**2018 EAU Male Infertility Guidelines Scope Search**

Database: Embase <1974 to 2017 May 23>, OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present, EBM Reviews - Cochrane Central Register of Controlled Trials <April 2017>, EBM Reviews - Cochrane Database of Systematic Reviews <2005 to May 19, 2017>

Search Strategy:

1. exp male infertility/ (62601)
2. (exp infertility/ or exp hypogonadism/) and male/ (88243)
3. (asthenozoospermia or oligospermia or azoospermia or teratozoospermia).tw.kw. (16886)
4. (oligoasthenoteratozoospermia or oligozoospermia or anejaculation).tw.kw. (4757)
5. ((male or males or men or man) and (infertil* or subfertil* or infecundity or sterility or hypogonadism*)).tw.kw. (72869)
6. ((male or males or men or man) and (fertility adj3 (failure or disorder* or dysfunction or impair* or problem* or disab* or abnormality or disturbance* or impotence or insufficiency))).tw. (3208)
7. exp ejaculation disorder/ (2402)
8. ((spermatogen* or ejaculation) adj3 (failure or disorder* or dysfunction or impair* or problem* or disab* or abnormal* or disturban* or impotence or insufficien*)).tw.kw. (7655)
9. or/1-8 (135988)
10. female/ not (male/ or (men or man or male*).tw.) (5234358)
11. female to male transgender/ or (male transgender* or transsexual or trans men).tw. (2841)
12. (In-vitro fertilization or IVF).ti. (30592)
13. or/10-12 (5251239)
14. 9 not 13 (131755)
15. random*.mp. (3129086)
16. clinical trial:.mp. (2637535)
17. (double-blind: or placebo: or blind*).mp. or (blind: or trial).tw. (2425145)
18. (randomized controlled trial or controlled clinical trial).pt. (1057860)
19. (systematic reivew or meta analysis).tw.kw. or "systematic review"/ or meta analysis/ (376317)
20. (Medline or Embase or Pubmed or Cochrane or literature search or literature review).ab. (439192)
21. or/15-20 (5787965)
22. 14 and 21 (16798)
23. limit 22 to english language [Limit not valid in CDSR; records were retained] (15228)
24 ((exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/) not (humans/ or human/)) or ((rats or mice or mouse or cats or dogs or animal* or cell lines) not (human* or men or women)).ti. (10995354)
25 23 not 24 (14232)
26 (case report/ or case reports/ or case report.ti.) not (literature review or systematic review).ti. (4101217)
27 25 not 26 (13914)
28 note/ or editorial/ or letter/ or Comment/ or news/ (3877437)
29 27 not 28 (13590)
30 conference abstract.pt. (2551764)
31 Congresses as Topic/ (119864)
32 29 not (30 or 31) (12351)
33 limit 32 to dd=20160407-20170524 use oemezd [Limit not valid in Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher,CCTR,CDSR; records were retained] (387)
34 limit 32 to ed=20160407-20170524 use ppez [Limit not valid in Embase,CCTR,CDSR; records were retained] (278)
35 limit 32 to yr="2016-Current" use coch (27)
36 limit 32 to yr="2016-current" use cctr (134)
37 (201606* or 201607* or 201608* or 201609* or 201610* or 201611* or 201612* or 2017*).dc. or 2017*.ep. (2916086)
38 32 and 37 (696)
39 34 or 35 or 36 or 38 (1055)
40 remove duplicates from 39 (799)

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1.
Dopa-testotoxicosis: disruptive hypersexuality in hypogonadal men with prolactinomas treated with dopamine agonists
De Sousa SMC, Chapman IM, Falhammar H, Torpy DJ
EBM Reviews - Cochrane Central Register of Controlled Trials
Dopamine agonists are the first line of therapy for prolactinomas, with high rates of biochemical control and tumour shrinkage. Toxicity is considered to be low and manageable by switching of agents and dose reduction. Dopamine agonist-induced impulse control disorders are well described in the neurology setting, but further data are required regarding this toxicity in prolactinoma patients. We performed a multicenter retrospective cohort study of eight men with prolactinomas and associated central hypogonadism. The eight men had no prior history of psychiatric disease, but each developed disruptive hypersexuality whilst on dopamine agonist therapy at various doses. Cabergoline, bromocriptine and quinagolide were all implicated. Hypersexuality had manifold consequences, including relationship discord, financial loss, reduced work performance, and illicit activity. We hypothesise that this phenomenon is due to synergy between reward pathway stimulation by dopamine agonists, together with rapid restoration of the eugonadal state after prolonged hypogonadism. We refer here to this distinct drug toxicity as 'dopa-testotoxicosis'. Given the profound impact in these patients and their families, cessation of dopamine agonists should be considered in men who develop hypersexuality, and pituitary surgery may be required to facilitate this. Awareness of this distinct impulse control disorder should enable further research into the prevalence, natural history and management of dopa-testotoxicosis. The condition is likely under-reported due to the highly personal nature of the symptoms and we suggest a simple written questionnaire to screen for hypersexuality and other behavioural symptoms within the first six months of dopamine agonist treatment. Copyright (C) 2016, Springer Science+Business Media New York.

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Publisher
Humana Press Inc. (E-mail: humana@humanapr.com)

2.
Dopa-testotoxicosis: a novel drug toxicity of dopamine agonists in male prolactinoma patients
De Sousa SMC, Chapman IM, Falhammar H, Torpy DJ
EBM Reviews - Cochrane Central Register of Controlled Trials
Background: Impulse control disorders (ICD) including gambling, hypersexuality, compulsive shopping and binge eating have recently been recognised as side effects of dopamine agonists (DAs). The vast majority has been described in the treatment of Parkinson's disease and restless legs syndrome where pathological gambling is the predominant DA-associated ICD (1). Little is known about the nature of ICDs in the prolactinoma setting where endocrine factors, specifically testosterone fluctuations, may influence behaviour (2). Methods: We performed a multicenter retrospective cohort study of eight men who developed hypersexuality following initiation of DA therapy for prolactinomas. Results: The men had no prior history of psychiatric disease, but each developed disruptive hypersexuality with manifold consequences, including relationship discord, financial loss, reduced work performance, and illicit activity. Two men also developed pathological gambling. Cabergoline, bromocriptine and quinagolide were all implicated. The onset of hypersexuality ranged from days to years after DA commencement. Some men notably had normal pre-treatment testosterone levels, however these values were in the lower half of the reference range and rose into the upper half with DA initiation suggesting they had relative hypogonadism at baseline. Six men received no androgen replacement and increases in testosterone were solely attributable to DA therapy. Prolactin and testosterone consistently improved to be close or within the reference range by the time of symptom onset. Symptoms were reversible with DA cessation. Conclusions: We hypothesise that this phenomenon is due to synergy between mesolimbic reward pathway stimulation by DAs, together with rapid restoration of the eugonadal state after prolonged hypogonadism. We refer to this unique drug toxicity as 'dopa-testotoxicosis'. The condition is likely under-reported due to the highly personal nature of the symptoms and we suggest a simple written questionnaire to screen for it. Treatment will generally include cessation of DAs in affected men, and often pituitary surgery for prolactinoma resection.

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Publisher
Blackwell Publishing Ltd
3.

An open-label clinical trial to investigate the efficacy and safety of corifollitropin alfa combined with hCG in adult men with hypogonadotropic hypogonadism

Nieschlag E, Bouloux P-MG, Stegmann BJ, Shankar RR, Guan Y, Tzontcheva A, McCrary Sisk C, Behre HM

EBM Reviews - Cochrane Central Register of Controlled Trials

[Journal: Article]
AN: CN-01335385 NEW

Background: Hypogonadotropic hypogonadism (HH) in men results in insufficient testicular function and deficiencies in testosterone and spermatogenesis. Combinations of human chorionic gonadotropin (hCG) and recombinant follicle-stimulating hormone (recFSH) have been successful in the treatment of HH. Corifollitropin alfa is a long-acting FSH-analog with demonstrated action in women seeking infertility care. The aim of this study was to investigate the efficacy and safety of corifollitropin alfa combined with hCG to increase testicular volume and induce spermatogenesis in men with HH.

Methods: This was a Phase III, multi-center, open-label, single-arm trial of corifollitropin alfa in azoospermic men aged 18 to 50 years with HH. After 16 weeks of pretreatment of 23 subjects with hCG alone, 18 subjects with normalized testosterone (T) levels who remained azoospermic entered the 52-week combined treatment phase with hCG twice-weekly and 150 mug corifollitropin alfa every other week. The increase in testicular volume (primary efficacy endpoint) and induction of spermatogenesis resulting in a sperm count >1 x 10^6/mL (key secondary efficacy endpoint) during 52 weeks of combined treatment were assessed. Safety was evaluated by the presence of anti-corifollitropin alfa antibodies and the occurrence of adverse events (AEs).

Results: Mean (+/-SD) testicular volume increased from 8.6 (+/-6.09) mL to 17.8 (+/-8.93) mL (geometric mean fold increase, 2.30 [95% CI: 2.03, 2.62]); 14 (77.8%) subjects reached a sperm count >1 x 10^6/mL. No subject developed confirmed anti-corifollitropin alfa antibodies during the trial. Treatment was generally well tolerated.

Conclusions: Corifollitropin alfa 150 mug administrated every other week combined with twice-weekly hCG for 52 weeks increased testicular volume significantly, and induced spermatogenesis in >75% of men with HH who had remained azoospermic after hCG treatment alone. Trial registration: ClinicalTrials.gov: NCT01709331. Copyright (C) 2017 The Author(s).

Institution
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Publisher
BioMed Central Ltd. (E-mail: info@biomedcentral.com)
Although culture-independent techniques have refuted lung sterility in health, controversy about contamination during bronchoscope passage through the upper respiratory tract (URT) has impeded research progress. We sought to establish whether bronchoscopic sampling accurately reflects the lung microbiome in health and to distinguish between two proposed routes of authentic microbial immigration, (i) dispersion along contiguous respiratory mucosa and (ii) subclinical microaspiration. During bronchoscopy of eight adult volunteers without lung disease, we performed seven protected specimen brushings (PSB) and bilateral bronchoalveolar lavages (BALs) per subject. We amplified, sequenced, and analyzed the bacterial 16S rRNA gene V4 regions by using the Illumina MiSeq platform. Rigorous attention was paid to eliminate potential sources of error or contamination, including a randomized processing order and the inclusion and analysis of exhaustive procedural and sequencing control specimens. Indices of mouth-lung immigration (mouth-lung community similarity, bacterial burden, and community richness) were all significantly greater in airway and alveolar specimens than in bronchoscope contamination control specimens, indicating minimal evidence of pharyngeal contamination. Ecological indices of mouth-lung immigration peaked at or near the carina, as predicted for a primary immigration route of microaspiration. Bacterial burden, diversity, and mouth-lung similarity were greater in BAL than PSB samples, reflecting differences in the sampled surface areas. (This study has been registered at ClinicalTrials.gov under registration no. NCT02392182.)

This study defines the bacterial topography of the healthy human respiratory tract and provides ecological evidence that bacteria enter the lungs in health primarily by microaspiration, with potential contribution in some subjects by direct dispersal along contiguous mucosa. By demonstrating that contamination contributes negligibly to microbial communities in bronchoscopically acquired specimens, we validate the use of bronchoscopy to investigate the lung microbiome. Copyright (C) 2017 Dickson et al.
5.
Fertility concerns among breast cancer patients in Mexico
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Article]
AN: CN-01336169  NEW
Objective Young women represent a high proportion of the total number of breast cancer (BC) patients in Mexico; however, no previous studies addressing their attitudes regarding the risk of chemotherapy-induced infertility and its contributing factors are available. The aim of this study was to evaluate the concerns of young women with BC towards the risk of infertility in two referral centers in Mexico with access to public health services. Methods A cross-sectional study including women with newly or previously detected BC aged 40 years or younger at diagnosis was conducted. Variables regarding concerns about fertility were collected from an adapted version of the Fertility Issues Survey. Results 134 consecutive eligible women responded to the in-person paper survey. 55% were partnered, 35.1% had no children, and 48% reported willingness to have children prior to BC diagnosis. Only 3% of patients considered to be able to afford extra expenses. At diagnosis, 44% of women expressed some level of concern about infertility risk. The only factor significantly associated with fertility concern was the desire of having children prior to diagnosis (OR 11.83, p = 0.006). Only 30.6% patients recalled having received information regarding infertility risk from their physicians. Conclusion A minority of young women with breast cancer in Mexico is informed about the risk of BC treatment-induced infertility, despite substantial interest. Informing all patients about infertility risk and available options for fertility preservation should be an essential aspect of the supportive care of young women with BC, even in low-middle income countries such as Mexico. Copyright (C) 2017 Elsevier Ltd
Gender differences in perception of psychosocial distress and coping mechanisms among infertile men and women in Saudi Arabia

EBM Reviews - Cochrane Central Register of Controlled Trials

The objective of the study was to evaluate the differences in psychosocial distress and coping mechanisms among infertile men and women in Saudi Arabia (SA). We performed a cross-sectional study of infertile patients (206 women and 200 men) attending infertility clinics in three referral hospitals in Riyadh, SA. A semi-structured questionnaire was developed to assess socio-demographic, clinical and psychosocial variables. Infertility-related psychosocial pressures were reported in 79 (39.7%) male and 97 (47.3%) female participants (p = 0.123). Males suffered more from intrusive questions and pressure to conceive, remarry or get divorced, while females were stressed more from psychological and emotional exhaustion, marital discord, attitudes of mothers-in-law or society, and persistent desire by the husband to have children. To cope with infertility, females engaged more in religious activities (p < 0.001) and spoke more to someone regarding their problems (p < 0.001). To solve their infertility problems, 50% tried to find solutions via the internet, and 38.5% of males and 51% of females reported using alternative medicines (p = 0.012). The patients with infertility in SA face multiple psychosocial stressors related to their infertility, and cope differently based on the gender and culture-specific knowledge of infertility. The female participants were significantly more affected from psychosocial stressors and the persistent desire by their spouse to have children. Copyright (C) 2016 The British Fertility Society.
Introduction: Spinal cord injury (SCI) is estimated to affect approximately 276,000 individuals in the United States. Since 2010, the mean age of individuals at the time of the SCI has been 42 years, with nearly 80% of cases involving men. This means that individuals with SCI generally are young men who typically place a great deal of importance on normal sexual and reproductive function. Aim: To assess the effect of sildenafil treatment on erectile function and the frequency of ejaculation in men with SCI. Methods: This study was a post hoc analysis of pooled data from two randomized, double-blinded, placebo-controlled, flexible-dose, crossover sildenafil trials conducted in Europe, Australia, and Turkey. Two hundred forty-eight men at least 18 years old with traumatic SCI of at least 6 months’ duration, with erectile dysfunction solely attributed to SCI, and in a stable heterosexual relationship were treated sequentially with sildenafil and placebo. Exclusion criteria included taking nitrate therapy, severe cardiac failure, and recent stroke or myocardial infarction. The starting sildenafil dose was 50 mg, taken approximately 1 hour before sexual activity, with subsequent dose adjustment to 100 or 25 mg based on efficacy and safety during treatment. There was a 2-week washout between 6-week treatments. Main Outcome Measures: Change from baseline in International Index of Erectile Function question 3 (frequency of penetration), question 4 (maintaining erection after penetration), question 9 (frequency of ejaculation), and erectile function domain scores; intercourse success; and treatment preference. Results: All International Index of Erectile Function outcomes, including achieving and maintaining erections and ejaculation frequency, were statistically significantly greater with sildenafil vs placebo, including the subgroup with complete SCI (P < .01 for all comparisons). The percentage of successful intercourse attempts with sildenafil (53% vs 12%) and preference for sildenafil (96% vs 4%) vs placebo were significant (P < .001), including the subgroup with complete SCI. The most common all-cause adverse events with sildenafil were headache.
(16.1%) and urinary tract infection (11.6%). Conclusion: Sildenafil significantly improves erections, intercourse success, and ejaculation frequency vs placebo, including in men with complete SCI. Sildenafil is an effective and well-tolerated treatment for sexual dysfunction in men with SCI. The increase in frequency of ejaculation could allow the possibility of having children without medical intervention in this patient population. Ohl DA, Carlsson M, Stecher VJ, Rippon GA. Efficacy and Safety of Sildenafil in Men With Sexual Dysfunction and Spinal Cord Injury. Sex Med Rev 2017;X:XX-XX. Copyright (C) 2017.

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Publisher
Elsevier B.V. (E-mail: customerservices@oxonblackwellpublishing.com)

8.
Nutrient patterns and asthenozoospermia: a case-control study
Eslamian G, Amirjannati N, Rashidkhani B, Sadeghi M-R, Hekmatdoost A
EBM Reviews - Cochrane Central Register of Controlled Trials
Andrologia. 49(3) (no pagination):2017.
[Journal: Article]
AN: CN-01337298  NEW
The association of dietary nutrient patterns and sperm motility is not yet well elucidated, and previous studies have just focused on the isolated nutrients. This case-control study examined the association of nutrient patterns with asthenozoospermia among Iranian men. In total, 107 incident asthenozoospermic men and 235 age-matched controls were interviewed through the infertility clinics in Tehran, Iran, from January 2012 to November 2013. Semen quality data were analysed according to the fifth edition of WHO guideline. Nutrient patterns were identified using principal component analysis based on semiquantitative 168-item food frequency questionnaires. All nutrient intakes were energy-adjusted by the residual method. In principal component analysis, three dietary patterns emerged. The first pattern, which was high in vitamin E, vitamin D, vitamin C, zinc, folate, total fibre, selenium and polyunsaturated fatty acids, was significantly associated with lower risk of asthenozoospermia. After adjustment for potential confounders, participants in the highest tertile of the first pattern scores had 51% lower risk of asthenozoospermia compared with those in the lowest (p-trend:.004). Our findings suggest that
adherence to the pattern comprising mainly of antioxidant nutrients may be inversely associated with asthenozoospermia. Copyright (C) 2016 Blackwell Verlag GmbH

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Publisher
Blackwell Publishing Ltd (E-mail: customerservices@oxonblackwellpublishing.com)

9.
Efficacy and safety of testosterone replacement gel for treating hypogonadism in men: phase III open-label studies
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Article In Press]
AN: CN-01339263 NEW

Efficacy and safety of testosterone gel 2% (TG) were evaluated in two phase 3, open-labelled, single-arm, multicentre studies (000023 and extension study 000077). Hypogonadal men having serum testosterone levels <300 ng/dl at two consecutive measurements were included. Study duration was 9 months (000023: 3 months; 000077: 6 months). Starting dose of TG (46 mg) was applied on upper arm/shoulder. The primary endpoint (000023) was responder rate (subjects with average 24-hour serum testosterone concentration 300-1050 ng/dl on Day 90). Study 000077 evaluated the safety of TG in patients rolling over from study 000023 over a period of 6 months. Of 180 subjects in 000023, 172 completed and 145 rolled over to 000077, with 127 completers. The responder rate was 85.5%. Fewer subjects in 000077 (12.7%) versus 000023 (31.8%) had maximum testosterone concentration (C<inf>max</inf>) >1500 ng/dl, with no significant safety concerns. Significant improvements in sexual function and quality of life were noted in both studies. Subjects experienced few skin reactions without notable increases in prostate-specific antigen and haematocrit levels. TG was efficacious with an acceptable safety profile. C<inf>max</inf> >1500 ng/dl did not exhibit distinct impact on safety parameters. However, further optimisation of titration schema to reduce C<inf>max</inf> is warranted while maintaining
10. Academic performance in adolescents born after ART - A nationwide registry-based cohort study
Spangmose AL, Malchau SS, Schmidt L, Vassard D, Rasmussen S, Loft A, Forman J, Pinborg A
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Article]
AN: CN-01339646  NEW
STUDY QUESTION: Is academic performance in adolescents aged 15-16 years and conceived
after ART, measured as test scores in ninth grade, comparable to that for spontaneously
conceived (SC) adolescents? SUMMARY ANSWER: ART singletons had a significantly lower
mean test score in the adjusted analysis when compared with SC singletons, yet the differences
were small and probably not of clinical relevance. WHAT IS KNOWN ALREADY: Previous studies
have shown similar intelligence quotient (IQ) levels in ART and SC children, but only a few have
been on adolescents. Academic performance measured with standardized national tests has not
previously been explored in a complete national cohort of adolescents conceived after ART.
STUDY DESIGN, SIZE, DURATION: A Danish national registry-based cohort including all 4766
ART adolescents (n = 2836 singletons and n = 1930 twins) born in 1995-1998 were compared
with two SC control cohorts: a randomly selected singleton population (n = 5660) and all twins (n
= 7064) born from 1995 to 1998 in Denmark. Nine children who died during the follow-up period
were excluded from the study. PARTICIPANTS/MATERIALS, SETTING, METHODS: Mean test
scores on a 7-point-marking scale from -3 to 12 were compared, and adjustments were made for
relevant reproductive and socio-demographic covariates including occupational and educational
level of the parents. MAIN RESULTS AND THE ROLE OF CHANCE: The crude mean test score
was higher in both ART singletons and ART twins compared with SC adolescents. The crude
mean differences were +0.41 (95% CI 0.30-0.53) and +0.45 (95% CI 0.28-0.62) between ART
and SC singletons and between ART and SC twins, respectively. However, the adjusted mean overall test score was significantly lower for ART singletons compared with SC singletons (adjusted mean difference -0.15 (95% CI -0.29 to -0.02)). For comparison, the adjusted mean difference was +2.05 (95% CI 1.82 to 2.28) between the highest and the lowest parental educational level, suggesting that the effect of ART is weak compared with the conventional predictors. The adjusted analyses showed significantly lower mean test scores in mathematics and physics/chemistry for ART singletons compared with SC singletons. Comparing ART twins with SC twins yielded no difference in academic performance in the adjusted analyses. Similar crude and adjusted overall mean test scores were found when comparing ART singletons and ART twins. LIMITATIONS, REASONS FOR CAUTION: Missing data on educational test scores occurred in 6.6% of adolescents aged 15-16 years for the birth cohorts 1995-1997, where all of the children according to their age should have passed the ninth grade exam at the time of data retrieval. As sensitivity analyses yielded no significant difference in the adjusted risk of having missing test scores between any of the groups, it is unlikely that this should bias our results. Adjustment for body mass index and smoking during pregnancy was not possible. WIDER IMPLICATIONS OF THE FINDINGS: As our results are based on national data, our findings can be applied to other populations. The findings of this paper suggest that a possible small negative effect of parental subfertility or ART treatment is counterbalanced by the higher educational level in the ART parents. Copyright (C) The Author 2016. Published by Oxford University Press on behalf of the European Society of Human Reproduction and Embryology. All rights reserved.

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Publisher
Oxford University Press (E-mail: jnl.info@oup.co.uk)

11.
Prevalence and risk factors of chlamydia infection in Hong Kong: a population-based geospatial household survey and testing
Wong WCW, Zhao Y, Wong NS, Parish WL, Miu HYH, Yang L-G, Emch M, Ho KM, Fong FY, Tucker JD
EBM Reviews - Cochrane Central Register of Controlled Trials
Background: Chlamydia causes infertility and increases risk of HIV infection, and population-based studies provide essential information for effective infection control and prevention. This study examined Chlamydia trachomatis prevalence and risk factors among a representative sample of 18-49-year-old residents in Hong Kong. Methods: Census boundary map of 412 constituency areas was used as primary sampling units to construct the sampling frame and, residential buildings and units were randomly selected using geospatial modelling. A questionnaire on sexual practice and health was conducted, and polymerase chain reaction was used to test the urine for genital chlamydial infection. Invitation letters were sent to the selected households and a team of interviewers were sent to recruit one subject per household. Prevalence data was weighted according to the 2011 census and risk factors identified through logistic regression. Results: Among 881 participants (response rate of 24.5%), the overall Chlamydia trachomatis prevalence was low at 1.4% (95%CI 0.8+/-2.5%) but sexually active young (18+/4-26 years) women had relatively high prevalence (5.8%, 95%CI 1.7+/4-18.2%) in Hong Kong. A unique U-shape disease burden was observed with peaks in younger and older (40+/4-49 years) women. Amongst the sexually active women, the risk factors of Chlamydia trachomatis infection were: younger age (aOR = 25.4, 95% CI 2.81+/4-230); living alone (aOR = 8.99, 95% CI 1.46+/4-55.40); and, among all the sexually active participants, males (including the male partners of the female participants) who had travelled out of Hong Kong in the previous 12 months had higher risks of infection (aOR = 5.35; 95% CI 1.25+/4-22.8). A core-peripheral geographical distribution of Chlamydia trachomatis prevalence was also observed. Conclusion: Young and older sexually active women in Hong Kong have high prevalence of chlamydia. Routine screening for sexually active women and young men should be considered. Further research on testing feasibility and linkage-to-care are urgently needed to control the infection. Copyright (C) 2017 Wong et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Publisher
Public Library of Science (E-mail: plos@plos.org)
Androgen Treatment Effects on Motor Function, Cognition, and Behavior in Boys with Klinefelter Syndrome
Ross JL, Kushner H, Kowal K, Bardsley M, Davis S, Reiss AL, Tartaglia N, Roeltgen D
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Article In Press]
AN: CN-01340267  NEW
Objectives: To examine the effects of early low-dose androgen on motor, cognitive, and behavioral function in prepubertal boys with Klinefelter syndrome (47,XXY). Study design: Double-blind trial of 84 boys, ages 4-12 years, randomized to oxandrolone (Ox; 0.06 mg/kg daily; n = 43) or placebo (Pl; n = 41) for 24 months. Standardized assessments were performed at baseline and every 12 months for 24 months evaluating motor, cognitive, and behavioral function.
Results: The 24-month outcomes were better in the Ox vs. Pl group on 1 of 5 primary endpoints (motor function/strength): Bruininks Visual-Motor scale (P = .005), without significant differences between the 2 groups for the other 4 components. Secondary analyses suggested improvement in the Ox vs. Pl group in the anxiety/depression (P = .03) and social problems (P = .01) scales on the Child Behavior Checklist, anxiety (P = .04) on the Piers Harris Self Concept Scale, and interpersonal problems (P = .02) on the Children's Depression Inventory, without significant differences in hyperactive or aggressive behaviors. Conclusions: This double-blind, randomized trial demonstrates that 24 months of childhood low-dose androgen treatment in boys with Klinefelter syndrome benefited 1 of 5 primary endpoints (visual-motor function). Secondary analyses demonstrated positive effects of androgen on aspects of psychosocial function (anxiety, depression, social problems), without significant effects on cognitive function, or hyperactive or aggressive behaviors. Trial registration: ClinicalTrials.gov: NCT00348946. Copyright (C) 2017 Elsevier Inc.
Institution
J.L. Ross, Thomas Jefferson University, Sidney Kimmel Jefferson Medical College, Department of Pediatrics, 833 Chestnut St, Philadelphia, PA 19107
Publisher
Mosby Inc. (E-mail: customerservice@mosby.com)
The association of a probiotic with a prebiotic (Flortec, Bracco) to improve the quality/quantity of spermatozoa in infertile patients with idiopathic oligoasthenoteratospermia: a pilot study

Marett C, Cavallini G

EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Article In Press]
AN: CN-01341624  NEW

The hypothesis that the assumption of a probiotic associated with a prebiotic (Flortec, Bracco; one sachet contains: Lactobacillus paracasei B21060 5 x 10^9 cells + arabinogalctan 1243 mg + oligo-fructosaccharides 700 mg + l-glutamine 500 mg) could improve the quality and quantity of spermatozoa in idiopathic oligoasthenoteratospermia (iAOT) patients to a larger extent than a control substance (starch) was tested. Forty-one patients with no chromosomal aberrations were randomized into two groups: 20 received Flortec, one sachet per day for 6 months, whereas 21 received the control substance. The following data were collected: clinical history, scrotal Doppler scans, Y microdeletion, karyotype and cystic fibrosis screens, follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), testosterone (T), and prolactin (PRL) levels, and two semen analyses. Both the Flortec and the starch groups underwent two semen analyses and one FSH, LH, T, E2, and PRL measurement in the blood, at the beginning of the study, and after 6 months. The comparisons were carried out using a non-parametric (Wilcoxon signed rank) test. The side effects were assessed and compared using the chi-squared test. Group 1 (Flortec) had their sperm count improved: volume of the ejaculate (median from 2.4 to 3.1 mL; p < 0.01), sperm concentration (median: from 15.2 x 10^6/mL to 28.3 x 10^6/mL; p < 0.01), progressive motility (median: from 16.2 to 42.0%; p < 0.01), and the percentage of typical forms (median: from 7 to 16.3%; p < 0.01); in addition, their FSH, LH, and T levels improved (p < 0.01), while those of E2 and PRL did not. Group 2 (control substance) had no modification in 42 of the parameters studied. There were no side effects in either group. These data showed that Flortec constitutes a safe therapy for improving the volume of the ejaculate and the quality/quantity of spermatozoa in iOAT patients.

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Publisher
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Testicular sperm aspiration (TESA) for infertile couples with severe or complete asthenozoospermia

Al-Malki AH, Alrabeeah K, Mondou E, Brochu-Lafontaine V, Phillips S, Zini A

EBM Reviews - Cochrane Central Register of Controlled Trials
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AN: CN-01331997 NEW

The aim of the study was to evaluate reproductive outcomes in a cohort of infertile couples with severe and complete asthenozoospermia undergoing TESA (testicular sperm aspiration) with ICSI. We conducted a retrospective study of 28 couples with complete or severe asthenozoospermia who underwent TESA between January 2010 and December 2015. We compared TESA-ICSI outcomes of these couples to ejaculate ICSI outcomes of 40 couples with severe asthenozoospermia treated during the same time period at our institution. Couples with female factor infertility and/or female aged >39 were excluded. Sperm retrieval rates and ICSI outcomes [(MII oocytes, fertilization rate, good embryo rate (transferred and frozen), couples with embryo transfer (per cycle started), clinical pregnancy (per embryo transfer)] were recorded. Patients were grouped based on whether they had ejaculated (Ej-group) or testicular (TESA-group) spermatozoa used. Testicular sperm patients were further classified based on whether they had complete asthenozoospermia (0% total motility) (Tc-group) or severe asthenozoospermia (<1% progressive motility) (Ts-group). Mean (+/-SD) male and female ages were 36 +/- 6 and 32 +/- 4, respectively. Sperm recovery by testicular sperm aspiration (TESA) was successful in 100% (28/28) of the men. The overall clinical pregnancy rate (CPR) per cycle started was 34% (23/68) with a mean of 1.1 +/- 0.4 embryos transferred per transfer. Fertilization rates were significantly lower in TESA-group compared to Ej-group (52% vs. 67%, respectively; p = 0.001), while male age was significantly higher in TESA-group compared to Ej-group (34 +/- 6 vs. 37 +/- 6, respectively; p = 0.03). Moreover, female age was significantly higher in Tc-group compared to Ts-group (30 +/- 4 vs. 33 +/- 3, respectively; p = 0.0285). However, there were no significant difference in clinical pregnancy rate per embryo transfer in the Tc-group, Ts-group, and Ej-group (50% vs. 45% vs. 57%, respectively; p = 0.8219). The data suggest that testicular sperm-ICSI is no better than ejaculated sperm-ICSI in couples with severe or complete asthenozoospermia. Randomized, controlled trials comparing ejaculated vs. testicular spermatozoa are needed to assess the true benefit of TESA-ICSI in these couples. Copyright (C) 2017 American Society of Andrology and European Academy of Andrology.

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Introduction: The prevalence of metabolic syndrome (MetS) is rapidly increasing in the United States and, because of its strong association with male hypogonadism, has become a significant topic of interest in the sexual medicine community. At the center of this conversation is the efficacy and safety of testosterone replacement therapy (TRT) as a therapeutic option for HG and MetS. Aim: To provide a review of the current literature pertaining to TRT and MetS. Methods: A thorough literature review was performed to review the relation between TRT and MetS using the PubMed online database from 1976 through 2016 with the keywords testosterone, hypogonadism, metabolic syndrome, and testosterone therapy. Main Outcome Measures: Outcomes pertaining to MetS including weight, waist circumference, body mass index, blood glucose control, cholesterol parameters, blood pressure, and quality of life. Results: From the plethora of contrasting literature on the efficacy and safety of TRT, it is increasingly clear that more well-designed studies are needed to clarify the efficacy and safety of TRT. Although most of the current literature shows that TRT has the potential to significantly lower the studied outcome variables associated with MetS, several studies provide more mixed results. Conclusion: TRT has the potential to alleviate some of the morbidity associated with hypogonadism and MetS. Larger multicenter well-designed studies are needed to better describe and quantify the relation between MetS and TRT. Anaissie J, Roberts NH, Wang P, et al. Testosterone Replacement Therapy and Components of the Metabolic Syndrome. Sex Med Rev 2017;X:XXX-XXX. Copyright (C) 2017 International Society for Sexual Medicine.

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Publisher
Testicular growth and spermatogenesis: new goals for pubertal hormone replacement in boys with hypogonadotropic hypogonadism? -a multicentre prospective study of hCG/rFSH treatment outcomes during adolescence -


EBM Reviews - Cochrane Central Register of Controlled Trials
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Context/objective: Testosterone treatment for pubertal induction in boys with hypogonadotropic hypogonadism (HH) provides virilization, but does not induce testicular growth or fertility. Larger studies evaluating the outcomes of gonadotropin replacement during adolescence have not been reported to date; whether previous testosterone substitution affects testicular responses is unresolved. We aimed to assess the effects of human chorionic gonadotropin (hCG) and recombinant FSH (rFSH) in boys and adolescents with HH with respect to a) testicular growth, b) spermatogenesis, c) quality of life (QoL) and to identify factors influencing therapeutic success.

Design/setting: A prospective case study was conducted in 26 paediatric endocrine centres.

Patients/interventions: HCG and rFSH were administered until cessation of testicular growth and plateauing of spermatogenesis to (1) prepubertal HH boys with absent or early arrested puberty (group A) and to (2) HH adolescents who had previously received full testosterone replacement (group B). Outcome measures: Bi-testicular volumes (BTVs), sperm concentrations and QoL.

Results: Sixty (34 A/26 B) HH patients aged 14-22 years were enrolled. BTVs rose from 5 +/- 5 to 34 +/- 3 ml in group A vs 5 +/- 3 to 32 +/- 3 ml in group B, with normal final BTVs (>24 ml) attained in 74%/70% after 25/23 months in A/B, respectively. Sperm in the ejaculate were found in 21/23(91%)/18/19(95%), with plateauing concentrations after 31/30 months of hCG and 25/25 months of combined treatment in A/B. Sperm concentrations were normal (>15 mill/ml) in 61%/32%, with mean concentrations of 40 +/- 73 vs 19 +/- 38 mill/ml in A/B (n.s.). Outcomes
were better in patients without bilateral cryptorchidism, with non-congenital HH causes, higher baseline BTVs, and higher baseline inhibin B and AMH levels. QoL increased in both groups.

Conclusions: HCG/rFSH replacement during adolescence successfully induces testicular growth and spermatogenesis, irrespective of previous testosterone replacement, and enhances QoL.

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17.
Diagnostic accuracy of Cancer Antigen 125 (CA125) for endometriosis in symptomatic women: a multi-center study
Hirsch M, Duffy JMN, Deguara CS, Davis CJ, Khan KS
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Article]
AN: CN-01288966  NEW
Study objective To assess the diagnostic accuracy of serum Cancer Antigen 125 (CA 125) > 30 units/milliliter (u/ml) for diagnosing endometriosis in symptomatic women. Study design
Prospective observational cohort study including patients with symptoms of pelvic pain or subfertility undergoing elective diagnostic laparoscopy at two tertiary referral hospitals. We excluded patients suspected to have other gynecological pathology. We evaluated the accuracy of serum CA 125 (index test) with histologically confirmed endometriosis (reference standard).
Main results Fifty-eight consecutive women recruited between October 2013 to March 2015. Women with endometriosis had a higher CA 125 level than those without endometriosis (mean 54.7 +/-71.6 vs 16.2 +/- 8.0). The specificity of CA 125 > 30 u/ml was 96% (95% CI 81.7-99.9%) and sensitivity was 57% (95% CI 37.4-74.5%). The positive likelihood ratio for the histological presence of endometriosis with a CA 125 > 30 u/ml was 15.8 (95% CI 2.3-112) providing a post-test probability of 94% (95% CI 71%-99%) in women with pelvic pain or subfertility. The area under the curve, 0.85 (95% CI 0.74-0.96) indicates high test accuracy. Conclusions CA 125 > 30 u/ml is highly predictive of endometriosis in women with symptoms of pain and/or subfertility. CA
125 should be considered as a rule-in test for expediting the diagnosis and management of endometriosis, CA 125 < 30 u/ml is, however, unable to rule out endometriosis. Copyright (C) 2016 Elsevier Ireland Ltd

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18.
Diagnosis of partial retrograde ejaculation in non-azoospermic infertile men with low semen volume
Mieusset R, Walschaerts M, Isus F, Almont T, Daudin M, Hamdi SM
EBM Reviews - Cochrane Central Register of Controlled Trials
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AN: CN-01298434 NEW
In non-azoospermic patients with low semen volume (LSV), looking for partial retrograde ejaculation (PRE) by searching sperm in the postejaculatory urine (PEU) is required. The use of a retro-ejaculatory index (R-ratio) was suggested to define PRE, but none of the studies indicated a specific threshold above which PRE must be considered. Our objective was to propose a threshold value for the R-ratio as indicative of PRE in patients with LSV selected to be devoid of any known causes or risk factors for retrograde ejaculation or LSV. Among our data base (2000-2009) including 632 patients with PEU, 245 male patients from infertile couples who had had a first semen analysis with LSV (< 2mL) and a second semen analysis associated with PEU, were selected on the previous criteria. A prospective control group was randomly constituted (2007-2008) of 162 first consulting male patients from infertile couples, with a normal semen volume (> 2mL) on a first semen analysis and who accepted to collect PEU with their usual second semen analysis, selected on the previous criteria. To define an R-ratio threshold indicative of PRE, we used a ROC curve analysis and a regression tree based on a classification and regression tree (CART) algorithm. Of the 245 LSV patients, 146 still presented low semen volume (< 2 mL) on the second semen analysis. From the use of the CART algorithm, two low (1.5% and 2.8%) and
two high R-values (7.1% and 8.3%) were defined, according to the lower reference limit for semen volume of 2.0 mL (WHO 1999) or 1.5 mL (WHO 2010) respectively. As only one or no patient with normal semen volume was observed above the two high R-values, we suggest an R-value higher than the range of [7.1-8.3]% as indicative of PRE until confirmation by a prospective multicenter study. Copyright (C) 2017 Mieusset et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

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19.
Randomised clinical trial of comparing effects of acupuncture and varicocelectomy on sperm parameters in infertile varicocele patients
Kadihasanoglu M, Ozbek E
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20.
Erythrocytosis Following Testosterone Therapy. [Review]
Ohlander SJ; Varghese B; Pastuszak AW.
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Sexual Medicine Reviews. , 2017 May 16.
[Journal Article. Review]
INTRODUCTION: A rapid increase in awareness of androgen deficiency has led to substantial increases in prescribing of testosterone therapy (TTh), with benefits of improvements in mood, libido, bone density, muscle mass, body composition, energy, and cognition. However, TTh can be limited by its side effects, particularly erythrocytosis. This review examines the literature on testosterone-induced erythrocytosis and polycythemia.

AIM: To review the available literature on testosterone-induced erythrocytosis, discuss possible mechanisms for pathophysiology, determine the significance of formulation, and elucidate potential thromboembolic risk.

METHODS: A literature review was performed using PubMed for articles addressing TTh, erythrocytosis, and polycythemia.

MAIN OUTCOME MEASURES: Mechanism, pharmacologic contribution, and risk of testosterone-induced erythrocytosis.

RESULTS: For men undergoing TTh, the risk of developing erythrocytosis compared with controls is well established, with short-acting injectable formulations having the highest associated incidence. Potential mechanisms explaining the relation between TTh and erythrocytosis include the role of hepcidin, iron sequestration and turnover, erythropoietin production, bone marrow stimulation, and genetic factors. High blood viscosity increases the risk for potential vascular complications involving the coronary, cerebrovascular, and peripheral vascular circulations, although there is limited evidence supporting a relation between TTh and vascular complications.

CONCLUSION: Short-acting injectable testosterone is associated with greater risk of erythrocytosis compared with other formulations. The mechanism of the pathophysiology and its role on thromboembolic events remain unclear, although some data support an increased risk of cardiovascular events resulting from testosterone-induced erythrocytosis. Ohlander SJ, Varghese B, Pastuszak AW. Erythrocytosis Following Testosterone Therapy. Sex Med Rev 2017;X:XXX-XXX.

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21.
High frequency of de novo DAZ microdeletion in sperm nuclei of subfertile men: possible involvement of genome instability in idiopathic male infertility.
Mozdarani H; Ghoraeian P; Mozdarani S; Fallahi P; Mohseni-Meybodi A.
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Human Fertility. 1-9, 2017 May 19.
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The occurrence and diagnosis of Y-chromosome microdeletions, specifically deletions of the DAZ (Deleted in Azoospermia) genes are an important issue in male infertility. Screening Y chromosome microdeletion is mainly done using polymerase chain reaction (PCR) on blood leukocytes. However, there is some evidence indicating that presence of DAZ in somatic cells might not be indicative of its presence in the germ cell lineage. Therefore, a total of 130 men with poor semen quality were examined for presence of DAZ microdeletion in their leukocytes. From these, sperm from 40 randomly selected men with no DAZ microdeletions in their leukocytes (n=10 oligozoospermia; n=10 asthenozoospermia; n=10 oligoasthenozoospermia; and n=10 near-azoospermia) were were compared to sperm from men of normal semen quality (n=10) using combined primed in situ labelling and fluorescent in situ hybridization (PRINS-FISH) technique as well as screening for sex chromosome aneuploidy. There was an increased frequency of DAZ microdeletion in blood samples from oligozoospermic (5%) (p<0.05) and near azoospermic patients (14%) (p<0.01). A high frequency of DAZ microdeletion was observed in the sperm of patients with no DAZ microdeletion in their leukocytes compared to control (p<0.01). The frequency of sex chromosome aneuploidy also increased, correlating with the severity of
infertility in the studied groups. A similar result was observed for sex chromosome aneuploidy. The results might be indicative of DAZ microdeletion induction during spermatogenesis.

Oxidative stress (OS) is the result of random cellular damage caused by reactive oxygen species that leads to cell death, ageing, or illness. Most physiological processes can result in OS, which in turn has been identified as a major cause of infertility. In promiscuous species, the fertilizing ability of the ejaculate partly determines the male reproductive success. When dominance
determines access to fertile females, theory predicts that lower ranking males should increase resource investment into enhancing ejaculate quality. We hypothesized that subordinate males should thus prioritize antioxidant protection of their ejaculates to protect them from OS. We put this hypothesis to the test, by chronically dosing wild House Sparrows with diquat (~1mg/kg), an herbicide that increases pro-oxidant generation. We found that, although they increased their antioxidant levels in the ejaculate, diquat-treated males produced sperm with reduced velocity. Importantly, and contrary to our hypothesis, males at the bottom of the hierarchy suffered the largest reduction in sperm velocity. We suggest that resource access hinders individuals' ability to cope with environmental hazards. Our results point at OS as a likely physiological mechanism mediating ejaculate quality, while individual ability to access resources may play a role in constraining the extent to which such resources can be allocated into the ejaculate.

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Validation study of the SCREENIVF: an instrument to screen women or men on risk for emotional maladjustment before the start of a fertility treatment.

Ockhuijsen HDL; van Smeden M; van den Hoogen A; Boivin J.

OBJECTIVE: To examine construct and criterion validity of the Dutch SCREENIVF among women and men undergoing a fertility treatment.

DESIGN: A prospective longitudinal study nested in a randomized controlled trial.

SETTING: University hospital.

PATIENT(S): Couples, 468 women and 383 men, undergoing an IVF/intracytoplasmic sperm injection (ICSI) treatment in a fertility clinic, completed the SCREENIVF.

MAIN OUTCOME MEASURE(S): Construct and criteria validity of the SCREENIVF.

RESULT(S): The comparative fit index and root mean square error of approximation for women and men show a good fit of the factor model. Across time, the sensitivity for Hospital Anxiety and Depression Scale subscale in women ranged from 61%-98%, specificity 53%-65%, predictive value of a positive test (PVP) 13%-56%, predictive value of a negative test (PVN) 70%-99%. The sensitivity scores for men ranged from 38%-100%, specificity 71%-75%, PVP 9%-27%, PVN 92%-100%. A prediction model revealed that for women 68.7% of the variance in the Hospital Anxiety and Depression Scale on time 1 and 42.5% at time 2 and 38.9% at time 3 was explained by the predictors, the sum score scales of the SCREENIVF. For men, 58.1% of the variance in the Hospital Anxiety and Depression Scale on time 1 and 46.5% at time 2 and 37.3% at time 3 was explained by the predictors, the sum score scales of the SCREENIVF.

CONCLUSION(S): The SCREENIVF has good construct validity but the concurrent validity is better than the predictive validity. SCREENIVF will be most effectively used in fertility clinics at the start of treatment and should not be used as a predictive tool.
Effects of testosterone replacement therapy on metabolic syndrome among Japanese hypogonadal men: A subanalysis of a prospective randomised controlled trial (EARTH study).

Shigehara K; Konaka H; Nohara T; Izumi K; Kitagawa Y; Kadono Y; Iwamoto T; Koh E; Mizokami A; Namiki M.

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Andrologia. , 2017 May 12.

[Journal Article]
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We investigated the effects of testosterone replacement therapy (TRT) on metabolic factors among hypogonadal men with a metabolic syndrome. From the study population of the EARTH study, which was a randomised controlled study in Japan, 65 hypogonadal patients with a metabolic syndrome, comprising the TRT group (n = 32) and controls (n = 33), were included in this study analysis. The TRT group was administered 250mg of testosterone enanthate as an intramuscular injection every 4 weeks for 12 months. Waist circumference, body mass index, body fat volume and blood pressure were measured in all patients at baseline and at 12 months. In addition, blood biochemical data, including total cholesterol, triglyceride (TG), HDL cholesterol, fasting plasma glucose (FPG) and haemoglobin A1c (HbA1c) levels, were also evaluated. Changes in these categories from baseline to 12 months were compared between the TRT and control groups, with significant differences observed in waist circumference, body fat percentage, FPG, TG and HbA1c levels. No significant differences were observed in other parameters. TRT
for 1 year was associated with improvements in some metabolic factors among Japanese men with hypogonadism and metabolic syndrome.
Testosterone treatment and cardiovascular and venous thromboembolism risk: what is 'new'?
Corona G; Dicuio M; Rastrelli G; Maseroli E; Lotti F; Sforza A; Maggi M.
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In men, testosterone (T) production declines as a function of ageing. Late-onset hypogonadism (LOH) is the most commonly used term to indicate this age-related condition. In LOH, the relative clinical significance and the potential benefit of testosterone treatment (TTh) are still the subject of strong criticisms in the scientific community. The debate is further complicated by the recent position statement of the US Food and Drug Administration (FDA) emphasizing that, in LOH, the benefits and safety of TTh have not been fully established. Hence, the FDA required a labeling change to inform patients about a possible increased cardiovascular (CV) risk of TTh. Similar considerations were previously released by the FDA and by Health Canada concerning a TTh-related venous thromboembolism (VTE) risk. In this review, we will summarize the available evidence concerning a possible link among TTh and CV and VTE risks. For this purpose, data derived from epidemiological studies analyzing relationships between the aforementioned risks and endogenous T levels will be analyzed. In addition, evidence deriving from interventional studies including pharmacoepidemiological and placebo-controlled randomized controlled trials (RCTs) will be examined. Our analysis shows that available data do not support an increased CV risk related to TTh. Similar considerations can be drawn for the relationship between TTh and VTE. The previously reported cases of TTh-related VTE were frequently related to a previously undiagnosed thrombophilia-hypofibrinolysis status. Hence, an anamnestic screening for thrombophilia before starting TTh is recommended, just as it is for the use of oral contraceptives.
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Condorelli RA; Russo GI; Calogero AE; Morgia G; La Vignera S.

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[Journal Article]

UI: 28488229

PURPOSE: Prostatitis is a very common urogenital disease of the male with prevalence ranging from 2.2 to 9.7% worldwide. Interestingly, some recent evidences have showed a significant association between chronic prostatitis (CP) and male infertility including a detrimental effect on sperm parameters, reduction of zinc concentration on semen sperm and production of anti-semen antibodies (ASAs). The aim of the current meta-analysis was to evaluate the association between CP and alteration of semen parameters.

METHODS: This analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines and we included in the final analysis 27
studies, with a total of 3241 participants, including 381 (11.75%) with chronic bacterial prostatitis (CBP), 1670 (51.53%) with chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) and 1190 (36.72%) controls.

RESULTS: CBP was associated with reduction of sperm concentration, sperm vitality, sperm total and progressive motility, while CP/CPPS was related to the reduction of semen volume, sperm concentration, sperm progressive motility and sperm normal morphology. We found that CP was significantly associated with reduced zinc concentration on seminal plasma (SMD: -20.73; p = 0.005). Finally, CP statistically increased the risk of developing ASA on seminal plasma (OR 3.26; p < 0.01).

CONCLUSION: In conclusion, chronic prostatitis showed a detrimental effect on sperm and both CPB or CP/CPPS may differently show negative impact on sperm.
Pulsatile GnRH therapy may restore hypothalamus-pituitary-testis axis function in patients with congenital combined pituitary hormone deficiency: a prospective, self-controlled trial.

Zheng J; Mao J; Xu H; Wang X; Huang B; Liu Z; Cui M; Xiong S; Ma W; Min L; Kaiser UB; Nie M; Wu X.

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[Journal Article]

UI: 28368486

Context: The effectiveness of pulsatile gonadotropin-releasing hormone (GnRH) therapy in congenital combined pituitary hormone deficiency (CCPHD) patients has not been investigated due to the limited number of patients as well as these patients’ presumed pituitary hypoplasia, poor gonadotrophic cell reserve, and impaired gonadotrophic response to GnRH.

Objective: To assess the pituitary response to pulsatile GnRH therapy in men with CCPHD.

Design: A prospective, self-controlled, 3 months clinical trial.

Settings: A University Endocrine Clinic.

Patients: Men with hypogonadotropic hypogonadism caused by CCPHD.

Intervention(s): Pulsatile GnRH was administered subcutaneously for three months.

Main outcome measures: Primary endpoints were total serum testosterone, testicular volume, and LH and FSH levels. Secondary endpoints included occurrence of spermatogenesis.

Results: A total of 40 male CCPHD patients completed the study. Of these, 60% (24/40) showed a good response to pulsatile GnRH treatment (response group), and their LH and FSH levels increased into the normal range and testosterone levels also increased to 8.67±4.83 nmol/L at three months. Of the patients in the response group, 33.3% (8/24) of them achieved spermatogenesis. The remaining 40% (16/40) of patients had a poor response to pulsatile GnRH treatment. MRI did not reveal any correlation between pituitary response and pituitary height and/or integrity of the pituitary stalk.

Conclusions: This study suggests that gonadotrophs in CCPHD patients can exist and be functional- even with MRI evidence of pituitary hypoplasia or dysplasia. Pulsatile GnRH therapy restored pituitary-testis axis function in 60% of patients with CCPHD. These results may directly guide the clinical therapeutic choice.
Risk of diabetes according to male factor infertility: a register-based cohort study.
STUDY QUESTION: Is male factor infertility associated with an increased risk of developing diabetes?

SUMMARY ANSWER: The study provides evidence that male factor infertility may predict later occurrence of diabetes mellitus with the risk being related to the severity of the underlying fertility problem.

WHAT IS KNOWN ALREADY: Previous cross-sectional studies have shown an increased prevalence of comorbidities among infertile men when compared to controls.

STUDY DESIGN, SIZE, DURATION: In this prospective cohort study, 39,516 men who had since 1994 undergone fertility treatment with their female partner were identified from the Danish national IVF register, which includes data on assumed cause of couple infertility (male/female factor, mixed and unexplained infertility) and type of fertility treatment. With a median follow-up time of 5.6 years, each man was followed for diabetes occurrence from enrollment until 31 December 2012 using the National Diabetes Register (NDR). Men with a history of diabetes prior to their fertility diagnosis were excluded. Hazard ratios (HR) were estimated by Cox proportional hazard models with age as the underlying time scale. In addition to analyzing the data for the entire IVF registration period (1994-2012), separate analyses were performed for men identified from the first (1994-2005) and second (2006-2012) IVF registration period owing to heterogeneity in the reporting of male factor infertility in these two time periods, because the reason for male factor infertility was not available from the first register.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Male factor infertility was identified from the variable 'yes' or 'no' from the first IVF register and through a diagnosis code (e.g. oligospermia, azoospermia) from the second IVF register. The reference group was men with male factor infertility (=‘no’) and those with normal semen quality or sterilized men. Of the included men, 18,499 (46.8%) had male factor infertility and 21,017 (53.2%) made up the reference group.

MAIN RESULTS AND THE ROLE OF CHANCE: A total of 651 (1.6%) diabetes cases were identified during the follow-up period. The adjusted HR's for diabetes risk among men with male factor infertility when compared to the reference group were HR = 1.08 (95% CI: 0.89, 1.31) and HR = 1.45 (95% CI: 1.06, 1.97) for the first and second IVF registration period, respectively. When assessing the effects of individual causes of male factor infertility, the adjusted HR's for
men with oligospermia, azoospermia and aspermia were HR = 1.44 (95% CI: 1.01, 2.06), HR = 2.10 (95% 1.25, 3.56) and HR = 3.20 (95% CI 1.00, 10.31), respectively.

LIMITATIONS, REASONS FOR CAUTION: We found no increased risk among men identified from the first IVF register, which may be related to exposure misclassification as the reason for male factor infertility was not available from this time period. The NDR does not distinguish between type 1 and type 2 diabetes.

WIDER IMPLICATIONS OF THE FINDINGS: These findings support previous studies that a man's reproductive and somatic health are closely intertwined and highlight the importance for further monitoring of these men. Further, implementation of diabetes screening may be especially relevant among aspermic and azoospermic men.

STUDY FUNDING/COMPETING INTERESTS: This article is part of the ReproUnion collaborative study, co-financed by the European Union, Intereg V Oresund-Kattegat-Skagerrak. None of the authors declare any conflict of interest.

TRIAL REGISTRATION NUMBER: None.
Prevalence of 'obesity-associated gonadal dysfunction' in severely obese men and women and its resolution after bariatric surgery: a systematic review and meta-analysis.

Escobar-Morreale HF; Santacruz E; Luque-Ramirez M; Botella Carretero JI.

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[Journal Article]

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BACKGROUND: Sexual dimorphism manifests noticeably in obesity-associated gonadal dysfunction. In women, obesity is associated with androgen excess disorders, mostly the polycystic ovary syndrome (PCOS), whereas androgen deficiency is frequently present in obese men in what has been termed as male obesity-associated secondary hypogonadism (MOSH). Obesity-associated gonadal dysfunction, consisting of PCOS in women and MOSH in men, is a frequent finding in patients with severe obesity and it may be ameliorated or even resolve with marked weight loss, especially after bariatric surgery.

OBJECTIVE AND RATIONALE: We aimed to obtain an estimation of the prevalence of obesity-associated gonadal dysfunction among women and men presenting with severe obesity and to evaluate the response to bariatric surgery in terms of resolution and/or improvement of this condition and changes in circulating sex hormone concentrations.

SEARCH METHODS: We searched PubMed and EMBASE for articles published up to June 2016. After deleting duplicates, the abstract of 757 articles were analyzed. We subsequently excluded 712 articles leaving 45 studies for full-text assessment of eligibility. Of these, 16 articles were excluded. Hence, 29 studies were included in the quantitative synthesis and in the different meta-analyses. Quality of the studies was assessed using the Quality index for prevalence studies and the Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group available from the National Heart, Lung and Blood Institute. For meta-analyses including more than 10 studies, we used funnel and Doi plots to estimate publication bias.
OUTCOMES: In severely obese patients submitted to bariatric surgery, obesity-associated gonadal dysfunction was very prevalent: PCOS was present in 36% (95CI 22-50) of women and MOSH was present in 64% (95CI 50-77) of men. After bariatric surgery, resolution of PCOS was found in 96% (95CI 89-100) of affected women and resolution of MOSH occurred in 87% (95CI 76-95) of affected men. Sex hormone-binding globulin concentrations increased after bariatric surgery in women (22 pmol/l, 95CI 2-47) and in men (22 pmol/l, 95CI 19-26) and serum estradiol concentrations decreased in women (-104 pmol/l, 95CI -171 to -39) and to a lesser extent in men (-22 pmol/l, 95CI -38 to -7). On the contrary, sex-specific changes were observed in serum androgen concentrations: for example, total testosterone concentration increased in men (8.1 nmol/l, 95CI 6-11) but decreased in women (-0.7 nmol/l, 95CI -0.9 to -0.5). The latter was accompanied by resolution of hirsutism in 53% (95CI 29-76), and of menstrual dysfunction in 96% (95CI 88-100), of women showing these symptoms before surgery.

WIDER IMPLICATIONS: Obesity-associated gonadal dysfunction is among the most prevalent comorbidities in patients with severe obesity and should be ruled out routinely during their initial diagnostic workup. Considering the excellent response regarding both PCOS and MOSH, bariatric surgery should be offered to severely obese patients presenting with obesity-associated gonadal dysfunction.

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30. Reproductive toxicity of Roundup herbicide exposure in male albino rat.
Owagboriaye FO; Dedeke GA; Ademolu KO; Olujimi OO; Ashidi JS; Adeyinka AA.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Experimental & Toxicologic Pathology. , 2017 May 01.
[Journal Article]
UI: 28473188
The incidence of infertility in human is on the increase and the use of Roundup herbicide and presence of its residues in foodstuff is a major concern. This study therefore aim to assess the effect of Roundup on the reproductive capacity of 32 adult male albino rats randomized into 4 groups of 8 rats per group orally exposed to Roundup at 3.6mg/kg body weight (bw), 50.4mg/kgbw and 248.4mg/kgbw of glyphosate concentrations for 12 weeks while the control group was given distilled water. Serum level of reproductive hormone (testosterone, luteinizing hormone (LH), follicle stimulating hormone (FSH) and prolactin), oxidative stress indices in the testicular tissue, epididymal sperm morphology assessment and testicular histopathology of the rats were used as a diagnostic marker of reproductive dysfunction. Significant (p<0.05) alterations in the level of all the reproductive hormones and oxidative stress markers assayed were observed in rats exposed to Roundup. Significant reductions (p<0.05) in sperm count, percentage motility and significant (p<0.05) increased in abnormal sperm cells were observed in the exposed rats. Histopathologically, severe degenerative testicular architectural lesions were seen in the Roundup exposed rats. Roundup may interfere with spermatogenesis and impair fertility in male gonad.
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31.
The impact of specific fertility treatments on cognitive development in childhood and adolescence: a systematic review.
Rumbold AR; Moore VM; Whitrow MJ; Oswald TK; Moran LJ; Fernandez RC; Barnhart KT; Davies MJ.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article]
UI: 28472417
STUDY QUESTIONS: Does fertility treatment influence cognitive ability in school-aged children, and does the impact vary with the type of treatment?

SUMMARY ANSWER: The available high-quality evidence indicates that specific treatments may give rise to different effects on cognitive development, with certain treatments, including ICSI, associated with cognitive impairment.

WHAT IS KNOWN ALREADY: Previous reviews of the literature concerning cognitive outcomes among children conceived with medical assistance have concluded that study findings are generally 'reassuring', but limited attention has been paid to the quality of this research. In addition, no review has separately assessed the range of treatment modalities available, which vary in invasiveness, and thus, potentially, in their effects on developmental outcomes.

STUDY DESIGN, SIZE, DURATION: A systematic review was undertaken. We searched PubMed, PsycINFO and the Educational Resources Information Centre database to identify English-language studies published up until 21 November 2016.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Two authors independently reviewed identified articles, extracted data and assessed study quality. Studies were eligible if they assessed cognitive development from age 4 years or more, among children conceived with fertility treatment compared with either children conceived naturally or children born from a different type of fertility treatment. Where available, data were extracted and reported separately according to the various components of treatment (e.g. mode of fertilization, embryo freezing, etc.). Risk of bias was assessed using the Newcastle-Ottawa Scale, with a score >7/9 indicative of high quality.

MAIN RESULTS AND THE ROLE OF CHANCE: The search identified 861 articles, of which 35 were included. Of these, seven were rated high quality. Most studies (n = 22) were subject to selection bias, due to the exclusion of children at increased risk of cognitive impairment. Among high-quality studies, there was no difference in cognitive outcomes among children conceived with conventional IVF and those conceived naturally. Findings among high-quality studies of children conceived with ICSI were inconsistent: when compared with children conceived naturally, one study reported lower intelligence quotient (IQ; 5-7 points, on average) among ICSI children whereas the remaining two high-quality studies reported no difference between groups. Furthermore, among the three high-quality studies comparing children conceived with ICSI compared with conventional IVF, one reported a significant increase in the risk of mental retardation, one reported a small difference in IQ (3 points lower, on average) and one no difference at all. There were scant studies examining exposure to embryo freezing, or less invasive treatments such as ovulation induction without IVF/ICSI.

LIMITATION, REASONS FOR CAUTION: Most existing studies had methodological limitations including selection bias and/or failure to address confounding by family background. In addition, a meta-analysis could not be performed due to heterogeneity in the assessment of cognitive
outcomes. These factors impeded our ability to synthesize the evidence and draw reliable conclusions.

WIDER IMPLICATIONS OF THE FINDINGS: The conflicting findings among studies of children conceived with ICSI require clarification, in light of the increasing use of this technique for reasons other than male-factor infertility. Further population-based studies are needed that utilize contemporary data to examine specific aspects of treatment and combinations of techniques (e.g. ICSI with frozen embryo cycles). Importantly, studies should include the complete group of children exposed to treatment.

STUDY FUNDING/COMPETING INTEREST(S): A.R.R. is supported by a Career Development Fellowship from the National Health and Medical Research Council of Australia. L.J.M. is funded by a fellowship from the Heart Foundation of Australia. The authors declare there are no competing interests.

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32.
Introduction of a male-harming mitochondrial haplotype via 'Trojan Females' achieves population suppression in fruit flies.
Wolff JN; Gemmell NJ; Tompkins DM; Dowling DK.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
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[Journal Article]
UI: 28467301
Pests are a global threat to biodiversity, ecosystem function, and human health. Pest control approaches are thus numerous, but their implementation costly, damaging to non-target species, and ineffective at low population densities. The Trojan Female Technique (TFT) is a prospective self-perpetuating control technique that is species-specific and predicted to be effective at low densities. The goal of the TFT is to harness naturally-occurring mutations in the mitochondrial genome that impair male fertility while having no effect on females. Here, we provide proof-of-concept for the TFT, by showing that introduction of a male fertility-impairing mtDNA haplotype into replicated populations of Drosophila melanogaster causes numerical population suppression, with the magnitude of effect positively correlated with its frequency at trial inception. Further development of the TFT could lead to establishing a control strategy that overcomes limitations of
conventional approaches, with broad applicability to invertebrate and vertebrate species, to control environmental and economic pests.

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A randomized trial of local endometrial injury during ovulation induction cycles.
Helmy MEE; Maher MA; Elkhouly NI; Ramzy M.
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OBJECTIVE: To investigate the effect of endometrial injury on pregnancy outcomes among infertile women taking clomifene citrate.
METHODS: A prospective randomized trial was undertaken at an Egyptian hospital between January 26, 2015, and July 17, 2016. Eligible women (>1 year primary/secondary/unexplained infertility, aged 20-35 years, day-2 follicle-stimulating hormone <12 IU/L, normal prolactin/thyroid function/uterine cavity, >1 patent tube, male partner with normal semen count and motility, 3
cycles of clomifene citrate without success) were randomly allocated (1:1) using computer-generated numbers into intervention (received endometrial injury on cycle day 15-24) or control groups (sham procedure). Women began ovulation induction on days 3-5 of the following cycle. Participants and investigators were not masked to group assignment. The primary outcomes were clinical pregnancy, spontaneous abortion, and multiple pregnancy rates. Women who completed follow-up were included in analyses.

RESULTS: The intervention group included 52 women and the control group 53 women. The clinical pregnancy rate was significantly higher in the intervention group (37% [n=19]) than in the control group (13% [n=7]; P=0.006). No differences between the intervention and control groups were noted for spontaneous abortion rate (11% [2/19] vs 29% [2/7]; P=0.287) or multiple pregnancy rate (11% [2/19] vs 14% [1/7]; P=0.790). No adverse effects were reported.

CONCLUSION: Endometrial injury before ovulation induction could improve chances of pregnancy and its outcomes. CLINICALTRIALS.GOV: NCT02345837.

The acceptability of stem cell-based fertility treatments for different indications.
STUDY QUESTION: What is the acceptability of using stem cell-based fertility treatments (SCFT) for different indications according to gynaecologists and the general public?

SUMMARY ANSWER: The majority of gynaecologists and the general public accept SCFT for the indications female or male infertility in young heterosexual couples, and female infertility in single women and same-sex couples.

WHAT IS KNOWN ALREADY: SCFT could result in genetic parenthood for intended parents with indications that cannot be treated using currently available methods, such as being in a same-sex relationship or female post-menopausal age. It is unclear whether the acceptability of SCFT differs between indications for treatment and whether gynaecologists and the general public differ in their assessments.

STUDY DESIGN SIZE, DURATION: In November 2015, a cross-sectional survey was disseminated among 179 gynaecologists and a panel of 1250 respondents comprising a representative sample of the Dutch general public.

PARTICIPANTS/MATERIALS, SETTING, METHODS: The potential indications for future SCFT to achieve genetic parenthood were identified by literature review. A questionnaire was developed, reviewed by experts from different disciplines and tested among the general public. The questionnaire asked whether treating eight groups of intended parents with SCFT was acceptable or not. Regression analysis examined whether demographic characteristics influenced choices and whether the general public and gynaecologists differed in opinion.

MAIN RESULTS AND THE ROLE OF CHANCE: A total of 82 (46%) gynaecologists and 772 (62%) members of the general public completed the survey. The acceptability of using SCFT varied according to both gynaecologists and the general public between the eight groups of intended parents (P < 0.001). The majority of the Dutch general public accepts SCFT for six out of eight possible indications, namely female infertility in young heterosexual couples (94%), male infertility in young heterosexual couples (94%), unexplained infertility in young heterosexual couples (83%), female infertility in single women (69%), lesbian couples (68%) and gay couples (62%). The majority of gynaecologists also found treating these groups acceptable, except for the indication of unexplained infertility, which was only accepted by a minority of gynaecologists (43%). A minority of both the general public and gynaecologists accepted SCFT for fertile women who want a child that is genetically only her own (27 and 6%, respectively) and for female infertility in heterosexual couples in which the woman is over 50 years of age (17% and 26%,
respectively). Attaching low importance to religion, having progressive political preferences, not having a university degree, having experienced infertility, being a woman, being older and not being of European ethnicity were positively associated with considering using SCFT acceptable for one or multiple indications.

LARGE SCALE DATA: N/A.

LIMITATIONS REASONS FOR CAUTION: The generalizability of our findings to future decades or other countries might be limited as opinions about novel technologies change over time and might vary across cultures. Support among gynaecologists and the general public is interesting but not proof of ethical acceptability.

WIDER IMPLICATIONS OF THE FINDINGS: Once proven safe and effective, fear of limited acceptability by the general public is unwarranted, and thus should not stop gynaecologists from offering SCFT to single infertile women and same-sex couples in addition to young infertile heterosexual couples.

STUDY FUNDING AND COMPETING INTEREST(S): Funded by the Young Academy of the Royal Netherlands Academy of Arts and Sciences and the Universities of Amsterdam and Leuven. No conflict of interest to declare.

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CFTR gene mutations and polymorphism are associated with non-obstructive azoospermia: From case-control study.
Jiang L; Jin J; Wang S; Zhang F; Dai Y; Shi L; Zhang S.
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A variety of experimental studies have yielded evidence that the cystic fibrosis transmembrane conductance regulator (CFTR) protein participates in the process of spermatogenesis. However, the association between CFTR gene and non-obstructive azoospermia (NOA) disease remained to be a question. First, we reviewed available data from the PubMed and Embase databases before May 2016 to find the most common mutations of CFTR gene in NOA patients. Second, an original case-control study was conducted on NOA patients (n=100) and a control group consisting of fertile males (n=100), selected from August 2015 to March 2017, to detect CFTR gene mutations and polymorphism. Peripheral blood samples from NOA patients and normal controls were analyzed for the presence of specific sequences of CFTR gene by polymerase chain reaction amplification followed by direct sequencing. From our comprehensive review, 12 case-control studies were found concerning the relation between CFTR gene mutations and polymorphism and NOA disease. Fifty-four mutations were mentioned and IVS8 poly-T, TG repeats, F508del and R117H mutations were the most common ones. Based on that, we detected IVS8 poly-T, TG repeats, F508del, R117H and M470V mutations in our case control study. We found that the T5 allele was present at a significantly higher rate in NOA patients than in the control group (5.00% versus 0.00%, p<0.01) with increased risk having NOA [Odds ratios (OR) 2.05, 95% confidence intervals (CI) 1.85-2.27]. The T5 variant was always accompanied by TG12 (10/10) and V470 allele participated in most TG12T5 haplotypes (8/10). TG12T5-V470 haplotype also enhanced risk of having NOA [OR 2.04, 95% CI 1.84-2.26]. F508del and R117H mutations were not found in either group. In conclusion, the polyvariant mutant genes of CFTR: T5 allele and TG12-T5-V470 genotype are correlated with NOA, but F508del and R117H mutations have low possibility to be associated with NOA.
36.

Meta-analysis of Results of Testosterone Therapy on Sexual Function Based on International Index of Erectile Function Scores.
Corona G; Rastrelli G; Morgentaler A; Sforza A; Mannucci E; Maggi M.
CONTEXT: The interpretation of available clinical evidence related to the effect of testosterone (T) treatment (TTh) on sexual function has been inconsistent, in part due to the use of different and self-reported measures to assess outcomes. The International Index of Erectile Function (IIEF) is the most frequently used validated tool to assess male sexual function.

OBJECTIVE: To perform a meta-analysis of available data evaluating the effect of TTh on male sexual function using IIEF as the primary outcome.

EVIDENCE ACQUISITION: An extensive Medline, Embase, and Cochrane search was performed including all placebo-controlled randomized clinical trials enrolling men comparing the effect of TTh on sexual function.

EVIDENCE SYNTHESIS: Out of 137 retrieved articles, 14 were included in the study enrolling 2298 participants, with a mean follow-up of 40.1 wk and mean age of 60.2+/6.5 yr. Using IIEF-erectile function domain (IIEF-EFD) as the outcome, we found that TTh significantly improved erectile function compared with placebo (mean difference=2.31 [1.41;3.22] IIEF-EFD score, p<0.0001). Patients with more severe hypogonadism (total T<8 nmol/l) reported greater changes in final IIEF-EFD score when compared with those with a milder T deficiency (total T<12 nmol/l; 1.47 [0.90;2.03] and 2.95 [1.86;4.03] for total T<12 nmol/l and <8 nmol/l, respectively, Q=5.61, p=0.02). The magnitude of the effect was lower in the presence of metabolic derangements, such as diabetes and obesity. Other aspects of sexual function, as evaluated by IIEF subdomains, were also improved with TTh including libido, intercourse satisfaction, orgasm, and overall sexual satisfaction.

CONCLUSIONS: TTh significantly improves erectile function and other sexual parameters as measured by IIEF in hypogonadal men. These results argue that sexual dysfunction should be considered a hallmark manifestation of T deficiency, since those symptoms can be significantly improved with normalization of serum T. In addition, these results suggest that TTh alone may be considered a reasonable treatment for hypogonadal men with milder degrees of erectile dysfunction, whereas the addition of other treatments, such as phosphodiesterase type 5 inhibitors, may be more appropriate for men with more severe erectile dysfunction.

PATIENT SUMMARY: We investigated the effect of testosterone treatment on sexual function by performing a meta-analysis of all available studies that used the most frequently used assessment tool, the International Index of Erectile Function. We found that testosterone treatment significantly improves erectile dysfunction, as well as other aspects of sexual function, in men with testosterone deficiency. This treatment may be all that is required for hypogonadal
men with milder erectile dysfunction; however, additional treatments may be necessary in more severe cases.

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37.
Long-Term Testosterone Therapy Improves Cardiometabolic Function and Reduces Risk of Cardiovascular Disease in Men with Hypogonadism.
Traish AM; Haider A; Haider KS; Doros G; Saad F.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
OBJECTIVES: In the absence of large, prospective, placebo-controlled studies of longer duration, substantial evidence regarding the safety and risk of testosterone (T) therapy (TTh) with regard to cardiovascular (CV) outcomes can only be gleaned from observational studies. To date, there are limited studies comparing the effects of long-term TTh in men with hypogonadism who were treated or remained untreated with T, for obvious reasons. We have established a registry to assess the long-term effectiveness and safety of T in men in a urological setting. Here, we sought to compare the effects of T on a host of parameters considered to contribute to CV risk in treated and untreated men with hypogonadism (control group).

PATIENTS AND METHODS: Observational, prospective, cumulative registry study in 656 men (age: 60.7 +/- 7.2 years) with total T levels <12.1 nmol/L and symptoms of hypogonadism. In the treatment group, men (n = 360) received parenteral T undecanoate (TU) 1000 mg/12 weeks following an initial 6-week interval for up to 10 years. Men (n = 296) who had opted against TTh served as controls. Median follow-up in both groups was 7 years. Measurements were taken at least twice a year, and 8-year data were analyzed. Mean changes over time between the 2 groups were compared by means of a mixed-effects model for repeated measures, with a random effect for intercept and fixed effects for time, group, and their interaction. To account for baseline differences between the 2 groups, changes were adjusted for age, weight, waist circumference, fasting glucose, blood pressure, and lipids.

RESULTS: There were 2 deaths in the T-treated group, none was related to CV events. There were 21 deaths in the untreated (control) group, 19 of which were related to CV events. The incidence of death in 10 patient-years was 0.1145 in the control group (95% confidence interval [CI]: 0.0746-0.1756; P < .000) and 0.0092 in the T-treated group (95% CI: 0.0023-0.0368; P < .000); the estimated difference between groups was 0.0804 (95% CI: 0.0189-0.3431; P < .001). The estimated reduction in mortality for the T-group was between 66% and 92%. There were also 30 nonfatal strokes and 26 nonfatal myocardial infarctions in the control group and none in the T-treated group.

CONCLUSION: Long-term TU was well tolerated with excellent adherence suggesting a high level of patient satisfaction. Mortality related to CV disease was significantly reduced in the T-group.

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OBJECTIVE: To examine and characterize the demographics and scholarly characteristics of academic urology chairmen at the time of appointment.

MATERIALS AND METHODS: The chairman of each United States urology residency program as of September 2016 was included in the study. Interim chairmen, as well as programs for which no clearly defined chair could be identified, were excluded. Demographic and academic data were collected via publically available curriculum vitae, departmental websites, Google search engine, and PubMed and Scopus websites.

RESULTS: One hundred thirteen chairmen were included in the study. The majority were male (96%) and mean age at appointment was 46 years (standard deviation=6.3 years). Mean number of publications and H-index at the time of appointment was 105 and 31.1, respectively. Fellowship training was completed by 75% of chairmen, of which urologic oncology (N=43), endourology (N=12), and infertility/andrology (N=10) were the most common. The most common additional
graduate degrees prior to appointment were MBA (N=7) and PhD (N=6). The most frequently attended institutions for residency were Johns Hopkins University (13) and Northwestern University (5), whereas Memorial Sloan Kettering Cancer Center (13) and Baylor University (7) were the most frequent for fellowship. Twenty percent of chairmen attained the chairman position at their former residency program and 7% at their former fellowship program.

CONCLUSION: Our study describes the demographic and academic characteristics of urology academic chairmen at the time of appointment. The majority of chairmen are male and specialize in urologic oncology. Chairmen often receive the chair appointment at their former residency program.

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Infertility and subfertility account for huge economic losses in the animal industry; indeed, 50% of animal breeding failure is associated with male infertility. Approximately 70% of cattle and 90% of pig livestock are currently produced by artificial insemination. Therefore, breeding-male selection is extremely important for the genetic benefits of progeny. Although conventional semen analysis provides an initial measure of male fertility, its clinical value is questionable. Proteomics approaches recently identified candidate protein markers in spermatozoa for evaluating male fertility. Fertility-related proteins in capacitated boar spermatozoa were shown to predict boar fertility more precisely than those detected in ejaculated spermatozoa, which motivated the development of more accurate and sensitive tools for the assessment of male fertility in relation to sperm function and fertilization. Although protein markers in spermatozoa are capable of differentiating between fertile and infertile males, clinical trials are required to validate their predictive utility. This review outlines recent findings regarding the capacitation-related proteome of spermatozoa, and discusses how these proteins may be utilized to better understand the fertility of domestic animals. This article is protected by copyright. All rights reserved.
To reassess the efficacy of varicocelectomy in the treatment of hypogonadism in subfertile males, we carried out a meta-analysis of clinical trials and retrospective studies that compared the pre-operative and postoperative serum testosterone. We searched Embase and PubMed (1980 to May 2016) for studies. Eight studies and 712 patients were included. The combined analysis of seven studies discovered that the mean serum testosterone of patients post-operation improved by 34.3 ng/dl (95% CI: 22.57-46.04, p < .00001, I^2 = 0.0%) compared with their pre-operative levels. In subgroup analysis, testosterone improvements in the hypogonadal treated subgroup were more significant (improved by 123 ng/dl, 95% CI: 114.61-131.35, p < .00001, I^2 = 37%) than in the eugonadal, or the untreated controls. In an analysis of surgery versus untreated control (three studies included), results showed that mean testosterone among hypogonadal increased by 105.65 ng/dl (95% CI: 77.99-133.32), favouring varicocelectomy, as the differences were significant (p < .00001). However, there were insignificant differences in eugonadal (p = .36). In conclusion, varicocelectomy significantly improved testosterone in hypogonadal men with subfertility. Active surgical treatment of varicocele might have a benefit of maintaining healthy androgen levels in subfertile men.
INTRODUCTION: Selective estrogen receptor modulators (SERMs) have been used off-label in men for more than 50 years. SERMs exert their action on the estrogen receptor agonistically or antagonistically. A fundamental knowledge of the complex molecular action and physiology of SERMs is important in understanding their use and future directions of study in men.

AIM: To review the basic science and mechanism of the action of estrogens, the estrogen receptor, and SERMs, and the existing clinical publications on the use of SERMs in men for infertility and hypogonadism with their strengths and weaknesses and to identify the need for future studies.

METHODS: After a review of publications on the basic science of estrogen receptors, a chronologic review of published evidence-based studies on the use of SERMs in men for infertility and hypogonadism was undertaken.
MAIN OUTCOME MEASURES: Clinical publications were assessed for type of study, inclusion criteria, outcome measurements, and results. Strengths and weaknesses of the publications were assessed and discussed.

RESULTS: Few prospective rigorously controlled trials have been undertaken on the use of SERMs in men. Most existing trials are largely retrospective anecdotal studies with inconsistent inclusion and end-point measurements. The SERMs are complex and at times can produce paradoxical results. Their action likely depends on the genetics of the individual, his tissue-specific composition of estrogen receptors, the molecular structure and pharmacodynamics of the SERMs, and their metabolism.

CONCLUSION: Rigorously controlled trials of the use of SERMs in men are needed to better identify their clinical benefit and long-term safety in infertile and hypogonadal men. Recent placebo-controlled pharmaceutical industry SERM trials have demonstrated short-term safety and efficacy in men with secondary hypogonadism and eventually might provide an alternative to exogenous testosterone replacement therapy in men with secondary hypogonadism. Helo S, Wynia B, McCullough A. "Cherchez La Femme": Modulation of Estrogen Receptor Function With Selective Modulators: Clinical Implications in the Field of Urology. Sex Med Rev 2017;X:XXX-XXX.

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Predictive value of FSH, testicular volume, and histopathological findings for the sperm retrieval rate of microdissection TESE in nonobstructive azoospermia: a meta-analysis.

Li H; Chen LP; Yang J; Li MC; Chen RB; Lan RZ; Wang SG; Liu JH; Wang T.

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We performed this meta-analysis to evaluate the predictive value of different parameters in the sperm retrieval rate (SRR) of microdissection testicular sperm extraction (TESE) in patients with nonobstructive azoospermia (NOA). All relevant studies were searched in PubMed, Web of Science, EMBASE, Cochrane Library, and EBSCO. We chose three parameters to perform the meta-analysis: follicle-stimulating hormone (FSH), testicular volume, and testicular histopathological findings which included three patterns: hypospermatogenesis (HS), maturation arrest (MA), and Sertoli-cell-only syndrome (SCOS). If there was a threshold effect, only the area under the summary receiver operating characteristic curve (AUSROC) was calculated. Otherwise, the pooled sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), and the diagnostic odds ratio (DOR) were also calculated. Twenty-one articles were included in our study finally. There was a threshold effect among studies investigating FSH and SCOS. The AUSROCs of FSH, testicular volume, HS, MA, and SCOS were 0.6119, 0.6389, 0.6758, 0.5535, and 0.2763, respectively. The DORs of testicular volume, HS, and MA were 1.98, 16.49, and 1.26, respectively. The sensitivities of them were 0.80, 0.30, and 0.27, while the specificities of them were 0.35, 0.98, and 0.76, respectively. The PLRs of them were 1.49, 10.63, and 1.15, respectively. And NLRs were 0.73, 0.72, and 0.95, respectively. All the investigated factors in our study had limited predictive value. However, the histopathological findings were helpful to some extent. Most patients with HS could get sperm by microdissection TESE.
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Dietary patterns, foods and nutrients in male fertility parameters and fecundability: a systematic review of observational studies.

Salas-Huetos A; Bullo M; Salas-Salvado J.


[Journal Article]

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BACKGROUND: Infertility is a global public health issue, affecting 15% of all couples of reproductive age. Male factors, including decreased semen quality, are responsible for ~25% of these cases. The dietary pattern, the components of the diet and nutrients have been studied as possible determinants of sperm function and/or fertility.

OBJECTIVE AND RATIONALE: Previous systematic reviews have been made of the few heterogeneous low-quality randomized clinical trials (RCTs) conducted in small samples of participants and investigating the effect of specific nutrients and nutritional supplements on male infertility. However, as yet there has been no systematic review of observational studies.

SEARCH METHODS: A comprehensive systematic review was made of the published literature, from the earliest available online indexing year to November 2016, in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses. We have included cross-sectional, case-control and prospective and retrospective studies in which fertile/infertile men were well defined (men with sperm disorders, sperm DNA damage, varicocele or idiopathic infertility). The primary outcomes were semen quality or fecundability. With the data extracted, we evaluated and scored the quality of the studies selected. We excluded RCTs, animal studies, review articles and low-quality studies.

OUTCOMES: A total of 1944 articles were identified, of which 35 were selected for qualitative analysis. Generally, the results indicated that healthy diets rich in some nutrients such as omega-3 fatty acids, some antioxidants (vitamin E, vitamin C, beta-carotene, selenium, zinc, cryptoxanthin and lycopene), other vitamins (vitamin D and folate) and low in saturated fatty acids and trans-fatty acids were inversely associated with low semen quality parameters. Fish, shellfish and seafood, poultry, cereals, vegetables and fruits, low-fat dairy and skimmed milk were positively associated with several sperm quality parameters. However, diets rich in processed meat, soy foods, potatoes, full-fat dairy and total dairy products, cheese, coffee, alcohol, sugar-sweetened beverages and sweets have been detrimentally associated with the quality of semen in some studies. As far as fecundability is concerned, a high intake of alcohol, caffeine and red
meat and processed meat by males has a negative influence on the chance of pregnancy or fertilization rates in their partners.

WIDER IMPLICATIONS: Male adherence to a healthy diet could improve semen quality and fecundability rates. Since observational studies may prove associations but not causation, the associations summarized in the present review need to be confirmed with large prospective cohort studies and especially with well-designed RCTs.

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44.
Men’s knowledge, attitudes and behaviours relating to fertility.
Hammarberg K; Collins V; Holden C; Young K; McLachlan R.
BACKGROUND: The increasingly common practice in high-income countries to delay childbearing to the fourth and fifth decades of life increases the risk of involuntary childlessness or having fewer children than desired. Older age also increases the risk of age-related infertility, the need for ART to conceive, and obstetric and neonatal complications. Existing research relating to childbearing focusses almost exclusively on women, and in public discourse declining fertility rates are often assumed to be the result of women delaying childbearing to pursue other life goals such as a career and travel. However, evidence suggests that the lack of a partner or a partner willing to commit to parenthood is the main reason for later childbearing.

OBJECTIVE AND RATIONALE: To better understand men's contributions to childbearing decisions and outcomes, the literature pertaining to men's fertility-related knowledge, attitudes and behaviours was reviewed.

SEARCH METHODS: The electronic databases of Medline, Embase and PsycINFO were searched to identify investigations of men's knowledge, attitudes and behaviours relating to fertility, infertility, reproductive health or childbearing using relevant fertility keyword search terms. Studies were included if they had investigated factors associated with men's fertility-related knowledge, attitudes and behaviours, had been conducted in a high-income country and were published in an English language peer-reviewed journal between January 2005 and August 2016.

OUTCOMES: The search yielded 1349 citations. Of these, 47 papers representing 43 unique studies were included in the review. Where response rate was reported, it ranged between 13 and 94%. Studies varied in terms of research design; inclusion and exclusion criteria; recruitment strategies; adequacy of sample size; recruitment and retention rates and data collection tools. However, findings were consistent and indicate that men almost universally value parenthood, want and expect to become fathers, and aspire to have at least two children. Yet most men have inadequate knowledge about the limitations of female and male fertility and overestimate the chance of spontaneous and assisted conception. Perceptions of ideal circumstances in which to have children included being in a stable and loving relationship, having completed studies, secured a permanent job and a dependable income, having achieved personal maturity, and having a partner who desires children and is 'suitable' as a potential co-parent. Although all studies were conducted in high-income countries, between-country social and cultural differences may have influenced the findings relating to attitudes.

WIDER IMPLICATIONS: Men aspire to parenthood as much as women do but have limited knowledge about the factors that influence fertility. The gap between ideal biological and ideal
social age for having children appears to be widening, narrowing the time frame in which parenthood can be achieved. This may lead to unfulfilled parenthood aspirations. The findings can inform government policies and public education strategies aimed to support childbearing during the most fertile years, reduce the personal and societal cost of infertility and ART use, and allow people to fulfil their parenthood goals.

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45.
The Effect of Oral Phosphodiesterase-5 Inhibitors on Sperm Parameters: A Meta-analysis and Systematic Review.
Tan P; Liu L; Wei S; Tang Z; Yang L; Wei Q.
OBJECTIVE: To perform a systematic review and meta-analysis to evaluate the effect of phosphodiesterase-5 (PDE5) inhibitors on sperm parameters.

METHODS: A systematic literature search was performed. Mean value and its standard deviation (mean +/- standard deviation) were used to perform quantitative analysis. Statistic heterogeneity scores were assessed with the standard Cochran Q test and I² statistic. All statistical analyses were conducted by RevMan 5.3.

RESULTS: Eleven studies embraced a total of 1317 participants and 19 subgroups or trials were included. Acute administration of PDE5 inhibitors had no effect on semen volume (mean value [MD]=0.26; 95% confidence interval [CI]: 0.00-0.48) and sperm concentration (MD=2.04; 95%CI: -2.95 to 7.04). However, the percentage of motile spermatozoa (MD=7.05; 95%CI: 2.59-11.51), the percentage of total progressive motility (MD=6.23; 95%CI: 2.43-10.04), and rapid progressive motility (MD=3.11; 95%CI: 0.23-5.99) were increased after oral PDE5 inhibitors treatment. Interestingly, these significant changes were observed only in infertile men but not in normal patients (MD=6.89, P<.001 vs MD=0.67, P=.71; MD=6.64, P=.001 vs MD=2.11, P>.05; and MD=3.89, P=.04 vs MD=0.92, P=.59, respectively). The percentage of morphologically normal spermatozoa also increased in infertile men (MD=12.15; 95%CI: 5.16-19.15). Limited evidence showed the linearity, abnormal forms of spermatozoa, as well as reproductive hormones (total testosterone, free testosterone, luteinizing hormone, and follicle-stimulating hormone) did not benefit from PDE5 inhibitors treatment.

CONCLUSION: Oral PDE5 inhibitors treatment could modestly increase the sperm motility and morphology in infertile men.

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Effects of Anabolic Androgenic Steroids on the Reproductive System of Athletes and Recreational Users: A Systematic Review and Meta-Analysis. [Review]
Christou MA; Christou PA; Markozannes G; Tsatsoulis A; Mastorakos G; Tigas S.
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BACKGROUND: Anabolic androgenic steroids (AAS) are testosterone derivatives used by athletes and recreational users to improve athletic performance and/or enhance appearance. Anabolic androgenic steroids use may have serious and potentially irreversible adverse effects on different organs and systems, including the reproductive system.

OBJECTIVE: This systematic review and meta-analysis aimed to critically assess the impact of AAS use on the reproductive system of athletes and recreational users.

METHODS: An electronic literature search was conducted using the databases MEDLINE, CENTRAL, and Google Scholar. Studies were included when the following criteria were fulfilled: participants were athletes or recreational users of any age, sex, level or type of sport; AAS use of
any type, dose, form or duration; AAS effects on the reproductive system were assessed as stated by medical history, clinical examination, hormone and/or semen analysis. Random-effects meta-analysis was performed to assess the weighted mean difference (WMD) of serum gonadotropin (luteinizing hormone, follicle-stimulating hormone) and testosterone levels compared with baseline, during the period of AAS use, as well as following AAS discontinuation.

RESULTS: Thirty-three studies (three randomized clinical trials, 11 cohort, 18 cross-sectional, and one non-randomized parallel clinical trial) were included in the systematic review (3879 participants; 1766 AAS users and 2113 non-AAS users). The majority of the participants were men; only six studies provided data for female athletes. A meta-analysis (11 studies) was conducted of studies evaluating serum gonadotropin and testosterone levels in male subjects: (1) prior to, and during AAS use (six studies, n = 65 AAS users; seven studies, n = 59, evaluating gonadotropin and testosterone levels respectively); (2) during AAS use and following AAS discontinuation (four studies, n = 35; six studies, n = 39, respectively); as well as (3) prior to AAS use and following AAS discontinuation (three studies, n = 17; five studies, n = 27, respectively).

During AAS intake, significant reductions in luteinizing hormone [weighted mean difference (WMD) -3.37 IU/L, 95% confidence interval (CI) -5.05 to -1.70, p < 0.001], follicle-stimulating hormone (WMD -1.73 IU/L, 95% CI -2.67 to -0.79, p < 0.001), and endogenous testosterone levels (WMD -10.75 nmol/L, 95% CI -15.01 to -6.49, p < 0.001) were reported. Following AAS discontinuation, serum gonadotropin levels gradually returned to baseline values within 13-24 weeks, whereas serum testosterone levels remained lower as compared with baseline (WMD -9.40 nmol/L, 95% CI -14.38 to -4.42, p < 0.001). Serum testosterone levels remained reduced at 16 weeks following discontinuation of AAS. In addition, AAS abuse resulted in structural and functional sperm changes, a reduction in testicular volume, gynecomastia, as well as clitoromegaly, menstrual irregularities, and subfertility.

CONCLUSION: The majority of AAS users demonstrated hypogonadism with persistently low gonadotropin and testosterone levels, lasting for several weeks to months after AAS withdrawal. Anabolic androgenic steroid use results in profound and prolonged effects on the reproductive system of athletes and recreational users and potentially on fertility.
47. Ethanol-induced male infertility: Effects of aqueous leaf extract of Tetracarpidium conophorum. Akomolafe SF; Oboh G; Akindahunsi AA; Afolayan AJ. OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present Andrologia. , 2017 Feb 06. [Journal Article] UI: 28164351

This study investigated the effects of Tetracarpidium conophorum leaf extract on infertility induced by ethanol in male rats. Thirty rats were randomly divided into six groups of five animals each: Group 1 (positive control) received 0.9% saline only; Group 2 (ethanol alone) were given only 30% ethanol orally at 7 ml/kg body weight per day, thrice in a week; groups 3, 4 and 5 were given ethanol and co-treated with 50, 500 and 1,000 mg/kg body weight of leaf extract, respectively, while Group 6 was given ethanol and co-treated with a fertility drug, clomiphene citrate. Ethanol treatment resulted in significant (p < .05) decrease in LDH activity, G-6PDH
activity, glycogen content, 3beta and 17beta HSD activities and testicular and epididymal Zn and Se contents and furthermore decrease in testicular sperm count, viability and marked increment in total sperm abnormalities, rate of sperm analysis parameters and consequently decreased reproductive hormone levels. Interestingly, co-administration of ethanol with either T. conophorum extract or drug almost ameliorated the toxic assault imposed by ethanol on reproductive organs and improved seminal qualities of the rats.

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The development of male infertility increased rapidly worldwide, which coinciding with the epidemic of obesity. However, the impact of weight abnormalities on sperm quality is still contestable. To assess the correlation between BMI and sperm parameters, we searched relevant articles in PubMed, Embase, Web of science, and Wanfang database published until June 2015 without language restriction. Otherwise, we also recruited some participants who attended fertility clinic as well as some general populations in this report. We performed a systematic review and meta-analysis about BMI and sperm parameters containing total sperm count, concentration, semen volume and sperm motility (overall and progressive). Metabolomic analysis of seminal plasma was performed to explore the mechanism from a new perspective. This study found standardized weighted mean differences (SMD) in sperm parameters (total sperm count, sperm concentration, and semen volume) of abnormal weight groups decreased to different degree compared to normal weight. Dose-response analysis found SMD of sperm count, sperm concentration and semen volume respectively fell 2.4%, 1.3% and 2.0% compared with normal weight for every 5-unit increase in BMI. Metabolomic analysis of seminal plasma showed that spermidine and spermine were likely to play a vital role in the spermatogenesis progress. This systematic review with meta-analysis has confirmed there was a relationship between BMI and sperm quality, suggesting obesity may be a detrimental factor of male infertility.
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Molecular modeling and dynamics simulation analysis of KATNAL1 for identification of novel inhibitor of sperm maturation.
Sarma K; Roychoudhury S; Bora SS; Dehury B; Parida P; Das S; Das R; Dohutia C; Nath S; Deb B; Modi MK.
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Combinatorial Chemistry & High Throughput Screening. , 2017 Jan 16.
[Journal Article]
UI: 28093975
Rapid growth of world population is one of the biggest challenges faced by the human race. Hormone based birth control often causes various side effects, as such development of non-hormonal based contraceptives is the need of the hour. A recent study revealed that temporary infertility without changing hormone levels can be attained by inhibiting Katanin p60 ATPase-containing subunit A-like 1 protein (KATNAL1) which is critical in sperm maturation in the testes. This study revealed that, KATNAL1 is a soluble protein retained in the cytoplasm having molecular weight of 55,392 Dalton. In the secondary structure of KATNAL1, percentage of random coils was found to be maximum followed by helices and strands. The protein is highly thermostable, mild acidic and hydrophilic in nature. Further molecular docking study confirmed its ATP binding with various hydrophobic and hydrogen bond interactions. Binding efficiency of various phytochemicals that have previously been reported as spermicidal were tested using molecular docking against KATNAL1. Calotropin, a cardenolide of Calotropis procera showed the highest binding efficiency against the target protein without toxicity. Molecular dynamics simulation (MD) of the docked complex validated the results of the docking study. In conclusion, our results revealed the ATP binding mode of KATNAL1 and identified calotropin as a potential lead molecule against it showing high binding efficiency with good bioavailability and no mutagenicity. Further in vitro and in vivo bioassay of calotropin could facilitate the development of novel non-hormonal male-specific contraceptive in near future.
Status
Publisher
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Grandmaternal smoke exposure reduces female fertility in a murine model, with great-grandmaternal smoke exposure unlikely to have an effect.

Camlin NJ; Jarnicki AG; Vanders RL; Walters KA; Hansbro PM; McLaughlin EA; Holt JE.
STUDY QUESTION: What effect does multigenerational (F2) and transgenerational (F3) cigarette smoke exposure have on female fertility in mice?

SUMMARY ANSWER: Cigarette smoking has a multigenerational effect on female fertility.

WHAT IS KNOWN ALREADY: It has been well established that cigarette smoking decreases female fertility. Furthermore, a growing body of evidence suggests that smoking during pregnancy decreases the fertility of daughters and increases cancer and asthma incidence in grandchildren and great-grandchildren.

STUDY DESIGN, SIZE, DURATION: Six-week-old C57BL/6 female mice were exposed nasally to cigarette smoke or room air (controls) for 5 weeks prior to being housed with males. Females continued to be exposed to smoke throughout pregnancy and lactation until pups were weaned. A subset of F1 female pups born to these smoke and non-smoke exposed females were bred to create the F2 grandmaternal exposed generation (multigenerational). Finally, a subset of F2 females were bred to create the F3 great-grandmaternal exposed generation (transgenerational). The reproductive health of F2 and F3 females was examined at 8 weeks and 9 months.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Ovarian and oocyte quality was examined in smoke exposed and control animals. A small-scale fertility trial was performed before ovarian changes were examined using ovarian histology and immunofluorescence and/or immunoblotting analysis of markers of apoptosis (TUNEL) and proliferation (proliferating cell nuclear antigen (PCNA) and anti-Mullerian hormone (AMH)). Oocyte quality was examined using immunocytochemistry to analyze the metaphase II spindle and ploidy status. Parthenogenetic activation of oocytes was used to investigate meiosis II timing and preimplantation embryo development. Finally, diestrus hormone serum levels (FSH and LH) were quantified.

MAIN RESULTS AND THE ROLE OF CHANCE: F2 smoke exposed females had no detectable change in ovarian follicle quality at 8 weeks, although by 9 months ovarian somatic cell proliferation was reduced (P = 0.0197) compared with non-smoke exposed control. Further investigation revealed changes between control and smoke exposed F2 oocyte quality, including altered meiosis II timing at 8 weeks (P = 0.0337) and decreased spindle pole to pole length at 9 months (P = 0.0109). However, no change in preimplantation embryo development was observed following parthenogenetic activation. The most noticeable effect of cigarette smoke exposure was related to the subfertility of F2 females; F2 smoke exposed females displayed significantly increased time to conception (P = 0.0042) and significantly increased lag time between pregnancies (P = 0.0274) compared with non-smoke exposed F2 females. Conversely, F3 smoke
exposed females displayed negligible oocyte and follicle changes up to 9 months of age, and normal preimplantation embryo development.

LARGE SCALE DATA: None.

LIMITATIONS, REASONS FOR CAUTION: This study focused solely on a mouse model of cigarette smoke exposure to simulate human exposure.

WIDER IMPLICATIONS OF THE FINDINGS: Our results demonstrate that grandmaternal cigarette smoke exposure reduces female fertility in mice, highlighting the clinical need to promote cessation of cigarette smoking in pregnant women.

STUDY FUNDING/COMPETING INTEREST(S): This study was funded by the Australian Research Council, National Health and Medical Research Council, Hunter Medical Research Institute, Newcastle Permanent Building Society Charitable Trust, and the University of Newcastle Priory Research Centers in Chemical Biology, Healthy Lungs and Grow Up Well. The authors declare no conflict of interest.

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Revisiting the human seminiferous epithelium cycle.
Nihi F; Gomes MLM; Carvalho FAR; Reis AB; Martello R; Melo RCN; Almeida FRCL; Chiarini-Garcia H.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article]
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STUDY QUESTION: Can all types of testicular germ cells be accurately identified by microscopy techniques and unambiguously distributed in stages of the human seminiferous epithelium cycle (SEC)?

SUMMARY ANSWER: By using a high-resolution light microscopy (HRLM) method, which enables an improved visualization of germ cell morphological features, we identified all testicular germ cells in the seminiferous epithelium and precisely grouped them in six well-delimited SEC stages, thus providing a reliable reference source for staging in man.

WHAT IS ALREADY KNOWN: Morphological characterization of germ cells in human has been done decades ago with the use of conventional histological methods (formaldehyde-based fixative -Zenker-formal- and paraffin embedding). These early studies proposed a classification of the SEC in six stages. However, the use of stages as baseline for morphofunctional evaluations
of testicular parenchyma has been difficult because of incomplete morphological identification of
germ cells and their random distribution in the human SEC.

STUDY DESIGN, SIZE, DURATION: Testicular tissue from adult and elderly donors with normal
spermatogenesis according to Levin’s, Johnsen’s and Bergmann’s scores were used to evaluate
germ cell morphology and validate their distribution and frequency in stages throughout human
spermatogenesis.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Testicular tissue from patients diagnosed
with congenital bilateral agenesis of vas deferens (n = 3 adults) or prostate cancer (n = 3 elderly)
were fixed in glutaraldehyde and embedded in araldite epoxy resin. Morphological analyses were
performed by both light and transmission electron microscopy.

MAIN RESULTS AND THE ROLE OF CHANCE: HRLM method enabled a reliable morphological
identification of all germ cells (spermatogonia, spermatocytes and spermatids) based on high-
resolution aspects of euchromatin, heterochromatin and nucleolus. Moreover, acrosomal
development of spermatids was clearly revealed. Altogether, our data redefined the limits of each
stage leading to a more reliable determination of the SEC in man.

LIMITATIONS, REASONS FOR CAUTION: Occasionally, germ cells can be absent in some
tubular sections. In this situation, it has to be taken into account the germ cell association
proposed in the present study to classify the stages.

WIDER IMPLICATIONS OF THE FINDINGS: Our findings bring a new focus on the morphology
and development of germ cells during the SEC in human. Application of HRLM may be a valuable
tool for research studies and clinical andrology helping to understand some testicular diseases
and infertility conditions which remain unsolved.

STUDY FUNDING/COMPETING INTEREST: Experiments were partially supported by
Coordenacao de Aperfeicoamento de Pessoal de Nivel Superior (CAPES), Fundacao de Amparo
a Pesquisa de Minas Gerais (FAPEMIG) and Conselho Nacional de Desenvolvimento Cientifico e
Tecnologico (CNPq). The authors declare that there are no conflicts of interest.

TRIAL REGISTRATION NUMBER: Not applicable.

Status
In-Process

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An update systematic review of fetal death, congenital anomalies, and fertility disorders among health care workers. [Review]

Warembourg C; Cordier S; Garlantezec R.

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[Journal Article. Review]

UI: 28514021

BACKGROUND: Health care workers (HCWs) are occupationally exposed to various hazards, some associated with adverse pregnancy outcomes in previous reviews. This systematic review
aims at synthesizing the recent literature on occupational exposures among HCWs related to fetal death, congenital anomalies, and fertility disorders.

METHODS: We searched the Medline database from 2000 to 2015 for articles about all potential occupational exposures of women and men working in this sector.

RESULTS: We retained 32 studies, most of them (n=30) among women HCWs. Studies based on job title reported excess risks of some congenital anomalies (especially nervous and musculoskeletal systems) among HCWs compared to non-HCWs but no evidence about fetal death. Excess risks associated with specific exposures includes reports of some congenital anomalies for women exposed to anesthetic gases. Exposure to some sterilizing agents and, with less evidence, to antineoplastic drugs and to ionizing radiation, is associated with increased risks of miscarriage but not stillbirth. Strenuous work schedules appear to be associated with fertility disorders, but the evidence is limited. Only a few studies have been published since 2000 about non-ionizing radiation, or about fertility disorders related to chemical or physical agents, or about male HCWs.

CONCLUSIONS: Despite the establishment of recommendations to limit exposures of HCWs, some excess risks of adverse pregnancy outcomes are still reported and need to be explained.

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OBJECTIVE: To compare the efficacy and safety of amoxapine and vitamin B12 for treating retrograde ejaculation (RE).

MATERIALS AND METHODS: Between May 2009 and November 2012, this open-label, randomized, crossover study enrolled 26 men suffering with RE at Department of Reproductive Medicine, Omori Hospital. Patients were randomly allocated into two groups (n=13 each). The amoxapine-B12 group received amoxapine (50 mg daily for 4 weeks, orally) followed (after a 1-week washout period) by vitamin B12 (500 mug three-times daily for 4 weeks). The B12-amoxapine group received the opposite regimen. All patients masturbated to ejaculation at least twice during each treatment period. The primary outcome was antegrade ejaculation of semen, as reported by the patient, on more than one occasion during either treatment period (defined as treatment success). Any adverse events were noted. Success rates were compared between treatments using Fisher's exact test.

RESULTS: One patient (B12-amoxapine group) withdrew for personal reasons (breakdown of marital relations); all other patients completed the study. Overall success rate was 88% (22/25). Success rate was higher for amoxapine than for vitamin B12 (80%, 20/25 vs 16%, 4/25; P<0.0001). 18 patients were responsive to amoxapine but not to vitamin B12, 2 patients were responsive to vitamin B12 but not amoxapine, 2 patients were responsive to both drugs, and 3 patients had no response to either drug. One patient (4%) reported sleepiness and 2 (8%) reported constipation while receiving amoxapine. No adverse events were reported during vitamin B12 treatment.

CONCLUSIONS: Amoxapine may be an effective, safe and well-tolerated therapy for RE.
BACKGROUND: Leptospirosis is a zoonotic bacterial disease with a worldwide distribution. In Vietnam, leptospirosis is considered endemic. In pigs, leptospirosis can result in reproductive problems (such as abortion and infertility) which lead to economic loss. In addition, transmission to people presents a public health risk. In Vietnam, few national studies have been conducted on...
The sero-prevalence of leptospirosis in pigs. The main objective of this study was to evaluate the sero-prevalence and incidence of presumptive infective leptospira serovars in fattening pigs from 5 provinces in Vietnam.

RESULTS: Blood samples from fattening pigs were randomly collected at slaughterhouses. We collected 1959 sera samples from 5 provinces (Son La, Hanoi, Nghe An, Dak Lak and An Giang) between January and early June 2016. The microscopic agglutination test (MAT) was used to identify the serogroups/serovars. Overall, the sero-prevalence was 8.17% (95% CI: 6.99-9.47) and serovar Tarassovi Mitis (2.19%) had the highest prevalence followed by Australis (1.94%), Javanica (1.68%) and Autumnalis (1.17%) using a cutoff (> 1:100). The sero-prevalence among female pigs (5.28%, 95% CI: 3.94-6.93) was slightly higher than among male pigs (4.88%, 95% CI: 3.51-6.58), but this difference was not statistically significant.

CONCLUSIONS: Leptospirosis in pigs may be a useful indicator of the human/animal burden in Vietnam and a risk assessment tool. The presence of some of the identified serovars suggests that wildlife may play an important role in the transmission of leptospirosis to domesticated pigs in Vietnam. Therefore, strengthened monitoring and surveillance systems are needed to better understand the epidemiology of the disease and prevent or reduce infection in humans and animals.

Status
In-Process

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Institution
Discrete survival model analysis of a couple’s smoking pattern and outcomes of assisted reproduction.

Vanegas JC; Chavarro JE; Williams PL; Ford JB; Toth TL; Hauser R; Gaskins AJ.

BACKGROUND: Cigarette smoking has been associated with worse infertility treatment outcomes, yet some studies have found null or inconsistent results.

METHODS: We followed 225 couples who underwent 354 fresh non-donor assisted reproductive technology (ART) cycles between 2006 and 2014. Smoking history was self-reported at study entry. We evaluated the associations between smoking patterns and ART success using multivariable discrete time Cox proportional hazards models with six time periods: cycle initiation to egg retrieval, retrieval to fertilization, fertilization to embryo transfer (ET), ET to implantation, implantation to clinical pregnancy, and clinical pregnancy to live birth to estimate hazard ratios (HR) and 95% CIs. Time-dependent interactions between smoking intensity and ART time period were used to identify vulnerable periods.

RESULTS: Overall, 26% of women and 32% of men reported ever smoking. The HR of failing in the ART cycle without attaining live birth for male and female ever smokers was elevated, but non-significant, compared to never smokers regardless of intensity (HR = 1.02 and 1.30, respectively). Female ever smokers were more likely to fail prior to oocyte retrieval (HR: 3.37; 95% CI: 1.00, 12.73). Every one cigarette/day increase in smoking intensity for females was associated with a HR of 1.02 of failing ART (95% CI: 0.97, 1.08), regardless of duration or current smoking status. Women with higher smoking intensities were most likely to fail a cycle prior to oocyte retrieval (HR: 1.07; 95% CI: 1.00, 1.16). Among past smokers, every additional year since
a man had quit smoking reduced the risk of failing ART by 4% (HR: 0.96; 95% CI: 0.91, 1.00) particularly between clinical pregnancy and live birth (HR: 0.86; 95% CI: 0.76, 0.96).

CONCLUSIONS: Female smoking intensity, regardless of current smoking status, is positively associated with the risk of failing ART cycles between initiation and oocyte retrieval. In men who ever smoked, smoking cessation may reduce the probability of failing ART, particularly between clinical pregnancy and live birth.


Status
In-Data-Review

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Institution
56. Multicentre study of Y chromosome microdeletions in 1,808 Chinese infertile males using multiplex and real-time polymerase chain reaction.
Zhu XB; Gong YH; He J; Guo AL; Zhi EL; Yao JE; Zhu BS; Zhang AJ; Li Z.
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Azoospermia factor (AZF) genes on the long arm of the human Y chromosome are involved in spermatogenesis, and microdeletions in the AZF region have been recognised to be the second major genetic cause of spermatogenetic failure resulting in male infertility. While screening for these microdeletions can avoid unnecessary medical and surgical treatments, current methods are generally time-consuming. Therefore, we established a new method to detect and analyse microdeletions in the AZF region quickly, safely and efficiently. In total, 1,808 patients with spermatogenetic failure were recruited from three hospitals in southern China, of which 600 patients were randomly selected for screening for Y chromosome microdeletions in AZF regions employing real-time polymerase chain reaction with a TaqMan probe. In our study, of 1,808 infertile patients, 150 (8.3%) were found to bear microdeletions in the Y chromosome using multiplex PCR, while no deletions were found in the controls. Among the AZF deletions detected, two were in AZFa, three in AZFb, 35 in AZFc, three in AZFb+c and two in AZFa+b+c. Our method is fast-it permits the scanning of DNA from a patient in one and a half hours-and reliable, minimising the risk of cross-contamination and false-positive and false-negative results.
A phytotherapeutic approach to reduce sperm DNA fragmentation in patients with male infertility.
INTRODUCTION: Infertility affects 50 to 80 million (between 8 and 12% of couples). Male factor is a cause of infertility in almost half of the cases, mainly due to oligoasthenoteratozoospermia. DNA fragmentation is now considered an important factor in the aetiology of male infertility. We studied the effects on semen analysis and on DNA fragmentation of in vivo administration of Myo-inositol and Tribulus Terrestris plus Alga Ecklonia plus Biovis (Tradafertil; Tradapharma Sagl, Switzerland) in men with previously diagnosed male infertility.

MATERIALS AND METHODS: Sixty patients were enrolled in the present study and were randomized into two subgroups: the group A who received Myo-inositol 1000 mg, Tribulus Terrestris 300 mg, Alga Ecklonia Bicyclis 200 mg and Biovis one tablet a day for 90 days, and the group B (placebo group) who received one placebo tablet a day for 90 days. The primary efficacy outcome was the improvement of semen characteristics after 3 months’ therapy and the secondary outcome was the reduction of the DNA fragmentation after treatment.

RESULTS: The groups were homogenous for age, hormonal levels, sperm concentration and all parameters of sperm analysis. Sperm concentration and progressive motility improved after treatment with Tradafertil (3.82 Mil/ml vs. 1.71 Mil/ml; p<0.05; 4.86% vs. 1.00%; p<0.05) as well as the DNA fragmentation (1.64% vs 0.39%, p<0.001). No side effects were revealed.

CONCLUSIONS: In conclusion, we can affirm that Tradafertil is safe and tolerable. It is a new phytotherapeutic approach to Oligoasthenoteratospermia (OAT) syndrome that could lead to good results without interacting with hypothalamic-pituitary-gonadal axis.
STUDY QUESTION: What are the relations among birthweight (BW), semen parameters and birth outcomes in a population-based sample?

SUMMARY ANSWER: BW is unrelated to semen parameters, which are in turn unrelated to birth outcomes.

WHAT IS KNOWN ALREADY: In clinical settings, there has been suggestion that semen parameters are related to BW when comparing fertile and infertile men; however, findings have been less clear in more general populations.

STUDY DESIGN, SIZE, DURATION: Questionnaire data and semen samples were collected at baseline from 427 male participants of the population-based Longitudinal Investigation of Fertility and the Environment (LIFE) prospective cohort study from 2005 to 2009, who were followed prospectively to assess pregnancy outcomes among 226 singleton births.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Men of at least 18 years of age who were married or in a committed relationship and trying to conceive were eligible for participation; physician-diagnosed infertility was an exclusion criterion. Participants were recruited from two geographic areas and semen samples were analyzed for 34 quality parameters categorized as general, motility, morphology, sperm head and sperm chromatin structure using methods
including computer-aided semen analysis integrated visual optical system and sperm chromatin structure assay. Linear and mixed models were used for statistical analysis of the relations between men’s BW, semen parameters, and BW, gestational age at delivery, birth length, head circumference and ponderal index of singleton births.

MAIN RESULTS AND THE ROLE OF CHANCE: No association was observed between male BW and semen parameters or birth outcomes. Few associations were observed between semen parameters and birth outcomes, and the observed statistically significant associations were isolated and without a consistent pattern that would suggest an association between BW and birth outcomes.

LIMITATIONS, REASONS FOR CAUTION: Men’s BW was self-reported and may be subject to some imprecision. Semen analysis was performed the day after collection, an approach that impacts the assessment of motility and that may limit inference from our analyses of motility measures. In addition, inclusion criteria for selection into the cohort limits generalizability to generally healthy couples trying to conceive and without known subfertility.

WIDER IMPLICATIONS OF THE FINDINGS: Despite suggestions from prior studies of male in utero exposures impacting BW and male reproductive health, there appears to be little support for such relations in this generally healthy population.

STUDY FUNDING/COMPETING INTEREST(S): Supported by the Intramural Research Program of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (N01-HD-3-3355, N01-HD-3-3356 and NOH-HD-3-3358). The authors report no competing interests, and a Memo of Understanding with the National Institute of Occupational Safety and Health (NIOSH) for semen analysis.

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BACKGROUND AND OBJECTIVES: This study aimed to investigate the effects of tomato juice consumption on seminal plasma lycopene levels and sperm parameters in infertile men.

METHODS AND STUDY DESIGN: Subjects were male infertility patients with poor sperm concentration (<20×10⁶/mL) and/or motility (<50%). Following a fourweek observation period, subjects were randomly assigned among three groups: a tomato juice group, an antioxidant group, and a control group. The subjects in the tomato juice group and the antioxidant group daily consumed one can of tomato juice (containing 30 mg of lycopene) or one antioxidant capsule (containing vitamin C 600 mg, vitamin E 200 mg, and glutathione 300 mg), respectively, for 12 weeks (feeding period). Seminal plasma lycopene levels and sperm parameters were measured every 6 weeks during the feeding period.

RESULTS: Forty-four patients completed the study (control group: 12, antioxidant group: 15, tomato juice group: 17). In the tomato juice group, plasma lycopene level was significantly increased at the 12th week of the feeding period. Moreover, a decrease in seminal plasma white
blood cells and an increase in sperm motility in the tomato juice group were statistically significant at the 12th and 6th weeks, respectively, compared to the control group. In the antioxidant capsule group, no significant improvement was observed in semen parameters.

CONCLUSIONS: In conclusion, regular consumption of tomato juice seems to improve sperm motility in infertile patients. This is the first report to show that commercially available food, such as tomato juice, might be beneficial for male infertility.

Status
In-Process
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Predicting the likelihood of live birth for elective oocyte cryopreservation: a counseling tool for physicians and patients.

Goldman RH; Racowsky C; Farland LV; Munne S; Ribustello L; Fox JH.
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STUDY QUESTION: Can a counseling tool be developed for women desiring elective oocyte cryopreservation to predict the likelihood of live birth based on age and number of oocytes frozen?

SUMMARY ANSWER: Using data from ICSI cycles of a population of women with uncompromised ovarian reserve, an evidence-based counseling tool was created to guide women and their physicians regarding the number of oocytes needed to freeze for future family-building goals.

WHAT IS KNOWN ALREADY: Elective oocyte cryopreservation is increasing in popularity as more women delay family building. By undertaking elective oocyte freezing at a younger age, women hope to optimize their likelihood of successful live birth(s) using their thawed oocytes at a future date. Questions often arise in clinical practice regarding the number of cryopreserved oocytes sufficient to achieve live birth(s) and whether or not additional stimulation cycles are likely to result in a meaningful increase in the likelihood of live birth. As relatively few women who have electively cryopreserved oocytes have returned to use them, available data for counseling patients wishing to undergo fertility preservation are limited.

STUDY DESIGN, SIZE, DURATION: A model was developed to determine the proportion of mature oocytes that fertilize and then form blastocysts as a function of age, using women with presumably normal ovarian reserve based on standard testing who underwent ICSI cycles in our program from January, 2011 through March, 2015 (n = 520). These included couples diagnosed exclusively with male-factor and/or tubal-factor infertility, as well as cycles utilizing egg donation. Age-specific probabilities of euploidy were estimated from 14 500 PGS embryo results from an external testing laboratory. Assuming survival of thawed oocytes at 95% for women <36 y and for
egg donors, and 85% for women >36 y, and 60% live birth rate per transferred euploid blastocyst, probabilities of having at least one, two or three live birth(s) were calculated.

PARTICIPANTS/MATERIALS, SETTING, METHOD: First fresh male-factor and/or tubal-factor only autologous ICSI cycles (n = 466) were analyzed using Poisson regression to calculate the probability that a mature oocyte will become a blastocyst based on age. Egg donation cycles (n = 54) were analyzed and incorporated into the model separately. The proportion of blastocysts expected to be euploid was determined using PGS results of embryos analyzed via array comparative genomic hybridization. A counseling tool was developed to predict the likelihood of live birth, based on individual patient age and number of mature oocytes.

MAIN RESULTS AND THE ROLE OF CHANCE: This study provides an evidence-based model to predict the probability of a woman having at least one, two or three live birth(s) based on her age at egg retrieval and the number of mature oocytes frozen. The model is derived from a surrogate population of ICSI patients with uncompromised ovarian reserve. A user-friendly counseling tool was designed using the model to help guide physicians and patients.

LIMITATIONS, REASONS FOR CAUTION: The data used to develop the prediction model are, of necessity, retrospective and not based on patients who have returned to use their cryopreserved oocytes. The assumptions used to create the model, albeit reasonable and data-driven, vary by study and will likely vary by center. Centers are therefore encouraged to consider their own blastocyst formation and thaw survival rates when counseling patients.

WIDER IMPLICATIONS OF THE FINDINGS: Our model will provide a counseling resource that may help inform women desiring elective fertility preservation regarding their likelihood of live birth(s), how many cycles to undergo, and when additional cycles would bring diminishing returns.

STUDY FUNDING/COMPETING INTERESTS: None.

TRIAL REGISTRATION NUMBER: Not applicable.

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Farland, L V. Center for Infertility and Reproductive Surgery, Department of Obstetrics, Gynecology and Reproductive Biology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115, USA.
INTRODUCTION: The aim of this systematic review is to establish the clinical impact of open (mesh and/or without mesh) and laparoscopic hernia repair (transabdominal pre-peritoneal (TAP) and/or totally extra-peritoneal (TEP)) on male fertility. The incidence of male infertility following various types of inguinal hernia repair is currently unknown. The lack of high-quality evidence has led to various speculations, suggestions and reliance on anecdotal experience in the clinical practice.

METHODS: An electronic search of the literature in Medline, Scopus, Embase and Cochrane library from 1966 to October 2015 according to PRISMA checklist was conducted. Quality assessment of articles was conducted using the Oxford Critical Appraisal Skills Programme (CASP) and their recommendation for practice was examined through National Institute for Health and Care Excellence (NICE). This resulted in ten studies (n = 10), comprising 35,740 patients.

RESULTS: Sperm motility could be affected following any type and/or technique of inguinal hernia repair but this is limited to the immediate postoperative period (<48 h). Obstructive azoospermia was noted in 0.03% of open and 2.5% of bilateral laparoscopic (TAP) hernia repair
with mesh. Male infertility was detected in 0.8% of the open hernia repair (mesh) with no correlation to the type of mesh (lightweight vs. heavyweight).

CONCLUSION: Inguinal hernia repair without mesh has no impact on male fertility and obstructive azoospermia. However, the use of mesh in bilateral open and/or laparoscopic repair may require the inclusion of male infertility as the part of informed consent in individuals that have not completed their family or currently under investigations.

Status
In-Process

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62.
Association between MTHFR A1298C polymorphism and male infertility: A meta-analysis.
Zhang Q; Yin GY; Liu J; Liang Y; Li YY; Zhao JY; Zhang LW; Wang BQ; Tang NJ.
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There have been several epidemiological studies evaluating the potential association between the methylenetetrahydrofolate reductase (MTHFR) A1298C polymorphism and the risk of male
infertility. However, the results obtained were inconsistent. Therefore, we performed a meta-
analysis to further examine the association between the MTHFR A1298C polymorphism and male
infertility. A comprehensive search was conducted to identify all eligible studies from the online
literature databases published prior to January 15th, 2016. A total of 20 studies with 4293 cases
and 4507 controls were included. An odds ratio (OR) and a 95% confidence interval (95% CI)
were calculated to assess the strength of the association. A cumulative meta-analysis, sensitivity
analysis and assessment of the publication bias were also performed in this study. The results
showed that in the overall analysis, the association between the MTHFR A1298C polymorphism
and male infertility was not significant. A stratified analysis by ethnicity revealed a significant
increase in the risk of male infertility in the Asian population with the MTHFR A1298C
polymorphism (especially in the heterozygote model: OR=1.20, 95% CI=1.01-1.44, P=0.994; the
dominant model: OR=1.23, 95% CI=1.04-1.45, P=0.996; and the allele model: OR=1.20, 95%
CI=1.04-1.39, P=0.985) but not in the Caucasian population. In the stratified analyses, no
significant association was observed between the different types of male infertility. This meta-
analysis suggests the MTHFR A1298C polymorphism may be a potential risk factor for male
infertility, especially in the Asian population.

Status
In-Process

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63.
The Relationship between the Amount of Saturated Fat Intake and Semen Quality in Men.
Dadkhah H; Kazemi A; Nasr-Isfahani MH; Ehsanpour S.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article]
UI: 28382058
INTRODUCTION: Infertility in men is one of the current problems of human society. Some studies suggest that the metabolic status of a man, including cholesterol intake, closely correlates with sperm function. The aim of this study was to evaluate the correlation between saturated fat intake and semen quality among men referring to the Isfahan Fertility and Infertility Center, Iran.
MATERIALS AND METHODS: This cross-sectional study was conducted on all men who referred to the Isfahan Fertility and Infertility Center. The study population consisted of 120 men selected through simple random sampling. The data collection tool consisted of a two-part questionnaire including a demographic and anthropometric characteristics form and the Food Frequency Questionnaire (FFQ). The FFQ consists of 168 items that assess food and nutrient intake for 3 months. The reliability and validity of the instruments were confirmed in previous studies. Semen analysis was performed using computer-aided semen analysis (CASA) method. Descriptive statistics and logistic regression test were used to analyze the data.
RESULTS: Results showed that the chances of having semen volume of higher than 1.5 ml (normal volume) increased by 27.5% for every 1 g increase in total fat (CI: 1.11-1.46) (P = 0.001) and reduced 38% for every 1 g increase in saturated fat (CI: 0.42-0.90, P = 0.010). No association was found between semen quality and intake of dietary fats.
CONCLUSIONS: Based on the findings of this study and the prevalence of infertility in recent decades, changes in diet and saturated fatty acids intake may improve semen quality.

Status
In-Data-Review

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Date Created
20170406

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2017

64.
Prevalence and risk factors of chlamydia infection in Hong Kong: A population-based geospatial household survey and testing.
Wong WC; Zhao Y; Wong NS; Parish WL; Miu HY; Yang LG; Emch M; Ho KM; Fong FY; Tucker JD.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

BACKGROUND: Chlamydia causes infertility and increases risk of HIV infection, and population-based studies provide essential information for effective infection control and prevention. This study examined Chlamydia trachomatis prevalence and risk factors among a representative sample of 18-49-year-old residents in Hong Kong.
METHODS: Census boundary map of 412 constituency areas was used as primary sampling units to construct the sampling frame and, residential buildings and units were randomly selected using geospatial modelling. A questionnaire on sexual practice and health was conducted, and polymerase chain reaction was used to test the urine for genital chlamydial infection. Invitation letters were sent to the selected households and a team of interviewers were sent to recruit one subject per household. Prevalence data was weighted according to the 2011 census and risk factors identified through logistic regression.

RESULTS: Among 881 participants (response rate of 24.5%), the overall Chlamydia trachomatis prevalence was low at 1.4% (95%CI 0.8-2.5%) but sexually active young (18-26 years) women had relatively high prevalence (5.8%, 95%CI 1.7-18.2%) in Hong Kong. A unique U-shape disease burden was observed with peaks in younger and older (40-49 years) women. Amongst the sexually active women, the risk factors of Chlamydia trachomatis infection were: younger age (aOR = 25.4, 95% CI 2.81-230); living alone (aOR = 8.99, 95% CI 1.46-55.40); and, among all the sexually active participants, males (including the male partners of the female participants) who had travelled out of Hong Kong in the previous 12 months had higher risks of infection (aOR = 5.35; 95% CI 1.25-22.8). A core-peripheral geographical distribution of Chlamydia trachomatis prevalence was also observed.

CONCLUSION: Young and older sexually active women in Hong Kong have high prevalence of chlamydia. Routine screening for sexually active women and young men should be considered. Further research on testing feasibility and linkage-to-care are urgently needed to control the infection.

Status
In-Data-Review

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Wong, Ngai Sze. Institute for Global Health & Infectious Diseases, University of North Carolina at Chapel Hill, Chapel Hill, United States of America.
Various studies (direct and indirect) have presented the effect of captopril, a universally used antihypertensive medication, on semen quality; yet, this effect is still collectively unreviewed. This review systematically discusses and summarises the effect of captopril on semen quality. We searched all published articles in the MEDLINE electronic database since June 1985 until January 2016 using the keywords "captopril" and "sperm," and certain supporting articles were reviewed and considered, if relevant. In conclusion, up to the present time, captopril does not
appear to induce a striking change in semen quality, and hence on male infertility, while it may affect the rate of spermatozoa-egg fusion as it inhibits the activity of angiotensin-converting enzyme that is released during capacitation and the acrosome reaction. Further research, mainly clinical, is still desired to prove these effects.

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66. Testosterone replacement therapy improves health-related quality of life for patients with late-onset hypogonadism: a meta-analysis of randomized controlled trials.
Nian Y; Ding M; Hu S; He H; Cheng S; Yi L; Li Y; Wang Y.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Andrologia. 49(4), 2017 May.
[Journal Article]
UI: 27389320

Although testosterone replacement therapy can restore serum testosterone concentrations to normal level in late-onset hypogonadism patients, whether it can improve patients' quality of life remains uncertain. Therefore, we perform a meta-analysis of randomized controlled trials on this issue. Five randomized controlled trials total 1,212 patients were included. Fixed-effect model was used to calculate the weighted mean difference of score of Aging Males' Symptom rating scale. Our result reveals that testosterone replacement therapy improves patients' health-related quality of life in terms of the decrease in the AMS total score [WMD = -2.96 (-4.21, -1.71), p <
.00001] and the psychological [WMD = -0.89 (-1.41, -0.37), p = .0008], somatic [WMD = -0.89 (-1.41, -0.37), p = .0008] and sexual [WMD = -1.29 (-1.75, -0.83), p < .00001] subscale score.

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Status
In-Process

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20160708

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67.
eNOS gene T786C, G894T and 4a4b polymorphisms and male infertility susceptibility: a meta-analysis.
Chang J; Pan F; Tang Q; Wu W; Chen M; Lu C; Ding H; Hu L; Chen D; Xia Y; Wang X.
The association between polymorphism of eNOS and male infertility in several studies was controversial. To explore a more precise estimation of the association, a meta-analysis of eight case-control studies, including 1,968 cases and 1,539 controls, were selected. The meta-analysis was conducted by calculating the pooled odds ratio (OR) with a 95% confidence interval (95% CI). Overall, the association between T786C and risk of male infertility was obvious (TC vs. TT: OR, 1.20; 95% CI, 1.01-1.42; CC vs. TT: OR, 3.37; 95% CI, 1.65-6.87; TC/CC vs. TT: OR, 1.47; 95% CI, 1.25-1.73; CC vs. TT/TC: OR, 3.18; 95% CI, 1.54-6.56; TC vs. TT: OR, 1.65; 95% CI, 1.27-2.03). However, no overall association was observed between the other two polymorphisms of eNOS (G894T and 4a4b) and male infertility. Stratified analysis showed that significantly strong association between T786C polymorphism and semen quality was present in all three types of male infertility (azoospermia, oligozoospermia and asthenozoospermia). In the subgroup analysis based on ethnicity, both T786C and 4a4b could influence the risk of male infertility in Asian and Caucasian. Further studies of polymorphisms of eNOS with their biological functions are needed to understand the role in the development of male infertility.

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Expanding the genetic spectrum of ANOS1 mutations in patients with congenital hypogonadotropic hypogonadism.

Goncalves CI; Fonseca F; Borges T; Cunha F; Lemos MC.
STUDY QUESTION: What is the prevalence and functional consequence of ANOS1 (KAL1) mutations in a group of men with congenital hypogonadotropic hypogonadism (CHH)?
SUMMARY ANSWER: Three of forty-two (7.1%) patients presented ANOS1 mutations, including a novel splice site mutation leading to exon skipping and a novel contiguous gene deletion associated with ichthyosis.

WHAT IS KNOWN ALREADY: CHH is characterized by lack of pubertal development and infertility, due to deficient production, secretion or action of GnRH, and can be associated with anosmia/hyposmia (Kallmann syndrome, KS) or with a normal sense of smell (normosmic CHH). Mutations in the anosmin-1 (ANOS1) gene are responsible for the X-linked recessive form of KS.

STUDY DESIGN, SIZE, DURATION: This cross-sectional study included 42 unrelated men with CHH (20 with KS and 22 with normosmic CHH).
PARTICIPANTS/MATERIALS, SETTING, METHODS: Patients were screened for mutations in the ANOS1 gene by DNA sequencing. Identified mutations were further investigated by RT-PCR analysis and multiplex ligation-dependent probe amplification (MLPA) analysis.
MAIN RESULTS AND THE ROLE OF CHANCE: Hemizygous mutations were identified in three (7.1%) KS cases: a novel splice acceptor site mutation (c.542-1G>C), leading to skipping of exon 5 in the ANOS1 transcript in a patient with self-reported normosmia (but hyposmic upon testing); a recurrent nonsense mutation (c.571C>T, p.Arg191*); and a novel 4.8 Mb deletion involving ANOS1 and eight other genes (VCX3B, VCX2, PNPLA4, VCX, STS, HDHD1, VCX3A and NLGN4X) in KS associated with ichthyosis.
LIMITATIONS, REASONS FOR CAUTION: Objective olfactory testing was not performed in all cases of self-reported normosmia and this may have underestimated the olfactory deficits.
WIDER IMPLICATIONS OF THE FINDINGS: This study further expands the spectrum of known genetic defects associated with CHH and suggests that patients with self-reported normal olfactory function should not be excluded from ANOS1 genetic testing.
STUDY FUNDING/COMPETING INTEREST(S): This study was funded by the Portuguese Foundation for Science and Technology. The authors have no conflicts of interest.
TRIAL REGISTRATION NUMBER: N/A.

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Goncalves, C I; Fonseca, F; Borges, T; Cunha, F; Lemos, M C.
OBJECTIVE: To assess the association between coenzyme Q10 (CoQ10) intake from food sources and semen quality. We assessed this association in a prospective cohort of men attending a fertility clinic. CoQ10 supplementation has been associated with improvements in semen parameters. However, the impact of CoQ10 intake from food sources on semen quality has not been investigated.

MATERIALS AND METHODS: Subfertile couples seeking fertility evaluation at the Massachusetts General Hospital Fertility Center were invited to participate in an ongoing study of environmental factors and fertility. In total, 211 male participants completed a validated food frequency questionnaire and provided 476 semen samples. Multivariable linear mixed models were used to examine the relation between CoQ10 intake from food and semen parameters while adjusting for potential confounders and accounting for within-person correlations.
RESULTS: Mean dietary CoQ10 intake was 19.2mg/day (2.4-247.2mg/day). No subjects were taking CoQ10 supplements. There were no associations between dietary CoQ10 intake from food and conventional semen parameters. The adjusted mean difference (95% confidence interval) comparing men in the top and bottom quartiles of CoQ10 intake from food were -3.1 mil/mL (95% confidence interval -29.5, 38.8 mil/mL) for sperm concentration, -4.5% (-15.1%, 6.0%) for total motility, -1.3% for progressive motility (-8.4%, 5.7%), and 0.3% (-1.4%, 2.0%) for sperm morphology.

CONCLUSION: CoQ10 intake from food was not related to semen parameters among subfertile men. Mean dietary intake of CoQ10 in this study was 10-fold lower than the supplemental dose used in clinical trials showing improved sperm motility. CoQ10 intake from food alone may be insufficient to optimize semen parameters.

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Status
In-Data-Review

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20161126

Year of Publication
2017
An updated systematic review on the possible effect of nonylphenol on male fertility.
Noorimotlagh Z; Haghighi NJ; Ahmadimoghadam M; Rahim F.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article]
UI: 27826822

Diverse industries like detergents, resins and polymers, hair dyes, intravaginal spermicides, and pesticides produce endocrine disruptor (ED)-containing wastewaters that have hazardous effects on the environment and public health. Nonylphenol (NP) is a chemical substance that consists of a phenolic group and an attached lipophilic linear nonyl chain. NP has weak estrogenic activity and affects estrogen receptor (ER), as well as induces male infertility via a negative impact on spermatogenesis and sperm quality. The aim of this study was to comprehensively review all available literature about the side effects of NP on the male genital system. We systematically searched Scopus and PubMed using MeSH terms that include "Organic Chemicals," "Infertility," "Infertility, Male," "Nonylphenol", ("Infertility, Male"[Mesh]) OR "Nonylphenol" [Supplementary Concept]) OR "Prostate"[Mesh]) OR "Spermatozoa"[Mesh]) OR "Sertoli Cells"[Mesh]) OR "Leydig Cells"[Mesh] OR "Male accessory gland" OR "Epididym" OR "Reproductive toxicity"), and all other possible combinations from January 1, 1970, to September 15, 2016, with language limit. The initial search identified 117,742 potentially eligible studies, of which 33 met the established inclusion criteria and were included in the analysis. Thirty-three selected studies include animal model (n = 18), cell line (n = 15), human model (n = 1), morphology (n = 13), sperm quality (n = 17), and toxicity (n = 14). This review highlighted the evidence for the ED effect of NP that acts through interference with ER, discussing male reproductive tract perturbations. We critically discuss the available evidence on the effect of NP on sperm quality (such as motility, viability, sperm count, and sperm concentration), dramatic morphological changes (such as change of weights of testes and epididymis), and biochemical changes related to oxidative stress in testes. Finally, it is important to take caution with the continued use of NP that disrupts male reproductive health.

Status
In-Process

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An open-label clinical trial to investigate the efficacy and safety of corifollitropin alfa combined with hCG in adult men with hypogonadotropic hypogonadism.

Nieschlag E; Bouloux PG; Stegmann BJ; Shankar RR; Guan Y; Tzontcheva A; McCrery Sisk C; Behre HM.

BACKGROUND: Hypogonadotropic hypogonadism (HH) in men results in insufficient testicular function and deficiencies in testosterone and spermatogenesis. Combinations of human chorionic gonadotropin (hCG) and recombinant follicle-stimulating hormone (recFSH) have been successful
in the treatment of HH. Corifollitropin alfa is a long-acting FSH-analog with demonstrated action in women seeking infertility care. The aim of this study was to investigate the efficacy and safety of corifollitropin alfa combined with hCG to increase testicular volume and induce spermatogenesis in men with HH.

METHODS: This was a Phase III, multi-center, open-label, single-arm trial of corifollitropin alfa in azoospermic men aged 18 to 50 years with HH. After 16 weeks of pretreatment of 23 subjects with hCG alone, 18 subjects with normalized testosterone (T) levels who remained azoospermic entered the 52-week combined treatment phase with hCG twice-weekly and 150 mug corifollitropin alfa every other week. The increase in testicular volume (primary efficacy endpoint) and induction of spermatogenesis resulting in a sperm count >1x10^6/mL (key secondary efficacy endpoint) during 52 weeks of combined treatment were assessed. Safety was evaluated by the presence of anti-corifollitropin alfa antibodies and the occurrence of adverse events (AEs).

RESULTS: Mean (+/-SD) testicular volume increased from 8.6 (+/-6.09) mL to 17.8 (+/-8.93) mL (geometric mean fold increase, 2.30 [95% CI: 2.03, 2.62]); 14 (77.8%) subjects reached a sperm count >1x10^6/mL. No subject developed confirmed anti-corifollitropin alfa antibodies during the trial. Treatment was generally well tolerated.

CONCLUSIONS: Corifollitropin alfa 150 mug administrated every other week combined with twice-weekly hCG for 52 weeks increased testicular volume significantly, and induced spermatogenesis in >75% of men with HH who had remained azoospermic after hCG treatment alone.

TRIAL REGISTRATION: ClinicalTrials.gov: NCT01709331 .

Status
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72.
Systematic Review of Premenstrual, Postmenstrual and Infertility Disorders of Vitex Agnus Castus. [Review]
Rafieian-Kopaei M; Movahedi M.
[Journal Article. Review]
UI: 28243425
INTRODUCTION: Vitex agnus-castus, also called vitex is aboriginal to the Mediterranean region, with long leaves, tender stem, flowers and ripening seeds. The aim of this study was to overview premenstrual, postmenstrual and infertility disorder of Vitex agnus-castus.
METHODS: This review article was carried out by searching studies in PubMed, Medline, Web of Science, and IranMedex databases. The initial search strategy identified about 87 references. In this study, 43 studies were accepted for further screening, and met all our inclusion criteria (in English, full text, therapeutic effects of Vitex agnus-castus and dated mainly from the year 2009 to 2016). The search terms were Vitex agnus-castus, premenstrual, postmenstrual, infertility disorder properties and pharmacological effects.
RESULT: Vitex agnus-castus was shown to contribute to the treatment of premenstrual syndrome (PMS). Moreover, the result of the present study showed that this valuable plant is helpful in alleviation of pain resulting from postmenstrual disease. Furthermore, it was found that Vitex agnus-castus is beneficial in infertility disorder.
CONCLUSION: Vitex agnus-castus (AC) is a phytopharmaceutical compound and is shown to be widely used to treat PMS and PMDD. In addition, it was shown to be beneficial in post-menstrual
cases and it can also contribute to treatment of infertility cases in both men and women. Dopaminergic compounds available in this plant help to treat premenstrual mastodynia as well as other symptoms of the premenstrual syndrome.

Status
In-Data-Review

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20170228

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73.
Ren Z; Ren P; Yang B; Fang K; Ren S; Liao J; Liu S; Liu L; Peng Z; Dong Q.
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[Journal Article]
UI: 28081209

BACKGROUND: Methylene-tetrahydrofolate reductase gene (MTHFR C677T and A1298C) and methionine synthase gene (MS A2756G) polymorphisms have shown an association with male infertility risk in several ethnic populations. Although several studies have evaluated these associations in Chinese populations, their small sample sizes and inconsistent outcomes have prevented strong conclusions. Therefore, the present meta-analysis was performed with published studies to evaluate the associations of the three single nucleotide polymorphisms (SNPs) and male infertility in a Chinese population.
METHODS: We conducted a search of PubMed, Embase, Web of Science, Chinese National Knowledge Infrastructure (CNKI), China biology medical literature (CBM), VIP, and Chinese literature (Wan Fang) databases up to May 31, 2016. Odds ratios (ORs) and 95% confidence intervals (95%CIs) were used to assess the strength of associations with a random-effect model or a fixed-effect model based on the heterogeneity analysis results. Sensitivity analysis was used to confirm the reliability and stability of the meta-analysis.

RESULTS: A total of nine studies, including 1,713 cases and 1,104 controls, were included in the meta-analysis. The pooled results indicated that the MTHFR C667T polymorphism was significantly associated with increased risk of male infertility in the Chinese population in the allele model (T vs. C: OR = 1.47, 95%CI = 1.32-1.63), the dominant model (TT + CT vs. CC: OR = 1.51, 95%CI = 1.30-1.77), the additive model (TT vs. CC: OR = 2.08, 95%CI = 1.68-2.58) and the recessive model (TT vs. CT+CC: OR = 1.58, 95%CI = 1.31-1.90), whereas the MTHFR A1298C and MS A2756G polymorphisms were not risk factors. There was no significant heterogeneity in any genotype contrasts among the studies. The sensitivity analysis indicated that the results of this meta-analysis were relatively stable.

CONCLUSION: This study suggests that the MTHFR C667T polymorphism may contribute to the genetic susceptibility to male infertility in the Chinese population, whereas MTHFR A1298C and MS A2756G polymorphisms may be unrelated to male infertility. Studies with larger sample sizes and representative population-based cases and well-matched controls are needed to validate our results.

Status

In-Data-Review

Authors Full Name

Ren, Zhengju; Ren, Pengwei; Yang, Bo; Fang, Kun; Ren, Shangqing; Liao, Jian; Liu, Shengzhao; Liu, Liangren; Peng, Zhufeng; Dong, Qiang.

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Diagnosis of Partial Retrograde Ejaculation in Non-Azoospermic Infertile Men with Low Semen Volume.


In non-azoospermic patients with low semen volume (LSV), looking for partial retrograde ejaculation (PRE) by searching sperm in the postejaculatory urine (PEU) is required. The use of a retro-ejaculatory index (R-ratio) was suggested to define PRE, but none of the studies indicated a specific threshold above which PRE must be considered. Our objective was to propose a threshold value for the R-ratio as indicative of PRE in patients with LSV selected to be devoid of any known causes or risk factors for retrograde ejaculation or LSV. Among our data base (2000-2009) including 632 patients with PEU, 245 male patients from infertile couples who had had a first semen analysis with LSV (< 2mL) and a second semen analysis associated with PEU, were selected on the previous criteria. A prospective control group was randomly constituted (2007-2008) of 162 first consulting male patients from infertile couples, with a normal semen volume (> 2mL) on a first semen analysis and who accepted to collect PEU with their usual second semen
analysis, selected on the previous criteria. To define an R-ratio threshold indicative of PRE, we used a ROC curve analysis and a regression tree based on a classification and regression tree (CART) algorithm. Of the 245 LSV patients, 146 still presented low semen volume (< 2 mL) on the second semen analysis. From the use of the CART algorithm, two low (1.5% and 2.8%) and two high R-values (7.1% and 8.3%) were defined, according to the lower reference limit for semen volume of 2.0 mL (WHO 1999) or 1.5 mL (WHO 2010) respectively. As only one or no patient with normal semen volume was observed above the two high R-values, we suggest an R-value higher than the range of [7.1-8.3]% as indicative of PRE until confirmation by a prospective multicenter study.

Status
In-Data-Review

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Management of infertile women with pelvic endometriosis: a literature review.
Guinard E; Collinet P; Lefebvre C; Robin G; Rubod C.

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INTRODUCTION: Endometriosis is a condition that affects women's fertility. Several mechanisms are involved in this process: anatomical changes, mechanical, immune or inflammatory factors, ovarian reserve alterations... There are different types of strategies to treat endometriosis-related infertility: medical treatment, surgical treatment and/or techniques of medically assisted procreation.

EVIDENCE ACQUISITION: We tried to consider various therapeutic strategies depending on the stage of the disease in order to offer appropriate management to patients with endometriosis who wish to become pregnant: we reviewed 58 articles between 1985 to 2016 searching in medline using the key words <<endometriosis and infertility>> and <<infertility and endometriosis treatment>>. And we divided the patients in subgroups mild and severe endometriosis, in vitro fertilization (IVF) versus surgery in deep infiltrating endometriosis (DIE) and others.

EVIDENCE SYNTHESIS: Surgery appears to be the chief treatment for minimal to mild endometriosis in a context of infertility. Concerning deep infiltrating endometriosis, data in insufficient to decide on the best treatment although surgery associated with IVF seems to bring clinical benefit.

CONCLUSIONS: Regarding optimal management of infertility - in case of stage III or IV endometriosis, there is yet no consensus. A multidisciplinary approach is essential in order to consider the various treatment options and provide optimum care and individualized to patients according to different parameters (patient age, degree of damage and location of DIE lesions, presence or absence of ovarian failure or other factors associated with subfertility, male infertility factors in the couple...). Indeed, optimal care of patients should be multidisciplinary and personalized.

Status
Reproductive hormones of ICSI-conceived young adult men: the first results.
Belva F; Roelants M; De Schepper J; Van Steirteghem A; Tournaye H; Bonduelle M.
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[Journal Article]
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STUDY QUESTION: Are reproductive hormone levels (FSH, LH, inhibin B and testosterone) in male offspring conceived by ICSI because of male infertility comparable with those from peers born after spontaneous conception?

SUMMARY ANSWER: In this cohort of 54 young men conceived by ICSI because of male-factor infertility, mean and median reproductive hormone levels were found to be comparable with
results from spontaneously conceived peers, but ICSI-conceived men were more likely to have low inhibin B (<10th percentile) and high FSH (>90th percentile) levels.

WHAT IS KNOWN ALREADY: Since the worldwide oldest ICSI offspring have recently reached young adulthood, their reproductive health can now be investigated. This typically involves semen analysis and a hormonal profiling including the measurement of FSH, LH, inhibin B and testosterone. Circulating levels of FSH and inhibin B are generally known as markers of the exocrine function of the testis, i.e. spermatogenesis, while LH and testosterone reflect its endocrine function. We have previously observed a normal pubertal development and comparable levels of inhibin B and testosterone among pubertal ICSI boys when compared to spontaneously conceived peers. However, at present, information on the gonadal function of ICSI offspring in adulthood is still lacking.

STUDY DESIGN, SIZE, DURATION: This study, conducted between March 2013 and April 2016 at the UZ Brussel, is part of a larger follow-up project focusing on reproductive and metabolic health of young adults between 18 and 22 years and conceived after ICSI because of male infertility. The ICSI men are part of a longitudinally followed cohort while the spontaneously conceived controls were recruited cross-sectionally.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Results of a single fasting blood sample from 54 young adult ICSI men were compared to that of 57 spontaneously conceived peers. Reproductive hormone analysis involved FSH, LH, testosterone and inhibin B measurement. Furthermore, the association between their reproductive hormones and their sperm parameters was examined. Data were analyzed by multiple linear and logistic regression adjusted for covariates.

MAIN RESULTS AND THE ROLE OF CHANCE: ICSI men had comparable mean levels of FSH, LH, testosterone and inhibin B in comparison to spontaneously conceived counterparts, even after adjustment for confounders, such as age, BMI and season. Young ICSI-conceived men were more likely to have inhibin B levels below the 10th percentile (<125.2 ng/l; Adjusted Odds Ratio (AOR) 4.0; 95% CI: 0.9-18.4; P = 0.07) compared with spontaneously conceived peers and were more likely to have FSH levels above the 90th percentile (>5.5 IU/L; AOR 3.3; 95% CI: 0.9-11.9; P = 0.06) compared with spontaneously conceived peers, but neither difference reached statistical significance. FSH, LH and inhibin B, but not testosterone, levels were significantly associated with sperm concentration and total sperm count.

LIMITATIONS, REASONS FOR CAUTION: The main limitation is the small study population. Furthermore, the results of this study should be interpreted according to the background of the participants: all subjects in our study group were conceived by ICSI because of severe male infertility and hence the results cannot be generalized to all ICSI offspring because the indications for performing ICSI have since been widened.
WIDER IMPLICATIONS OF THE FINDINGS: These first results in a small group of ICSI men show reassuring reproductive hormonal levels. However, larger studies are required to confirm our results. Since inhibin B and FSH are consistently correlated with semen characteristics, we would suggest that the reproductive status of young adults conceived by ICSI is explored with a hormonal assessment given its easier acceptance compared to semen sampling.

STUDY FUNDING/COMPETING INTERESTS: This study was supported by Methusalem grants and by grants from Wetenschappelijk Fonds Willy Gepts, all issued by the Vrije Universiteit Brussel (VUB). A grant from the Belgian Society for Pediatric Endocrinology and Diabetology was received for this project. All co-authors, except M.B. and H.T., declare no conflict of interest. M.B. has received consultancy fees from MSD, Serono Symposia and Merck. The Universitair Ziekenhuis Brussel (UZ Brussel) and the Centre for Medical Genetics have received several educational grants from IBSA, Ferring, Organon, Shering-Plough, Merck for establishing the database for follow-up research and organizing the data collection. The institution of HT receives research grants from the 'Research Fund of Flanders' (FWO), an unconditional grant from Ferring for research on testicular stem cells and research grants from Ferring, Merck, MSD, Roche, Besins, Goodlife and Cook for several research projects in female infertility. H.T. has received consultancy fees from Finox, Abbott and ObsEva for research projects in female infertility.

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COMPI Fertility Problem Stress Scales is a brief, valid and reliable tool for assessing stress in patients seeking treatment.

Sobral MP; Costa ME; Schmidt L; Martins MV.

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[Journal Article]

UI: 27979919

STUDY QUESTION: Are the Copenhagen Multi-Centre Psychosocial Infertility research program Fertility Problem Stress Scales (COMPI-FPSS) a reliable and valid measure across gender and culture?

SUMMARY ANSWER: The COMPI-FPSS is a valid and reliable measure, presenting excellent or good fit in the majority of the analyzed countries, and demonstrating full invariance across genders and partial invariance across cultures.

WHAT IS KNOWN ALREADY: Cross-cultural and gender validation is needed to consider a measure as standard care within fertility. The present study is the first attempting to establish comparability of fertility-related stress across genders and countries.

STUDY DESIGN SIZE, DURATION: Cross-sectional study. First, we tested the structure of the COMPI-FPSS. Then, reliability and validity (convergent and discriminant) were examined for the final model. Finally, measurement invariance both across genders and cultures was tested.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Our final sample had 3923 fertility patients (1691 men and 2232 women) recruited in clinical settings from seven different countries: Denmark, China, Croatia, Germany, Greece, Hungary and Sweden. Participants had a mean age of 34 years and the majority (84%) were childless.
MAIN RESULTS AND THE ROLE OF CHANCE: Findings confirmed the original three-factor structure of the COMPI-FPSS, although suggesting a shortened measurement model using less items that fitted the data better than the full version model. While data from the Chinese and Croatian subsamples did not fit, all other counties presented good fit (chi2/df < 5.4; comparative fit index > 0.94; root-mean-square error of approximation < 0.07; modified expected cross-validation index < 0.77). In general, reliability, convergent validity, and discriminant validity were observed in all subscales from each country (composite reliability > 0.63; average variance extracted > 0.38; squared correlation > 0.13). Full invariance was established across genders, and partial invariance was demonstrated across countries.

LIMITATIONS REASONS FOR CAUTION: Generalizability regarding the validation of the COMPI-FPSS cannot be made regarding infertile individuals not seeking treatment, or non-European patients. This study did not investigate predictive validity, and hence the capability of this instrument in detecting changes in fertility-specific adjustment over time and predicting the psychological impact needs to be established in future research.

WIDER IMPLICATIONS OF THE FINDINGS: Besides extending knowledge on the psychometric properties of one of the most used fertility stress questionnaire, this study demonstrates both research and clinical usefulness of the COMPI-FPSS.

STUDY FUNDING/COMPETING INTERESTS: This study was supported by European Union Funds (FEDER/COMPETE-Operational Competitiveness Program, and by national funds (FCT-Portuguese Foundation for Science and Technology) under the projects PTDC/MHC-PSC/4195/2012 and SFRH/BPD/85789/2012). There are no conflicts of interest to declare.

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A meta-analysis of sperm donation offspring health outcomes.

Adams DH; Clark RA; Davies MJ; de Lacey S.

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[Journal Article]
UI: 27573256

Although the use of donor sperm as a treatment modality for male infertility has become common place, the health outcomes for those conceived has been poorly studied. A structured search of the literature using PubMed, EMBASE and Cochrane Reviews was performed to investigate the health outcomes of offspring conceived from donor sperm. Eight studies were eligible and included in the review, and of these, three were included in a meta-analysis. Meta-analysis of clinical outcomes showed that donor sperm neonates are not at increased risk of being born of low birth weight (<2500 g), preterm (<37 weeks) or with increased incidences of birth defects, than spontaneously conceived neonates.

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Association between adherence to the Mediterranean diet and semen quality parameters in male partners of couples attempting fertility.

Karayiannis D; Kontogianni MD; Mendorou C; Douka L; Mastrominas M; Yiannakouris N.

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[Journal Article]

UI: 27994040

STUDY QUESTION: Is adherence to the Mediterranean diet (MedDiet) associated with better semen quality in men of subfertile couples attempting fertility?

SUMMARY ANSWER: Greater adherence to the MedDiet, as assessed through the validated Mediterranean diet score (MedDietScore), was significantly associated with higher sperm concentration, total sperm count and sperm motility.

WHAT IS KNOWN ALREADY: A-posteriori dietary pattern approaches have revealed that dietary patterns characterized by high intakes of fruits, vegetables, whole grains, fish and low intake of meat are associated with better semen quality. Yet, whether adherence to the MedDiet is associated with better semen profile remains largely unexplored.

STUDY DESIGN, SIZE, AND DURATION: This was a cross-sectional study of 225 men from couples attending a fertility clinic in Athens, Greece, recruited between November 2013 and May 2016. The study was designed to evaluate the influence of habitual dietary intake and lifestyle on fertility outcomes.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Men aged 26-55 years, 51.1% overweight or obese, 20.9% smokers, with complete dietary data were analyzed. Diet was assessed via a food-frequency questionnaire and adherence to the MedDiet was assessed through the MedDietScore (range: 0-55; higher scores indicating greater adherence to MedDiet). Semen quality was evaluated according to World Health Organization 2010 guidelines. Multiple logistic
regression analysis was used to evaluate associations between tertiles of the MedDietScore and the likelihood of having abnormal semen parameters, after adjusting for potential confounders.

**MAIN RESULTS AND THE ROLE OF CHANCE:** Compared to men in the highest tertile of the MedDietScore (>37, N = 66), a higher percentage of men in the lowest tertile of the score (<30, N = 76) exhibited below the WHO reference values for sperm concentration (47.4% vs 16.7%, P < 0.001), total sperm count (55.3% vs 22.7%, P < 0.001), total motility (65.8% vs 31.8%, P < 0.001), progressive motility (84.2 vs 62.1%, P = 0.011) and sperm morphology (50.0 vs 28.8%, P = 0.023). In the multivariable adjusted models, men in the lowest tertile of the MedDietScore had ~2.6 times higher likelihood of having abnormal sperm concentration, total sperm count and motility, compared to men in the highest tertile of the score.

**LIMITATIONS, REASONS FOR CAUTION:** The main limitation of the study stems from its cross-sectional nature, limiting our ability to determine causality.

**WIDER IMPLICATIONS OF THE FINDINGS:** The results suggest that greater compliance to the MedDiet may help improve semen quality. Whether this translates into differences in male fertility remains to be elucidated. Our findings are consistent with previous studies showing that dietary patterns with some of the characteristics of the MedDiet, i.e. rich in fruit, vegetables, legumes and whole grains, are associated with better measures of semen quality.

**STUDY FUNDING/COMPETING INTERESTS:** No funding was obtained. The authors have no competing interests to declare.

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80.
Risk of childhood mortality in family members of men with poor semen quality.
Hanson HA; Mayer EN; Anderson RE; Aston KI; Carrell DT; Berger J; Lowrance WT; Smith KR; Hotaling JM.
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STUDY QUESTION: What is the familial childhood mortality in first-degree (FDR) and second-degree relatives (SDR) of patients undergoing semen analysis (SA)?
SUMMARY ANSWER: The relationship between infertility and congenital malformations (CM) in offspring is complex, with an increased risk of death due to CM in FDR, but not SDR, of men with lower semen parameters.
WHAT IS KNOWN ALREADY: Semen quality is an established predictor of men's somatic health. We can gain a better understanding of possible genetic or environmental determinants of the infertility phenotype by exploring familial aggregation of childhood mortality in relatives of men with poor semen quality.
STUDY DESIGN, SIZE, DURATION: Retrospective cohort study from the Subfertility, Health and Assisted Reproduction study (cohort compiled 1996-2011) linked with patient/familial information from the Utah Population Database (UPDB). Index cases included a clinic-referred sample of 12889 men who underwent SA and had adequate familial and follow-up data in the UPDB. Parameters of semen quality included: semen concentration, sperm count, motility, total motile count, sperm head morphology, sperm tail morphology and vitality.
PARTICIPANTS/MATERIALS, SETTING, METHODS: SA data were collected from two tertiary medical center andrology laboratories that have captured ~90% of all SA performed in Utah since
2004. Age- and sex-matched fertile controls were selected to create the comparison group for determining risk of childhood death (to age 20 years) in family members. A total of 79,750 siblings and 160,016 aunts/uncles were used to investigate the familial aggregation of childhood mortality. The main outcome was childhood mortality in FDR and SDR of men with SA and their matched controls. All-cause and cause-specific Cox proportional hazard models were used to test the association between semen quality and childhood mortality in family members. Cause-specific models were considered for cancer and CM.

MAIN RESULTS AND THE ROLE OF CHANCE: In the cohort of men with SA, there were 406 (1.0%) deaths in FDR and 772 (1.1%) deaths in SDR due to any cause. There was no significant difference in the risk of all-cause childhood mortality between the relatives of men with SA and the fertile control group [hazard ratio (HR)Female = 1.08, 95% CI = 0.88, 1.32; HRMale = 0.88, 95% CI = 0.75, 1.04]. We found no association between semen quality and risk for childhood cancer mortality in FDR or SDR (HRFDR = 0.98, 95% CI = 0.62, 1.54; HRSBR = 1.12, 95% CI = 0.83, 1.50). The FDR of men with SA and fertile controls were followed on average for 19.71 and 19.73 years, respectively. During this period of follow-up, FDR of men with SA had an unadjusted 40% relative risk of increased CM-related death. After stratifying by semen parameters and adjusting for birth year, we found FDR of men with worse semen quality, and notably azoospermic men (HR = 2.69, 95% CI = 1.24, 5.84), were at higher risk of CM-related death.

LIMITATIONS REASONS FOR CAUTION: A large proportion of men with SA in the study had normal semen parameters. It is important to note that these men themselves may not be subfertile, but they were subfertile at the couple level (i.e. the female partner may be infertile). In addition, care is needed when interpreting our results, as we do not have semen measures on our sample of fertile men. Second, we were unable to include potential confounders such as medical comorbidities, smoking status, or environmental exposures. Third, men with SA were seen at the University of Utah or Intermountain Health Care clinics for a fertility evaluation thereby suggesting a more select population. Fourth, we chose to categorize morphology into equally distributed quartiles as a response to the fact that the World Health Organization threshold for normal motility changed multiple times during our study period. Lastly, we do not know the proportion of female partners with diagnosed infertility. We chose not to subcategorize each infertile male by infertile diagnosis because our goal was to understand how semen parameters influenced familial childhood mortality.

WIDER IMPLICATIONS OF THE FINDINGS: We are not the first study to show a relationship between fertility and CMs. Children conceived through ART may be at higher risk of birth defects, however it is not known if the relationship is causal or if there is some underlying factor linking infertility and birth outcomes. This study provides further evidence that the increased risk of congenital birth defects may not be due to the ART, but rather genetic or environmental factors
that link the two outcomes. We encourage further research in order to confirm a relationship between semen quality and increased risk for CM.

STUDY FUNDING/COMPETING INTERESTS: This work was supported by the National Institutes of Health - National Institute of Aging [Grant numbers 1R21AG036938-01, 2R01 AG022095 and 1K12HD085852-01]. Authors have no competing interests to disclose.

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STUDY QUESTION: Is female exposure to phthalate metabolites associated with reduced fecundity, as estimated by prolonged time to pregnancy (TTP)?

SUMMARY ANSWER: Female exposure to monoethyl phthalate (MEP) but not monobutyl phthalate (MBP), monobenzyl phthalate (MBzP) and monoethylhexyl phthalate (MEHP) was associated with a longer TTP.

WHAT IS KNOWN ALREADY: Male exposure to phthalates is potentially associated with adverse effects on human fecundity in epidemiological studies, but little is known about the potential effects on female reproduction.

STUDY DESIGN SIZE AND DURATION: A cohort study with prospective data based on 229 women from a Danish cohort of 430 first pregnancy planning couples enrolled in 1992-1994. In 2009, urinary analyses of phthalate metabolites were performed on stored urine samples from this cohort.
PARTICIPANTS/MATERIALS, SETTING AND METHODS: We analyzed MEP, MBP, MBzP and MEHP in female morning spot urine samples collected daily during the first 10 days of menstrual cycles after discontinuation of contraception. The exposure assessment was based on the mean of two measurements from each woman collected in a period of 6 menstrual cycles. We used Cox regression with discrete time to estimate fecundability ratios (FRs) and 95% CI in relation to the average urine metabolite concentration exposure level, controlled for age and BMI, and the time-varying variables smoking and alcohol.

MAIN RESULT AND ROLE OF CHANCE: Urinary concentration of MEP was associated with a decreased fecundity (adjusted FR 0.79; 95% CI: 0.63; 0.99) corresponding to a 21% decreased probability of conception for each natural log (ln) unit increase in MEP. No significant association with TTP was found for MBP, MBzP and MEHP.

LIMITATIONS REASONS FOR CAUTION: Subfertile women were overrepresented in the study population due to exclusion of 77 high fertile women who became pregnant in the first cycle when urine collection began.

WIDER IMPLICATIONS OF THE FINDINGS: Our results suggest that female exposure to MEP may have an adverse effect on female fecundity, but these findings need to be replicated in a larger and newer cohort study with sufficient exposure contrast if the use of diethyl phthalate (DEP) and thereby MEP in the future potentially should be regulated in cosmetics and industrial consumer products.

STUDY FUNDING/COMPETING INTERESTS: The original data collected were founded by Aarhus University Research Foundation, the Danish Medical Research Council and the Danish Medical Health Insurance Foundation. There are no conflicts of interest to be declared.

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The role of intracytoplasmic sperm injection in non-male factor infertility in advanced maternal age.

Tannus S; Son WY; Gilman A; Younes G; Shavit T; Dahan MH.

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[Journal Article]

UI: 27852688

STUDY QUESTION: Does ICSI improve reproductive outcomes compared with conventional IVF when used for non-male factor infertility in women aged 40 years and over?

SUMMARY ANSWER: There is no advantage of ICSI over conventional IVF in women aged 40 years and over when used for non-male factor infertility.
WHAT IS KNOWN ALREADY: The use of ICSI has increased dramatically in recent years and is being applied for indications other than male factor infertility. Currently, ICSI is used in 65% of IVF cycles in Europe and in 76% of cycles in the USA. Despite its increase use, there is no clear evidence of a benefit in using ICSI over conventional IVF. Older women undergoing infertility treatments are at an increased risk of having diminished ovarian reserve and lower oocyte quality, which could make ICSI the preferred insemination method in this group. However, studies that have examined the benefits of ICSI in this age group are lacking.

STUDY DESIGN, SIZE, DURATION: A retrospective, single center study included women, aged 40-43 years, who underwent IVF treatments for non-male factor infertility between January 2012 until June 2015.

PARTICIPANTS/MATERIALS, SETTING, METHODS: A total of 745 women were included in the study. Of these, 490 women underwent ICSI and 255 women underwent conventional IVF. In order to be included in the study, women had to be at least 40 years of age at the beginning of ovarian stimulation and their male partner had to have normal sperm parameters according to World Health Organisation (WHO) fifth edition. Exclusion criteria included: more than three previous IVF cycles, a history of fertilization failure or low fertilization (<50%), the use of donor or frozen oocytes and the use of donor or frozen sperm samples. The primary outcome was the live birth rate. Secondary outcomes included fertilization rates, fertilization failure and embryo quality.

MAIN RESULTS AND THE ROLE OF CHANCE: Baseline characteristics were similar between the two groups, except for the number of previous IVF cycles, which was higher in the ICSI group (1.0 vs. 0.6, P = 0.0001). Despite similar numbers of oocytes retrieved (7.2 vs. 6.5), when examining oocytes maturity (performed 2 h after oocyte retrieval in the ICSI group and after 18 h in the conventional IVF group), the conventional IVF group had a higher number of Metaphase II (MII) oocytes (6.1 vs. 4.7, P < 0.0001). The conventional IVF group also had higher numbers of zygotes formed (4.48 vs. 3.66, P = 0.001), more cycles with embryos transferred at the blastocyst stage (36 vs. 26%, P = 0.005) and more cycles where embryos were available for cryopreservation (26.4 vs. 19.7%, P = 0.048), compared with the ICSI group. The fertilization rates (64 vs. 67%) and fertilization failure (9.0 vs. 9.7%) were similar. After logistic regression analysis controlling for confounders, the live birth rates were similar between the groups (11.9 vs. 9.6%). Subgroup analyses of women undergoing their first IVF cycle and women with <3 oocytes retrieved did not show an advantage of ICSI over conventional IVF.

LIMITATIONS, REASONS FOR CAUTION: The retrospective nature of this study was a major limitation. The ICSI group had a higher number of previous IVF cycles, which could mean that ICSI was performed in poorer prognosis patients. Moreover, although this study is one of the largest studies to examine the question of whether ICSI is of value for older women with non-male factor infertility, based on a post hoc power analysis, it was still underpowered to detect
differences in live birth rates, which can limit the conclusions of the study. Prospective studies are needed to confirm our findings.

WIDER IMPLICATIONS OF THE FINDINGS: The decision regarding performing ICSI should be based on sperm parameters and previous history. The use of ICSI for the sole indication of advanced maternal age shows no benefit over conventional IVF.

STUDY FUNDING/COMPETING INTERESTS: None.

TRIAL REGISTRATION NUMBER: N/A.

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Status
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Effects of two-year testosterone replacement therapy on cognition, emotions and quality of life in young and middle-aged hypogonadal men.

Lasaite L; Ceponis J; Preiksa RT; Zilaitiene B.

The aim of the study was to examine the effects of two-year testosterone replacement therapy on cognitive functioning, emotional state and quality of life in young and middle-aged men with hypogonadotropic hypogonadism. Nineteen males diagnosed with hypogonadotropic hypogonadism participated in the study. Cognitive functions were assessed by Trail Making Test and Digit Span Test of Wechsler Adult Intelligence Scale. Emotional state was evaluated by Profile of Mood States. Quality of life was evaluated by WHO Brief Quality of Life Questionnaire.

Changes after two-year testosterone replacement therapy were detected in Trail Making A (42.9 +/- 22.3 vs. 36.2 +/- 22.5, p = .050) and B (90.6 +/- 55.3 vs. 65.6 +/- 21.4, p = .025) tests, showing improvement in attention and visual scanning abilities, executive function and psychomotor speed, as well as in Digit Span Test forward score (5.4 +/- 2.0 vs. 6.1 +/- 2.6, p = .046), showing improvement in attention capacity and psychomotor speed. No significant differences were observed in emotional state and quality of life. In conclusion, beneficial effect in cognitive functioning (improved attention and visual scanning ability, executive function and psychomotor speed), but not in emotional state and quality of life, was observed in young and middle-aged hypogonadal men after two-year testosterone replacement therapy.

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Lasaite, L; Ceponis, J; Preiksa, R T; Zilaitiene, B.

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Obstetric and perinatal outcome of babies born from sperm selected by MACS from a randomized controlled trial.

Romany L; Garrido N; Cobo A; Aparicio-Ruiz B; Serra V; Meseguer M.

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[Journal Article. Randomized Controlled Trial]

Ui: 27882439

PURPOSE: The purpose of this study is to assess outcomes after magnetic-activated cell sorting (MACS) technology on obstetric and perinatal outcomes compared with those achieved after swim up from randomized controlled trial.

METHODS: This is a two-arm, unicentric, prospective, randomized, and triple-blinded trial and has a total of 237 infertile couples, between October 2010 and January 2013. A total of 65 and 66 newborns from MACS and control group, respectively, were described.

RESULTS: MACS had no clinically relevant adverse effects on obstetric and perinatal outcomes. No differences were found for obstetric problems including premature rupture of membranes 6.1% (CI95% 0-12.8) vs. 5.9% (CI95% 0-12.4), 1st trimester bleeding 28.6% (CI95% 15.9-41.2) vs. 23.5% (CI95% 11.9-35.1), invasive procedures as amniocentesis 2.0% (CI95% 0-5.9) vs. 3.9% (CI95% 0-9.2), diabetes 14.3% (CI95% 4.5-24.1) vs. 9.8% (CI95% 1.6-17.9), anemia 6.1% (CI95% 0-12.8) vs. 5.9%(CI95% 0-12.4), 2nd and 3rd trimesters 10.2% (CI95% 1.7-18.7) vs.
5.9% (CI95% 0-12.4), urinary tract infection 8.2% (CI95% 0.5-15.9) vs. 3.9% (CI95% 0-9.2), pregnancy-induced hypertension 6.1% (CI95% 0-12.8) vs. 15.7% (CI95% 5.7-25.7), birth weight (g) 2684.10 (CI95% 2499.48-2868.72) vs. 2676.12 (CI95% 2499.02-2852.21), neonatal height (cm) 48.3 (CI95% 47.1-49.4) vs. 46.5 (CI95% 44.6-48.4), and gestational cholestasis 0%(CI95% 0-0) vs. 3.9% (CI95% 0-9.2), respectively, in MACS group compared with control group.

CONCLUSIONS: Our data suggest that MACS technology does not increase or decrease adverse obstetric and perinatal outcomes in children conceived when this technology was performed, being the largest randomized control trial with live birth reported results with MACS.
To evaluate the association between the SPO11 gene C631T polymorphism and the risk of male infertility. We conducted a search on PubMed, Embase, Web of Science, Chinese National Knowledge Infrastructure (CNKI), China biology medical literature database (CBM), VIP, and Chinese literature database (Wan Fang) on 31 March 2016. Odds ratio (OR) and 95% confidence interval (95%CI) were used to assess the strength of associations. A total of five studies including 542 cases and 510 controls were involved in this meta-analysis. The pooled results indicated that the SPO11 gene C631T polymorphism was significantly associated with increased risk of male infertility (TT+CT vs. CC: OR=4.14, 95%CI=2.48-6.89; CT vs. CC: OR=4.34, 95%CI=2.56-7.34; T vs. C: OR=4.35, 95%CI=2.58-7.34). Subgroup analysis of different countries proved the relationship between SPO11 gene C631T polymorphism and male infertility risk in Chinese, but not in Iranian peoples. In conclusion, this study suggested that SPO11 gene C631T polymorphism may contribute as a genetic factor susceptible to cause male infertility. Furthermore, more large sample and representative population-based cases and well-matched controls are needed to validate our results.

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MEDLINE
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Association and meta-analysis of HLA and non-obstructive azoospermia in the Han Chinese population.
Zou S; Song P; Meng H; Chen T; Chen J; Wen Z; Li Z; Li Z; Shi Y; Hu H.
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Andrologia. 49(2), 2017 Mar.
[Journal Article. Meta-Analysis]
UI: 27597543
The exact aetiology and pathogenesis of most non-obstructive azoospermia (NOA) are still unknown. The previous two genomewide association studies (GWASs) have identified three different loci within the HLA region for NOA in the Han Chinese population, including rs3129878, rs498422 and rs7194. To further validate the risk of three GWAS-linked loci for NOA, we conducted a case-control study of these three risk loci in an independent Han Chinese male population, with 603 NOA patients and 610 controls. Furthermore, we also performed a meta-analysis of five studies on these three NOA-risk loci. The case-control study strongly suggested a significant association between loci rs3129878, rs498422 and rs7194 and NOA (P = 6.75 x 10^-21 (OR = 2.2586), P = 0.0060 (OR = 1.4013) and P = 0.0128 (OR = 1.2626) respectively). Our meta-analyses also supported the susceptibility of these three risk loci to NOA (P < 0.01). The risk variants within the HLA region potentially have a strong effect on males at risk of NOA, and may serve as diagnostic markers for male infertility. However, considering genetic difference between
different populations, future validating studies in larger independent samples and animal experiments are suggested.

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87.
Sex steroids in relation to cardiac structure and function in men. [Review]
De Smet MA; Lapauw B; De Backer T.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present Andrologia. 49(2), 2017 Mar.
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The prevalence of testosterone substitution as well as of androgen deprivation therapy in men is increasing. This review aims to summarise available knowledge of the effects of sex steroids on cardiac structure and function in men. MEDLINE was searched through PubMed. Original studies, systematic reviews and meta-analyses, and relevant citations were screened. A short-term hormonal intervention study in healthy young men with respect to echocardiographic parameters of structure and function was performed. Preclinical research provides sufficient evidence for the heart as a substrate for sex hormones. In animals, administration of oestradiol appears to have beneficial effects on cardiac structure and function, whereas administration of testosterone to noncastrated animals adversely affects cardiac function. However, the effects of sex steroids on cardiac function and structure appear more heterogeneous in human observational studies while comparative, prospective studies in humans are lacking. It is concluded that although effects of testosterone substitution as well as of androgen deprivation on cardiac structure and function can be expected based on pre-clinical research, there exists an important knowledge gap of the effects of hormonal intervention in men. As such, there is a need to address this question in future prospective intervention trials.
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Status
MEDLINE
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Studies suggest a relationship between semen quality and the concentration of trace elements in serum or seminal plasma. However, trace elements may be linked to DNA and capable of altering the gene expression patterns. Thus, trace element interactions with DNA may contribute to the mechanisms for a trans-generational reproductive effect. We developed an analytical method to determine the amount of trace elements bound to the sperm DNA, and to estimate their affinity for the sperm DNA by the ratio: 

\[ R = \log \left( \frac{\text{metal concentration in the sperm DNA}}{\text{metal concentration in seminal plasma}} \right) \]

We then analyzed the concentrations of 15 trace elements (Al, Cd, Cr, Cu, Hg, Mn, Mo, Ni, Pb, Ti, V, Zn, As, Sb, and Se) in the seminal plasma and the sperm DNA in 64 normal and 30 abnormal semen specimens with Inductively Coupled Plasma/Mass Spectrometry (ICP-MS). This study showed all trace elements were detected in the seminal plasma and only metals were detected in the sperm DNA. There was no correlation between the metals' concentrations in the seminal plasma and the sperm DNA. Al had the highest affinity for DNA followed by Pb and Cd. This strong affinity is consistent with the known mutagenic effects of these metals. The lowest affinity was observed for Zn and Ti. We observed a significant increase of Al linked to the sperm DNA of patients with oligozoospermia and teratozoospermia. Al's reproductive toxicity might be due to Al linked to DNA, by altering spermatogenesis and expression patterns of genes involved in the function of reproduction.
Status
MEDLINE

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Association and meta-analysis of HLA and non-obstructive azoospermia in the Han Chinese population.
Zou S; Song P; Meng H; Chen T; Chen J; Wen Z; Li Z; Li Z; Shi Y; Hu H.
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[Journal Article. Meta-Analysis]
UI: 27597543
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Sex steroids in relation to cardiac structure and function in men. [Review]
De Smet MA; Lapauw B; De Backer T.
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91.
Sexual Rehabilitation After Treatment For Prostate Cancer-Part 2: Recommendations From the Fourth International Consultation for Sexual Medicine (ICSM 2015).
Embase
[Article]
AN: 614681526
Introduction Sexual dysfunction is common in patients after radical prostatectomy (RP) for prostate cancer. Aim To provide the International Consultation for Sexual Medicine (ICSM) 2015 recommendations concerning management strategies for post-RP erectile function impairment and to analyze post-RP sexual dysfunction other than erectile dysfunction. Methods A literature search was performed using Google and PubMed database for English-language original and review articles published up to August 2016. Main Outcome Measures Levels of evidence (LEs) and grades of recommendations (GRs) are provided based on a thorough analysis of the literature and committee consensus. Results Nine recommendations are provided by the ICSM 2015 committee on sexual rehabilitation after RP. Recommendation 6 states that the recovery of postoperative erectile function can take several years (LE = 2, GR = C). Recommendation 7 states there are conflicting data as to whether penile rehabilitation with phosphodiesterase type 5 inhibitors improves recovery of spontaneous erections (LE = 1, GR = A). Recommendation 8 states that the data are inadequate to support any specific regimen as optimal for penile rehabilitation (LE = 3, GR = C). Recommendation 9 states that men undergoing RP (any technique) are at risk of sexual changes other than erectile dysfunction, including decreased libido, changes in orgasm, anejaculation, Peyronie-like disease, and changes in penile size (LE = 2, GR = B). Conclusion This article discusses Recommendations 6 to 9 of the ICSM 2015 committee on sexual rehabilitation after RP. Salonia A, Adaikan G, Buvat J, et al. Sexual Rehabilitation After Treatment For Prostate Cancer-Part 2: Recommendations From the Fourth International Consultation for Sexual Medicine (ICSM 2015). J Sex Med 2017;14:297-315.
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PMID
Status
EMBASE
Comparison of transurethral incision of the prostate and silodosin in patients having benign prostatic obstruction in terms of retrograde ejaculation.

Cakiroglu B., Hazar A.I., Sinanoglu O., Arda E., Ekici S.

Embase
Archivio Italiano di Urologia e Andrologia. 89 (1) (pp 31-33), 2017. Date of Publication: 2017.

Background: To compare the functional outcomes and retrograde ejaculation (RE) after transurethral incision of the prostate (TUIP) or silodosin in bladder outlet obstruction (BOO) secondary to a small prostate. Methods: Prospectively collected data from December 2011
through December 2014 of 192 LUTS patients having fertility concerns with prostate volume smaller than 40 ml receiving either TUIP or silodosin treatment were prospectively reviewed. The treatment outcomes were evaluated and compared. Results: TUIP was performed in 96 cases and silodosin 8 mg was prescribed in 96 cases. At 12th months after TUIP or continuous silodosin treatment, the decrease in mean International Prostate Symptom Score (IPSS) and postvoiding residual urine (PVR) and the improvement of mean maximal flow rate (Qmax) were significant (p = 0.000). The improvement in IPSS and Qmax was significantly higher in TUIP group compared to silodosin group (p = 0.005, p = 0.000) with a lower rate of retrograde ejaculation (RE) in TUIP group. (11/96 vs 33/96) (p = 0.000) Conclusions: Both TUIP and silodosin ensures comparable improvement in PVR, IPSS and Qmax with a lower rate of RE on the TUIP group in prostates weighing less than 40 grams suggesting that TUIP is a better choice in younger patients seeking preservation of ejaculation with fertility concerns.

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93.

Physiological and psychological effects of testosterone during severe energy deficit and recovery: A study protocol for a randomized, placebo-controlled trial for Optimizing Performance for Soldiers (OPS).
Background The physiological consequences of severe energy deficit include hypogonadism and the loss of fat-free mass. Prolonged energy deficit also impacts physical performance, mood, attentiveness, and decision-making capabilities. This study will determine whether maintaining a eugonadal state during severe, sustained energy deficit attenuates physiological decrements and maintains mental performance. This study will also assess the effects of normalizing testosterone levels during severe energy deficit and recovery on gut health and appetite regulation. Methods Fifty physically active men will participate in a 3-phase, randomized, placebo-controlled study. After completing a 14-d, energy-adequate, diet acclimation phase (protein: 1.6 g · kg⁻¹ · d⁻¹; fat: 30% total energy intake), participants will be randomized to undergo a 28-d, 55% energy deficit phase with (DEF + TEST: 200 mg testosterone enanthate per week) or without (DEF) exogenous testosterone. Diet and physical activity will be rigorously controlled. Recovery from the energy deficit (ad libitum diet, no testosterone) will be assessed until body mass has been recovered within +/- 2.5% of initial body mass. Body composition, stable isotope methodologies, proteomics, muscle biopsies, whole-room calorimetry, molecular biology, activity/sleep monitoring, personality and cognitive function assessments, functional MRI, and comprehensive biochemistries will be used to assess physiological and psychological responses to energy restriction and recovery feeding while volunteers are in an expected hypogonadal versus eugonadal state. Discussion The Optimizing Performance for Soldiers (OPS) study aims to determine whether preventing hypogonadism will mitigate declines in physical and mental function that typically occur during prolonged energy deficit, and the efficacy of testosterone replacement on recovery from severe underfeeding. Trial Registration: NCT02734238.

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94.

Outer dense fiber proteins: Bridging between male infertility and cancer.
Azizi F., Ghafoun-Fard S.

Embase
[Review]

AN: 616123460

Background: The similarities between gametogenic and carcinogenesis processes have been noted for more than decades. Among prominent similarities between these two processes is expression of a group of antigens, namely cancer-testis antigens in both the testes and various cancer tissues. Outer dense fiber (ODF) proteins are testis-specific proteins localized to sperm tails and involved in sperm motility. Methods: We performed a computerized search of the MEDLINE/PUBMED databases with keywords "outer dense fiber, ODF, cancer, testis, gametogenesis and infertility". Results: The results of animal and human studies show ODF contribution to male fertility. In addition, ODFs are expressed in some cancers, including prostate adenocarcinoma, breast cancer, chronic myeloid leukemia and basal cell carcinoma. Conclusion:
ODF expression analysis in cancer may pave the way for identification of cancer biomarkers or therapeutic targets.

95.
Preconception maternal lipoprotein levels in relation to fecundability.

Summary
Fecundability was reduced for all abnormal female lipid levels including total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and total triglyceride levels. What is Known Already Subfecundity affects 7-15% of the population and lipid disorders are hypothesized to play a role since cholesterol acts as a substrate for the synthesis of steroid hormones. Evidence illustrating this relationship at the mechanistic level is mounting but few studies in humans have explored the role of preconception lipids in fecundity. Study Design, Size, Duration A secondary analysis of the Effects of Aspirin in Gestation and Reproduction (EAGeR) trial (2007-2011), a block-randomized, double-blind, placebo-controlled trial.

Participants/Materials, Setting, Methods A total of 1228 women, with 1-2 prior pregnancy losses
and without a diagnosis of infertility, attempting pregnancy for up to six menstrual cycles were recruited from clinical sites in Utah, New York, PA and Colorado. Time to pregnancy was the number of menstrual cycles to pregnancy as determined by positive hCG test or ultrasound. Individual preconception lipoproteins were measured at baseline, prior to treatment randomization and dichotomized based on clinically accepted cut-points as total cholesterol >200 mg/dl, LDL-C >130 mg/dl, HDL-C <50 mg/dl and triglycerides >150 mg/dl. Main Results and The Role of chance There were 148 (12.3%) women with elevated total cholesterol, 94 (7.9%) with elevated LDL-C, 280 (23.2%) with elevated triglycerides and 606 (50.7%) with low HDL-C. The fecundability odds ratio (FOR) was reduced for all abnormal lipids before and after confounder adjustment, indicating reduced fecundability. Total cholesterol >200 mg/dl was associated with 24% (FOR: 0.76, 95% CI: 0.59, 0.97) and 29% (FOR: 0.71, 95% CI: 0.55, 0.93) reduced fecundability for hCG-detected and ultrasound-confirmed pregnancy, respectively, compared with total cholesterol <200 mg/dl. There was a 19-36% decrease in the probability of conception per cycle for women with abnormal lipoprotein levels, though additional adjustment for central adiposity and BMI attenuated observed associations. Limitations, Reasons For Caution Although the FOR is a measure of couple fecundability, we had only measures of female lipid levels and can therefore not confirm the findings from a previous study indicating the independent role of male lipids in fecundity. The attenuated estimates and decreased precision after adjustment for central adiposity and obesity indicate the complexity of potential causal lipid pathways, suggesting other factors related to obesity besides dyslipidemia likely contribute to reduced fecundability. Wider Implications of The Findings Our results are consistent with one other study relating preconception lipid concentrations to fecundity and expand these findings by adding critically important information about individual lipoproteins. As lipid levels are modifiable they may offer an inexpensive target to improve female fecundability. Study Funding and Competing Interest(S) This study was funded by the Intramural Research Program of the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

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Status
INPROCESS

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96. Effects of testosterone replacement therapy on metabolic syndrome among Japanese hypogonadal men: A subanalysis of a prospective randomised controlled trial (EARTH study). Shigehara K., Konaka H., Nohara T., Izumi K., Kitagawa Y., Kadono Y., Iwamoto T., Koh E., Mizokami A., Namiki M. Embase Andrologia. (no pagination), 2017. Date of Publication: 2017. [Article In Press] AN: 616204553 We investigated the effects of testosterone replacement therapy (TRT) on metabolic factors among hypogonadal men with a metabolic syndrome. From the study population of the EARTH study, which was a randomised controlled study in Japan, 65 hypogonadal patients with a metabolic syndrome, comprising the TRT group (n = 32) and controls (n = 33), were included in this study analysis. The TRT group was administered 250mg of testosterone enanthate as an intramuscular injection every 4 weeks for 12 months. Waist circumference, body mass index, body fat volume and blood pressure were measured in all patients at baseline and at 12 months. In addition, blood biochemical data, including total cholesterol, triglyceride (TG), HDL cholesterol,
fasting plasma glucose (FPG) and haemoglobin A1c (HbA1c) levels, were also evaluated. Changes in these categories from baseline to 12 months were compared between the TRT and control groups, with significant differences observed in waist circumference, body fat percentage, FPG, TG and HbA1c levels. No significant differences were observed in other parameters. TRT for 1 year was associated with improvements in some metabolic factors among Japanese men with hypogonadism and metabolic syndrome.

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Status
ARTICLE IN PRESS

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97.
Multicentre study of Y chromosome microdeletions in 1,808 Chinese infertile males using multiplex and real-time polymerase chain reaction.

Embase
Andrologia. 49 (5) (no pagination), 2017. Article Number: e12662. Date of Publication: June 2017.

AN: 613537944
Azoospermia factor (AZF) genes on the long arm of the human Y chromosome are involved in spermatogenesis, and microdeletions in the AZF region have been recognised to be the second
major genetic cause of spermatogenetic failure resulting in male infertility. While screening for these microdeletions can avoid unnecessary medical and surgical treatments, current methods are generally time-consuming. Therefore, we established a new method to detect and analyse microdeletions in the AZF region quickly, safely and efficiently. In total, 1,808 patients with spermatogenetic failure were recruited from three hospitals in southern China, of which 600 patients were randomly selected for screening for Y chromosome microdeletions in AZF regions employing real-time polymerase chain reaction with a TaqMan probe. In our study, of 1,808 infertile patients, 150 (8.3%) were found to bear microdeletions in the Y chromosome using multiplex PCR, while no deletions were found in the controls. Among the AZF deletions detected, two were in AZFa, three in AZFb, 35 in AZFc, three in AZFb+c and two in AZFa+b+c. Our method is fast-it permits the scanning of DNA from a patient in one and a half hours-and reliable, minimising the risk of cross-contamination and false-positive and false-negative results.

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2017
Effect of oral administration of Tribulus terrestris extract on semen quality and body fat index of infertile men.

Salgado R.M., Marques-Silva M.H., Goncalves E., Mathias A.C., Aguiar J.G., Wolff P.

Embase
Andrologia. 49 (5) (no pagination), 2017. Article Number: e12655. Date of Publication: June 2017.

AN: 613017557

Male fertility can be evaluated through complete semen analysis. Plants belonging to the Tribulus genus are known for their role in enhancing sex hormone levels and semen quality. The aim of this study was to evaluate the effects of T. terrestris on semen quality and physiological parameters. Sixty-five men with abnormal semen evaluation were included in this study, in which they were prescribed with oral administration of Androsten (250 mg of Tribulus terrestris dried extract per capsule). Body fat percentage, lean muscle mass gain, fluctuation in steroid hormone levels and all semen parameters were analysed during the period of treatment. The results demonstrated that decrease in the percentage of body fat and increase in lean mass were significant, as well as increase in dihydrotestosterone levels. Complete semen analysis evaluated at the end of treatment showed significant enhancement in sperm concentration, motility and liquefaction time. Protodioscin, the main phytochemical agent of the Tribulus genus, acts on sertoli cells, germ cell proliferation and growth of seminiferous tubules. This component is known to convert testosterone into dihydrotestosterone, which plays important roles in male attributes. Our results indicate the therapeutic use of Tribulus terrestris by men presenting altered semen parameters, and/or undergoing infertility treatment.

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INPROCESS

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20170516

Year of Publication
2017
Umbilical cord-derived mesenchymal stem cells on scaffolds facilitate collagen degradation via upregulation of MMP-9 in rat uterine scars.


Embase

Stem Cell Research and Therapy. 8 (1) (no pagination), 2017. Article Number: 84. Date of Publication: 18 Apr 2017.

[Article]

AN: 615550061

Background: Severe injuries of the uterus may trigger uterine scar formation, ultimately leading to infertility or obstetrical complications. To date, few methods have adequately solved the problem of collagen deposition in uterine scars. Umbilical cord-derived mesenchymal stem cells (UC-MSCs) have shown great promise in clinical applications. The objective of this study was to investigate the effect of a scaffold/UC-MSCs construct on collagen degradation and functional regeneration in rat uterine scars following full-thickness excision of uterine walls. Methods: In order to establish a rat model of uterine scars, the uterine wall of approximately 1.0 cm in length and 0.5 cm in width (one-third of the uterine circumference) was excised from each uterine horn. A total of 128 scarred uterine horns from 64 rats were randomly assigned to four groups, including a PBS group (n = 32 uterine horns), scaffold group (n = 32 uterine horns), UC-MSCs group (n = 32 uterine horns) and scaffold/UC-MSCs group (n = 32 uterine horns) to investigate the effect of different treatments on the structure and function of uterine scars. PBS, degradable collagen fibres, UC-MSCs or UC-MSCs mixed with gelatinous degradable collagen fibres were injected into four pre-marked points surrounding each uterine scar, respectively. At days 30 and 60 post-transplantation, a subset of rats (n = 8 uterine horns) from each group was euthanized and serial sections of uterine tissues containing the operative region were prepared. Haematoxylin-eosin staining, Masson's trichrome staining, and immunohistochemical staining for MMP-2, MMP-9, alpha-SMA and VWF were performed. Finally, another subset of rats (n = 16 uterine horns) from each group was mated with male rats at day 60 post-transplantation and euthanized 18 days after the presence of vaginal plugs to check numbers, sizes and weights of fetuses, as well as sites of implantation. Results: The scaffold/UC-MSCs group exhibited obvious collagen degradation compared with the other three groups. At day 60 post-transplantation, the number of MMP-9-positive cells in the scaffold/UC-MSCs group (25.96 +/- 3.63) was significantly higher than that in the PBS group (8.19 +/- 1.61, P < 0.01), the scaffold group (7.25 +/- 2.17, P < 0.01) and the UC-MSCs group (8.31 +/- 2.77, P < 0.01). The pregnancy rate in the scaffold/UC-MSCs group (10/16) was also significantly higher than that in the PBS group (2/16, P < 0.017),
the scaffold group (1/16, P < 0.017) and the UC-MSCs group (3/16, P < 0.017). Conclusions: The scaffold/UC-MSCs system facilitated collagen degradation in uterine scars via upregulation of MMP-9, which was secreted by transplanted UC-MSCs, and promoted regeneration of the endometrium, myometrium and blood vessels in uterine scars. Furthermore, the scaffold/UC-MSCs-treated uterine scars showed nearly complete restoration of receptive fertility.

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100.

Western-style diet, sex steroids and metabolism.
Varlamov O.

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[Article]
AN: 610761020
The evolutionary transition from hunting to farming was associated with introduction of carbohydrate-rich diets. Today, the increased consumption of simple sugars and high-fat food brought about by Western-style diet and physical inactivity are leading causes of the growing obesity epidemic in the Western society. The extension of human lifespan far beyond reproductive age increased the burden of metabolic disorders associated with overnutrition and age-related hypogonadism. Sex steroids are essential regulators of both reproductive function and energy metabolism, whereas their imbalance causes infertility, obesity, glucose intolerance, dyslipidemia, and increased appetite. Clinical and translational studies suggest that dietary restriction and weight control can improve metabolic and reproductive outcomes of sex hormone-related pathologies, including testosterone deficiency in men and natural menopause and hyperandrogenemia in women. Minimizing metabolic and reproductive decline through rationally designed diet and exercise can help extend human reproductive age and promote healthy aging. This article is part of a Special Issue entitled: Oxidative Stress and Mitochondrial Quality in Diabetes/Obesity and Critical Illness Spectrum of Diseases - edited by P. Hemachandra Reddy. Copyright © 2016 Elsevier B.V.

101.

From sperm to offspring: Assessing the heritable genetic consequences of paternal smoking and potential public health impacts.

Beal M.A., Yauk C.L., Marchetti F.

Embase
Individuals who smoke generally do so with the knowledge of potential consequences to their own health. What is rarely considered are the effects of smoking on their future children. The objective of this work was to review the scientific literature on the effects of paternal smoking on sperm and assess the consequences to offspring. A literature search identified over 200 studies with relevant data in humans and animal models. The available data were reviewed to assess the weight of evidence that tobacco smoke is a human germ cell mutagen and estimate effect sizes. These results were used to model the potential increase in genetic disease burden in offspring caused by paternal smoking, with specific focus on aneuploid syndromes and intellectual disability, and the socioeconomic impacts of such an effect. The review revealed strong evidence that tobacco smoking is associated with impaired male fertility, and increases in DNA damage, aneuploidies, and mutations in sperm. Studies support that these effects are heritable and adversely impact the offspring. Our model estimates that, with even a modest 25% increase in sperm mutation frequency caused by smoke-exposure, for each generation across the global population there will be millions of smoking-induced de novo mutations transmitted from fathers to offspring. Furthermore, paternal smoking is estimated to contribute to 1.3 million extra cases of aneuploid pregnancies per generation. Thus, the available evidence makes a compelling case that tobacco smoke is a human germ cell mutagen with serious public health and socio-economic implications. Increased public education should be encouraged to promote abstinence from smoking, well in advance of reproduction, to minimize the transmission of harmful mutations to the next-generation.
Validation study of the SCREENIVF: An instrument to screen women or men on risk for emotional maladjustment before the start of a fertility treatment.


Embase

Fertility and Sterility. (no pagination), 2017. Date of Publication: January 24, 2017.

[Article In Press]

AN: 616131002

Objective: To examine construct and criterion validity of the Dutch SCREENIVF among women and men undergoing a fertility treatment. Design: A prospective longitudinal study nested in a randomized controlled trial. Setting: University hospital. Patient(s): Couples, 468 women and 383 men, undergoing an IVF/intracytoplasmic sperm injection (ICSI) treatment in a fertility clinic, completed the SCREENIVF. Main Outcome Measure(s): Construct and criteria validity of the SCREENIVF. Result(s): The comparative fit index and root mean square error of approximation for women and men show a good fit of the factor model. Across time, the sensitivity for Hospital Anxiety and Depression Scale subscale in women ranged from 61%-98%, specificity 53%-65%, predictive value of a positive test (PVP) 13%-56%, predictive value of a negative test (PVN) 70%-99%. The sensitivity scores for men ranged from 38%-100%, specificity 71%-75%, PVP 9%-27%, PVN 92%-100%. A prediction model revealed that for women 68.7% of the variance in the Hospital Anxiety and Depression Scale on time 1 and 42.5% at time 2 and 38.9% at time 3 was explained by the predictors, the sum score scales of the SCREENIVF. For men, 58.1% of the variance in the Hospital Anxiety and Depression Scale on time 1 and 46.5% at time 2 and 37.3% at time 3 was explained by the predictors, the sum score scales of the SCREENIVF.

Conclusion(s): The SCREENIVF has good construct validity but the concurrent validity is better than the predictive validity. SCREENIVF will be most effectively used in fertility clinics at the start of treatment and should not be used as a predictive tool.

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Status

ARTICLE IN PRESS

Institution
Fluid intelligence, traits of personality and personality disorders in a cohort of adult KS patients with the classic 47, XXY karyotype.

Liberato D., Granato S., Grimaldi D., Rossi F.M., Tahani N., Gianfrilli D., Anzuini A., Lenzi A., Cavaggioni G., Radicioni A.F.

Embase


[Article In Press]

AN: 616100303

Purpose: Klinefelter's syndrome (KS) is associated with specific neurobehavioral features and personality traits. The aim of our study was to investigate fluid intelligence, personality traits and personality disorders (PD) and possible correlations with testosterone in a cohort of adult KS patients. Methods: We analyzed 58 adult KS patients with the classic 47, XXY karyotype. The Structured Clinical Interview for axis II disorders was used to assess DSM IV personality disorders. Personality traits were assessed using MMPI-2. Fluid intelligence was tested by using Raven's Standard Progressive Matrices (SPM) Test. Testosterone blood concentration was measured by CMIA. Results: PD prevalence was 31%. Four altered MMPI scales (Social Responsibility, Dominance, Ego Strength and Repression) were found in more than 40% of patients. Overcontrolled hostility and MacAndrew Alcoholism Scale-Revised scales were altered in the PD-group only. Biz-Odd Thinking and Post-Traumatic Stress Disorder scale were
associated with the presence of personality disorder. The raw SPM score was 44 +/- 10.8 without any significant correlation with testosterone. No significant difference in mean age, SPM raw score and MMPI score was observed between eugonadal, hypogonadal and treated patients. Conclusions: Most KS patients had average fluid intelligence. PD prevalence was higher than in the general population. Testosterone was not correlated with fluid intelligence, personality traits or PD, but a reduction in marital distress was observed in treated patients. This could suggest that testosterone therapy can improve physical symptoms and this effect could also improve relationship abilities and wellness awareness.

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104.

Chronic prostatitis and its detrimental impact on sperm parameters: a systematic review and meta-analysis.

Condorelli R.A., Russo G.I., Calogero A.E., Morgia G., Ia Vignera S.

Embase

Prostatitis is a very common urogenital disease of the male with prevalence ranging from 2.2 to 9.7% worldwide. Interestingly, some recent evidences have showed a significant association between chronic prostatitis (CP) and male infertility including a detrimental effect on sperm parameters, reduction of zinc concentration on semen sperm and production of anti-semen antibodies (ASAs). The aim of the current meta-analysis was to evaluate the association between CP and alteration of semen parameters. Methods: This analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines and we included in the final analysis 27 studies, with a total of 3241 participants, including 381 (11.75%) with chronic bacterial prostatitis (CBP), 1670 (51.53%) with chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) and 1190 (36.72%) controls. Results: CBP was associated with reduction of sperm concentration, sperm vitality, sperm total and progressive motility, while CP/CPPS was related to the reduction of semen volume, sperm concentration, sperm progressive motility and sperm normal morphology. We found that CP was significantly associated with reduced zinc concentration on seminal plasma (SMD: -20.73; p = 0.005). Finally, CP statistically increased the risk of developing ASA on seminal plasma (OR 3.26; p < 0.01). Conclusion: In conclusion, chronic prostatitis showed a detrimental effect on sperm and both CPB or CP/CPPS may differently show negative impact on sperm.
The impact and management of sexual dysfunction secondary to pharmacological therapy of benign prostatic hyperplasia.


Embase

Translational Andrology and Urology. 6 (2) (pp 295-304), 2017. Date of Publication: 01 Apr 2017.

[Review]

AN: 615924625

Benign prostatic hyperplasia (BPH) is one of the most common genitourinary complications in men over 50 years of age and typically presents with lower urinary tract symptoms (LUTS). Classes of medications include alpha1-adrenoceptor blockers, 5alpha-reductase inhibitors, and phosphodiesterase 5 inhibitors. Today, alpha1-adrenoceptor blockers and 5alpha-reductase inhibitors are often combined to give a synergistic effect. A review of the current literature identified several adverse sexual side effects, including erectile dysfunction (ED), decreased libido, orgasmic disorders, and ejaculatory disorders. We believe it is important to know the extent of these side effects, as the clinician and patient will need to decide the cost of improved voiding symptoms. The chief adverse effect is ejaculatory disorders, including the absence of ejaculation. Clinical consideration for BPH should include the elements of male sexual function, patients’ age, and the characteristics and comprehensive effects of each group of drugs. Methodological bias in clinical studies, such as the subjective evaluation of the sexual side effect, makes it difficult to determine the ideal drug for treatment.

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The effectiveness of zinc supplementation in men with isolated hypogonadotropic hypogonadism.

Embase

A multicenter, open-label, randomized, controlled superiority trial with 18 months of follow-up was conducted to investigate whether oral zinc supplementation could further promote spermatogenesis in males with isolated hypogonadotropic hypogonadism (IHH) receiving sequential purified urinary follicular-stimulating hormone/human chorionic gonadotropin (uFSH/hCG) replacement. Sixty-seven Chinese male IHH patients were recruited from the Departments of Endocrinology in eight tertiary hospitals and randomly allocated into the sequential uFSH/hCG group (Group A, n = 34) or the sequential uFSH plus zinc supplementation group (Group B, n = 33). In Group A, patients received sequential uFSH (75 U, three times a week every other 3 months) and hCG (2000 U, twice a week) treatments. In Group B, patients received oral zinc supplementation (40 mg day-1) in addition to the sequential uFSH/hCG treatment given to patients in Group A. The primary outcome was the proportion of patients with a sperm concentration >1.0 x 106 ml-1 during the 18 months. The comparison of efficacy between Groups A and B was analyzed. Nineteen of 34 (55.9%) patients receiving sequential uFSH/hCG and 20 of 33 (60.6%) patients receiving sequential uFSH/hCG plus zinc supplementation achieved sperm concentrations >1.0 x 106 ml-1 by intention to treat analyses. No differences between Group A and Group B were observed as far as the efficacy of inducing spermatogenesis (P = 0.69). We concluded that the sequential uFSH/hCG plus zinc supplementation regimen had a similar efficacy to the sequential uFSH/hCG treatment alone. The additional improvement of 40 mg day-1 oral zinc supplementation on spermatogenesis and masculinization in male IHH patients is very subtle.

Status
107.
Apostolidis A., Rantell A., Anding R., Kirchner-Hermanns R., Cardozo L.

Embase
Neurology and Urology. 36 (4) (pp 869-875), 2017. Date of Publication: April 2017.
[Review]
AN: 615708517

AIM: To discuss available data on the links between LUTD and sexual dysfunction, what is still unknown about the causative effect of disease processes on sexual function (SF), and to suggest proposals for further research. METHODS: At the 2015 International Consultation on Incontinence-Research Society (ICI-RS), a multi-disciplinary group presented a literature search of what is known about the effect of LUTD on SF in men and women. Wider discussions regarding knowledge gaps, and ideal research methodology ensued and are presented.

RESULTS: The underlying mechanisms of the impact of LUTD on SF remain largely unknown. Risk factors for the metabolic syndrome may cause both LUTS and ED in men, and their improvement may improve both conditions. In women, neurovascular changes may be common in LUTD and FSD. Successful LUTS management results in FSD improvement, but the mechanisms are ill understood. Gaps in standardization of sexual dysfunction terminology, variations of assessment, and treatment in clinical practice and research make most studies not comparable. The sensitive knowledge and subjective nature of the problem present challenges and often result in neglecting it.

CONCLUSION: Neurovascular and hormonal factors, but also indirect effects may link LUTD to SD in both sexes, but the evidence is not robust and the mechanisms unclear. There is a need for defining the terminology and standardizing outcomes assessed in clinical trials. The multifactorial nature of SF in both sexes makes trial design challenging and "real world" studies may prove more beneficial for patients' outcomes and clinicians' understanding.

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2017
The aim was to examine the value of different covariates in the prediction of intrauterine insemination (IUI) success. Between July 2011 and September 2015, data from 1401 IUI cycles with homologous semen in 556 couples were collected prospectively, by questionnaire, in a tertiary referral infertility centre. Statistical analysis was performed using generalized estimating equations (GEEs). GEEs were used instead of an ordinary logistic regression model to take into account the correlation between observations from the same person. The primary outcome parameter was clinical pregnancy rate (CPR), confirmed with a gestational sac and fetal heartbeat on ultrasonography at 7-8 weeks. An overall CPR of 9.5% per cycle was observed. Univariate statistical analysis revealed female and male age, male smoking, female body mass index, ovarian stimulation and inseminating motile count (IMC) as covariates significantly influencing CPR per cycle. Multivariate GEE analysis revealed that the only valuable prognostic covariates included female age, male smoking and infertility status (i.e. primary/secondary infertility). IMC showed a significant curvilinear relationship, with first an increase and then a decrease in pregnancy rate. Copyright © 2017 Reproductive Healthcare Ltd.
Testosterone replacement therapy improves health-related quality of life for patients with late-onset hypogonadism: a meta-analysis of randomized controlled trials.


Andrologia. 49 (4) (no pagination), 2017. Article Number: e12630. Date of Publication: 01 May 2017.

Although testosterone replacement therapy can restore serum testosterone concentrations to normal level in late-onset hypogonadism patients, whether it can improve patients' quality of life remains uncertain. Therefore, we perform a meta-analysis of randomized controlled trials on this issue. Five randomized controlled trials total 1,212 patients were included. Fixed-effect model was used to calculate the weighted mean difference of score of Aging Males' Symptom rating scale. Our result reveals that testosterone replacement therapy improves patients' health-related quality of life in terms of the decrease in the AMS total score \[WMD = -2.96 (-4.21, -1.71), p < .00001\] and the psychological \[WMD = -0.89 (-1.41, -0.37), p = .0008\], somatic \[WMD = -0.89 (-1.41, -0.37), p = .0008\] and sexual \[WMD = -1.29 (-1.75, -0.83), p < .00001\] subscale score.

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The association between polymorphism of eNOS and male infertility in several studies was controversial. To explore a more precise estimation of the association, a meta-analysis of eight case-control studies, including 1,968 cases and 1,539 controls, were selected. The meta-analysis was conducted by calculating the pooled odds ratio (OR) with a 95% confidence interval (95% CI). Overall, the association between T786C and risk of male infertility was obvious (TC vs. TT: OR, 1.20; 95% CI, 1.01-1.42; CC vs. TT: OR, 3.37; 95% CI, 1.65-6.87; TC/CC vs. TT: OR, 1.47; 95% CI, 1.25-1.73; CC vs. TT/TC: OR, 3.18; 95% CI, 1.54-6.56; TC vs. TT: OR, 1.65; 95% CI, 1.27-2.03). However, no overall association was observed between the other two polymorphisms of eNOS (G894T and 4a4b) and male infertility. Stratified analysis showed that significantly strong association between T786C polymorphism and semen quality was present in all three types of male infertility (azoospermia, oligozoospermia and asthenozoospermia). In the subgroup analysis based on ethnicity, both T786C and 4a4b could influence the risk of male infertility in Asian and Caucasian. Further studies of polymorphisms of eNOS with their biological functions are needed to understand the role in the development of male infertility.
111.
Effect of captopril on semen quality.
Banihani S.A.
Embase
Andrologia. 49 (4) (no pagination), 2017. Article Number: e12641. Date of Publication: 01 May 2017.
[Review]
AN: 611348073
Various studies (direct and indirect) have presented the effect of captopril, a universally used antihypertensive medication, on semen quality; yet, this effect is still collectively unreviewed. This review systematically discusses and summarises the effect of captopril on semen quality. We searched all published articles in the MEDLINE electronic database since June 1985 until January 2016 using the keywords "captopril" and "sperm," and certain supporting articles were reviewed and considered, if relevant. In conclusion, up to the present time, captopril does not appear to induce a striking change in semen quality, and hence on male infertility, while it may affect the rate of spermatozoa-egg fusion as it inhibits the activity of angiotensin-converting enzyme that is released during capacitation and the acrosome reaction. Further research, mainly clinical, is still desired to prove these effects.

Copyright © 2016 Blackwell Verlag GmbH
Current perspective of diethylstilbestrol (DES) exposure in mothers and offspring.
Al Jishi T., Sergi C.
Embase
Reproductive Toxicology. 71 (pp 71-77), 2017. Date of Publication: 01 Aug 2017.
[Review]
AN: 615924388
Diethylstilbestrol (DES) was an orally active estrogen prescribed to the pregnant women to prevent miscarriages. DES is known as a 'biological time bomb' and long-term effects of DES have been recorded in the mothers exposed to DES and their offspring (DES-daughters and DES-sons). Adverse pregnancy outcomes, infertility, cancer, and early menopause have been discovered in women exposed to DES, and some events occur in their offspring and subsequent generations. An increased risk of breast cancer is not limited to the DES-exposed daughters. There is an urgent need to find ways to stop the inheritance cycle of DES and prevent adverse effects of DES in the future generations. The present article reviews the health implications of DES exposure and screening exams currently recommended to DES daughters and their offspring. Copyright © 2017 Elsevier Inc.
Selective serotonin reuptake inhibitors versus placebo in patients with major depressive disorder. A systematic review with meta-analysis and Trial Sequential Analysis.


Embase


[Article]

AN: 614343148

Background: The evidence on selective serotonin reuptake inhibitors (SSRIs) for major depressive disorder is unclear. Methods: Our objective was to conduct a systematic review assessing the effects of SSRIs versus placebo, 'active' placebo, or no intervention in adult participants with major depressive disorder. We searched for eligible randomised clinical trials in The Cochrane Library's CENTRAL, PubMed, EMBASE, PsycLIT, PsycINFO, Science Citation Index Expanded, clinical trial registers of Europe and USA, websites of pharmaceutical companies, the U.S. Food and Drug Administration (FDA), and the European Medicines Agency until January 2016. All data were extracted by at least two independent investigators. We used
Cochrane systematic review methodology, Trial Sequential Analysis, and calculation of Bayes factor. An eight-step procedure was followed to assess if thresholds for statistical and clinical significance were crossed. Primary outcomes were reduction of depressive symptoms, remission, and adverse events. Secondary outcomes were suicides, suicide attempts, suicide ideation, and quality of life. Results: A total of 131 randomised placebo-controlled trials enrolling a total of 27,422 participants were included. None of the trials used ‘active’ placebo or no intervention as control intervention. All trials had high risk of bias. SSRIs significantly reduced the Hamilton Depression Rating Scale (HDRS) at end of treatment (mean difference -1.94 HDRS points; 95% CI -2.50 to -1.37; P < 0.00001; 49 trials; Trial Sequential Analysis-adjusted CI -2.70 to -1.18); Bayes factor below predefined threshold (2.01*10^-23). The effect estimate, however, was below our predefined threshold for clinical significance of 3 HDRS points. SSRIs significantly decreased the risk of no remission (RR 0.88; 95% CI 0.84 to 0.91; P < 0.00001; 34 trials; Trial Sequential Analysis adjusted CI 0.83 to 0.92); Bayes factor (1426.81) did not confirm the effect). SSRIs significantly increased the risks of serious adverse events (OR 1.37; 95% CI 1.08 to 1.75; P = 0.009; 44 trials; Trial Sequential Analysis-adjusted CI 1.03 to 1.89). This corresponds to 31/1000 SSRI participants will experience a serious adverse event compared with 22/1000 control participants. SSRIs also significantly increased the number of non-serious adverse events. There were almost no data on suicidal behaviour, quality of life, and long-term effects. Conclusions: SSRIs might have statistically significant effects on depressive symptoms, but all trials were at high risk of bias and the clinical significance seems questionable. SSRIs significantly increase the risk of both serious and non-serious adverse events. The potential small beneficial effects seem to be outweighed by harmful effects. Systematic review registration: PROSPERO CRD42013004420. Copyright © 2017 The Author(s).

Status
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Institution
(Jakobsen, Katakam, Schou, Hellmuth, Stallknecht, Leth-Moller, Iversen, Banke, Petersen, Klingenberg, Ebert, Timm, Lindschou, Gluud) Copenhagen University Hospital, The Copenhagen Trial Unit, Centre for Clinical Intervention Research, Department 7812 Rigshospitalet, Blegdamsvej 9, Rigshospitalet, Copenhagen DK 2100, Denmark
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20170309
The mean age of the world population has steadily increased in the last decades, as a result of increased life expectancy and reduced birth rate. Global aging has led to a greater worldwide cost for healthcare: hormonal alterations contribute to the pathogenesis of several conditions and might cause a significant reduction in the perceived sense of well-being. Menopause is archetypal of hormonal alterations occurring during aging: in males, sex hormones do not decrease abruptly, yet testosterone levels decrease steadily and continuously during aging, ultimately resulting in late-onset hypogonadism. Treatment of this condition might mitigate most symptoms; however, testosterone replacement therapy (TRT) should be prescribed only in selected patients and it should not be considered as an antiaging treatment. In recent years, different authors have questioned health risks associated with testosterone treatment; while position statements from many scientific societies seem to be reassuring, the Food and Drug Administration has issued a warning in regard to the possible side effects of this therapy. We aim to review recent controversies and discoveries in regard to TRT.
Oral probenecid improves sperm motility in men with spinal cord injury.
Ibrahim E., Aballa T.C., Lynne C.M., Brackett N.L.

Embase
[Article In Press]
AN: 615890380

Study Design: Prospective cohort study (twenty men with spinal cord injury [SCI]). Objective: Determine if administration of oral probenecid results in improved sperm motility in men with SCI.
Setting: Major university medical center. Methods: Twenty men with SCI were administered probenecid for 4 weeks (250 mg twice a day for 1 week, followed by 500 mg twice a day for 3 weeks). Semen quality was assessed at three time points: pre-treatment, post-treatment (immediately after the 4-week treatment), and follow-up (4 weeks after the last pill was ingested).
Result(s): Probenecid was well-tolerated by all subjects. Sperm motility improved in each subject after 4 weeks of oral probenecid. The mean percent of sperm with progressive motility increased from 19% to 26% (P < 0.05). A more striking increase was seen in the mean percent of sperm with rapid linear motility, from 5% to 17%, (P <0.001). This improvement continued into the four week follow up period. Similar improvements were seen in the total motile sperm count (15 million, 28 million, and 27 million at pre-treatment, post-treatment, and follow-up, respectively). Sperm concentration was not significantly different at pre-treatment, post-treatment, and follow-up, (52 million, 53 million and 53 million, respectively). Conclusion: This study showed that administration of an oral agent (probenecid) known to interfere with the pannexin-1 cellular membrane channel, can improve sperm motility in men with spinal cord injury. It is the first study to report improved sperm motility after oral medication in men with SCI. Copyright © 2017 The Author(s). Published by Taylor & Francis.

Status
ARTICLE IN PRESS

Institution
Evaluation of the effect of indomethacin and piroxicam administration before embryo transfer on pregnancy rate.
Kumbasar S., Gul O., Sik A.

Embase

[Article]
AN: 614477838

Aim: The aim of this study was to evaluate the effect of non-steroidal anti-inflammatory drug (NSAID) administration before embryo transfer (ET) on pregnancy rates in women undergoing in vitro fertilization/intracytoplasmic sperm injection ET. Methods: Our study included 255 patients diagnosed with primary or secondary infertility caused by a male or tubal-related factor, endometriosis or unexplained factors. The patients were divided randomly into three groups. Two groups were administered oral piroxicam (10 mg capsules) or 100 mg indomethacin (rectal suppository), respectively, 1-2 h before ET. As a control, the third group did not receive any form of treatment before ET. Basal levels of follicle-stimulating hormone, luteinizing hormone, and level 17beta-estradiol on the day of human chorionic gonadotropin administration, the collected and transferred number of embryos, and the number of grade A embryos obtained were determined in all patients. Results: The implantation, clinical pregnancy, and miscarriage rates of the groups were compared. The clinical pregnancy rate per ET and the implantation rate were 35.2% and 12.15% in the piroxicam group, 31.7% and 10.9% in the indomethacin group, and 32.9% and 12.5% in the control, respectively. The miscarriage rates of groups 1, 2 and 3 were 12%, 11.7%
and 11.7%, respectively (P = 0.964). The differences in clinical pregnancy rates among the groups were not statistically significant (P = 0.887). There were also no significant differences in the implantation rates (P = 0.842). Conclusion: These results suggest that NSAID administration before ET has no additional effect on pregnancy outcome in patients undergoing in vitro fertilization. Copyright © 2017 Japan Society of Obstetrics and Gynecology Status
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2017

117.
Rapid and visual Chlamydia trachomatis detection using loop-mediated isothermal amplification and hydroxynaphthol blue.
Choopara I., Arunrut N., Kiatpathomchai W., Dean D., Somboonna N.
Embase
Letters in Applied Microbiology. 64 (1) (pp 51-56), 2017. Date of Publication: 01 Jan 2017. [Article]
AN: 613711900
We developed an assay comprising crude DNA lysis by simple heat treatment coupled loop-mediated isothermal amplification with hydroxynaphthol blue for Chlamydia trachomatis detection (petty patent pending), and evaluated the developed assay for its feasibility as a one-step point-of-care detection on 284 endocervical swab specimens from clinically symptomatic C. trachomatis and healthy subjects. This assay is sensitive to 0.04 pg of ompA, specific with six primers targeting C. trachomatis ompA region, rapid (45 min total assay time), inexpensive
(approx. 3 USD/reaction), does not require sophisticated instrumentation, and has comparable assay effectiveness (95% specificity, 90-100% sensitivity) to bacterial DNA isolation by a commercial kit coupled with polymerase chain reaction and gel electrophoresis (98-100% specificity, 87-100% sensitivity) based on the clinical samples test. The test result could be read by naked eye through the colour change from violet (negative) to sky blue (positive) for C. trachomatis-infected specimens. Further, this assay uses all safe chemical reagents and is hence safe to the users. Significance and Impact of the Study: Chlamydia trachomatis is the major bacterial sexually transmitted disease worldwide. The clinical symptoms are broad, and chronic C. trachomatis infections could lead to blindness, ectopic pregnancy, sterility in males and females, and a higher risk of the development of cervical cancer. The result indicates the potential usefulness of our crude DNA lysis coupled loop-mediated isothermal amplification with hydroxynaphthol blue for a simple, rapid, specific, sensitive and cost-effective assay for C. trachomatis detection from suspected specimens. This assay offers an alternative in the clinical diagnosis of C. trachomatis in resource-limited health-care facilities and clinical laboratories in developing countries, and in field tests.  Copyright © 2016 The Society for Applied Microbiology

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The comparison of laparoscopic and microsurgical varicocelectomy in infertile men with varicocele on paternity rate 12 months after surgery: a prospective randomized controlled trial.
Bryniarski P., Taborowski P., Rajwa P., Kaletka Z., Zyczkowski M., Paradysz A.

Embase
Andrology. 5 (3) (pp 445-450), 2017. Date of Publication: May 2017.
[Article]
AN: 615119256

The best surgical approach for varicocelectomy is still unknown, however more and more physicians favour subinguinal microsurgery. The aim of this study was to find whether microsurgical approach is superior to laparoscopic varicocelectomy in terms of pregnancy rate, fertility potential, endocrinological function of the testis, erectile dysfunction and testicle volume increase. It was a prospective, non-masked, parallel-group randomized controlled trial with one to one allocation. It was conducted at authors' institution and designed as per protocol study. From 2012 till 2015 84 patients were randomly allocated to two groups. First group consisted of 42 patients who underwent laparoscopic varicocelectomy, whereas patients from the second group underwent microsurgical varicocelectomy. The indications for varicocelectomy consisted of infertility >1 year, palpable left-sided varicocele and at least one impaired semen parameter (sperm concentration <15 mln/mL; total motility<40%; progressive motility <32%, vitality <58% or normal morphology <4%). The primary goal was to show superiority of microsurgical varicocelectomy over laparoscopic varicocelectomy in terms of pregnancy rate. The secondary endpoints comprised assessment of sperm parameters in three-month intervals after intervention until one year. Other points included, LH, FSH and testosterone levels as well as testicle volume and International Index of Erectile Function. From each group five patients were lost during the follow-up period. The primary endpoint was not achieved - pregnancy rate in first and second group was 29.7% and 40.5% respectively (p = 0.34). Analysis of the sperm parameters after surgery revealed significant statistical difference in total motility, progressive motility and morphology in favour of microsurgical approach. Both methods showed improvement in all sperm parameters. There were no differences in hormonal levels as well as in erectile function and testicle volume between groups. Small number of patients in both groups are the main limitation.
119.
The Dilemma of Adolescent Varicoceles: Do They Really Have to Be Repaired?.
Sack B.S., Schafer M., Kurtz M.P.
Embase
Current Urology Reports. 18 (5) (no pagination), 2017. Article Number: 38. Date of Publication: 01 May 2017.
[Review]
AN: 614857955
The primary indication for varicocele repair in adults, that of failed paternity, must be substituted in the adolescent population with surrogate parameters of testicular size differential and semen analysis. Making recommendations based on these two parameters is incredibly difficult because studies often have contradictory findings, different patient populations, and lack of long-term follow up of the key endpoint, paternity. Therefore, it is not a surprise that recommendations for adolescent varicocele repair are general (with some exceptions) and necessarily so because of limitations in quality of evidence. Apart from pain, all indications for varicocele repair in adolescence remain controversial. This highlights the most important task for future studies: to prevent pediatric urologists from allowing a potentially damaging process to go untreated, while at
the same time avoiding unnecessary intervention on a highly prevalent condition. Copyright © 2017, Springer Science+Business Media New York.


Status EMBASE

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Year of Publication 2017

120.

Embase Andrology. 5 (3) (pp 414-422), 2017. Date of Publication: May 2017. [Article]

AN: 614869364

The standard FSH treatment is based on a 3 months period, after which both quantitative/qualitative improvement of sperm parameters and increased pregnancy rate were reported. In this prospective clinical trial, for the first time, we studied (i) Sperm hyaluronic acid binding capacity after highly purified FSH (hpFSH) treatment; (ii) the effect after short-term and standard treatment on this functional parameter. As secondary objective, we analyzed three SNPs on FSHbeta and FSHR genes to define their potential predictive value for responsiveness. From a total of 210 consecutive patients, 40 oligo- and/or astheno- and/or teratozoospermic
patients fulfilled the inclusion criteria. Treatment consisted in hpFSH 75 IU/L every other day for 3 months. To avoid potential biases derived from the lack of placebo, we analyzed each patient after 4-6 months of 'wash-out' period. After FSH treatment, we observed a statistically significant (p < 0.001) improvement of the percentage of hyaluronic acid bound spermatozoa from basal to T1 (after 1 month) and to T3 (after 3 months). Importantly, these values returned to near-baseline value after the wash-out. The same results were detected for total motile sperm count after 3 months with return to baseline after wash-out. Forty-two percent of patients responded to the therapy with increasing hyaluronic acid binding capacity above the double of the Intraindividual Variation (IV) while 24% of patients reached above the normal Sperm-Hyaluronan Binding Assay (HBA) value. Further increase in 'responders' was observed at T3. The responsiveness to treatment resulted independent from FSHR/FSHbeta polymorphisms. The significant positive effect on sperm maturity after 1 month opens novel therapeutic perspectives. In view of both the high cost and the relative invasiveness of treatment, the short protocol (1 month) could represent a viable FSH treatment option prior Assisted Reproductive Techniques since FSH, by acting on sperm maturation, increases the proportion of functionally competent cells. Copyright © 2017 American Society of Andrology and European Academy of Andrology


Status EMBASE

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The association of a probiotic with a prebiotic (Flortec, Bracco) to improve the quality/quantity of spermatozoa in infertile patients with idiopathic oligoasthenoteratospermia: a pilot study.
Maretti C., Cavallini G.

Embase
Andrology. 5 (3) (pp 439-444), 2017. Date of Publication: May 2017.

The hypothesis that the assumption of a probiotic associated with a prebiotic (Flortec, Bracco; one sachet contains: Lactobacillus paracasei B21060 5 x 10^9 cells + arabinogalctan 1243 mg + oligo-fructosaccharides 700 mg + l-glutamine 500 mg) could improve the quality and quantity of spermatozoa in idiopathic oligoasthenoteratospermia (iAOT) patients to a larger extent than a control substance (starch) was tested. Forty-one patients with no chromosomal aberrations were randomized into two groups: 20 received Flortec, one sachet per day for 6 months, whereas 21 received the control substance. The following data were collected: clinical history, scrotal Doppler scans, Y microdeletion, karyotype and cystic fibrosis screens, follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), testosterone (T), and prolactin (PRL) levels, and two semen analyses. Both the Flortec and the starch groups underwent two semen analyses and one FSH, LH, T, E2, and PRL measurement in the blood, at the beginning of the study, and after 6 months. The comparisons were carried out using a non-parametric (Wilcoxon signed rank) test. The side effects were assessed and compared using the chi-squared test. Group 1 (Flortec) had their sperm count improved: volume of the ejaculate (median from 2.4 to 3.1 mL; p < 0.01), sperm concentration (median: from 15.2 x 10^6/mL to 28.3 x 10^6/39 mL; p < 0.01), progressive motility (median: from 16.2 to 42.0%; p < 0.01), and the percentage of typical forms (median: from 7 to 16.3%; p < 0.01); in addition, their FSH, LH, and T levels improved (p < 0.01), while those of E2 and PRL did not. Group 2 (control substance) had no modification in 42 of the parameters studied. There were no side effects in either group. These data showed that Flortec constitutes a safe therapy for improving the volume of the ejaculate and the quality/quantity of spermatozoa in iOAT patients. Copyright © 2017 American Society of Andrology and European Academy of Andrology

PMID

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122.
Treatment of osteoporosis secondary to hypogonadism in prostate cancer patients: A prospective randomized multicenter international study with denosumab vs. alendronate.
Doria C., Mosele G.R., Solla F., Maestretti G., Balsano M., Scarpaa R.M.
Embase
Minerva Urologica e Nefrologica. 69 (3) (pp 271-277), 2017. Date of Publication: 2017.
[Article]
AN: 615774801
BACKGROUND: Osteoporosis is a complication of androgen deprivation therapy (ADT) in men with prostate carcinoma. This is a multicenter, randomized, double-blind prospective study on use of denosumab versus alendronate in the therapy of secondary osteoporosis related to ADT. METHODS: A total of 234 patients with diagnosis of osteoporosis underwent ADT for prostate cancer were enrolled. Patients were randomly assigned 1:1 to receive denosumab 60 mg subcutaneously every 6 months or alendronate (70 mg/week) for 2 years. All patient received supplemental Vitamin D (600 I U/day) and supplemental calcium to maintain a calcium intake of 1200 mg per day. Effectiveness of therapy in both groups (denosumab group and alendronate group) was assessed by changes in bone turnover markers (BTMs), bone mineral density, fracture incidence, Visual Analogue Scale score for back pain, and Short Form-8 health survey score for health-related quality of life. RESULTS: In the denosumab study group, level of BTMs for bone formation were significantly increased from baseline at all time points during the study (P<0.001); in the alendronate study group level of BTMs for bone formation were increased too (P>0.05). Mean changes in BMD at final follow-up differed significantly between two groups. BMD changes at the lumbar spine at 24 months were 5.6% with denosumab vs.-1.1% with alendronate (P<0.001). CONCLUSIONS: Denosumab and alendronate showed similar clinical efficacy in the therapy of ADT-related osteoporosis in men with prostate carcinoma; both drugs provided significant improvements in back pain and general health conditions. Denosumab showed
significant increase of BTMs and BMD than alendronate with lower rate of new vertebral fractures.

Status
INPROCESS

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123.
Feng S., Tian Y., Liu W., Li Z., Deng T., Li H., Wang K.

Embase

[Article]
AN: 613373648

Purpose: To evaluate the clinical efficiency and safety of PAE treating moderate-to-severe LUTS related to BPH. Materials and Methods: A systematic literature search was performed using PUBMED, EMBASE, Cochrane database of systematic review, and Web of Science, up to April 2016, to identify eligible studies. The Cochrane Collaboration's RevMan 5.3 was used to analyze the extracted data. Random- or fixed-effect model was selected to fit the pooled out heterogeneity. Results: 20 eligible studies were included in this meta-analysis. Synthetic data
showed that there were statistically significant improvements in IPSS (MD = -13.25; 95% CI -14.81 to -11.69; P < 0.00001), QoL score (MD = -2.34; 95% CI -2.69 to -2.00, P < 0.00001), PSA level (MD = -1.33; 95% CI -1.86 to -0.80; P < 0.00001), PV (MD = -28.00; 95% CI -35.94 to -20.07; P < 0.00001), Qmax (MD = 5.51; 95% CI 4.62 to 6.40; P < 0.00001), and PVR (MD = -67.8; 95% CI -81.35 to -53.60; P < 0.00001). There was no significant difference in IIEF score (MD = 0.93; 95% CI 0.43-1.42; P = 0.07). Major complications following PAE include pain in the perineum, retropubic area, and/or urethra (9.4%), and hematuria (9.0%). Conclusions: PAE should be considered to be the very promising alternative treatment for those who do not want or cannot tolerate surgical treatment, with its benefits on IPSS, QoL score, PSA level, PV, Qmax, and PVR without affecting erectile function. Copyright © 2016, Springer Science+Business Media New York and the Cardiovascular and Interventional Radiological Society of Europe (CIRSE).


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124.
The mechanisms of cyclophosphamide-induced testicular toxicity and the protective agents.
Ghobadi E., Moloudizargari M., Asghari M.H., Abdollahi M.
Introduction: Cyclophosphamide (CP) is an alkylating antineoplastic agent with known toxicity to the male reproductive system. Areas covered: This review summarizes the known mechanisms by which CP exerts its toxic effects on the male reproductive system and the methods utilized to prevent such effects so that it could be further investigated and applied in clinical use. Keywords including ['Cyclophosphamide' AND 'male reproductive' OR 'sperm toxicity' OR 'spermatotoxicity' OR 'infertility'] were searched through Google Scholar, PubMed and Scopus databases based on PRISMA guidelines. After removing duplicates and irrelevant data, 76 papers were reviewed concerning the outcomes of treatment of male mice, rats, and humans with CP and the effects of co-administration of various natural and synthetic compounds on male reproductive system.

Expert opinion: CP exerts its effect mainly by inducing oxidative stress and changing gene expression in spermatocytes variably during different stages of development. These effects could be either restored or prevented by the administration of compounds with antioxidant properties and those which target the biochemical alterations induced by CP.

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Association between methionine synthase reductase A66G polymorphism and male infertility: A meta-analysis.

Xu W., Zhang L., Wu X., Jin F.

Embase


[Article]

AN: 615633343

The aim of this meta-analysis was to assess the methionine synthase reductase (MTRR) gene 66A > G polymorphism and male infertility susceptibility. Studies were identified in PubMed and Embase databases. An odds ratio (OR) was used to assess the relationship between MTRR 66A > G polymorphism and male infertility risk. A total of seven case-control studies containing 1438 patients and 1363 controls were enrolled in the meta-analysis. Our results showed that no association exists between the MTRR 66A > G polymorphism and male infertility risk in the total population (GG vs. AA: OR = 1.29, 95% confidence interval [CI] = 1.00-1.66; GA vs. AA: OR = 1.09, 95% CI = 0.92-1.30; dominant model: OR = 1.13, 95% CI = 0.96-1.34; recessive model: OR = 0.83, 95% CI = 0.67-1.03). In a subgroup analysis by nationality, the 66A > G polymorphism was not associated with male infertility in both Asians and Caucasians. In a subgroup analysis stratified by male infertility type, significant association was found with oligoasthenozoospermia (OAT) (GG vs. AA: OR = 1.83, 95% CI = 1.24-269; GA vs. AA: OR = 1.36, 95% CI = 0.88-2.11; dominant model: OR = 1.51, 95% CI = 1.13-2.01; recessive model: OR = 0.62, 95% CI = 0.46-0.85). In summary, the present meta-analysis suggests that MTRR 66A > G polymorphism may be associated with OAT risk. Copyright © 2017 Begell House, Inc.

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Efficacy of Holmium Laser Transurethral Incision of the Prostate in Symptomatic Mild-to-Moderate Benign Prostate Enlargement Based on Preoperative Characteristics.
Suh Y.S., Ko K.J., Kim T.H., Sung H.H., Lee K.-S.

[Article In Press]
AN: 615681833

Objective: To investigate the efficacy of Holmium laser transurethral incision of the prostate (Ho-TUIP) with preoperative characteristics based on urodynamic parameters. Methods: The medical records of 40 consecutive cases of Ho-TUIP in patients unresponsive to medical treatment were retrospectively reviewed. The efficacy of Ho-TUIP was analyzed according to preoperative factors, including urodynamic parameters. Treatment success was confirmed if overall efficacy demonstrated an improvement that was "good or greater" according to the criteria developed by Homma et al. Predictive factors of treatment success were analyzed using logistic regression analysis with demographics, symptom questionnaires, prostate size, and urodynamic parameters. Postoperative complications and Global Response Assessment (GRA) were investigated.

Results: Mean age was 60.9 years (range 37-84), mean follow-up period was 36.6 months (range 6.3-114.8), and mean prostate size was 23.5 mL (range 12.7-39.5). All patients underwent medical treatment before Ho-TUIP, and mean medication duration was 50.5 months (range 3.4-140.0). The treatment success rate was 60.0%. Treatment success rates were higher in the bladder outlet obstruction index (BOOI) >20 group (n = 26) than in the BOOI <20 group (n = 14) (p = 0.003). In logistic regression analysis, BOOI >20 was a predictor of treatment success (OR 7.60, 95% CI 1.60-35.90, P = 0.010). Among patients who maintained an active sex life, 77.8% (14/18) reported retrograde ejaculation. In terms of GRA, 81.5% (31/38, two patients expired) of patients improved at the final follow-up. Conclusions: Ho-TUIP is an effective procedure with tolerable complications for the treatment of symptomatic mild-to-moderate BPE in patients with BOOI >20 that are unresponsive to medical treatment. Copyright © 2017 Wiley Publishing Asia Pty Ltd.
127.
Meta-analysis of Results of Testosterone Therapy on Sexual Function Based on International Index of Erectile Function Scores.
Corona G., Rastrelli G., Morgentaler A., Sforza A., Mannucci E., Maggi M.
Embase
[Article In Press]
AN: 615612217
Context: The interpretation of available clinical evidence related to the effect of testosterone (T) treatment (TTh) on sexual function has been inconsistent, in part due to the use of different and self-reported measures to assess outcomes. The International Index of Erectile Function (IIEF) is the most frequently used validated tool to assess male sexual function. Objective: To perform a meta-analysis of available data evaluating the effect of TTh on male sexual function using IIEF as the primary outcome. Evidence acquisition: An extensive Medline, Embase, and Cochrane search was performed including all placebo-controlled randomized clinical trials enrolling men comparing the effect of TTh on sexual function. Evidence synthesis: Out of 137 retrieved articles, 14 were
included in the study enrolling 2298 participants, with a mean follow-up of 40.1 wk and mean age of 60.2. +/- 6.5 yr. Using IIEF-erectile function domain (IIEF-EFD) as the outcome, we found that TTh significantly improved erectile function compared with placebo (mean difference = 2.31 [1.41;3.22] IIEF-EFD score, p < .0001). Patients with more severe hypogonadism (total T. < .8 nmol/l) reported greater changes in final IIEF-EFD score when compared with those with a milder T deficiency (total T. < .12 nmol/l; 1.47 [0.90;2.03] and 2.95 [1.86;4.03] for total T. < .12 nmol/l and <8 nmol/l, respectively, Q = 5.61, p = 0.02). The magnitude of the effect was lower in the presence of metabolic derangements, such as diabetes and obesity. Other aspects of sexual function, as evaluated by IIEF subdomains, were also improved with TTh including libido, intercourse satisfaction, orgasm, and overall sexual satisfaction. Conclusions: TTh significantly improves erectile function and other sexual parameters as measured by IIEF in hypogonadal men. These results argue that sexual dysfunction should be considered a hallmark manifestation of T deficiency, since those symptoms can be significantly improved with normalization of serum T. In addition, these results suggest that TTh alone may be considered a reasonable treatment for hypogonadal men with milder degrees of erectile dysfunction, whereas the addition of other treatments, such as phosphodiesterase type 5 inhibitors, may be more appropriate for men with more severe erectile dysfunction. Patient summary: We investigated the effect of testosterone treatment on sexual function by performing a meta-analysis of all available studies that used the most frequently used assessment tool, the International Index of Erectile Function. We found that testosterone treatment significantly improves erectile dysfunction, as well as other aspects of sexual function, in men with testosterone deficiency. This treatment may be all that is required for hypogonadal men with milder erectile dysfunction; however, additional treatments may be necessary in more severe cases. The present meta-analysis investigates the effect of testosterone treatment (TTh) on sexual function over placebo considering the International Index of Erectile Function (IIEF) as final outcome. Our data indicate that TTh significantly improves erectile function and other sexual parameters as measured by IIEF. The effects of TTh on erectile dysfunction are greater in patients with lower testosterone levels at baseline and lower in the presence of metabolic derangements, such as diabetes and obesity. The observed mean 2.3-point increase in IIEF-erectile function domain score is clinically meaningful, suggesting that TTh alone may be a reasonable treatment option in men with milder form of erectile dysfunction whereas the addition of other treatments, such as phosphodiesterase type 5 inhibitors, may be more appropriate for men with more severe erectile dysfunction. Copyright © 2017.

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(Corona, Sforza) Endocrinology Unit, Medical Department, Azienda Usl Bologna Maggiore-Bellaria Hospital, Bologna, Italy (Rastrelli, Mannucci, Maggi) Andrology and Sexual Medicine
128.
Early weight loss predicts the reduction of obesity in men with erectile dysfunction and hypogonadism undergoing long-term testosterone replacement therapy.

Salman M., Yassin D.-J., Shoukfeh H., Nettleship J.E., Yassin A.

Embase
Aging Male. 20 (1) (pp 45-48), 2017. Date of Publication: 02 Jan 2017.
[Article]
AN: 614212785

We and others have previously shown that testosterone replacement therapy (TRT) results in sustained weight loss in the majority of middle-aged hypogonadal men. Previously, however, a small proportion failed to lose at least 5% of their baseline weight. The reason for this is not yet understood. In the present study, we sought to identify early indicators that may predict successful long-term weight loss, defined as a reduction of at least 5% of total body weight relative to baseline weight (T0), in men with hypogonadism undergoing TRT. Eight parameters measured were assessed as potential predictors of sustained weight loss: loss of 3% or more of baseline weight after 1 year of TU treatment, severe hypogonadism, BMI, waist circumference, International Prostate Symptom Score (IPSS), glycated hemoglobin (HbA1C), age and use of vardenafil. Among the eight measured parameters, three factors were significantly associated with sustained weight loss over the entire period of TU treatment: (1) a loss of 3% of the baseline body weight after 1 year of TRT; (2) baseline BMI over 30; and (3) a waist circumference >102 cm. Age was not a predictor of weight loss. Copyright © 2017 Informa UK Limited, trading as Taylor & Francis Group.
Glutathione S-transferase P1 Ile105Val polymorphism and male infertility risk: An updated meta-analysis.


Embass
[Article]
AN: 615440465

Background: Several studies concerning the association between glutathione S-transferase P1 (GSTP1) Ile105Val polymorphism and male infertility risk have reported controversial findings. The present study was aimed to explore this association using a meta-analysis. Methods: The PubMed, EMBASE, China National Knowledge Infrastructure (CNKI), and Wanfang databases were searched. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to estimate the strength of the association. Results: A total of 3282 cases and 3268 controls in nine case-control studies were included. There was no significant association between GSTP1 Ile105Val polymorphism and male infertility in the overall population, but significant associations were found under the dominant (OR = 1.23, 95% CI = 1.04-1.46, I² = 32.2%) and heterozygote (OR = 1.29, 95% CI = 1.08-1.53, I² = 26.8%) models after excluding studies for which the data
did not satisfy Hardy-Weinberg equilibrium (HWE). Similarly, subgroup analyses revealed no significant association in Asians or Chinese population although a significant association was apparent among Chinese population in studies with HWE under the heterozygote model (OR = 1.25, 95% CI = 1.03-1.52, I² = 44.1%). Significant heterogeneity could be observed in some genetic models, but this heterogeneity was not significant when stratified by HWE. No evidence for publication bias was found. Conclusions: The GSTP1 Ile105Val polymorphism might not be associated with male infertility risk, and thus additional well-designed studies with larger sample size are warranted. Copyright © 2017 Chinese Medical Journal.

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Publisher
Chinese Medical Association
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20170424
Year of Publication
2017

130.
Embase
[Article]
AN: 615135984
Background: Area-wide integrated pest management strategies that include a sterile insect technique component have been successfully used to eradicate tsetse fly populations in the past. To ensure the success of the sterile insect technique, the released males must be adequately sterile and be able to compete with their native counterparts in the wild. Methodology/Principal findings: In the present study the radiation sensitivity of colonised Glossina brevipalpis Newstead (Diptera; Glossinidae) males, treated either as adults or pupae, was assessed. The mating performance of the irradiated G. brevipalpis males was assessed in walk-in field cages. Glossina brevipalpis adults and pupae were highly sensitive to irradiation, and a dose of 40 Gy and 80 Gy induced 93% and 99% sterility respectively in untreated females that mated with males irradiated as adults. When 37 to 41 day old pupae were exposed to a dose of 40 Gy, more than 97% sterility was induced in untreated females that mated with males derived from irradiated pupae. Males treated as adults with a dose up to 80 Gy were able to compete successfully with untreated fertile males for untreated females in walk-in field cages. Conclusions/Significance: The data emanating from this field cage study indicates that, sterile male flies derived from the colony of G. brevipalpis maintained at the Agricultural Research Council-Onderstepoort Veterinary Institute in South Africa are potential good candidates for a campaign that includes a sterile insect technique component. This would need to be confirmed by open field studies. Copyright © 2017 de Beer et al.
Complications associated with bone morphogenetic protein in the lumbar spine.
Kang D.G., Hsu W.K., Lehman R.A.
Embase
Orthopedics. 40 (2) (pp e229-e237), 2017. Date of Publication: March-April 2017.
[Review]
AN: 615090090
Complications associated with the use of recombinant human bone morphogenetic protein in the lumbar spine include retrograde ejaculation, ectopic bone formation, vertebral osteolysis and subsidence, postoperative radiculitis, and hematoma and seroma. These complications are controversial and remain widely debated. This article discusses the reported complications and possible implications for the practicing spine surgeon. Understanding the complications associated with the use of recombinant human bone morphogenetic protein and the associated controversies allows for informed decision making by both the patient and the surgeon.
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2017
High Prevalence of Low Serum Biologically Active Testosterone in Older Male Veterans.
Conover C.F., Yarrow J.F., Garrett T.J., Ye F., Quinlivan E.P., Cannady D.F., Peterson M.D.,
Borst S.E.
Embase
Journal of the American Medical Directors Association. 18 (4) (pp 366.e17-366.e24), 2017. Date
of Publication: 01 Apr 2017.
[Article]
AN: 614440730
Objectives Assess the prevalence of hypogonadism in older male Veterans by comparing direct
measurements of total testosterone (T) and bioavailable testosterone (BioT) versus indirect BioT
values derived from existing and newly developed regression analyses. Design Cohort study.
Setting Malcom Randall VA Medical Center, Gainesville, FL. Participants Community-dwelling
male Veterans aged 60 and older (n = 203). Measurements Total T, BioT, albumin, sex hormone-
binding globulin (SHBG), and body mass index were evaluated. Blood values were assessed via
liquid chromatography-tandem mass spectrometry (LC-MS/MS) and clinical or commercially
available immunoassays to compare accuracy among assessment techniques. Existing and
newly developed multiple regression analyses were evaluated to assess accuracy in predicting
BioT. Results Total T was 13.80 +/- 6.25 nmol/L (398 +/- 180 ng/dL) and was low (<10.4 nmol/L
or <300 ng/dL) in 34% of participants. SHBG was 58 +/- 35 nmol/L and elevated (>62 nmol/L) in
36% of participants. BioT was 1.94 +/- 0.97 nmol/L (56 +/- 28 ng/dL), with 72% of participants
below the clinical cutoff (<2.43 nmol/L or <70 ng/dL). Albumin was within the normal clinical
range. Total T and BioT measured via immunoassay and LC-MS/MS were moderately to highly
correlated, with no differences between assessment methods. Several existing predictive
equations overestimated BioT by 74% to 166% within our cohort (P < .001). A newly developed
regression model that included total T, SHBG, albumin, and age more accurately predicted BioT,
with values correlated (r = 0.508, P < .001) and comparable to LC-MS/MS. Conclusion In our
cohort, the prevalence of low total T was higher and low BioT was markedly higher than reported
in the general age-matched population, indicating a greater incidence of hypogonadism in older
male Veterans. In addition, existing empiric formulae, derived from other populations produced
BioT values that were considerably greater than those directly measured, whereas our newly
developed regression analysis provides improved predictive capabilities for older male Veterans.
The Conception and Evaluation of Sexual Health Literature.
DeLay K.J., Voznesensky I., Hellstrom W.J.G.
Embase
Sexual Medicine Reviews. 5 (2) (pp 135-145), 2017. Date of Publication: 01 Apr 2017.
[Review]
AN: 613993634

Introduction
Understanding the appropriate evaluation and development methods for studying the literature as it pertains to sexual health is important for those practicing within the subspecialty.

Aim
To further understand the methodology that is necessary to evaluate and design optimal studies in sexual health. Methods A PubMed search was performed using the terms urologic
study design, urologic validated questionnaires, clinical trials, and study bias. Articles with current and relevant topics in sexual health were selected for evaluation. Main Outcome Measure Summary of the current state of sexual medicine literature with insights into the evaluation and development of this literature. Results Most of the urologic and sexual medicine literature consists of retrospective studies that have resulted in low levels of evidence. Case series, case-control studies, cohort studies, and experimental studies are designs commonly used in sexual health. There are numerous types of bias that decrease the validity of the results within the literature. There are multiple validated questionnaires that can decrease bias when collecting data. These instruments are preferred over non-validated questionnaires and can help discern whether an intervention improves a patient's quality of life. The quality of the literature varies and often reflects the incidence of the condition being studied. Conclusion Those caring for patients with sexual dysfunction need to recognize the quality of the literature they read and understand the means of developing the highest quality studies, recommendations, and published literature. DeLay KJ, Voznesensky I, Hellstrom WJG. The Conception and Evaluation of Sexual Health Literature. Sex Med Rev 2017;5:135-145. Copyright © 2016 International Society for Sexual Medicine

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134.
Testosterone Replacement Therapy and Components of the Metabolic Syndrome.

Embase
Sexual Medicine Reviews. 5 (2) (pp 200-210), 2017. Date of Publication: 01 Apr 2017.
Introduction The prevalence of metabolic syndrome (MetS) is rapidly increasing in the United States and, because of its strong association with male hypogonadism, has become a significant topic of interest in the sexual medicine community. At the center of this conversation is the efficacy and safety of testosterone replacement therapy (TRT) as a therapeutic option for HG and MetS. Aim To provide a review of the current literature pertaining to TRT and MetS. Methods A thorough literature review was performed to review the relation between TRT and MetS using the PubMed online database from 1976 through 2016 with the keywords testosterone, hypogonadism, metabolic syndrome, and testosterone therapy. Main Outcome Measures Outcomes pertaining to MetS including weight, waist circumference, body mass index, blood glucose control, cholesterol parameters, blood pressure, and quality of life. Results From the plethora of contrasting literature on the efficacy and safety of TRT, it is increasingly clear that more well-designed studies are needed to clarify the efficacy and safety of TRT. Although most of the current literature shows that TRT has the potential to significantly lower the studied outcome variables associated with MetS, several studies provide more mixed results. Conclusion TRT has the potential to alleviate some of the morbidity associated with hypogonadism and MetS. Larger multicenter well-designed studies are needed to better describe and quantify the relation between MetS and TRT. Anaissie J, Roberts NH, Wang P, et al. Testosterone Replacement Therapy and Components of the Metabolic Syndrome. Sex Med Rev 2017;5:200-210. Copyright © 2017 International Society for Sexual Medicine
Male Hypogonadism and Osteoporosis: The Effects, Clinical Consequences, and Treatment of Testosterone Deficiency in Bone Health. 
Golds G., Houdek D., Arnason T. 
Embase 
Date of Publication: 2017. 
[Review] 
AN: 615076623 
It is well recognized that bone loss accelerates in hypogonadal states, with female menopause being the classic example of sex hormones affecting the regulation of bone metabolism. Underrepresented is our knowledge of the clinical and metabolic consequences of overt male hypogonadism, as well as the more subtle age-related decline in testosterone on bone quality. While menopause and estrogen deficiency are well-known risk factors for osteoporosis in women, the effects of age-related testosterone decline in men on bone health are less well known. Much of our knowledge comes from observational studies and retrospective analysis on small groups of men with variable causes of primary or secondary hypogonadism and mild to overt testosterone deficiencies. This review aims to present the current knowledge of the consequences of adult male hypogonadism on bone metabolism. The direct and indirect effects of testosterone on bone cells will be explored as well as the important differences in male osteoporosis and assessment as compared to that in females. The clinical consequence of both primary and secondary hypogonadism, as well as testosterone decline in older males, on bone density and fracture risk in men will be summarized. Finally, the therapeutic options and their efficacy in male osteoporosis and hypogonadism will be discussed. Copyright © 2017 Gary Golds et al. 
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Publisher
136.
Long-term efficacy of a combination therapy with an anticholinergic agent and an alpha1-blocker for patients with benign prostatic enlargement complaining both voiding and overactive bladder symptoms: A randomized, prospective, comparative trial using a urodynamic study.
Matsukawa Y., Takai S., Funahashi Y., Kato M., Yamamoto T., Gotoh M.
Embase
Neurourology and Urodynamics. 36 (3) (pp 748-754), 2017. Date of Publication: 01 Mar 2017.
[Article]
AN: 609896815
Aims: We evaluated long-term efficacy and safety of a combination therapy (CT) with an anticholinergic agent and an alpha1-blocker for patients with benign prostatic enlargement (BPE) complaining of voiding and overactive bladder (OAB) symptoms, in comparison with those of alpha1-blocker monotherapy (MT), by conducting a urodynamic study (UDS). Methods: This was a randomized prospective study involving 120 outpatients with untreated BPE associated with urinary urgency at least once per week and OABSS of >3. The patients were randomly assigned to receive MT with silodosin at 8 mg/day or CT with silodosin at 8 mg/day and propiverine at 20 mg/day. Changes in parameters from baseline to 12 weeks and 1 year after administration were assessed based on IPSS, IPSS-QOL, OABSS, and voiding and storage functions as measured by UDS. Results: In efficacy analysis, 53 patients with MT and 51 with CT were included. Although mean IPSS and OABSS significantly improved in both groups, the CT group showed statistically significant improvement in OABSS (-3.4 in CT, -2.4 in MT, P = 0.04), IPSS-QOL (-1.9, -1.2, P = 0.01), and OAB-urgency score (-1.8, -1.2, P < 0.01) at the long-term evaluation. In storage function, both groups showed significant improvements, but the CT group demonstrated a greater improvement in terms of disappearance rate of detrusor overactivity (54.5% in CT, 34.2% in MT, P = 0.07) and bladder capacity (+61 mL, +33 mL, P = 0.02). Conclusions: Long-term combination treatment with silodosin and propiverine was effective and safe for BPE

137.
Effect of Chinese Herbal Medicine on Male Infertility.
Jiang D., Coscione A., Li L., Zeng B.-Y.

Male infertility normally refers a male’s inability to cause pregnancy in a fertile female partner after 1 year of unprotected intercourse. Male infertility in recent years has been attracting increasing interest from public due to the evidence in decline in semen quality. There are many factors contributing to the male infertility including abnormal spermatogenesis; reproductive tract anomalies or obstruction; inadequate sexual and ejaculatory functions; and impaired sperm motility, imbalance in hormone levels, and immune system dysfunction. Although conventional treatments such as medication, surgical operation, and advanced techniques have helped many male with infertility cause pregnancy in their female partners, effectiveness is not satisfactory and associated with adverse effects. Chinese herbal medicine (CHM) has been used to improve male infertility in China for a very long time and has now been increasingly popular in Western countries for treating infertility. In this chapter we summarized recent development in basic research and clinical studies of CHM in treating male infertility. It has showed that CHM improved
sperm motility and quality, increased sperm count and rebalanced inadequate hormone levels, and adjusted immune functions leading to the increased number of fertility. Further, CHM in combination with conventional therapies improved efficacy of conventional treatments. More studies are needed to identify the new drugs from CHM and ensure safety, efficacy, and consistency of CHM. Copyright © 2017 Elsevier Inc.

138.

Efficacy of varicocelectomy in the treatment of hypogonadism in subfertile males with clinical varicocele: A meta-analysis.

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[Article In Press]
AN: 615331072

To reassess the efficacy of varicocelectomy in the treatment of hypogonadism in subfertile males, we carried out a meta-analysis of clinical trials and retrospective studies that compared the pre-operative and postoperative serum testosterone. We searched Embase and PubMed (1980 to May 2016) for studies. Eight studies and 712 patients were included. The combined analysis of seven studies discovered that the mean serum testosterone of patients post-operation improved by 34.3 ng/dl (95% CI: 22.57-46.04, p < .00001, I2 = 0.0%) compared with their pre-operative
levels. In subgroup analysis, testosterone improvements in the hypogonadal treated subgroup were more significant (improved by 123 ng/dl, 95% CI: 114.61-131.35, p < .00001, I² = 37%) than in the eugonadal s, or the untreated controls. In an analysis of surgery versus untreated control (three studies included), results showed that mean testosterone among hypogonadal s increased by 105.65 ng/dl (95% CI: 77.99-133.32), favouring varicocelectomy, as the differences were significant (p < .00001). However, there were insignificant differences in eugonadal s (p = .36). In conclusion, varicocelectomy significantly improved testosterone in hypogonadal men with subfertility. Active surgical treatment of varicocele might have a benefit of maintaining healthy androgen levels in subfertile men. Copyright © 2017 Blackwell Verlag GmbH.

Status
ARTICLE IN PRESS

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139.
Efficacy of treatment with pseudoephedrine in men with retrograde ejaculation.
Shoshany O., Abhyankar N., Elyaguov J., Niederberger C.

Embase
[Article In Press]

AN: 615291960

The use of pseudoephedrine, an alpha agonist, for the treatment of retrograde ejaculation is well-known, however, there is no clear consensus from the literature regarding its efficacy and treatment protocol. We evaluated the efficacy of pseudoephedrine treatment in patients with retrograde ejaculation, utilizing a yet undescribed short-period treatment protocol. Twenty men were medically treated with pseudoephedrine for retrograde ejaculation between January 2010
and May 2016 (12 with complete retrograde ejaculation and 8 with partial retrograde ejaculation).
All patients had a semen analysis and post-ejaculatory urinalysis before and after treatment. The
treatment protocol consisted of 60 mg of pseudoephedrine every 6 h on the day before semen
analysis and two more 60 mg doses on the day of the semen analysis. Diabetes was the most
common etiology for complete retrograde ejaculation (60%), whereas an idiopathic cause was the
most common etiology for partial retrograde ejaculation (82%). Of the 12 complete retrograde
ejaculation patients treated with pseudoephedrine prior to semen analysis, 7 (58.3%) recovered
spermatozoa in the antegrade ejaculate, with a mean total sperm count of 273.5 +/- 172.5 million.
Of the eight patients with partial retrograde ejaculation, five (62.5%) had a >50% increase in the
antegrade total sperm count. In this group, the mean total sperm count increased from 26.9 +/-
8.5 million before treatment to 84.2 +/- 24.6 million after treatment, whereas the percentage of
spermatozoa in the urine declined from 43.2 +/- 9% to 17 +/- 10%, respectively (both p < 0.05).
Overall, in men with retrograde ejaculation treated with a pseudoephedrine regimen prior to
ejaculation, some improvement in seminal parameters occurred in 14 (70%) patients, with 10
patients (38.5% of all patients) achieving antegrade total sperm counts over 39 million.
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140.
Chairmen in Academic Urologic Practice: A Descriptive Analysis.
Farber N.J., Friel B.J., Kwon Y.S., Cruz A., Elsamra S.E.
Embase
Objective: To examine and characterize the demographics and scholarly characteristics of academic urology chairmen at the time of appointment. Materials and Methods: The chairman of each United States urology residency program as of September 2016 was included in the study. Interim chairmen, as well as programs for which no clearly defined chair could be identified, were excluded. Demographic and academic data were collected via publically available curriculum vitae, departmental websites, Google search engine, and PubMed and Scopus websites. Results: One hundred thirteen chairmen were included in the study. The majority were male (96%) and mean age at appointment was 46 years (standard deviation = 6.3 years). Mean number of publications and H-index at the time of appointment was 105 and 31.1, respectively. Fellowship training was completed by 75% of chairmen, of which urologic oncology (N = 43), endourology (N = 12), and infertility/andrology (N = 10) were the most common. The most common additional graduate degrees prior to appointment were MBA (N = 7) and PhD (N = 6). The most frequently attended institutions for residency were Johns Hopkins University (13) and Northwestern University (5), whereas Memorial Sloan Kettering Cancer Center (13) and Baylor University (7) were the most frequent for fellowship. Twenty percent of chairmen attained the chairman position at their former residency program and 7% at their former fellowship program. Conclusion: Our study describes the demographic and academic characteristics of urology academic chairmen at the time of appointment. The majority of chairmen are male and specialize in urologic oncology. Chairmen often receive the chair appointment at their former residency program. Copyright © 2017 Elsevier Inc.
Efficacy and Safety of Continuous Subcutaneous Infusion of Recombinant Human Gonadotropins for Congenital Micropenis during Early Infancy.


Hormone Research in Paediatrics. 87 (2) (pp 103-110), 2017. Date of Publication: 01 Mar 2017.

AN: 615138653

Background: Early postnatal administration of gonadotropins to infants with congenital hypogonadotropic hypogonadism (CHH) can mimic minipuberty, thereby increasing penile growth. We assessed the effects of gonadotropin infusion on stretched penile length (SPL) and hormone levels in infants with congenital micropenis. Methods: Single-center study including 6 males with micropenis in case of isolated CHH (n = 4), panhypopituitarism (n = 1), and partial androgen insensitivity syndrome (PAIS; n = 1). Patients were evaluated at baseline, monthly and at the end of the study through a clinical examination (SPL, testicular position and size), serum hormone assays (testosterone, luteinizing hormone, follicle-stimulating hormone, inhibin B, anti-Mullerian hormone [AMH]), and ultrasound of penis/testes. Results: In CHH, significant increases occurred in serum testosterone (from undetectable level to 3.5 +/- 4.06 ng/mL [12.15 +/- 14.09 nmol/L]), SPL (from 13.8 +/- 4.5 to 42.6 +/- 5 mm; p < 0.0001), inhibin B (from 94.8 +/- 74.9 to 469.4 +/- 282.5 pg/mL, p = 0.04), and AMH (from 49.6 +/- 30.6 to 142 +/- 76.5 ng/mL, p = 0.03). Micropenis was corrected in all patients, except one. On treatment, in the patient with PAIS, SPL was increased from 13 to 38 mm. Conclusions: Early gonadotropin infusion is a safe, well-tolerated and effective treatment. The effect in PAIS has not been reported previously. Long-term follow-up is needed to assess the impact, if any, on future fertility and reproduction.

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Add-on mirtazapine improves orgasmic functioning in patients with schizophrenia treated with first-generation antipsychotics.

Terevnikov V., Stenberg J.-H., Tiihonen J., Burkin M., Joffe G.

Embase

[Article]
AN: 612619108

Aim: Sexual dysfunction, common in schizophrenia, may be further exaggerated by antipsychotics, especially those of First Generation (FGAs), and antidepressants, such as Selective Serotonin Reuptake Inhibitors (SSRs). Mirtazapine, an antidepressant characterized by its different action mechanism compared with that of the majority of other antidepressants, may improve SSRI-induced sexual dysfunction in patients with depression. It is unknown, however, whether mirtazapine improves sexual functioning in schizophrenia. Methods: This study randomly assigned FGA-treated patients with schizophrenia to receive either an add-on mirtazapine (n = 20) or a placebo (n = 19) for 6 weeks. Sexual functioning was prospectively measured using five
relevant items from the Udvalg for Kliniske Undersogelser side-effect rating scale (UKU-SERS).

Results: Orgasmic function improved with statistical significance in the mirtazapine group (\(p = .03\)), with no changes in any other sexual functions in either group. Conclusion: Add-on mirtazapine appears to relieve orgasmic dysfunction in FGA-treated patients with schizophrenia.

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PMID

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143.
The effectiveness of intrauterine insemination: A matched cohort study.
Embase
Objective To study the effectiveness of an intrauterine insemination (IUI) program compared to no treatment in subfertile couples with unexplained subfertility and a poor prognosis on natural conception. Study design A retrospective matched cohort study in which ongoing pregnancy rates in 72 couples who voluntarily dropped out of treatment with IUI were compared to ongoing pregnancy rates in 144 couples who continued treatment with IUI. Couples with unexplained subfertility, mild male subfertility or cervical factor subfertility who started treatment with IUI between January 2000 and December 2008 were included. Couples were matched on hospital, age, duration of subfertility, primary or secondary subfertility and diagnosis. Primary outcome was cumulative ongoing pregnancy rate after three years. Time to pregnancy was censored at the moment couples were lost to follow up or when their child wish ended and, for the no-treatment group, when couples re-started treatment. Results After three years, there were 18 pregnancies in the stopped treatment group (25%) versus 41 pregnancies in the IUI group (28%) (RR 1.1 (0.59-2.2)(p = 0.4)). The cumulative pregnancy rate after three years was 40% in both groups, showing no difference in time to ongoing pregnancy (shared frailty model \( p = 0.86 \)). Conclusions In couples with unexplained subfertility and a poor prognosis for natural conception, treatment with IUI does not add to expectant management. There is need for a randomized clinical trial comparing IUI with expectant management in these couples.
A perspective on middle-aged and older men with functional hypogonadism: Focus on holistic management.

Grossmann M., Matsumoto A.M.

Embase

[Review]

AN: 614843999

Context: Middle-aged and older men (50 years), especially those who are obese and suffer from comorbidities, not uncommonly present with clinical features consistent with androgen deficiency and modestly reduced testosterone levels. Commonly, such men do not demonstrate anatomical hypothalamic-pituitary-testicular axis pathology but have functional hypogonadism that is potentially reversible. Evidence Acquisition: Literature review from 1970 to October 2016. Evidence Synthesis: Although definitive randomized controlled trials are lacking, evidence suggests that in such men, lifestyle measures to achieve weight loss and optimization of comorbidities, including discontinuation of offending medications, lead to clinical improvement and a modest increase in testosterone. Also, androgen deficiency-like symptoms and end-organ deficits respond to targeted treatments (such as phosphodiesterase-5 inhibitors for erectile dysfunction) without evidence that hypogonadal men are refractory. Unfortunately, lifestyle interventions remain difficult and may be insufficient even if successful. Testosterone therapy should be considered primarily for men who have significant clinical features of androgen deficiency and unequivocally low testosterone levels. Testosterone should be initiated either concomitantly with a trial of lifestyle measures, or after such a trial fails, after a tailored diagnostic work-up, exclusion of contraindications, and appropriate counseling. Conclusions: There is modest evidence that functional hypogonadism responds to lifestyle measures and optimization
of comorbidities. If achievable, these interventions may have demonstrable health benefits beyond the potential for increasing testosterone levels. Therefore, treatment of underlying causes of functional hypogonadism and of symptoms should be used either as an initial or adjunctive approach to testosterone therapy. Copyright © 2017 by the Endocrine Society.

145.
Associations of C677T polymorphism in methylenetetrahydrofolate reductase (MTHFR) gene with male infertility risk: A meta-analysis.
Embase
Date of Publication: 01 May 2017.
[Article]
AN: 615017474
Purpose Methylenetetrahydrofolate reductase is one of the key enzymes in folate metabolism. But the association between polymorphism and the risk of male infertility is still controversial. Therefore, this study used a meta-analysis on the collection of data to analyze MTHFR gene
C677T polymorphism (known as c.665 C > T, rs1801133, p.Ala222Val). Methods PubMed, EMBASE, China National Knowledge Infrastructure (CNKI), and Wan fang. Data were searched to identify eligible studies. We sifted the data collection by Hardy-Weinberg equilibrium calculator and used odds ratios (ORs) and 95% confidence intervals (95% CIs) to conduct data through RevMan5.0 and StataSE12.0 software. Results A total of 15 studies have 3853 patients with infertility and 3613 healthy controls in this meta-analysis. Our results showed that T variant of MTHFR C677T gene polymorphism was significantly associated with an increased risk of male infertility (for T vs. C: OR = 1.38, 95% CI = 1.18-1.63; for TT vs. CC: OR = 1.86, 95% CI = 1.36-2.54; for CT vs. CC: OR = 1.34, 95% CI = 1.03-1.74; for TT vs. CT: OR = 1.52, 95% CI = 1.26-1.84; for TT vs. CT + CC: OR = 1.42, 95% CI = 1.19-1.70; for TT + CT versus CC: OR = 1.46, 95% CI = 1.05-2.04). In addition, the results indicated that T allele had the positive association which was driven by East-asian populations (random: OR = 1.44, 95% CI = 1.2-1.74; fixed: OR = 1.39, 95% CI = 1.20-1.61), Middle-eastern populations (random: OR = 1.30, 95% CI = 1.05-1.63; fixed: OR = 1.30, 95% CI = 1.05-1.63) and Mixed-race (random: OR = 1.96, 95% CI = 1.35-2.85; fixed: OR = 1.31, 95% CI = 1.20-1.43). Conclusion This meta-analysis suggests that MTHFR C677T polymorphism is associated with male infertility. Copyright © 2017 Elsevier B.V.

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The effect of slow release insemination on pregnancy rates: report of two randomized controlled pilot studies and meta-analysis.


Embase
Archives of Gynecology and Obstetrics. 295 (4) (pp 1025-1032), 2017. Date of Publication: 01 Apr 2017.
[Article]
AN: 614436497

Purpose: A modified application technique of intrauterine insemination (IUI) is slow release insemination (SRI), first described by Muharib et al. (Hum Reprod 7(2):227-229, 1992), who postulated higher pregnancy rates with a slow release of spermatozoa for 3 h. Methods: To investigate this approach, two randomized controlled, cross-over pilot studies were performed from 2004 to 2006 in Israel and Germany to compare SRI with the standard bolus IUI. We aimed to present the results and perform a meta-analysis on available data for SRI. Univariate comparisons of pregnancy rates were performed using one-tailed z tests for method superiority. For meta-analysis, a fixed-effect Mantel-Haentzel weighted average of relative risk was performed. Results: Fifty treatment cycles (IUI: n = 25, SRI: n = 25) were performed in Germany, achieving four pregnancies (IUI: 4%, SRI: 12%, p > 0.05). Thirty-nine treatment cycles (IUI: n = 19, SRI: n = 20) were performed in Israel achieving six pregnancies (IUI: 10.5%, SRI: 20%; p > 0.05). Meta-analysis of all eligible studies for SRI (n = 3) revealed a combined relative risk for pregnancy after SRI of 2.64 (95% CI 1.04-6.74), p = 0.02). Conclusions: In conclusion, these results lend support to the hypothesis that the pregnancy rate might be improved by SRI compared to the standard bolus technique. Copyright © 2017, The Author(s).

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Publisher
Klinefelter syndrome (KS) is the most common male sex chromosome disorder, affecting 1/660 men. It is caused by the presence of extra X chromosomes. The KS phenotype is traditionally described as a tall, slim, narrow-shouldered, broad-hipped man with hypergonadotropic hypogonadism and small testes. An association between KS and type 2 diabetes has long been recognized, but the pathogenesis is still unknown. If both hypogonadism and visceral obesity play a role in the development of insulin resistance in men, KS offers an interesting window into this relationship. Indeed, in addition to hypergonadotropic hypogonadism, with variable degrees of androgen deficiency, most 47,XXY KS patients present an unfavorable change in body composition, with increased truncal fat. In KS, both hypotestosteronemia and visceral obesity not only play an important and independent role in determining impaired insulin sensitivity, but may also be reciprocally influenced in a self-perpetuating vicious circle. Other possible mechanisms that may lead to insulin resistance in KS involve the extra copies of X chromosomes. This chapter discusses the main evidence linking KS and impaired insulin sensitivity, leading to insulin resistance and type 2 diabetes. Copyright © 2017 S. Karger AG, Basel.
148.
Role of silodosin as medical expulsive therapy in ureteral calculi: a meta-analysis of randomized controlled trials.
Embase
Urolithiasis. (pp 1-8), 2017. Date of Publication: 01 Apr 2017.
[Article In Press]
AN: 615110595
The objective of this study is to investigate the efficacy of silodosin in medical expulsive therapy (MET) for ureteral stones. We conducted a systematic review and meta-analysis to determine the efficacy and safety of silodosin in MET for ureteral calculi. We searched PubMed, Embase, Medline, Central (the Cochrane Library, Issue 1,2013), Google Scholar from the inception to March 2015 for randomized controlled trials (RCTs), comparing silodosin with tamsulosin or control on ureteral stone passage. Eight RCTs with a total of 1145 ureteral stone patients (300 patients in the control group, 287 patients in the tamsulosin group, 558 patients in the silodosin group) were included in this meta-analysis. When compared with control, silodosin significantly improved expulsion rate of distal ureteral stones (RR: 1.42; 95% CI, 1.21-1.67; P < 0.0001), while there was no significant difference between silodosin and the control in expulsion rate of proximal (RR: 0.99; 95% CI, 0.69-1.43; P < 0.97) or mid (RR: 1.13; 95% CI, 0.60-2.16; P < 0.0001) ureteral stones. There was no significant difference between silodosin and tamsulosin in terms of expulsion time (WMD: -2.47; 95% CI, -5.32 to 0.39; P = 0.09), analgesic use (WMD: -0.39; 95% CI, -0.91 to 0.13; P = 0.14) and retrograde ejaculation rate (RR: 1.85; 95% CI, 0.95-3.59; P = 0.07) in MET for distal ureteral stones. However, silodosin provided a significantly higher
expulsion rate (RR: 1.25; 95% CI, 1.13-1.37; P < 0.0001) than tamsulosin for distal ureteral stones. Silodosin significantly improved expulsion rate of distal ureteral stones and was clinically superior to tamsulosin. Silodosin was ineffective in MET for proximal and mid ureteral stones. More RCT studies are needed to compare the efficacy of silodosin versus tamsulosin in MET for distal ureteral stones. Copyright © 2017 Springer-Verlag Berlin Heidelberg

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ARTICLE IN PRESS

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149.
"Cherchez La Femme": Modulation of Estrogen Receptor Function With Selective Modulators: Clinical Implications in the Field of Urology.
Helo S., Wynia B., McCullough A.

Embase
[Article In Press]
AN: 615092466

Introduction: Selective estrogen receptor modulators (SERMs) have been used off-label in men for more than 50 years. SERMs exert their action on the estrogen receptor agonistically or antagonistically. A fundamental knowledge of the complex molecular action and physiology of SERMs is important in understanding their use and future directions of study in men. Aim: To
review the basic science and mechanism of the action of estrogens, the estrogen receptor, and SERMs, and the existing clinical publications on the use of SERMs in men for infertility and hypogonadism with their strengths and weaknesses and to identify the need for future studies. Methods: After a review of publications on the basic science of estrogen receptors, a chronologic review of published evidence-based studies on the use of SERMs in men for infertility and hypogonadism was undertaken. Main Outcome Measures: Clinical publications were assessed for type of study, inclusion criteria, outcome measurements, and results. Strengths and weaknesses of the publications were assessed and discussed. Results: Few prospective rigorously controlled trials have been undertaken on the use of SERMs in men. Most existing trials are largely retrospective anecdotal studies with inconsistent inclusion and end-point measurements. The SERMs are complex and at times can produce paradoxical results. Their action likely depends on the genetics of the individual, his tissue-specific composition of estrogen receptors, the molecular structure and pharmacodynamics of the SERMs, and their metabolism. Conclusion: Rigorously controlled trials of the use of SERMs in men are needed to better identify their clinical benefit and long-term safety in infertile and hypogonadal men. Recent placebo-controlled pharmaceutical industry SERM trials have demonstrated short-term safety and efficacy in men with secondary hypogonadism and eventually might provide an alternative to exogenous testosterone replacement therapy in men with secondary hypogonadism. Helo S, Wynia B, McCullough A. "Cherchez La Femme": Modulation of Estrogen Receptor Function With Selective Modulators: Clinical Implications in the Field of Urology. Sex Med Rev 2017;X:XXX-XXX. Copyright © 2017 The Authors.
Testosterone treatment and cognitive function in older men with low testosterone and age-associated memory impairment.


Embase

Importance: Most cognitive functions decline with age. Prior studies suggest that testosterone treatment may improve these functions. Objective: To determine if testosterone treatment compared with placebo is associated with improved verbal memory and other cognitive functions in older men with low testosterone and age-associated memory impairment (AAMI). Design, Setting, and Participants: The Testosterone Trials (TTrials) were 7 trials to assess the efficacy of testosterone treatment in older men with low testosterone levels. The Cognitive Function Trial evaluated cognitive function in all TTrials participants. In 12 US academic medical centers, 788 men who were 65 years or older with a serum testosterone level less than 275 ng/mL and impaired sexual function, physical function, or vitality were allocated to testosterone treatment (n = 394) or placebo (n = 394). A subgroup of 493 men met criteria for AAMI based on baseline subjective memory complaints and objective memory performance. Enrollment in the TTrials began June 24, 2010; the final participant completed treatment and assessment in June 2014.

Interventions: Testosterone gel (adjusted to maintain the testosterone level within the normal range for young men) or placebo gel for 1 year. Main Outcomes and Measures: The primary outcome was the mean change from baseline to 6 months and 12 months for delayed paragraph recall (score range, 0 to 50) among men with AAMI. Secondary outcomes were mean changes in visual memory (Benton Visual Retention Test; score range, 0 to -26), executive function (Trail-Making Test B minus A; range, -290 to 290), and spatial ability (Card Rotation Test; score range, -80 to 80) among men with AAMI. Tests were administered at baseline, 6 months, and 12 months. Results: Among the 493 men with AAMI (mean age, 72.3 years [SD, 5.8]; mean baseline testosterone, 234 ng/dL [SD, 65.1]), 247 were assigned to receive testosterone and 246 to receive placebo. Of these groups, 247 men in the testosterone group and 245 men in the placebo completed the memory study. Therewas no significant mean change from baseline to 6 and 12 months in delayed paragraph recall score among men with AAMI in the testosterone and placebo groups (adjusted estimated difference, -0.07 [95%CI, -0.92 to 0.79]; P = .88). Mean scores for
delayed paragraph recall were 14.0 at baseline, 16.0 at 6 months, and 16.2 at 12 months in the testosterone group and 14.4 at baseline, 16.0 at 6 months, and 16.5 at 12 months in the placebo group. Testosterone was also not associated with significant differences in visual memory (-0.28 [95%CI, -0.76 to 0.19]; P = .24), executive function (-5.51 [95%CI, -12.91 to 1.88]; P = .14), or spatial ability (-0.12 [95%CI, -1.89 to 1.65]; P = .89). Conclusions and Relevance: Among older men with low testosterone and age-associated memory impairment, treatment with testosterone for 1 year compared with placebo was not associated with improved memory or other cognitive functions.

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Embase

[Article]
Importance: Recent studies have yielded conflicting results as to whether testosterone treatment increases cardiovascular risk. Objective: To test the hypothesis that testosterone treatment of older men with low testosterone slows progression of noncalcified coronary artery plaque volume. Design, Setting, and Participants: Double-blinded, placebo-controlled trial at 9 academic medical centers in the United States. The participants were 170 of 788 men aged 65 years or older with an average of 2 serum testosterone levels lower than 275 ng/dL (82 men assigned to placebo, 88 to testosterone) and symptoms suggestive of hypogonadism who were enrolled in the Testosterone Trials between June 24, 2010, and June 9, 2014. Intervention: Testosterone gel, with the dose adjusted to maintain the testosterone level in the normal range for young men, or placebo gel for 12 months. Main Outcomes and Measures: The primary outcome was noncalcified coronary artery plaque volume, as determined by coronary computed tomographic angiography. Secondary outcomes included total coronary artery plaque volume and coronary artery calcium score (range of 0 to >400 Agatston units, with higher values indicating more severe atherosclerosis). Results: Of 170 men who were enrolled, 138 (73 receiving testosterone treatment and 65 receiving placebo) completed the study and were available for the primary analysis. Among the 138 men, the mean (SD) age was 71.2 (5.7) years, and 81% were white. At baseline, 70 men (50.7%) had a coronary artery calcification score higher than 300 Agatston units, reflecting severe atherosclerosis. For the primary outcome, testosterone treatment compared with placebo was associated with a significantly greater increase in noncalcified plaque volume from baseline to 12 months (from median values of 204 mm³ to 232 mm³ vs 317 mm³ to 325 mm³, respectively; estimated difference, 41 mm³; 95% CI, 14 to 67 mm³; P = .003). For the secondary outcomes, the median total plaque volume increased from baseline to 12 months from 272 mm³ to 318 mm³ in the testosterone group vs from 499 mm³ to 541 mm³ in the placebo group (estimated difference, 47 mm³; 95% CI, 13 to 80 mm³; P = .006), and the median coronary artery calcification score changed from 255 to 244 Agatston units in the testosterone group vs 494 to 503 Agatston units in the placebo group (estimated difference, -27 Agatston units; 95% CI, -80 to 26 Agatston units). No major adverse cardiovascular events occurred in either group. Conclusions and Relevance: Among older men with symptomatic hypogonadism, treatment with testosterone gel for 1 year compared with placebo was associated with a significantly greater increase in coronary artery noncalcified plaque volume, as measured by coronary computed tomographic angiography. Larger studies are needed to understand the clinical implications of this finding. Copyright © 2017 American Medical Association. All rights reserved.

An open-label clinical trial to investigate the efficacy and safety of corifollitropin alfa combined with hCG in adult men with hypogonadotropic hypogonadism.


[Article]

AN: 614684133

Background: Hypogonadotropic hypogonadism (HH) in men results in insufficient testicular function and deficiencies in testosterone and spermatogenesis. Combinations of human chorionic gonadotropin (hCG) and recombinant follicle-stimulating hormone (recFSH) have been successful in the treatment of HH. Corifollitropin alfa is a long-acting FSH-analog with demonstrated action in women seeking infertility care. The aim of this study was to investigate the efficacy and safety of corifollitropin alfa combined with hCG to increase testicular volume and induce spermatogenesis in men with HH. Methods: This was a Phase III, multi-center, open-label, single-arm trial of corifollitropin alfa in azoospermic men aged 18 to 50 years with HH. After 16 weeks of pretreatment of 23 subjects with hCG alone, 18 subjects with normalized testosterone (T) levels who remained azoospermic entered the 52-week combined treatment phase with hCG twice-weekly and 150 mug corifollitropin alfa every other week. The increase in testicular volume (primary efficacy endpoint) and induction of spermatogenesis resulting in a sperm count >1 x 106/mL (key secondary efficacy endpoint) during 52 weeks of combined treatment were assessed. Safety was evaluated by the presence of anti-corifollitropin alfa antibodies and the occurrence of adverse events (AEs). Results: Mean (+/-SD) testicular volume increased from 8.6 (+/-6.09) mL to 17.8 (+/-8.93) mL (geometric mean fold increase, 2.30 [95% CI: 2.03, 2.62]); 14
(77.8%) subjects reached a sperm count >1 x 10^6/mL. No subject developed confirmed anti-corifollitropin alfa antibodies during the trial. Treatment was generally well tolerated. Conclusions: Corifollitropin alfa 150 mug administrated every other week combined with twice-weekly hCG for 52 weeks increased testicular volume significantly, and induced spermatogenesis in >75% of men with HH who had remained azoospermic after hCG treatment alone. Trial registration: ClinicalTrials.gov: NCT01709331. Copyright © 2017 The Author(s).

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153.
Prednisone treatment in infertile patients with oligozoospermia and accessory gland inflammatory alterations.

Embase
Andrology. 5 (2) (pp 268-273), 2017. Date of Publication: 01 Mar 2017.
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AN: 614838820
The association between inflammation of the male reproductive system and oligozoospermia has been frequently reported in the clinical work-up of male infertility. To improve sperm parameters in infertile patients with genital inflammation, many phytochemical and nutraceutical drugs are currently being used. However, their use is still empirical and no conclusive data have been provided about their efficacy. The treatment with steroid anti-inflammatory drugs might be useful in reducing inflammation and improving sperm parameters, thus increasing the fertility outcome. The aim of this study was to evaluate if glucocorticoid treatment improves seminal parameters in infertile oligozoospermic patients presenting signs of accessory gland inflammation at genital ultrasound. A total of 90 infertile patients were enrolled in the study. They presented normal testicular volume, normal FSH plasma levels, the presence of various degrees of oligozoospermia, associated with scrotal and trans-rectal ultrasound signs indicative of accessory gland inflammation, but negative microbiological analysis on semen and/or prostatic secretions. Patients were randomly allocated into three groups of treatment, receiving, respectively, 5, 12.5, and 25 mg daily oral Prednisone for one month. Seminal parameters were evaluated at admission and after treatment. In patients undergoing Prednisone treatment at a daily dose of 5 mg we observed a significant increase in total sperm count. At a daily dose of 12.5 mg, Prednisone treatment improved sperm concentration, total sperm count, and the percentage of sperm motility. Twenty-five mg of Prednisone led to significant improvement in all the sperm parameters, except for semen volume. These results clearly demonstrate that Prednisone treatment can significantly improve sperm parameters in a selected population of oligozoospermic patients. These findings suggest that Prednisone treatment should be considered in idiopathic oligozoospermic patients with supposed normal spermatogenesis and accessory gland inflammatory alterations, in order to improve sperm parameters and fertility outcome. Copyright © 2016 American Society of Andrology and European Academy of Andrology.

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Effects of testosterone replacement therapy on hypogonadal men with osteopenia or osteoporosis: a subanalysis of a prospective randomized controlled study in Japan (EARTH study).


Embase
[Article In Press]
AN: 615054625

Objective: We investigated the effects of testosterone replacement therapy (TRT) on bone mineral density (BMD) among hypogonadal men with osteopenia/osteoporosis. Methods: From our previous EARTH study population, 74 patients with a clinical diagnosis of osteopenia or osteoporosis and hypogonadism were included in this study, as the TRT (n=35) and control (n=34) groups. The TRT group was administered 250mg of testosterone enanthate injection every 4 weeks for 12 months. The BMD, waist circumference, body mass index, body fat percentage, and muscle volume were measured at baseline and at 12 months. Blood biochemical data, including total cholesterol, triglycerides, HDL-cholesterol, hemoglobin A1c, and adiponectin values were also evaluated. Results: At the 12-month visit, BMD significantly increased in both groups. However, comparisons on changes of parameter values from baseline to the 12-month visit between the TRT and control groups were significantly different in BMD (5.0+/−5.0 vs. 3.0+/−3.2; p=.0434) and in adiponectin value (-0.90+/−3.33 vs. 0.10+/−2.04; p=.0192). There were no significant changes in other parameters. Conclusions: TRT for 12 months could improve BMD with a decrease in adiponectin levels among hypogonadal men with osteopenia/osteoporosis.
Managing subfertility in patients with heart disease: What are the choices?
Embase
[Review]
AN: 614583847
More women with heart disease are reaching reproductive age and will want to embark upon pregnancy. Furthermore, many of these women are delaying pregnancy until later in life when they may be exposed to a greater number of complications from their heart disease. A relatively high proportion of these women will pursue fertility treatment to achieve a pregnancy; consequently, the management of subfertile couples where the woman (or man) has heart disease is of growing importance. In this review, we discuss how fertility investigations and treatment can impact a women with heart disease and how some of the potential complications can be minimized or avoided. We also consider surrogacy, which is an important option when pregnancy is contraindicated. Copyright © 2017 Elsevier Inc.

Cauldwell, Matthew; ORCID: http://orcid.org/0000-0003-2366-3133
156.
Biological characters of human dermal fibroblasts derived from foreskin of male infertile patients.
Fang F., Ni K., Cai Y., Ye Z., Shang J., Shen S., Xiong C.
Embase
Tissue and Cell. 49 (1) (pp 56-63), 2017. Date of Publication: 01 Feb 2017.
[Article]
AN: 614063980
Dermal fibroblasts play a vital role in maintaining skin function. They not only synthesize and secrete extracellular matrix molecules, but also produce a complex mixture of bioactive factors, which both contribute to immune regulation and wound healing. Fibroblasts isolated from skin tissue exhibit wide range of potentials, especially in regenerative medicine. The use of fibroblast cultures for medical purposes requires standardization of cell preparations. To achieve this, we isolated and characterized dermal fibroblasts from human foreskin with a standardized method. The obtained cells grew as typical morphology of fibroblasts, and expressed intermediate filament protein vimentin and nestin. Immunophenotypic analysis indicated that the isolated fibroblasts expressed mesenchymal surface markers CD73, CD90, CD44 and CD105, and were negative for haematopoietic markers CD45 and CD34. Growth kinetics analysis of the cells showed high proliferative properties. Furthermore, cryopreservation had no influence on cell morphology and growth properties. Here, we describe a standardized, repeatable method for isolation of
fibroblasts from human foreskin tissues and identify their biological characters according to morphologic, immunohistologic and proliferative criteria, which would be meaningful for future clinical trials and regenerative medicine purposes. Copyright © 2016


Status EMBASE

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157.

Eurycoma Longifolia as a potential adoptogen of male sexual health: a systematic review on clinical studies.
Thu H.E., Mohamed I.N., Hussain Z., Jayusman P.A., Shuid A.N.

Embase

[Article]
AN: 614621595
Eurycoma longifolia (EL) has been well recognized as a booster of male sexual health. Over the past few decades, numerous in vivo animal studies and human clinical trials have been conducted across the globe to explore the promising role of EL in managing various male sexual disorders, which include erectile dysfunction, male infertility, low libido, and downregulated testosterone levels. The aim of the present review is to analyze and summarize the literature on human clinical trials which revealed the clinical significance and therapeutic feasibility of EL in improving male sexual health. This systematic review is focused on the following databases: Medline, Wiley Online Library, BioMed Central, Hindawi, Web of Knowledge, PubMed Central and Google Scholar, using search terms such as "Eurycoma longifolia", "EL", "Tongkat Ali", "male sexual health", "sexual infertility", "erectile dysfunction", "male libido", and "testosterone levels". Notably, only human clinical studies published between 2000 and 2014 were selected and thoroughly reviewed for relevant citations. Out of 150 articles, 11 met the inclusion criteria. The majority of articles included were randomized placebo-controlled trials, multiple cohort studies, or pilot trials. All these studies demonstrated considerable effects of EL on male sexual health disorders. Among them, 7 studies revealed remarkable association between the use of EL and the efficacy in the treatment of male sexual disorders, and remaining 4 studies failed to demonstrate sufficient effects on male sexual health. In summary, there is convincing evidence for the prominence of EL in improving the male sexual health. The review also substantiates the use of current methodology in the development of novel and more rationale natural herbal medicines for the management of male sexual disorders. Copyright © 2017 China Pharmaceutical University

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20170324

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2017
Transmission of double FMR1 allelic premutations in a family.
Sun M., Ning J., Zhang H., Li S.
Embase
Genes and Genomics. 39 (4) (pp 409-415), 2017. Date of Publication: 01 Apr 2017.
[Article]
AN: 613923856
The fragile X mental retardation 1 (FMR1) gene is the only gene known responsible for fragile X related disorders, including fragile X syndrome (FXS), fragile X-associated primary ovarian insufficiency, and fragile X-associated tremor/ataxia. Although FMR1 premutation carriers are common, double mutations of the FMR1 gene is very rare. To our knowledge, only twelve such reports including twenty-three cases from fourteen families have been documented. We report here another family with a FXS family history in which the proband's maternal grandmother had compound FMR1 gene premutations and we review twelve published papers associated with double allelic mutations. Our study and literature review indicated that compound premutations may have influences regarding the early onset of fragile X-associated primary ovarian insufficiency and severity of psychiatric issues, and less likely aggravate the cognitive deficits compared with one allele mutant patients. Further detailed studies of similar cases are needed to clarify the profile of double FMR1 premutations. Copyright © 2016, The Genetics Society of Korea and Springer-Science and Media.

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Date Created
Hyaluronan-binding system for sperm selection enhances pregnancy rates in ICSI cycles associated with male factor infertility.


Embase

Jornal Brasileiro de Reproducao Assistida. 21 (1) (pp 2-6), 2017. Date of Publication: 2017.

[Article]

AN: 614901138

Objectives: The aim of the present study was to compare two procedures for sperm selection in ICSI cycles - conventional morphology sperm selection (ICSI-PVP) and chemical selection through Hyaluronan-treated petri dishes (PICS), when male factor was associated. Methods: The evaluated parameters were semen quality, fertilization and cleavage rates, chemical and clinical pregnancy rates, as well as abortion rate. Fifty-six ICSI cycles were included in this report, 19 cycles using PICS and 37 using conventional ICSI. Results: PICS and ICSI showed, respectively, the following outcome: fertilization rates 71.93% (123/171) and 64.14% (127/198); cleavage rates 95.12% (117/123) and 95.27% (121/127); chemical pregnancy rates 63.15% (12/19) and 27.03% (10/37); clinical pregnancy rates 42.10% (8/19) and 16.21% (6/37); and abortion rates 33.33% (4/12) and 40.00% (4/10). According to both Fisher's Exact Test and Chi-square Test, chemical pregnancy (p = 0.05) and clinical pregnancy (p = 0.09) rates were significantly higher in the PICS group. p values < 0.05 were consider statistically significant. Conclusions: The present data indicates that ICSI cycles that used the PICS technique had a considerably higher chance (=5 fold) to achieve pregnancy than those who had sperm selected only by morphology assessment. Teratozoospermic patients were those who benefited most with PICS. Therefore, the technique should be included in laboratory routine with low cost, avoiding the selection of immature sperm with increased rates of peroxidation and DNA fragmentation. Prospective and randomized studies should be applied to strengthen this suggestion. Copyright © 2017, Sociedade Brasileira de Reproducao Assistida. All rights reserved.

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Aims: Varicocelectomy is the most common operation carried out by doctors for male infertility treatment. The aim of varicocele treatment is to hinder the refluxing venous drainage to the testis, retaining arterial inflow, and lymphatic drainage. A lot of pain is generated after this surgery, and the use of opium should be reduced to nearest minimum, as all drugs are toxins. Thus the aim of the present study is to facilitate morphine usage reduction after varicocelectomy surgery. 

Material and Methods: One-hundred (100) patients who were varicocelectomy candidate were randomized into two groups: experimental group contain 50 patients and control group contain 50 patients as well. In experimental group, 2 mL magnesium sulfate in 2 mL normal saline was injected into patient immediately after surgery. The control group received only 4 mL normal saline. Morphine dosage administered, and severity of pain monitoring was accessed and recorded with a visual analogue scale (VAS). Result: Result indicated that administration of morphine dosage in the test group 0.21 +/- 0.64 mg was significantly lower as compared to the control group 0.75 +/- 1.30 mg during the first 24-hour after surgery (p = 0.01). Average VAS scores in the experimental and control groups in the first 4-hour interval were 0.91 +/- 1.30 and 2.9 +/- 2.50 (p = 0.02) respectively. We observed a significant difference in the VAS score for pain severity and the
dosages of morphine administered. Conclusions: The experimental group with magnesium sulfate in its drug formulation showed better pain control compared to the control group which received only normal saline, whose pain manifested after every few hours. This can be used for the formulation of opium for this surgery in a large scale. Copyright © 2017 Taylor & Francis Group, LLC

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161.

Testicular sperm aspiration (TESA) for infertile couples with severe or complete asthenozoospermia.

Al-Malki A.H., Alrabeeah K., Mondou E., Brochu-Lafontaine V., Phillips S., Zini A.

Embase
Andrology. 5 (2) (pp 226-231), 2017. Date of Publication: 01 Mar 2017.

[Article]
AN: 614394595

The aim of the study was to evaluate reproductive outcomes in a cohort of infertile couples with severe and complete asthenozoospermia undergoing TESA (testicular sperm aspiration) with ICSI. We conducted a retrospective study of 28 couples with complete or severe asthenozoospermia who underwent TESA between January 2010 and December 2015. We compared TESA-ICSI outcomes of these couples to ejaculate ICSI outcomes of 40 couples with severe asthenozoospermia treated during the same time period at our institution. Couples with female factor infertility and/or female aged > 39 were excluded. Sperm retrieval rates and ICSI
outcomes [(MII oocytes, fertilization rate, good embryo rate (transferred and frozen), couples with embryo transfer (per cycle started), clinical pregnancy (per embryo transfer)] were recorded. Patients were grouped based on whether they had ejaculated (Ej-group) or testicular (TESA-group) spermatozoa used. Testicular sperm patients were further classified based on whether they had complete asthenozoospermia (0% total motility) (Tc-group) or severe asthenozoospermia (<1% progressive motility) (Ts-group). Mean (+/-SD) male and female ages were 36 +/- 6 and 32 +/- 4, respectively. Sperm recovery by testicular sperm aspiration (TESA) was successful in 100% (28/28) of the men. The overall clinical pregnancy rate (CPR) per cycle started was 34% (23/68) with a mean of 1.1 +/- 0.4 embryos transferred per transfer. Fertilization rates were significantly lower in TESA-group compared to Ej-group (52% vs. 67%, respectively; p = 0.001), while male age was significantly higher in TESA-group compared to Ej-group (34 +/- 6 vs. 37 +/- 6, respectively; p = 0.03). Moreover, female age was significantly higher in Tc-group compared to Ts-group (30 +/- 4 vs. 33 +/- 3, respectively; p = 0.0285). However, there were no significant difference in clinical pregnancy rate per embryo transfer in the Tc-group, Ts-group, and Ej-group (50% vs. 45% vs. 57%, respectively; p = 0.8219). The data suggest that testicular sperm-ICSI is no better than ejaculated sperm-ICSI in couples with severe or complete asthenozoospermia. Randomized, controlled trials comparing ejaculated vs. testicular spermatozoa are needed to assess the true benefit of TESA-ICSI in these couples. Copyright © 2017 American Society of Andrology and European Academy of Andrology.

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Publisher Blackwell Publishing Ltd (E-mail: customerservices@oxonblackwellpublishing.com)
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Testosterone prevents protein loss via the hepatic urea cycle in human.
Lam T., Poljak A., McLean M., Bahl N., Ho K.K.Y., Birzniece V.
Embase
[Article]
AN: 614784586
Context: The urea cycle is a rate-limting step for amino acid nitrogen elimination. The rate of urea synthesis is a true indicator of whole-body protein catabolism. Testosterone reduces protein and nitrogen loss. The effect of testosterone on hepatic urea synthesis in humans has not been studied. Objective: To determine whether testosterone reduces hepatic urea production. Design: An open-label study. Patients and intervention: Eight hypogonadal men were studied at baseline, and after two weeks of transdermal testosterone replacement (Testogel, 100 mg/day). Main outcomes measures: The rate of hepatic urea synthesis was measured by the urea turnover technique using stable isotope methodology, with 15N2-urea as tracer. Whole-body leucine turnover was measured, from which leucine rate of appearance (LRa), an index of protein breakdown and leucine oxidation (Lox), a measure of irreversible protein loss, were calculated. Results: Testosterone administration significantly reduced the rate of hepatic urea production (from 544.4 +/- 71.8 to 431.7 +/- 68.3 mumol/min; P < 0.01), which was paralleled by a significant reduction in serum urea concentration. Testosterone treatment significantly reduced net protein loss, as measured by percent Lox/LRa, by 19.3 +/- 5.8% (P < 0.05). There was a positive association between Lox and hepatic urea production at baseline (r² = 0.60, P < 0.05) and after testosterone administration (r² = 0.59, P < 0.05). Conclusion: Testosterone replacement reduces protein loss and hepatic urea synthesis. We conclude that testosterone regulates whole-body protein metabolism by suppressing the urea cycle.   Copyright © 2017 European Society of Endocrinology.
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Nutrient patterns and asthenozoospermia: a case-control study.

Embase
Andrologia. 49 (3) (no pagination), 2017. Article Number: e12624. Date of Publication: 01 Apr 2017.

The association of dietary nutrient patterns and sperm motility is not yet well elucidated, and previous studies have just focused on the isolated nutrients. This case-control study examined the association of nutrient patterns with asthenozoospermia among Iranian men. In total, 107 incident asthenozoospermic men and 235 age-matched controls were interviewed through the infertility clinics in Tehran, Iran, from January 2012 to November 2013. Semen quality data were analysed according to the fifth edition of WHO guideline. Nutrient patterns were identified using principal component analysis based on semiquantitative 168-item food frequency questionnaires. All nutrient intakes were energy-adjusted by the residual method. In principal component analysis, three dietary patterns emerged. The first pattern, which was high in vitamin E, vitamin D, vitamin C, zinc, folate, total fibre, selenium and polyunsaturated fatty acids, was significantly associated with lower risk of asthenozoospermia. After adjustment for potential confounders, participants in the highest tertile of the first pattern scores had 51% lower risk of asthenozoospermia compared with those in the lowest (p-trend:.004). Our findings suggest that adherence to the pattern comprising mainly of antioxidant nutrients may be inversely associated with asthenozoospermia.
164.
The SPO11-C631T gene polymorphism and male infertility risk: a meta-analysis.
Embase
Renal Failure. (pp 1-7), 2017. Date of Publication: 03 Jan 2017.
[Article In Press]
AN: 613984949
To evaluate the association between the SPO11 gene C631T polymorphism and the risk of male infertility. We conducted a search on PubMed, Embase, Web of Science, Chinese National Knowledge Infrastructure (CNKI), China biology medical literature database (CBM), VIP, and Chinese literature database (Wan Fang) on 31 March 2016. Odds ratio (OR) and 95% confidence interval (95%CI) were used to assess the strength of associations. A total of five studies including 542 cases and 510 controls were involved in this meta-analysis. The pooled results indicated that
the SPO11 gene C631T polymorphism was significantly associated with increased risk of male infertility (TT+CT vs. CC: OR=4.14, 95%CI=2.48-6.89; CT vs. CC: OR=4.34, 95%CI=2.56-7.34; T vs. C: OR=4.35, 95%CI=2.58-7.34). Subgroup analysis of different countries proved the relationship between SPO11 gene C631T polymorphism and male infertility risk in Chinese, but not in Iranian peoples. In conclusion, this study suggested that SPO11 gene C631T polymorphism may contribute as a genetic factor susceptible to cause male infertility. Furthermore, more large sample and representative population-based cases and well-matched controls are needed to validate our results. Copyright © 2016 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group.

PMID

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ARTICLE IN PRESS

Institution
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165.
Leptin as a predictive marker in unexplained infertility in north indian population.
Kumari P., Jaiswar S.P., Shankhwar P., Deo S., Ahmad K., Iqbal B., Mahdi A.A.
Embase
[Article]
AN: 614670702
Introduction: According to WHO, the primary infertility in India is about 3.9% (age-standardized to 25-49 year) and 16.8% (age-standardized to 15-49 year), using the "age but no birth" definition. Several factors which affect fertility include low sperm production in men, poor egg quality and blocked fallopian tubes in women and also hormonal imbalances. Leptin plays a critical role in women's reproduction and neuroendocrine health. It is used for treating exercise-induced bone loss, eating disorders and infertility. Aim: To evaluate the serum leptin levels in Indians and to ascertain the relationship between serum leptin levels, Unexplained Infertility (UI) and related variables [height, weight, Waist Hip Ratio (WHR), Body Mass Index (BMI)] between obese infertile, non-obese infertile and healthy subjects. Materials and Methods: The present case-control study was conducted at the Department of Obstetrics and Gynaecology, King George's Medical University (KGMU), Lucknow, India and funded by Department of Science and Technology, New Delhi, India. The study included 229 female participants in the age group of 18-40 years (120 cases and 109 controls) who were randomly selected. The blood samples were collected from the Infertility Clinic, Queen Mary's Hospital, KGMU, Lucknow, India. All the participants underwent complete physical examination. Initially, the participants were categorized into fertile and infertile groups, they were further divided on the basis of BMI, normal (BMI - 18.5-24.5) and overweight or obese (BMI>25). Leptin level was measured by Active Human Leptin ELISA kit and BMI of all subjects was calculated in kg/m2 (weight in kg and height in m). Results: A highly positive linear correlation (R=0.754, p<0.001) was found between BMI and serum leptin in unexplained infertile women, which indicates a strong relationship between BMI and serum leptin. The variation in serum leptin is explained by the independent variable, BMI. There was a partial positive linear correlation between BMI and serum leptin in the control group. Statistically there was no significant correlation (R=0.109, p=0.258) between BMI and serum leptin in the control group. Conclusion: The present study clearly demonstrates that level of leptin is higher in unexplained infertile than in the fertile group, and also shows that a strong relationship exists between BMI and serum leptin in the obese group. Serum leptin level was significantly higher in obese than non-obese subjects. Thus, leptin is an important factor for normal reproductive function. Obesity, the main cause of infertility may be controlled by regulating the leptin concentration. Copyright © 2017, Journal of Clinical and Diagnostic Research. All rights reserved.

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Male hormonal contraception: hope and promise.
Piotrowska K., Wang C., Swerdloff R.S., Liu P.Y.

Family planning is a shared responsibility, but available male-directed contraceptive methods are either not easily reversible (vasectomy) or not sufficiently effective (condom). However, roughly 20% of couples using a contraceptive method worldwide, and up to 80% in some countries, still choose a male-directed method. Male hormonal contraception is highly effective, with perfect use failure rates of 0.6% (95% CI 0.3-1.1) if sperm concentrations of less than 1 million per mL are maintained. After cessation of male hormonal contraception, sperm output fully recovers in a predictable manner, resulting in pregnancies and livebirths. Spontaneous miscarriage and fetal malformation rates after recovery of sperm output overlap those in the general population. Short-term adverse events-acne, night sweats, increased weight, and altered mood and libido-are recognised, but are generally mild. Further optimisation of specific androgen-progesterin regimens and phase 3 studies of lead combinations are still needed to successfully develop an approved male hormonal contraceptive and to identify long-term side-effects.
Comparison of the efficacy and safety of aripiprazole versus bupropion augmentation in patients with major depressive disorder unresponsive to selective serotonin reuptake inhibitors: A randomized, prospective, open-label study.


Embase

[Article]
AN: 614244057

Purpose The purpose of this study was to compare the efficacy and safety of aripiprazole versus bupropion augmentation in patients with major depressive disorder (MDD) unresponsive to selective serotonin reuptake inhibitors (SSRIs). Methods This is the first randomized, prospective, open-label, direct comparison study between aripiprazole and bupropion augmentation. Participants had at least moderately severe depressive symptoms after 4 weeks or more of SSRI treatment. A total of 103 patients were randomized to either aripiprazole (n = 56) or bupropion (n = 47) augmentation for 6 weeks. Concomitant use of psychotropic agents was prohibited. Montgomery Asberg Depression Rating Scale, 17-item Hamilton Depression Rating scale, Iowa Fatigue Scale, Drug-Induced Extrapyramidal Symptoms Scale, Psychotropic-Related Sexual Dysfunction Questionnaire scores were obtained at baseline and after 1, 2, 4, and 6 weeks of treatment. Results Overall, both treatments significantly improved depressive symptoms without causing serious adverse events. There were no significant differences in the Montgomery Asberg Depression Rating Scale, 17-item Hamilton Depression Rating scale, and Iowa Fatigue Scale.
scores, and response rates. However, significant differences in remission rates between the 2 groups were evident at week 6 (55.4% vs 34.0%, respectively; P = 0.031), favoring aripiprazole over bupropion. There were no significant differences in adverse sexual events, extrapyramidal symptoms, or akathisia between the 2 groups. Conclusions The present study suggests that aripiprazole augmentation is at least comparable to bupropion augmentation in combination with SSRI in terms of efficacy and tolerability in patients with MDD. Both aripiprazole and bupropion could help reduce sexual dysfunction and fatigue in patients with MDD. Aripiprazole and bupropion may offer effective and safe augmentation strategies in patients with MDD who are unresponsive to SSRIs. Double-blinded trials are warranted to confirm the present findings.

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168.
Cryopreserved oocyte versus fresh oocyte assisted reproductive technology cycles, United States, 2013.
Crawford S., Boulet S.L., Kawwass J.F., Jamieson D.J., Kissin D.M.
Objective: To compare characteristics, explore predictors, and compare assisted reproductive technology (ART) cycle, transfer, and pregnancy outcomes of autologous and donor cryopreserved oocyte cycles with fresh oocyte cycles. Design: Retrospective cohort study from the National ART Surveillance System. Setting: Fertility treatment centers. Patients: Fresh embryo cycles initiated in 2013 utilizing embryos created with fresh and cryopreserved, autologous and donor oocytes. Intervention(s): Cryopreservation of oocytes versus fresh. Main Outcomes Measure(s): Cancellation, implantation, pregnancy, miscarriage, and live birth rates per cycle, transfer, and/or pregnancy. Result(s): There was no evidence of differences in cancellation, implantation, pregnancy, miscarriage, or live birth rates between autologous fresh and cryopreserved oocyte cycles. Donor cryopreserved oocyte cycles had a decreased risk of cancellation before transfer (adjusted risk ratio [aRR] 0.74, 95% confidence interval [CI] 0.57-0.96) as well as decreased likelihood of pregnancy (aRR 0.88, 95% CI 0.81-0.95) and live birth (aRR 0.87, 95% CI 0.80-0.95); however, there was no evidence of differences in implantation, pregnancy, or live birth rates when cycles were restricted to those proceeding to transfer. Donor cryopreserved oocyte cycles proceeding to pregnancy had a decreased risk of miscarriage (aRR 0.75, 95% CI 0.58-0.97) and higher live birth rate (aRR 1.05, 95% CI 1.01-1.09) with the transfer of one embryo, but higher miscarriage rate (aRR 1.28, 95% CI 1.07-1.54) and lower live birth rate (aRR 0.95, 95% CI 0.92-0.99) with the transfer of two or more. Conclusion(s): There was no evidence of differences in ART outcomes between autologous fresh and cryopreserved oocyte cycles. There was evidence of differences in per-cycle and per-pregnancy outcomes between donor cryopreserved and fresh oocyte cycles, but not in per-transfer outcomes. Copyright © 2016

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Publisher
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AN: 614860035
Purpose: The purpose of this study is to determine the possible preoperative predictors of spontaneous pregnancy (SPR) for infertile males with varicocele after microsurgical subinguinal varicocelectomy (MVL) performed in two medical centers in a prospective cohort study. Methods: A total of 120 males with varicocele that underwent MVL between June 2013 and June 2014 in two medical centers were documented. Related data, including male and female partner age, male body mass index (BMI), female BMI, preoperative semen parameters, hormone levels, testicular volume, grade and side of varicocele, were collected and analyzed. The follow-up assessment was also conducted within a 2-year period after the surgery. The outcome measure was SPR within the 2-year follow-up reported. The possible determinants of SPR were also analyzed and indentified using Cox regression analysis. Results: Of the 110 patients that accomplished the 2-year follow-up, 42 patients reported pregnancy outcome. Using Cox regression analysis, total motile sperm count [TMC; RR (95% CI) = 1.362 (1.120-1.560), p = 0.003] and follicle-stimulating hormone [FSH; RR (95% CI) = 0.726 (0.541-0.980), p = 0.020] levels posed significant determinants for SPR. Conclusion: Our study indicated that males who underwent MVL with higher TMC and lower FSH preoperatively have higher possibility of pregnancy postoperatively. Copyright © 2017 Springer Science+Business Media Dordrecht
Status
ARTICLE IN PRESS
Institution
(Zhang, Wang, Xu, Tian) Department of Urology Surgery, The First Affiliated Hospital of Zhengzhou University, #1 Jian She Dong Road, Zhengzhou, Henan 450052, China (Xu, Kuang)
Local endometrial scratching under ultrasound-guidance after failed intrauterine insemination and cycle outcome: A randomized controlled trial.

Soliman B.S., Harira M.

Embase


[Article]

AN: 613645898

Background: Interaction between the embryo and endometrium plus endometrial receptivity is considered as two strong issues affecting the implantation outcome. Purpose: To investigate the effect of local endometrial scratching on pregnancy rate after failed previous intra uterine insemination. Study design: A prospective, randomized, control trial. Setting: At Cytogenetic and Endoscopy Unit, Zagazig University Hospital. Patients and methods: A total of 226 women either with unexplained or with mild male factor infertility were divided randomly into approximately two groups: in study group, 114 women and in control group, 112 women. For both groups, folliculometry was started at cycle day 7 additionally and at the same setting; endometrial scratching was done only for the study group. Outcome results: Biochemical and clinical pregnancy rates. Results: The biochemical and clinical pregnancy rates were significantly higher in the endometrial scratching group compared to the control group [27/106 (25.5%) vs. 15/106 (14.1%) p = 0.03 and 24/106 (22.6%) vs. 12/106 (11.3%); p = 0.02] respectively. Also, ongoing pregnancy rate was statistically significantly different between both groups [22/106 (20.7%) vs. 11/106 (10.4%); p = 0.03]. Conclusion: Endometrial scratching is useful in increasing pregnancy rates after failed previous intra uterine insemination trials when it is performed in the mid proliferative phase. Copyright © 2016 Middle East Fertility Society
Curative effect of surgery in combination with compound xuanju capsule in treating subclinical varicocele induced infertility.
Qu X., Shan Z., Zhang N., Guo L.

Biomedical Research (India). 28 (3) (pp 1247-1250), 2017. Date of Publication: 2017.

[Article]
AN: 614479853

Objective: To discuss over the clinical effect of treating subclinical varicocele induced infertility with varicocelectomy in combination with compound Xuanju capsule and the effect of the therapy on levels of sex hormone and anti-sperm antibody (AsAb). Methods: Eighty-eight patients with subclinical varicocele were selected and randomly divided into a treatment group and a control group (N=44). Patients in the control group underwent varicocelectomy, while patients in the treatment group were given compound Xuanju capsule besides surgery. Clinical effects, the level of sex hormone and the level of AsAb of two groups were observed and analyzed. Results: The clinical effective rate of the treatment group was 84.09%, much higher than 68.18% in the control group. Sperm density, the percentage of forward movement sperm and sperm survival rate of the control group were (29.32 +/- 3.48) x 10^6, (45.68 +/- 3.03) and (57.17 +/- 3.42) respectively after treatment, much higher than the values before treatment, and the differences had statistical significance (P<0.05); the percentage of normal morphological sperms, sperm density, the percentage of forward movement sperm and sperm survival rate of the treatment group were
much higher to those of the control group, and the differences had statistical significance (P<0.05); except for semen volume, the other indexes of the treatment group were superior to those of the control group after treatment, and the differences had statistical significance (P<0.05). The hormone level of the treatment group was higher than that of the control group, and the difference had statistical significance (P<0.05); the reduction amplitude of serum AsAb positive rate of the treatment group was more obvious than that of the control group, and the difference had statistical significance (P<0.05). Conclusions: Surgery in combination with compound Xuanju capsule can effectively improve semen quality and sexual hormone level and reduce the level of serum AsAb in the treatment of subclinical varicocele. Copyright © 2017, Scientific Publishers of India. All rights reserved.

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20170316
Year of Publication
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172.
Effectiveness of a video intervention on fertility knowledge among university students: a randomised pre-test/post-test study.
Conceicao C., Pedro J., Martins M.V.
Embase
European Journal of Contraception and Reproductive Health Care. 22 (2) (pp 107-113), 2017.
Date of Publication: 04 Mar 2017.
[Article]
AN: 614436635
Objectives: Recent evidence has shown that young adults have poor knowledge about reproductive health and fertility, and that interventions are needed to increase fertility awareness.
The aim of this study was to assess the effectiveness of a brief video in increasing knowledge about fertility and infertility in young adults. Methods: We carried out a two-arm, parallel-group, randomised controlled trial with a pre-test/post-test design (NCT02607761, ClinicalTrials.gov). The sample was composed of 173 undergraduates who completed a self-report questionnaire. Participants were randomly assigned to exposure or no exposure to an educational video about reproductive health and infertility (intervention group, n = 89; control group, n = 84). Results: At baseline, participants revealed poor knowledge of infertility risk factors and fertility issues, and average knowledge of the definition of infertility. Interaction effects between group and time were found for all variables targeted in the video. Participants in the intervention group significantly increased their knowledge of fertility issues, infertility risk factors and the definition of infertility. No significant differences in post-test knowledge were observed in the control group, except for the age at which there is a marked decrease in female fertility. Conclusions: A short video intervention is effective in increasing short-term knowledge about reproductive health and infertility. If future research using longer intervals corroborates our findings, video intervention could be a useful tool in public health prevention campaigns. Copyright © 2017 The European Society of Contraception and Reproductive Health.

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173.
FDA-approved medications that impair human spermatogenesis.
We herein provide an overview of the single-ingredient U.S. Food and Drug Administration (FDA)-approved drugs that affect human spermatogenesis, potentially resulting in a negative impact on male fertility. To provide this information, we performed an in-depth search of DailyMed, the official website for FDA-approved drug labels. Not surprisingly, hormone-based agents were found to be the drugs most likely to affect human spermatogenesis. The next category of drugs most likely to have effects on spermatogenesis was the antineoplastic agents. Interestingly, the DailyMed labels indicated that several anti-inflammatory drugs affect spermatogenesis, which is not supported by the peer-reviewed literature. Overall, there were a total of 65 labels for drugs of various classes that showed that they have the potential to affect human sperm production and maturation. We identified several drugs indicated to be spermatotoxic in the drug labels that were not reported in the peer-reviewed literature. However, the details about the effects of these drugs on human spermatogenesis are largely lacking, the mechanisms are often unknown, and the clinical impact of many of the findings is currently unclear. Therefore, additional work is needed at both the basic research level and during clinical trials and post-marketing surveillance to fill the gaps in the current knowledge. The present findings will be of interest to physicians and pharmacists, researchers, and those involved in drug development and health care policy.
Preliminary study of the efficacy of the combination of tamsulosin and trospium as a medical expulsive therapy for distal ureteric stones.

Abdelaziz A.S., Badran Y.A., Aboelsaad A.Y., Elhilaly H.

Objectives To evaluate and compare the efficacy of tamsulosin (0.4 mg, once/day) and combinations of it with trospium (20 mg, twice/day) in the treatment of single small lower ureteral stones. Patients and methods A total of 126 patients presenting to urology outpatient clinics from July 2012 to May 2015, with a single 5-10 mm sized lower ureteral stone were randomly classified into two treatment groups. Patients in group A (n = 62) received an oral dose of 0.4 mg tamsulosin once daily and 20 mg trospium chloride twice daily. Patients in group B (n = 64) received 0.4 mg tamsulosin once daily and placebo twice daily. The spontaneous passage of stones, the stone expulsion time, and adverse effects were evaluated. Results There were no significant differences in baseline characteristic of the patients in both groups. Stone expulsion was observed in 47 patients (75.8%), and 58 (90.62%) in groups A and B respectively. The average time to expulsion was 11.65 +/- 5.32 days in group A and 17.35 +/- 6.21 days in group B. The spontaneous stone passage rate through the ureter was significantly higher and the stone expulsion time was faster in groups A than in group B (p < 0.05). The adverse effects observed in both groups were comparable and were mild. Conclusions The combination of 0.4 mg tamsulosin and 40 mg trospium as MET for single lower ureteral stones <10 mm is safe and more effective than 0.4 mg tamsulosin as a mono-therapy. Copyright © 2016 Pan African Urological Surgeons Association

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Abdelkader O., Mohyelden K., Sherif M.H., Metwaly A.H., Aldaquadossi H., Shelbaya A., Khairy H., Elnashar A.

Embase

Objectives To compare the role of alpha-blocker (Tamsulosin) monotherapy, anticholinergic (Tolterodine) monotherapy or combination of both drugs versus analgesics in improving post-ureteroscopy (URS) lower urinary tract symptoms related to double-J ureteral stent. Patients and methods Between January 2009 and June 2013, 160 consecutive patients with ureteric stones were included in this study at 2 tertiary care centers'. Patients were randomized into 4 groups; group A (n = 40) received 0.4 mg Tamsulosin once a day, group B (n = 40) received 4 mg Tolterodine once a day, group C (n = 40) received Tamsulosin 0.4 mg and Tolterodine 4 mg once a day and group D (n = 40) as a control group, received placebo once a day. All patients received analgesics on demand. Pre-treatment evaluation was done followed by among-groups comparison after 14 days including ureteral stent symptom questionnaire (USSQ) [Urinary symptom index (USI), pain symptom index (PSI), general health index (GHI), work perform index (WPI), need for pain killer (PK), need for analgesia, visual analogue scale (VAS) for pain and quality of life (QOL)]. Side effects were recorded and compared. Results Out of 160 patients, 153 patients (40, 38, 37 and 38 patients in groups A, B, C and D, respectively) completed the study with a mean age of 34.3 +/- 7.6 (20-50) years. All groups were comparable in terms of age, gender, stone size and stone location, USSQ items and QOL. After 14 days, the USSQ and QOL were significantly lower in group A, B and C in comparison with group D (p < 0.05). Patients in group C had significantly much improvement than those of groups A and B (p < 0.05). Conclusion
Combination of alpha blockers (Tamsulosin) and Anticholinergics (Tolterodine) seems to significantly improve post-URS lower urinary tract symptoms secondary to ureteral stents with lower need for analgesia and better quality of life. Adverse effect of used drugs mentioned as transient and tolerated by the patients without need for auxiliary medication. Copyright © 2016 Pan African Urological Surgeons’ Association

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176.
Jasuja G.K., Bhasin S., Reisman J.I., Hanlon J.T., Miller D.R., Morreale A.P., Pogach L.M., Cunningham F.E., Park A., Berlowitz D.R., Rose A.J.
Embase
[Article]
AN: 613790122
Background: There has been concern about the growing off-label use of testosterone. Understanding the context within which testosterone is prescribed may contribute to interventions to improve prescribing. Objective: To evaluate patient characteristics associated with receipt of testosterone. Design: Cross-sectional. Setting: A national cohort of male patients, who had
received at least one outpatient prescription within the Veterans Affairs (VA) system during Fiscal Year 2008- Fiscal Year 2012. Participants: The study sample consisted of 682,915 non-HIV male patients, of whom 132,764 had received testosterone and a random 10% sample, 550,151, had not. Main Measures: Conditions and medications associated with testosterone prescription. Key Results: Only 6.3% of men who received testosterone from the VA during the study period had a disorder of the testis, pituitary or hypothalamus associated with male hypogonadism. Among patients without a diagnosed disorder of hypogonadism, the use of opioids and obesity were the strongest predictors of testosterone prescription. Patients receiving >100 mg/equivalents of oral morphine daily (adjusted odds ratio = 5.75, p < 0.001) and those with body mass index (BMI) >40 kg/m² (adjusted odds ratio = 3.01, p < 0.001) were more likely to receive testosterone than non-opioid users and men with BMI <25 kg/m². Certain demographics (age 40-54, White race), comorbid conditions (sleep apnea, depression, and diabetes), and medications (antidepressants, systemic corticosteroids) also predicted a higher likelihood of testosterone receipt, all with an adjusted odds ratio less than 2 (p < 0.001). Conclusions: In the VA, 93.7% of men receiving testosterone did not have a diagnosed condition of the testes, pituitary, or hypothalamus. The strongest predictors of testosterone receipt (e.g., obesity, receipt of opioids), which though are associated with unapproved, off-label use, may be valid reasons for therapy. Interventions should aim to increase the proportion of testosterone recipients who have a valid indication. Copyright © 2016, Society of General Internal Medicine.

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An update on the diagnosis, surgical management, and fertility outcomes for women with endometrioma. Cranney R., Condous G., Reid S. Embase


AN: 614789347

Endometriosis is estimated to affect up to 50% of infertile women, and severity of endometriosis stage appears to correlate with reduced fertility. Ovarian endometriomas are found in up to 44% of women with endometriosis, and are significantly associated with the presence of pelvic deep infiltrating endometriosis, ovarian adhesions, and pouch of Douglas obliteration. Through the use of MEDLINE and PubMed databases, we conducted a literature review of all available research
related to the diagnosis, surgical management and fertility outcomes for women with endometrioma. The evolving use of specialized transvaginal ultrasound for the diagnosis of endometrioma and related endometriotic pathologies can allow for preoperative mapping/staging of the disease, as well as appropriate surgical planning and fertility counseling. Surgical management of endometriomas appears to reduce markers of ovarian reserve, such as anti-Mullerian hormone, prompting concern of reduced fertility following surgery. Ovarian cystectomy appears to be superior to ablation in terms of endometrioma recurrence, pain symptoms and increased spontaneous conception rate among subfertile patients. Research is inconclusive as to which surgical method least damages ovarian reserve in the long term; however, bipolar hemostasis appears to be the most damaging technique and should be avoided. Surgical management should be individualized for women with endometrioma, and strong consideration should be given to the preoperative ovarian reserve status prior to performing ovarian cystectomy. Current evidence suggests that ovarian cystectomy does not improve reproductive outcomes for women with endometrioma undergoing assisted reproductive technology; however, the majority of studies have been performed retrospectively and more prospective studies are needed. Copyright © Nordic Federation of Societies of Obstetrics and Gynecology.

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Is there a protective role of testosterone against high-grade prostate cancer? Incidence and severity of prostate cancer in 553 patients who underwent prostate biopsy: a prospective data register.

Yassin A., Salman M., Talib R.A., Yassin D.-J.

Embase

[Article In Press]
AN: 614783849

This study investigated the role of testosterone replacement therapy (TRT) in prostate safety and cancer progression. A cohort of 553 patients, 42 treated and 162 untreated hypogonadal men, and 349 eugonadal men were included. Pathological analysis of prostate biopsies examining the incidence and severity of PCa revealed that: 16.7% of treated hypogonadal men had a positive biopsy, a Gleason score of <6 in 71.4% and >6 in 28.6% of men, a predominant score of 3 and tumour staging of II in 85.7% men; 51.9% of untreated hypogonadal men had a positive biopsy, a Gleason score of <6 in 40.5% and >6 in 59.5% men, a predominant score of 3 (77.4%) and tumour staging of II (41.7%) or III (40.5%); 37.8% of eugonadal men had a positive biopsy, a Gleason score of <6 in 42.4% and >6 in 57.6% of men, a predominant score of 3 (82.6%) and tumour staging of II (44.7%) or III (47.7%). The incidence of positive prostate biopsies was lowest in hypogonadal men receiving TRT, with significantly lower severity of PCa in terms of staging and grading in the same group. These results suggest that TRT might have a protective effect against high-grade PCa. Copyright © 2017 Informa UK Limited, trading as Taylor & Francis Group.

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Publisher
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2017
Sex steroids in relation to cardiac structure and function in men.
De Smet M.A.J., Lapauw B., De Backer T.

Embase
Andrologia. 49 (2) (no pagination), 2017. Article Number: e12610. Date of Publication: 01 Mar 2017.
[Article]
AN: 614376848

The prevalence of testosterone substitution as well as of androgen deprivation therapy in men is increasing. This review aims to summarise available knowledge of the effects of sex steroids on cardiac structure and function in men. MEDLINE was searched through PubMed. Original studies, systematic reviews and meta-analyses, and relevant citations were screened. A short-term hormonal intervention study in healthy young men with respect to echocardiographic parameters of structure and function was performed. Preclinical research provides sufficient evidence for the heart as a substrate for sex hormones. In animals, administration of oestradiol appears to have beneficial effects on cardiac structure and function, whereas administration of testosterone to noncastrated animals adversely affects cardiac function. However, the effects of sex steroids on cardiac function and structure appear more heterogeneous in human observational studies while comparative, prospective studies in humans are lacking. It is concluded that although effects of testosterone substitution as well as of androgen deprivation on cardiac structure and function can be expected based on pre-clinical research, there exists an important knowledge gap of the effects of hormonal intervention in men. As such, there is a need to address this question in future prospective intervention trials. Copyright © 2016 Blackwell Verlag GmbH

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Association and meta-analysis of HLA and non-obstructive azoospermia in the Han Chinese population.
Zou S., Song P., Meng H., Chen T., Chen J., Wen Z., Li Z., Shi Y., Hu H.
Embase
Andrologia. 49 (2) (no pagination), 2017. Article Number: e12600. Date of Publication: 01 Mar 2017.
[Article]
AN: 612061017
The exact aetiology and pathogenesis of most non-obstructive azoospermia (NOA) are still unknown. The previous two genomewide association studies (GWASs) have identified three different loci within the HLA region for NOA in the Han Chinese population, including rs3129878, rs498422 and rs7194. To further validate the risk of three GWAS-linked loci for NOA, we conducted a case-control study of these three risk loci in an independent Han Chinese male population, with 603 NOA patients and 610 controls. Furthermore, we also performed a meta-analysis of five studies on these three NOA-risk loci. The case-control study strongly suggested a significant association between loci rs3129878, rs498422 and rs7194 and NOA (P = 6.75 x 10-21 (OR = 2.2586), P = 0.0060 (OR = 1.4013) and P = 0.0128 (OR = 1.2626) respectively). Our meta-analyses also supported the susceptibility of these three risk loci to NOA (P < 0.01). The risk variants within the HLA region potentially have a strong effect on males at risk of NOA, and may serve as diagnostic markers for male infertility. However, considering genetic difference between different populations, future validating studies in larger independent samples and animal experiments are suggested. Copyright © 2016 Blackwell Verlag GmbH
PMID
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EMBASE
Efficacy and safety of testosterone replacement gel for treating hypogonadism in men: Phase III open-label studies.
Belkoff L., Brock G., Carrara D., Neijber A., Ando M., Mitchel J.
Embase
[Article In Press]
AN: 614765889
Efficacy and safety of testosterone gel 2% (TG) were evaluated in two phase 3, open-labelled, single-arm, multicentre studies (000023 and extension study 000077). Hypogonadal men having serum testosterone levels <300 ng/dl at two consecutive measurements were included. Study duration was 9 months (000023: 3 months; 000077: 6 months). Starting dose of TG (46 mg) was applied on upper arm/shoulder. The primary endpoint (000023) was responder rate (subjects with average 24-hour serum testosterone concentration 300-1050 ng/dl on Day 90). Study 000077 evaluated the safety of TG in patients rolling over from study 000023 over a period of 6 months. Of 180 subjects in 000023, 172 completed and 145 rolled over to 000077, with 127 completers. The responder rate was 85.5%. Fewer subjects in 000077 (12.7%) versus 000023 (31.8%) had maximum testosterone concentration (Cmax) >1500 ng/dl, with no significant safety concerns. Significant improvements in sexual function and quality of life were noted in both studies. Subjects experienced few skin reactions without notable increases in prostate-specific antigen
and haematocrit levels. TG was efficacious with an acceptable safety profile. Cmax >1500 ng/dl did not exhibit distinct impact on safety parameters. However, further optimisation of titration schema to reduce Cmax is warranted while maintaining the average steady state total testosterone concentration. Copyright © 2017 Blackwell Verlag GmbH.

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182.
Androgen Treatment Effects on Motor Function, Cognition, and Behavior in Boys with Klinefelter Syndrome.
Ross J.L., Kushner H., Kowal K., Bardsley M., Davis S., Reiss A.L., Tartaglia N., Roeltgen D.
Embase
[Article In Press]
AN: 614748549

Objectives: To examine the effects of early low-dose androgen on motor, cognitive, and behavioral function in prepubertal boys with Klinefelter syndrome (47,XXY). Study design: Double-blind trial of 84 boys, ages 4-12 years, randomized to oxandrolone (Ox; 0.06 mg/kg daily; n = 43) or placebo (Pl; n = 41) for 24 months. Standardized assessments were performed at baseline and every 12 months for 24 months evaluating motor, cognitive, and behavioral function.
Results: The 24-month outcomes were better in the Ox vs. Pl group on 1 of 5 primary endpoints (motor function/strength): Bruininks Visual-Motor scale (P = .005), without significant differences between the 2 groups for the other 4 components. Secondary analyses suggested improvement in the Ox vs. Pl group in the anxiety/depression (P = .03) and social problems (P = .01) scales on the Child Behavior Checklist, anxiety (P = .04) on the Piers Harris Self Concept Scale, and interpersonal problems (P = .02) on the Children’s Depression Inventory, without significant differences in hyperactive or aggressive behaviors. Conclusions: This double-blind, randomized trial demonstrates that 24 months of childhood low-dose androgen treatment in boys with Klinefelter syndrome benefited 1 of 5 primary endpoints (visual-motor function). Secondary analyses demonstrated positive effects of androgen on aspects of psychosocial function (anxiety, depression, social problems), without significant effects on cognitive function, or hyperactive or aggressive behaviors. Trial registration: ClinicalTrials.gov: NCT00348946. Copyright © 2017 Elsevier Inc.

Effect of soy in men with type 2 diabetes mellitus and subclinical hypogonadism: A randomized controlled study.
Context: Isoflavones found in soy products have a chemical structure similar to estrogen, leading to concerns of an adverse estrogenic effect in men, particularly in those with type 2 diabetes mellitus (T2DM) who have low testosterone levels due to hypogonadism. Objective: The primary outcome was change in total testosterone levels. The secondary outcomes were the changes in glycemia and cardiovascular risk markers. Design: This was a randomized double-blind parallel study. Setting: This study occurred in a secondary care setting in United Kingdom. Participants: Two hundred men with T2DM and a total testosterone level <12 nmol/L were included. Intervention: Fifteen grams of soy protein with 66 mg of isoflavones (SPI) or 15 g soy protein alone without isoflavones (SP) daily as snack bars for 3 months were administered. Results: There was no change in either total testosterone or in absolute free testosterone levels with either SPI or SP. There was an increase in thyrotropin (TSH) and reduction in free thyroxine (fT4; P < 0.01) after SPI supplementation. Glycemic control improved with a significant reduction in hemoglobin A1c (24.19 [7.29]mmol/mol, P,0.01) and homeostasis model of assessment - insulin resistance after SPI. Cardiovascular risk improved with a reduction in triglycerides, C-reactive protein, and diastolic blood pressure (DBP; P <0.05) with SPI vs SP supplementation. There was a 6% improvement in 10-year coronary heart disease risk after 3 months of SPI supplementation. Endothelial function improved with both SPI and SP supplementation (P < 0.01), with an increased reactive hyperemia index that was greater for the SPI group (P < 0.05). Conclusions: Testosterone levels were unchanged and there was a substantial improvement in glycaemia and cardiovascular risk markers with SPI compared with SP alone over 3 months. There was also a substantial increase in TSH and a reduction in fT4. Copyright © 2017 by the Endocrine Society.
184.
The effect of expressive writing intervention for infertile couples: A randomized controlled trial.
Frederiksen Y., O'Toole M.S., Mehlsen M.Y., Hauge B., Elbaek H.O., Zachariae R., Ingerslev H.J.
Embase
[Article]
AN: 614691067
STUDY QUESTION: Is expressive writing intervention (EWI) efficacious in reducing distress and improving pregnancy rates for couples going through ART treatment? SUMMARY ANSWER: Compared to controls, EWI statistically significantly reduced depressive symptoms but not anxiety and infertility-related distress. WHAT IS KNOWN ALREADY: ART treatment is considered stressful. So far, various psychological interventions have been tested for their potential in reducing infertility-related distress and the results are generally positive. It remains unclear whether EWI, a brief and potentially cost-effective intervention, could be advantageous. STUDY DESIGN SIZE, DURATION: Between November 2010 and July 2012, a total of 295 participants (163 women, 132 men) were randomly allocated to EWI or a neutral writing control group. PARTICIPANTS/MATERIALS, SETTING, METHODS: Participants were couples undergoing IVF/ICSI treatment. Single women and couples with Preimplantation Genetic Diagnosis or acute change of procedure from insemination to IVF, were excluded. EWI participants participated in three 20-min home-based writing exercises focusing on emotional disclosure in relation to infertility/fertility treatment (two sessions) and benefit finding (one session). Controls wrote non-emotionally in three 20-min sessions about their daily activities. The participants completed questionnaires at the beginning of treatment (t1), prior to the pregnancy test (t2), and 3 months later (t3). In total, 26.8% (79/295) were lost to follow-up. Mixed linear models were chosen to compare the two groups over time for psychological outcomes (depression, anxiety and infertility-
related distress), and a Chi2 test was employed in order to examine group differences in pregnancy rates.

MAIN RESULTS AND THE ROLE OF CHANCE:

One hundred and fifty-three participants received EWI (women = 83; men = 70) and 142 participants were allocated to the neutral writing control group (women = 83; men = 62). Both women and partners in the EWI group exhibited greater reductions in depressive symptoms compared with controls (P = 0.049; [CI 95%: -0.04; -0.01] Cohen's d = 0.27). The effect of EWI on anxiety did not reach statistical significance. Overall infertility-related distress increased marginally for the partners in the EWI group compared to the partners in the control group (P = 0.06; Cohen's d = 0.17). However, in relation to the personal subdomain, the increase was statistically significant (P = 0.01; Cohen's d = 0.24). EWI had no statistically significant effect on pregnancy rates with 42/83 (50.6%) achieving pregnancy in the EWI group compared with 40/80 (49.4%) in the control group (RR = 0.99 [CI 95% = 0.725, 1.341]; P = 0.94).

LIMITATIONS, REASONS FOR CAUTION:
The results for depressive symptoms corresponded to a small effect size and the remaining results failed to reach statistical significance. This could be due to sample characteristics leading to a possible floor-effect, as we did not exclude participants with low levels of emotional distress at baseline. Furthermore, men showed increased infertility-related distress over time.

WIDER IMPLICATIONS OF THE FINDINGS:

EWI is a potentially cost-effective and easy to implement home-based intervention, and even small effects may be relevant. When faced with infertility, EWI could thus be a relevant tool for alleviating depressive symptoms by allowing the expression of feelings about infertility that may be perceived as socially unacceptable. However, the implications do not seem to be applicable for men, who presented with increased infertility-related distress overtime.

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Pregnancy and live birth rates after microsurgical vasoepididymostomy for azoospermic patients with epididymal obstruction.

Peng J., Zhang Z., Yuan Y., Cui W., Song W.

Embase


[Article]

STUDY QUESTION: Can microsurgical vasoepididymostomy (MVE) be an effective treatment for azoospermic men with epididymal obstruction? SUMMARY ANSWER: MVE is an effective treatment for epididymal obstruction, with overall patency and live birth rates of 76.3% and 34.8%, respectively. WHAT IS KNOWN ALREADY: We showed that MVE was an effective treatment for non-vasectomized patients with epididymal obstruction and prior failed sperm retrieval for ICSI. ICSI is the preferred treatment for obstructive azoospermia in some reproductive centers. Some small studies documented that MVE could achieve high patency and pregnancy rates. STUDY DESIGN, SIZE, DURATION: This retrospective study was designed to investigate the natural pregnancy and live birth rates after MVE and to identify possible predictors of pregnancy. From January 2011 to July 2013, 241 patients underwent MVE for epididymal obstruction in our andrology center. PARTICIPANTS/MATERIALS, SETTING, METHODS: All patients underwent scrotal exploration and MVE. Semen was analyzed every 3 months postoperatively until pregnancy was achieved. Patency, pregnancy and live birth rates were evaluated. Preoperative and intraoperative data were compared between patent and non-patent groups to identify factors affecting the patency rate. Predictors of pregnancy were identified by univariate and multivariate analyses with Cox regression models. MAIN RESULTS AND THE ROLE OF CHANCE: Data from 198 males (82.2%) were analyzed. The mean (+/-SD) age of males and female partners was 31.0 +/- 5.8 and 28.4 +/- 4.4 years, respectively. Sperm was present in the ejaculate of 151 patients (76.3%) postoperatively. Patency rates were increased for patients with bilateral anastomosis, distant anastomosis and motile sperm in epididymal fluid. Overall, 81/198 males (40.9%) reported pregnancy in partners and 73 newborns were delivered.
The overall live birth rate was 34.8%. Male age (hazard ratio (HR) [95% CI] 0.407 [0.203-0.816], P = 0.011), sperm concentration (HR [95% CI] 4.988 [2.777-8.957], P < 0.001) and forward motility (HR [95% CI] 1.751 [1.042-2.945], P = 0.035) were predictors of pregnancy.

LIMITATIONS, REASONS FOR CAUTION: A randomized control trial comparing pregnancy rates, live birth rates, risks and medical costs of MVE and IVF/ICSI is needed. The sample size of females >35 years old was small, so we could not determine whether female age was a predictor of pregnancy. WIDER IMPLICATIONS OF THE FINDINGS: MVE is an effective therapy for azoospermic patients with epididymal obstruction. Sperm concentration and forward motility may predict pregnancy after the procedure. Microsurgical reconstruction could be a first choice for epididymal obstruction. Copyright © The Author 2016. Published by Oxford University Press on behalf of the European Society of Human Reproduction and Embryology. All rights reserved.

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186.
Stability of the human sperm DNA methylome to folic acid fortification and short-term supplementation.
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[Article]
AN: 614690961
STUDY QUESTION: Do short-term and long-term exposures to low-dose folic acid supplementation alter DNA methylation in sperm? SUMMARY ANSWER: No alterations in sperm DNA methylation patterns were found following the administration of low-dose folic acid supplements of 400 mug/day for 90 days (short-term exposure) or when pre-fortification of food with folic acid and post-fortification sperm samples (long-term exposure) were compared. WHAT IS KNOWN ALREADY: Excess dietary folate may be detrimental to health and DNA methylation profiles due to folate's role in one-carbon metabolism and the formation of S-adenosyl methionine, the universal methyl donor. DNA methylation patterns are established in developing male germ cells and have been suggested to be affected by high-dose (5 mg/day) folic acid supplementation. STUDY DESIGN, SIZE, DURATION: This is a control versus treatment study where genome-wide sperm DNA methylation patterns were examined prior to fortification of food (1996-1997) in men with no history of infertility at baseline and following 90-day exposure to placebo (n = 9) or supplement containing 400 mug folic acid/day (n = 10). Additionally, pre-fortification sperm DNA methylation profiles (n = 19) were compared with those of a group of post-fortification (post-2004) men (n = 8) who had been exposed for several years to dietary folic acid fortification. PARTICIPANTS/MATERIALS, SETTING, METHODS: Blood and seminal plasma folate levels were measured in participants before and following the 90-day treatment with placebo or supplement. Sperm DNA methylation was assessed using the whole-genome and genome-wide techniques, MassArray epityper, restriction landmark genomic scanning, methyl-CpG immunoprecipitation and Illumina Human Methylation 450 Bead Array. MAIN RESULTS AND THE ROLE OF CHANCE: Following treatment, supplemented individuals had significantly higher levels of blood and seminal plasma folates compared to placebo. Initial first-generation genome-wide analyses of sperm DNA methylation showed little evidence of changes when comparing pre- and post-treatment samples. With Illumina Human Methylation 450 Bead Chip arrays, no significant changes were observed in individual probes following low-level supplementation; when compared with those of the post-fortification cohort, there were also few differences in methylation despite exposure to years of fortified foods. LARGE SCALE DATA: Illumina Human Methylation 450 BeadChip data from this study have been submitted to the NCBI Gene Expression Omnibus under the accession number GSE89781. LIMITATIONS, REASONS FOR CAUTION: This study was limited to the number of participants available in each cohort, in particular those who were not exposed to early (pre-1998) fortification of food with folic acid. While genome-wide DNA methylation was assessed with several techniques that targeted genic and CpG-rich regions, intergenic regions were less well interrogated. WIDER IMPLICATIONS OF THE FINDINGS: Overall, our findings provide evidence that short-term exposure to low-dose folic acid supplements of 400 mug/day, over a period of 3 months, a duration of time that might occur during infertility treatments, has no major impact on the sperm DNA methylome. Copyright ©
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187.
Human MTHFR-G1793A transition may be a protective mutation against male infertility: a genetic association study and in silico analysis.
Karimian M., Hosseinzadeh Colagar A.

Embase
[Article In Press]
AN: 614735584
In this paper, we evaluate the association of the human methylenetetrahydrofolate reductase (MTHFR)-G1793A transition with male infertility using a case-control study, a meta-analysis and an in silico analysis. In the case-control study, 308 blood samples (169 infertile and 139 fertile men) were collected. MTHFR-G1793A genotyping was performed by PCR-RFLP. The study revealed a significant protective association between the GA genotype (OR: 0.3737, 95%CI: 0.1874-0.7452, p=0.0052) and A allele (OR: 0.4266, 95%CI: 0.2267-0.8030, p = 0.0083) with male infertility. Meta-analysis showed that the G1793A transition might be a protective mutation against male infertility in both A vs. G (OR: 0.608, 95%CI: 0.466-0.792, p<0.001), and GA vs. GG (OR: 0.534, 95%CI: 0.394-0.724, p<0.001) genetic models. In silico-analysis revealed that although G1793A could not make fundamental changes in the function and structure of MTHFR, it could modify the structure of the mRNA (Distance =0.1809, p=0.1095; p<0.2 is significant). The results suggest that G1793A substitution might be a protective genetic factor against male infertility. However, further case-control studies are required to provide a more robust conclusion.

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Status
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2017
Prevalence and risk factors of chlamydia infection in Hong Kong: A population-based geospatial household survey and testing.


[Article]

AN: 614515025

Background: Chlamydia causes infertility and increases risk of HIV infection, and population-based studies provide essential information for effective infection control and prevention. This study examined Chlamydia trachomatis prevalence and risk factors among a representative sample of 18-49-year-old residents in Hong Kong. Methods: Census boundary map of 412 constituency areas was used as primary sampling units to construct the sampling frame and, residential buildings and units were randomly selected using geospatial modelling. A questionnaire on sexual practice and health was conducted, and polymerase chain reaction was used to test the urine for genital chlamydial infection. Invitation letters were sent to the selected households and a team of interviewers were sent to recruit one subject per household. Prevalence data was weighted according to the 2011 census and risk factors identified through logistic regression. Results: Among 881 participants (response rate of 24.5%), the overall Chlamydia trachomatis prevalence was low at 1.4% (95%CI 0.8+/−2.5%) but sexually active young (18+/−26 years) women had relatively high prevalence (5.8%, 95%CI 1.7+/−18.2%) in Hong Kong. A unique U-shape disease burden was observed with peaks in younger and older (40+/−49 years) women. Amongst the sexually active women, the risk factors of Chlamydia trachomatis infection were: younger age (aOR = 25.4, 95% CI 2.81+/−230); living alone (aOR = 8.99, 95% CI 1.46+/−55.40); and, among all the sexually active participants, males (including the male partners of the female participants) who had travelled out of Hong Kong in the previous 12 months had higher risks of infection (aOR = 5.35; 95% CI 1.25+/−22.8). A core-peripheral geographical distribution of Chlamydia trachomatis prevalence was also observed. Conclusion: Young and older sexually active women in Hong Kong have high prevalence of chlamydia. Routine screening for sexually active women and young men should be considered. Further research on testing feasibility and linkage-to-care are urgently needed to control the infection.

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189.
Men with a complete absence of normal sperm morphology exhibit high rates of success without assisted reproduction.

Kovac J., Smith R., Cajipe M., Lamb D., Lipshultz L.

Embase


[Article]

AN: 614019271
In couples with infertility, abnormal strict morphology of 0% normal forms (NF) is a criterion to proceed rapidly to in vitro fertilization (IVF). Since no data currently exist, we investigated the outcomes for men with 0% NF to determine reproductive success without the use of assisted reproductive technologies (ART). A cohort of 24 men with 0% NF were identified (2010-2013) with 27 randomly selected men with >4% NF as controls. Patient charts were reviewed with men contacted and administered an Institutional Review Board (IRB)-approved telephone questionnaire to ascertain outcomes. After a median follow-up time of 2.5 years, 29.2% of men with 0% NF did not require ART for their first pregnancy (controls = 55.6%, P < 0.05). When all pregnancies were analyzed together, men with 0% NF achieved twenty pregnancies of which 75% did not require IVF (controls = thirty pregnancies; 76.7% did not require IVF). The average age of men and female partners was similar between men with 0% NF and >4% NF. All men had normal follicle-stimulating hormone (FSH), testosterone, prolactin, sex hormone-binding globulin (SHBG), and estradiol. Although, global semen parameters were worse in men with 0% NF, when a first pregnancy was a natural conception (NC), 100% of men with 0% NF (n = 7/7) and 37.5% of controls (n = 3/8) went on to have a subsequent pregnancy via NC. Men with 0% NF conceived without IVF in 29.2% of cases compared to 55.6% of controls. Strict morphology should not be used to predict fertilization, pregnancy, or live birth potential. In men with 0% NF, alternative modalities should be considered before immediate IVF. Copyright © 2017 AJA, SIMM and SJTU. All rights reserved.

Two-micrometer thulium laser resection of the prostate-tangerine technique in benign prostatic hyperplasia patients with previously negative transrectal prostate biopsy.


Embase

Asian Journal of Andrology. 19 (2) (pp 244-247), 2017. Date of Publication: 01 Mar 2017.

[Article]

AN: 614337283

The 2-mum thulium laser resection of the prostate-tangerine technique (TmLRP-TT) has been introduced as a minimally invasive treatment for benign prostatic hyperplasia (BPH). This study was undertaken to assess the clinical efficacy and safety of TmLRP-TT for the treatment of BPH patients with previously negative transrectal prostate biopsy. A prospective analysis of 51 patients with previously negative transrectal prostate biopsy who underwent surgical treatment using TmLRP-TT was performed from December 2011 to December 2013. Preoperative status, surgical details, and perioperative complications were recorded. The follow-up outcome was evaluated with subjective and objective tests at 1 and 6 months. TmLRP-TT was successfully completed in all patients. Mean prostate volume, operative duration, and catheterization time were 93.3 +/- 37.9 ml, 69.5 +/- 39.5 min, and 6.5 +/- 1.3 days, respectively. The mean International Prostate Symptom Score, quality of life score, maximum urinary flow rate, and post-void residual urine volume changed notably at 6-month follow-up (22.5 +/- 6.9 vs 6.1 +/- 3.2, 4.8 +/- 1.3 vs 1.1 +/- 0.9, 7.3 +/- 4.5 vs 18.9 +/- 7.1 ml s^-1_ , and 148.7 +/- 168.7 vs 28.4 +/- 17.9 ml). Two (3.9%) patients required blood transfusion perioperatively, while 3 (5.9%) patients experienced transient hematuria postoperatively, and 2 (3.9%) patients received 3 days recatheterization due to clot retention. TmLRP-TT is a safe and effective minimally invasive technique for patients with previously negative transrectal prostate biopsy during the 6-month follow-up. This promising technology may be a feasible surgical method for previously negative transrectal prostate biopsy in the future.  Copyright © 2017 AJA, SIMM & SJTU. All rights reserved.


Status

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The aim of this study is to evaluate the benefits of laparoscopic Doppler ultrasound (LDU) application during laparoscopic varicocelectomy (LV), and to compare the surgical outcomes and complications between LDU-assisted LV (LDU-LV) and conventional LV for infertile patients with varicoceles; 147 infertile patients were randomly divided into two groups. Operative and postoperative parameters, semen parameters, and the pregnancy rate were compared. There were no differences in baseline demographics. The operative time was significantly longer in LDU-LV group than LV group. The incidence of postoperative hydrocele was 1.4% (1/72) in LDU-LV group versus 10.7% (8/75) in LV group, which showed a significant difference (P < 0.05). However, other surgical outcomes, such as postoperative hospital stay, postoperative recurrence, and testicular atrophy, were similar between the two groups. Sperm concentration and sperm motility were significantly increased in both groups at 3, 6, and 12 months after surgery (P < 0.01), and they were higher in LDU-LV than LV group in 12 months after surgery (34.21 +/- 6.36 vs 29.99 +/- 6.04 for concentration, P < 0.05; 40.72 +/- 8.12 vs 37.31 +/- 6.12 for motility, P < 0.05). Sperm morphology was comparable between the two groups. The pregnancy rate showed no significant difference (44.4% of the LDU-LV vs 37.3% of the LV, P > 0.05). In conclusion, compared with LV, LDU-LV could safely and effectively ligate all spermatic veins and preserve spermatic arteries without leading to high varicocele recurrence and postoperative hydrocele.
Given the benefits that sperm counts as well as sperm motility favoring LDU-LV, we recommend that LDU should be routinely used as an effective tool to improve outcomes and safety of laparoscopic varicocelectomy. Copyright © 2017 AJA, SIMM & SJTU. All rights reserved.


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192.

46 XX karyotype during male fertility evaluation; Case series and literature review. Majzoub A., Arafa M., Starks C., Elbardisi H., Al Said S., Sabanegh E.


Forty-six XX disorder of sex development is an uncommon medical condition observed at times during the evaluation of a man's fertility. The following is a case series and literature review of phenotypically normal men diagnosed with this karyotype. Our goal is to comprehend the patients' clinical presentation as well as their laboratory results aiming to explore options available for their management. A formal literature review through PubMed and MEDLINE databases was performed using "46 XX man" as a word search. A total of 55 patients, including those conveyed in this article were diagnosed with a 46 XX karyotype during their fertility
evaluation. The patients' mean age +/- s.d. was 34 +/- 10 years and their mean height +/- s.d. was 166 +/- 6.5 cm. Overall, they presented with hypergonadotropic hypogonadism. Sexual dysfunction, reduced hair distribution, and gynecomastia were reported in 20% (4/20), 25.8% (8/31), and 42% (13/31) of the patients, respectively. The SRY gene was detected in 36 (83.7%) and was absent in the remaining seven (16.3%) patients. We found that a multidisciplinary approach to management is preferred in 46 XX patients. Screening for remnants of the mullerian ducts and for malignant transformation in dysgenetic gonads is imperative. Hypogonadism should be addressed, while fertility options are in vitro fertilization with donor sperm or adoption.

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Recommendations for gonadotoxicity surveillance in male childhood, adolescent, and young adult cancer survivors: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group in collaboration with the PanCareSurFup Consortium.

Treatment with chemotherapy, radiotherapy, or surgery that involves reproductive organs can cause impaired spermatogenesis, testosterone deficiency, and physical sexual dysfunction in male pubertal, adolescent, and young adult cancer survivors. Guidelines for surveillance and management of potential adverse effects could improve cancer survivors' health and quality of life. Surveillance recommendations vary considerably, causing uncertainty about optimum screening practices. This clinical practice guideline recommended by the International Late Effects of Childhood Cancer Guideline Harmonization Group in collaboration with the PanCareSurFup Consortium, developed using evidence-based methodology, critically synthesises surveillance recommendations for gonadotoxicity in male childhood, adolescent, and young adult (CAYA) cancer survivors. The recommendations were developed by an international multidisciplinary panel including 25 experts in relevant medical specialties, using a consistent and transparent process. Recommendations were graded according to the strength of underlying evidence and potential benefit gained by early detection and appropriate management. The aim of the recommendations is to enhance evidence-based care for male CAYA cancer survivors. The guidelines reveal the paucity of high-quality evidence, highlighting the need for further targeted research. Copyright © 2017 Elsevier Ltd

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Erectile dysfunction, metabolic syndrome, and cardiovascular risks: Facts and controversies.
Sanchez E., Pastuszak A.W., Khera M.
Translational Andrology and Urology. 6 (1) (pp 28-36), 2017. Date of Publication: 2017.
[Review]
AN: 614521438
Erectile dysfunction (ED) is the most common male sexual dysfunction, and shares many risk factors with systemic conditions including cardiovascular disease (CVD) and the metabolic syndrome (MetS). ED is considered to be an independent risk factor for CVD and can be a harbinger of future cardiovascular events. Given this relationship, each encounter for ED should be viewed by healthcare providers as an opportunity to screen for CVD and other comorbid conditions, including the MetS, that can significantly affect a man's overall health. While universally accepted screening guidelines are lacking, expert panels do recommend an approach to risk stratification in men with ED. In this review, we discuss the current state of understanding of the relationship between ED, the MetS, and CV risk, and how this impacts the approach to the patient presenting with ED. Copyright © Translational Andrology and Urology. All rights reserved.
Prostatic artery embolization in treating benign prostatic hyperplasia: a systematic review.
Embase
International Urology and Nephrology. 49 (2) (pp 197-203), 2017. Date of Publication: 01 Feb 2017.
[Article]
AN: 613476597
Introduction: We systemically reviewed the current evidence on prostatic artery embolization (PAE) in treating men with benign prostatic hyperplasia. Methods: A systemic literature search was conducted in PubMed, EMBASE and Web of Science on 1 May 2016 without time constraints. Outcomes of interest included the changes in the International Prostate Symptom Score (IPSS), quality-of-life (QOL) score, peak urinary flow (Qmax), post-void residual urine (PVR), International Index of Erectile Function (IIEF) score, prostate volume (PV) and prostate-specific antigen (PSA) level. Results: A total of 987 records were identified through database searching. After removing duplicates, screening and reviewing full-length texts, a total of five records remained, with two randomized controlled trials and three non-randomized cohort studies. Transurethral resection of prostate resulted in better IPSS than PAE. Open prostatectomy had better IPSS, QOL score, Qmax and PVR, but worse IIEF score than PAE at 1 year. Unilateral PAE had higher rate of poor clinical outcome than bilateral PAE, but the difference became statistically insignificant after adjusting for age; IPSS, QOL score, Qmax, PVR, IIEF score, PV and PSA did not differ between the two groups. PAE with 100 mum PVA particles resulted in greater reduction in PSA level, but worse IIEF score than PAE with 200 mum PVA particles; IPSS, QOL score, Qmax, PVR, PV and poor clinical outcome did not differ between the two groups. Conclusion: Evidence on different aspects of PAE was limited. Further studies are warranted to investigate the role of PAE as compared to other forms of medical and surgical treatment. Copyright © 2016, Springer Science+Business Media Dordrecht.
Status
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Frailty is a clinical condition related to changes in metabolism, to sarcopenia, and to decline in muscle mass and strength, bone mineral density, and physical function with aging. The pathophysiology of frailty is multifactorial and associated with comorbidities. Testosterone is implicated in regulating metabolic functions, maintenance of muscle and bone, and inhibition of adipogenesis. In older individuals, reduced testosterone is thought to contribute to an altered state of metabolism, loss of muscle and bone, and increased fat, leading to sarcopenia, sarcopenic obesity, and frailty. While no direct relationship between testosterone deficiency (commonly known as hypogonadism) and frailty has been established (due to the multifactorial nature of frailty), clinical evidence suggests that testosterone deficiency is associated with increased sarcopenia and obesity. Testosterone treatment in frail older men with limited mobility and with testosterone deficiency improved insulin resistance, glucose metabolism, and body composition. These changes contribute to better physical function and improved quality of life. Because frailty increases disability, comorbidities, and the risk of hospitalization, institutionalization, and mortality in older men, it is warranted to explore the potential usefulness
of testosterone treatment in frail men with hypogonadism in order to attenuate the progression of sarcopenia and frailty. In this paper, we will discuss the impact of testosterone deficiency on frailty and the potential role of testosterone treatment in ameliorating and reducing the progression of frailty. Such an approach may reduce disability and the risk of hospitalization and increase functional independence and quality of life. Copyright © 2016 S. Karger AG, Basel.

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197.
Investigating the success rate of sex selection in cycles of intrauterine insemination of sperm using an albumin gradient method in infertile couples referring to the omid persian gulf infertility center of bushehr, iran.
Ahmadi S., Rahmani E., Motamed N., Sadeghi F.

Embase
Date of Publication: April 2017.
Objectives: Sex selection is an important concern for some couples. One of the relatively more simple and inexpensive methods, which does not need to use toxic chemicals to separate the Y and X sperms, is the Ericsson method. Therefore, the aim of this study is to evaluate the results of sex selection in infertile couples by using the albumin gradient method. Materials and Methods: The present study is a quasi-experimental clinical trial study, conducted on 80 infertile couples. After the induction of ovulation and a vaginal sonography, sperm samples were prepared using the albumin gradient method, after which intrauterine insemination (IUI) was conducted. The rate of successful sex selection was then calculated. Results: Among 80 cases of performed IUI, 22 cases (27.5%) were successful, among which 3 cases (8.3%) suffered miscarriages and 19 cases (23.7%) were associated with a successful pregnancy. The success rate of sex selection was 59.1% in successful pregnancies. In general, the sex selection success rate was higher for the male gender; as a result, the success rates in 68 requests for male sex and 12 requests for female sex totaled 12 cases (17.6%) and 1 case (3.8%), respectively. Conclusion: Albumin gradient is an appropriate sex determination method in IUI cycles due to a 23.7% chance of pregnancy in infertile women, while the success rate is 59.1% in sex determination. Copyright © 2017 The Author(s).
By definition, a drug is a medicine or substance that exerts a physiologic effect on an organism. In dermatology, various medications and substances are utilized on a daily basis, ranging from topical treatments to anesthetics in micrographic surgery. The purpose of this section is to focus on some of the more common substances, specifically how they work, how they are utilized, and their routine alternatives (if available). The mechanism of action, usage, and alternative options of the medication finasteride are discussed. Copyright © 2017 Dermatology Nurses' Association.
The aim of this study is to evaluate the effects of vilazodone on sexual functioning in healthy, sexually active adults and assess the impact of medication nonadherence in this type of trial. Participants were randomized to vilazodone (20 or 40 mg/day), paroxetine (20 mg/day), or placebo for 5 weeks of double-blind treatment. The primary endpoint was change from baseline to day 35 in Change in Sexual Functioning Questionnaire (CSFQ) total score in the intent-to-treat (ITT) population. Post-hoc analyses were carried out in modified intent-to-treat (mITT) populations that excluded participants in the active-treatment groups with undetectable plasma drug concentrations at all visits (mITT-I) or at least one visit (mITT-II). In the ITT population (N=199), there were no statistically significant differences between any treatment groups for CSFQ total score change: Placebo, -1.0; vilazodone 20 mg/day, -1.4; vilazodone 40 mg/day, -1.9; and paroxetine, -3.5. In mITT-I (N=197) and mITT-II (N=159), CSFQ total score change was not significantly different between vilazodone (either dose) versus placebo; the CSFQ total score decreased significantly (P<0.05) with paroxetine versus both placebo and vilazodone 20 mg/day, but not versus vilazodone 40 mg/day. Vilazodone exerted no significant effect on sexual functioning in healthy adults. Medication nonadherence can alter study results and may be an important consideration in trials with volunteer participants. Copyright © 2016 Wolters Kluwer Health, Inc.
Conservative Nonhormonal Options for the Treatment of Male Infertility: Antibiotics, Anti-Inflammatory Drugs, and Antioxidants.

Calogero A.E., Condorelli R.A., Russo G.I., Vignera S.L.

Embase


[Review]

AN: 614179880

The nonhormonal medical treatment can be divided into empirical, when the cause has not been identified, and nonempirical, if the pathogenic mechanism causing male infertility can be solved or ameliorated. The empirical nonhormonal medical treatment has been proposed for patients with idiopathic or noncurable oligoasthenoteratozoospermia and for normozoospermic infertile patients. Anti-inflammatory, fibrinolytic, and antioxidant compounds, oligo elements, and vitamin supplementation may be prescribed. Infection, inflammation, and/or increased oxidative stress often require a specific treatment with antibiotics, anti-inflammatory drugs, and/or antioxidants. Combined therapies can contribute to improve sperm quality.

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Frailty and treatments for benign prostatic hyperplasia.
Chaplin S.
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202.
Current and emergent pharmacologic treatments for irritable bowel syndrome with diarrhea: Evidence-based treatment in practice.
Lucak S., Chang L., Halpert A., Harris L.A.
Embase
Therapeutic Advances in Gastroenterology. 10 (2) (pp 253-275), 2017. Date of Publication: 2017.
Irritable bowel syndrome with diarrhea (IBS-D) is a common, chronic functional gastrointestinal disorder with symptoms that can be distressing for patients and often result in substantially impaired quality of life. This review focuses on providing clinicians with information on practical, evidence-based treatment for IBS-D. Current therapies commonly used for the treatment of IBS-D, including pharmacologic and nonpharmacologic interventions, are briefly reviewed, followed by discussion of the emergent pharmacologic treatments (rifaximin and eluxadoline) and medical foods (IBgard and EnteraGam). Given the lack of a standard treatment algorithm for IBS-D and the emergence of new pharmacologic therapies, treatment needs to be tailored to the individual patient and take into account the severity of disease. In this context, the latter part of this manuscript examines how treatments for IBS-D can be used in clinical practice by presenting three patient case scenarios with varying degrees of IBS-D severity. For each case, the patient's medical history and clinical presentation are related to the Rome Foundation multidimensional clinical profile (MDCP) and potential treatment options with current and emergent therapies are reviewed. The interplay of gastrointestinal symptoms and their psychosocial impact, as well as the importance of a patient-centered approach to therapy, are discussed. Consideration is given to the potential need for combination therapies and how emergent treatments could fit into the treatment pathway for mild, moderate, and severe cases of IBS-D in clinical practice. Copyright © The Author(s) 2017.

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Ejaculation and sperm characteristics in men with cauda equina and conus medullaris syndromes.

Hadiji N., Mieusset R., Previnaire J.G., Castel-Lacanal E., Soler J.M.

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[Article In Press]

AN: 614423375

Study design: Retrospective. Objectives: The objective of the study was to describe the type of ejaculation in patients with cauda equina (CE) and conus medullaris (CM) lesions, and to analyse sperm quality. Setting: France. Methods: One hundred sixty-six patients with CE and CM lesions were included. Diagnosis was based on clinical (no motor responses, sensation or sacral reflexes) and urodynamic assessments (no detrusor activity). Vibromassage (VM) was used to induce ejaculation according to the recommendations for patients with spinal cord injury. If ejaculation did not occur, oral midodrine was administered in progressive doses. Retrograde ejaculation was systematically sought. Sperm parameters were analysed according to World Health Organisation recommendations (2010). Results: Eighty-nine patients were included. Eleven ejaculated on the first VM trial (four anterograde (AE), six retrograde (RE) and one antero-retrograde (ARE)). Five patients continued trials of VM alone, two of whom ejaculated following a mean 1.9 trials (one RE, one ARE). Twenty-six patients underwent trials of VM+ midodrine, 18 of whom ejaculated following a mean 4.4 trials with a mean dose of 22.5g of midodrine (2 AE, 13 RE and 5 ARE). Fifty-three ejaculates from 26 patients were analysed. Sperm concentration was low in 90.6% of samples; total necrospermia was found in 65% and asthenospermia in 95% of samples. Conclusion: Ejaculation is difficult to induce using VM in patients with CE and CM lesions, and requires high doses of midodrine. Sperm counts were generally low, and asthenospermia and necrospermia were found in the majority of specimens. Cryopreservation of sperm should be systematic in case of medically assisted procreation. Spinal Cord advance online publication, 14 February 2017; doi:10.1038/sc.2017.5. Copyright © 2017 International Spinal Cord Society

Status

ARTICLE IN PRESS

Institution
The treatment of hypogonadism in men is of great interest to both patients and providers. There are a number of testosterone formulations currently available and several additional formulations under development. In addition, there are some lesser-used alternative therapies for the management of male hypogonadism, which may have advantages for certain patient groups. The future of hypogonadism therapy may lie in the development of selective androgen receptor modulators that allow the benefits of androgens whilst minimizing unwanted side effects.

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205.
A systematic review of Mancozeb as a reproductive and developmental hazard.
Runkle J., Flocks J., Economos J., Dunlop A.L.
Embase
[Review]
AN: 614188344
Background The potential adverse reproductive and developmental effects of Mancozeb, especially in sensitive subpopulations, have not been fully reviewed for this widely used fungicide. Objective To review the experimental and epidemiologic evidence for the association between exposure to Mancozeb and reproductive and developmental health outcomes using an adaptation of the National Toxicology Program's Office of Health Assessment and Translation (OHAT) systematic review framework. Data sources Four databases (PubMed, TOXNET, Web of Science, Google Scholar) were searched for published studies on Mancozeb. Of 403 identified articles, 30 met our inclusion criteria for systematic review. Results Results from in vitro studies provide evidence that Mancozeb may indirectly disrupt or impair reproduction at the cellular level and should be regarded as a reproductive toxicant. Animal studies confirm reproductive and developmental toxicity in mammals and suggest that males chronically exposed to Mancozeb experience significant changes in physiological, biochemical, and pathological processes that may lead to infertility. Epidemiological studies were limited to indirect methods of exposure assessment and examined the effect of fungicides more broadly during pre-conception, pregnancy, and birth, yielding mixed results. Conclusions High confidence ratings from in vitro and animal studies, in combination with moderate confidence ratings from epidemiologic studies employing indirect methods of exposure assessment, provide evidence that Mancozeb should be regarded as a suspected developmental hazard and a presumed reproductive hazard in humans. More population-based studies linking direct measures and/or biomarkers of exposure to adverse effects on male and female fertility, as well as in utero and early life development, are needed to improve the quality of the evidence base concerning the human reproductive and developmental consequences of Mancozeb exposure. Copyright © 2016 Elsevier Ltd
Status
Expression of hOvol2 in the XY body of human spermatocytes.
Taniguchi H., Katano T., Nishida K., Yao I., Morimoto Y., Matsuda T., Ito S.
Embase
Andrologia. 49 (1) (no pagination), 2017. Article Number: e12599. Date of Publication: 01 Feb 2017.
[Article]
AN: 610202733
Male infertility is common at infertile clinics, and 10-20% of infertile males are azoospermic. Non-obstructive azoospermia is a complex multifactorial disease, and the process of spermatogenesis remains largely unknown. Ovol1 and Ovol2, a family of zinc finger transcription factors, are expressed in spermatocytes at the pachytene stage and are suggested to be critical regulators of pachytene progression in male germ cells. In this study, we examined the expression of human Ovol2 (hOvol2) in the seminiferous tubes of patients subjected to testicular sperm extraction. We first cloned hOvol1 and hOvol2 from the testis of one of the patients and found no alteration in these nucleotide sequences of this patient. While hOvol1 and hOvol2 were detected by RT-PCR in the testis of patients capable of spermatogenesis, they were not detected in those with Sertoli cell-only syndrome. We recently succeeded in preparing anti-Ovol2 antibody by immunising rats
with recombinant mouse Ovol2 (mOvol2) and confirmed the specificity and cross-reactivity of this antibody with hOvol2 in cells transfected with hOvol1 or hOvol2 cDNA. hOvol2 expression was restricted to the XY body of spermatocytes at the pachytene stage. This study demonstrates that hOvol2 is expressed in germ cells and may be involved in spermatogenesis.  Copyright © 2016 Blackwell Verlag GmbH

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Year of Publication
2017

207.
The toxicity of methotrexate in male fertility and paternal teratogenicity.
Gutierrez J.C., Hwang K.

Embase
Expert Opinion on Drug Metabolism and Toxicology. 13 (1) (pp 51-58), 2017. Date of Publication: 02 Jan 2017.
[Review]
AN: 613653720
Introduction: There is a high prevalence of methotrexate (MTX) use in males of reproductive age. The scope of this paper reviews what is known regarding risks to fertility and partners' pregnancy
outcomes with regard to MTX use in men. Areas covered: This paper reviews the evidence for current recommendations for MTX use and male fertility and aims to educate professionals regarding MTX use in reproducing males so that patients may be counseled appropriately. A literature search included peer-reviewed sources from PubMed searches and the literature referenced within. Expert opinion: There is a lack of evidence regarding effects of MTX on male fertility. The recommendation to stop MTX three months prior to conception is safe, but is not evidenced by an understanding of the impact of MTX on spermatogenesis or paternal-mediated teratogenicity but rather the timeframe of spermatogenesis. Given the unclear evidence, patients treated with MTX must be counseled on the likelihood of adverse effects of MTX and role of sperm cryopreservation. Future studies are needed to help elucidate the unclear evidence of MTX effects on male fertility and pregnancy outcomes. Copyright © 2016 Informa UK Limited, trading as Taylor & Francis Group.

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Publisher
Taylor and Francis Ltd (E-mail: healthcare.enquiries@informa.com)

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2017

208.

Relationship between mean platelet volume, platelet distribution width, plateletcrit and varicocele.
Polat H., Gulpinar M.T., Sarica M.A., Benlioglu C.

Embase
Andrologia. 49 (1) (no pagination), 2017. Article Number: e12594. Date of Publication: 01 Feb 2017.
[Article]
AN: 614078822

Increases in platelet count and platelet indices such as mean platelet volume (MPV), platelet distribution width (RDW) and plateletcrit (PCT) have been reported in a wide range of pathological settings. The aetiology of varicocele, a vascular disease, is poorly defined. In this study, we aimed to examine the relationship between varicocele, platelet count and a series of platelet indices. A total of 69 patients with varicocele and 56 patients without varicocele were enrolled in the study. Patient sperm parameters, platelet, MPV, PDW and PCT values were analysed. There were semen abnormalities in 37 (53.6%) patients in the varicocele group and 19 (33.9%) patients in nonvaricocele group (P < 0.05). There was no significant difference in platelet count or platelet indices (MPV, PDW and PCT) between the patients with and without varicocele (P < 0.05). There was no statistically significant difference in platelet count or MPV, PDW and PCT between patients with varicocele and the control subjects. Copyright © 2016 Blackwell Verlag GmbH

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209.


Steroidogenic factor-1 (SF-1), also known as nuclear receptor subfamily 5 group A member 1 (NR5A1), is a member of orphan receptor subfamily and located on chromosome 9 (9q33). In 46, XY individuals with mutation of SF-1 gene, adrenal failure, testis dysgenesis, androgen synthesis defects, hypospadias and anorchia with microphallus, infertility can occur from severe to mild. We report a case of a 20-day-old male who is admitted to our clinic due to ambiguous genitalia. In this report, we describe a novel heterozygous c.814A > C (p. T272P) NR5A1 mutation in a patient with 46, XY DSD without adrenal insufficiency. We describe a novel missense mutation c.814A > C (p. T272P) in NR5A1 gene which had not previously been reported. Also this report highlights that the potential diagnostic utility of next-generation sequencing is an effective strategy versus Sanger sequencing to identify genetic mosaicism in clinical practice.

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2017
4-Methylcatechol inhibits cell growth and testosterone production in TM3 Leydig cells by reducing mitochondrial activity.

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Andrologia. 49 (1) (no pagination), 2017. Article Number: e12581. Date of Publication: 01 Feb 2017.

[Article]
AN: 610269781

4-Methylcatechol (4-MC) is a potential neuroprotective drug because it stimulates the synthesis of brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF) in neurons. The present study explored the effect of 4-MC on cell growth and testosterone synthesis in the TM3 Leydig cells of mice. 4-MC did not enhance expression of both BDNF and NGF in these cells. However, this compound significantly inhibited cell proliferation and increased the number of apoptotic cells in a dose-dependent manner. The expression profile of Bax/Bcl-2 gene was altered considerably, and mitochondrial activity was significantly decreased in cells. 4-Methylcatechol also inhibited testosterone synthesis in TM3 Leydig cells. The inhibitory roles of this compound in relation to growth and testosterone synthesis in TM3 Leydig cells maybe associated with increased Bax gene expression and decreased mitochondrial activity. As a result, caspase cascade is activated.

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Institution
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2017
The effect of wet cupping on quality of life of adult patients with chronic medical conditions in King Abdulaziz University Hospital.


Embase


[Article]

AN: 614191435

Objectives: To assess the effect of wet cupping on health-related quality of life (HRQOL) of adult patients with chronic medical conditions, who were referred to the Cupping Clinic of King Abdulaziz University Hospital (KAUH), Jeddah, Kingdom of Saudi Arabia. Methods: A controlled, quasi-experimental study design was carried out among 629 patients referred for cupping from the KAUH Specialty Clinics, during the period from January to December 2014. Patients in the intervention group (309 patients) completed a pre-test included WHO quality of life-BREF, received one wet-cupping session, and filled-out the post-test (1 month later). Patients in the control group (320 patients) completed the pre-test during their enrollment in the study and post-test one month later. Both groups received their ordinary treatment. Descriptive and inferential statistics were performed. Results: Pain was the most common cause for cupping referral. After cupping intervention, the mean scores of most of the HRQOL domains, especially the physical domain, improved significantly among patients in the intervention group. The mean total score of physical HRQOL domain was 61.6 +/- 13.6 before cupping, and reached 69.7 +/- 12.6 after intervention (paired t-test=11.3, p=0.000). Improvements in HRQOL were noticed for almost all types of pain and other medical conditions. Conclusion: There are promising effects in favor of using wet cupping for improving HRQOL of patients with chronic conditions. Cupping is recommended as a complementary treatment modality for chronic medical conditions, especially pain. Copyright © 2017, Saudi Arabian Armed Forces Hospital. All rights reserved.

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In silico analysis of candidate proteins sharing homology with Streptococcus agalactiae proteins and their role in male infertility.

Parida R., Samanta L.

Embase


[Article]

AN: 613084941

Leukocytospermia is a physiologic condition defined as human semen with a leukocyte count of >1 x 106 cells/ml that is often correlated with male infertility. Moreover, bacteriospermia has been associated with leukocytospermia ultimately leading to male infertility. We have found that semen samples with >1 x 106/ml leukocytes and/or bacteriospermia have oxidative predominance as evidenced by augmented protein carbonyl and lipid peroxidation status of the semen which is implicated in sperm dysfunction. It has been reported that Streptococcus agalactiae is present in bacteriospermic samples. Previous research has shown that human leukocyte antigen beta chain paralog (HLA-DRB) alleles interact best with the infected sperm cells rather than the non-infected cells. Little is known about the interaction of major histocompatibility complex (MHC) present on
leukocytes with the sperm upon bacterial infection and how it induces an immunological response which we have addressed by epitope mapping. Therefore, we examined MHC class II derived bacterial peptides which might have human sperm-related functional aspects. Twenty-two S. agalactiae proteins were obtained from PUBMED protein database for our study. Protein sequences with more than two accession numbers were aligned using CLUSTAL Omega to check their conservation pattern. Each protein sequence was then analyzed for T-cell epitope prediction against HLA-DRB alleles using the immune epitope database (IEDB) analysis tool. Out of a plethora of peptides obtained from this analysis, peptides corresponding to proteins of interest such as DNA binding response regulator, hyaluronate lyase and laminin binding protein were screened against the human proteome using Blastp. Interestingly, we have found bacterial peptides sharing homology with human peptides deciphering some of the important sperm functions. Antibodies raised against these probable bacterial antigens of fertility will not only help us understand the mechanism of leukocytospermia/bacteriospermia induced male factor infertility but also open new avenues for immunocontraception. Abbreviations: AA: amino acid; ASA: antisperm antibodies; GBS: group B streptococcus; HLA: human leukocyte antigen; HAS3: hyaluronan synthase 3; IEDB: immune epitope database; MAPO2: O6-methylguanine-induced apoptosis 2; MHC: major histocompatibility complex; ROS: reactive oxygen species; Rosbin1: round spermatid basic protein 1; S. agalactiae: Streptococcus agalactiae; SA: sperm antigen; SPATA17: spermatogenesis associated protein17; SPNR: spermatid perinuclear RNA binding protein; TEX15: testis-expressed sequence 15 protein; TOPAZ: testis- and ovary-specific PAZ domain-containing protein; TPABP: testis-specific poly-A binding protein; TPAP: testis-specific poly(A) polymerase; WHO: World Health Organization Copyright © 2017 Taylor & Francis.
This paper reviews the recently published scientific information regarding ANCA-associated vasculitis (AAV), aiming to highlight the most important data from the clinical nephrologists' perspective. The classification, pathomechanism, recent achievements of the treatment, short-term and long-term outcomes of the disease, and the difficulties nephrologists face when taking care for patients with AAV are summarized. There has been significant progress in the understanding of the genetic and pathologic background of the disease in the last years, and results of histological studies guide us to predict long-term renal function. Findings of several multicentered trials with reasonable number of participants provide comparison of the efficacy and safety of different remission induction and maintenance therapies, and evaluate recently introduced immunosuppressive agents. Although the clinical outcome of patients with AAV has improved significantly since modern immunosuppressive drugs are available, the treatment-related complications still contribute to the morbidity and mortality. To improve the survival and quality of life of patients with AAV further, knowledge of the predictors of relapse, end-stage kidney disease, and mortality, also prevention of infections and other treatment-related adverse events are important. The eligibility for renal transplantation and the option for successful pregnancies for young women are also important factors which influence the patients' quality of life. In order to provide favorable outcome, the clinicians need to establish personalized treatment strategies to optimize the intensity and minimize the toxicity of the immunosuppressive therapy.
Methylenetetrahydrofolate Reductase C677T Polymorphism and Risk for Male Infertility in Asian Population.
Rai V., Kumar P.
Embase
[Article In Press]
AN: 614361414

Methylenetetrahydrofolate reductase (MTHFR) is a critical enzyme of folate pathway and required for DNA synthesis and methylation. MTHFE C677T polymorphisms is reported as risk factors for various diseases and disorders like birth defects, metabolic, neurological, psychiatric disorders, and cancers. Several studies have investigated association between the MTHFR C677T polymorphism and male infertility. To assess the risk associated with MTHFR C677T polymorphism in Asian population, a meta-analysis was performed. Included articles were collected from the following electronic databases: PubMed, Google Scholar, and Science direct up to March 2015. Risk was estimated as pooled odds ratios (ORs) with confidence intervals (CIs) for assessment. Seventeen case-control studies involving 4392 breast infertile males and 3667 fertile males were found suitable for the inclusion in the present meta-analysis. Results showed that the C677T polymorphism was significantly associated with male infertility in Asian population using all the five genetic models (ORT vs. C (allele contrast model) = 1.86, 95% CI 1.7-2.0; ORTT vs. CC (homozygote model) = 1.96, 95% CI 1.67-2.30; ORCT vs. CC (codominant model) = 1.40, 95% CI 1.18-1.62; ORTT+CT vs. CC (dominant model) = 1.53, 95% CI 1.30-1.77; ORTT vs. CT+CC (recessive model) = 1.67, 95% CI 1.44-1.92). In conclusion, results of present meta-analysis strongly supported an association between C677T polymorphism and male infertility in Asians. Copyright © 2017 Association of Clinical Biochemists of India
Status
ARTICLE IN PRESS
Fawzy M., Sabry M., Nour M., Abdelrahman M.Y., Roshdy E., Magdi Y., Abdelghafar H.
Embase
Fertility and Sterility. 107 (2) (pp 405-412), 2017. Date of Publication: 01 Feb 2017.
[Article]
AN: 613929607
Objective To evaluate the effect of supplementing single-step embryo culture medium with insulin on human embryo development. Design Comparative study. Setting Two private centers. Patient(s) The study involved a sibling oocyte split of 5,142 retrieved oocytes from 360 patients. Intervention(s) Sibling oocytes split after intracytoplasmic sperm injection for culture from day 0 through day 5 or 6 in insulin-supplemented or control medium. Women were split to receive their embryos from insulin-supplemented or control medium. Main Outcome Measure(s) Clinical pregnancy rate. Result(s) There were significantly higher rates of clinical, ongoing, and twin pregnancies in the insulin-supplemented arm than in the control arm. On day 3, embryo quality and compaction were higher in insulin-supplemented medium. On day 5, insulin supplementation showed higher rates of blastocyst formation, quality, and cryopreservation. Conclusion(s) Insulin supplementation of single-step embryo culture medium from day 0 through day 5 or 6 improved clinical pregnancy rate and human embryo development. However, these findings need further confirmation through a multicenter randomized controlled trial that may include other patient populations and different culture media. Copyright © 2016 American Society for Reproductive Medicine
Status
Cystic fibrosis (CF), a monogenic disease caused by mutations in the CFTR gene on chromosome 7, is complex and greatly variable in clinical expression. Airways, pancreas, male genital system, intestine, liver, bone, and kidney are involved. The lack of CFTR or its impaired function causes fat malabsorption and chronic pulmonary infections leading to bronchiectasis and progressive lung damage. Previously considered lethal in infancy and childhood, CF has now attained median survivals of 50 years of age, mainly thanks to the early diagnosis through neonatal screening, recognition of mild forms, and an aggressive therapeutic attitude. Classical treatment includes pancreatic enzyme replacement, respiratory physiotherapy, mucolitics, and aggressive antibiotic therapy. A significant proportion of patients with severe symptoms still
requires lung or, less frequently, liver transplantation. The great number of mutations and their diverse effects on the CFTR protein account only partially for CF clinical variability, and modifier genes have a role in modulating the clinical expression of the disease. Despite the increasing understanding of CFTR functioning, several aspects of CF need still to be clarified, e.g., the worse outcome in females, the risk of malignancies, the pathophysiology, and best treatment of comorbidities, such as CF-related diabetes or CF-related bone disorder. Research is focusing on new drugs restoring CFTR function, some already available and with good clinical impact, others showing promising preliminary results that need to be confirmed in phase III clinical trials.

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Publisher
Birkhauser Verlag AG
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20170208
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2017

217.
The putative effects of D-Aspartic acid on blood testosterone levels: A systematic review.
Roshanzamir F., Safavi S.M.
Embase
International Journal of Reproductive BioMedicine. 15 (1) (pp 1-10), 2017. Date of Publication:
[Review]
AN: 614250032
Background: D-Aspartic acid (D-Asp) is in invertebrate and vertebrate neuroendocrine tissues, where it carries out important physiological functions. Recently, it has been reported that D-Asp is involved in the synthesis and release of testosterone and is assumed can be used as a testosterone booster for infertile men, and by athletes to increase muscle mass and strength.
Objective: The aim of this review is to summarize available evidence related to the effects of D-Asp on serum testosterone levels. Materials and Methods: We conducted a systematic review of all type studies, which evaluated the effect of the D-Asp on blood testosterone including published papers until October 2015, using PubMed, ISI Web of Science, ProQuest and Scopus database. Results: With 396 retrieved records, 23 animal studies and 4 human studies were included. In vivo and in vitro animal studies revealed the effect of D-Asp depending on species, sex and organ-specific. Our results showed that exogenous D-Asp enhances testosterone levels in male animal's studies, whereas studies in human yielded inconsistent results. The evidence for this association in man is still sparse, mostly because of limited number and poor quality studies. Conclusion: There is an urgent need for more and well-designed human clinical trials with larger sample sizes and longer duration to investigate putative effects of D-Asp on testosterone concentrations. Copyright © 2017, Research and Clinical Center for Infertility. All rights reserved.

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Research and Clinical Center for Infertility (E-mail: IJRM@yazdivf.org)
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20170208
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2017
Introduction: The aim of this systematic review is to establish the clinical impact of open (mesh and/or without mesh) and laparoscopic hernia repair (transabdominal pre-peritoneal (TAP) and/or totally extra-peritoneal (TEP)) on male fertility. The incidence of male infertility following various types of inguinal hernia repair is currently unknown. The lack of high-quality evidence has led to various speculations, suggestions and reliance on anecdotal experience in the clinical practice.

Methods: An electronic search of the literature in Medline, Scopus, Embase and Cochrane library from 1966 to October 2015 according to PRISMA checklist was conducted. Quality assessment of articles was conducted using the Oxford Critical Appraisal Skills Programme (CASP) and their recommendation for practice was examined through National Institute for Health and Care Excellence (NICE). This resulted in ten studies (n = 10), comprising 35,740 patients.

Results: Sperm motility could be affected following any type and/or technique of inguinal hernia repair but this is limited to the immediate postoperative period (<48 h). Obstructive azoospermia was noted in 0.03% of open and 2.5% of bilateral laparoscopic (TAP) hernia repair with mesh. Male infertility was detected in 0.8% of the open hernia repair (mesh) with no correlation to the type of mesh (lightweight vs. heavyweight).

Conclusion: Inguinal hernia repair without mesh has no impact on male fertility and obstructive azoospermia. However, the use of mesh in bilateral open and/or laparoscopic repair may require the inclusion of male infertility as the part of informed consent in individuals that have not completed their family or currently under investigations.
New horizons for cystic fibrosis treatment.
Fajac I., De Boeck K.

Embase
Pharmacology and Therapeutics. 170 (pp 205-211), 2017. Date of Publication: 01 Feb 2017.
[Review]
AN: 613949207

Cystic fibrosis is an inherited multi-system disease associated with chronic lung infection, malabsorption, salt loss syndromes, male infertility and leading to numerous comorbidities. The landscape in cystic fibrosis care has changed markedly with currently more adult patients than children in many countries. Over 2000 different mutations in the CFTR gene have been reported and the majority are extremely rare. Understanding how CFTR mutations translate to disturbed synthesis or function of the CFTR protein has opened the way to 'personalized' treatments to correct the basic defect. The first 2 drugs have reached the clinic: a CFTR potentiator to augment CFTR channel function, and the combination of this potentiator with a corrector to increase CFTR expression at the cell membrane. To obtain robust correction of CFTR expression at the cell membrane, combinations of correctors with additive efficacy are under investigation. Other mutation type-specific treatments under clinical investigation are premature stop codon-read through drugs and antisense oligonucleotides that correct the basic defect at the mRNA level. Restoring the defective gene by gene editing can already be achieved ex vivo. Mutation agnostic treatments are explored as well: stabilizing CFTR expression at the cell membrane, circumventing the CFTR channel by blocking or activating other ion channels, and gene therapy. Combinations of these therapies can be anticipated. The pipeline of corrective strategies under clinical investigation is increasing continuously and a rising number of pharmaceutical companies are entering the field. Copyright © 2016 Elsevier Inc.

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Bulbocavernosus muscle area as a novel marker for hypogonadism.
Gupta N., Carvajal M., Jurewicz M., Gilbert B.R.

Embase

Objective Late-onset hypogonadism, or androgen deficiency in the aging male, is a significant cause of morbidity in older men. Many men in the low normal or equivocal range for low testosterone level exhibit signs and symptoms of hypogonadism. Serum testosterone is an imperfect maker for hypogonadism as symptoms vary greatly within the low to low normal range in addition to variations among testosterone assays. Perineal ultrasound can be effectively used to examine the bulbocavernosus muscle (BCM), an androgenized tissue that may be impacted by androgen receptor activity.

Methods This study was a retrospective analysis of men who underwent perineal ultrasound for hypogonadism. The ultrasound data were used to calculate the area of the BCM and correlate it with indices of hypogonadism in symptomatic men including free and total testosterone and dual-energy X-ray absorptiometry (DEXA).

Results The results demonstrate that there is a significant correlation between total and free testosterone and BCM area in hypogonadal patients. Comparison between BCM area and total testosterone showed R² = 0.061 and p = 0.0187 and comparison between BCM area and free testosterone showed R² = 0.0957 and p = 0.0034. In addition, low BCM was also correlated with DEXA results showing osteoporosis and osteopenia (R² = 0.2239, p = 0.0027).

Conclusion There has been recent controversy over the safety of testosterone replacement therapy. This might be particularly important in men with hypogonadal symptoms but a low normal testosterone level. Our study investigated the use of perineal ultrasound to measure BCM as a surrogate marker for poor androgenized men presenting with hypogonadism.

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221.
Embase
BJU International. 119 (2) (pp 216-224), 2017. Date of Publication: 01 Feb 2017.
[Article]
AN: 611664257
Objectives: To evaluate the effects of testosterone-replacement therapy (TRT) on prostate health indicators in hypogonadal men, including rates of prostate cancer diagnoses, changes in prostate-specific antigen (PSA) levels and lower urinary tract symptoms (LUTS) over time.
Patients and Methods: The Registry of Hypogonadism in Men (RHYME) is a multi-national patient registry of treated and untreated, newly-diagnosed hypogonadal men (n = 999). Follow-up assessments were performed at 3-6, 12, 24, and 36 months. Baseline and follow-up data collection included medical history, physical examination, blood sampling, and patient questionnaires. Prostate biopsies underwent blinded independent adjudication for the presence and severity of prostate cancer; PSA and testosterone levels were measured via local and central laboratory assays; and LUTS severity was assessed via the International Prostate Symptom Score (IPSS). Incidence rates per 100 000 person-years were calculated. Longitudinal mixed models were used to assess effects of testosterone on PSA levels and IPSS. Results: Of the 999
men with clinically diagnosed hypogonadism (HG), 750 (75%) initiated TRT, contributing 23,900 person-months of exposure. The mean testosterone levels increased from 8.3 to 15.4 nmol/L in treated men, compared to only a slight increase from 9.4 to 11.3 nmol/L in untreated men. In all, 55 biopsies were performed for suspected prostate cancer, and 12 non-cancer related biopsies were performed for other reasons. Overall, the proportion of positive biopsies was nearly identical in men on TRT (37.5%) compared to those not on TRT (37.0%) over the course of the study. There were no differences in PSA levels, total IPSS, or the IPSS obstructive sub-scale score by TRT status. Lower IPSS irritative sub-scale scores were reported in treated compared to untreated men. Conclusions: Results support prostate safety of TRT in newly diagnosed men with HG.

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MTHFR C677T, A1298C and MS A2756G gene polymorphisms and male infertility risk in a Chinese population: A meta-analysis.
Ren Z., Ren P., Bo Y., Kun F., Ren S., Liao J., Liu S., Liu L., Peng Z., Qiang D.
Embase
[Article]
AN: 614055465
Background Methylenetetrahydrofolate reductase gene (MTHFR C677T and A1298C) and methionine synthase gene (MS A2756G) polymorphisms have shown an association with male infertility risk in several ethnic populations. Although several studies have evaluated these associations in Chinese populations, their small sample sizes and inconsistent outcomes have prevented strong conclusions. Therefore, the present meta-analysis was performed with published studies to evaluate the associations of the three single nucleotide polymorphisms (SNPs) and male infertility in a Chinese population. Methods We conducted a search of PubMed, Embase, Web of Science, Chinese National Knowledge Infrastructure (CNKI), China biology medical literature (CBM), VIP, and Chinese literature (Wan Fang) databases up to May 31, 2016. Odds ratios (ORs) and 95% confidence intervals (95%CIs) were used to assess the strength of associations with a random-effect model or a fixed-effect model based on the heterogeneity analysis results. Sensitivity analysis was used to confirm the reliability and stability of the meta-analysis. Results A total of nine studies, including 1,713 cases and 1,104 controls, were included in the metaanalysis. The pooled results indicated that the MTHFR C667T polymorphism was significantly associated with increased risk of male infertility in the Chinese population in the allele model (T vs. C: OR = 1.47, 95%CI = 1.32 +/- 1.63), the dominant model (TT + CT vs. CC: OR = 1.51, 95%CI = 1.30 +/- 1.77), the additive model (TT vs. CC: OR = 2.08, 95%CI = 1.68 +/- 2.58) and the recessive model (TT vs. CT+CC: OR = 1.58, 95%CI = 1.31 +/- 1.90), whereas the MTHFR A1298C and MS A2756G polymorphisms were not risk factors. There was no significant heterogeneity in any genotype contrasts among the studies. The sensitivity analysis indicated that the results of this meta-analysis were relatively stable. Conclusion This study suggests that the MTHFR C667T polymorphism may contribute to the genetic susceptibility to male infertility in the Chinese population, whereas MTHFR A1298C and MS A2756G polymorphisms may be unrelated to male infertility. Studies with larger sample sizes and representative population-based
cases and well-matched controls are needed to validate our results. Copyright © 2017 Ren et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

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2017

223.
Diverse role of survival motor neuron protein.
Singh R.N., Howell M.D., Ottesen E.W., Singh N.N.
Embase
Date of Publication: 01 Mar 2017.
[Review]
AN: 614108943
The multifunctional Survival Motor Neuron (SMN) protein is required for the survival of all organisms of the animal kingdom. SMN impacts various aspects of RNA metabolism through the formation and/or interaction with ribonucleoprotein (RNP) complexes. SMN regulates biogenesis of small nuclear RNPs, small nucleolar RNPs, small Cajal body-associated RNPs, signal recognition particles and telomerase. SMN also plays an important role in DNA repair, transcription, pre-mRNA splicing, histone mRNA processing, translation, selenoprotein synthesis, macromolecular trafficking, stress granule formation, cell signaling and cytoskeleton
maintenance. The tissue-specific requirement of SMN is dictated by the variety and the abundance of its interacting partners. Reduced expression of SMN causes spinal muscular atrophy (SMA), a leading genetic cause of infant mortality. SMA displays a broad spectrum ranging from embryonic lethality to an adult onset. Aberrant expression and/or localization of SMN has also been associated with male infertility, inclusion body myositis, amyotrophic lateral sclerosis and osteoarthritis. This review provides a summary of various SMN functions with implications to a better understanding of SMA and other pathological conditions. Copyright © 2017 Elsevier B.V.

224.
Moderate aerobic exercise training for improving reproductive function in infertile patients: A randomized controlled trial.
Hajizadeh Maleki B., Tartibian B.
Embase
Cytokine. 92 (pp 55-67), 2017. Date of Publication: 01 Apr 2017.
[Article]
AN: 614046906
This study investigated for the first time the changes in seminal markers of inflammation, oxidative stress status, semen parameters, sperm DNA integrity as well as pregnancy rate following 24 weeks of moderate aerobic exercise in infertile patients. A total of 1026 sedentary men (aged 25-40 years) attending the infertility clinic with history of more than one year of infertility, were screened and 419 were randomized to either exercise (EX, n = 210) or non-
exercise (NON-EX, n = 209) groups. Exercise training favorably attenuated seminal markers of both inflammation (IL-1beta, IL-6, IL-8, and TNF-alpha) and oxidative stress (ROS, MDA, 8-Isoprostane) as well as enhanced antioxidant defense system (SOD, catalase and TAC) (P < 0.05). These changes correlate with favorable improvements in semen parameters, sperm DNA integrity and pregnancy rate (P < 0.05). The results provide information about the effectiveness of moderate aerobic exercise training as a treatment option for male factor infertility. The 4-week detraining period was not enough to reverse all benefits promoted by exercise intervention.

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225.

Zinc Deficiency after Gastric Bypass for Morbid Obesity: a Systematic Review.
Mahawar K.K., Bhasker A.G., Bindal V., Graham Y., Dudeja U., Lakdawala M., Small P.K.

Embase
Obesity Surgery. 27 (2) (pp 522-529), 2017. Date of Publication: 01 Feb 2017.

[Review]
AN: 613425245

Up to 50% of patients have zinc deficiency before bariatric surgery. Roux-en-Y gastric bypass (RYGB) is the commonest bariatric procedure worldwide. It can further exacerbate zinc deficiency by reducing intake as well as absorption. The British Obesity and Metabolic Surgery Society, therefore, recommends that zinc level should be monitored routinely following gastric bypass. However, the American guidance does not recommend such monitoring for all RYGB patients
and reserves it for patients with 'specific findings'. This review concludes that clinically relevant Zn deficiency is rare after RYGB. Routine monitoring of zinc levels is hence unnecessary for asymptomatic patients after RYGB and should be reserved for patients with skin lesions, hair loss, pica, dysgeusia, hypogonadism or erectile dysfunction in male patients, and unexplained iron deficiency anaemia. Copyright © 2016, Springer Science+Business Media New York.

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Springer New York LLC (E-mail: barbara.b.bertram@gsk.com)

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226.
A meta-analysis of the efficacy of venlafaxine extended release 75-225 mg/day for the treatment of major depressive disorder.
Thase M., Asami Y., Wajsbrot D., Dorries K., Boucher M., Pappadopulos E.

Embase
Current Medical Research and Opinion. 33 (2) (pp 317-326), 2017. Date of Publication: 01 Feb 2017.
Objective: To evaluate the short-term efficacy of venlafaxine extended release (ER) 75-225 mg/day compared with placebo for treating major depressive disorder (MDD) and to examine associations between baseline characteristics and efficacy outcomes in MDD patients treated with venlafaxine ER 75-225 mg/day. Research design and methods: This meta-analysis included published and unpublished short-term, double-blind, placebo-controlled, Wyeth/Pfizer sponsored studies of venlafaxine ER at doses up to 225 mg/day in adults with MDD. Clinical trial registration: All trials were conducted before trial registration became mandatory. Main outcome measures: Change from baseline in the 17-item Hamilton Rating Scale for Depression (HAM-D17) total score was analyzed over time using a mixed-effects model for repeated measures with terms for study, treatment group, visit, interaction between treatment group and visit, and baseline score as a covariate. Associations between baseline demographic and clinical characteristics and the probability of HAM-D17 response and remission at week 8 were evaluated using logistic regression models, with terms for study, treatment group, and baseline characteristics in the models. Safety and tolerability was assessed based on adverse events (AEs) and discontinuations due to AEs. Results: The full analysis set included 1087 patients from five studies that fulfilled selection criteria. Statistically significant separation between venlafaxine ER and placebo groups for HAM-D17 total score was seen at week 2 and all subsequent assessments (p-values < .0001). There was no significant interaction between treatment and baseline HAM-D17 total score. Probability of HAM-D17 remission at week 8 decreased with increasing baseline HAM-D17 total score (p = .0012; OR: 0.94); however, baseline HAM-D17 total score did not predict response. Discontinuations due to AEs were reported for 9.4% of venlafaxine-ER-treated patients compared with 3.6% of placebo-treated patients. Key limitations: Five studies met the criteria for inclusion. Several differences in design between included studies limited the analysis: one study did not include a week 3 assessment (the week 3 time point was therefore dropped from the analysis), one study had two venlafaxine ER dose arms, which were combined into one group for the meta-analysis, and mixed- and flexible-dose studies were pooled. Conclusions: Venlafaxine ER 75-225 mg/day effectively reduced symptoms of depression in patients with MDD overall and in patients with either lower (<23) or higher (>23) HAM-D17 total score at baseline. Copyright © 2016 Informa UK Limited, trading as Taylor & Francis Group.

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Review Article: Past, Present and Future of Cancer Survivorship and the Importance of the Urologist.
Selph J.P., Peterson A.C.
Embase
Urology Practice. 4 (1) (pp 60-70), 2017. Date of Publication: 01 Jan 2017.
[Review]
AN: 613902947
Introduction Cancer survivorship is a concept that focuses on the complete medical and holistic care of the patient with cancer from the time of diagnosis to the time of death. In 2015 the number of cancer survivors in the United States was expected to exceed 14.5 million people and a significant portion of these patients have malignancies that affect the genitourinary health of the survivor. In this review we describe the concept of cancer survivorship and review the important role of the urologist in cancer survivor care. Methods A literature search concerning cancer survivorship and urogenital neoplasms was performed. We systematically searched Medline from inception until July 2015 with the objective of identifying studies specifically targeting broad survivorship care concerns for genitourinary neoplasms. We also included nonsystematically identified publications, and governmental and agency produced reports that are currently available through various government entities and organizations. Results Systematic searching yielded 35 articles and 7 reports for inclusion in our literature review. Urology relevant Medline findings were categorized into review articles, biopsychosocial aspects of cancer care, guidelines or society recommendations, diet and exercise related materials, models or coordination of care, or other. We found that the development of guidelines and recommendations for survivorship care in urology has been limited by the quality of the studies published to date. Conclusions More
patients are surviving cancer and living with the consequences of treatment of the primary disease. Awareness of the components of survivorship will be critical as more national organizations require specific survivorship care programs to address these issues. Given that a large number of cancer survivors in the United States have survived urological malignancy or have urological side effects of treatment, the urology community must be familiar with the global concept of survivorship. Copyright © 2017 American Urological Association Education and Research, Inc.

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228.
Diagnosis of partial retrograde ejaculation in non-azoospermic infertile men with low semen volume.
Mieusset R., Walschaerts M., Isus F., Almont T., Daudin M., Hamdi S.M.

Embase

[Article]
AN: 614015472

In non-azoospermic patients with low semen volume (LSV), looking for partial retrograde ejaculation (PRE) by searching sperm in the postejaculatory urine (PEU) is required. The use of a retro-ejaculatory index (R-ratio) was suggested to define PRE, but none of the studies indicated a specific threshold above which PRE must be considered. Our objective was to propose a
threshold value for the R-ratio as indicative of PRE in patients with LSV selected to be devoid of any known causes or risk factors for retrograde ejaculation or LSV. Among our data base (2000-2009) including 632 patients with PEU, 245 male patients from infertile couples who had had a first semen analysis with LSV (< 2mL) and a second semen analysis associated with PEU, were selected on the previous criteria. A prospective control group was randomly constituted (2007-2008) of 162 first consulting male patients from infertile couples, with a normal semen volume (>2mL) on a first semen analysis and who accepted to collect PEU with their usual second semen analysis, selected on the previous criteria. To define an R-ratio threshold indicative of PRE, we used a ROC curve analysis and a regression tree based on a classification and regression tree (CART) algorithm. Of the 245 LSV patients, 146 still presented low semen volume (< 2 mL) on the second semen analysis. From the use of the CART algorithm, two low (1.5% and 2.8%) and two high R-values (7.1% and 8.3%) were defined, according to the lower reference limit for semen volume of 2.0 mL (WHO 1999) or 1.5 mL (WHO 2010) respectively. As only one or no patient with normal semen volume was observed above the two high R-values, we suggest an R-value higher than the range of [7.1-8.3]% as indicative of PRE until confirmation by a prospective multicenter study. Copyright © 2017 Mieusset et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.
Introduction The goal of any medical or surgical treatment for benign prostatic hyperplasia (BPH) is to improve quality of life. It is important to consider the sexual side effects of these treatments, which can directly affect quality of life. Aim To review the published literature on the sexual side effects of different medical and surgical treatments for BPH. Methods A literature review was performed of the various approved medical and surgical treatments for BPH and their respective sexual side effects. Main Outcome Measures The main outcome measure was sexual dysfunction associated with different treatments in the form of ejaculatory dysfunction, erectile dysfunction, decreased libido, and sexual dissatisfaction. Results The most common side effect for medical and surgical treatments of BPH is ejaculatory dysfunction, although its prevalence after any individual treatment varies greatly. Surgical therapies have a greater relative impact on erectile dysfunction compared with medical therapies; the exact mechanism of this erectile dysfunction has yet to be fully elucidated. The degree of decreased libido and sexual dissatisfaction associated with most treatments is poorly described in the literature and often contradictory. Conclusion There are numerous medical and surgical therapies available for treating BPH. Most of these therapies have sexual side effects that can negatively affect a patient's quality of life. It is important for physicians to consider these sexual side effects and to discuss them with their patients before initiating treatment. Copyright © 2016 International Society for Sexual Medicine
Introduction The question of whether to initiate men on testosterone replacement therapy (TRT) and for how long remains a relevant question to be answered. Aim To determine when to start patients on TRT, determine the benefits of TRT, and whether starting patients on TRT condemns them to a lifetime of hormonal replacement. Methods A literature review of relevant publications in PubMed was used. Main Outcome Measures Main outcome measures were evidence for initiating TRT, benefits of TRT, pathophysiology of TRT, and evidence for duration of TRT. Results Although the exact threshold of serum testosterone levels that define hypogonadism is still strongly debated, the presence of symptoms associated with low levels of testosterone can be considered to help make the diagnosis. Although the proper duration of TRT has yet to be established, maintenance of symptom improvement after discontinuing TRT has been observed, which is a promising result. Studies also have shown a return to hormonal baseline after discontinuation of TRT. Conclusion It has been established that patients with testosterone deficiency benefit from TRT. Preliminary evidence seems to show that men who are initiated on TRT are not condemned to a lifetime of hormonal therapy, although many men might choose to continue treatment because of improvement in their symptoms. Copyright © 2016 International Society for Sexual Medicine
Introduction Deterioration in sexual functioning is one of the major and serious complications of diabetes. This common metabolic disorder not only affects sexuality through microvascular and nerve damage but also has psychological aspects. In men, the primary complications are erectile dysfunction, ejaculatory dysfunction, and loss of libido. Women similarly experience sexual problems, including decreased libido and painful intercourse. Aim To summarize the effects of diabetes on sexuality, evaluate the impact of diabetes on sexual function, and assess the conventional and novel treatment approaches based on recent studies. Methods A literature review of peer-reviewed journal articles and guidelines was performed. Main Outcome Measures To assess the effects of diabetes on sexuality and to focus on treatment approaches. Results Male and female sexual dysfunctions are a significant complication of diabetes. Tight glycemic control seems to be beneficial in delaying the onset of sexual problems and ameliorating them when they are present. Erectile dysfunction occurs as one of the first problems. The current mainstay of treatment for erectile dysfunction is therapy with phosphodiesterase type 5 inhibitors and then a stepwise approach of management. Men also can experience ejaculation problems and loss of libido. Diabetes also can decrease testosterone levels, which further decreases libido. Hypogonadal men with diabetes might benefit from testosterone replacement therapy. Diabetic women also can have sexual problems. These problems mainly include loss of libido, decrease in arousal and lubrication resulting in painful intercourse, and loss of orgasm. All these challenges require a multidisciplinary approach. Conclusion Diabetes has detrimental effects on the sexual function of patients. Diabetologists who primarily care for the patient should not only focus on the
glycemic control of their patients but also address their sexual complaints, because these problems can significantly impair their quality of life. Urologists, gynecologists, endocrinologists, and psychiatrists should work in a multidisciplinary manner for the treatment of decreased sexual functioning as a result of diabetes. Copyright © 2016 International Society for Sexual Medicine Status EMBASE Institution (Kizilay) Department of Urology, Turgutlu State Hospital, Manisa, Turkey (Gali) University of California-San Diego School of Medicine, San Diego, CA, United States (Serefoglu) Department of Urology, Bagcilar Training and Research Hospital, Istanbul, Turkey Publisher Elsevier B.V. (E-mail: customerservices@oxonblackwellpublishing.com) Date Created 20170117 Year of Publication 2017

232.
Diagnostic application of oxidation-reduction potential assay for measurement of oxidative stress: clinical utility in male factor infertility.
Agarwal A., Roychoudhury S., Sharma R., Gupta S., Majzoub A., Sabanegh E.
Embase Reproductive BioMedicine Online. 34 (1) (pp 48-57), 2017. Date of Publication: 01 Jan 2017. [Article] AN: 613768421
The objectives of this study were to: (i) describe a protocol measuring the oxidation-reduction potential (ORP) by MiOXSYS System as an alternative method of seminal oxidative stress (OS) testing; (ii) establish a reference value for static ORP (sORP) to distinguish between controls and male factor infertility patients; (iii) evaluate intra-observer and inter-observer reliability; and (iv) examine association of sORP with sperm parameters predictive of male factor infertility. Elevated levels of sORP were seen in infertile patients (6.22 +/- 1.10mV/106 sperm/ml) compared with controls (1.59 +/- 0.29mV/106 sperm/ml) (P = 0.004). A sORP cut-off value 1.36mV/106 sperm/ml identified normal semen and abnormal semen quality with a sensitivity 69.6%, specificity 83.1%,
positive predictive value 85.3% and negative predictive value 65.9%. The test demonstrated strong intra-observer (CV 8.39%) and inter-observer reliability (correlations >0.97). Higher sORP levels were associated with poor sperm parameters across the fertility status of subjects. Negative correlations were noted with sperm parameters (concentration, total sperm count, motility and morphology) indicating these male infertility parameters are related to OS. In conclusion, the introduction of ORP as a novel clinical test for assessment of OS will help clinicians to better diagnose and manage male factor infertility patients. Copyright © 2016 Reproductive Healthcare Ltd.

Deyhoul N., Mohamaddoost T., Hosseini M. Infertility-related risk factors: A systematic review. Embase
Date of Publication: January 2017. [Review]
AN: 613959928

Objectives: Infertility is a universal barrier affecting people all over the world and its cause and importance may vary according to the geographical location and socio-economic condition. Infertility Awareness is the first step in maintaining pregnancy power in lifestyle modification. Materials and Methods: Some studies were conducted on some databases such as PubMed, Scopus, Springer and Science Direct. Twenty-five English papers with similar subject as ours published from 2010 to 2015 were reviewed. Results: Reproductive system disorders, the symptoms of sexually transmitted diseases and hormonal disorders are among the infertility causes in men and women. Lifestyle-related factors such as obesity, nutrition, smoking and alcohol consumption, mobile phone use, sexual violence and anxiety were evaluated as pregnancy changers. Conclusion: Having a healthy lifestyle, running regular tests and checkups under medical supervision and maintaining normal body weight can prevent from fertility problems. Infertility in women will be treated by medicine, minor surgery, laparoscopic procedures, and hormone therapy and by avoiding early pregnancy failure. This article is useful and beneficial for all medical and scientific researchers who want to uproot infertility. Copyright © 2017 The Author(s).

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234.
Oxidative stress and polycystic ovary syndrome: An evaluation during ovarian stimulation for intracytoplasmic sperm injection.
Oxidative stress (OS) may affect the natural fertility and the results of assisted reproduction techniques (ARTs). Subfertility associated with polycystic ovary syndrome (PCOS) may be related to OS. This process may intensify during controlled ovarian stimulation (COS) for ARTs because of increased ovarian metabolic activity and hypoestrogenism with the use of gonadotropin-releasing hormone agonists (GnRHas). The objective of this study was to investigate the presence of systemic OS in non-stimulated cycles and to determine OS markers (malondialdehyde (MDA), advanced oxidation protein products (AOPP), hydroperoxides (FOX), glutathione (GSH) and Vitamin E) during COS in non-obese infertile women with and without PCOS who were subjected to ARTs. A prospective cohort study was conducted on non-obese women (16 with PCOS and 60 ovulatory patients with infertility due to male and/or tubal factors). The OS markers were determined during the following time points: The follicular phase of the natural cycle (D1), after pituitary downregulation with GnRHa and before the use of gonadotropins (D2), on the day of administration of human chorionic gonadotropin (D3), and at oocyte retrieval (D4). Intergroup analysis showed that serum MDA concentrations were higher in the PCOS group at D3 (P = 0.048) and D4 (P = 0.002). On an intragroup analysis, the control group had higher MDA concentrations at D2 than at D1 (P = 0.01) or D4 (P = 0.004). The AOPP concentrations were higher at D2 (P < 0.0001), D3 (P < 0.001) and D4 (P < 0.0001) compared to D1. The FOX concentrations were lower at D2 (P < 0.0001), D3 (P < 0.0001) and D4 (P < 0.001) than at D1. Serum GSH concentrations were significantly higher at D4 than at D1 (P = 0.02). An intragroup analysis of the PCOS subjects showed that the five OS markers did not differ significantly among the four time points when they were analyzed (D1, D2, D3 and D4). In conclusion, non-obese infertile women with PCOS showed evidence of systemic OS after COS with gonadotropins for ICSI. On the other hand, non-obese ovulatory infertile women and women with infertility due to male and/or tubal factors showed a possible systemic oxidative balance until the final COS. Copyright © 2017 Society for Reproduction and Fertility.
235.
Pharmacotherapy Pearls for the Geriatrician: Focus on Oral Disease-Modifying Antirheumatic Drugs Including Newer Agents.
Biehl A.J., Katz J.D.

Embase
[Review]
AN: 613410974

Providing safe and effective pharmacotherapy to the geriatric patients with rheumatological disorders is an ongoing struggle for the rheumatologist and geriatrician alike. Cohesive communication and partnership can improve the care of these patients and subvert adverse outcomes. Disease-modifying antirheumatic drugs, including methotrexate, hydroxychloroquine, sulfasalazine, and leflunomide, and the newest oral agent for treatment of rheumatoid arthritis, tofacitinib, have distinctive monitoring and adverse effect profiles. This article provides the general practitioner or geriatrician with clinically relevant pearls regarding the use of these interventions in older patients. Copyright © 2016 Elsevier Inc.
Clinical features and morbidities of Hb H disease in Taiwan
Lu MY, Kuo MC, Wang SC, Chen SH, Ko BS, Chang C-S, Tang J-L

EBM Reviews - Cochrane Central Register of Controlled Trials

[Journal: Conference Abstract]
AN: CN-01334878 NEW

Introduction Patients with non-transfusion-dependent thalassemia experience a wide array of clinical complications despite their independence from frequent, regular red blood cell transfusions. They have the higher incidence of osteoporosis, extramedullary hematopoiesis (EMH), hypogonadism, cholelithiasis, thromboembolic disease, pulmonary hypertension, silent cerebral ischemia, and leg ulcers. Thalassemia is highly prevalent in Taiwan and Hb H disease is predominant. But limited data are available about clinical features and morbidities. Here, we studied clinical features and morbidities in Taiwanese patients with Hb H disease.

Methods & Results We collected 90 patients with Hb H disease in three hospitals since 2014 Nov till 2016 July. Male to female were 43/59. The mean age was 33.1 years (from 0.5 to 92.3 years). Two cases died of pulmonary hypertension and old age at 31 years old and 87 years old. Alpha-globin gene genotype studies were done in 44 cases. The (- (SEA)) type of alpha(0)-thalassemia mutation was detected in all patients. Twenty- four (57.1%) cases were deletional (alpha(3.7)/alpha(4.2)/unknown 19/4/1) and 20 (42.9%) were nondeletional (CS/RS 18/2) type. The mean of Hemoglobin (Hb) and serum ferritin level were 8.7 g/dL and 730 ng/mL. We also revealed the positive correlation between age and serum ferritin level. The liver iron concentration (LIC) were 6.694 mg Fe/g dw (n=35). The Hb, ferritin and LIC level were not different between deletional and non- deletional groups. They received the transfusion management: 1 with regular transfusion 6 weeks interval, 5 with irregular transfusion 6 weeks interval, 27 with occasional transfusion and 57 without transfusion. Fifteen cases received splenectomy. There were significantly higher
prevalence for transfusion frequency and splenectomy in non-deletional group. The prevalence of morbidities were 16/79 for cholelithiasis, 12/90 for thromboembolic event, 4/90 for heart failure symptoms (2 for pulmonary hypertension), 5/90 for arrhythmia, 3/90 for bone fracture, 5/20 for osteoporosis and 0 for renal stone. There were non-significantly higher prevalence for morbidities in non-deletional group. Discussion & Conclusion The study provides the clinical features and the prevalence of morbidities in Hb H disease in Taiwan. Surprisingly, the prevalence of thromboembolic event and pulmonary hypertension are overlooked in our routine Hb H disease care. We need to schedule close and careful clinical follow up of Hb H patients as they get older, they get some morbidities or they are nondeletional genotype.

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American Society of Hematology

237.
Effectiveness of lifestyle intervention in subgroups of obese infertile women: a subgroup analysis of a RCT
Van Oers AM, Groen H, Mutsaerts MAQ, Burggraaff JM, Kuchenbecker WKH, Perquin DAM, Koks CAM, Van Golde R, Kaaijk EM, Schierbeek JM, Oosterhuis GJE, Broekmans FJ, Vogel NEA, Land JA, Mol BWJ, Hoek A
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Article]
AN: CN-01339811 NEW
STUDY QUESTION: Do age, ovulatory status, severity of obesity and body fat distribution affect the effectiveness of lifestyle intervention in obese infertile women? SUMMARY ANSWER: We did not identify a subgroup in which lifestyle intervention increased the healthy live birth rate however it did increase the natural conception rate in anovulatory obese infertile women. WHAT IS KNOWN ALREADY: Obese women are at increased risk of infertility and are less likely to conceive after infertility treatment. We previously demonstrated that a 6-month lifestyle intervention preceding infertility treatment did not increase the rate of healthy live births (vaginal live birth of a healthy singleton at term) within 24 months of follow-up as compared to prompt infertility treatment in obese infertile women. Natural conceptions occurred more frequently in
women who received a 6-month lifestyle intervention preceding infertility treatment. STUDY DESIGN, SIZE, DURATION: This is a secondary analysis of a multicentre RCT (randomized controlled trial), the LIFestyle study. Between 2009 and 2012, 577 obese infertile women were randomly assigned to a 6-month lifestyle intervention followed by infertility treatment (intervention group) or to prompt infertility treatment (control group). Subgroups were predefined in the study protocol, based on frequently used cut-off values in the literature: Age (>36 or <36 years), ovulatory status (anovulatory or ovulatory), BMI (>35 or <35 kg/m²) and waist-hip (WH) ratio (>0.8 or <0.8). PARTICIPANTS/MATERIALS, SETTING, METHODS: Data of 564 (98%) randomized women who completed follow-up were analyzed. We studied the effect of the intervention program in various subgroups on healthy live birth rate within 24 months, as well as the rate of overall live births (live births independent of gestational age, mode of delivery and health) and natural conceptions within 24 months. Live birth rates included pregnancies resulting from both treatment dependent and natural conceptions. Logistic regression models with randomization group, subgroup and the interaction between randomization group and subgroup were used. Significant interaction was defined as a P-value <0.1. MAIN RESULTS AND THE ROLE OF CHANCE: Neither maternal age, ovulatory status nor BMI had an impact on the healthy live birth rate within 24 months, nor did they influence the overall live birth rate within 24 months after randomization. WH ratio showed a significant interaction with the effect of lifestyle intervention on healthy live birth rate (P = 0.05), resulting in a lower healthy live birth rate in women with a WH ratio <0.8. WH ratio had no interaction regarding overall live birth rate (P = 0.27) or natural conception rate (P = 0.38). In anovulatory women, the effect of lifestyle intervention resulted in more natural conceptions compared to ovulatory women (P-value for interaction = 0.02). There was no interaction between other subgroups and the effect of the intervention on the rate of natural conception. LIMITATIONS, REASONS FOR CAUTION: Since this was a subgroup analysis of a RCT and sample size determination of the trial was based on the primary outcome of the study, the study was not powered for analyses of all subgroups. WIDER IMPLICATIONS OF THE FINDINGS: Our finding that lifestyle intervention leads to increased natural conception in anovulatory obese women could be used in the counselling of these women, but requires further research using an appropriately powered study in order to confirm this result. Copyright (C) The Author 2016.

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Publisher
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Exercise improves the effects of testosterone replacement therapy and the durability of response after cessation of treatment: a pilot randomized controlled trial
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Article]
AN: CN-01341533 NEW
The effects of the combination of exercise and TRT on symptoms of late-onset hypogonadism (LOH) and the durability of response after cessation of TRT were investigated. A total of fifty patients with erectile dysfunction (ED) who had a sedentary lifestyle and low serum total testosterone (T) levels were enrolled and followed for 20 weeks. Patients were randomly divided into two groups; all of them received T gel for 12 weeks and it was discontinued for 8 weeks. Patients assigned to Group II were offered a supervised exercise program for 20 weeks. Measurement of serological testing was performed and self-assessment questionnaires and Global Assessment Question (GAQ) were asked. Baseline characteristics and the initial symptom scores showed no significant difference between the two groups. Serum total T levels and the symptom scores were increased at 12 weeks in both groups, and Group II showed better results with statistical significance. There was a decrease in T levels and worsening of symptom scores at week 20 compared to week 12 in both groups, and Group II showed better results with statistical significance. On the GAQ, Group II showed higher ratio of "yes" at week 12 and the same tendency was sustained at week 20 with significant difference between two groups. The combination of exercise and TRT showed significant improvements in serum T levels and LOH symptoms compared to TRT alone. In addition, these improvements were maintained in the combination group with continuous exercise, even after cessation of TRT. Copyright (C) 2016 AJA, SIMM & SJTU. All rights reserved.
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Effect of yoga on quality of life and seminal quality in male infertility patients with Major Depressive Disorder (MDD): randomized controlled trial
Tolahunase M, Bisht S, Sagar R, Yadav RK, Khan S, Dada R
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Conference Abstract]
AN: CN-01213944

MSc[Med]) Introduction: Infertile men diagnosed with major depressive disorder (MDD) are at risk for poor quality of life and poor sperm quality due to cellular aging. Targeted interventions are needed to address the needs of this vulnerable group. Methods: This trial of a short term yoga intervention for infertile men was designed to evaluate improvement of sperm quality (DNA fragmentation Index (DFI), reactive oxygen species (ROS) and total anti-oxidant capacity (TAC)) as a primary outcome. Secondary outcomes included improvement in quality of life (WHOQOL-BREF scale) and reduction in depression severity (Beck Depression Inventory-II (BDI-II)), cellular aging and neurodegeneration (cortisol, ROS, TAC, telomere length, and brain derived neurotrophic factor (BDNF)). Infertile men with MDD were randomly assigned to a 12-week yoga intervention group (n = 27) or to a wait-list control group (n = 22). Participants were examined and semen and blood samples were collected before and after the intervention for assessment. Basic semen analysis based on WHO (2010) guidelines was also performed. Results: In linear mixed models, the yoga intervention led to significant improvements in basic semen analysis based on WHO (2010) guidelines and significant reductions in sperm DFI (p = .004). Compared to controls, the ROS levels were lower in the yoga group (p = 0.006), whereas the TAC levels were higher in the yoga group (p = 0.001). Yoga group showed significant reductions in depressive symptoms (p = .044) and improvement in quality of life (p=.022), as well as significant reductions in cortisol, blood ROS and increase in other circulating biomarkers, which include, telomere length, TAC and BDNF at post intervention (p < .05 for all). Conclusion: A brief, yoga intervention demonstrated preliminary short-term efficacy in improving sperm quality. Components of yoga, including asanas (physical postures), dhyana (meditation) and pranayama (breathing exercises), improve quality of life, which brings about decreases in both psychological and oxidative stress. The resulting reduction in depression severity, and improvement in biomarkers of cellular aging and neurodegeneration in males suffering from major depression influences improvement in quality of
semen and sperm. Further research is needed to analyze effects of yoga on infertile couples with MDD for benefits in fertility.

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Publisher
Blackwell Publishing Ltd

240.
Can early clinical parameters predict post-traumatic pituitary dysfunction in severe traumatic brain injury?
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Article]
AN: CN-01243703

Background: Post-traumatic hypopituitarism is a major complication after severe head trauma. The aim of our study was to evaluate the possible role of early clinical parameters in the development of endocrine deficits. Methods: Data on endocrine function, on-admission clinical-, laboratory-, and ICU-monitored parameters were available in 63 patients of the surviving 86 severe head injury patients (post-resuscitation GCS under 8) treated at one neurosurgical center during a 10-year period. Results: Hypopituitarism was diagnosed in 68.3 % of the patients. The most frequently affected pituitary axis was the growth hormone (GH): GH deficiency or insufficiency was present in 50.8 %. Central hypogonadism affected 23.8 % of male patients; hypothyroidism and secondary adrenal failure were found in 22.2 and 9.5 % of the investigated population, respectively. Early onset (within 1 year of brain injury) hypopituitarism was found in 24 patients. No connection was found between the development of hypopituitarism and any of the clinical parameters assessed on-admission or at ICU. Significant correlations were found between early endocrine dysfunctions and surgical intervention (OR: 4.64) and the diagnosis of subdural hematoma (OR: 12). In our population, after road traffic accidents, the development of late-onset hypopituitarism was less prevalent (OR: 0.22). Conclusions: Since our results do not indicate any reliable predictive parameter for the development of endocrine dysfunction in a
cohort of patients with severe traumatic brain injury, regular endocrine screening of this specific patient population seems obligatory. Copyright (C) 2016, Springer-Verlag Wien.

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241.
Intrauterine administration of hCG immediately after oocyte retrieval and the outcome of ICSI: a randomized controlled trial
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Article]
AN: CN-01244206
STUDY QUESTION Does the intrauterine administration of hCG immediately after oocyte retrieval in antagonist cycles with ICSI and fresh embryo transfer (ET) influence the implantation rate or chemical and clinical pregnancy rates? SUMMARY ANSWER The intrauterine administration of hCG after oocyte retrieval increases the implantation rate and chemical and clinical pregnancy rates. WHAT IS KNOWN ALREADY Over half of IVF/ICSI cycles fail due to implantation failure. Intrauterine administration of hCG, a few minutes before ET, increased the implantation and pregnancy rates in most but not in all studies. The effect of intrauterine administration of hCG, after oocyte retrieval, has not yet been studied. STUDY DESIGN, SIZE, DURATION The study was a parallel, triple-blind randomized clinical trial (RCT) performed from September 2015 to February 2016, in a university hospital. We recruited women undergoing antagonist ovarian stimulation, ICSI and ET. For an effect size of 0.2, power of 80% at a significance level of 0.05, we needed 150 participants. Accounting for a 7% dropout rate, a total of 160 women was considered appropriate. A computer-generated randomization list with a block size of 4, with 1:1 allocation was used. The treatment allocation was placed in a sealed, opaque, envelope and picked up consecutively. Immediately after oocyte retrieval, patients in the intervention and control groups were treated with intrauterine injection of hCG and saline, respectively. Participants underwent ET on Day 3. A beta-hCG test was done at 2 weeks. If
positive, three transvaginal-ultrasonographies (TVSs) were done at 3, 4 and 10 weeks after ET. The participants were called up thereafter and questioned about the continuity of their pregnancy.

PARTICIPANTS/MATERIALS, SETTING, METHOD Of 1990 women attending the infertility clinic of our university hospital, 508 were IVF/ICSI candidates during the study period, and 245 of the patients on an antagonist cycle met the criteria to be invited into our trial. Inclusion criteria were normal ovarian reserve, age <41, undergoing ICSI, and fresh ET and normal TSH and prolactin. Uncontrolled chronic disease, severe hydrosalpinx, severe endometriosis, morphologic embryo deficiencies, non-obstructive azospermia and high risk of severe ovarian hyperstimulation syndrome were criteria for exclusion. After taking an informed consent, a total of 158 participants were recruited, of which 80 were randomly allocated to receive intrauterine 500 IU hCG in up to 0.5 ml normal saline and 78 to receive intrauterine 0.5 ml normal saline immediately after oocyte retrieval, during general anaesthesia. ICSI was performed conventionally. The 4-8 cell embryos were transferred on the third day after oocyte retrieval. Implantation rate, chemical and clinical pregnancy rates were analysed and compared between the two groups.

MAIN RESULTS AND THE ROLE OF CHANCE Patients’ demographic and baseline characteristics were comparable. The clinical results showed statistically significant differences between the two groups regarding the biochemical pregnancy rate (59.2 versus 31.3%; P = 0.001; odds ratio (OR) = 1.88; 95% CI, 1.26-2.82; risk difference (RD) = 27.8; 95% CI, 11.2-42.3), implantation rate (37 versus 17%; P = 0.012; OR = 2.29; 95% CI, 1.02-5.14; RD = 20.2; 95% CI, 5.4-33.8), clinical pregnancy rate (50.7 versus 16.4%; P < 0.001; OR = 3.08; 95% CI, 1.71-5.55; RD = 34.3; 95% CI, 18.7-47.6) and ongoing pregnancy rate (40.1 versus 13.4%; P = 0.001; OR = 3.04; 95% CI, 1.55-5.93; RD = 27.4; 95% CI, 12.7-40.6). The abortion and ectopic pregnancy rates were not statistically different between the two groups.

LIMITATIONS, REASONS FOR CAUTION The insertion of an intrauterine insemination catheter and the injection of a small amount of saline into the uterine cavity (without hCG) may also have some impact on implantation. This effect could be studied by comparing this intervention with another study group without any intrauterine injection. There are no specific side effects mentioned in the literature for the intrauterine administration of hCG, neither were any observed in our study, but it is best to be cautious about probable side effects, because this type of intervention is relatively new and experimental, and deserves more studies before being entered into routine clinical practice.

WIDER IMPLICATIONS OF THE FINDINGS Intrauterine administration of hCG immediately after oocyte pick up increases its effectiveness; however, further investigations are required before this procedure can be recommended for clinical practice.

STUDY FUNDING/COMPETING INTEREST(S) This study was supported by the Women's Health Research Center, Tabriz University of Medical Sciences, Iran. No external funds were used. The authors have no conflicts of interest to declare.

TRIAL REGISTRATION NUMBER IRCT201206165485N4. TRIAL REGISTRATION DATE 2 September 2015. DATE OF FIRST PATIENT'S ENROLMENT 2 September 2015. Copyright (C) 2016 The Author 2016.
Impact of luteal phase support with vaginal progesterone on the clinical pregnancy rate in intrauterine insemination cycles stimulated with gonadotropins: a randomized multicenter study
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Article]
AN: CN-01245226
Objective To evaluate the effect of luteal phase support (LPS) in intrauterine insemination (IUI) cycles stimulated with gonadotropins. Design Randomized multicenter trial. Setting Academic tertiary care centers and affiliated secondary care centers. Patient(s) Three hundred and ninety-three normo-ovulatory patients, <43 years, with body mass index <30 kg/m<sup>2</sup>, in their first IUI cycle, with at least one patent tube, a normal uterine cavity, and a male partner with total motile sperm count >5 million after capacitation. Intervention(s) Gonadotropin stimulation, IUI, randomization to LPS using vaginal progesterone gel (n = 202) or no LPS (n = 191). Main Outcome Measure(s) Clinical pregnancy rate, live-birth rate, miscarriage rate, and duration of the luteal phase. Result(s) The primary outcome, the clinical pregnancy rate, was not statistically different between the treatment group (16.8%) and the control group (11%) (relative risk [RR] 1.54; 95% confidence interval [CI], 0.89-2.67). Similarly, the secondary outcome, the live-birth rate, was 14.9% in the treatment group and 9.4% in the control group (RR 1.60; 95% CI, 0.89-2.87). The mean duration of the luteal phase was about 2 days longer in the treatment group (16.6 +/- 2.2 days) compared with the control group (14.6 +/- 2.5 days) (mean difference 2.07; 95% CI, 1.58-2.56). Conclusion(s) Although a trend toward a higher clinical pregnancy rate as
Feasibility of a brief, intensive weight loss intervention to improve reproductive outcomes in obese, subfertile women: a pilot study


EBM Reviews - Cochrane Central Register of Controlled Trials

Objective To evaluate the feasibility of a brief, intensive weight loss intervention (IWL) to improve reproductive outcomes in obese subfertile women. Design Pilot study of IWL versus standard-of-care nutrition counseling (SCN). Setting Single-site, academic institution. Patient(s) Obese women (body mass index, 35-45 kg/m<sup>2</sup>) with anovulatory subfertility. Intervention(s) Women were rigorously prescreened to rule out secondary causes of subfertility. Eligible women were randomized to IWL or SCN. IWL consisted of 12 weeks of very-low-energy diet (800 kcal/day) + 4 weeks of a low-calorie conventional food-based diet (CFD) to promote 15% weight loss. SCN consisted of 16 weeks of CFD to promote >5% weight loss. Women were transitioned to weight maintenance diets and referred back to reproductive endocrinology for ovulation induction. Main Outcome Measure(s) Feasibility of recruitment, randomization, intervention implementation, and retention. Result(s) Thirty-nine women were screened; 25 (64%) were eligible to participate, and 14 of those eligible (56%) agreed to be randomized, seven in each group. One withdrew from the IWL group and two from the SCN group. Percent weight loss was greater in the IWL group than in the SCN group (13% +/- 5% vs. 4% +/- 4%). Three of six women in the IWL group conceived and delivered term pregnancies. No pregnancies occurred in the SCN group. Conclusion(s) After rigorous screening, 44% of eligible women completed the study.
IWL was associated with greater percentage weight loss and improvements in insulin sensitivity.

Clinical Trial Registration NCT01894074. Copyright (C) 2016 American Society for Reproductive Medicine
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Publisher
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244.
Intracytoplasmic sperm injection outcomes with freshly ejaculated sperms and testicular or epididymal sperm extraction in patients with idiopathic cryptozoospermia
Ketabchi AA
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Article]
AN: CN-01246778
Background: Cryptozoospermia (CO) is a situation in which spermatozoa cannot be observed in a fresh semen sample unless an extended centrifugation and microscopic search are performed. CO patients are suggested to use only intracytoplasmic sperm injection (ICSI) as infertility treatment. But still there is debate about the choice of sperm source in cryptozoospermic men candidate for ICSI. Objectives: This study was conducted to evaluate fertility outcomes in men with idiopathic cryptozoospermia who were treated using ICSI with freshly ejaculated sperm and testis sperm extraction (TESE) or percutaneous epididymal sperm aspiration (PESA). Methods: In this prospective cohort study carried out in an academic institution, 83 out of 92 couples with cryptozoospermia undergoing their first ICSI cycle were recruited. These patients were randomly allocated to two groups: group one (n = 42) who produced freshly ejaculated sperm and, group two (n = 41) who produced a sample by TESE or PESA. The groups were analyzed and compared in terms of fertilization rate, cleavage rate, embryo quality, implantation rate, and clinical pregnancy rate. Results: There was a significant difference in fertilization rate, embryo quality, implantation rate, and pregnancy rates between the group of surgically extracted sperm and those of naturally ejaculated sperm using conventional ICSI (P < 0.05). Conclusions: Sperm quality extracted by percutaneous PESA and TESE procedures
increases fertility outcomes compared to naturally ejaculated sperm in men with idiopathic CO. More specifically, embryo quality, which is most relevant to fertility outcome, improved when surgically extracted sperm was used for ICSI. Copyright (C) 2016, Nephrology and Urology Research Center.

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Publisher
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245.
Low Testosterone in Men with Cardiovascular Disease or Risk Factors: to Treat or Not To Treat?
Cassimatis DC, Crim MT, Wenger NK
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Review]
AN: CN-01247787
Current evidence supports the use of testosterone replacement in men with the clinical-biochemical syndrome of hypogonadism, defined as low testosterone serum levels and symptoms such as fatigue, exercise intolerance, erectile dysfunction, low libido, or depression. Although the evidence consistently shows that hypogonadism is associated with elevated cardiovascular risk, evidence is mixed regarding whether testosterone (T) replacement provides cardiovascular (CV) benefit or harm. For a man with symptomatic hypogonadism in the setting of CV disease, clinical heart failure, and/or traditional CV risk factors (hypertension, diabetes, and hyperlipidemia), a balanced approach would be to counsel him that overall, the evidence should not dissuade him from utilizing T replacement for non-cardiac symptom relief but that more data are needed before a definitive recommendation can be made about T replacement for CV benefit.

The preponderance of available evidence, reviewed in this article, suggests that T replacement, at appropriate doses and with monitored response, is likely to be safe for men with CV disease or CV risk factors and may even reduce major adverse cardiovascular events (MACE). The 2015 American Association of Clinical Endocrinologists and American College of Endocrinology position statement supports this stance and calls for improved prospective data. There is a clear need for a large, prospective randomized trial evaluating the impact of T replacement on MACE,
for men both with and without CV disease or CV risk factors. Clinicians should be aware that all men who elect to take T replacement therapy require regular follow-up with the prescribing physician to include both clinical assessment and surveillance laboratory assessment of total T level, complete blood count, and prostate specific antigen. Copyright (C) 2016, Springer Science+Business Media New York.

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Publisher
Springer Healthcare

246.
Clinical utility of SNP Microarray's (SNPM) in recurrent pregnancy loss (RPL) and infertility on formalin-fixed, paraffin-embedded (FFPE) samples versus karyotype on blinded samples
Kolhe R, Pundkar C, Mondal A, Lee W, Chaubey A

EBM Reviews - Cochrane Central Register of Controlled Trials

[Journal: Conference Abstract]
AN: CN-01252514

Introduction: A correct diagnosis is critical in separating spontaneous pregnancy loss and RPL and for determining appropriate therapeutic options. Traditionally, karyotyping has been used in molecular analysis of RPL and IF and been overall very helpful in RPL workup. Unfortunately Karyotype analysis also has multiple limitations such as low diagnostic yield, long turnaround time, missing cryptic changes (<5MB), required trained people to perform analysis and is a subjective method prone to human error. Methods: We performed an internal audit at our institution (2012 to 2015) and out of the 578 samples sent to cytogenetics lab for karyotype analysis only few (< 6%) cases had information which helped patient care. This led us to re-examine our RPL cases (FFPE samples) on SNPM. Archival blocks with slides were retrieved and reviewed. Clinical information was obtained from patient charts under approved IRB protocol. H&E slides were examined and chorionic villi (fetal tissue) was identified and marked for DNA isolation by surgical pathologist. The whole genome SNPM was performed on the DNA isolated
from FFPE specimens following manufacturer’s protocol (OncoScan FFPE Assay Kit, Affymetrix, Inc.). The raw data was analyzed in Chromosome Analysis Suite 3.0 software and were matched to in silico FFPE reference sets. This platform consists of 274,000 probes including 74 somatic mutations from 9 genes (BRAF, KRAS, EGFR, IDH1, IDH2, PTEN, PIK3CA, NRAS and TP53). The IF cases were examined on Cytoscan (Affymetrix, Inc.) on blood. Results: All the RPL and IF cases (n=10) resulted in substantial information helping the diagnosis and patient prognosis on SNPM. e.g., Case 1: 38 YO female with history of 7 miscarriages with failed multiple attempts for karyotyping. Her SPMN analysis demonstrated mosaic trisomies of chromosomes 21 (~75% mosaic gain) and 22 (~70% mosaic gain) were observed. Case 2: 32 YO male with infertility/testicular failure with 46XY on karyotype. SNPM analysis showed Y chromosome micro deletion. Conclusion: There is high failure rate in accurately karyotyping products of conceptions (POC) for multiple reasons (Blinded sampling error in OR by D&C, overgrowth of maternal cells resulting in 46, XX, culture failure, microbial overgrowth etc.). SNPM technology has a remarkably higher resolution than conventional cytogenetics (karyotyping and FISH) in identifying cryptic deletions and duplications within the human genome. Having any additional genetic information from POC is very comforting to the patient and extremely beneficial to the reproductive medicine clinic to plan the next pregnancy. We anticipate that this approach of obtaining high-resolution data from an FFPE sample will facilitate studies of RPL which was not previously possible.

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Publisher
Elsevier Inc.

247.
Effectiveness of gonadotropin-releasing hormone antagonists in the management of multifollicular recruitment in intrauterine insemination cycles

Espejo-Catena M, Bano I, Puertos J

EBM Reviews - Cochrane Central Register of Controlled Trials

[Journal: Article]
AN: CN-01265135 NEW
Introduction: To evaluate the efficacy of GnRH antagonists in terms of increasing the pregnancy rates in intrauterine insemination (IUI) after controlled ovarian stimulation (COS) when more than one dominant follicle is recruited. Methods: This is a prospective and randomized clinical trial that included 300 couples with primary or secondary infertility that underwent their first or second COS-IUI cycle with recombinant FSH. In all of these patients two or three leading follicles > 14 mm of mean diameter where detected by vaginal ultrasound (US) and were randomized into two groups. In group A the patients received rFSH+GnRH antagonists until the day that the hCG was given, while in group B the patients followed a standard COS received rFSH only. Results: Total amount of rFSH units (620.8+245.1 vs 575.5+296.4) and clinical pregnancy rates (31.16% vs 19.15%) were statistically significantly higher in patients who were treated with GnRH antagonists. A similar number of twin pregnancies and miscarriages occurred in both groups. Conclusion: Multiple doses of GnRH antagonists in COS-IUI significantly increase pregnancy rates in multifollicular cycles.

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248.
Effectiveness of gonadotropin-releasing hormone antagonists in the management of multifollicular recruitment in intrauterine insemination cycles Effectiveness of gonadotropin-releasing hormone antagonists in the management of multifollicular recruitment in intrauterine insemination cycles EBM Reviews - Cochrane Central Register of Controlled Trials Acta medica international. 3 (1) (pp 13-18). 2016. Date of publication: 01 jan 2016. 2016. [Journal: Article] AN: CN-01265337 NEW

Introduction: To evaluate the efficacy of GnRH antagonists in terms of increasing the pregnancy rates in intrauterine insemination (IUI) after controlled ovarian stimulation (COS) when more than one dominant follicle is recruited. Methods: This is a prospective and randomized clinical trial that included 300 couples with primary or secondary infertility that underwent their first or second COS-IUI cycle with recombinant FSH. In all of these patients two or three leading follicles > 14 mm of mean diameter where detected by vaginal ultrasound (US) and were randomized into two
groups. In group A the patients received rFSH+GnRH antagonists until the day that the hCG was given, while in group B the patients followed a standard COS received rFSH only. Results: Total amount of rFSH units (620.8+245.1vs 575.5+296.4) and clinical pregnancy rates (31.16% vs 19.15%) were statistically significantly higher in patients who were treated with GnRH antagonists. A similar number of twin pregnancies and miscarriages occurred in both groups. Conclusion: Multiple doses of GnRH antagonists in COS-IUI significantly increase pregnancy rates in multifollicular cycles.

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Impact of the oxytocin receptor antagonist (atosiban) administered shortly before embryo transfer on pregnancy outcome after intracytoplasmic sperm injection (ICSI)

Hebisha SA, Aboelazm BA, Adel HM, Ahmed AI

EBM Reviews - Cochrane Central Register of Controlled Trials


[Journal: Conference Abstract]
AN: CN-01267826  NEW

OBJECTIVE: To evaluate the impact of the oxytocin receptor antagonist (Atosiban) administered shortly before embryo transfer on implantation and pregnancy rates in patients undergoing intracytoplasmic sperm injection (ICSI) using long agonist protocol. DESIGN: Randomised controlled trial. MATERIALS AND METHODS: one hundred and eighty two women, prepared for intracytoplasmic sperm injection for male or tubal factor infertility, using long agonist protocol were divided randomly into two groups; Group A (n=91) who received 7.5 mg Atosiban by slow IV injection and Group B (n=91) who received placebo as sodium chloride 0.9% solution also by IV injection 20 minutes before embryo transfer (blastocyst stage ET). Pregnancy and implantation
rates were compared among the two study groups. RESULTS: Pregnancy rate was significantly higher in group A (atosiban group) (58/91) compared to group B (44/91); (63.7% vs 48.4% respectively, \(p=0.037^*\)). Also, implantation rate was significantly higher in group A (atosiban group) compared to group B; (45.20% vs 34.69% respectively, \(P=0.045^*\)). All of the intermediate cycle parameters were also comparable. CONCLUSIONS: Atosiban in the given dose and regimen improved both implantation and ongoing pregnancy rates in patients undergoing ICSI using blastocyst stage embryo transfer. (Table Presented).

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Publisher
Elsevier Inc.

250.
Gentamicin versus ceftriaxone for the treatment of gonorrhoea (G-TOG trial): study protocol for a randomised trial
EBM Reviews - Cochrane Central Register of Controlled Trials
Trials. 17(1) (no pagination):2016.
[Journal: Article]
AN: CN-01286152 NEW
Background: Gonorrhoea is a common sexually transmitted infection which causes genital pain and discomfort; in women it can also lead to pelvic inflammatory disease and infertility, and in men to epididymo-orchitis. Current treatment is with ceftriaxone, but there is increasing evidence of antimicrobial resistance which is reducing its effectiveness against gonorrhoea. A small, but increasing, number of patients have already been found to have highly resistant strains of gonorrhoea which has been associated with clinical failure. This trial aims to determine whether gentamicin is not clinically worse than ceftriaxone in the treatment of gonorrhoea.
Methods/design: This is a blinded, two-arm, multicentre, noninferiority randomised trial. Patients are eligible if they are aged 16-70 years with a diagnosis of genital, pharyngeal and/or rectal gonorrhoea. Exclusion criteria are: known concurrent sexually transmitted infection(s) (excluding chlamydia); bacterial vaginosis and/or Trichomonas vaginalis infection; contraindications or an allergy to gentamicin, ceftriaxone, azithromycin or lidocaine; pregnancy or breastfeeding;
complicated gonorrhoeal infection; weight under 40 kg; use of ceftriaxone, gentamicin or azithromycin within the preceding 28 days. Randomisation is to receive a single intramuscular injection of either gentamicin or ceftriaxone, all participants receive 1 g oral azithromycin as standard treatment. The estimated sample size is 720 participants (noninferiority limit 5%). The primary outcome is clearance of Neisseria gonorrhoeae at all infected sites by a negative Nucleic Acid Amplification Test, 2 weeks post treatment. Secondary outcomes include clinical resolution of symptoms, frequency of adverse events, tolerability of therapy, relationship between clinical effectiveness and antibiotic minimum inhibitory concentration for N. gonorrhoeae, and cost-effectiveness. Discussion: The options for future treatment of gonorrhoea are limited. Results from this randomised trial will demonstrate whether gentamicin is not clinically worse than ceftriaxone for the treatment of gonorrhoea. This will inform clinical practice and policy for the treatment of gonorrhoea when current therapy with cephalosporins is no longer effective, or is contraindicated. Trial registration: International Standard Randomised Controlled Trial Number - ISRCTN51783227, Registered on 18 September 2014. Current protocol version 2.0 17 June 2015. Copyright (C) 2016 The Author(s).

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251.
Local endometrial scratching under ultrasound-guidance after failed intrauterine insemination and cycle outcome: a randomized controlled trial
Soliman BS, Harira M
EBM Reviews - Cochrane Central Register of Controlled Trials
AN: CN-01289575 NEW
. Background: Interaction between the embryo and endometrium plus endometrial receptivity is considered as two strong issues affecting the implantation outcome. . Purpose: To investigate the effect of local endometrial scratching on pregnancy rate after failed previous intra uterine insemination. . Study design: A prospective, randomized, control trial. . Setting: At Cytogenetic
and Endoscopy Unit, Zagazig University Hospital. Patients and methods: A total of 226 women either with unexplained or with mild male factor infertility were divided randomly into approximately two groups: in study group, 114 women and in control group, 112 women. For both groups, folliculometry was started at cycle day 7 additionally and at the same setting; endometrial scratching was done only for the study group. Outcome results: Biochemical and clinical pregnancy rates. Results: The biochemical and clinical pregnancy rates were significantly higher in the endometrial scratching group compared to the control group [27/106 (25.5%) vs. 15/106 (14.1%) \( p=0.03 \) and 24/106 (22.6%) vs. 12/106 (11.3%); \( p=0.02 \)] respectively. Also, ongoing pregnancy rate was statistically significantly different between both groups [22/106 (20.7%) vs. 11/106 (10.4%); \( p=0.03 \)]. Conclusion: Endometrial scratching is useful in increasing pregnancy rates after failed previous intrauterine insemination trials when it is performed in the mid proliferative phase. Copyright (C) 2016 Middle East Fertility Society.

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Middle East Fertility Society

252.
Dopamine agonists for preventing ovarian hyperstimulation syndrome
Tang H, Mourad S, Zhai S-D, Hart RJ
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Review]
AN: CN-01291136 NEW
Background: Ovarian hyperstimulation syndrome (OHSS) is a potentially serious complication of ovarian stimulation in assisted reproduction technology (ART). It is characterised by enlarged ovaries and an acute fluid shift from the intravascular space to the third space, resulting in bloating, increased risk of venous thromboembolism and decreased organ perfusion. Most cases are mild, but forms of moderate or severe OHSS appear in 3% to 8% of in vitro fertilisation (IVF) cycles. The dopamine agonist cabergoline was introduced as a secondary prevention intervention for OHSS in women at high risk of OHSS undergoing ART treatment. As cabergoline seemed to be effective in preventing OHSS, other types of dopamine agonists, such as quinagolide and
bromocriptine, have since been studied in ART to prevent OHSS. Objectives: To assess the effectiveness and safety of dopamine agonists in preventing OHSS in high-risk women undergoing ART treatment. Search methods: We searched several databases from inception to August 2016 (Cochrane Gynaecology and Fertility Specialised Register of trials, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, CINAHL, PsycINFO, Clinicaltrials.gov and the World Health Organization International Trials Registry Platform (ICTRP)) for randomised controlled trials (RCTs) assessing the effect of dopamine agonist in preventing OHSS. We handsearched the reference lists of relevant studies. Selection criteria: We considered RCTs which compared dopamine agonists with placebo/no intervention or another intervention for preventing OHSS in high-risk women for inclusion. Primary outcome measures were incidence of moderate or severe OHSS and live birth rate. Secondary endpoints were clinical pregnancy rate, multiple pregnancy rate, miscarriage rate and any other adverse effects of the treatment. Data collection and analysis: Two authors independently screened titles, abstracts and full texts of publications, selected studies, extracted data and assessed risk of bias. We resolved any disagreements by consensus. We reported pooled results as odds ratios (OR) and 95% confidence interval (95% CI) by the Mantel-Haenszel method. In addition, we graded the overall quality of the evidence using GRADE criteria. Main results: The search identified 14 new RCTs since the last published version of this review, resulting in 16 included RCTs involving 2091 high-risk women for this updated review. They evaluated three types of dopamine agonists: cabergoline, quinagolide and bromocriptine. When compared with placebo or no intervention, dopamine agonists seemed effective in the prevention of moderate or severe OHSS (OR 0.27, 95% CI 0.19 to 0.39; 1022 participants; 8 studies; I² = 0%; moderate quality evidence). This suggests that if 29% of women undergoing ART experience moderate or severe OHSS, the use of dopamine agonists will lower this to 7% to 14% of women. There was no evidence of a difference in live birth rate, clinical pregnancy rate, multiple pregnancy rate or miscarriage rate (very low to moderate quality evidence). However, taking dopamine agonists (especially quinagolide) may increase the incidence of adverse events such as gastrointestinal adverse effects (OR 4.54, 95% CI 1.49 to 13.84; 264 participants; 2 studies; I² = 49%, very low quality evidence). When we compared dopamine agonist plus co-intervention with co-intervention, there was no evidence of a difference in the outcomes of moderate or severe OHSS, live birth rate, clinical pregnancy rate, miscarriage rate or adverse events. The co-interventions were hydroxyethyl starch (two RCTs) and albumin (one RCT). Cabergoline was associated with a lower risk of moderate or severe OHSS compared with human albumin (OR 0.21, 95% CI 0.12 to 0.38; 296 participants; 3 studies; I² = 72%). However, there was no evidence of a difference between cabergoline and hydroxyethyl starch, coasting (withholding any more ovarian stimulation for a few days) or prednisolone. There was an increased clinical pregnancy rate in the cabergoline group when cabergoline was compared with
coasting (OR 2.65, 95% CI 1.13 to 6.21; 120 participants; 2 studies; I² = 0%). In other respects, there was no evidence of a difference in clinical pregnancy rate, multiple pregnancy rate or miscarriage rate between cabergoline and other active interventions. The quality of the evidence between dopamine agonist and placebo or no intervention ranged from very low to moderate, mainly due to poor reporting of study methods (mostly a lack of details on randomisation or blinding) and serious imprecision for some comparisons. Authors’ conclusions: Dopamine agonists appear to reduce the incidence of moderate or severe OHSS in women at high risk of OHSS (moderate quality evidence). If a fresh embryo transfer is performed, the use of dopamine agonists does not affect the pregnancy outcome (live birth rate, clinical pregnancy rate and miscarriage rate) (very low to moderate quality evidence). However, dopamine agonists might increase the risk of adverse events, such as gastrointestinal symptoms. Further research should focus on dose-finding, comparisons with other effective treatments and consideration of combination treatments. Therefore, large, well-designed and well-executed RCTs that involve more clinical endpoints (e.g., live birth rate) are necessary to further evaluate the role of dopamine agonists in OHSS prevention. Copyright (C) 2016 The Cochrane Collaboration.

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253.

Human chorionic gonadotrophin priming for fertility treatment with in vitro maturation
Reavey J, Vincent K, Child T, Granne IE
EBM Reviews - Cochrane Central Register of Controlled Trials
 [Journal: Review]
AN: CN-01291222 NEW

Background: In vitro maturation (IVM) is a fertility treatment that involves the transvaginal retrieval of immature oocytes, and their subsequent maturation and fertilisation. Although the live birth rate is lower than conventional in vitro fertilisation (IVF) with ovarian stimulation, it is a useful treatment, as it avoids the risk of ovarian hyperstimulation syndrome (OHSS). Women with
polycystic ovaries (PCO) or polycystic ovarian syndrome (PCOS) are at an increased risk of OHSS. Thus, IVM may be a more useful treatment in this patient group. Strategies to maximise the maturation rates of the immature oocytes are important. This review focuses on the administration of human chorionic gonadotrophin (hCG) prior to immature oocyte retrieval.

Objectives: To determine the effectiveness and safety of hCG priming in subfertile women who are undergoing IVM treatment in the context of assisted reproduction. Search methods: We searched the following electronic databases up to 29 August 2016: Cochrane Gynaecology and Fertility Group Specialised Register of controlled trials, CENTRAL, MEDLINE, Embase, PsycINFO, and CINAHL. We also searched the trial registries ClinicalTrials.gov and WHO ICTPR to identify ongoing and registered trials. We sought recently published papers not yet indexed in the major databases, and reviewed the reference lists of reviews and retrieved studies as sources of potentially relevant studies. There were no language restrictions. Selection criteria: We included randomised controlled trials (RCTs) that compared hCG priming with placebo or no priming in women undergoing IVM. We also included RCTs that compared different doses of hCG, or the timing of oocyte retrieval. The primary outcomes were live birth rate and miscarriage rate per woman randomised. Data collection and analysis: Two review authors independently selected studies for inclusion, and with a third author, assessed risk of bias and extracted data. We contacted the original authors where data were missing. For dichotomous outcomes, we used the Mantel-Haenszel method to calculate odds ratios (OR). For continuous outcomes, we calculated the mean differences (MD) between treatment groups. We assessed statistical heterogeneity using the I2 statistic. We assessed the overall quality of the evidence using GRADE methods. Main results: We included four studies, with a total of 522 women, in the review. One of these studies did not report outcomes per woman randomised, and so was not included in formal analysis. Three studies investigated 10,000 units hCG priming compared to no priming. One study investigated 20,000 units hCG compared to 10,000 units hCG priming. Three studies only included women with PCOS (N = 122), while this was an exclusion criteria in the fourth study (N = 400). We rated all four studies as having an unclear risk of bias in more than one of the seven domains assessed. The quality of the evidence was low, the main limitations being lack of blinding and imprecision. When 10,000 units hCG priming was compared to no priming, we found no evidence of a difference in the live birth rates per woman randomised (OR 0.65, 95% confidence intervals (CI) 0.24 to 1.74; one RCT; N = 82; low quality evidence); miscarriage rate (OR 0.60, 95% CI 0.21 to 1.72; two RCTs; N = 282; I2 statistic = 21%; low quality evidence), or clinical pregnancy rate (OR 0.52, 95% CI 0.26 to 1.03; two RCTs, N = 282, I2 statistic = 0%, low quality evidence). Though inconclusive, our findings suggested that hCG may be associated with a reduction in clinical pregnancy rates; 22% of women who received no priming achieved pregnancy, while between 7% and 23% of women who received hCG priming did so. The study comparing 20,000 units hCG with 10,000 units hCG did not report sufficient
No studies reported on adverse events (other than miscarriage) or drug reactions. Authors’ conclusions: This review found no conclusive evidence that hCG priming had an effect on live birth, pregnancy, or miscarriage rates in IVM. There was low quality evidence that suggested that hCG priming may reduce clinical pregnancy rates, however, these findings were limited by the small number of data included. As no data were available on adverse events (other than miscarriage) or on drug reactions, we could not adequately assess the safety of hCG priming. We need further evidence from well-designed RCTs before we can come to definitive conclusions about the role of hCG priming, and the optimal dose and timing. Copyright (C) 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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254.
Possible influence of vitamin D on male reproduction
Boisen IM, Bollehuus Hansen L, Mortensen LJ, Lanske B, Juul A, Blomberg Jensen M

Vitamin D is a versatile signaling molecule with an established role in the regulation of calcium homeostasis and bone health. In recent years the spectrum of vitamin D target organs has expanded and a reproductive role is supported by the presence of the vitamin D receptor (VDR) and the vitamin D metabolizing enzymes in the gonads, reproductive tract, and human spermatozoa. Interestingly, expression levels of VDR and the vitamin D inactivating enzyme CYP24A1 in human spermatozoa serve as positive predictive markers of semen quality and are higher expressed in spermatozoa from normal than infertile men. VDR mediates a non-genomic increase in intracellular calcium concentration, sperm motility, and induces the acrosome reaction. Furthermore, functional animal model studies have shown that vitamin D is important for
sex steroid production, estrogen signaling, and semen quality. Cross-sectional clinical studies have supported the notion of a positive association between serum 25-hydroxyvitamin D (25-OHD) level and semen quality in both fertile and infertile men. However, it remains to be determined whether this association reflects a causal effect. The VDR is ubiquitously expressed and activated vitamin D is a regulator of insulin, aromatase, and osteocalcin. Hence, it is plausible that the influence of vitamin D on gonadal function may be mediated indirectly through other vitamin D regulated endocrine factors. Recent studies have indicated that vitamin D supplementation may be beneficial for couples in need of assisted reproductive techniques as high serum vitamin D levels were found to be associated with a higher chance of achieving pregnancy. Randomized clinical trials are needed to determine whether systemic changes in vitamin D metabolites can influence semen quality, fertility, and sex steroid production in infertile men. In this review known and possible future implications of vitamin D in human male reproduction function will be discussed. Copyright (C) 2016.

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Publisher
Elsevier Ltd

255.
Multicentre study of Y chromosome microdeletions in 1,808 Chinese infertile males using multiplex and real-time polymerase chain reaction
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Article In Press]
AN: CN-01291513  NEW
Azoospermia factor (AZF) genes on the long arm of the human Y chromosome are involved in spermatogenesis, and microdeletions in the AZF region have been recognised to be the second major genetic cause of spermatogenic failure resulting in male infertility. While screening for these microdeletions can avoid unnecessary medical and surgical treatments, current methods
are generally time-consuming. Therefore, we established a new method to detect and analyse microdeletions in the AZF region quickly, safely and efficiently. In total, 1,808 patients with spermatogenetic failure were recruited from three hospitals in southern China, of which 600 patients were randomly selected for screening for Y chromosome microdeletions in AZF regions employing real-time polymerase chain reaction with a TaqMan probe. In our study, of 1,808 infertile patients, 150 (8.3%) were found to bear microdeletions in the Y chromosome using multiplex PCR, while no deletions were found in the controls. Among the AZF deletions detected, two were in AZFa, three in AZFb, 35 in AZFc, three in AZFb+c and two in AZFa+b+c. Our method is fast—it permits the scanning of DNA from a patient in one and a half hours and reliable, minimising the risk of cross-contamination and false-positive and false-negative results. Copyright (C) 2016 Blackwell Verlag GmbH.

Intracytoplasmic sperm injection outcomes with freshly ejaculated sperms and testicular or epididymal sperm extraction in patients with idiopathic cryptozoospermia

Ketabchi AA

EBM Reviews - Cochrane Central Register of Controlled Trials

Nephro-urology monthly. 8(6) (no pagination):2016.[Journal: Article]

AN: CN-01291704 NEW

Background: Cryptozoospermia (CO) is a situation in which spermatozoa cannot be observed in a fresh semen sample unless an extended centrifugation and microscopic search are performed. CO patients are suggested to use only intracytoplasmic sperm injection (ICSI) as infertility treatment. But still there is debate about the choice of sperm source in cryptozoospermic candidate for ICSI. Objectives: This study was conducted to evaluate fertility outcomes in men with idiopathic cryptozoospermia who were treated using ICSI with freshly ejaculated sperm and testis sperm extraction (TESE) or percutaneous epididymal sperm aspiration (PESA). Methods: In this prospective cohort study carried out in an academic institution,
83 out of 92 couples with cryptozoospermia undergoing their first ICSI cycle were recruited. These patients were randomly allocated to two groups: group one (n = 42) who produced freshly ejaculated sperm and, group two (n = 41) who produced a sample by TESE or PESA. The groups were analyzed and compared in terms of fertilization rate, cleavage rate, embryo quality, implantation rate, and clinical pregnancy rate. Results: There was a significant difference in fertilization rate, embryo quality, implantation rate, and pregnancy rates between the group of surgically extracted sperm and those of naturally ejaculated sperm using conventional ICSI (P < 0.05). Conclusions: Sperm quality extracted by percutaneous PESA and TESE procedures increases fertility outcomes compared to naturally ejaculated sperm in men with idiopathic CO. More specifically, embryo quality, which is most relevant to fertility outcome, improved when surgically extracted sperm was used for ICSI. Copyright (C) 2016, Nephrology and Urology Research Center.

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Publisher
Kowsar Corp (E-mail: info@anesthpain.com)

257.

Prolactin related symptoms during risperidone maintenance treatment: results from a prospective, multicenter study of schizophrenia
Bo Q, Dong F, Li X, Wang Z, Ma X, Wang C

EBM Reviews - Cochrane Central Register of Controlled Trials
BMC psychiatry. 16(1) (no pagination):2016.

[Journal: Article]

AN: CN-01292001 NEW

Background: This study aimed to investigate prolactin related symptoms (PRS) in individuals with schizophrenia during risperidone maintenance treatment for one year, as well as to identify the risk factors for PRS. Methods: In a multicenter, randomized, controlled, longitudinal study, clinically stabilized schizophrenia patients (N = 374) were randomized to a no-dose-reduction group (N = 129) and 4-week (N = 125) and 26-week (N = 120) reduction groups, in which the original dose was followed by a 50 % reduction over 8 weeks and subsequently maintained. PRS were assessed via a scale of prolactin related adverse events, which included 16 items:
menstrual cycle, menstrual period, menstrual volume, menstrual irregularities, amenorrhea, dysmenorrhea, postpartum lactation, gynecomastia, breast tenderness, sexual dysfunction, decreased sexual desire, erectile dysfunction, ejaculatory dysfunction, impotence, increased body hair, and acne. The occurrence of PRS was assessed at baseline and monthly for six months, followed by every two months. A mixed model was used. Results: PRS at baseline were reported in 18.4, 15.0, and 14.0 % of the 4-week, 26-week, and no-dose-reduction groups, respectively. Female gender, younger age at onset, and the Positive and Negative Syndrome Scale (PANSS) total scores at entry predicted the development of PRS. The mixed model indicated that PRS were more severe in females and at a high dose. In the 237 patients who remained in the study after one year, the incidence of PRS decreased to 9.6, 11.1, and 7.6 % in the 4-week, 26-week, and no-dose-reduction groups, respectively. Conclusion: These findings indicate that the PRS severity was alleviated during the one year treatment period because of the dose reduction. Attention should focus on the side effects of hyperprolactinemia during long-term treatment, especially with a high dose, females, younger age at onset, and more severe patients. Trial registration: ClinicalTrials.gov identifier: NCT00848432. Registered February 19, 2009. Copyright (C) 2016 The Author(s).

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258.
Safety and tolerability of metformin for chemoprevention in Li-Fraumeni syndrome (LFS)
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Conference Abstract]
AN: CN-01294312 NEW
Background: Metformin is FDA approved for the treatment of type II diabetes. Frequently reported side effects of metformin use in diabetics are abdominal cramping, nausea, and diarrhea. Lactic acidosis, a lifethreatening accumulation of lactic acid in the blood, is also a potential adverse effect of metformin. The primary goal of this phase I study was to assess the safety and tolerability of metformin in nondiabetic patients with germline mutations in TP53 and a clinical diagnosis of LFS. LFS is a highlypenetrant, autosomal dominant, cancer predisposition disorder characterized by early onset of breast, sarcoma, adrenocortical, brain, and other cancers. Further, LFS patients have been shown to have increased oxidative phosphorylation capacity in skeletal muscle and oxidative stress markers. Evidence suggests metformin inhibits oxidative phosphorylation in mitochondria, reducing available energy for cancer cell proliferation, and decreasing the production of reactive oxygen species that can cause DNA damage. Although metformin is used safely in nondiabetic individuals for off label indications such as polycystic ovarian syndrome and infertility, its use in nondiabetic patients with germline TP53 mutations has never been documented. Objectives: To assess safety and tolerability of metformin dosages from 500 mg to 2000 mg per day in patients with germline mutations in TP53 and a clinical diagnosis of LFS. Methodology: Adult LFS patients (?18 years old) with documented germline mutation in TP53 were enrolled for 20 weeks. Patients with a history of cancer had to be in remission (surgery and chemotherapy completed 6 and 12 months prior respectively). Patients could not have a history of diabetes or prior metformin use. Metformin was initiated at 500 mg per day and increased in 500 mg dose increments every two weeks to a maximum dose of 2000 mg by week 8. Patients were maintained on 2000 mg of metformin for six additional weeks (week 14). For the last six weeks of the study, patients were taken off metformin (week 20). The targeted accrual goal was ?22 subjects. Results: Of 24 nondiabetic, LFS patients enrolled, 18 (75%) were female, and 6 (25%) were male. Thirteen (54%) females and 1 male (16%) had a prior history of cancer. The age range for females and males was 25-52 and 20-54 years old respectively. One patient developed cancer, and 2 withdrew from the study before starting treatment; 1 dropped out of the study due to personal issues after reaching a dose of 1500 mg. Of the remaining 20 patients, 1 dropped out of the study due to intolerable dyspepsia/reflux at a dose of 500 mg and 1 patient could only tolerate a maximum dose of 1500 mg due to headaches and nausea; the remaining 18 patients tolerated 2000 mg of metformin. Of 22 patients who took metformin, 20 (90%) experienced abdominal pain/nausea/diarrhea. Five patients (22%) experienced headaches. Three patients (13%) experienced reflux/dyspepsia. Two patients experienced one episode of vomiting (9%). None of the patients experienced lactic acidosis. Fasting glucose at week 14 on 2000 mg of metformin daily for females ranged from 7696 mg/dL and for males 8698 mg/dL. Conclusions: Metformin was safe and tolerable in nondiabetic LFS patients with germline mutations in TP53. LFS patients report similar side effects as diabetic patients on metformin. No cases of lactic acidosis occurred.
Effect of testosterone therapy combined with a very low caloric diet on fat mass in obese men with a low-to-low-normal testosterone level: a randomized controlled trial

Fui MNT, Hoermann R, Dupuis P, Raval M, Zajac JD, Grossmann M

EBM Reviews - Cochrane Central Register of Controlled Trials


[Journal: Conference Abstract]

AN: CN-01294863 NEW

Effect of Testosterone Therapy Combined with a Very Low Caloric Diet on Fat Mass in Obese Men with a Low- to Low-Normal Testosterone Level: A Randomized Controlled Trial

Context In men, obesity is strongly associated with low testosterone levels. Weight loss due to caloric restriction is associated with increases in circulating testosterone, and testosterone treatment reduces fat mass. However, whether combining testosterone treatment with caloric restriction reduces fat mass more so than caloric restriction alone is not known. Objective We hypothesised that testosterone treatment will reduce body fat mass more so than caloric restriction alone.

Design, setting and participants We conducted a 56-week double-blind randomised placebo-controlled trial at a tertiary referral centre. We recruited 100 obese men (BMI > 30 kg/m<sup>2</sup>) aged 18-75 years with a low- to lownormal serum total testosterone level (average of 2 consecutive morning fasting levels of <12nmol/L [<346ng/dL]). Intervention All men underwent a weight-loss phase with a very low-calorie diet (providing approximately 600 kcal/ d) for 10 weeks followed by reinstitution of normal foods with the aim of weight maintenance for the next 46 weeks. In addition, men were randomised in a concealed 1:1 allocation to receive 10-weekly intramuscular 1000 mg testosterone undecanoate or placebo injections for the 56-week duration of the study. Main outcome measures: The primary outcome was fat mass measured by DEXA. Secondary outcomes were visceral fat mass by abdominal CT and lean body mass by DEXA. Results Baseline characteristics of the 100 men were as follows: median [interquartile
range] age 53.2 y [47.4-59.9y], BMI 37.4 kg/m^2 [34.7-41.2kg/m^2], fat
mass 45.1kg [37.8-51.9kg] and total testosterone 7.1nmol/L [6.1-8.2nmol/L] (204ng/dL [175-237ng/dL]) by LCMS-MS. The study will be completed by November 2015 and results will be
reported at the meeting Conclusions There is an epidemic of obesity and related functional
hypogonadism yet testosterone treatment remains controversial. This trial will assess whether in
middle-aged obese men with a low to low-normal testosterone, testosterone treatment has fat
lowering effects beyond that achieved by caloric restriction alone.
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completed the study. Free testosterone concentrations increased from 4.5+/−1.3 to 13.8+/−4.1ng/dl (p<0.001) after testosterone therapy but did not change in placebo group. The hematocrit increased from 42.0+/−2.7% to 45.4+/−4.6% (p<0.001) but did not change after placebo (40.7+/−2.9% to 41.6+/−3.1%, p=0.22). There was a 30+/−7% decrease in plasma hepcidin (p<0.01) and 29+/−8% increase in erythropoietin concentrations (p<0.05) after testosterone therapy. There was no significant change in iron or ferritin concentrations but transferrin concentration increased by 21+/−7% and transferrin saturation decreased by 30+/−10% (p<0.01). Ferroportin mRNA expression in MNC increased by 70+/−13% (p<0.01) at 4 weeks and 15 weeks but came back to baseline at 24 weeks after testosterone therapy when the hematocrit normalized. There was no change in any of these parameters after placebo. We conclude that the administration of testosterone to restore normal testosterone concentration led to a significant increase in plasma erythropoietin concentrations, reduction in plasma hepcidin concentration, marked increase in ferroportin expression which was transient, a smaller but significant increase in transferrin and a small reduction in plasma iron concentrations. Clearly, therefore, the increase in hematocrit is supported by an increase in erythropoietin and an increase in iron transport through an increase in ferroportin. This increase is probably through the known suppression of hepcidin which suppresses ferroportin expression.

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Endocrine Society

Maximal oxygen uptake (VO$_2$) is markedly decreased in prader-willii syndrome (PWS)

Hirsch HJ, Gross I, Constantini N, Nice S, Pollak Y, Genstil L, Eldar-Geva T, Gross-Tsur V
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Conference Abstract]
AN: CN-01294895 NEW
Background: PWS, due to lack of expression of paternal genes in 15q11-13, is characterized by obesity, hypotonia, hypogonadism, abnormal body composition, and variable cognitive and behavioral disorders. Regimens to prevent morbid obesity in this population include a very restricted diet (800 kcal/day or less) and daily exercise. $\text{VO}_{2}\max$, the maximal amount of $\text{O}_2$ consumption during incremental exercise, is the single best measurement of cardiovascular fitness and maximal aerobic capacity. $\text{VO}_{2}\max$ is an important measure in prescribing exercise regimens. Indirect methods using heart rate at rest and during exercise to estimate $\text{VO}_{2}\max$ in normal individuals may not be accurate for PWS. Direct measurement of $\text{VO}_{2}\max$ has not been previously reported in PWS.

Objectives: Assess the efficacy of exercise in PWS by determining $\text{VO}_{2}\max$, anaerobic threshold, and other fitness components in young adults with PWS and compare the findings with a group of age and BMI-matched non-syndromic overweight controls.

Methods: The study group consisted of 17 (12 male, 5 female) individuals ages 19-35 (28.6 +/- 4.9) years with PWS (10 deletion, 6 uniparental disomy, and 1 imprinting center defect). The control group (OC) consisted of 32 (22 male, 10 female) overweight/obese but otherwise healthy young adults of comparable ages 19-36 (29.3 +/- 5.2) years. BMI was similar in both groups: 19.4-38.1 (27.8 +/- 5) kg/m$^2$ for PWS and 21.1-48.1 (26.3 +/- 4.9) kg/m$^2$ for controls (NS). During a graded treadmill exercise test, $\text{VO}_{2}\max$ was determined by direct measurements of oxygen consumption and CO$_2$ production using a metabolic analyzer (QUARK CPET, Cosmed, Italy). Maximal effort was reached within 8-14 minutes. Anaerobic threshold was determined by observing when the rise in VCO$_2$ was no longer parallel with the increase in VO$_2$ (Cardiopulmonary Exercise Training (CPET) V slope). Strength (hand dynamometer) and flexibility (sit and reach) tests were performed by all participants and a balance test was performed for the PWS group.

Results: $\text{VO}_{2}\max$ for PWS individuals was significantly lower than for OC (24.6 +/- 3.4 vs 46.5 +/- 12.2 ml/kg/min, $p<0.001$). $\text{VO}_{2}\max$ and pulse rate at the anaerobic threshold were significantly lower (20 +/- 2 vs 36.2 +/- 10.5 ml/kg/min, $p<0.001$ and 130 +/- 20 vs 152 +/- 13 beats per minute, $p<0.001$) for PWS and OC, respectively. Maximal strength of both hands (36 +/- 4 vs. 91.4 +/- 21.2 kgm, $p<0.001$) and flexibility (15.2 +/- 9.5 vs. 26 +/- 11.1 cm, $p=0.001$) were significantly lower for PWS compared to OC.

Conclusions: Exercise programs which do not take into account the significantly lower $\text{VO}_{2}\max$ in PWS may fail to attain adequate energy expenditure in these individuals. Direct measurement of $\text{VO}_{2}\max$ along with strength, flexibility, and balance assessment are needed to tailor appropriate exercise regimens in order to achieve more effective weight control in PWS as well as in other special need populations.

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Publisher
Endocrine Society
Co-infusion of KNDY (kisspeptin, neurokinin b and dynorphin) neuropeptides potently stimulate LH pulsatility and gonadotrophin release in healthy male volunteers


EBM Reviews - Cochrane Central Register of Controlled Trials

[Journal: Conference Abstract]

AN: CN-01294922  NEW

Introduction: In a subpopulation of neurons in the hypothalamus, 3 neuropeptides namely kisspeptin, neurokinin B and dynorphin co-localize in a group of cells called the KNDy neurons. Data in animals shows that KNDy neuropeptides interact together to affect pulsatile GnRH release. Kisspeptin stimulates and neurokinin B may modulate GnRH pulsatility, whilst dynorphin acting at the kappa opioid receptor (KOR) has inhibitory effects. To investigate the importance of KNDy neuropeptides in humans, we assessed for the first time the effects of co-administration of kisspeptin-54, neurokinin-B and a KOR antagonist on LH pulsatility (surrogate marker for GnRH pulsatility in humans) and gonadotrophin release. Methods: We undertook an ethically approved prospective, single-blinded placebo-controlled study. Healthy male volunteers (n=5/group) each attended on 8 different study visits, each lasting 9h and received a different treatment intervention at each visit: 1. Intravenous infusion (IV) of vehicle (control) 2. IV kisspeptin-54 (0.1nmol/kg/h) (KP) 3. IV NKB (2.56nmol/kg/h) (NKB) 4. Oral naltrexone (50mg) (NAL) 5. Co-treatment of KP+NAL 6. Co-treatment of KP+NKB 7. Co-treatment of NKB+NAL 8. Co-treatment of KP+NKB+NAL Blood sampling was performed every 10mins throughout each study to determine plasma LH and FSH levels. After 1h of baseline blood sampling the intervention was started for 8h. LH pulsatility was determined using the blinded deconvolution analysis. Results: 1. KP alone potently increased LH and FSH release, whilst NKB or NAL alone had no significant effect. Co-administration of KP+NAL resulted in the highest effects on LH and FSH release: AUC mean change from baseline LH (h.IU/L): control 6.1+/−139; KP 3440+/−831, p<0.01 vs control; KP+NAL 3659+/−920, p<0.01 vs control. AUC mean change from baseline FSH (h.IU/L): control -46.3+/−31; KP 578.9+/−132, p<0.01 vs control; KP+NAL 673.1+/−191, p<0.01 vs control).
significantly increased LH pulsatility whilst NKB alone had no effect. However, co-administration of KP+NKB significantly increased LH pulsatility (number LH pulses: control 4.0+/0.3; NKB 4.4+/0.5, p=0.62 vs control; KP 5.8+/0.7, p=0.08 vs control; KP+NKB 7.2+/0.5, p=0.01 vs control).

NAL alone or co-administration of KP+NAL also significantly increased LH pulsatility (number LH pulses: control 4.0+/0.3; KP 5.8+/0.7, p=0.08 vs control; NAL 6.4+/0.4, p<0.01 vs control; KP+NAL 6.6+/0.7, p<0.05 vs control). Conclusions: We show for the first time in humans significant interactions between the KNDy neuropeptides on LH pulsatility and gonadotrophin release. NKB significantly augments LH pulsatility when co-administered with KP. Co-administration of KP+NAL significantly increased not only LH pulsatility but most potently stimulated gonadotrophin release, which has important therapeutic implications in treating patients with reproductive failure and infertility.

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Publisher
Endocrine Society

Vitamin D and calcium as novel regulators of reproductive hormones and sex steroids in copenhagen bone gonadal study: a randomized clinical trial

EBM Reviews - Cochrane Central Register of Controlled Trials

[Journal: Conference Abstract]
AN: CN-01294934  NEW

Context: Newer studies have indicated that vitamin D may have more widespread effects than the classical effects on bone and calcium-phosphate homeostasis. The presence of the vitamin D receptor in the testis and male reproductive tract indicates a role for vitamin D in male reproduction Objective: To investigate changes in the reproductive, skeletal and endocrine organs following 5 months supplementation with high dose vitamin D and calcium or placebo in infertile men. Design: A single center, double blinded randomized clinical trial of 330 Danish infertile men with vitamin D insufficiency (serum 25-OHD < 50 nmol/l) conducted from 2011-2015.
Setting: Tertiary referral centre for andrology. Participants: All men were part of an infertile couple and were referred due to low semen quality. In total, 1421 infertile men were screened. 1090 men were excluded due to high vitamin D levels, azoospermia, serious associated comorbidities, medication or no desire to participate, yielding 330 men eligible for inclusion in the study. Of the 330 men who gave informed consent 309 showed up day 1 and started treatment with vitamin D + calcium or placebo. Main Outcome Measures: All 309 men underwent DXA scanning, delivered two semen samples and one blood sample prior to treatment start and again after 150 days intervention. The effect of one oral 300,000 IE cholecalciferol loading dose in addition to a daily 1400 IE cholecalciferol + 500 mg calcium dose for 5 months was compared with placebo on semen quality, clinical pregnancies, serum 25-hydroxyvitamin D, 1,25dihydroxyvitamin D, calcium ion, AMH, Inhibin B, LH, FSH and sex steroid levels. Results: More than 88% of the infertile men completed the study. Two semen analyses prior to the intervention and at follow up day 150 provide a reliable estimate of semen quality before and after the intervention. Serum analyses are being conducted currently using LCMS for vitamin D metabolites and validated ELISAs for sex steroids, AMH, Inhibin B, FSH and LH. The study will be un-blinded December 2015. Conclusions: This is the first randomized clinical trial investigating the effect of vitamin D supplementation to infertile men. This study will show whether supplementation with cholecalciferol and calcium influences reproductive function and changes the endocrine crosslink between bone and gonads in infertile men.

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Publisher
Endocrine Society

Proinflammatory cytokine infusion attenuates LH's feedforward on testosterone secretion: modulation by age
Veldhuis JD, Yang RY, Roelfsema F, Takahashi PY
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Conference Abstract]
Context. In the experimental animal, inflammatory signals quench luteinizing hormone’s (LH) feedforward drive of testosterone (T) secretion and appear to impair gonadotropin-releasing hormone (GnRH)-LH output. The degree to which such suppressive effects operate in the human is not known. Objective. To test the hypothesis that interleukin-2 (IL2) impairs LH’s feedforward drive on T and T’s feedback inhibition of LH secretion in healthy men. Setting. Mayo Clinic’s Center for Clinical and Translational Science. Participants. 35 healthy men, 17 young and 18 older. Interventions. Randomized prospective double-blind saline-controlled study of IL2 infusion in 2 doses with concurrent 10-min blood sampling for 24 h. Outcomes. Deconvolution analysis of LH and T secretion. Results. After saline injection, older compared with young men exhibited reduced LH feedforward drive on T secretion (P<0.001), and decreased T feedback inhibition of LH secretion (P<0.01). After IL2 injection, LH’s feedforward onto T secretion declined markedly especially in young subjects (P<0.001). Concomitantly, IL2 potentiated T’s proportional feedback on LH secretion especially in older volunteers. Conclusion. This investigation (a) confirms combined feedforward and feedback deficits in older relative to young men given saline, and (b) demonstrates: (1) joint mechanisms by which IL2 enforces biochemical hypogonadism, viz.: combined feedforward block and feedback amplification; and (2) unequal absolute inhibition of T and LH secretion by IL2 in young and older men. These outcomes establish that the male gonadal axis is susceptible to dual-site suppression by a prototypic inflammatory mediator. Thus, we postulate that selected interleukins might also enforce male hypogonadism in chronic systemic inflammation.

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Publisher
Endocrine Society

Clinical and immunological characteristics of autoimmune addison's disease in Sweden: a nationwide multicenter analysis of 660 patients
EBM Reviews - Cochrane Central Register of Controlled Trials
Autoimmune Addison's disease (AAD) is a rare disease and larger cohort studies are occasional. Deeper insights into clinical and immunological features are needed to optimize monitoring. To provide upgraded data regarding autoimmune comorbidities, autoantibody profiles, metabolic factors and replacement therapy we identified 660 patients with AAD utilizing the Swedish Addison Registry (SAR). Clinical data were analysed and autoantibodies in serum determined. 3627 individuals from the population-based survey Northern Sweden MONICA (MONItoring of Trends and Determinants of CArdiovascular Disease) served as controls when analyzing metabolic factors. The SAR cohort consisted of 59.4% women. The mean age at diagnosis was significantly higher for women (p<0.0001). The proportion of 21-hydroxylase (21-OH) autoantibody positive patients was 83.0%. The majority of patients (62%) had one or more associated autoimmune disease with a women to men ratio of 1.03:0.64 (p<0.0001). The most frequently associated disease among both women and men was hypothyroidism, which was more common among women than men (p<0.0001). Also hyperthyroidism (p=0.0028), hypogonadism (p=0.0015), and alopecia (p=0.0454) had a female preponderance. Regular hydrocortisone was used by 89% of patients; mean dose 28.1 mg/day (SD: 8.5). The mean hydrocortisone equivalent dose normalized to body surface was 14.8 mg/m<sup>2</sup>/day (SD: 4.4). Mineralocorticoid substitution was used in 88% of patients. BMI (p<0.0001) and the risk of hypertension (p=0.042) were significantly lower in patients with AAD compared with control subjects. No overall significant differences were found for the risk of type 2 diabetes or hyperlipidemia. However, a significant interaction between age and AAD was observed for hyperlipidemia (p=0.013); AAD patients <65 years but not >65 years had a higher risk of hyperlipidemia compared with control subjects. AAD patients are prone to develop other autoimmune conditions. Careful monitoring especially of clinically latent cases is warranted. The mean daily hydrocortisone dose in Swedish AAD patients is slightly higher than generally recommended but the patients do not have an overall unfavorable metabolic profile.

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Publisher
Endocrine Society
Unexpectedly dramatic weight loss in a Prader-Willi syndrome patient treated by Liraglutide

Pirson N, Patricia E, Jean-Paul T

EBM Reviews - Cochrane Central Register of Controlled Trials


[Journal: Conference Abstract]
AN: CN-01295562  NEW

Prader-Willi syndrome is the most common genetic disorder responsible for a life-threatening obesity. The weight gain results mostly from hyperphagia, but its physiopathology remains unsettled. Hence, the treatment is generally poorly effective. Liraglutide is a Glugacon-Like Peptide (GLP)-1 analog approved for the treatment of type 2 diabetes and more recently for the treatment of the obesity. This medication induces generally a moderate weight loss resulting from enhanced satiety. We report the case of a 48-year-old man with a classical PWS associated with a super morbid obesity (W: 179.8 kg and H: 156 cm; BMI 73.9 kg/m<sup>2</sup>) and type 2 diabetes almost well controlled (HbA1c = 7.1%) with tritherapy (Metformine-Gliclazide-Sitagliptine). In addition to diabetes, obesity was complicated with arterial hypertension, sleep apnea syndrome and hypogonadism. At the first visit in our center, Sitagliptine was stopped for Liraglutide 1.2 mg/day to encourage weight loss. During the next three years, the weight loss was dramatic and continued over the years of treatment with Liraglutide (-90 kg /3 years) to reach a BMI of 37.4 kg/m<sup>2</sup>, below the threshold of morbid obesity at the most recent visit. In parallel, glycemic control improved markedly allowing a reduction in the hypoglycemic treatment (HbA1c = 5.6%) despite the stop of gliclazide. To our best knowledge, few PWS patients treated by GLP-1 analogs have been reported in the literature. However, in these cases, the amplitude of weight loss was lower and the length of the follow up shorter. Since therapeutic options are limited and bariatric surgery controversial in this population, randomized controlled studies should be designed to assess the efficacy of GLP-1 analogs.

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Publisher
Taylor and Francis Ltd.
Neuroendocrine phenotype, genetics and hormonal treatment outcome in idiopathic normosmic hypogonadism and Kallmann syndrome patients: a multicenter Belgian study


EBM Reviews - Cochrane Central Register of Controlled Trials


[Journal: Conference Abstract]

AN: CN-01295567  NEW

Aim: To study the clinical phenotype, the genetics and therapeutic responses in a series of 35 consecutive patients with hypogonadotropic hypogonadism and normosmia (nIHH) /hyposmia (KS).

Methods: The study of the genes FGFR1 and KAL1 (anosmin), is performed in our center since 2013. Recently, a panel of genes is available for analysis of the following genes: KAL1, FGFR1, PROKR2, PROK2, CHD7, FGF8, KISS1, KISS1R, APR3, TACR3, GNRHR, GNRH1, NELF, WDR11, HS6ST1, SEMA3A. Results: the series includes 35 patients (32 H/3F, 18 +/- 9 years) belonging to 31 families. We have identified by olfactometry 26 nIHH and 9 KS. Brain MRI was performed in all patients: two patients had a malformation of Chiari I, two patients showed a partially empty sella, one patient had a cyst of the pouch of Rathke and another one had a cleft palate. Preliminary genetic analysis demonstrated a FGFR1 mutation in three patients and in a family. Identified mutations were: c.1663 + 1 G > A, c.1025T > A (p.Leu342*) and c.937 - 1234C > T (new mutation: exon 8A of the isoform IIIb). An anosmin mutation was also identified in another patient: c.827-856 + 49delins, p.Ala276-asp286delinsGlyAsn. A last patient had a new mutation TAC3 c.238 + 1 G > A. concerning fertility outcomes, an oligospermia was obtained in 6/12 men treated with hCG and FSH. Hormonal treatment allowed the development of secondary sexual characters in all patients. The patient with FGFR1:c.937 - 1234C > T showed a reversibility of hypogonadism, after 4 years of treatment. Conclusions: Patients with nIHH FGFR1 mutation may also present with neuro developmental anomalies, which they should be screened for. The association of normosmic IHH and Chiari malformation is intriguing: it was reported just once in the literature (Kulmar & al. Pituitary 2010). We demonstrated hypogonadism reversibility in a patient with one FGFR1 mutation. Finally, we report two novel TAC3 and FGFR1 mutations.
Background: The aim of this study was to investigate the prevalence of obesity in Korean men with Klinefelter syndrome (KS) and the associated risk factors for obesity and hyperglycemia. Methods: Data were collected retrospectively from medical records from 11 university hospitals in Korea between 1994 and 2014. Subjects aged >18 years with newly diagnosed KS were enrolled. The following parameters were recorded at baseline before treatment: chief complaint, height, weight, fasting glucose level, lipid panel, blood pressure, testosterone, luteinizing hormone, follicle-stimulating hormone, karyotyping patterns, and history of hypertension, diabetes, and dyslipidemia. Results: Data were analyzed from 376 of 544 initially enrolled patients. The rate of the 47 XXY chromosomal pattern was 94.1%. The prevalence of obesity (body mass index >25 kg/m$^2$) in Korean men with KS was 42.6%. The testosterone level was an independent risk factor for obesity and hyperglycemia. Conclusion: Obesity is common in Korean men with KS. Hypogonadism in patients with KS was associated with obesity and hyperglycemia. Copyright (C) 2016 Korean Endocrine Society.
The attitudes of infertile couples towards assisted reproductive techniques in Yazd, Iran: a cross sectional study in 2014
Afshani SA, Abdoli AM, Hashempour M, Baghbaheshti M, Zolfaghari M
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Article]
AN: CN-01302021 NEW
Background: Knowledge about assisted reproductive techniques (ART) and its procedures affect the attitude of infertile people. Making decisions about the use of ART is affected by one's perception and attitude. Objective: The aim of this cross-sectional study was to determine the attitude of infertile couples toward applying ART, and to investigate its related factors. Materials and Methods: A randomized cross-sectional study was conducted on 184 infertile couples who had referred to the Research and Clinical Center of Infertility, Yazd, Iran for diagnosis and treatment in June 2014. The data was collected using a two-part questionnaire containing demographic and attitudinal statements. For data analysis, SPSS statistical software and statistical tests of mean differences (t-test), Pearson correlation and analysis of variance were used. Results: A significant relationship between spouse's attitude (p<0.01), relative's attitude (p<0.01), the applied knowledge of ART (p<0.01), and attitude of infertile couples toward applying the ART was observed; however, there was not any significant relationship between gender and socioeconomic status toward applying ART (p>0.05). Conclusion: In conclusion, making a decision and accepting ART can be influenced by couple's attitude, their family's attitude and applied knowledge of ART. Copyright (C) 2016, Research and Clinical Center for Infertility. All rights reserved.
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Comparison of the effect of a combination of eight micronutrients versus a standard mono preparation on sperm parameters
Lipovac M, Bodner F, Imhof M, Chedraui P
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Article]
AN: CN-01302192 NEW

Background: There are reports showing that l-carnitine alone or in combination with other micronutrients improve sperm parameters. However, comparative studies are still lacking. This study was carried out to compare the short term effects of a combination of eight micronutrients including l-carnitine vs. a mono-substance (l-carnitine alone) on sperm parameters. Methods: This was a prospective, open-labelled, nonrandomized study that included male subjects (20 to 60 years) with at least 1 year of subfertility and at least one pathological semen analysis who received 3 months treatment with a mono-substance (500 mg l-carnitine/twice a day, n = 156) or a combined compound (440 mg l-carnitine + 250 mg l-arginine + 40 mg zinc + 120 mg vitamin E + 80 mg glutathione + 60 mug selenium + 15 mg coenzyme Q10 + 800 mug folic acid/once a day, n = 143) for the same time period. Sperm parameters were analyzed before and after treatment and groups comparisons performed. Results: Baseline characteristics were similar among studied groups (age and body mass indices). Semen parameters (volume, density, overall progressive motility [including slow and fast motility]) and percentage of sperm with normal morphology improved after 3 months in both groups as compared to baseline. However, relative change (expressed as % increase of absolute values) for sperm density and overall progressive motility (including fast motility) was found to be higher for the combined micronutrient treatment group as compared to the mono-treatment using l-carnitine alone. Conclusion: Both analyzed groups displayed a positive short term effect on all sperm parameters; however effect on density and motility was significantly better for the combined formulation. There is need for more research in this matter that includes long term outcome data. Trial registration: Retrospectively registered at ISRCTN (7th October 2016). Study ID: ISRCTN48594239 Copyright (C) 2016 The Author(s).
Frequency of severe iatrogenic hyperprolactinaemia with atypical long acting and oral antipsychotics: paliperidone, risperidone, olanzapine, quetiapine and aripiprazole
EBM Reviews - Cochrane Central Register of Controlled Trials
AN: CN-01303826 NEW
Background: Iatrogenic hyperprolactinaemia (IHPRL) is a common but heterogeneous side effect that has been more frequently related with some antipsychotic (APS) drugs like haloperidol, risperidone, amisulpride and paliperidone. Increased awareness between clinicians and a careful attention about some severe physical risk is needed. IHPRL frequency and symptoms could be underestimated without routine exploration. Short-term symptoms include amenorrhea, galactorrhea and sexual dysfunction (decrease of libido and erectile difficulties related to hypogonadism). Medium and long-term symptoms related to estrogen decrease like low bone mass density, hipogonadism, praecox menopause, some types of cancer risk increase (breast and endometrial), cardiovascular risk increase, immune system disorders lipids and cognitive dysfunction could be observed. Routinely explore sexual dysfunction is recommended due to possible poor patient tolerance and low compliance. Severity of IHPRL (mild <25 ng/ml; moderate 25-75 ng/ml; severe >100 ng/ml) must be taken into account in order to avoid clinical consequences and follow treatment strategies. Published consensus states that special care for elderly, child and adolescents and patients with PRI levels >50 ng/ml should be taken. 
Objective: To evaluate the frequency and severity of hyperprolactinemia associated to different APS, including oral and longacting in clinical settings. Methods: Multicentre and observational cross-sectional study. Adult patients treated with either ILD or oral paliperidone, risperidone, olanzapine, aripiprazole and oral quetiapine for at least 4 weeks and with no other PRL-rising treatment were included at clinically approved dosages. Hyperprolactinaemia was defined as 25 ng/ml in women or 20 ng/ml in men. Patients under more than one antipsychotic treatment were excluded. Results: 363 patients suffering for severe mental disorders (psychosis or bipolar disorder) were evaluated. Oral paliperidone was associated with the higher frequency of severe hyperprolactinaemia (>100 ng/ml): 46.4% (mean dosage 7.6 mg/day) followed by paliperidone ILD (26.8%; 125 mg/monthly); risperidone ILD (23.1%; 71 mg/15 days); oral risperidone (19.4%;
4.7 mg/day); olanzapine ILD (8.3%; 338 mg/monthly); quetiapine (3.2%; 466 mg/day) and oral olanzapine (1.5%; 12.5 mg/day). Aripiprazol did not show any severe IHPRL (15 mg/day).

Conclusion: Prolactin levels should be checked in all patients receiving antipsychotics at baseline although praecox symptoms (amenorrhea-galactorrhea) could not be present in order to determine severity of IHPRL and not underestimate other tardive symptoms sometimes severe (osteoporosis, increased of cardiovascular/ cancer risk. Intervention strategies (dosage decrease, drug substitution, dopaminergic agonist) should be approached in all moderate/severe hyperprolactinaemia. A possible prolactinoma should be investigated in patients with PRL levels >100 ng/ml with special attention to patients with breast/endometrial cancer history. Densitometry should be prescribed for males >50 years old, amenorrhea >6 months or praecox menopause to avoid fractures risk. This frequency of severe IHPRL must be taken in consideration when choosing a long-term antipsychotic for patients, given the important clinical consequences associated to severe sustained hyperprolactinaemia.

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Publisher
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their 80s and nearly 100% in the ninth decade, supporting a urologic dogma that all men will have BPH if they live long enough. Patients with mild LUTS are generally treated with watchful waiting or lifestyle modification. Medical treatment is usually the firstline option and is indicated for patients with moderate LUTS. The two main categories of medications for management of BPH are alpha-blockers and 5alpha-reductase inhibitors. Patients with a refractory disease or complications because of medical treatment are considered for surgical therapy. Instead transurethral resection of the prostate (TURP) is the goldstandard surgical treatment. It is effective, with IPSS (international prostate symptom score) reduced on average by 70% even though it is related to a higher rate of complications with increased gland size >80 ml. The most important side effect of this treatment is retrograde ejaculation (70-86%); other complications are bleeding requiring blood transfusion (2.5-7.2%), TUR syndrome (3.4-4.7%), erectile dysfunction (6.5%), urinary incontinence (0.7-1.4%), and urethral stenosis (3.8-4%). Open prostatectomy is the procedure of choice for prostates larger than 80-100 cm3, but it is an invasive surgical procedure with concomitant morbidity and extended hospitalization. Several other less invasive therapies have been popularized in the past two decades, including photoselective vaporization of the prostate, transurethral needle ablation, transurethral microwave therapy, and holmium laser enucleation of the prostate. Despite of promising results of laser enucleation, the learning curve is very protracted. Prostatic artery embolization (PAE) as an emerging interventional technique to treat LUTS secondary to BPH (LUTS/BPH) has recently gained in popularity worldwide. The therapeutic potential of PAE in the management of symptomatic BPH was first described by DeMeritt et al. in 2000. The authors treated a spontaneous prostatic bleeding in patients with BPH and during the follow-up they noted shrinkage of the enlarged prostate and a relief of symptoms. However, this milestone clinical report did not attract much academic attention until 2008, when Sun et al. first published an animal experimental study that confirmed the technical feasibility and safety of PAE for the treatment of symptomatic BPH. Since then there have principally been two authors, Prof. Carnevale from Sao Paulo, Brazil, and Prof. Pisco from Lisbon, Portugal, who have obtained the preliminary results of PAE. In 2009 and 2011, Carnevale et al. reported the preliminary results and midterm follow-up in two patients treated with PAE. Both patients reported a significant improvement in IPSS and QoL (Quality of Life) scores at 18 months. However the first large series was described by Pisco et al in 2013, they performed PAE in 89 patients with LUTS associated with BPH using 200-mum nonspherical polyvinyl alcohol particles. An average decrease in IPSS score, an increased in QoL score, a mean PV (Prostate Volume) reduction were detected after a 7,9 months follow-up, with only one mayor complication consisting in a necrosis of the bladder inferior wall. The only randomized trial comparing TURP and PAE has been published in Radiology in march 2014 by Yuan-an Gao's Chinese group (1); surgical treatment showed superior improvement at one and 3 months but at 6 and 12 months follow-up the results of both groups are similar regarding IPPS, QoL, peak urinary flow and
postvoiding residual volume. Clinical failure of PAE was 9.4% and there were more frequent complication associated (post-embolization syndrome 11.1% and 25.9% of acute urinary retention). Bagla et al. have reported the first US experience (2); 20 patients have been treated with up to six months results: clinical success was obtained in 19/20; there were no minor or major complications. Registers in Italy and US are now ongoing; in Southampton UK a multidisciplinary register comparing PAE and TURP has been launched with over 50 patients recruited in PAE arm and 25 in the TURP one. Since May 2012, in our Interventional Radiology Department (3) were treated 35 patients with LUTS in BPH, refractory to medical therapy. The indication for treatment was given by a team made up of urologist and interventional radiologists. Patients enrolled were ineligible or refusing traditional surgical endoscopic treatment. PAE was technically successful in 96.7% of cases, without any complications. All the eleven patients with indwelling catheter before the procedure removed it from one to four weeks after PAE. We achieved a statistically significant volume reduction, IPSS reduction, and QoL improvement. Pisco et al. in CIRSE 2015 have obtained long-term results of PAE in 240 patients: technical success 233 patients (97.1%), 72.1% of clinical success at the time of discharge, and 70% long-term improvement; in this paper, a major complication (bladder wall ischemia treated by surgery) was described. One of the latest studies proposed by Pisco et al., in 2016 (4), evaluates the efficacy of PAE in patients with a high prostate volume > 100 cm³. The treatment was performed in 152 patients, with a technical success in 149. Instead, 33 cases resulted in a clinical failure (23.6%), of which 23 in the short term (< 6 months) and the remaining 10 in the medium-term. Cumulative clinical success rates were 90%, ending in 72.4% from 18 until 66 months. Hence, PAE provides sustained short-, medium-, long-term control for LUTS in patients with prostate volume > 100 cm³. To improve the results of PAE Carnevale has developed the PErFecTED technique (Proximal Embolization First Then Embolize Distal) with promising outcomes (5). He has prospectively randomized 30 patients to receive TURP or original PAE compared them to a cohort of patients treated with PErFecTED PAE. TURP and PErFecTED PAE both resulted in significantly lower IPSS than oPAE but were not significantly different from one another. Therefore, TURP and PAE are both safe and effective treatments. TURP and PErFecTED PAE yield similar symptom improvement, but TURP is associated with both better urodynamic results and more adverse events. Also, in case of recurrence of symptoms after PAE, prostatic artery re-embolization has been proposed by Costa et al. at CIRSE 2015; 30 patients were re-embolized with PVA particles with 93.72% of technical success, at 6 months' follow-up. 80% of clinical success was reached with an IPSS mean decrease of 31%. In conclusion, PAE is a minimally invasive procedure performed under local anaesthesia, feature that makes it suitable to old patients with comorbidity. The treatment is indicated in patients with either small or large prostates. This technique has many positive sides such as absence of retrograde ejaculation, impotence, and urethral stenosis. Furthermore, the typical contraindications of TURP like heart
disease, metallic implant or penile prosthesis, several urethral stenosis, artificial sphincter and elevated ASA score are not restrictions for PAE. Even if PAE seems to be really safe some complications have been underlined by Schreuder et al. in a recent systematic review (6). They described as mayor complication important pain due to bladder ischemia (0.57%), acute urinary retention (2.97%) and cases of rectum, anus, or corpus cavernosum ischemia. They found out also few minor complications like hematoma on puncture site (3.68%), hematuria (8.36%), hematospermia (5.38%), urinary tract infection (9.49%), prostatitis, and balanitis (1.42%). In spite of complications, 89% of patients were discharged on the day of the procedure and the remaining 11% the day after. After all, evidence demonstrates that PAE is safe and effective, with a low complication rate, and in accordance with the latest studies, it can also be repeated in the same patients.

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Publisher
Springer New York LLC

Utility of a single serum testosterone measurement to determine response to topical testosterone replacement in hypogonadal men.

EBM Reviews - Cochrane Central Register of Controlled Trials
Current Medical Research and Opinion. 32 (2) (pp 263-269), 2016. Date of Publication: 01 Feb 2016. 2016.

[Journal: Article]

AN: CN-01193093 NEW

Objective: To evaluate the utility of single serum testosterone measurement in patients receiving transdermal testosterone therapy. Research design and methods: Data were from an open-label, 120 day, multi-center titration trial in androgen-deficient men receiving an initial daily dose of 60 mg testosterone (testosterone topical solution 2%) applied to axillae (30 mg/axilla). Average concentration (Cavg) of serum testosterone (TT) was determined on days 15, 60, and 120; doses were adjusted to maintain normal Cavg (300-1050 ng/dL [10.4-36.4 nmol/L]). Accuracy of single serum TT measurements (2, 4, 8, 12, 16, and 20 hours post-dose) was assessed in patients with Cavg TT within and below (<300 ng/dL [<10.4 nmol/L]) the normal range. Clinical trial registration: Clinicaltrials.gov - NCT00702650. Main outcome measure: Serum testosterone
levels. Results: In patients with normal Cavg (n = 85), 79% to 92% had serum testosterone levels within normal range 2, 4, 8, 12, 16, and 20 hours post-dose; significant effects of time post-dose for single testosterone measurement accuracy (P = 0.01) were observed: testing accuracy peaked 4-8 hours post-dose and tapered ~16 hours post-dose. In 28/63 instances with low Cavg TT throughout the study a normal 2 hour serum TT level was observed. The average percentage (across all days) of discordant results between Cavg (<300 ng/dL [<10.4 nmol/L]) and single serum TT measurements (300-1050 ng/dL [10.4-36.4 nmol/L]) declined with increasing time from dose application (44% at 2 hours, 38% at 4 hours, 22% at 8 hours, 3% at 16 hours). Conclusions: Reliance on a single serum testosterone measurement to determine the need for dose adjustment of testosterone topical solution 2% may lead clinicians to change the dose unnecessarily, or alternatively, not increase the dose when necessary. The results reported here are limited to testosterone topical solution 2% and may not be applicable to other topical agents.

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Publisher
Taylor and Francis Ltd (E-mail: healthcare.enquiries@informa.com)

274.

The influence of ginger (Zingiber officinale) on human sperm quality and DNA fragmentation: A double-blind randomized clinical trial.

EBM Reviews - Cochrane Central Register of Controlled Trials

[Journal: Article]

AN: CN-01193460 NEW

Background: Although the effectiveness of ginger as an antioxidant agent has been exploited, little human research has been conducted on its activity on male reproductive functions.

Objective: This study was designed to investigate the effects of ginger (Zingiber officinale) on sperm DNA fragmentation (SDF) in infertile men. Materials and Methods: This randomized double-blind, placebo-controlled trial with a 1:1 allocation was performed on 100 infertility treatment candidates who were admitted to Royan Institute for Reproductive Biomedicine,
Tehran, Iran. Patients were randomly assigned to receive one of two treatments: ginger and placebo. Patients were given a 3-month oral treatment (members received capsules containing 250 mg of ginger powder twice a day in ginger and a placebo in other group). Before and after treatment, standardized semen samples were obtained to determine sperm concentration, motility, and SDF according to World Health Organization. Results: There was no significant difference between two groups regarding SDF at baseline (53.48, 95%CI: 37.95-69.02) in cases and (56.75, 95%CI: 40.01-73.5) in controls. The average positive percentage of SDF in patients receiving ginger (17.77, 95%CI: 6.16-29.39) was lower compared with placebo (40.54, 95%CI: 23.94-57.13) after three month of treatment (p=0.02). In multivariate analysis, SDF was significantly lower in patients receiving ginger compared with placebo (mean difference: 3.21, 95%CI: 0.78-5.63, p=0.009). There were no significant differences between two groups regarding to semen parameters. Conclusion: The present study has demonstrated that ginger in a controlled study of efficacy was effective in decreasing SDF in infertile men. Copyright (C) 2016, Research and Clinical Center for Infertility. All rights reserved.

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275.
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Article]
AN: CN-01194475 NEW
Introduction. Novel pathways to parenthood [oocyte cryopreservation, allowance of surrogacy, uterus transplantation, and assisted reproductive treatments (ART) for single women] are currently being discussed. This study investigates women's attitudes towards oocyte cryopreservation and ART procedures that are not allowed or are still under investigation in Sweden, and whether the attitudes differ between urban women and women from a national
cohort. Materials and methods. Two thousand randomly selected Swedish females aged 30-39 years, 1000 residents of Stockholm (urban cohort) and 1000 from the remainder of Sweden (national cohort), were invited to complete a postal questionnaire on attitudes about existing and novel ARTs. Results. Response rates for the national and urban cohorts were 52.1% and 48.9%. Ninety-four per cent of women were positive towards oocyte cryopreservation for medical reasons. Seventy per cent considered that this treatment was also indicated for social reasons. Seventy-six per cent found it acceptable to offer ART to single women. Uterus transplantation was found to be more acceptable than surrogacy (80% vs. 47%). Urban women were more positive to both oocyte cryopreservation for social reasons and fertility treatment of single women than the national cohort. Urban women were also more tolerant regarding age limits for attempting pregnancy with cryopreserved gametes and regarding permission for a longer duration of maintaining cryopreserved gametes. Conclusions. Swedish women have a high acceptance of most new ARTs, with the exception of surrogacy. Urban women seem to have a greater acceptance for social egg-freezing, longer duration of cryopreservation of oocytes, and higher age limit for their use. Copyright (C) 2015 Nordic Federation of Societies of Obstetrics and Gynecology.

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Publisher
Taylor and Francis Ltd (E-mail: info@royensoc.co.uk)

276.
The impact of vitamin E supplementation on semen parameters and pregnancy rates after varicocelectomy: a randomised controlled study.
EBM Reviews - Cochrane Central Register of Controlled Trials
Andrologia. 48 (7) (pp 829-834),. 2016. Date of Publication: 01 Sep 2016. 2016.
[Journal: Article]
AN: CN-01195158  NEW
In this study, we aimed to investigate the impact of vitamin E supplementation on semen parameters and pregnancy after varicocelectomy. Forty-five infertile male patients who were diagnosed with varicocele and underwent subinguinal varicocelectomy were included in the study. After performing subinguinal varicocelectomy, the patients were randomised into two
groups: 22 receiving vitamin E for 12 months, and 23 as the control group without receiving any supplementation. The pre-operative parameters of semen analyses and pregnancy rates of both groups were compared with those of post-operative parameters. There were no statistically significant differences between the groups in terms of sperm count and motile sperm percentage, in pre-operative, post-operative 3rd month, post-operative 6th month and post-operative 12th month periods. Repeated-measures anova was performed, and sperm count, percentage of change in sperm count, motile sperm count and percentage of change in motile sperm count of the groups were compared. The administration of vitamin E increased all of these parameters; however, they were not found to be statistically significant. In conclusion, vitamin E supplementation might improve the sperm parameters after varicocelectomy; however, further studies including larger number of samples are needed to make a proper decision on vitamin E supplementation after varicocelectomy. Copyright (C) 2016 Blackwell Verlag GmbH
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277.
Testosterone treatment is not associated with increased risk of prostate cancer or worsening of lower urinary tract symptoms: Prostate health outcomes in the Registry of Hypogonadism in Men. EBM Reviews - Cochrane Central Register of Controlled Trials BJU International. (no pagination),. 2016. Date of Publication: 2016. 2016.
[Journal: Article In Press]
AN: CN-01195848 NEW
Objectives: To evaluate the effects of testosterone-replacement therapy (TRT) on prostate health indicators in hypogonadal men, including rates of prostate cancer diagnoses, changes in prostate-specific antigen (PSA) levels and lower urinary tract symptoms (LUTS) over time.
Patients and Methods: The Registry of Hypogonadism in Men (RHYME) is a multi-national patient registry of treated and untreated, newly-diagnosed hypogonadal men (n = 999). Follow-up assessments were performed at 3-6, 12, 24, and 36 months. Baseline and follow-up data collection included medical history, physical examination, blood sampling, and patient questionnaires. Prostate biopsies underwent blinded independent adjudication for the presence
and severity of prostate cancer; PSA and testosterone levels were measured via local and central laboratory assays; and LUTS severity was assessed via the International Prostate Symptom Score (IPSS). Incidence rates per 100,000 person-years were calculated. Longitudinal mixed models were used to assess effects of testosterone on PSA levels and IPSS. Results: Of the 999 men with clinically diagnosed hypogonadism (HG), 750 (75%) initiated TRT, contributing 23,900 person-months of exposure. The mean testosterone levels increased from 8.3 to 15.4 nmol/L in treated men, compared to only a slight increase from 9.4 to 11.3 nmol/L in untreated men. In all, 55 biopsies were performed for suspected prostate cancer, and 12 non-cancer related biopsies were performed for other reasons. Overall, the proportion of positive biopsies was nearly identical in men on TRT (37.5%) compared to those not on TRT (37.0%) over the course of the study. There were no differences in PSA levels, total IPSS, or the IPSS obstructive sub-scale score by TRT status. Lower IPSS irritative sub-scale scores were reported in treated compared to untreated men. Conclusions: Results support prostate safety of TRT in newly diagnosed men with HG. Copyright (C) 2016 BJU International.

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Publisher
Blackwell Publishing Ltd (E-mail: customerservices@oxonblackwellpublishing.com)

278.
A perspective on the evolving landscape in male reproductive medicine.
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Article]
AN: CN-01196565 NEW
Context: Men's health and aging are emerging as important areas of research opportunity because of advances in reproductive biology and the recognition of men's health as a unique and important aspect of public health. Evidence Acquisition: A perspective of the evolving landscape in male reproductive medicine. Evidence Synthesis: Remarkable discoveries in reproductive biology have greatly advanced the treatment of erectile dysfunction, androgen deficiency, infertility, hormone sensitive cancers, and prostate diseases. Although the off-label use of
testosterone in middle-aged and older men has grown, the management of androgen deficiency syndromes remains suboptimal. There is a pressing need for wider adoption of accurate testosterone assays and harmonized reference ranges and large randomized trials of testosterone's efficacy and cardiovascular and prostate safety. The transformation in idealized body image towards greater muscularity has contributed to increasing prevalence of body image disorders and the use of muscle building drugs in men. Therapeutic options for fertility regulation in men remain limited, the pathophysiologic basis of infertility in a vast majority of infertile men remains unknown, and assisted reproductive technologies remain inaccessible to many infertile men. Much of the dogma on testosterone's binding to its binding proteins remains inaccurate, and the role of free and albumin-bound testosterone poorly understood. The reproductive health of cancer survivors and the availability of wider contraceptive choices form ene are other areas of unmet need. Suboptimal care of transgender persons has framed transgender medicine as an important healthcare disparities issue. Conclusions: Transformative changes in societal attitudes towards men's sexual health, body image, and gender identity, and in the economics of reproductive healthcare services, offer extraordinary opportunities for translational science that is patient focused, mechanism based, and integrated with healthcare. Copyright (C) 2016 by the Endocrine Society.

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Publisher
Endocrine Society (E-mail: mzendell@endo-society.org)

279.
Cabozantinib (COMETRIQdegree): In medullary thyroid cancer: More harmful than beneficial, as is Vandetanib. Cabozantinib (COMETRIQdegree): In medullary thyroid cancer: More harmful than beneficial, as is Vandetanib.
Anonymous
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Article]
AN: CN-01198584 NEW
Surgery is the mainstay of treatment for medullary thyroid cancer. Cytotoxic chemotherapy is generally ineffective in patients with progressive, inoperable, advanced-stage or metastatic tumours. Vandetanib is also authorised in this setting, but it has more harms than benefits. Cabozantinib, like vandetanib, inhibits several tyrosine kinases involved in angiogenesis. Cabozantinib has been authorised in the European Union for use in this setting. In a randomised, placebo-controlled trial in 330 patients, adding cabozantinib to tailored symptomatic treatment did not prolong survival or improve symptoms, despite a favourable effect on tumour imaging and certain laboratory parameters. On the contrary, cabozantinib appeared to undermine quality of life and aggravate diarrhoea. The known adverse effects of cabozantinib are numerous and often severe: diarrhoea, hand-foot syndrome, hypertension, venous and arterial thrombosis, bleeding and fistulae. Deaths unrelated to tumour progression were more frequent with cabozantinib than with placebo. Cabozantinib carries a risk of multiple pharmacokinetic interactions by interfering with cytochrome P450 isoenzyme CYP3A4 and P-glycoprotein. In animals, cabozantinib is teratogenic and also impairs male and female fertility. Contraception is required for women, and also for the partners of treated men, who must use condoms. These precautions must be maintained for at least 4 months after the end of treatment. In practice, in mid-2015, cabozantinib, like vandetanib, has an unfavourable harm-benefit balance in medullary thyroid cancer. The focus should remain on tailored symptomatic care.

Publisher
Association Mieux Prescrire

Data from the EORTC cancer survivorship task force.
vrieling C, Moser L, Liu L, Meunier F
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Conference Abstract] AN: CN-01172132 NEW
During the past decades, important progress has been made in the treatment of cancer. With early detection and more effective treatments, cancer has become a curable disease for many
patients, while for others it could now be considered a chronic disease. As a consequence, the number of long-term cancer survivors is rapidly increasing, in particular among patients treated for Hodgkin's lymphoma, testicular, prostate, colo-rectal, breast cancer or children's leukemia. Most of these patients, however, face immediate (mostly transient) and long term (mostly irreversible) physical and mental side effects: hair loss, changes in body image, fatigue, depression, cognitive dysfunction, as well as increased risk of cardiovascular disease, bone loss, infertility and secondary malignancies. Cancer survivors are also confronted with socio-economical consequences of their disease, including too often exclusion from insurances, mortgages and loss of jobs. Most of the current knowledge regarding the long-term side effects of cancer and its treatment is based on registry data that is missing important treatment details. Clinical trial databases on the other hand include treatment and outcome data, but often fail to produce very long-term follow-up of outcome and late effects because of the high costs of conducting such long-term follow-up. The European Organisation for Research and Treatment of Cancer (EORTC) Survivorship Task Force aims to use and, if needed, to complete the impressive EORTC databases accumulated over 50 years of conducting cancer clinical trials. The goal is to document and analyse how long-term outcomes and side effects are associated with cancer treatment. With experience in updates of lymphoma and leukemia trials, early breast cancer trials are now being assessed as well. These studies provide large patient numbers (over 6000 patients for the lymphoma studies and over 10,000 patients for the early breast cancer cohort). For the lymphoma trials, the first results on cardiovascular disease and secondary malignancies (incidence and mortality) have recently been published. The effects of the different treatment components on these endpoints have been quantified. Additional information will be gathered through a number of questionnaires sent to survivors, asking them about the impact of cancer diagnosis and treatment on relationships (social situation, parenthood), education, work and insurance, fatigue, emotional well-being and quality of life. To estimate the relative risks compared to the general population, a linkage with data of registries from several geographic areas is needed. Establishing such a network will enable us to quantify the impact of cancer treatment on late side effects in absolute terms. The information that the EORTC will gather through this series of projects is expected to help and guide future patients in trading off treatment efficacy and late side effects, seen as important costs in surviving cancer.

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Publisher
Elsevier Ireland Ltd
Effects of avanafil on semen quality and sperm cytoskeleton in oligoasthenospermic infertile men: A randomized controlled trial.
EBM Reviews - Cochrane Central Register of Controlled Trials
CONFERENCE END: 2016 Feb 6, 18th Congress of the European Society for Sexual Medicine
Madrid Spain., [Journal: Conference Abstract]
AN: CN-01167664 NEW

Objective: We evaluated the effects of avanafil on semen quality in oligoasthenospermic infertile (OAI) men. Methods: The present study was initially scheduled to include 39 OAI-men. When each patient was recruited they were randomly assigned to one of three groups A, B, and C. In all, 13 OAI-men were treated daily for 12 weeks with avanafil (50 mg three times a day; group A), or L-carnitine (14 men; positive control group; 1.5 g per day group B); another group of 12 OAI-men (group C; negative control group) received no treatment. Semen parameters, the mean length of sperm midpiece (LMP), the outcome of hypoosmotic swelling test (%HPST), and the seminal plasma citrate concentration (secreted by the prostate) were evaluated before and after the end of the treatment in each of groups A and B and before and at the end of the 12-week-experimental period (EP) in group C, respectively. Serum levels of testosterone were evaluated before and at the end of the EP in each of groups A, B, or C. Wilcoxon paired test was used for statistical analysis. A probability P smaller than 0.05 was considered as significant. Results: Within group A the peripheral serum mean testosterone concentration (ng/ml), semen citrate concentration (mg/dl), percentage of motile spermatozoa (%), the mean LMP (micrometers), the %HOST (%) and percentage of morphologically normal spermatozoa (%) were significantly greater after avanafil treatment (8.85, 385, 39, 4.5, 59, and 9, respectively) than before treatment (7.99, 297, 26, 4.1, 46, and 3, respectively). Within each group B and C, differences in the above parameters prior to the EP and at the end of the EP were not significant. Conclusion: The enhancement of prostatic secretory function, the longer LMP, and the increase in testosterone may explain the increase in sperm motility after avanafil administration.

Institution
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Publisher
Elsevier
Erectile and ejaculatory function preserved with convective water vapor energy treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia: Randomized controlled study.
EBM Reviews - Cochrane Central Register of Controlled Trials
[Journal: Article]
AN: CN-01159145 NEW

Introduction: Most surgical treatments for male lower urinary tract symptoms and benign prostatic hyperplasia affect erectile and ejaculatory functions negatively, leading to patient dissatisfaction.

Aim: To determine whether water vapor thermal therapy, when conducted in a randomized controlled trial, would significantly improve lower urinary tract symptoms secondary to benign prostatic hyperplasia and urinary flow rate while preserving erectile and ejaculatory functions.

Methods: Men at least 50 years old with International Prostate Symptom Scores of at least 13, a peak flow rate of at least 5 to no higher than 15 mL/s, and prostate volume of 30 to 80 cm$^3$ were randomized 2:1 between Rezum System thermal therapy and control. Thermal water vapor (103$^\circ$C) was injected into lateral and median lobes as required for treatment of benign prostatic hyperplasia. The control procedure entailed rigid cystoscopy with simulated active treatment sounds. Main Outcome Measures: Blinded group (active = 136, control = 61) comparison occurred at 3 months and the active arm was followed to 12 months for International Prostate Symptom Score, peak flow rate, and sexual function using the International Index of Erectile Function and the Male Sexual Health Questionnaire for Ejaculatory Function. The minimal clinically important difference in erectile function perceived by subjects as beneficial was determined for each erectile function severity category. Subjects not sexually active were censored from sexual function analysis. Results: No treatment- or device-related de novo erectile dysfunction occurred after thermal therapy. International Index of Erectile Function and Male Sexual Health Questionnaire for Ejaculatory Function scores were not different from the control group at 3 months or from baseline at 1 year. Ejaculatory bother score improved 31% over baseline ($P = .0011$). Also, 32% of subjects achieved minimal clinically important differences in erectile function scores at 3 months, and 27% at 1 year, including those with moderate to severe
erectile dysfunction. International Prostate Symptom Score and peak flow rate were significantly superior to controls at 3 months and throughout 1 year (P < .0001). Conclusion: Convective water vapor thermal therapy provides sustainable improvements for 12 months to lower urinary tract symptoms and urinary flow while preserving erectile and ejaculatory functions.

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Publisher
Elsevier

283.
Assisted reproductive outcomes in women with different polycystic ovary syndrome phenotypes: The predictive value of anti-Mullerian hormone.
Ramezanali F, Ashrafi M, Hemat M, Arabipoor A, Jalali S, Moini A
EBM Reviews - Cochrane Central Register of Controlled Trials
Reproductive biomedicine online. 32 (5):503-12, 2016.
[Journal: Article]
AN: CN-01153979 NEW
This cross-sectional study aimed to evaluate IVF/intracytoplasmic sperm injection (ICSI) outcomes in different polycystic ovary syndrome (PCOS) phenotypes (A, B, C and D) compared with a control group and the predictive values of serum anti-Mullerian hormone (AMH) in PCOS phenotypes for main outcomes. This study evaluated 386 PCOS women and 350 patients with male factor infertility. Women with phenotypes A and C had significantly higher concentrations of AMH than those with phenotype B (P < 0.001). Clinical pregnancy rate (CPR) in the phenotype D group (53.3%) was higher than other groups (32.5%, 26.4% and 36.8%, respectively, in phenotypes A, B and C), but not to a significant level. Multivariable regression analysis, after adjusting for women's age and body mass index, revealed that PCOS phenotypes A and B were associated with a decreased CPR compared with the control group (odds ratio [OR]: 0.46, confidence interval [CI]: 0.26-0.8, P = 0.007 and OR: 0.34, CI: 0.18-0.62, P = 0.001, respectively).
It seems a combination of hyperandrogenism and chronic anovulation is associated with a negative impact on the CPR in these patients. These results demonstrated that AMH concentration is related to PCO morphology but not predictive for CPR and live birth rate.
Mid-term results using aquablation, an image guided robot-assisted water jet ablation of the prostate, for the treatment of benign prostatic hyperplasia (BPH).

Gilling P, Anderson P, Tan A, Desai M

EBM Reviews - Cochrane Central Register of Controlled Trials


CONFERENCE END: 2016 May 10, 2016 Annual Meeting of the American Urological Association, AUA San Diego, CA United States.,

[Journal: Conference Abstract]

AN: CN-01142655 NEW

INTRODUCTION AND OBJECTIVES: The mid-term results from the multicenter clinical experience of the use of Aquablation to treat lower urinary tract symptoms secondary to BPH are reported. The AquaBeam System is an image-guided robotic system delivering Aquablation, a minimally invasive waterjet therapy for the targeted removal of prostate tissue without the production of heat. Using the real-time transrectal ultrasound image and an integrated conformal planning station, the target region of the prostate is identified and the contour and depth of resection are programmed into the system by the surgeon

METHODS: Men over 50 years of age with an International Prostate Symptom Score (IPSS) greater than 12, a maximum flow rate of 12 ml/sec, and a prostate volume of 25 - 100 ml were treated using the AquaBeam System (PROCEPT BioRobotics, Redwood Shores, CA). Clinical parameters and safety were assessed out to 1 year after surgery. RESULTS: A total of fifty-seven males were enrolled at four centers and treated with Aquablation. The mean age was 69 +/- 7 years with a mean prostate size of 48 +/- 20 ml and the presence of a median lobe was noted in twenty-six of the fifty-seven (46%) patients. All procedures were technically successful with a mean total operative time of 38 +/- 15 minutes and Aquablation resection time of 7 +/- 5 minutes. There were no intra-operative complications and adverse events were typically mild and transient. Other peri-operative
complications were comparable to those observed with other available BPH therapies. There were no procedure related cases of retrograde ejaculation, urinary incontinence, or erectile dysfunction. At the time of this report, fifty one subjects and thirty three subjects had completed their six-month and one-year follow up, respectively. At six month and one year follow up, statistically significant improvement was observed in IPSS, QoL, Qmax, and PVR. IPSS reduced from 22.9 to 6.8, QoL from 5.0 - 1.6, PVR from 105 - 57 ml, and Qmax improved from 7.8 - 16.7 ml/s from baseline to 12 months. Prostate size reduced to 30 ml at six months. CONCLUSIONS: The results of this multicenter experience are promising and Aquablation appears to be safe, feasible, and efficient. The outcomes of this multicenter study support further research in a prospective randomized controlled clinical trial.

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Publisher
Elsevier Inc.

285.
Treatment of lower urinary tract symptoms due to benign prostatic hyperplasia with convective water vapor energy ablation: Preserved erectile and ejaculatory function.
EBM Reviews - Cochrane Central Register of Controlled Trials
CONFERENCE END: 2016 May 10, 2016 Annual Meeting of the American Urological Association, AUA San Diego, CA United States.,
[Journal: Conference Abstract]
AN: CN-01142657 NEW
INTRODUCTION AND OBJECTIVES: To report the prospective analysis of sexual function evaluated in a randomized controlled study of transurethral prostate convective water vapor thermal energy (Rezum System) to treat lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH). RF-generated wet thermal energy (water vapor), dispersed by convection can be targeted to defined prostate zones including the median lobe to achieve rapid tissue ablation. METHODS: Men >50 years old with IPSS > 13, Qmax <15 ml/ s, prostates of 30-80 cc were stratified by International Prostate Symptom Score (IPSS) severity and randomized
2:1 to thermal therapy with the Rezum System and control. The control procedure was rigid cystoscopy with mimicked active treatment sounds. A wash-out period was required for all daily use of drugs for LUTS and/or erectile dysfunction (ED). The blinded group was compared at 3 months and treatment group evaluated over 1 year for LUTS with IPSS, flow rate (Qmax) and sexual function with the International Index of Erectile Function (IIEF-EF) and the Male Sexual Health Questionnaire for Ejaculatory Dysfunction (MSHQ-EjD). RESULTS: 197 men were randomized. LUTS improved 11 points in the active group (N=136) at 3 months vs. 4.3 points for control group (N=61), p<0.0001. In men with severe LUTS (IPSS >19), 85% achieved > 30% reduction in symptoms. Qmax increased 68% (6.2 ml/ s) at 3 months vs. no change in controls (p <0.0001). These improvements were sustained in 96% of treated subjects who completed their 1-year follow-up (p<0.0001). At study entry, 52% of treatment subjects had a history of erectile dysfunction (ED) and 26% had decreased stoppage ejaculation. Only sexually active men (91/136) 67% were included in the sexual function analyses. In these, the IIEF-EF baseline mean was 17.2 (30 max score) and the MSHQ-EjD mean was 7.8 (15 max). There were no clinically meaningful negative changes in scores over 12 months. Modest decreases in ejaculatory volume occurred in 6 men (4.4%), anejaculation in 4 men (2.9%). No de novo ED was reported.

CONCLUSIONS: Conservation of sexual function is a fundamental QOL issue for men contemplating a nonsurgical treatment options for LUTS/ BPH. Convective water vapor thermal energy therapy is a minimally invasive treatment that provides rapid and durable LUTS improvements and no clinically significant changes in erectile and ejaculatory function. The thermal energy treatment was developed for in-office use and shown to be applicable to treatment of all prostate zones including median lobes.

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286.
Altered preconception fatty acid intake is associated with improved pregnancy rates in overweight and obesewomen undertaking in Vitro fertilisation.
Moran LJ, Tsagareli V, Noakes M, Norman R
EBM Reviews - Cochrane Central Register of Controlled Trials
Nutrients. 8(1) (no pagination):2016.
Maternal preconception diet is proposed to affect fertility. Prior research assessing the effect of altering the fatty acid profile on female fertility is conflicting. The aim of this study was to assess the effect of preconception maternal diet, specifically fatty acid profile, on pregnancies and live births following in vitro fertilisation (IVF). Forty-six overweight and obese women undergoing IVF were randomised to a diet and physical activity intervention (intervention) or standard care (control). Outcome measures included pregnancy, live birth and pre-study dietary intake from food frequency questionnaire. Twenty pregnancies (n = 12/18 vs. n = 8/20, p = 0.12) and 12 live births (n = 7/18 vs. n = 5/20, p = 0.48) occurred following the intervention with no differences between the treatment groups. On analysis adjusted for BMI and smoking status, women who became pregnant had higher levels of polyunsaturated fatty acid (PUFA) intake (p = 0.03), specifically omega-6 PUFA and linoleic acid (LA) (p = 0.045) with a trend for an elevated intake of omega-3 PUFA (p = 0.06). There were no dietary differences for women who did or did not have a live birth. Maternal preconception PUFA, and specifically omega-6 and LA intake, are associated with improved pregnancy rates in overweight and obese women undergoing IVF. This has implications for optimising fertility through preconception nutrition.

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287.
Pulsatile gonadotropin-releasing hormone therapy is associated with earlier spermatogenesis compared to combined gonadotropin therapy in patients with congenital hypogonadotropic hypogonadism.
Mao JF; Liu ZX; Nie M; Wang X; Xu HL; Huang BK; Zheng JJ; Min L; Kaiser UB; Wu XY.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Asian Journal of Andrology, 2016 Dec 27.

UI: 28051040
Both pulsatile gonadotropin-releasing hormone (GnRH) infusion and combined gonadotropin therapy (human chorionic gonadotropin and human menopausal gonadotropin [HCG/HMG]) are effective to induce spermatogenesis in male patients with congenital hypogonadotropic hypogonadism (CHH). However, evidence is lacking as to which treatment strategy is better. This retrospective cohort study included 202 patients with CHH: twenty had received pulsatile GnRH and 182 had received HCG/HMG. Patients had received therapy for at least 12 months. The total follow-up time was 15.6 +/- 5.0 months (range: 12-27 months) for the GnRH group and 28.7 +/- 13.0 months (range: 12-66 months) for the HCG/HMG group. The median time to first sperm appearance was 6 months (95% confidence interval [CI]: 1.6-10.4) in the GnRH group versus 18 months (95% CI: 16.4-20.0) in the HCG/HMG group (P < 0.001). The median time to achieve sperm concentrations >5 x 10^6 ml^-1 was 14 months (95% CI: 5.8-22.2) in the GnRH group versus 27 months (95% CI: 18.9-35.1) in the HCG/HMG group (P < 0.001), and the median time to concentrations >10 x 10^6 ml^-1 was 18 months (95% CI: 10.0-26.0) in the GnRH group versus 39 months (95% CI unknown) in the HCG/HMG group. Compared to the GnRH group, the HCG/HMG group required longer treatment periods to achieve testicular sizes of >4 ml, >8 ml, >12 ml, and >16 ml. Sperm motility (a + b + c percentage) evaluated in semen samples with concentrations >1 x 10^6 ml^-1 was 43.7% +/- 20.4% (16 samples) in the GnRH group versus 43.2% +/- 18.1% (153 samples) in the HCG/HMG group (P = 0.921). Notably, during follow-up, the GnRH group had lower serum testosterone levels than the HCG/HMG group (8.3 +/- 4.6 vs 16.2 +/- 8.2 nmol l^-1, P < 0.001). Our study found that pulsatile GnRH therapy was associated with earlier spermatogenesis and larger testicular size compared to combined gonadotropin therapy. Additional prospective randomized studies would be required to confirm these findings.
Female Adult Aedes albopictus Suppression by Wolbachia-Infected Male Mosquitoes.

Mains JW; Brelsfoard CL; Rose RI; Dobson SL.

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present Scientific Reports. 6:33846, 2016 Sep 23.

[D] [Journal Article]

UI: 27659038

Dengue, chikungunya and zika viruses are pathogens with an increasing global impact. In the absence of an approved vaccine or therapy, their management relies on controlling the mosquito vectors. But traditional controls are inadequate, and the range of invasive species such as Aedes albopictus (Asian Tiger Mosquito) is expanding. Genetically modified mosquitoes are being tested, but their use has encountered regulatory barriers and public opposition in some countries. Wolbachia bacteria can cause a form of conditional sterility, which can provide an alternative to genetic modification or irradiation. It is unknown however, whether openly released, artificially...
infected male Ae. albopictus can competitively mate and sterilize females at a level adequate to suppress a field population. Also, the unintended establishment of Wolbachia at the introduction site could result from horizontal transmission or inadvertent female release. In 2014, an Experimental Use Permit from the United States Environmental Protection Agency approved a pilot field trial in Lexington, Kentucky, USA. Here, we present data showing localized reduction of both egg hatch and adult female numbers. The artificial Wolbachia type was not observed to establish in the field. The results are discussed in relation to the applied use of Wolbachia-infected males as a biopesticide to suppress field populations of Ae. albopictus.

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Date Created
20160923
Year of Publication
2016

289.
Changes occurred in the testes and DNA pattern of males wax moth (Galleria mellonella) first generation as a result of irradiation of their parents.
Rizk SA; Abdalla RS; Sayed RM.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Bulletin of Entomological Research. 1-6, 2016 Dec 15.
[Journal Article]
Nowadays, the sterile insect technique is broadly used as a pest control measure. Therefore, the present study was conducted to investigate the alteration occurred in testes and DNA pattern as an effect of inherited sterility. Full grown pupae of the wax moth, Galleria mellonella were irradiated with 80 and 160 Gy of gamma irradiation. The size of the testes was decreased by increasing of gamma irradiation dose. Also, the size of the testes was decreased in F 1 males comparing with the size of the testes of both the parents and the untreated control. The effects of gamma rays on the DNA patterns of adult male parents and F 1 males showed alterations among the controls, the treated parents and F 1 individuals. Exposure to radiation caused very frequently the appearance of some extra bands and the deficiency of others in the arbitrary random amplified polymorphic DNA-polymerase chain reaction amplification patterns of the irradiated insects.

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20161215

Year of Publication
2016

290.
The Role of Sexual Dysfunction and Infertility on Reproductive Health in Diabetics: Pathogenesis, Evaluation, and Management.
Gandhi J; Dagur G; Warren K; Smith N; Khan SA.
BACKGROUND: Uncontrolled or long-term diabetes mellitus is conducive to vascular and oxidative stress disturbances that impede several physiological systems, which may in turn elicit psychological symptoms.

OBJECTIVE: We assess the sexual and hormonal complications of diabetes mellitus that impair reproductive function in males and females.

METHOD: A comprehensive MEDLINE search was guided using key words relevant to diabetes mellitus and reproductive health.

RESULTS: We reviewed the pathogenesis, clinical manifestations, imaging modalities, pharmacological treatment, and intervention options for each diabetic reproductive complication in males and females. Erectile dysfunction secondary to angiopathic, neuropathic, and myopathic damage is a leading complication of diabetes in males. Other reproductive complications include ejaculatory dysfunction, hypogonadism, modified semen parameters, and delayed puberty. Specifics of reproductive dysfunction in diabetic women are less definite than in men due to the lack of standardized evaluation of sexual function in women as well as the increased role of psychological morbidity. Despite this, it is known to manifest as hypogonadism, hypoactive sexual desire disorder, dyspareunia, menstrual dysfunction, and polycystic ovarian syndrome.

CONCLUSION: Longitudinal studies with larger sample sizes are necessary to better comprehend the connection between diabetes and sexual dysfunction, chiefly in females. Understanding and dividing the role of fertility and sexual issues in reproductive dysfunction can help guide evaluation and management.
Ignorance could hurt: an assessment of fertility awareness, childbirth intentions and parenting attitudes among university students.

Abiodun O; Alausa K; Olasehinde O.

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article]
UI: 27740927

BACKGROUND: An emerging pattern of increasing median age at first birth among women has been well documented in Western countries. A similar but less remarkable trend is being experienced in sub-Saharan Africa. There is a paucity of information in Sub-Saharan Africa about awareness of age-related fertility decline. The aim of this study was to assess the perception of fertility, childbirth intentions and parenting attitudes among university students.

MATERIALS AND METHODS: A cross-sectional survey of 231 female and 158 male students randomly selected university undergraduates in Nigeria using a self-reported questionnaire.

RESULTS: The respondents overestimated the ages of slight (92.1%) and marked decline (89.4%) in female fertility. The chance of pregnancy after unprotected sex during ovulation was overestimated by 93.1% of the respondents. Over three-quarters of them overestimated the success rate of in-vitro fertilization. The sources of information regarding fertility issues were mainly school (40.1%), the media (20.6%) and family members (18.8%). About 98.7% of the childless respondents reported an intention to have children in the future. The mean number of children desired was 3.29+/-1.14. Females desire to have their first and last children earlier than males (p=0.000). The perceived potential obstacles to having the desired children were the pursuit of career aspirations (35.5%) and the pursuit of personal interests (20.8%).

CONCLUSIONS: Misconceptions about fertility issues have grave implications for involuntary childlessness and secondary infertility. Comprehensive family planning education that will address the misconceptions about female fecundity and parenting issues are required.

Status
Publisher
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Abiodun, Olumide; Alausa, Kamil; Olasehinde, Olanrewaju.
Comparing calculated free testosterone with total testosterone for screening and diagnosing late-onset hypogonadism in aged males: A cross-sectional study.

Liu Z; Liu J; Shi X; Wang L; Yang Y; Tao M; Fu Q.

OBJECTIVE: The aim of this study is to compare calculated free testosterone (cFT) and total testosterone (T) in predicting late-onset hypogonadism (LOH) in middle-aged and elderly males.

METHODS: We surveyed a random sample of 608 males between the ages of 45 and 87 years from Shanghai, China. The Aging Male Symptoms (AMS) questionnaire and the Androgen Deficiency in Aging Male (ADAM) questionnaire were completed by the subjects. Testosterone (T), sex hormone-binding globulin (SHBG), albumin, and other blood biochemical indexes were measured in 332 males. The corresponding cFT was obtained using the Vermeulen formula and the correlations between T and cFT were analyzed by SPSS statistical software.

RESULTS: Among the 332 males who underwent biochemical evaluation, 289 males (87.0%) was positively screened by the ADAM questionnaire and 232 males (69.9%) by the AMS questionnaire. As suggested by linear regression, cFT exhibited a negative correlation with age in both ADAM+ and AMS+ group, whereas T did not appear to have significant correlation with age. Besides, there were statistically significant differences in cFT (P<.001) in the AMS questionnaire.

CONCLUSIONS: Calculated free testosterone levels are more reliable than T levels for diagnosing LOH in middle-aged and elderly males.

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293.
Possible influence of vitamin D on male reproduction. [Review]
Boisen IM; Bollehuus Hansen L; Mortensen LJ; Lanske B; Juul A; Blomberg Jensen M.
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[Review. Journal Article]
UI: 27693423
Vitamin D is a versatile signaling molecule with an established role in the regulation of calcium homeostasis and bone health. In recent years the spectrum of vitamin D target organs has expanded and a reproductive role is supported by the presence of the vitamin D receptor (VDR)
and the vitamin D metabolizing enzymes in the gonads, reproductive tract, and human spermatozoa. Interestingly, expression levels of VDR and the vitamin D inactivating enzyme CYP24A1 in human spermatozoa serve as positive predictive markers of semen quality and are higher expressed in spermatozoa from normal than infertile men. VDR mediates a non-genomic increase in intracellular calcium concentration, sperm motility, and induces the acrosome reaction. Furthermore, functional animal model studies have shown that vitamin D is important for sex steroid production, estrogen signaling, and semen quality. Cross-sectional clinical studies have supported the notion of a positive association between serum 25-hydroxyvitamin D (25-OHD) level and semen quality in both fertile and infertile men. However, it remains to be determined whether this association reflects a causal effect. The VDR is ubiquitously expressed and activated vitamin D is a regulator of insulin, aromatase, and osteocalcin. Hence, it is plausible that the influence of vitamin D on gonadal function may be mediated indirectly through other vitamin D regulated endocrine factors. Recent studies have indicated that vitamin D supplementation may be beneficial for couples in need of assisted reproductive techniques as high serum vitamin D levels were found to be associated with a higher chance of achieving pregnancy. Randomized clinical trials are needed to determine whether systemic changes in vitamin D metabolites can influence semen quality, fertility, and sex steroid production in infertile men. In this review known and possible future implications of vitamin D in human male reproduction function will be discussed.

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Screening for genital chlamydia infection. [Review]
Low N; Redmond S; Uuskula A; van Bergen J; Ward H; Andersen B; Gotz H.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present Cochrane Database of Systematic Reviews. 9:CD010866, 2016 Sep 13. [Review. Journal Article]
UI: 27623210
BACKGROUND: Genital infections caused by Chlamydia trachomatis are the most prevalent bacterial sexually transmitted infection worldwide. Screening of sexually active young adults to detect and treat asymptomatic infections might reduce chlamydia transmission and prevent
reproductive tract morbidity, particularly pelvic inflammatory disease (PID) in women, which can cause tubal infertility and ectopic pregnancy.

OBJECTIVES: To assess the effects and safety of chlamydia screening versus standard care on chlamydia transmission and infection complications in pregnant and non-pregnant women and in men.

SEARCH METHODS: We searched the Cochrane Sexually Transmitted Infections Group Specialised Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, LILACS, Cinahl, DARE, PsycINFO and Web of Science electronic databases up to 14 February 2016, together with World Health Organization International Clinical Trials Registry (ICTRP) and ClinicalTrials.gov. We also handsearched conference proceedings, contacted trial authors and reviewed the reference lists of retrieved studies.

SELECTION CRITERIA: Randomised controlled trials (RCTs) in adult women (non-pregnant and pregnant) and men comparing a chlamydia screening intervention with usual care and reporting on a primary outcome (C. trachomatis prevalence, PID in women, epididymitis in men or incidence of preterm delivery). We included non-randomised controlled clinical trials if there were no RCTs for a primary outcome.

DATA COLLECTION AND ANALYSIS: Two review authors independently assessed trials for inclusion, extracted data and assessed the risk of bias. We resolved disagreements by consensus or adjudication by a third reviewer. We described results in forest plots and conducted meta-analysis where appropriate using a fixed-effect model to estimate risk ratios (RR with 95% confidence intervals, CI) in intervention vs control groups. We conducted a pre-specified sensitivity analysis of the primary outcome, PID incidence, according to the risks of selection and detection bias.

MAIN RESULTS: We included six trials involving 359,078 adult women and men. One trial was at low risk of bias in all six specific domains assessed. Two trials examined the effect of multiple rounds of chlamydia screening on C. trachomatis transmission. A cluster-controlled trial in women and men in the general population in the Netherlands found no change in chlamydia test positivity after three yearly invitations (intervention 4.1% vs control 4.3%, RR 0.96, 95% CI 0.84 to 1.09, 1 trial, 317,304 participants at first screening invitation, low quality evidence). Uptake of the intervention was low (maximum 16%). A cluster-randomised trial in female sex workers in Peru found a reduction in chlamydia prevalence after four years (adjusted RR 0.72, 95% CI 0.54 to 0.98, 1 trial, 4465 participants, low quality evidence). Four RCTs examined the effect of chlamydia screening on PID in women 12 months after a single screening offer. In analysis of four trials according to the intention-to-treat principle, the risk of PID was lower in women in intervention than control groups, with little evidence of between-trial heterogeneity (RR 0.68, 95% CI 0.49 to 0.94, I² 7%, 4 trials, 21,686 participants, moderate quality evidence). In a sensitivity analysis, the estimated effect of chlamydia screening in two RCTs at low risk of detection bias (RR 0.80, 95%
CI 0.55 to 1.17) was compatible with no effect and was lower than in two RCTs at high or unclear risk of detection bias (RR 0.42, 95% CI 0.22 to 0.83). The risk of epididymitis in men invited for screening, 12 months after a single screening offer, was 20% lower risk for epididymitis than in those not invited; the confidence interval was wide and compatible with no effect (RR 0.80, 95% CI 0.45 to 1.42, 1 trial, 14,980 participants, very low quality evidence). We found no RCTs of the effects of chlamydia screening in pregnancy and no trials that measured the harms of chlamydia screening.

AUTHORS’ CONCLUSIONS: Evidence about the effects of screening on C. trachomatis transmission is of low quality because of directness and risk of bias. There is moderate quality evidence that detection and treatment of chlamydia infection can reduce the risk of PID in women at individual level. There is an absence of RCT evidence about the effects of chlamydia screening in pregnancy. Future RCTs of chlamydia screening interventions should determine the effects of chlamydia screening in pregnancy, of repeated rounds of screening on the incidence of chlamydia-associated PID and chlamydia reinfection in general and high risk populations.
A limited number of studies have reported an association between male factor infertility (MFI) and dental health status (DHS). The aim of the present study was to assess the association between DHS and MFI through a systematic review of indexed literature. To address the focused question: "Is there a relationship between DHS and MFI?"-indexed databases were searched up to March 2016 using various key words "infertility," "periodontal disease," "periodontitis," "dental infection," "caries," and "odontogenic infection." Letters to the editor, case reports, commentaries, historic reviews, and experimental studies were excluded. In total seven studies were included in the present systematic review and processed for data extraction. All the studies reported a positive association between MFI and DHS. The number of study participants ranged between 18 and 360 individuals. Results from six studies showed a positive association between chronic periodontitis and MFI. Three studies reported a positive relationship between MFI and odontogenic infections associated to necrotic pulp, chronic apical osteitis, and radicular cysts. One study reported a relationship between caries index and MFI. From the literature reviewed, there seems to be a positive association between MFI and DHS; however, further longitudinal studies and randomized control trials assessing confounders are needed to establish real correlation. Dentists and general practitioners should be aware that oral diseases can influence the systemic health. Andrological examination should include comprehensive oral evaluation, and physicians detecting oral diseases should refer the patient to a dentist for further evaluation.

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Date Created
20160624
We evaluated the role of Tribulus terrestris in males with unexplained infertility and its effect on serum testosterone and semen parameters. Thirty randomized male patients presenting to Andrology outpatient clinic complaining of idiopathic infertility were selected. They were given Tribulus terrestris (750 mg) in three divided doses for three months. The effect of Tribulus terrestris on serum testosterone (total and free) and luteinizing hormone (LH), as well as its impact on semen parameters in those patients, was studied. No statistically significant difference was observed in the levels of testosterone (total and free) and LH and semen parameters (sperm concentration or motility, or abnormal forms) before and after the treatment. In addition, no statistically significant correlations were observed between testosterone (free and total) and LH and semen parameters before and after the treatment. Tribulus terrestris was ineffective in the treatment of idiopathic infertility.
The control of male fertility by spermatid-specific factors: searching for contraceptive targets from spermatozoon's head to tail. [Review]
Chen SR; Batool A; Wang YQ; Hao XX; Chang CS; Cheng CY; Liu YX.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Review. Journal Article]
UI: 27831554

Male infertility due to abnormal spermatozoa has been reported in both animals and humans, but its pathogenic causes, including genetic abnormalities, remain largely unknown. On the other hand, contraceptive options for men are limited, and a specific, reversible and safe method of male contraception has been a long-standing quest in medicine. Some progress has recently been made in exploring the effects of spermatid-specific genetic factors in controlling male fertility. A comprehensive search of PubMed for articles and reviews published in English before July 2016 was carried out using the search terms 'spermiogenesis failure', 'globozoospermia', 'spermatid-specific', 'acrosome', 'infertile', 'manchette', 'sperm connecting piece', 'sperm annulus', 'sperm ADAMs', 'flagellar abnormalities', 'sperm motility loss', 'sperm ion exchanger' and 'contraceptive targets'. Importantly, we have opted to focus on articles regarding spermatid-specific factors. Genetic studies to define the structure and physiology of sperm have shown that spermatozoa appear to be one of the most promising contraceptive targets. Here we summarize how these spermatid-specific factors regulate spermiogenesis and categorize them according to their localization and function from spermatid head to tail (e.g., acrosome, manchette, head-tail conjunction, annulus, principal piece of tail). In addition, we emphatically introduce small-molecule contraceptives, such as BRDT and PPP3CC/PPP3R2, which are currently being developed to target spermatogenic-specific proteins. We suggest that blocking the differentiation
of haploid germ cells, which rarely affects early spermatogenic cell types and the testicular microenvironment, is a better choice than spermatogenic-specific proteins. The studies described here provide valuable information regarding the genetic and molecular defects causing male mouse infertility to improve our understanding of the importance of spermatid-specific factors in controlling fertility. Although a male contraceptive 'pill' is still many years away, research into the production of new small-molecule contraceptives targeting spermatid-specific proteins is the right avenue.

Status
In-Data-Review

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Chen, Su-Ren; Batool, Aalia; Wang, Yu-Qian; Hao, Xiao-Xia; Chang, Chawn-Shang; Cheng, C Yan; Liu, Yi-Xun.

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Date Created
20161110

Year of Publication
2016
Etiology, transmission and protection: Chlamydia trachomatis is the leading cause of bacterial sexually transmitted infection (STI) globally. However, C. trachomatis also causes trachoma in endemic areas, mostly Africa and the Middle East, and is a leading cause of preventable blindness worldwide. Epidemiology, incidence and prevalence: The World Health Organization estimates 131 million new cases of C. trachomatis genital infection occur annually. Globally, infection is most prevalent in young women and men (14-25 years), likely driven by asymptomatic infection, inadequate partner treatment and delayed development of protective immunity. Pathology/Symptomatology: C. trachomatis infects susceptible squamocolumnar or transitional epithelial cells, leading to cervicitis in women and urethritis in men. Symptoms are often mild or absent but ascending infection in some women may lead to Pelvic Inflammatory Disease (PID), resulting in reproductive sequelae such as ectopic pregnancy, infertility and chronic pelvic pain. Complications of infection in men include epididymitis and reactive arthritis. Molecular mechanisms of infection: Chlamydiae manipulate an array of host processes to support their obligate intracellular developmental cycle. This leads to activation of signaling pathways resulting in disproportionate influx of innate cells and the release of tissue damaging proteins and pro-inflammatory cytokines. Treatment and curability: Uncomplicated urogenital infection is treated with azithromycin (1 g, single dose) or doxycycline (100 mg twice daily x 7 days). However, antimicrobial treatment does not ameliorate established disease. Drug resistance is rare but treatment failures have been described. Development of an effective vaccine that protects against upper tract disease or that limits transmission remains an important goal. Status
In-Data-Review
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OBJECTIVE: To determine whether a uterus from the mother of a woman with absolute uterine factor infertility can be transplanted to daughter and carry a pregnancy with delivery of a healthy child.

DESIGN: Part of an observational study.

SETTING: University teaching hospital.

PATIENT(S): Twenty eight-year-old woman with uterine agenesis, her male partner, and her 50-year-old mother.

INTERVENTION(S): In vitro fertilization with embryo cryopreservation before live donor uterus transplantation (UTx). Induction immunosuppression. Embryo transfer 12 months after UTx, pregnancy controls, delivery, and hysterectomy.

MAIN OUTCOME MEASURE(S): Results of IVF-ET, parameters of pregnancy/birth, and surgical data of transplantation/cesarean section/hysterectomy.

RESULT(S): Two IVF cycles before UTx resulted in 10 cryopreserved embryos. Donor surgery included hysterectomy with vascular pedicles of uterine vessels and proximal vessels up to and including parts of internal iliacs. Recipient surgery was by bilateral vascular connections to external iliacs, vaginal-vaginal anastomosis, and uterine fixation. Pregnancy occurred at the first single ET, and the pregnancy proceeded uneventfully until gestational week 34, when the patient developed cholestasis with intense pruritus. Cesarean section was performed at 34+6, with
delivery of a healthy boy (weight 2,335 g). Hysterectomy was performed 3.5 months after delivery. The weight of the healthy child at 12 months was 9.3 kg. Grandmother (uterus donor) and mother are in good health 3 years after UTx.

CONCLUSION(S): This is the first report of a live birth after mother-to-daughter UTx, and it also represents the second birth ever after human UTx.

CLINICAL TRIAL REGISTRATION: NCT01844362.

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status
In-Data-Review

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Sperm ejaculates contain a heterogeneous population of nonviable and viable spermatozoal cells. Ejaculates with high concentrations of poor quality or damaged spermatozoa can greatly impair the overall fertility of males. Recently, a novel technique termed nanopurification has been developed (Feugang et al. 2015 IVF Reprod. Med. Genet. 3, 2) to noninvasively target and remove poor quality spermatozoa from boar semen. Such removal will enrich insemination doses with high quality spermatozoa to enhance fertility successes. However, effects associated with offspring born from nanopurified semen and possible meat quality assurance have yet to be extensively studied. The objective of this study was to measure the growth performance and market characteristics of pigs born from standard or nanopurified spermatozoa. Boar semen was obtained in insemination doses from a local stud and was mixed with (nanopurified) magnetic
nanoparticles (iron-oxide) specifically designed to interact with acrosome-reacted and apoptotic spermatozoa. After incubation, mixed semen were placed under an electromagnetic field trapping moribund sperm to allow collection of intact and viable spermatozoa. Six gilts were bred with standard non-purified (control; n=3) or nanopurified (n=3) semen, with subsequent pregnancies leading to full-term birth of viable offspring. At weaning, pigs of equal sexes (5 male and 5 female) were randomly selected from control (n=10) and nanopurified (n=10) litters. Pigs were fed and measured until market weight, at which meat quality and carcass characteristics were assessed. Data (mean+/-SEM) were analysed with Student's t-test and SAS software (SAS Institute Inc., Cary, NC, USA). The threshold of significance was set as P<0.05. Patterns of growth between groups were comparable up to market size (P>0.05). Standard pork quality parameters (lean carcass weight, loin eye area, percentage of lean cuts, loin and ham colouring, etc.) revealed no significant differences between groups (P>0.05). Dressing percentage was found higher in the nanopurified group compared with control, with a 1.5% increase (P<0.05). Marbling score tended to be significantly higher in the nanopurified group (2.7+/-0.15) when compared with the control (2.3+/-0.15). Findings indicate that sperm nanopurification does not impair growth of offspring and could ultimately lead to a higher pork carcass quality. Additional research is being conducted to confirm current findings and identify further effects of nanopurification regarding offspring and carcass quality.

Status
In-Process

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301.
Effect of Testosterone Replacement Therapy on Cognitive Performance and Depression in Men with Testosterone Deficiency Syndrome.
Jung HJ; Shin HS.
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[Journal Article]
UI: 28053949
PURPOSE: We aimed to evaluate the effect of testosterone replacement therapy (TRT) on cognitive function and depression in men with testosterone deficiency syndrome.
MATERIALS AND METHODS: We carried out a prospective, placebo-controlled trial involving 106 men with total testosterone levels <3.3 ng/mL and symptoms of hypogonadism. Based on whether the patients received TRT (injection with 1,000 mg testosterone undecanoate) or a placebo (advice to modify lifestyle), the study population was divided into a TRT group (n=54) and a control group (n=52).
RESULTS: The age among patients in the TRT and control groups was 56.7+/−12.6 years and 57.8+/−11.4 years, respectively (p> 0.05). At baseline, no significant differences between the TRT and control groups were noted regarding serum testosterone or prostate-specific antigen levels, or regarding the scores for aging symptoms (Aging Males' Symptoms scale), erectile function (5-item International Index of Erectile Function questionnaire), cognitive function (Korean Mini-Mental State Examination), and depression (Beck Depression Inventory). At 8 months after intervention total serum testosterone levels and erectile function scores had significantly increased (p<0.05), whereas the scores for aging symptoms and depression had significantly decreased (p<0.05) in the TRT group; no significant improvement in any parameters was noted for the control group. Notably, significant improvement in cognitive function was noted among patients with cognitive impairment at baseline (cognitive function score <25) who received TRT.
CONCLUSIONS: TRT may be considered in men with testosterone deficiency syndrome if low testosterone levels are associated with depression or cognitive impairment.
Status
In-Data-Review
Authors Full Name
Study of pentoxifylline effects on motility and viability of spermatozoa from infertile asthenozoospermic males.

Ghasemzadeh A; Karkon-Shayan F; Yousefzadeh S; Naghavi-Behzad M; Hamdi K.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article]
UI: 27942099

BACKGROUND: The quality of semen is one of the major parameters in male infertility. Pentoxifylline, a methylxanthine derivative, is an agent primarily used in the treatment of intermittent claudication and other vascular disorders. Studies have shown that pentoxifylline enhances the quality and quantity of sperms. In this study, we have investigated the in vitro effects of pentoxifylline on viability and motility of spermatozoa in samples of infertile oligoasthenozoospermic males.

MATERIALS AND METHODS: In this observer-blinded clinical trial, semen samples of 25 infertile oligoasthenozoospermic males were collected in Alzahra Educational Medical Center of Tabriz University of Medical Sciences from August 2010 to August 2012. After the isolation of spermatozoa by the swim-up method, they were randomized into four groups in ISM1 environment: The controls treated normally: Group 1 treated by pentoxifylline at a dose of 50 mug/ml, Group 2 treated by pentoxifylline at a dose of 100 mug/ml, and Group 3 treated by pentoxifylline at a dose of 200 mug/ml. Sperm viability and motility were compared among the groups on 45 min, 24 h, 36 h, and 48 h intervals.
RESULTS: Mean percentages of live sperms were 98.40%, 51.40%, 20.60%, and 6.00% in control group and 98.40%, 69.20%, 38.60%, and 14.60% in Group 3 on the mentioned intervals, respectively. This mean percentage decrease of live sperms was significantly lower in Group 3 comparing with that of other groups (P = 0.01). Mean percentages of motile sperms were 54%, 8.40%, 2.80%, and 0% in control group; and 54%, 16%, 4.80%, and 1.40% in Group 3 on the mentioned intervals, respectively. There was not a significant difference between the four groups in this regard (P = 0.19).

CONCLUSION: Pentoxifylline can enhance the viability of sperm of infertile oligoasthenozoospermic males with no significant effect on its motility.

Status
In-Data-Review

Authors Full Name
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20161212

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2016

303.
Wolffian Origin of Vagina Unfolds the Embryopathogenesis of OHVIRA (Obstructed Hemivagina and Ipsilateral Renal Anomaly) Syndrome and Places OHVIRA as a Female Counterpart of Zinner Syndrome in Males.

Aswani Y; Varma R; Choudhary P; Gupta RB.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid
MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article]
UI: 27920841

BACKGROUND: The classical theory of Mullerian origin of upper vagina fails to explain complex urogenital malformations like OHVIRA syndrome; the Acien's hypothesis, however, unravels the hidden embryopathogenesis. As per Acien, Wolffian (mesonephric) ducts instead of Mullerian ducts and sinovaginal bulbs, give rise to the vagina. The new hypothesis, however, retains the concept of origin of the ureters (with ureters inducing renal development) by the former and the uterus by Mullerian ducts. Thus, a failure of development of mesonephros/mesonephric duct gives rise to absent ureters and hence absent homolateral kidney; blind ending (obstructed) ipsilateral hemivagina and cessation of support to paramesonephric ducts which leads to unfused uterus (uterus didelphys). Hence, the new hypothesis explains all components of OHVIRA syndrome. On a parallel track, unilateral anomalous development of the mesonephros in males causes atresia of the homolateral ejaculatory duct that results in obstruction of the proximally placed seminal vesicle. Besides, there is absence of the ipsilateral kidney (Zinner syndrome).

CASE REPORT: In this manuscript, we describe four cases of OHVIRA syndrome. Case 1 was a 34-year-old nulligravida, married since fourteen years, who presented with a 5-month history of pelvic inflammatory disease and dyspareunia. Regular menses in the patient and azoospermia in her husband delayed the diagnosis. Case 2 was a 14-year-old girl who presented with dysmenorrhea and lower abdominal pain since a few months. Case 3 was a 27-year-old female who presented with infertility and dysmenorrhea. Case 4 was a 15-year-old female who presented with a one-year history of dysmenorrhea and cyclic pelvic pain. In all cases, one of the uterine horns revealed collection due to a hemivaginal septum and an absent ipsilateral kidney; thus, establishing the diagnosis of OHVIRA syndrome. The case 4 additionally revealed homolateral vaginal agenesis.

CONCLUSIONS: On the basis of our 4 cases, we support the Acien's hypothesis of Wolffian origin of vagina which explains the development of OHVIRA syndrome. Besides, we emphasize the need to suspect this syndrome in a female with a pelvic mass and absence of homolateral kidney. Finally, we believe that OHVIRA due to its Wolffian origin is a female equivalent of Zinner syndrome in males. Therefore, we propose OSVIRA (Obstructed Seminal Vesicle and Ipsilateral Renal Agenesis) as an acronym for Zinner syndrome analogous to OHVIRA.
Status
In-Data-Review

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304.
Evaluation of Role of GnRH Antagonist in Intrauterine Insemination (IUI) Cycles with Mild Ovarian Hyperstimulation (MOH): A Prospective Randomised Study.
Wadhwa L; Khanna R; Gupta T; Gupta S; Arora S; Nandwani S.
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[Journal Article]
UI: 27651646
AIMS AND OBJECTIVE: To evaluate the role of GnRH antagonist in prevention of premature LH surge and increasing pregnancy rates in IUI cycle with mild ovarian hyperstimulation (MOH).
STUDY DESIGN: Prospective parallel, randomised controlled study.
MATERIAL AND METHODS: Couples diagnosed with unexplained, male factor subfertility and with one or both tubes patent were randomised to receive either a GnRH antagonist (study group) or no intervention (control group). All women were treated with clomiphene citrate (D3-D7) followed by HMG. A GnRH antagonist was added when one or more follicles of 16 mm diameter
or more were visualised in the study group. When at least one follicle reached a size of >18 mm, ovulation was induced by hCG injection. A single IUI was performed 36 h later. The primary outcome was premature LH surge and pregnancy rate. The secondary outcomes were the amount of gonadotropins used, duration of use of GnRH antagonist and incidence and severity of OHSS.

RESULTS: A total of seventy patients attending the infertility clinic in the outpatient department of Obstetrics and Gynecology, of a tertiary care centre, were recruited in the study which was carried out from August 2011 to March 2013. The study group included 34 women and 36 in the control arm. The incidence of premature LH surge was significantly lower in the antagonist group as compared to the control group 2.9 vs. 13.9 %, with a p value of <0.001. The clinical pregnancy rates were similar in both the groups 8.8 vs. 11.1 %, p value being 1.000. The amount of gonadotropins used in GnRH antagonist group was lower than in control group but not statistically significant. Duration of GnRH antagonist was 1.85 +/- 0.61 days in the study group.

CONCLUSION: The delayed administration of GnRH antagonists in MOH with IUI cycles when follicle size is >16 mm is beneficial in terms of preventing the occurrence of premature LH surge but with no improvement in pregnancy rates.

Status
PubMed-not-MEDLINE

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INTRODUCTION: Iatrogenic hyperprolactinaemia (IHPRL) has been more frequently related to some antipsychotic drugs that provoke an intense blockade of dopamine D2 receptors. There is a wide variation in clinical practice, and perhaps some more awareness between clinicians is needed. Due to the high frequency of chronic treatment in severe mental patients, careful attention is recommended on the physical risk. IHPRL symptoms could be underestimated without routine examination.

METHODOLOGY: An intense scientific literature search was performed in order to draw up a multidisciplinary consensus, including different specialists of psychiatry, endocrinology, oncology and internal medicine, and looking for a consensus about clinical risk and detection of IHPRL following evidence-based medicine criteria levels (EBM I-IV).

RESULTS: Short-term symptoms include amenorrhea, galactorrhoea, and sexual dysfunction with decrease of libido and erectile difficulties related to hypogonadism. Medium and long-term symptoms related to oestrogens are observed, including a decrease bone mass density, hypogonadism, early menopause, some types of cancer risk increase (breast and endometrial), cardiovascular risk increase, immune system disorders, lipids, and cognitive dysfunction.
Prolactin level, gonadal hormones and vitamin D should be checked in all patients receiving antipsychotics at baseline although early symptoms (amenorrhea-galactorrhoea) may not be observed due to the risk of underestimating other delayed symptoms that may appear in the medium term. Routine examination of sexual dysfunction is recommended due to possible poor patient tolerance and low compliance. Special care is required in children and adolescents, as well as patients with PRL levels >50ng/ml (moderate hyperprolactinaemia). A possible prolactinoma should be investigated in patients with PRL levels >150ng/ml, with special attention to patients with breast/endometrial cancer history. Densitometry should be prescribed for males >50 years old, amenorrhea>6 months, or early menopause to avoid fracture risk.

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Status
In-Process

Authors Full Name
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Beneficial effects of microsurgical varicocelectomy on sperm maturation, DNA fragmentation, and nuclear sulfhydryl groups: a prospective trial.

Alhathal N; San Gabriel M; Zini A.

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present Andrology. 4(6):1204-1208, 2016 Nov.

[Journal Article]
There is evidence to show that varicocele repair can improve conventional sperm parameters but the effects on sperm chromatin integrity have not been fully elucidated. We sought to examine the effects of varicocelectomy on sperm maturation, nuclear chromatin integrity and nuclear sulfhydryl groups. We conducted a prospective study of consecutive infertile men (n=29) that underwent a microsurgical sub-inguinal varicocelectomy for treatment of a clinically palpable varicocele and abnormal semen parameters. Six healthy sperm donors served as controls. We evaluated conventional sperm parameters and markers of sperm chromatin and DNA integrity (aniline blue (AB) staining, iodoacetamide fluorescein (IAF) fluorescence and, % DNA fragmentation index (%DFI) and percent high DNA stainability (%HDS) by sperm chromatin structure assay) before and 6 months after surgery. The sperm %DFI, %HDS, % 5-IAF staining (diffuse head staining) and % AB staining (dark blue) were all significantly lower in the control group compared to infertile men with varicocele (8 vs. 20%, 4.0 vs. 9.6%, 1.7 vs. 16.3%, and 2.5 vs. 13.5% respectively). The %HDS and %DFI decreased significantly after surgery (from 10% to 6% and from 20% to 13%, respectively). Similarly, the %5-IAF and %AB staining also decreased significantly after surgery (from 16.3% to 5.4%, and from 13.5% to 5.4%, respectively). We observed significant inversely relationships between sperm progressive motility and both %IAF staining and %DFI (r=-0.44 and -0.43, respectively). The data show that varicocelectomy is associated with an improvement in sperm DNA integrity and chromatin compaction using three different assays of sperm chromatin integrity.

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Status
In-Data-Review

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20160827

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2016
The epidemiologic evidence linking prenatal and postnatal exposure to endocrine disrupting chemicals with male reproductive disorders: a systematic review and meta-analysis. [Review] Bonde JP; Flachs EM; Rimborg S; Glazer CH; Giwercman A; Ramlau-Hansen CH; Hougaard KS; Hoyer BB; Haervig KK; Petersen SB; Rylander L; Specht IO; Toft G; Brauner EV. OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present Human Reproduction Update. 23(1):104-125, 2016 Dec. [Review. Journal Article] UI: 27655588

BACKGROUND: More than 20 years ago, it was hypothesized that exposure to prenatal and early postnatal environmental xenobiotics with the potential to disrupt endogenous hormone signaling might be on the causal path to cryptorchidism, hypospadias, low sperm count and testicular cancer. Several consensus statements and narrative reviews in recent years have divided the scientific community and have elicited a call for systematic transparent reviews. We aimed to fill this gap in knowledge in the field of male reproductive disorders.

OBJECTIVE AND RATIONALE: The aim of this study was to systematically synthesize published data on the risk of cryptorchidism, hypospadias, low sperm counts and testicular cancer following in utero or infant exposure to chemicals that have been included on the European Commission's list of Category 1 endocrine disrupting chemicals defined as having documented adverse effects due to endocrine disruption in at least one intact organism.

SEARCH METHODS: A systematic literature search for original peer reviewed papers was performed in the databases PubMed and Embase to identify epidemiological studies reporting associations between the outcomes of interest and exposures documented by biochemical analyses of biospecimens including maternal blood or urine, placenta or fat tissue as well as amnion fluid, cord blood or breast milk; this was followed by meta-analysis of quantitative data.

OUTCOMES: The literature search resulted in 1314 references among which we identified 33 papers(28 study populations) fulfilling the eligibility criteria. These provided 85 risk estimates of links between persistent organic pollutants and rapidly metabolized compounds (phthalates and Bisphenol A) and male reproductive disorders. The overall odds ratio (OR) across all exposures and outcomes was 1.11 (95% CI 0.91-1.35). When assessing four specific chemical subgroups with sufficient data for meta-analysis for all outcomes, we found that exposure to one of the four compounds, p,p’-DDE, was related to an elevated risk: OR 1.35 (95% CI 1.04-1.74). The data did not indicate that this increased risk was driven by any specific disorder.

WIDER IMPLICATIONS: The current epidemiological evidence is compatible with a small increased risk of male reproductive disorders following prenatal and postnatal exposure to some
persistent environmental chemicals classified as endocrine disruptors but the evidence is limited. Future epidemiological studies may change the weight of the evidence in either direction. No evidence of distortion due to publication bias was found, but exposure-response relationships are not evident. There are insufficient data on rapidly metabolized endocrine disruptors and on specific exposure-outcome relations. A particular data gap is evident with respect to delayed effects on semen quality and testicular cancer. Although high quality epidemiological studies are still sparse, future systematic and transparent reviews may provide pieces of evidence contributing to the narrative and weight of the evidence assessments in the field.

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Status
In-Data-Review

Authors Full Name
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Inflammatory bowel diseases and reproductive health. [Review]
Kokoszko-Bilska A; Sobkiewicz S; Fichna J.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article. Review]
UI: 27117378

Inflammatory bowel diseases (IBD) constitute a group of chronic intestinal diseases, including Crohn's disease and ulcerative colitis, which typically involve patients of reproductive age and may influence several features of human reproduction. There are many concerns regarding the interactions between the course of IBD, applied treatment (pharmacological or surgical), and
fertility, reproductive outcomes, and also neonatal outcomes. To review the literature describing fertility in IBD patients (separately for female and male), and possible infertility treatment in this group of patients, a PubMed search for English only publications (articles and/or abstracts) was conducted. Initially, the titles of publications and their abstracts were screened, and the most appropriate articles were selected and reviewed. Overall, in patients with quiescent IBD, fertility is almost identical to the general population, but particular subgroups of patients (with active disease, on pharmacological treatment, and after pelvic or abdominal surgery) may be affected by reduced fertility. Additionally, patients with IBD have fewer children than the general population, mainly as a result of voluntary childlessness. The main objectives for successful reproductive outcomes in IBD patients are proper guidance and also optimal treatment for achieving and maintaining disease remission. Recently, the European Evidence-Based Consensus on Reproduction and Pregnancy in IBD (the European Crohn's and Colitis Organization Guidelines) has been established to optimize preconceptional counseling and to promote an appropriate clinical management for patients planning to conceive. However, further studies are needed regarding the preservation of fertility in IBD patients and introduction of optimal infertility treatment in this group of patients.

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Status
In-Process

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Intracytoplasmic Sperm Injection Outcomes with Freshly Ejaculated Sperms and Testicular or Epididymal Sperm Extraction in Patients with Idiopathic Cryptozoospermia.
Ketabchi AA.
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[Journal Article]
UI: 27896242

BACKGROUND: Cryptozoospermia (CO) is a situation in which spermatozoa cannot be observed in a fresh semen sample unless an extended centrifugation and microscopic search are performed. CO patients are suggested to use only intracytoplasmic sperm injection (ICSI) as infertility treatment. But still there is debate about the choice of sperm source in cryptozoospermic men candidate for ICSI.

OBJECTIVES: This study was conducted to evaluate fertility outcomes in men with idiopathic cryptozoospermia who were treated using ICSI with freshly ejaculated sperm and testis sperm extraction (TESE) or percutaneous epididymal sperm aspiration (PESA).

METHODS: In this prospective cohort study carried out in an academic institution, 83 out of 92 couples with cryptozoospermia undergoing their first ICSI cycle were recruited. These patients were randomly allocated to two groups: group one (n = 42) who produced freshly ejaculated sperm and, group two (n = 41) who produced a sample by TESE or PESA. The groups were analyzed and compared in terms of fertilization rate, cleavage rate, embryo quality, implantation rate, and clinical pregnancy rate.

RESULTS: There was a significant difference in fertilization rate, embryo quality, implantation rate, and pregnancy rates between the group of surgically extracted sperm and those of naturally ejaculated sperm using conventional ICSI (P < 0.05).

CONCLUSIONS: Sperm quality extracted by percutaneous PESA and TESE procedures increases fertility outcomes compared to naturally ejaculated sperm in men with idiopathic CO. More specifically, embryo quality, which is most relevant to fertility outcome, improved when surgically extracted sperm was used for ICSI.
310.
Gentamicin versus ceftriaxone for the treatment of gonorrhoea (G-TOG trial): study protocol for a randomised trial.
Brittain C; Childs M; Duley L; Harding J; Hepburn T; Meakin G; Montgomery AA; Tan W; Ross JD.
[Journal Article]
UI: 27881151
BACKGROUND: Gonorrhoea is a common sexually transmitted infection which causes genital pain and discomfort; in women it can also lead to pelvic inflammatory disease and infertility, and in men to epididymo-orchitis. Current treatment is with ceftriaxone, but there is increasing evidence of antimicrobial resistance which is reducing its effectiveness against gonorrhoea. A small, but increasing, number of patients have already been found to have highly resistant strains of gonorrhoea which has been associated with clinical failure. This trial aims to determine whether gentamicin is not clinically worse than ceftriaxone in the treatment of gonorrhoea.
METHODS/DESIGN: This is a blinded, two-arm, multicentre, noninferiority randomised trial. Patients are eligible if they are aged 16-70 years with a diagnosis of genital, pharyngeal and/or rectal gonorrhoea. Exclusion criteria are: known concurrent sexually transmitted infection(s) (excluding chlamydia); bacterial vaginosis and/or Trichomonas vaginalis infection; contraindications or an allergy to gentamicin, ceftriaxone, azithromycin or lidocaine; pregnancy or breastfeeding; complicated gonorrhoeal infection; weight under 40 kg; use of ceftriaxone, gentamicin or azithromycin within the preceding 28 days. Randomisation is to receive a single intramuscular injection of either gentamicin or ceftriaxone, all participants receive 1 g oral azithromycin as standard treatment. The estimated sample size is 720 participants (noninferiority
The primary outcome is clearance of Neisseria gonorrhoeae at all infected sites by a negative Nucleic Acid Amplification Test, 2 weeks post treatment. Secondary outcomes include clinical resolution of symptoms, frequency of adverse events, tolerability of therapy, relationship between clinical effectiveness and antibiotic minimum inhibitory concentration for N. gonorrhoeae, and cost-effectiveness.

DISCUSSION: The options for future treatment of gonorrhoea are limited. Results from this randomised trial will demonstrate whether gentamicin is not clinically worse than ceftriaxone for the treatment of gonorrhoea. This will inform clinical practice and policy for the treatment of gonorrhoea when current therapy with cephalosporins is no longer effective, or is contraindicated.


Status
In-Data-Review
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Date Created
Low Testosterone in Men with Cardiovascular Disease or Risk Factors: To Treat or Not To Treat?. [Review]
Cassimatis DC; Crim MT; Wenger NK.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid
Current Treatment Options in Cardiovascular Medicine. 18(12):75, 2016 Dec.
[Review. Journal Article]
UI: 27807794
OPINION STATEMENT: Current evidence supports the use of testosterone replacement in men with the clinical-biochemical syndrome of hypogonadism, defined as low testosterone serum levels and symptoms such as fatigue, exercise intolerance, erectile dysfunction, low libido, or depression. Although the evidence consistently shows that hypogonadism is associated with elevated cardiovascular risk, evidence is mixed regarding whether testosterone (T) replacement provides cardiovascular (CV) benefit or harm. For a man with symptomatic hypogonadism in the setting of CV disease, clinical heart failure, and/or traditional CV risk factors (hypertension, diabetes, and hyperlipidemia), a balanced approach would be to counsel him that overall, the evidence should not dissuade him from utilizing T replacement for non-cardiac symptom relief but that more data are needed before a definitive recommendation can be made about T replacement for CV benefit. The preponderance of available evidence, reviewed in this article, suggests that T replacement, at appropriate doses and with monitored response, is likely to be safe for men with CV disease or CV risk factors and may even reduce major adverse cardiovascular events (MACE). The 2015 American Association of Clinical Endocrinologists and American College of Endocrinology position statement supports this stance and calls for improved prospective data. There is a clear need for a large, prospective randomized trial evaluating the impact of T replacement on MACE, for men both with and without CV disease or CV risk factors. Clinicians should be aware that all men who elect to take T replacement therapy require regular follow-up with the prescribing physician to include both clinical assessment and surveillance laboratory assessment of total T level, complete blood count, and prostate specific antigen.
Semen quality impairment is associated with sexual dysfunction according to its severity.
Lotti F; Corona G; Castellini G; Maseroli E; Fino MG; Cozzolino M; Maggi M.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article]
UI: 27733531
STUDY QUESTION: Is sexual dysfunction associated with severity of semen quality impairment in men with couple infertility?
SUMMARY ANSWER: In males of infertile couples the prevalence of erectile dysfunction (ED) increases as a function of semen quality impairment severity.
WHAT IS KNOWN ALREADY: Infertile men are at a higher risk for sexual dysfunction, psychopathological and general health disorders. However, it has never been systematically investigated if these problems are associated with severity of semen quality impairment.
STUDY DESIGN, SIZE, DURATION: Cross-sectional analysis of a first-time evaluation of 448 males of infertile couples attending an outpatient clinic from September 2010 to November 2015. In addition, 74 age-matched healthy, fertile men from an ultrasound study on male fertility were studied for comparison.
PARTICIPANTS/MATERIALS, SETTING, METHODS: All subjects underwent a complete physical, biochemical, scrotal and flaccid penile colour-Doppler ultrasound evaluation and semen analysis. Patients had already undergone at least one semen analysis; therefore, the majority were aware of their sperm quality before taking part in the study. Validated tools, such as the International Index of Sexual Function-15 (IIEF-15), Premature Ejaculation Diagnostic Tool (PEDT), Middlesex Hospital Questionnaire (MHQ), National Institutes of Health-Chronic Prostatitis Symptom Index (NIH-CPSI), International Prostate Symptom Score and Chronic Disease Score (CDS), were used to evaluate, respectively, sexual dysfunction, premature ejaculation (PE), psychopathological traits, prostatitis-like symptoms, lower urinary tract symptoms and general health status.

MAIN RESULTS AND THE ROLE OF CHANCE: Among men with couple infertility, 96 showed azoospermia (Group #1), 245 at least one sperm abnormality (Group #2) and 107 normozoospermia (Group #3). Fertile men were considered as a control group (Group #4). After adjusting for age, we observed a higher prevalence of ED (IIEF-15-erectile function domain score <26) (18.3% versus 0%; P = 0.006) and PE (PEDT score >8) (12.9% versus 4.1%; P = 0.036) in males of infertile couples compared with fertile men. The ED prevalence increases as a function of semen quality impairment severity (P < 0.0001), even after adjusting for confounders (age, CDS, MHQ and NIH-CPSI total score), despite similar hormonal, glyco-metabolic and penile vascular status. Compared to fertile men, all three groups of males with couple infertility showed a poorer erectile function, associated with an overall psychopathological burden (MHQ total score), particularly with somatized anxiety (MHQ-S). Azoospermic men showed the worst erectile function and general health: in this group, erectile function was negatively associated not only with psychopathological disturbances (MHQ total and MHQ-S scores; P < 0.0001) but also with a less healthy phenotype (higher CDS; P = 0.015). In addition, azoospermic men reported higher PE prevalence and lower sexual desire and orgasmic function when compared to fertile men (all P < 0.05), all of which were related to psychopathological symptoms.

LIMITATIONS, REASONS FOR CAUTION: The cross-sectional nature of the study represents its main limitation. A possible selection bias concerning the control group of healthy, fertile men recruited into an ultrasound study might have occurred. Finally, causality cannot be inferred in this type of study design and hence there should be some caution in interpreting the results.

WIDER IMPLICATIONS OF THE FINDINGS: Investigation of male sexual function, general health and psychological status in infertile couples, especially if azoospermic, is advisable, in order to improve not only reproductive but also general and sexual health.

STUDY FUNDING/COMPETING INTERESTS: Grants were received from the Ministry of University and Scientific Research (SIR project to F.L., protocol number: RBSI14LFMQ). There are no conflicts of interest.

TRIAL REGISTRATION NUMBER: None.
Metabolic Syndrome in Childhood: Rare Case of Alstrom Syndrome with Blindness.

Ahmad A; D'Souza B; Yadav C; Agarwal A; Kumar A; Nandini M; D'Souza V; Poornima AM; Kamath N.
Alstrom's syndrome (AS) is a rare autosomal recessive ciliopathic condition affecting 1:10,00,000 children. It's a single gene disorder of ALMS1 on chromosome 2 with multisystem involvement with cone-rod retinal dystrophy causing juvenile blindness, obesity, insulin resistance, type 2 Diabetes mellitus, hypogonadism and sensorineural hearing loss. Till now only 800 patients with this disorder has been identified so far. In this report, we describe the case of a 9-year old male boy from south India. He had been initially referred for polyphagia, polyuria, polydipsia, generalized weakness from 1 weeks. On examination he was demonstrated features suggestive of AS, including blindness, obesity, type 2 diabetes, altered lipid profile, hypogonadism, acanthosis nigricans, seborrhoeic dermatitis, right ear discharge and episodes of respiratory tract infections. So, diagnosis of AS is critical as it can easily be overlooked because of the many features associated with metabolic syndrome starting at age 7, a relatively early age.

Status
PubMed-not-MEDLINE

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Infertility in men with inflammatory bowel disease. [Review]

Shin T; Okada H.

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present


[Journal Article. Review]

UI: 27602237

Inflammatory bowel disease (IBD) predominantly affects young adults. Fertility-related issues are therefore important in the management of patients with IBD. However, relatively modest attention has been paid to reproductive issues faced by men with IBD. To investigate the effects of IBD and its treatment on male fertility, we reviewed the current literature using a systematic search for published studies. A PubMed search were performed using the main search terms "IBD AND male infertility", "Crohn's disease AND male infertility", "ulcerative colitis AND male infertility". References in review articles were used if relevant. We noted that active inflammation, poor nutrition, alcohol use, smoking, medications, and surgery may cause infertility in men with IBD. In surgery such as proctocolectomy with ileal pouch-anal anastomosis, rectal incision seems to be associated with sexual dysfunction. Of the medications used for IBD, sulfasalazine reversibly reduces male fertility. No other medications appear to affect male fertility significantly, although small studies suggested some adverse effects. There are limited data on the effects of drugs for IBD on male fertility and pregnancy outcomes; however, patients should be informed of the possible effects of paternal drug exposure. This review provides information on fertility-related issues in men with IBD and discusses treatment options.

Status
X-ray radiation and developmental inhibition of Drosophila suzukii (Matsumura) (Diptera: Drosophilidae).

Kim J; Kim J; Park CG.

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[Journal Article]

UI: 27585819

PURPOSE: Different doses of X-ray radiation were tested to assess the developmental inhibition effects on different stages of Drosophila suzukii, spotted wing drosophila (SWD). Efficacy of a potential quarantine treatment dose was evaluated for its practicality by a small scale-up validation test at a commercial facility.

MATERIALS AND METHODS: X-ray treatments at different doses of 50, 100, 200, and 300Gy were carried out with eggs, larvae, pupae and adults of SWD. The trial at the commercial facility was performed with pupae at 150Gy.

RESULTS: X-ray radiation inhibited development of all stages of SWD, and the estimated dose to cause 99% mortality or to prevent emergence (ED99) are reported here. Irradiation to eggs...
inhibited hatching, pupariation and adult emergence at 1962, 649 and 31Gy, respectively. The inhibition of irradiated larvae to adult emergence was 66Gy. Irradiation to pupae could not inhibit adult emergence completely even at 300Gy. However, irradiation at 100Gy and above induced complete adult sterility. Irradiation to pupae inhibited hatching of F1 eggs at 73Gy, while for adults, total inhibition of F1 egg hatching was observed at 822Gy. In the trial at the commercial facility, radiation at 150Gy to pupae induced complete adult sterility in all combinations of cross-mating between treated or untreated males and females.

CONCLUSION: This study suggests that X-ray radiation can be recommended as an alternative to methyl bromide as phytosanitary treatment for quarantine purpose.

Status
In-Data-Review

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2016

Vitamin D deficiency and low ionized calcium are linked with semen quality and sex steroid levels in infertile men.
Blomberg Jensen M; Gerner Lawaetz J; Andersson AM; Petersen JH; Nordkap L; Bang AK; Ekbom P; Joensen UN; Praetorius L; Lundstrom P; Boujida VH; Lanske B; Juul A; Jorgensen N. OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
STUDY QUESTION: Are low vitamin D levels linked with semen quality and sex steroids in infertile men?

SUMMARY ANSWER: Infertile men with vitamin D deficiency had lower sperm motility, total numbers of motile sperm, Inhibin B, sex-hormone-binding-globulin (SHBG) and testosterone/estradiol ratio, but higher levels of free sex steroids, than infertile men with normal vitamin D levels.

WHAT IS KNOWN ALREADY: Low vitamin D levels have been associated with decreased sperm motility in healthy men, but a relationship between vitamin D and calcium with semen quality and especially sex steroids has not been sufficiently described in infertile men.

STUDY DESIGN, SIZE, DURATION: This study comprises baseline characteristics of 1427 infertile men screened from 2011 to 2014 for inclusion in a randomized clinical trial, the Copenhagen-Bone-Gonadal Study.

PARTICIPANTS/MATERIALS, SETTING, METHODS: In total 1427 infertile men, consecutively referred to our tertiary andrological centre for fertility workup, underwent a physical examination and had semen quality assessed based on two samples and blood analysed for serum testosterone, SHBG, estradiol, inhibin B, luteinizing hormone, follicle-stimulating hormone (FSH), 25-hydroxyvitamin D (25-OHD), ionized calcium (Ca(2+)) and karyotype. There were 179 men excluded due to serious comorbidities or anabolic steroid usage, leaving 1248 patients for analyses.

MAIN RESULTS AND THE ROLE OF CHANCE: Men with 25-OHD >75 nmol/l had higher sperm motility and 66 and 111% higher total numbers of motile spermatozoa after 45 and 262 min, respectively, than men with 25-OHD <25 nmol/l (all P < 0.05). SHBG levels and testosterone/estradiol ratios were 15 and 14% lower, respectively, while free testosterone and estradiol ratios were 6 and 13% higher, respectively, in men with 25-OHD <25 nmol/l (all P < 0.05). Men with lower Ca(2+) levels had higher progressive sperm motility and inhibin B/FSH ratio but lower testosterone/estradiol ratio (all P < 0.05).

LIMITATIONS, REASONS FOR CAUTION: All outcomes presented are predefined end-points but inferral of causality is compromised by the descriptive study design. It remains to be shown whether the links between vitamin D, calcium, semen quality and sex steroids in infertile men are causal.

WIDER IMPLICATIONS OF THE FINDINGS: The associations between vitamin D deficiency and low calcium with semen quality and sex steroids support the existence of a cross-link between regulators of calcium homeostasis and gonadal function in infertile men.
STUDY FUNDING/COMPETING INTERESTS: This study was supported by the Danish Agency for Science, Technology and Innovation, Horslev Fonden, Danish Cancer Society and Novo Nordisk Foundation. There are no conflicts of interest.

TRIAL REGISTRATION NUMBER: NCT01304927.


DATE OF ENROLMENT OF FIRST PATIENT: 8 March 2011.

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Status
In-Data-Review

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20160806

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2016
Protective effect of pentoxifylline on male Wistar rat testicular germ cell apoptosis induced by 3,4-methylenedioxymethamphetamine.

Nouri M; Movassaghi S; Foroumadi A; Soleimani M; Sharifi ZN.

OBJECTIVES: 3, 4-methylenedioxymethamphetamine (MDMA) one of the methamphetamine derivatives that affect the reproductive system, has not been well understood. Many young people are consumers of drugs such as MDMA that can affect their reproductive capability. Apoptosis is the main mechanism for male infertility. Pentoxifylline (PTX) increases cAMP intracellularly and reduces tumor necrosis factor-alpha. This study aimed to investigate the protective effect of PTX administration in MDMA-induced apoptosis in testes of male Wistar rats.

MATERIALS AND METHODS: Thirty male Wistar rats weighing 250-300 g were randomly divided into five groups: control group (without any intervention), group receiving 7.5 mg/kg MDMA three times every two hours for one day, first experimental group receiving 100 mg/kg PTX just at the time of third injection of MDMA, second experimental group receiving 100 mg/kg PTX a week before MDMA administration, and the vehicle group, which received MDMA+saline. Two weeks later, testes were removed and prepared for H&E staining, TUNEL and Western blot techniques.

RESULTS: There was a significant decrease of the score in the MDMA group compared with the control group. In first and second experimental groups, the quality of seminiferous epithelium was improved compared with the MDMA group. The number of TUNEL-positive cells/tubule increased in MDMA and vehicle groups, which is decreased by administration of PTX before MDMA. Expression of active caspase-3 significantly increased in MDMA group, which is significantly decreased by administration of PTX before MDMA.

CONCLUSION: PTX can significantly reduce the severity of lesions in the testes following administration of MDMA.
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PMID
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4951604

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20160802
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2016

318.
Re: Six Months of Daily Treatment with Vardenafil Improves Parameters of Endothelial Inflammation and of Hypogonadism in Male Patients with Type 2 Diabetes and Erectile Dysfunction: A Randomized, Double-Blind, Prospective Trial.
Seftel AD.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article]
UI: 27479419
Status
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Authors Full Name
Seftel, Allen D.
Date Created
20160802
Zeta Sperm Selection Improves Pregnancy Rate and Alters Sex Ratio in Male Factor Infertility Patients: A Double-Blind, Randomized Clinical Trial.

Nasr Esfahani MH; Deemeh MR; Tavalaee M; Sekhavati MH; Gourabi H.

BACKGROUND: Selection of sperm for intra-cytoplasmic sperm injection (ICSI) is usually considered as the ultimate technique to alleviate male-factor infertility. In routine ICSI, selection is based on morphology and viability which does not necessarily preclude the chance injection of DNA-damaged or apoptotic sperm into the oocyte. Sperm with high negative surface electrical charge, named "Zeta potential", are mature and more likely to have intact chromatin. In addition, X-bearing spermatozoa carry more negative charge. Therefore, we aimed to compare the clinical outcomes of Zeta procedure with routine sperm selection in infertile men candidate for ICSI.

MATERIALS AND METHODS: From a total of 203 ICSI cycles studied, 101 cycles were allocated to density gradient centrifugation (DGC)/Zeta group and the remaining 102 were included in the DGC group in this prospective study. Clinical outcomes were compared between the two groups. The ratios of X and Y bearing sperm were assessed by fluorescence in situ hybridization (FISH) and quantitative polymerase chain reaction (qPCR) methods in 17 independent semen samples.

RESULTS: In the present double-blind randomized clinical trial, a significant increase in the percentage of top quality embryos and pregnancy rate were observed in DGC/Zeta group compared to DGC group. Moreover, sex ratio (XY/XX) at birth significantly was lower in the DGC/Zeta group compared to DGC group despite similar ratio of X/Y bearing spermatozoa following Zeta selection.

CONCLUSION: Zeta method not only improves the percentage of top embryo quality and pregnancy outcome but also alters the sex ratio compared to the conventional DGC method, despite no significant change in the ratio of X and Y bearing sperm population (Registration number: IRCT201108047223N1).
320.
Demographic and Clinical Correlates of Patient-Reported Improvement in Sex Drive, Erectile Function, and Energy With Testosterone Solution 2.
Wu F; Zitzmann M; Heiselman D; Donatucci C; Knorr J; Patel AB; Kinchen K.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article]
UI: 27329542
INTRODUCTION: Evidence from well-designed studies documenting the benefit of testosterone replacement therapy as a function of patient demographic and clinical characteristics is lacking.

AIM: To determine demographic and clinical predictors of treatment outcomes in hypogonadal men with low sex drive, low energy, and/or erectile dysfunction.

METHODS: Post hoc analysis of a randomized, multicenter, double-blinded, placebo-controlled, 16-week study of 715 hypogonadal men (mean age = 55.3 years, age range = 19-92 years) presenting with low sex drive and/or low energy who received placebo or testosterone solution 2% for 12 weeks.

MAIN OUTCOMES AND MEASURES: Two levels defined patient-reported improvement (PRI) in sex drive or energy: level 1 was at least "a little better" and level 2 was at least "much better" in energy or sex drive on the Patient Global Impression of Improvement at study end point. PRI in erectile function was stratified by erectile dysfunction severity at baseline as measured by the erectile function domain of the International Index for Erectile Function: mild at baseline (change of 2), moderate at baseline (change of 5), and severe at baseline (change of 7). Associations of demographic and clinical characteristics with PRI were calculated with stepwise forward multiple logistic regression analysis. Odds ratios represented the likelihood of PRI in symptoms among variable categories.

RESULTS: Higher levels of end-point testosterone were associated with higher rates of PRI (at levels 1 and 2) in sex drive and energy (P < .001 for the two comparisons). Lower baseline testosterone levels were associated with higher rates of level 1 PRI in sex drive (P = .028); and classic hypogonadism (vs non-classic hypogonadism) was associated with higher rates of level 2 PRI in sex drive (P = .005) and energy (P = .006).

CONCLUSION: When assessing the potential for improvements in men with testosterone deficiency using patient-reported outcome questionnaires, possible predictors of treatment outcomes to consider include the etiology of hypogonadism and testosterone levels (baseline and end point).

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Status
In-Data-Review

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New discovery of cryptorchidism: Decreased retinoic acid in testicle.

Peng J; Shen L; Chen J; Cao X; Zhou Y; Weng H; Long C; Zhang D; Tu S; Zhang Y; He D; Lin T; Wei G.

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[Journal Article]

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This study focuses on investigation of cryptorchidism induced by flutamide (Flu) and its histopathological damage, and detects retinoic acid concentration in testicle tissue, in order to find a new method for clinical treatment to infertility caused by cryptorchidism. Twenty SD (Sprague Dawley) pregnant rats were randomly divided into Flu cryptorchidism group (n = 10) and normal control group (n = 10). HE stained for observing morphological difference.

Transmission electron microscope (TEM) was used for observing the tight junction structure between Sertoli cells. Epididymal caudal sperms were counted and observed in morphology. The expression of stimulated by retinoic acid gene 8 (Stra8) was detected using immunohistochemistry, western blot, and Q-PCR. High performance liquid chromatography (HPLC) analysis was made on retinoic acid content. Sperm count and morphology observation confirmed cryptorchidism group was lower than normal group in sperm quantity and quality. The observation by TEM showed a loose structure of tight junctions between Sertoli cells.

Immunohistochemistry, western blot, and Q-PCR showed that cryptorchidism group was significantly lower than normal group in the expression of Stra8. HPLC showed that retinoic acid content was significantly lower in cryptorchid testis than in normal testis. In the cryptorchidism
model, retinoic acid content in testicular tissue has a significant reduction; testicles have significant pathological changes; damage exists in the structure of tight junctions between Sertoli cells; Stra8 expression has a significant reduction, perhaps mainly contributing to spermatogenesis disorder.

Status
PubMed-not-MEDLINE

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20160609
Prevalence of Urogenital Mycoplasmas in Iran and Their Effects on Fertility Potential: A Systematic Review and Meta-Analysis. [Review]
Ahmadi MH; Mirsalehian A; Bahador A.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article. Review]
UI: 27252910

BACKGROUND: Urogenital mycoplasmas are potentially pathogenic species causing genitourinary tract infections that may be initially asymptomatic but can progress and lead to severe complications and threaten reproductive health. However, the overall prevalence rate of this bacterium and its probable impacts on fertility potential have yet to be determined.

METHODS: We searched both English and Persian electronic databases using key words such as "Mycoplasma," "Ureaplasma," "M. hominis," "M. genitalium," "U. urealyticum," "U. parvum," "prevalence," and "Iran". Finally, after some exclusion, 29 studies from different regions of Iran were included in our study, and a meta-analysis was performed on collected data.

RESULTS: Urogenital mycoplasmas prevalence for women and men was high and ranged from 2%-40.5% and 2%-44.3%, respectively. The pooled prevalence in the male population was 11.1% (95% CI, 7.4%-16.4%) and in female was 12.8% (95% CI, 9.8%-16.5%). The prevalence of these bacteria was significantly higher in infertile men compared with that in fertile men. A high level of heterogeneity was observed for both men (I(2) = 92.4%; P<0.001) and women (I(2) = 93.3%; P<0.001). Some evidence for publication bias was observed in both men [Egger's test (two-tailed P=0.0007), and Begg's test (two-tailed P=0.0151)] and women [Egger's test (two-tailed P=0.0006), and Begg's test (two-tailed P=0.0086)] analysis.

CONCLUSION: Since urogenital mycoplasmas may play a role in male infertility, screening strategies, particularly for asymptomatic individuals, and treatment of infected ones, which can reduce consequent complications, looks to be necessary.

Status
PubMed-not-MEDLINE
Combined Effect of Trolox and EDTA on Frozen-Thawed Sperm Quality.
Keshtgar S; Iravanpour F; Gharesi-Fard B; Kazerooni M.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article]
UI: 27217608
The freezing and thawing process not only is associated with serious damage to sperm such as damage to the plasma membrane and the acrosomal membrane but also changes the membrane permeability to some ions including calcium. Also, the generation of oxygen free radicals is increased during the freezing-thawing process. The purpose of this study was to evaluate the effects of Trolox as an antioxidant and edetic acid (EDTA) as a calcium chelator on frozen-thawed (FT) sperm and compare these effects with those on fresh sperm. This study was done on these men of 25 healthy men, who referred to Shiraz Infertility Center between 2012 and 2013. Normal samples were transferred to the Reproductive Physiology Laboratory, Department of Physiology, Shiraz University of Medical Sciences, Shiraz. The samples were divided into two groups randomly: fresh and FT sperm groups. Each group was divided into five subgroups:
control group, the solvent group (0.1% dimethyl sulfoxide [DMSO]), Trolox group (200 µM), EDTA group (1.1 mM), and Trolox+EDTA group. The percentages of motility, viability, and acrosome-reacted sperm were tested. The percentages of motility and viability in the FT sperm were lower than those in the fresh sperm. The progressive motility of the FT sperm was improved nonsignificantly with Trolox+EDTA. However, the effect of Trolox+EDTA on the progressive motility of the FT sperm was much more than that on the fresh sperm. The fewest acrosome-reacted sperm were observed in the EDTA-containing FT sperm. Antioxidant supplementation or omission of extracellular calcium may partly improve motility and also reduce acrosomal damage in FT sperm.

Status
PubMed-not-MEDLINE

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324.
Comparison of the Effects of Varicocelectomy and Oral L-carnitine on Sperm Parameters in Infertile Men with Varicocele.
Sofimajidpour H; Ghaderi E; Ganji O.
BACKGROUND: Varicocele is defined as dilated and twisted veins of the pampiniform plexus in the spermatic cord. It is the most common cause of male infertility. There are various medical and surgical procedures for the treatment of this disease.

AIM: This study was aimed to compare the effects of oral administration of L-Carnitine and varicocelectomy on spermogram parameters.

MATERIALS AND METHODS: This study was conducted as a double blind clinical trial without randomization. Inclusion criteria were, all married infertile men with varicocele. Patients chose their treatment personally and spermogram was carried out for all patients before and after the third and sixth months of treatment. Then, the sperm parameters of the two groups were compared using repeated measures ANOVA.

RESULTS: In our study, trend of sperm count in the surgery group changed from 22 to 28.61 million (vs 34.6 to 45.37 in L-Carnitine group), motility changed from 21.74 to 35.38 percent (vs 33.9 to 47.48 in L-Carnitine group), normal sperm morphology changed from 46.25 to 60 percent (vs 56.61 to 69.7 in L-Carnitine group) and volume of semen changed from 3.5 to 4.17 cc (vs 2.95 to 4.33 in L-Carnitine group). These values were not statistically different between the two groups.

CONCLUSION: Based on the results of this study, we can say that medicinal treatment by administration of oral L-Carnitine is as effective as varicocelectomy in improving semen parameters and can be used as an alternative to surgery for varicocele grade II.

Status
PubMed-not-MEDLINE

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PMID
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4866177
Endometrial Injury May Increase the Pregnancy Rate in Patients Undergoing Intrauterine Insemination: An Interventional Randomized Clinical Trial.
Bahaa Eldin AM; Abdelmaabud KH; Laban M; Hassanin AS; Tharwat AA; Aly TR; Elbohoty AE; Elsayed HM; Ibrahim AM; Ibrahim ME; Sabaa HM; Abdelrazik AA; Abdelhady I.

OBJECTIVE: This study aimed to investigate the effect of endometrial injury using Pipelle catheter in the follicular phase (cycle day 5, 6, or 7) of the stimulation cycle on pregnancy rates in patients undergoing intrauterine insemination.

METHODS: This prospective randomized controlled study was carried out in the Assisted Reproductive Technology Unit of Ain Shams University Maternity Hospital, Cairo, Egypt, from July 1, 2013 to August 31, 2015. Three hundred sixty women, 20 to 35 years of age, with patent fallopian tubes, mild male factor infertility, or unexplained infertility were recruited. Participants were allocated randomly into 2 groups: experimental arm and control arm. Women in the experimental arm underwent endometrial biopsy using a Pipelle catheter on day 5, 6, or 7 of the stimulation cycle combined with intrauterine insemination. Women in the control group underwent intrauterine insemination with no endometrial biopsy done. The primary outcomes were the clinical and chemical pregnancy rates.

RESULTS: Data of 344 participants were statistically analyzed. The chemical pregnancy rate was 23.66% in the experimental arm and 10.85% in the control arm (P = .002). The clinical pregnancy rate was 18.93% in the experimental arm and 7.42% in the control arm (P = .003).

CONCLUSION: Endometrial injury using a Pipelle catheter in the stimulation cycle may improve pregnancy rates in women undergoing intrauterine insemination.
Status
In-Data-Review

Authors Full Name
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20160916

Year of Publication
Correlation of Adiponectin mRNA Abundance and Its Receptors with Quantitative Parameters of Sperm Motility in Rams.
Kadivar A; Heidari Khoei H; Hassanpour H; Golestanfar A; Ghanaei H.
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UI: 27123210

BACKGROUND: Adiponectin and its receptors (AdipoR1 and AdipoR2), known as adiponectin system, have some proven roles in the fat and glucose metabolisms. Several studies have shown that adiponectin can be considered as a candidate in linking metabolism to testicular function. In this regard, we evaluated the correlation between sperm mRNA abundance of adiponectin and its receptors, with sperm motility indices in the present study.

MATERIALS AND METHODS: In this completely randomized design study, semen samples from 6 adult rams were fractionated on a two layer discontinuous percoll gradient into high and low motile sperm cells, then quantitative parameters of sperm motility were determined by computer-assisted sperm analyzer (CASA). The mRNA abundance levels of Adiponectin, AdipoR1 and AdipoR2 were measured quantitatively using real-time reverse transcriptase polymerase chain reaction (qRT-PCR) in the high and low motile groups.

RESULTS: Firstly, we showed that adiponectin and its receptors (AdipoR1 and AdipoR2) were transcriptionally expressed in the ram sperm cells. Using Pfaff based method qRT-PCR, these levels of transcription were significantly higher in the high motile rather than low motile samples. This increase was 3.5, 3.6 and 2.5 fold change rate for Adiponectin, AdipoR1 and AdipoR2, respectively. Some of sperm motility indices [curvilinear velocity (VCL), straight-line velocity (VSL), average path velocity (VAP), linearity (LIN), wobble (WOB) and straightness (STR)] were also significantly correlated with Adiponectin and AdipoR1 relative expression. The correlation of AdipoR2 was also significant with the mentioned parameters, although this correlation was not comparable with adiponectin and AdipoR1.
CONCLUSION: This study revealed the novel association of adiponectin system with sperm motility. The results of our study suggested that adiponectin is one of the possible factors which can be evaluated and studied in male infertility disorders.

Status
PubMed-not-MEDLINE

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327.
A Preliminary Study: N-acetyl-L-cysteine Improves Semen Quality following Varicocelectomy.
Barekat F; Tavalaee M; Deemeh MR; Bahreinian M; Azadi L; Abbasi H; Rozbahani S; Nasr-Esfahani MH.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
BACKGROUND: Surgery is considered the primary treatment for male infertility from clinical varicocele. One of the main events associated with varicocele is excessive production of reactive oxygen species (ROS). N-acetyl-L-cysteine (NAC), an antioxidant that scavenges free radicals, is considered a supplement to alleviate glutathione (GSH) depletion during oxidative stress. Despite beneficial effects of NAC in other pathological events, there is no report on the effect of NAC in individuals with varicocele. Therefore, the aim of this study is to evaluate the outcome of NAC on semen quality, protamine content, DNA damage, oxidative stress and fertility following varicocelectomy.

MATERIALS AND METHODS: This prospective clinical trial included 35 infertile men with varicocele randomly divided into control (n=20) and NAC (n=15) groups. We assessed semen parameters, protamine content [chromomycin A3 (CMA3)], DNA integrity [terminal deoxynucleotidyltransferase-mediated dUTP nick-end labeling (TUNEL)] and oxidative stress [2', 7'-dichlorodihydrofluorescein-diacetate (DCFH-DA)] before and three months after varicocelectomy.

RESULTS: Percentage of abnormal semen parameters, protamine deficiency, DNA fragmentation and oxidative stress were significantly decreased in both groups compared to before surgery. We calculated the percentage of improvement in these parameters compared to before surgery for each group, then compared the results between the groups. Only percentage of protamine deficiency and DNA fragmentation significantly differed between the NAC and control groups.

CONCLUSION: The results of this study, for the first time, revealed that NAC improved chromatin integrity and pregnancy rate when administered as adjunct therapy post-varicocoelectomy (Registration Number: IRCT201508177223N5).

Status
PubMed-not-MEDLINE
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328.
Efficacy of Compound Therapy by Ginseng and Ciprofloxacin on Bacterial Prostatitis.
Miri M; Shokri S; Darabi S; Alipour Heidari M; Ghalyanchi A; Karimfar MH; Shirazi R.
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[Journal Article]
UI: 27054125

OBJECTIVE: Genitourinary tract infections play a significant role in male infertility. Infections of reproductive sex glands, such as the prostate, impair function and indirectly affect male fertility. The general aim of this study is to investigate the protective effect of Korean red ginseng (KRG) on prostatitis in male rats treated with ciprofloxacin (CIPX).
MATERIALS AND METHODS: In this experimental study, we randomly divided 72 two male Wistar rats into 9 groups. The groups were treated as follows for 10 days: i. Control (no
medication), ii. Sham [(normal saline injection into the vas deferens and oral administration of phosphate-buffered saline (PBS))], iii. Ginseng, iv. CPIX, v. CIPX+ginseng, vi. Uropathogenic Escherichia coli (E. coli) (UPEC), vii. UPEC+ginseng, viii. UPEC+CIPX, and ix. UPEC+ginseng+CIPX. The rats were killed 14 days after the last injection and the prostate glands were removed. After sample preparation, routine histology was performed using hematoxylin and eosin staining. The terminal deoxynucleotidyl transferase mediated dUTP-biotin nick end labeling (TUNEL) method was used to determine the presence of apoptotic cells.

RESULTS: The severity score for acinar changes and inflammatory cell infiltration in the UPEC+CIPX group did not significantly different from the UPEC group. However this score significantly decreased in the UPEC+CIPX+ginseng group compared to the UPEC group. Apoptotic index of all ginseng treated groups significantly decreased compared to the UPEC and CPIX groups.

CONCLUSION: These results suggested that ginseng might be an effective adjunct in CIPX treatment of prostatitis. The combined use ginseng and CIPX was more effective than ginseng or CIPX alone.

Status
PubMed-not-MEDLINE

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The Role of Date Palm (Phoenix dactylifera L) Pollen in Fertility: A Comprehensive Review of Current Evidence.
Tahvilzadeh M; Hajimahmoodi M; Rahimi R.
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UI: 26438718
Date palm pollen (DPP) is the male reproductive dust of palm flowers used as dietary supplement especially as aphrodisiac and fertility enhancer in both women and men from ancient times. Although there are few clinical trials evaluating the beneficial effects of DPP in humans, various experimental studies have been conducted on the reproductive effects of DPP. Among the compounds isolated from DPP are amino acids, fatty acids, flavonoids, saponins, and estroles. The present review summarizes comprehensive information concerning the phytochemistry and pharmacological activities of DPP and its application in fertility disorders.
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Status
In-Data-Review
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Date Created
Computational Analysis of Missense Variants of G Protein-Coupled Receptors Involved in the Neuroendocrine Regulation of Reproduction.

Min L; Nie M; Zhang A; Wen J; Noel SD; Lee V; Carroll RS; Kaiser UB.

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present


[Journal Article]
UI: 26088945

INTRODUCTION: Many missense variants in G protein-coupled receptors (GPCRs) involved in the neuroendocrine regulation of reproduction have been identified by phenotype-driven or large-scale exome sequencing. Computational functional prediction analysis is commonly performed to evaluate their impact on receptor function.

METHODS: To assess the performance and outcome of functional prediction analyses for these GPCRs, we performed a statistical analysis of the prediction performance of SIFT and PolyPhen-2 for variants with documented biological function as well as variants retrieved from Ensembl. We obtained missense variants with documented biological function testing from patients with reproductive disorders from a comprehensive literature search. Missense variants from individuals with known reproductive disorders were retrieved from the Human Gene Mutation Database. Missense variants from the general population were retrieved from the Ensembl genome database.

RESULTS: The accuracies of SIFT and PolyPhen-2 were 83 and 85%, respectively. The performance of both prediction tools was greater in predicting loss-of-function variants (SIFT: 92%; PolyPhen-2: 95%) than in predicting variants that did not affect function (SIFT: 54%; PolyPhen-2: 57%). Concordance between SIFT and PolyPhen-2 did not improve accuracy. Surprisingly, approximately half of the variants retrieved from Ensembl were predicted as loss-of-function variants by SIFT (47%) and PolyPhen-2 (54%).

CONCLUSION: Our findings provide new guidance for interpreting the results and limitations of computational functional prediction analyses for GPCRs and will help to determine which variants
require biological function testing. In addition, our findings raise important questions regarding the link between genotype and phenotype in the general population.

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331.
Comparison of the effect of a combination of eight micronutrients versus a standard mono preparation on sperm parameters.

Lipovac M; Bodner F; Imhof M; Chedraui P.

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[Clinical Trial. Journal Article]

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BACKGROUND: There are reports showing that l-carnitine alone or in combination with other micronutrients improve sperm parameters. However, comparative studies are still lacking. This study was carried out to compare the short term effects of a combination of eight micronutrients including l-carnitine vs. a mono-substance (l-carnitine alone) on sperm parameters.
METHODS: This was a prospective, open-labelled, nonrandomized study that included male subjects (20 to 60 years) with at least 1 year of subfertility and at least one pathological semen analysis who received 3 months treatment with a mono-substance (500 mg l-carnitine/twice a day, n=156) or a combined compound (440 mg l-carnitine+250 mg l-arginine+40 mg zinc+120 mg vitamin E+80 mg glutathione+60 mug selenium+15 mg coenzyme Q10+800 mug folic acid/once a day, n=143) for the same time period. Sperm parameters were analyzed before and after treatment and groups comparisons performed.

RESULTS: Baseline characteristics were similar among studied groups (age and body mass indices). Semen parameters (volume, density, overall progressive motility [including slow and fast motility]) and percentage of sperm with normal morphology improved after 3 months in both groups as compared to baseline. However, relative change (expressed as % increase of absolute values) for sperm density and overall progressive motility (including fast motility) was found to be higher for the combined micronutrient treatment group as compared to the mono-treatment using l-carnitine alone.

CONCLUSION: Both analyzed groups displayed a positive short term effect on all sperm parameters; however effect on density and motility was significantly better for the combined formulation. There is need for more research in this matter that includes long term outcome data.

TRIAL REGISTRATION: Retrospectively registered at ISRCTN (7th October 2016). Study ID: ISRCTN48594239.

Status

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Undescended testis (UDT) is the most common disorder of sexual development in boys and affects 3.5% of male newborns. Although approximately half of newborn UDTs descend spontaneously, some boys develop an ascending testis later in childhood. Recent guideline recommendations advocate orchiopexy by 18 months of age to maximize potential for fertility and perhaps reduce the risk for testicular carcinoma in the future. For palpable testes, a standard inguinal approach is appropriate. However, the prescrotal approach is often effective for low inguinal testes and reduces surgical time and patient discomfort with an equivalent success rate in boys with an ascending testis. Some advocate monitoring until adolescence to determine whether the testis will spontaneously descend into the scrotum, but data do not support this approach. Instead, prompt orchiopexy is recommended. In boys with a nonpalpable testis, approximately 50% are abdominal or high in the inguinal canal and 50% are atrophic, typically in the scrotum. Routine inguinal/scrotal ultrasound is not recommended, although in an older boy who is overweight, it is appropriate. If the patient has contralateral testicular hypertrophy, scrotal exploration is appropriate, and removal of the testicular remnant and contralateral scrotal orchiopexy to prevent future contralateral testicular torsion is recommended. In most cases, diagnostic laparoscopy is advised to determine whether the testis is abdominal. For the abdominal testis, there are numerous treatment options. If the testis is mobile or a peeping testis just distal to the internal inguinal ring, standard one-stage laparoscopic or open orchiopexy
should be attempted using the Prentiss maneuver. If the testicular vessels are short or the testis is not mobile, a two-stage Fowler-Stephens orchiopexy is appropriate. The second stage can be performed laparoscopically or open. Another option is microvascular testicular autotransplantation, which is a technically demanding procedure. Surgical results of abdominal orchiopexy are highly variable, short term, and highly subjective. Prospective clinical trials with follow-up into adolescence and adulthood are necessary to assess the success of various surgical approaches.

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333.
Artificial oocyte activation after intracytoplasmic morphologically selected sperm injection: A prospective randomized sibling oocyte study.
Aydinuraz B; Dirican EK; Olgan S; Aksunger O; Erturk OK.
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[Journal Article. Randomized Controlled Trial]
UI: 27734719
This study aimed to evaluate the effect of artificial oocyte activation (AOA) by calcium ionophore after intracytoplasmic morphologically selected sperm injection (IMSI) on fertilization, cleavage rate and embryo quality. A total of 194 oocytes from 21 cycles from women with a history of low fertilization rate accompanying teratozoospermia were enrolled over a 3-month period. Mature
oocytes from each patient were randomly allocated into two groups after IMSI. In the study group, half of the patients’ oocytes (n=97) were exposed to AOA, and in the control group (n=97), AOA was not applied. The mean number of mature oocytes, fertilization and cleavage rates were similar between the study and control groups (p>0.05 for each). However, fertilized oocytes of the AOA group were less likely to produce top quality embryos when calculated per fertilized oocyte (28/80; 35.0% versus 38/71; 53.5%, respectively; p=0.024) and also per cycle (13/21; 61.9% versus 20/21; 95.24%, respectively; p=0.006). Our study indicates that AOA may not improve fertilization rates after IMSI and may even reduce the ability of a successfully fertilized oocyte to develop into a top quality embryo. AOA should, therefore, be applied to cases with a defined oocyte activating deficiency.

Status
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334.

Due to its palindromic setup, AZFc (Azoospermia Factor c) region of chromosome Y is one of the most unstable regions of the human genome. It contains eight gene families expressed mainly in the testes. Several types of rearrangement resulting in changes in the cumulative copy number of the gene families were reported to be associated with diseases such as male infertility and testicular germ cell tumors. The best studied AZFc rearrangement is gr/gr deletion. Its carriers show widespread phenotypic variation from azoospermia to normospermia. This phenomenon was initially attributed to different gr/gr subtypes that would eliminate distinct members of the affected gene families. However, studies conducted to confirm this hypothesis have brought controversial results, perhaps, in part, due to the shortcomings of the utilized subtyping methodology. This proof-of-concept paper is meant to introduce here a novel method aimed at subtyping AZFc rearrangements. It is able to differentiate the partial deletion and partial duplication subtypes of the Deleted in Azoospermia (DAZ) gene family. The keystone of the method is the determination of the copy number of the gene family member-specific variant(s) in a series of sequence family variant (SFV) positions. Most importantly, we present a novel approach for the correct interpretation of the variant copy number data to determine the copy number of the individual DAZ family members in the context of frequent interloci gene conversion. Besides DAZ1/DAZ2 and DAZ3/DAZ4 deletions, not yet described rearrangements such as DAZ2/DAZ4 deletion and three duplication subtypes were also found by the utilization of the novel approach. A striking feature is the extremely high concordance among the individual data pointing to a certain type of rearrangement. In addition to being able to identify DAZ deletion subtypes more reliably than the methods used previously, this approach is the first that can discriminate DAZ duplication subtypes as well.
Can we identify subfertile couples that benefit from immediate in vitro fertilisation over intrauterine insemination?.

Tjon-Kon-Fat RI; Tajik P; Custers IM; Bossuyt PM; van der Veen F; van Wely M; Mol BW; Zafarmand MH.

OBJECTIVE: Available treatment options in couples with unexplained or mild male subfertility are intrauterine insemination with controlled ovarian hyperstimulation (IUI-COH) and in vitro fertilisation (IVF). IUI-COH is a less invasive treatment that is often used before proceeding with IVF. Yet as the IVF success rates might be higher and time to pregnancy shorter, expedited access to IVF might be the preferred option. To identify couples that could benefit from immediate IVF over IUI-COH, we assessed whether female age, duration of subfertility or prewash total motile count (TMC) can help to identify couples that would benefit from IVF over IUI-COH.

STUDY DESIGN: We performed a secondary data-analysis of a multicentre open-label randomised controlled trial in three university and six teaching hospitals in the Netherlands.
couples with unexplained or mild male subfertility were randomised to one cycle of IVF with elective single embryo transfer with subsequent frozen-thawed embryo transfers or 3 cycles of IUI-COH. The primary outcome was an ongoing pregnancy within 4 months after randomisation. Our aim was to explore a possible differential effect of specific markers on the effectiveness of treatment. We chose to therefore assess female age, duration of subfertility and TMC as these have previously been identified as predictors. For each prognostic factor we developed a logistic regression model to predict ongoing pregnancy with that prognostic factor, treatment and a factor-by-treatment interaction term.

RESULTS: Female age and duration of subfertility were not associated with better ongoing pregnancy chances after IVF compared to IUI-COH (p-value for interaction=0.65 and 0.26, respectively). Only when TMC was lower than 110 (x10(6)spermatozoa/mL), the probability of ongoing pregnancy was higher in women allocated to IVF (p-value for interaction=0.06).

CONCLUSION: In couples with unexplained or mild male subfertility, a low TMC might lead to higher pregnancy rates after IVF than after IUI-COH. This finding needs to be validated in a larger trial before it can be applied in clinical practice.

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336.
Dosage of Sex Chromosomal Genes in Blood Deposited on Filter Paper for Neonatal Screening of Sex Chromosome Aneuploidy.
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OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present Genetic Testing & Molecular Biomarkers. 20(12):786-790, 2016 Dec.
[Journal Article]

UI: 27997249

AIMS: In this study, we examined the doses of the stature homeobox (SHOX), vesicle-associated membrane protein 7 (VAMP7), and SRY genes to establish a protocol for using peripheral blood samples deposited on filter paper for the screening of sex chromosome aneuploidy in neonates. We also measured correlations with karyotypes to assess this method as a neonatal screening strategy.

MATERIALS AND METHODS: This was an observational, descriptive, comparative blind study. Thirty-two healthy young adults (17 women, 15 men; age, >18 years), four patients with known sex chromosome aneuploidy (positive control group), and 1000 healthy newborns were included. Gene dosages were determined using quantitative real-time polymerase chain reaction (RT-PCR). Values with standard deviations (SDs) of three or more were considered abnormal.
RESULTS: Men and women differed in the gene dosage of the SRY gene. Cases with Turner syndrome showed values below 3 SDs for SHOX and VAMP7 genes, and cases with Klinefelter syndrome showed values above 3 SDs for SHOX and VAMP7 genes. Two suspected cases of sex chromosome aneuploidy were diagnosed using our neonatal screening strategy; these cases were confirmed as Turner syndrome and 47,XYY syndrome by karyotyping.

CONCLUSIONS: Our data establish a basis for the determination of chromosomal sex and neonatal screening of sex chromosome aneuploidy using RT-PCR.

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In the literature, there is growing evidence that subfertile patients who conceived after infertility treatments have an increased risk of pregnancy and perinatal complications and this is particularly true for patients who conceived through use of high technology infertility treatments. Moreover, high technology infertility treatments include many concomitant clinical and biological risk factors. This review aims to summarize in a systematic fashion the current evidence regarding the relative effect of the different procedures for high technology infertility treatments on the risk of adverse pregnancy and perinatal outcome. A literature search up to August 2016 was performed in IBSS, SocINDEX, Institute for Scientific Information, PubMed, Web of Science and Google Scholar and an evidence-based hierarchy was used to determine which articles to include and analyze. Data on prepregnancy maternal factors, low technology interventions, specific procedures for male factor, ovarian tissue/ovary and uterus transplantation, and chromosomal abnormalities and malformations of the offspring were excluded. The available evidences were analyzed assessing the level and the quality of evidence according to the Oxford Centre for Evidence-Based Medicine guidelines and the Grading of Recommendations Assessment, Development, and Evaluation system, respectively. Current review highlights that every single procedure of high technology infertility treatments can play a crucial role in increasing the risk of
pregnancy and perinatal complications. Due to the suboptimal level and quality of the current
evidence, further well-designed studies are needed.

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338.
Testosterone undecanoate improves lipid profile in patients with type 1 diabetes and
hypogonadotrophic hypogonadism.
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Testosterone deficiency (Td) has been associated with the metabolic syndrome. Few studies have evaluated this condition in type 1 diabetes (T1D). The primary aim of this study was to evaluate the effectiveness of testosterone undecanoate (TU) on insulin sensitivity, glycemic control, anthropometric parameters, blood pressure and lipid profile in patients with Td and T1D.

We performed a randomized placebo-controlled multicenter study.

INCLUSION CRITERIA: a) age > 18 years; b) autoimmune diabetes; c) Td (total testosterone <10 nmol/L or calculated free testosterone <225 pmol/L and low/normal LH; d) ability to sign informed consent; e) comply with the study protocol.

EXCLUSION CRITERIA: a) pituitary tumor, empty sella, hyperprolactinemia, panhypopituitarism or secondary hypogonadism; b) contraindications for treatment with testosterone undecanoate (TU); c) patients who did not agree to sign their informed consent. Six patients were randomly assigned to testosterone undecanoate (TU) treatment and 7 to placebo with the following dosing schedule: baseline, 6 weeks and 16 weeks. Blood test, anthropometric parameters, blood pressure and insulin sensitivity were determined at baseline, 6, 16 and 22 weeks. No differences were observed regarding insulin sensitivity, HbA1c or basal glucose, anthropometric parameters or blood pressure. At 22 weeks, the decrease in total cholesterol was 37.4 +/- 27.5 mg/dL in the TU group compared with an increase of 13.2 +/- 17.8 mg/dL in the placebo group (P<0.005), and LDL cholesterol concentration decreased 30.2 +/- 22.1 mg/dL, compared with an increase of 10.5 +/- 13.4 mg/dL in the placebo group (P=0.004). We conclude that treatment with TU in patients with T1D and Td improves lipid profile, with no effects on metabolic control or anthropometric parameters.
BACKGROUND: Pregnancy failure and placenta mediated pregnancy complications affect >25% of pregnancies. Although there is biological plausibility for a procoagulant mechanism underlying some of these events, antithrombotic intervention trials demonstrate limited benefit, possibly through lack of stratification in heterogeneous patient groups. The ANXA5 M2 haplotype is a possible procoagulant biomarker and was tested pragmatically to determine whether this screening and LMWH treatment normalized the outcome for ANXA5 M2 positive couples. This was a pragmatic study that aimed to measure the effectiveness of a testing (for the M2 haplotype) and treatment (LMWH) pathway in routine clinical practice where there is variation between patients. Such a study in couples with fertility problems can inform choices between treatments; it is then the management protocol which is the subject of the investigation, not the individual treatments.

METHODS: Couples (N=77) with one or both partners ANXA5 M2 positive demonstrated association of this haplotype with adverse IVF outcome. A pragmatic, multicenter, prospective cohort study of ANXA5 M2 haplotype screening, and LWMH treatment following embryo transfer (ET) in 103 IVF couples positive for ANXA5 M2 was performed. They were compared with a group of 1000 contemporaneous randomly selected unscreened and untreated couples undergoing assisted conception, from which 103 matched control couples were derived. The primary outcome measure was live birth incidence. Secondary outcomes were results following embryo transfer (ET) and live birth outcome by gender and M2 carriage, and allelic dose influence.
FINDINGS: The tested and treated cohort of ANXA5 M2 carriers achieved a similar live birth rate (37.9%) per ET cycle compared to both the more fertile comparison group (38.5%), and to the 103 matched controls (33.0%). Significantly more treated male carrier only couples had a live birth versus female M2 only (47.7% vs. 25.0% p=0.045).

INTERPRETATION: Pragmatic ANXA5 M5 screening and treatment with LMWH in couples undergoing IVF is associated with similar outcome to couples with more favorable prognostic factors. The difference in live birth outcome for treated male only carrier couples may be consistent with an additional maternal thrombophilic factor that may adversely affect pregnancy, although other mechanisms are possible. This study suggests that LMWH treatment should be started prior to clinical pregnancy.

[Review]
Currow DC; Phillips J; Clark K.
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Chronic non-cancer pain (lasting more than 3 months) is highly prevalent in Australia (17% of males and 20% of females) and its optimal management is crucial to the health and wellbeing of the community. For 5% of the population, such pain interferes markedly with daily function. Part of the treatment for acute non-cancer pain for many people will include opioid analgesics at least for days to weeks. However, as pain becomes chronic, evidence to support ongoing prescription of opioids is lacking. There is increasing pressure to ensure that prescribing opioid analgesics is minimised to reduce not only the risk of dependence and illicit diversion but also the potential harms associated with tolerance, side effects and complications. Frameworks for considering opioid prescribing include assessing suitability of the patient for opioids; initiating a trial of therapy; and monitoring long term use. There is limited evidence of the long term efficacy of opioids for chronic non-cancer pain, and documented clinical consequences beyond addiction include acceleration of loss of bone mineral density, hypogonadism and an association with increased risk of acute myocardial infarction. Careful clinical selection of patients can help optimise the evidence-based use of opioids for chronic non-cancer pain: only treat pain that has been as well defined as possible when non-opioid therapies have not been effective; consider referral to specialist services for assessment if doses are above 100 mg oral morphine equivalent per 24 hours or the duration of therapy is longer than 4 weeks; limit prescribing to only one practitioner; seek an agreement with the patient for the initiation and potential withdrawal of opioids if the therapeutic trial is not effective.
AIMS AND OBJECTIVES: This critical review aims to identify, summarize and critically appraise the current literature evaluating the effectiveness of psychosocial interventions to improve infertile couples’ well-being. It also aims to identify the design implications of effective psychosocial interventions for the management of psychosocial distress in infertile couples, especially culturally specific interventions for Chinese infertile couples. Directions for future research are discussed.

BACKGROUND: Infertility is a life crisis affecting 15% of couples in most countries. The affected couples experience considerable psychological distress and impaired interpersonal relationships. Assisted reproductive technologies offer couples hope for pregnancy, but pose an unbearable psychological burden. Psychosocial interventions have been developed to offer support; however, their effectiveness has been inconsistent.

DESIGN: A thorough analysis of the literatures on the topic of psychosocial interventions for infertile couples.
METHODS: A systematic search of MEDLINE, CINAHL, PsycINFO, British Nursing Index and GoogleScholar from 2003-2015 was conducted to identify English language articles with the keywords 'psychosocial intervention' and 'infertility'. Two authors assessed all of the identified articles independently for inclusion in the review.

RESULTS: Twelve studies were included in the review: seven were interventional studies and five were review studies. The findings indicated that the psychosocial interventions in general improved psychological outcomes, marital relationships and pregnancy rates among infertile couples.

CONCLUSIONS: Psychosocial interventions should be incorporated into routine practice for infertile couples to provide timely support and counselling.

RELEVANCE TO CLINICAL PRACTICE: The implications of the review findings for the effective design of psychosocial interventions, including the content, format, duration and intervener for clinical practice are discussed. In confirming the efficacy of such intervention design, randomized controlled trials are needed to compare the interventions and usual care at clinical setting. Longitudinal design is also needed to examine the long-term effects of psychosocial interventions in infertile couples' well-being.

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Sperm DNA Fragmentation Index and Hyaluronan Binding Ability in Men from Infertile Couples and Men with Testicular Germ Cell Tumor.

Marchlewksa K; Filipiak E; Walczak-Jedrzejowska R; Oszukowska E; Sobkiewicz S; Wojt M; Chmiel J; Kula K; Slowikowska-Hilczer J.

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Objective. To investigate sperm DNA fragmentation and sperm functional maturity in men from infertile couples (IC) and men with testicular germ cell tumor (TGCT). Materials and Methods. Semen samples were collected from 312 IC men and 23 men with TGCT before unilateral orchiectomy and oncological treatment. The sperm chromatin dispersion test was performed to determine DNA fragmentation index (DFI) and the ability of sperm to bind with hyaluronan (HA) was assessed. Results. In comparison with the IC men, the men with TGCT had a higher percentage of sperm with fragmented DNA (median 28% versus 21%; p < 0.01) and a lower percentage of HA-bound sperm (24% versus 66%; p < 0.001). Normal results of both analyses were observed in 24% of IC men and 4% of men with TGCT. Negative Spearman's correlations were found between DFI and the percentage of HA-bound sperm in the whole group and in IC subjects and those with TGCT analyzed separately. Conclusions. Approximately 76% of IC men and 96% with TGCT awaiting orchiectomy demonstrated DNA fragmentation and/or sperm immaturity. We therefore recommend sperm banking after unilateral orchiectomy, but before irradiation and chemotherapy; the use of such a deposit appears to be a better strategy to obtain functionally efficient sperms.
Microsporogenesis is an indispensable period for investigating microspore development and cytoplasmic male sterility (CMS) occurrence. Radish CMS line plays a critical role in elite F1 hybrid seed production and heterosis utilization. However, the molecular mechanisms of microspore development and CMS occurrence have not been thoroughly uncovered in radish. In this study, a comparative analysis of radish floral buds from a CMS line (NAU-WA) and its maintainer (NAU-WB) was conducted using next generation sequencing (NGS) technology. Digital gene expression (DGE) profiling revealed that 3504 genes were significantly differentially expressed between NAU-WA and NAU-WB library, among which 1910 were upregulated and 1594 were downregulated. Gene ontology (GO) analysis showed that these differentially......
expressed genes (DEGs) were mainly enriched in extracellular region, catalytic activity, and response to stimulus. KEGG enrichment analysis revealed that the DEGs were predominantly associated with flavonoid biosynthesis, glycolysis, and biosynthesis of secondary metabolites. Real-time quantitative PCR analysis showed that the expression profiles of 13 randomly selected DEGs were in high agreement with results from Illumina sequencing. Several candidate genes encoding ATP synthase, auxin response factor (ARF), transcription factors (TFs), chalcone synthase (CHS), and male sterility (MS) were responsible for microsporogenesis. Furthermore, a schematic diagram for functional interaction of DEGs from NAU-WA vs. NAU-WB library in radish plants was proposed. These results could provide new information on the dissection of the molecular mechanisms underlying microspore development and CMS occurrence in radish.

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20160902

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2016
CAG-repeat polymorphisms in the polymerase gamma gene and male infertility: a meta-analysis.
Zhang J; Jiang W; Zhou Q; Ni M; Liu S; Zhu P; Wu Q; Li W; Zhang M; Xia X.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid
MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Andrologia. 48(9):882-889, 2016 Nov.
[Journal Article. Meta-Analysis]
UI: 26790834
CAG-repeat in the polymerase gamma (POLG) gene encoding polymerase gamma for mitochondria is important to spermatogenesis. Compared with a few researchers who raised alteration of CAG-repeat-affected male reproductive ability, others did not find the association between CAG-repeat polymorphisms and male infertility. Therefore, a comprehensive meta-analysis is necessary to determine the association; 13 case-control studies were screened out using keywords search. From these studies, characteristics were extracted for conducting meta-analysis. Odds ratio (OR) and 95% confidence interval (CI) were used to describe the results; the results indicated that CAG-repeat allele was not a risk factor to male infertility (pooled OR = 1.03, 95% CI: 0.79-1.34, P = 0.828). Four different genetic comparisons also demonstrated a negative result: heterozygote comparison (not 10/10 versus 10/10. Pooled OR = 0.99, 95% CI: 0.77-1.27, P = 0.948), homozygote comparison (not 10/not 10 versus 10/10. Pooled OR = 1.08, 95% CI: 0.56-2.06, P = 0.816), the recessive genetic comparison (not 10/not 10 versus not 10/10 + 10/10. Pooled OR = 1.07, 95% CI: 0.58-1.95, P = 0.829) and the dominant genetic comparison (not 10/not 10 + not 10/10 versus 10/10. Pooled OR = 0.97, 95% CI: 0.72-1.29, P = 0.804); based on current researches, this meta-analysis demonstrated no apparent association between POLG-CAG-repeat and male infertility. Similarly, CAG-repeat was not a sensitive site to male infertility.
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Association between C677T and A1298C polymorphisms of the MTHFR gene and risk of male infertility: a meta-analysis.

Yang Y; Luo YY; Wu S; Tang YD; Rao XD; Xiong L; Tan M; Deng MZ; Liu H. OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present, Genetics & Molecular Research. 15(2), 2016 Apr 26. [Journal Article. Meta-Analysis] 
UI: 27173242

Published studies on the association between the C677T and A1298C polymorphisms of the methylenetetrahydrofolate reductase (MTHFR) gene and male infertility risk are controversial. To obtain a more precise evaluation, we performed a meta-analysis based on published case-control studies.
studies. We conducted an electronic search of PubMed, EMBASE, the Cochrane Library, the Web of Science, and the China Knowledge Resource Integrated Database for papers on MTHFR gene C677T and A1298C polymorphisms and male infertility risk. Pooled odds ratios (ORs) with 95% confidence intervals (95%CIs) were used to assess the strength of association in homozygote, heterozygote, dominant, recessive, and additive models. Statistical heterogeneity, test of publication bias, and sensitivity analysis were carried out using the STATA software (Version 13.0). Overall, 21 studies of C677T (4505 cases and 4024 controls) and 13 studies of A1298C (2785 cases and 3094 controls) were included in this meta-analysis. For C677T, the homozygote comparison results were OR = 1.629, 95%CI (1.215-2.184), and the recessive model results were OR = 1.462 (1.155-1.850). For A1298C, the homozygote comparison results were OR = 1.289 (1.029-1.616), and the recessive model results were OR = 1.288 (1.034-1.604).

In conclusion, the current meta-analysis showed that the MTHFR C677T polymorphism was associated with a significantly increased male infertility risk in the Asian and overall populations, but not in the Caucasian population, and there was a significant association between the A1298C polymorphism and male infertility risk in the Asian, Caucasian, and overall groups.

Status
MEDLINE
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Date Created 20160513
Year of Publication
Aim. This study aimed to assess seminal miRNA relationship with seminal apoptotic markers and oxidative stress (OS) in infertile men associated with varicocele (Vx). Methods. In all, 220 subjects were divided into the following groups: fertile normozoospermic men, fertile normozoospermic men with Vx, infertile oligoasthenoteratozoospermic (OAT) men without Vx, and infertile OAT men with Vx. They were subjected to history taking, clinical examination, and semen analysis. In their semen, the following were estimated: miRNA-122, miRNA-181a, and miRNA-34c5 using quantitative real-time PCR, apoptotic markers (BAX, BCL2) protein expression, and OS markers [malondialdehyde (MDA) and glutathione peroxidase (GPx)]. Results. The mean levels of seminal miRNA-122, miRNA-181a, and miRNA-34c5 were significantly reduced in infertile OAT men with Vx compared with other groups coupled with Vx grade and Vx bilaterality. Seminal miRNA-122, miRNA-181a, and miRNA-34c5 were positively correlated with sperm concentration, total sperm motility, sperm normal morphology, seminal GPx, and seminal BCL2 and negatively correlated with seminal MDA and seminal BAX. Conclusions. Seminal miRNA-122, miRNA-181a, and miRNA-34c5 are decreased in infertile OAT men with Vx associated with increased Vx grade and Vx bilaterality. In addition, they are positively correlated with sperm parameters and negatively correlated with OS, apoptotic markers.

Status
MEDLINE
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Flavor perception test: evaluation in patients with Kallmann syndrome.

Maione L; Cantone E; Nettore IC; Cerbone G; De Brasi D; Maione N; Young J; Di Somma C; Sinisi AA; Iengo M; Macchia PE; Pivonello R; Colao A.

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Endocrine. 52(2):236-43, 2016 May.

[Comparative Study. Controlled Clinical Trial. Journal Article]

UI: 26209039

In Kallmann syndrome (KS), congenital hypogonadism is associated with olfactory impairment. To evaluate flavor perception-related disability in KS patients, 30 patients with KS, 12 with normosmic hypogonadism (nIHH), 24 with acquired anosmia (AA), and 58 healthy controls entered the study. All participants completed questionnaires concerning dietary habits, olfaction-related quality of life (QoL), and self-determined olfactory, flavor, and taste abilities prior to
undergoing standardized olfactometry and gustometry. Each subject underwent flavor testing, using orally administered aqueous aromatic solutions, identifying 21 different compounds by choosing each out of 5 alternative items. Flavor score (FS) was calculated as the sum of correct answers (range 0-21). Flavor perception by self-assessment was similar between KS, nIHH, and controls, and was mostly reduced only in AA. FS was similar between KS (5.4 +/- 1.4) and AA (6.4 +/- 1.9), and lower than in nIHH (16.2 +/- 2.4, p < 0.001) and controls (16.8 +/- 1.7, p < 0.0001). FS showed strong reproducibility, and correlated with olfactory scores in the overall population. KS and AA patients identified aromatics eliciting trigeminal stimulation better than pure odorants. Olfaction-related QoL was more impaired in AA than in KS. We report significant flavor impairment in KS. This contrasts with routine clinic evidence; KS patients, in contrast with AA, do not complain of flavor perception impairment, perhaps owing to the congenital nature of the dysfunction. Flavor perception impairment should be considered a specific KS disability, because of important detrimental effects on physical and mental health and on QoL. KS patients should also be advised of this impairment in order to prevent accidental and life-threatening events.

Status

MEDLINE

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348.
Effect of Lifestyle Intervention on the Hormonal Profile of Frail, Obese Older Men.
Armamento-Villareal R; Aguirre LE; Qualls C; Villareal DT.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
UI: 26892583
OBJECTIVE: Obesity-associated hypogonadism is hypothesized to be due to the suppressive effect of high estradiol (from an increase in aromatase activity present in the abundant adipose tissue) on the hypothalamic-pituitary-gonadal unit resulting in low testosterone production. Although weight loss has been found to be effective in reducing estradiol and raising testosterone levels in studies of younger men, its effect in frail, obese older men is understudied. Thus, the objective of this study was to determine the effect of lifestyle intervention on hormone levels in frail, obese older men.
DESIGN: Randomized controlled trial of lifestyle intervention in frail, obese older men (>65 yo) for 1 year.

SETTING: University hospital.

METHODS: Forty frail, obese elderly men were randomized, for a 52-week study, to any of the following treatment groups: (1) control group, (2) diet-induced weight loss group (diet group), (3) exercise training group (exercise group), and (4) diet-induced weight loss and exercise training group (diet-exercise group). The objective was to achieve a ~10 % weight loss at 6 months and maintain this weight for an additional 6 months. Physical function was assessed by the modified physical performance testing (modified PPT). Estradiol was measured by radioimmunoassay, testosterone by automated immunoassay, and sex hormone-binding globulin by enzyme-linked immunoassay.

RESULTS: After 12 months of intervention, diet alone resulted in a weight loss of -10.1 +/- 1.9 kg in the diet group and -9.1 +/- 0.9 kg in the diet-exercise group. This resulted in a significant decrease (both p<0.05) in total estradiol compared to baseline among subjects in the diet (2.5 +/- 1.3 pg/ml) and diet-exercise group (2.2 +/- 4.0 pg/ml). Free estradiol index also significantly decreased (both p <0.05) in both the diet (-0.39 +/- 0.14 pmol/nmol) and diet-exercise (-0.52 +/- 0.12 pmol/nmol) group. Total testosterone significantly increased (p<0.05) in response to diet (71.0 +/- 21.0 ng/dl) and diet-exercise (49.9 +/- 15.5 pg/ml) resulting in values of 287.0 +/- 28.1 ng/dl in the diet and 317.6 +/- 33.1 ng/dl in the diet-exercise group. However, because there was a significant increase in sex hormone-binding globulin levels in both the diet and diet-exercise groups, free testosterone index and the changes in free testosterone index were not significant compared to baseline. Regardless of changes in hormonal levels, patients in the diet, exercise, and diet-exercise groups experienced significant improvements in the modified PPT from baseline.

CONCLUSION: Weight loss from lifestyle intervention resulted in significant decreases in total and free estradiol levels in frail, obese older men, but this did not result in a clinically important increase in total testosterone nor a significant increase in free testosterone. Thus, alternative forms of treatment in addition to lifestyle intervention may be necessary to improve the hormonal profile among these patients. Nevertheless, whether further improvement in hormonal profile would result in better physical performance than what can be achieved by lifestyle alone in these subjects remains uncertain.

Status
MEDLINE
Authors Full Name
Armamento-Villareal, R; Aguirre, L E; Qualls, C; Villareal, D T.
Institution
The efficacy and safety of silodosin for the treatment of ureteral stones: a systematic review and meta-analysis. [Review]
Yang D; Wu J; Yuan H; Cui Y.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
UI: 27233621
BACKGROUND: To evaluate the efficacy and safety of silodosin as a medical expulsive therapy for ureteral stones by means of a systematic review and meta-analysis.
METHODS: We searched MEDLINE, EMBASE and the Cochrane Controlled Trials Register to identify randomized controlled trials (RCTs) of silodosin in the treatment of ureteral stones. The reference lists of retrieved studies were also investigated.
RESULTS: Six RCTs, including 916 participants and comparing silodosin with controls, were used in the meta-analysis. Silodosin was superior to controls in terms of stone expulsion rate, the primary efficacy end point in all six RCTs (odds ratio [OR] for expulsion 2.16, 95% confidence interval [CI] 1.62 to 2.86, p <0.00001). Silodosin was also more effective for secondary efficacy end points; the stone expulsion time (standardized mean difference [SMD] -3.66, 95% CI -6.61 to -0.71; p =0.01) and analgesic requirements (SMD -0.89, 95% CI -1.19 to -0.60; p<0.00001) were significantly reduced compared with those of controls. Other than the incidence of abnormal
ejaculation, which was higher in the silodosin groups (OR 2.84, 95 % CI 1.56 to 5.16, p =0.0006), few adverse effects were observed.

CONCLUSION: This meta-analysis indicates silodosin is an effective and safe treatment option for ureteral stones with a low occurrence of side effects.

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https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4882785
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350.
A novel stepwise micro-TESE approach in non obstructive azoospermia.
Franco G; Scarselli F; Casciani V; De Nunzio C; Dente D; Leonardo C; Greco PF; Greco A; Minasi MG; Greco E.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Clinical Trial. Journal Article]
BACKGROUND: The purpose of the study was to investigate whether micro-TESE can improve sperm retrieval rate (SRR) compared to conventional single TESE biopsy on the same testicle or to contralateral multiple TESE, by employing a novel stepwise micro-TESE approach in a population of poor prognosis patients with non-obstructive azoospermia (NOA).

METHODS: Sixty-four poor prognosis NOA men undergoing surgical testicular sperm retrieval for ICSI, from March 2007 to April 2013, were included in this study. Patients inclusion criteria were a) previous unsuccessful TESE, b) unfavorable histology (SCOS, MA, sclerahyalinosis), c) Klinefelter syndrome. We employed a stepwise micro-TESE consisting three-steps: 1) single conventional TESE biopsy; 2) micro-TESE on the same testis; 3) contralateral multiple TESE.

RESULTS: SRR was 28.1% (18/64). Sperm was obtained in both the initial single conventional TESE and in the following micro-TESE. The positive or negative sperm retrieval was further confirmed by a contralateral multiple TESE, when performed. No significant pre-operative predictors of sperm retrieval, including patients' age, previous negative TESE or serological markers (LH, FSH, inhibin B), were observed at univariate or multivariate analysis. Micro-TESE (step 2) did not improve sperm retrieval as compared to single TESE biopsy on the same testicle (step 1) or multiple contralateral TESE (step 3).

CONCLUSIONS: Stepwise micro-TESE could represent an optimal approach for sperm retrieval in NOA men. In our view, it should be offered to NOA patients in order to gradually increase surgical invasiveness, when necessary. Stepwise micro-TESE might also reduce the costs, time and efforts involved in surgery.

Status
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351.
Testofen, a specialised Trigonella foenum-graecum seed extract reduces age-related symptoms of androgen decrease, increases testosterone levels and improves sexual function in healthy aging males in a double-blind randomised clinical study.
Rao A; Steels E; Inder WJ; Abraham S; Vitetta L.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article. Randomized Controlled Trial]
UI: 26791805
This study examined the effect of Testofen, a specialised Trigonella foenum-graecum seed extract on the symptoms of possible androgen deficiency, sexual function and serum androgen concentrations in healthy aging males. This was a double-blind, randomised, placebo-controlled trial involving 120 healthy men aged between 43 and 70 years of age. The active treatment was standardised Trigonella foenum-graecum seed extract at a dose of 600mg/day for 12 weeks. The primary outcome measure was the change in the Aging Male Symptom questionnaire (AMS), a measure of possible androgen deficiency symptoms; secondary outcome measures were sexual function and serum testosterone. There was a significant decrease in AMS score over time and between the active and placebo groups. Sexual function improved, including number of morning
erections and frequency of sexual activity. Both total serum testosterone and free testosterone increased compared to placebo after 12 weeks of active treatment. Trigonella foenum-graecum seed extract is a safe and effective treatment for reducing symptoms of possible androgen deficiency, improves sexual function and increases serum testosterone in healthy middle-aged and older men.

Status
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Date Created
20160609
Year of Publication
2016

352.
Pipelle for Pregnancy (PIP): study protocols for three randomised controlled trials.
Lensen S; Martins W; Nastri C; Sadler L; Farquhar C.
[Journal Article. Multicenter Study. Pragmatic Clinical Trial. Randomized Controlled Trial. Research Support, Non-U.S. Gov't]
UI: 27121007
BACKGROUND: The success rate of infertility treatments remains modest. Endometrial injury has been suggested as an intervention to increase the probability of pregnancy in women
undergoing assisted reproductive technologies such as in vitro fertilisation (IVF). The majority of studies and systematic reviews have reported that endometrial injury improves the outcomes of IVF, intrauterine insemination and natural conception; however, the size and quality of the studies are poor. The low quality of the available evidence questions the presence of any real beneficial effect, and the applicability of the intervention in different populations remains unclear.

METHODS/DESIGN: The PIP trials are three multi-centre, randomised controlled trials designed to test three separate hypotheses: whether endometrial injury increases the probability of live birth in women or couples 1) who are undergoing autologous embryo transfer as part of an IVF cycle (PIP-IVF), 2) with unexplained infertility who are attempting to conceive naturally (PIP-UE) and 3) with subfertility related to polycystic ovarian syndrome (PCOS) who are on ovulation induction medication and attempting to conceive (PIP-PCOS). Participants will be randomised to either undergo endometrial injury by endometrial pipelle biopsy or to: * no intervention (PIP-IVF), or * a sham procedure (PIP-PCOS and PIP-UE). In PIP-IVF, endometrial injury will be carried out between day three of the cycle prior to the IVF cycle, and day three of the IVF cycle. In PIP-UE and PIP-PCOS, endometrial injury or a sham procedure will be undertaken between days 1-12 of a menstrual cycle or ovulation induction cycle respectively. Participants in PIP-UE and PIP-PCOS will then be followed for three cycles during which time they will attempt to conceive from sexual intercourse. To ensure allocation concealment, randomisation will be carried out using a web-based system or sequentially numbered, opaque, sealed envelopes. The primary outcome is live birth. Secondary outcomes include ongoing pregnancy, clinical pregnancy and miscarriage. The required sample sizes for the PIP studies have been estimated at 840 (PIP-IVF), 350 (PIP-UE) and 280 (PIP-PCOS). Primary analysis will be as per intention-to-treat principles.

DISCUSSION: The PIP trials are designed to address the gaps in the utility of endometrial scratching as a treatment for subfertility in three different populations. If the beneficial effect of this intervention can be confirmed in these settings, endometrial scratching will provide a cost-effective method for helping women and couples to conceive.


Status
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Comparing the Effectiveness of Dietary Vitamin C and Exercise Interventions on Fertility Parameters in Normal Obese Men.

Rafiee B; Morowvat MH; Rahimi-Ghalati N.

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present


[Journal Article. Multicenter Study. Randomized Controlled Trial. Research Support, Non-U.S. Gov't]

UI: 27085565

PURPOSE: Comparing the effectiveness of dietary vitamin C and weight loss exercises interventions for weight loss on semen characteristics in normal obese men.

MATERIALS AND METHODS: A total number of 200 men were randomly allocated into two groups based on body mass index, exercise and vitamin C groups. Also, 50 men with normal spermogram were placed in a control group. In exercise group, a 6 months intensive exercise program was designed under a coach's supervision to reduce the body weight. In vitamin C group, 1,000 mg of vitamin C were given every other day as supplement.

RESULTS: Weight loss increased the volume of semen in participants with 25-30 (P = .02) and more than 30 body mass index (P = .001). The increased concentration of sperm per mL of semen in body mass index (BMI) 25-30 group (P = .01) and more than 30 (P = .003) BMI was
significant. Improving sperm motility after two hours in participants with more than 30 (P = .01) BMI was significant. In vitamin C group, the improvement of sperm concentration in participants who had less than 25 (P = .01), between 25 and 30 (P = .01), more than 30 (P = .02) BMI was significant. Sperm motility improved in all three groups (P = .001, P = .02 and P = .003, respectively).

CONCLUSION: Weight loss can significantly increase semen volume, its concentration, its mobility and percentage of normal morphology. Consuming vitamin C significantly improves sperm concentration and mobility, but the semen volume and the percentage of normal morphology will not change significantly.

Status
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Date Created
20160418
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2016

Content Validity of the Hypogonadism Impact of Symptoms Questionnaire (HIS-Q): A Patient-Reported Outcome Measure to Evaluate Symptoms of Hypogonadism.
Gelhorn HL; Vernon MK; Stewart KD; Miller MG; Brod M; Althof SE; DeRogatis LR; Dobs A; Seftel AD; Revicki DA.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
BACKGROUND: Hypogonadism, or low testosterone, is a common disorder. There are currently no patient-reported outcome (PRO) instruments designed to comprehensively evaluate the symptoms of hypogonadism and to detect changes in these symptoms in response to treatment.

OBJECTIVE: The purpose of this study was to develop a PRO instrument, the Hypogonadism Impact of Symptoms Questionnaire (HIS-Q) and to assess its content validity.

METHODS: A literature review, expert clinician input, and qualitative concept elicitation with 39 male hypogonadism patients (four focus groups: n = 25; individual interviews: n = 14; mean age 52.3 +/- 14.3 years) from the USA were used to develop the draft HIS-Q. Subsequent cognitive interviews (n = 29; mean age 51.5 +/- 15.4 years) were used to evaluate content validity.

RESULTS: Emergent discussion with participants yielded symptoms within the sexual, physical, energy, sleep, cognition, and mood domains. Low libido and tiredness were most commonly reported. The initial version of the HIS-Q includes 53 items that were consistently understood by the participants, who found the instrument to be relevant to their experiences with hypogonadism and comprehensive in the content coverage of symptoms.

CONCLUSION: The HIS-Q is a comprehensive PRO measure of hypogonadism symptom severity in males. Its design elements, including the response options and recall period, were suitable, and content validity was confirmed.

Status
MEDLINE
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355.
Male infertility: lifestyle factors and holistic, complementary, and alternative therapies. [Review]
Yao DF; Mills JN.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article. Review]
UI: 26952957
While we may be comfortable with an allopathic approach to male infertility, we are also responsible for knowledge about lifestyle modifications and holistic, complementary, and alternative therapies that are used by many of our patients. This paper provides an evidence-based review separating fact from fiction for several of these therapies. There is sufficient literature to support weight reduction by diet and exercise, smoking cessation, and alcohol moderation. Supplements that have demonstrated positive effects on male fertility on small randomized controlled trial (RCT) include aescin, coenzyme Q 10, glutathione, Korean red ginseng, L-carnitine, nigella sativa, omega-3, selenium, a combination of zinc and folate, and the Menevit antioxidant. There is no support for the use of Vitamin C, Vitamin E, or saffron. The data for Chinese herbal medications, acupuncture, mind-body practice, scrotal cooling, and faith-based healing are sparse or inconclusive.
Status
MEDLINE
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Comments
PMID
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4854092
A combination of tryptophan, Satureja montana, Tribulus terrestris, Phyllanthus emblica extracts is able to improve sexual quality of life in patient with premature ejaculation.

Sansalone S; Russo GI; Mondaini N; Cantiello F; Antonini G; Cai T.

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Comparative Study. Journal Article. Multicenter Study. Randomized Controlled Trial]
UI: 27711088

OBJECTIVE: The management of patient affected by premature ejaculation (PE) is nowadays not highly satisfactory. Here, we aimed to evaluate the tolerability and efficacy of a combination of tryptophan, Satureja montana, Tribulus terrestris, Phyllanthus emblica extracts in order to improve sexual quality of life in patients with premature ejaculation.

MATERIALS AND METHODS: All patients attending to 5 urological centers from January 2015 to March 2015, due to premature ejaculation were enrolled in this study. At the enrolment visit, all subjects underwent self-administered IIEF-5, Male Sexual Health Questionnaire-Ejaculation Disorder (MSHQeJ), PEDT and IELTS (calculated as mean from that perceived by partner and that perceived by patient) and underwent urological visit and laboratory examinations. All patients received one tablet per day of a combination of tryptophan, Satureja montana, Tribulus terrestris, Phyllanthus emblica extracts for 3 months (Group A). After 3 months all patients underwent follow-up visit with the same investigations that have been carried out in the enrolment visit. The results were compared with a cohort of patients enrolled in the same period in another urological center and considered as a control group (Group B). All patients in the control group underwent counseling and sexual behavioral treatment without any pharmacological compound.

RESULTS: At the follow-up analysis, significant changes in terms of IELT in the Group A (mean difference: 31.90; p < 0.05) at 3 months and versus Group B at the intergroup analysis (mean difference: 30.30; p < 0.05) were reported. In the group A, significant differences from baseline to
last follow-up were observed relative to IIEF-5 (mean difference: 1.04; p < 0.05), PEDT (mean difference: -2.57; p < 0.05) and FSH (mean difference: -16.46; p < 0.05).

CONCLUSION: In conclusion, patients affected by PE may significantly benefit from oral therapy with a combination of tryptophan, Satureja montana, Tribulus terrestris, Phyllanthus emblica extracts in terms of IELT and PEDT scores improvement.

Status
MEDLINE

Authors Full Name
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2016

Infertile women below the age of 40 have similar anti-Mullerian hormone levels and antral follicle count compared with women of the same age with no history of infertility.
ALREADY?: The management of patients with a low ovarian reserve and a poor response to controlled ovarian stimulation (COS) remains a challenge in assisted reproductive technologies (ART). Both AMH levels and AFC reflect the ovarian reserve and are valuable predictors of the ovarian response to exogenous gonadotrophins. However, there is a large inter-individual variation in the age-related depletion of the ovarian reserve and a broad variability in the levels of AMH and AFC compatible with conception. Women with an early depletion of the ovarian reserve may experience infertility as a consequence of postponement of childbearing. Thus, low ovarian reserve is considered to be overrepresented among infertile patients.

STUDY DESIGN, SIZE, DURATION: A prospective cohort study including 382 women with a male partner referred to fertility treatment at Rigshospitalet, Copenhagen, Denmark during 2011-2013 compared with a control group of 350 non-users of hormonal contraception with no history of infertility recruited during 2008-2010.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Included patients and controls were aged 20-39 years. Women with polycystic ovary syndrome were excluded. On Cycle Days 2-5, AFC and ovarian volume were measured by transvaginal sonography, and serum levels of AMH, FSH and LH were assessed.

MAIN RESULTS AND THE ROLE OF CHANCE: Infertile patients had similar AMH levels (11%, 95% confidence interval (CI): -1;24%) and AFC (1%, 95% CI: -7;8%) compared with controls with no history of infertility in an age-adjusted linear regression analysis. The prevalence of very low AMH levels (<5 pmol/l) was similar in the two cohorts (age-adjusted odds ratio: 0.9, 95% CI: 0.5;1.7). The findings persisted after adjustment for smoking status, body mass index, gestational age at birth, previous conception and chronic disease in addition to age.

LIMITATIONS, REASON FOR CAUTION: The comparison of ovarian reserve parameters in women recruited at different time intervals could be a reason for caution. However, all women were examined at the same centre using the same sonographic algorithm and AMH immunoassay.

WIDER IMPLICATIONS OF THE FINDINGS: This study indicates that the frequent observation of patients with a poor response to COS in ART may not be due to an overrepresentation of women with an early depletion of the ovarian reserve but rather a result of the expected age-related decline in fertility.

STUDY FUNDING/COMPETING INTERESTS: The study received funding from MSD and the Interregional European Union (EU) projects 'ReproSund' and 'ReproHigh'. The authors have no conflict of interest.

TRIAL REGISTRATION NUMBER: Not applicable.

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An open-label, phase 2, single centre, randomized, crossover design bioequivalence study of AndroForte 5 testosterone cream and Testogel 1% testosterone gel in hypogonadal men: study LP101.

Wittert GA; Harrison RW; Buckley MJ; Wlodarczyk J.

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
We compared a novel 5% testosterone (T) cream (AndroForte 5, Lawley Pharmaceuticals, Australia) with a 1% T gel (Testogel, Besins Healthcare, Australia). Using an open-label crossover design, subjects were randomized to one of two treatment sequences using either the T gel or T cream first in a 1:1 ratio. Each treatment period was 30 days with a 7-14 days washout period between them. On Days 1 and 30 of each treatment period blood was sampled at -15, -5 min, 0, 2, 4, 5, 6, 7, 8, 9, 10, 12 and 16 h post study drug administration. Sixteen men with established androgen deficiency aged between 29 and 73 years, who had undertaken a washout from prior testosterone therapy participated in the study. One subject failed to complete both arms and another was excluded post-completion because of a major protocol violation.

Bioequivalence was established based on key pharmacokinetic (PK) variables: AUC, C(avg), C(max), T(max), % fluctuation (with and without baseline correction) for the two formulations of testosterone on Day 1 and Day 30. The ratio and 90% CI of AUC 0.99 (0.86-1.14), C(max) 1.02 (0.84-1.24) and C(avg) 0.99 (0.86-1.14) for T cream/T gel were within the predetermined bioequivalence criteria of 80% to 125% at Day 30. There were no statistically significant differences between secondary biochemical markers: serum dihydrotestosterone (DHT), oestradiol (E2), sex hormone-binding globulin (SHBG), luteinizing hormone (LH) and (FSH). The two testosterone formulations were shown to be bioequivalent.

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MEDLINE

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Institution

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20160119

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2016
Effect of male body mass index on clinical outcomes following assisted reproductive technology: a meta-analysis.
Le W; Su SH; Shi LH; Zhang JF; Wu DL.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article. Meta-Analysis]
UI: 26276351
Overweight and obese males might exhibit a great risk of infertility. However, according to the current studies, the association between elevated male body mass index (BMI) and the clinical adverse results after assisted reproductive technology (ART) remains controversial. Hence, we conducted a meta-analysis to evaluate the effects of raised male BMI on clinical outcomes following ART. PubMed, EMBASE and three Chinese databases were used to identify relevant studies. The primary outcome was clinical pregnancy rate. Secondary outcomes included live birth rate and sperm parameters. A total of 5262 male participants from 10 cohort studies were subjected to meta-analysis. Results indicated that overweight or obese had no significant impact on clinical pregnancy rate [in vitro fertilisation (IVF): odds ratio (OR), 0.73; 95% confidence interval (CI), 0.39-1.39; intracytoplasmic sperm injection (ICSI): OR, 1.03; 95% CI, 0.92-1.15], live birth rate (IVF: OR, 0.91; 95% CI, 0.78-1.06; ICSI: OR, 1.00; 95% CI, 0.50-1.99) and sperm concentration (SMD, -0.28; 95% CI, -0.65 to 0.08) compared with normal weight following IVF/ICSI treatments. Exclusion of any single study and almost all the sensitivity analyses showed that our results were reliable. At present, the role of male BMI in the process of ART is only partly understood and should be further investigated.
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Status
MEDLINE
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Advantages of testosterone nasal gel include ease of administration, low dose, and no risk of secondary transference. The efficacy and safety of testosterone nasal gel was evaluated in hypogonadal males. The ninety-day, randomized, open-label, dose-ranging study, included potential dose titration and sequential safety extensions to 1 year. At 39 US outpatient sites, 306 men (mean age 54.4 years) with two fasting morning total serum testosterone levels <300 ng/dL were randomized (n = 228, b.i.d. dosing; n = 78, t.i.d. dosing). Natesto(TM) Testosterone Nasal Gel was self-administered, using a multiple-dose dispenser, as two or three daily doses (5.5 mg per nostril, 11.0 mg single dose). Total daily doses were 22 mg or 33 mg. The primary endpoint was the Percentage of patients with Day-90 serum total testosterone average concentration
(C(avg)) value within the eugonadal range (>300 ng/dL, <1050 ng/dL). At Day 90, 200/273 subjects (73%; 95% CI 68, 79) in the intent-to-treat (ITT) population and 180/237 subjects (76%; 71, 81) in the per-protocol (PP) population were in the normal range. Also, in the normal range were 68% (61, 74) of ITT subjects and 70% (63, 77) of PP subjects in the titration arm, as well as, 90% (83, 97) of ITT subjects and 91% (84, 98) of PP subjects in the fixed-dose arm. Natesto(TM) 11 mg b.i.d. or 11 mg t.i.d. restores normal serum total testosterone levels in most hypogonadal men. Erectile function, mood, body composition, and bone mineral density improved from baseline. Treatment was well tolerated; adverse event rates were low. Adverse event discontinuation rates were 2.1% (b.i.d.) and 3.7% (t.i.d.). This study lacked a placebo or an active comparator control which limited the ability to adequately assess some measures.

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20160119

Year of Publication
2016

361.
The Role of Levomilnacipran in the Management of Major Depressive Disorder: A Comprehensive Review. [Review]
Bruno A; Morabito P; Spina E; Muscatello MR.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article. Review]
UI: 26572745
Levomilnacipran, the more active enantiomer of the serotonin and norepinephrine reuptake inhibitor (SNRI) milnacipran, was recently approved in the US for the treatment of major depressive disorder (MDD). The drug was developed as an extended release (ER) capsule formulation to allow for once-daily administration, thereby improving patient adherence. This agent differs from other available SNRIs in having a greater potency for inhibition of norepinephrine relative to serotonin reuptake. The efficacy of levomilnacipran ER has been evaluated in seven randomised, double-blind clinical trials (one Phase II and four Phase III trials, and two long-term efficacy studies). These studies documented that levomilnacipran is generally more effective than placebo for the treatment of MDD in the short-term, whereas no firm evidence exists on long-term efficacy for relapse prevention. Preliminary evidence suggests that levomilnacipran ER may be effective in improving not only depressive symptoms but also symptoms related to functioning (social life, work, and family life). Short-and longer-term studies found that the rate of withdrawal from levomilnacipran therapy due to adverse events was rather low. Moreover the drug appeared to be generally well tolerated. The most common adverse effects included nausea, hyperhidrosis, constipation, tachycardia, palpitations, erectile dysfunction and ejaculation disorder. As hypertension or orthostatic hypotension may occur in a few patients, the cardiovascular safety of levomilnacipran needs to be more extensively investigated especially on long-term treatment. Additional active comparator trials evaluating efficacy, tolerability and cost-effectiveness are required to better define the role of levomilnacipran ER in the treatment of MDD in relation to currently available antidepressants including other SNRIs.
Association of the methylenetetrahydrofolate reductase gene C677T polymorphism with the risk of male infertility: a meta-analysis.
Zhu X; Liu Z; Zhang M; Gong R; Xu Y; Wang B.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid
MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article. Meta-Analysis]
UI: 26584688
Several molecular epidemiological studies have been conducted to examine the association between methylenetetrahydrofolate reductase (MTHFR) C677T polymorphism and male infertility susceptibility, but the results remain inconclusive. To derive a more precise estimation of the relationship, a meta-analysis was performed. In this meta-analysis, a total of 26 case-control studies including 5659 infertility cases and 5528 controls were selected to evaluate the possible association. The pooled odds ratios (ORs) with 95% confidence intervals (95% CIs) were used to assess the strength of association of C677T polymorphism with male infertility in the additive model, dominant model, recessive model and allele-frequency genetic model. In the overall analysis, the frequency of the 677T allele was significantly associated with male infertility susceptibility (OR=2.32, 95%CI=2.04-2.65 for TT vs. CC genotype; OR=1.09, 95%CI=1.00-1.19 for CT vs. CC genotype; OR=1.19, 95%CI=1.10-1.29 for CT/TT vs. CC genotype; OR=1.54, 95%CI=1.36-1.74 for TT vs. CC/TT genotype; OR=1.22, 95%CI=1.15-1.30 for T vs. C allele). A subgroup analysis of the subjects showed that significantly strong association between MTHFR C677T polymorphism and male infertility was present only in Asians, but not in Caucasians. Additionally, MTHFR C677T was associated with a significant increase in the risk of azoospermia in all genetic models. Meanwhile, no significantly increased risks of oligoasthenotertozoospermia (OAT) were found in most of the genetic models. In conclusion, this meta-analysis is in favor that the MTHFR C677T polymorphism is capable of causing male infertility susceptibility, especially in Asians and the subgroup of azoospermia.
Status
MEDLINE
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Zhu, Xudong; Liu, Zhiguo; Zhang, Maochen; Gong, Ruihong; Xu, Yajun; Wang, Baoming.
Institution
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OBJECTIVE: To compare the efficacy and safety of single half-dose silodosin and single full-dose tamsulosin in Japanese men with lower urinary tract symptoms secondary to benign prostatic hyperplasia (LUTS/BPH).

METHODS: Japanese men aged >50 years with LUTS/BPH and an International Prostate Symptom Score (IPSS) of >8 were enrolled in the randomized crossover study and divided into silodosin-preceding (S-T) and tamsulosin-preceding (T-S) groups. The S-T group received 4 mg silodosin once daily for 4 weeks followed by 0.2 mg tamsulosin once daily for 4 weeks. The T-S group received the reverse treatment sequence. A washout period prior to drug crossover was not included. Subjective and objective efficacy parameters including IPSS, quality of life (QOL) index, uroflowmetry, and safety were compared between the two groups.

RESULTS: Thirty of 34 men (S-T group n = 16; T-S group n = 14) completed the study. Both drugs significantly improved all IPSS items and QOL index in the first treatment period. Subjective improvement in nocturia by silodosin was observed in both the first and crossover treatment periods. Objective improvement in maximum flow rate by silodosin was only observed in the first
treatment period. Adverse events occurred more frequently with silodosin than with tamsulosin; however, none of the adverse events required treatment discontinuation. Ejaculation disorders occurred in three participants (10%) and were associated with silodosin use.

CONCLUSION: Single half-dose silodosin has a similar efficacy to full-dose tamsulosin in Japanese men with LUTS/BPH and thus, may represent an effective, safe, and affordable treatment option.

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From Karimian M; Hosseinzadeh Colagar A. OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present Molecular & Cellular Endocrinology. 425:1-10, 2016 Apr 15.

Methionine synthase A2756G transition might be a risk factor for male infertility: Evidences from seven case-control studies.
Methionine synthase (MTR) has a crucial role in DNA synthesis and methylation reactions. The aim of this study was to investigate the association of the MTR-A2756G polymorphism with idiopathic male infertility. Blood samples were collected from 217 idiopathic infertile- and 233 healthy-men, and MTR-A2756G genotyping was performed by PCR-RFLP. Meta-analysis was conducted by pooling our data with the data obtained from 6 previous studies. Also, the effects of this substitution on protein structure were evaluated by bioinformatics tools. Our study revealed the association of AG-genotype, GG-genotype, and G-allele with male infertility. Meta-analysis showed a significant association between A2756G transition and male infertility. In addition, structural analysis of the transition effect on protein revealed a significant influence on MTR function (with score: 38; expected accuracy: 66%). These findings suggest that the A2756G substitution might be a genetic risk factor and a potential biomarker for idiopathic male infertility.

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365.
Onset Manifestations of Spinal and Bulbar Muscular Atrophy (Kennedy's Disease). [Review]
Finsterer J; Soraru G.
Spinal and bulbar muscular atrophy (SBMA) is regarded as a disorder with adult onset between third and fifth decade of life. However, there is increasing evidence that SBMA may start already before adulthood. The present study investigated the following: (1) Which clinical manifestations have been described so far in the literature as initial manifestations? (2) Which was the age at onset of these manifestations? and (3) Is age at onset dependent on the CAG-repeat length if non-motor manifestations are additionally considered? Data for this review were identified by searches of MEDLINE using appropriate search terms. Onset manifestations in SBMA can be classified as frequent, rare, motor, non-motor, or questionable. Frequent are muscle weakness, cramps, fasciculations/twitching, tremor, dysarthria, dysphagia, or gynecomastia. Rare are myalgia, easy fatigability, exercise intolerance, polyneuropathy, hyper-CKemia, under-masculinized genitalia, scrotal hypospadias, microphallus, laryngospasm, or oligospermia. Questionable manifestations include sensory disturbances, cognitive impairment, increased pituitary volume, diabetes, reduced tongue pressure, elevated creatine-kinase, or low androgens/high estrogens. Age at onset is highly variable ranging from 4-76 years. Non-motor manifestations develop usually before motor manifestations. Age at onset depends on what is considered as an onset manifestation. Considering non-motor onset manifestations, age at onset is independent of the CAG-repeat size. In conclusion, age at onset of SBMA depends on what is regarded as onset manifestation. If non-motor manifestations are additionally considered, age at onset is independent of the CAG-repeat length. Since life expectancy is hardly reduced in SBMA, re-investigation of patients from published studies with regard to their initial disease profiles is recommended.
Assessment of testicular dose during preoperative radiotherapy for rectal cancer. Buchli C; Al Abani M; Ahlberg M; Holm T; Fokstuen T; Bottai M; Frodin JE; Lax I; Martling A. OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present Acta Oncologica. 55(4):496-501, 2016. [Clinical Trial. Journal Article. Research Support, Non-U.S. Gov't] UI: 26362484

BACKGROUND: Radiotherapy (RT) for rectal cancer can have adverse effects on testicular function resulting in azoospermia and low testosterone levels. Variability of testicular dose (TD) due to differences in position of testes has been assessed with scrotal dosimeters and resulted in substantial variability of delivered TD. The aim of this study was to estimate planned and delivered TD using a treatment planning system (TPS).

METHODS: In 101 men treated with RT for rectal cancer the cumulative mean TD (mTD) was calculated by TPS based on plan-computed tomography (CT) to evaluate the effect of different predictors on planned TD. The delivered TD was estimated by TPS based on repeated cone-beam CTs in 32 of 101 men to assess within-person variability of planned and delivered TD in a longitudinal analysis.

RESULTS: The median planned mTD for short course RT was 0.57 Gy (range 0.06-14.37 Gy) and 0.81 Gy (range 0.36-10.80 Gy) for long course RT. The median planned mTD was similar to the median delivered mTD in the 32 men analysed over the entire course of RT (p=0.84). The mTD did not change significantly over time of planning and delivering RT. The variation in proximity between testes and planning target volume (PTV) was related to within-person variability of mTD in men on the 50th and 75th percentile of mTD and as expected the absolute difference between planned and delivered mTD increased with higher mTD.

CONCLUSION: Testicular doses calculated based on plan-CT are an accurate estimation of delivered TD based on repeated cone beam (CB)CT. The within-person variability of TD is related to variation in proximity between testes and PTV in men with moderate to high TD.
Aromatase inhibitors in the treatment of oligozoospermic or azoospermic men: a systematic review of randomized controlled trials. [Review]
Ribeiro MA; Gameiro LF; Scarano WR; Briton-Jones C; Kapoor A; Rosa MB; El Dib R.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
JBRA Assisted Reproduction. 20(2):82-8, 2016 May 01.
The aim of this study was to analyze published evidence regarding the effectiveness of aromatase inhibitor therapy on improving spermatogenesis in infertile men. We carried out a systematic review of randomized controlled trials. The date of the most recent search was October 4, 2015. Two authors independently selected relevant clinical trials, assessing their methodological quality and extracting data. Three studies were included in this review with a total of 100 participants; however, we were able to include data from only 54 participants in the analysis. In the representation of meta-analysis with a single study comparing testolactone versus placebo, related to the hormone concentrations, there was a statistically significance difference favoring the use of testolactone for Luteinizing Hormone (LH); Estrogen (E2); free Testosterone (free T); free Estrogen (free E2); 17-Hydroxyprogesterone (17OHP); prolactin (PRL). In another analysis from a single study comparing letrozole versus anastrozole, there was also a statistically significance difference favoring the use of letrozole for the increase in both the sperm count and LH. There is only low quality evidence regarding the effectiveness of aromatase inhibitor therapy in infertile men. Further trials are needed with standardized interventions and outcomes.

Status
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El Dib, Regina. McMaster Institute of Urology, at St. Joseph's Healthcare, Hamilton, ON, Canada. El Dib, Regina. Department of Anesthesiology, Faculdade de Medicina de Botucatu (FMB), Sao Paulo State University, UNESP, Botucatu, SP, Brazil.
Date Created
20160601
Year of Publication
Acute endothelial response to testosterone gel administration in men with severe hypogonadism and its relationship to androgen receptor polymorphism: a pilot study.

Franchomano D; Fattorini G; Gianfrilli D; Paoli D; Sgro P; Radicioni A; Romanelli F; Di Luigi L; Gandini L; Lenzi A; Aversa A.

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present


[Journal Article. Randomized Controlled Trial]

UI: 26162521

PURPOSE: Testosterone (T) exerts different effects on the cardiovascular system. Despite this knowledge, the acute vascular effect of androgen remains still poorly understood.

METHODS: We investigated the acute effects of T on vascular function in ten men (18-40 years age) with hypogonadism and severe hypotestosteronemia [serum total testosterone (TT) = 0.6 +/- 0.3 ng/mL]. In a 4-day double-blind, randomized, placebo-controlled crossover study, we administered 80 mg daily dose of transdermal-T gel (TG) and evaluated endothelial variations with Endopat2000 (reactive hyperemia index, RHI and the augmentation index, AI); also, CAG repeat polymorphism in exon 1 of the androgen receptor gene was investigated.

RESULTS: After TG administration, RHI significantly improved at 4 h (p < 0.05), while AI improvement was recorded at 4 and 96 h, also when adjusted for heart rate (AI@75; p < 0.01 and p < 0.001, respectively). Direct relationships between DELTAT, DELTADHT and DELTARHI variations (r = 0.37, p < 0.01; r = 0.17, p < 0.05, respectively) as well as between "CAG repeats" length and DELTALnRHI at 96 h (p < 0.03, r (2) = 0.47) were found. An inverse relationship between DELTAT and DELTAAI (p < 0.01, r = -0.35) and DELTAAI@75 (p < 0.01, r = -0.38) were found.

CONCLUSION: Administration of TG causes an acute vasodilation and improves arterial stiffness probably due to non-genomic actions of T. Endothelial vasodilatory response was more pronounced depending on higher plasma TT and DHT levels attained. Clinical implications in elderly frail populations are discussed.

Status

MEDLINE
Elastography to assess the effect of varicoceles on testes: a prospective controlled study.
Dede O; Teke M; Daggulli M; Utangac M; Bas O; Penbegul N.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Controlled Clinical Trial. Journal Article]
UI: 26011193
Varicoceles are the most common and treatable cause of male infertility. The pathophysiology of varicoceles primarily includes elevated temperature, adrenal hormone reflux, gonadotoxic metabolite reflux, altered testicular blood flow, antisperm antibody formation and oxidative stress. The diagnosis of a varicocele is mainly clinical. However, a Doppler ultrasound is used to obtain clinical data and to more accurately measure testicular size. Acoustic radiation force impulse (ARFI) is an additional technique to simultaneously show different areas with different densities in a colour-coded image and a B-mode or greyscale image. This can be used for structural analysis of testicular tissue and has become an additional method for detecting pathologic tissue alterations. We enrolled 30 patients who had clinically diagnosed with left varicoceles and male infertility (Group 1). All patients were evaluated by history taking, physical examination, a spermiogram and an endocrine profile. Thirty control patients (Group 2) were randomly chosen from patients who had applied to an andrology clinic for infertility; their physical examinations and laboratory results showed normal findings. Mean elastography results were significantly different between the groups, and significantly lower in patients who had varicoceles. The relationship between hormonal profiles and elastography parameters was calculated as statistically significant negative correlations between FSH and elasticity. Additionally, a negative correlation was determined between varicocele grade and elasticity of testes. In conclusion, our prospective study showed that ARFI imaging may be more useful than palpation for determining early damage of testicular structure by varicoceles.
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Status
MEDLINE
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The association between polymorphism of androgen receptor gene CAG (AR-CAG) and male infertility in several studies was controversial. Based on studies on association between AR-CAG repeat length and male infertility in recent years, an updated meta-analysis is needed. We aimed to evaluate the association between AR-CAG repeat length and male infertility in advantage of the data in all published reports. We searched for reports published before August 2015 using PubMed, CNKI, VIP, and WanFang. Data on sample size, mean, and standard deviation (SD) of AR-CAG repeat length were extracted independently by 3 investigators. Forty-four reports were selected based on criteria. The overall infertile patients and azoospermic patients were found to have longer AR-CAG repeat length (standard mean difference (SMD) = 0.19, 95% confidence interval (CI): 0.10-0.28, P < 0.01; SMD = 0.36, 95% CI: 0.10-0.61, P < 0.01). AR-CAG repeat length was longer in infertile men in Asian, Caucasian, and mixed races (SMD = 0.25, 95% CI: 0.08-0.43, P <0.01; SMD = 0.13, 95% CI: 0.02-0.25, P <0.05; SMD = 0.39, 95% CI: 0.15-0.63, P <0.01). The overall study shows that increased AR-CAG repeat length was associated with male infertility. The subgroup study on races shows that increased AR-CAG repeat length was associated with male infertility in Asian, Caucasian, and mixed races. Increased AR-CAG repeat
length was also associated with azoospermia. This meta-analysis supports that increased androgen receptor CAG length is capable of causing male infertility susceptibility.

Status
MEDLINE

Authors Full Name
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2016

371.
A randomized, double-blind, placebo-controlled study of escitalopram in patients with social anxiety disorder in Japan.
Asakura S; Hayano T; Hagino A; Koyama T.
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OBJECTIVE: This randomized, double-blind placebo-controlled study compared the efficacy and tolerability of escitalopram (10 and 20mg/day) in Japanese patients with social anxiety disorder (SAD).

RESEARCH DESIGN AND METHODS: Patients aged 18-64 years with a primary diagnosis of DSM-IV-TR defined SAD, a Liebowitz Social Anxiety Scale Japanese version (LSAS-J) total score $>60$ and a Clinical Global Impression-Severity (CGI-S) score $>4$ at baseline were randomly assigned (1:1:1) to placebo, escitalopram 10mg or escitalopram 20mg. The primary endpoint was change from baseline to Week 12 in the LSAS-J total score for both escitalopram 10mg and 20mg versus placebo (ANCOVA, FAS, LOCF), using a hierarchical testing procedure. Pre-specified secondary endpoints included LSAS-J sensitivity analyses.

CLINICAL TRIAL REGISTRATION: This study has the www.japic.or.jp identifier: JapicCTI-121842.

RESULTS: For the primary efficacy endpoint, the difference from placebo in the LSAS-J was $-3.9$ (p=0.089) for escitalopram 10mg. Since the superiority of escitalopram 10mg over placebo was not confirmed, an analysis without multiplicity adjustment was made, which showed a difference for escitalopram 20mg versus placebo of $-9.8$ (p<0.001). In pre-specified sensitivity analyses, the difference versus placebo was $-4.9$ (p=0.035) (ANCOVA, FAS, OC) and $-5.0$ (p=0.028) (MMRM, FAS) (escitalopram 10mg) and $-10.1$ (p<0.001) (ANCOVA, FAS, OC) and $-10.6$ (p<0.001) (MMRM, FAS) (escitalopram 20mg). Common adverse events (incidence $>5\%$ and significantly different from placebo) were somnolence, nausea and ejaculation disorder.

CONCLUSION: Escitalopram was efficacious, safe and well tolerated by patients with SAD in Japan. Study limitations are discussed including patient characteristics.

Status
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Date Created
20160322
Late-onset hypogonadism: the advantages of treatment with human chorionic gonadotropin rather than testosterone.

La Vignera S; Condorelli RA; Cimino L; Russo GI; Morgia G; Calogero AE.

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[Journal Article. Randomized Controlled Trial]

UI: 26488941

The traditional pharmacological treatment of patients with late onset hypogonadism (LOH) is represented by different formulations of testosterone (T) or alternatively by the extractive human chorionic gonadotropin (HCG). The hormone replacement treatment (HRT) is associated with the potential increase of hematocrit, serum concentrations of prostate-specific antigen (PSA) and prostate volume. Moreover, the gynecomastia represent a condition frequently associated with HRT. Recent evidences showed the role of leydig cells in the 25-hydroxylation of vitamin D and the elevated frequency of hypovitaminosis D among LOH patients. Finally, another important aspect of LOH is represented by the frequency of secondary infertility due to age or to traditional HRT. This study evaluated 40 LOH patients treated for 6 months with extractive HCG (n=10 patients) and three different formulations of T: transdermal (n=10 patients), undecaonate (n=10 patients) and enantate (n=10 patients). Hormonal, anthropometric, metabolic and sperm parameters were evaluated and compared. Moreover, the main safety parameters and the results of the main questionnaires were evaluated. After treatment, HCG group showed serum concentrations of 25-OH-vitamin D significantly higher (p<0.05) and serum concentrations of oestrogens significantly lower (p<0.05) compared with other groups. Moreover, they showed a mean value of hematocrit, PSA and prostate volume significantly lower (p<0.05) compared with other groups. Finally, all the groups treated with T showed a significant reduction (p<0.05) of sperm density and of percentage of spermatozoa with progressive motility compared with HCG group.

Status

MEDLINE
Incarcerated Inguinal Hernia Mesh Repair: Effect on Testicular Blood Flow and Sperm Autoimmunity.

Krnic D; Druzijanic N; Stula I; Capkun V; Krnic D.
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Medical Science Monitor. 22:1524-33, 2016 May 05.
[Clinical Trial. Journal Article. Research Support, Non-U.S. Gov't]
UI: 27149257

BACKGROUND The aim of our study was to determine an influence of incarcerated inguinal hernia mesh repair on testicular circulation and to investigate consequent sperm autoimmunity as a possible reason for infertility. MATERIAL AND METHODS This prospective study was performed over a 3-year period, and 50 male patients were included; 25 of these patients underwent elective open mesh hernia repair (Group I). Group II consisted of 25 patients who had surgery for incarcerated inguinal hernia. Doppler ultrasound evaluation of the testicular blood flow and blood samplings for antisperm antibodies (ASA) was performed in all patients before the surgery, on the second day, and 5 months after. Main outcome ultrasound measures were resistive index (RI) and pulsative index (PI), as their values are inversely proportional to testicular
blood flow. RESULTS In Group I, RI, and PI temporarily increased after surgery and then returned to basal values in the late postoperative period. Friedman analysis showed a significant difference in RI and PI for all measurements in Group II (p<0.05), with a significant decrease between the preoperative, early, and late postoperative periods. All final values were within reference range, including ASA, despite significant increase of ASA in the late postoperative period. CONCLUSIONS Although statistically significant differences in values of testicular flow parameters and immunologic sensitization in observed time, final values remained within the reference ranges in all patients. Our results suggest that the polypropylene mesh probably does not cause any clinically significant effect on testicular flow and immunologic response in both groups of patients.

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Gr/gr deletions on Y-chromosome correlate with male infertility: an original study, meta-analyses, and trial sequential analyses.

Bansal SK; Jaiswal D; Gupta N; Singh K; Dada R; Sankhwar SN; Gupta G; Rajender S.

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Scientific Reports. 6:19798, 2016 Feb 15.

[Journal Article. Meta-Analysis. Research Support, Non-U.S. Gov't]

UI: 26876364

We analyzed the AZFc region of the Y-chromosome for complete (b2/b4) and distinct partial deletions (gr/gr, b1/b3, b2/b3) in 822 infertile and 225 proven fertile men. We observed complete AZFc deletions in 0.97% and partial deletions in 6.20% of the cases. Among partial deletions, the frequency of gr/gr deletions was the highest (5.84%). The comparison of partial deletion data between cases and controls suggested a significant association of the gr/gr deletions with infertility (P = 0.0004); however, the other partial deletions did not correlate with infertility. In cohort analysis, men with gr/gr deletions had a relatively poor sperm count (54.20 +/- 57.45 million/ml) in comparison to those without deletions (72.49 +/- 60.06), though the difference was not statistically significant (p = 0.071). Meta-analysis also suggested that gr/gr deletions are significantly associated with male infertility risk (OR = 1.821, 95% CI = 1.39-2.37, p = 0.000). We also performed trial sequential analyses that strengthened the evidence for an overall significant association of gr/gr deletions with the risk of male infertility. Another meta-analysis suggested a significant association of the gr/gr deletions with low sperm count. In conclusion, the gr/gr deletions show a strong correlation with male infertility risk and low sperm count, particularly in the Caucasian populations.

Status
MEDLINE

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Gonadotropin suppression in men leads to a reduction in claudin-11 at the Sertoli cell tight junction.

McCabe MJ; Tarulli GA; Laven-Law G; Matthiesson KL; Meachem SJ; McLachlan RI; Dinger ME; Stanton PG.

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[Comparative Study. Journal Article. Randomized Controlled Trial. Research Support, Non-U.S. Gov't]
UI: 26908839

STUDY QUESTION: Are Sertoli cell tight junctions (TJs) disrupted in men undergoing hormonal contraception?

SUMMARY ANSWER: Localization of the key Sertoli cell TJ protein, claudin-11, was markedly disrupted by 8 weeks of gonadotropin suppression, the degree of which was related to the extent of adluminal germ cell suppression.

WHAT IS KNOWN ALREADY: Sertoli cell TJs are vital components of the blood-testis barrier (BTB) that sequester developing adluminal meiotic germ cells and spermatids from the vascular compartment. Claudin-11 knockout mice are infertile; additionally claudin-11 is spatially disrupted in chronically gonadotropin-suppressed rats coincident with a loss of BTB function, and claudin-11 is disorganized in various human testicular disorders. These data support the Sertoli cell TJ as a potential site of hormonal contraceptive action.
STUDY DESIGN, SIZE, DURATION: BTB proteins were assessed by immunohistochemistry (n = 16 samples) and mRNA (n = 18 samples) expression levels in available archived testis tissue from a previous study of 22 men who had undergone 8 weeks of gonadotropin suppression and for whom meiotic and post-meiotic germ cell numbers were available. The gonadotropin suppression regimens were (i) testosterone enanthate (TE) plus the GnRH antagonist, acyline (A); (ii) TE + the progestin, levonorgestrel, (LNG); (iii) TE + LNG + A or (iv) TE + LNG + the 5alpha-reductase inhibitor, dutasteride (D). A control group consisted of seven additional men, with three archived samples available for this study.

PARTICIPANTS/MATERIALS, SETTINGS, METHODS: Immunohistochemical localization of claudin-11 (TJ) and other junctional type markers [ZO-1 (cytoplasmic plaque), beta-catenin (adherens junction), connexin-43 (gap junction), vinculin (ectoplasmic specialization) and beta-actin (cytoskeleton)] and quantitative PCR was conducted using matched frozen testis tissue.

MAIN RESULTS AND THE ROLE OF CHANCE: Claudin-11 formed a continuous staining pattern at the BTB in control men. Regardless of gonadotropin suppression treatment, claudin-11 localization was markedly disrupted and was broadly associated with the extent of meiotic/post-meiotic germ cell suppression; claudin-11 staining was (i) punctate (i.e. 'spotty' appearance) at the basal aspect of tubules when the average numbers of adluminal germ cells were <15% of control, (ii) presented as short fragments with cytoplasmic extensions when numbers were 15-25% of control or (iii) remained continuous when numbers were >40% of control. Changes in localization of connexin-43 and vinculin were also observed (smaller effects than for claudin-11) but ZO-1, beta-catenin and beta-actin did not differ, compared with control.

LIMITATIONS, REASONS FOR CAUTION: Claudin-11 was the only Sertoli cell TJ protein investigated, but it is considered to be the most pivotal of constituent proteins given its known implication in infertility and BTB function. We were limited to testis samples which had been gonadotropin-suppressed for 8 weeks, shorter than the 74-day spermatogenic wave, which may account for the heterogeneity in claudin-11 and germ cell response observed among the men. Longer suppression (12-24 weeks) is known to suppress germ cells further and claudin-11 disruption may be more uniform, although we could not access such samples.

WIDER IMPLICATIONS OF THE FINDINGS: These findings are important for our understanding of the sites of action of male hormonal contraception, because they suggest that BTB function could be ablated following long-term hormone suppression treatment.

STUDY FUNDING/COMPETING INTERESTS: National Health and Medical Research Council (Australia) Program Grants 241000 and 494802; Research Fellowship 1022327 (to R.I.M.) and the Victorian Government’s Operational Infrastructure Support Program. None of the authors have any conflicts to disclose.

TRIAL REGISTRATION NUMBER: Not applicable.
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Thiocolchicoside has long been used as a muscle relaxant, despite a lack of proven efficacy beyond the placebo effect. Its chemical structure consists of colchicine, a sugar (ose) and a sulphur-containing radical (thio), and its adverse effects are therefore likely to be similar to those of colchicine. Using the standard Prescrire methodology, we reviewed the available data on the adverse effects of thiocolchicoside. Liver injury, pancreatitis, seizures, blood cell disorders, severe cutaneous disorders, rhabdomyolysis and reproductive disorders have all been recorded in the French and European pharmacovigilance databases and in the periodic updates that the companies concerned submit to regulatory agencies. These data do not specify the frequency of the disorders nor do they identify the most susceptible patient populations. Thiocolchicoside is teratogenic in experimental animals and also damages chromosomes. Human data are limited to a follow-up of about 30 pregnant women (no major malformations) and reports of altered spermatogenesis, including cases of azoospermia. In practice, there is no justification for exposing patients to the adverse effects of thiocolchicoside. It is better to use an effective, well-known analgesic for patients complaining of muscle pain, starting with paracetamol.
Psychological and educational interventions for subfertile men and women. [Review]
Verkuijlen J; Verhaak C; Nelen WL; Wilkinson J; Farquhar C.
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Cochrane Database of Systematic Reviews. 3:CD011034, 2016 Mar 31.
[Journal Article. Research Support, Non-U.S. Gov't. Review]
UI: 27031818

BACKGROUND: Approximately one-fifth of all subfertile couples seeking fertility treatment show clinically relevant levels of anxiety, depression, or distress. Psychological and educational interventions are frequently offered to subfertile couples, but their effectiveness, both in improving mental health and pregnancy rates, is unclear.

OBJECTIVES: To assess the effectiveness of psychological and educational interventions for subfertile couples on psychological and fertility treatment outcomes.

SEARCH METHODS: We searched (from inception to 2 April 2015) the Cochrane Gynaecology and Fertility Group Specialised Register of Controlled Trials, the Cochrane Central Register of Controlled Trials (CENTRAL; Issue 2, 2015), MEDLINE, EMBASE, PsycINFO, EBSCO CINAHL, DARE, Web of Science, OpenGrey, LILACS, PubMed, and ongoing trials registers. We handsearched reference lists and contacted experts in the field.

SELECTION CRITERIA: We included published and unpublished randomised controlled trials (RCTs), cluster randomised trials, and cross-over trials (first phase) evaluating the effectiveness of psychological and educational interventions on psychological and fertility treatment outcomes in subfertile couples.

DATA COLLECTION AND ANALYSIS: Two review authors independently assessed trial risk of bias and extracted data. We contacted study authors for additional information. Our primary outcomes were psychological measures (anxiety and depression) and fertility rates (live birth or ongoing pregnancy). We assessed the overall quality of the evidence using GRADE criteria. As we did not consider the included studies to be sufficiently similar to permit meaningful pooling, we summarised the results of the individual studies by presenting the median and interquartile range (IQR) of effects as well as the minimum and maximum values. We calculated standardised mean differences (SMDs) for continuous variables and odds ratios (ORs) for dichotomous outcomes.
MAIN RESULTS: We included 39 studies involving 4925 participants undergoing assisted reproductive technology. Studies were heterogeneous with respect to a number of factors, including nature and duration of interventions, participants, and comparator groups. As a result, we judged that pooling results would not result in a clinically meaningful estimate of a treatment effect. There were substantial methodological weaknesses in the studies, all of which were judged to be at high risk of bias for one or more quality assessment domains. There was concern about attrition bias (24 studies), performance bias for psychological outcomes (27 studies) and fertility outcomes (18 studies), and detection bias for psychological outcomes (26 studies). We therefore considered study-specific estimates of intervention effects to be unreliable. Thirty-three studies reported the outcome mental health. Only two studies reported the outcome live birth, and both of these had substantial attrition. One study reported ongoing pregnancy, again with substantial attrition. We have combined live birth and ongoing pregnancy in one outcome.

Psychological outcomes: Studies utilised a variety of measures of anxiety and depression. In all cases a low score denoted benefit from the intervention. SMDs for anxiety were as follows: psychological interventions versus attentional control or usual care: median (IQR) = -0.30 (-0.84 to 0.00), minimum value -5.13; maximum value 0.84, 17 RCTs, 2042 participants; educational interventions versus attentional control or usual care: median = 0.03, minimum value -0.38; maximum value 0.23, 4 RCTs, 330 participants. SMDs for depression were as follows: psychological interventions versus attentional control or usual care: median (IQR) = -0.45 (-0.68 to -0.08), minimum value -3.01; maximum value 1.23, 12 RCTs, 1160 participants; educational interventions versus attentional control or usual care: median = -0.33, minimum value -0.46; maximum value 0.17, 3 RCTs, 304 participants. Fertility outcomes: When psychological interventions were compared with attentional control or usual care, ORs for live birth or ongoing pregnancy ranged from minimum value 1.13 to maximum value 10.05. No studies of educational interventions reported this outcome.

AUTHORS’ CONCLUSIONS: The effects of psychological and educational interventions on mental health including distress, and live birth or ongoing pregnancy rates is uncertain due to the very low quality of the evidence. Existing trials of psychological and educational interventions for subfertility were generally poorly designed and executed, resulting in very serious risk of bias and serious inconsistency in study findings. There is a need for studies employing appropriate methodological techniques to investigate the benefits of these treatments for this population. In particular, attentional control groups should be employed, that is groups receiving a treatment that mimics the amount of time and attention received by the treatment group but is not thought to have a specific effect upon the participants, in order to distinguish between therapeutic and non-specific effects of interventions. Where attrition cannot be minimised, appropriate statistical techniques for handling drop-out must be applied. Failure to address these issues in study design
has resulted in studies that do not provide a valid basis for answering questions about the effectiveness of these interventions.

Status
MEDLINE

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[Review]
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[Journal Article. Research Support, Non-U.S. Gov't. Review]
UI: 27030583

Infertility and adverse pregnancy outcomes are significant public health concerns with global prevalence. Over the past 35 years, research has addressed whether exposure to power-frequency magnetic fields is one of the etiologic factors attributed to these conditions. However, no apparent authoritative reviews on this topic have been published in the peer-reviewed literature for nearly 15 years. This review provides an overview and critical analysis of human studies that were published in the peer-reviewed literature between 2002 and July 2015. Using PubMed, 13 epidemiology studies published during this time frame that concern exposure to magnetic fields and adverse prenatal (e.g., miscarriage), neonatal (e.g., preterm birth or birth
defects), and male fertility (e.g., poor semen quality) outcomes were identified. Some of these studies reported associations whereas others did not, and study design limitations may explain these inconsistencies. Future investigations need to be designed with these limitations in mind to address existing research gaps. In particular, the following issues are discussed: (1) importance of selecting the appropriate study population, (2) need for addressing confounding due to unmeasured physical activity, (3) importance of minimizing information bias from exposure measurement error, (4) consideration of alternative magnetic field exposure metrics, and (5) implications and applications of personal exposure data that are correlated within female-male couples. Further epidemiologic research is needed, given the near ubiquitous exposures to power-frequency magnetic fields in the general population.

Status
MEDLINE

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Treatment for osteoporosis in people with s-thalassaemia. [Review]
Bhardwaj A; Swe KM; Sinha NK; Osunkwo I.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present Cochrane Database of Systematic Reviews. 3:CD010429, 2016 Mar 10.
UI: 26964506

BACKGROUND: Osteoporosis is a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture. Osteoporosis represents an important cause of morbidity in people with beta-thalassaemia and its pathogenesis is multifactorial. Factors include bone marrow expansion due to ineffective erythropoiesis, resulting in reduced trabecular bone tissue with cortical thinning; endocrine dysfunction secondary to excessive iron loading, leading to increased bone turnover; and lastly, a predisposition to physical inactivity due to disease complications with a subsequent reduction in optimal bone mineralization. A number of therapeutic strategies have been applied to treat osteoporosis in people with beta-thalassaemia, which include bisphosphonates, with or without, hormone replacement therapy. There are various forms of bisphosphonates, such as clodronate, pamidronate, alendronate and zoledronic acid. Other treatments include calcitonin, calcium, zinc supplementation, hydroxyurea and hormone replacement therapy for preventing hypogonadism.

OBJECTIVES: To review the evidence on the efficacy and safety of treatment for osteoporosis in people with beta-thalassaemia.

SEARCH METHODS: We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group's Haemoglobinopathies Trials Register comprising references identified from comprehensive electronic database searches and handsearches of relevant journals and abstract books of conference proceedings. Date of most recent search: 04 February 2016.

SELECTION CRITERIA: Randomised, placebo-controlled trials in people with thalassaemia with a bone mineral density z score of less than -2 standard deviations for: children less than 15 years
old; adult males (15 to 50 years old); and all pre-menopausal females above 15 years and a bone mineral density t score of less than -2.5 standard deviations for post-menopausal females and males above 50 years old.

DATA COLLECTION AND ANALYSIS: Two review authors assessed the eligibility and risk of bias of the included trials, extracted and analysed data and completed the review. We summarised results using risk ratios or rate ratios for dichotomous data and mean differences for continuous data. We combined trial results where appropriate.

MAIN RESULTS: Four trials (with 211 participants) were included; three trials investigated the effect of bisphosphonate therapies and one trial investigated the effect of zinc supplementation. Only one trial was judged to be of good quality (low risk of bias); the remaining trials had a high or unclear risk of bias in at least one key domain. One trial (data not available for analysis) assessing the effect of neridronate (118 participants) reported significant increases in favour of the bisphosphonate group for bone mineral density at the lumbar spine and hip at both six and 12 months. For the femoral neck, a significant difference was noted at 12 months only. A further trial (25 participants) assessed the effect of alendronate and clodronate and found that after two years, bone mineral density increased significantly in the alendronate and clodronate groups as compared to placebo at the lumbar spine, mean difference 0.14 g/cm(2) (95% confidence interval 0.05 to 0.22) and at the femoral neck, mean difference 0.40 g/cm(2) (95% confidence interval 0.22 to 0.57). One 12-month trial (26 participants) assessed the effects of different doses of pamidronate (30 mg versus 60 mg) and found a significant difference in bone mineral density in favour of the 60 mg dose at the lumbar spine and forearm, mean difference 0.43 g/cm(2) (95% CI 0.10 to 0.76), mean difference 0.87 g/cm(2) (95% CI 0.23 to 1.51), respectively, but not at the femoral neck. In a zinc sulphate supplementation trial (42 participants), bone mineral density increased significantly compared to placebo at the lumbar spine after 12 months (37 participants), mean difference 0.15 g/cm(2) (95% confidence interval 0.10 to 0.20) and after 18 months (32 participants), mean difference 0.34 g/cm(2) (95% confidence interval 0.28 to 0.40). The same was true for bone mineral density at the hip after 12 months, mean difference 0.15 g/cm(2) (95% confidence interval 0.11 to 0.19) and after 18 months, mean difference 0.26 g/cm(2) (95% confidence interval 0.21 to 0.31). Fractures were not observed in one trial and not reported in three trials. There were no major adverse effects reported in two of the bisphosphonate trials; in the neridronate trial there was a reduction noted in the use of analgesic drugs and in the reported back pain score in favour of bisphosphonate treatment. Adverse effects were not reported in the trial of different doses of pamidronate or the zinc supplementation trial.

AUTHORS’ CONCLUSIONS: There is evidence to indicate an increase in bone mineral density at the femoral neck, lumbar spine and forearm after administration of bisphosphonates and at the lumbar spine and hip after zinc sulphate supplementation. The authors recommend that further
long-term randomised control trials on different bisphosphonates and zinc supplementation therapies in people with beta-thalassaemia and osteoporosis are undertaken.

Status
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380.
Assisted reproductive technologies for male subfertility. [Review][Update of Cochrane Database Syst Rev. 2007;(4):CD000360; PMID: 17943739]
Cissen M; Bensdorp A; Cohlen BJ; Repping S; de Bruin JP; van Wely M.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Cochrane Database of Systematic Reviews. 2:CD000360, 2016 Feb 26.
UI: 26915339

BACKGROUND: Intra-uterine insemination (IUI), in vitro fertilisation (IVF) and intracytoplasmic sperm injection (ICSI) are frequently used fertility treatments for couples with male subfertility. The use of these treatments has been subject of discussion. Knowledge on the effectiveness of fertility treatments for male subfertility with different grades of severity is limited. Possibly, couples are exposed to unnecessary or ineffective treatments on a large scale.

OBJECTIVES: To evaluate the effectiveness and safety of different fertility treatments (expectant management, timed intercourse (TI), IUI, IVF and ICSI) for couples whose subfertility appears to be due to abnormal sperm parameters.

SEARCH METHODS: We searched for all publications that described randomised controlled trials (RCTs) of the treatment for male subfertility. We searched the Cochrane Menstrual
Disorders and Subfertility Group Specialised Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL, PsycINFO and the National Research Register from inception to 14 April 2015, and web-based trial registers from January 1985 to April 2015. We applied no language restrictions. We checked all references in the identified trials and background papers and contacted authors to identify relevant published and unpublished data.

SELECTION CRITERIA: We included RCTs comparing different treatment options for male subfertility. These were expectant management, TI (with or without ovarian hyperstimulation (OH)), IUI (with or without OH), IVF and ICSI. We included only couples with abnormal sperm parameters.

DATA COLLECTION AND ANALYSIS: Two review authors independently selected the studies, extracted data and assessed risk of bias. They resolved disagreements by discussion with the rest of the review authors. We performed statistical analyses in accordance with the guidelines for statistical analysis developed by The Cochrane Collaboration. The quality of the evidence was rated using the GRADE methods. Primary outcomes were live birth and ovarian hyperstimulation syndrome (OHSS) per couple randomised.

MAIN RESULTS: The review included 10 RCTs (757 couples). The quality of the evidence was low or very low for all comparisons. The main limitations in the evidence were failure to describe study methods, serious imprecision and inconsistency. IUI versus TI (five RCTs)Two RCTs compared IUI with TI in natural cycles. There were no data on live birth or OHSS. We found no evidence of a difference in pregnancy rates (2 RCTs, 62 couples: odds ratio (OR) 4.57, 95% confidence interval (CI) 0.21 to 102, very low quality evidence; there were no events in one of the studies). Three RCTs compared IUI with TI both in cycles with OH. We found no evidence of a difference in live birth rates (1 RCT, 81 couples: OR 0.89, 95% CI 0.30 to 2.59; low quality evidence) or pregnancy rates (3 RCTs, 202 couples: OR 1.51, 95% CI 0.74 to 3.07; I(2) = 11%, very low quality evidence). One RCT reported data on OHSS. None of the 62 women had OHSS. One RCT compared IUI in cycles with OH with TI in natural cycles. We found no evidence of a difference in live birth rates (1 RCT, 44 couples: OR 3.14, 95% CI 0.12 to 81.35; very low quality evidence). Data on OHSS were not available. IUI in cycles with OH versus IUI in natural cycles (five RCTs) We found no evidence of a difference in live birth rates (3 RCTs, 346 couples: OR 1.34, 95% CI 0.77 to 2.33; I(2) = 0%, very low quality evidence) and pregnancy rates (4 RCTs, 399 couples: OR 1.68, 95% CI 1.00 to 2.82; I(2) = 0%, very low quality evidence). There were no data on OHSS. IVF versus IUI in natural cycles or cycles with OH (two RCTs) We found no evidence of a difference in live birth rates between IVF versus IUI in natural cycles (1 RCT, 53 couples: OR 0.77, 95% CI 0.25 to 2.35; low quality evidence) or IVF versus IUI in cycles with OH (2 RCTs, 86 couples: OR 1.03, 95% CI 0.43 to 2.45; I(2) = 0%, very low quality evidence). One RCT reported data on OHSS. None of the women had OHSS. Overall, we found no evidence of a
difference between any of the groups in rates of live birth, pregnancy or adverse events (multiple pregnancy, miscarriage). However, most of the evidence was very low quality. There were no studies on IUI in natural cycles versus TI in stimulated cycles, IVF versus TI, ICSI versus TI, ICSI versus IUI (with OH) or ICSI versus IVF.

AUTHORS' CONCLUSIONS: We found insufficient evidence to determine whether there was any difference in safety and effectiveness between different treatments for male subfertility. More research is needed.

Status
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381.
Apparently-Different Clearance Rates from Cohort Studies of Mycoplasma genitalium Are Consistent after Accounting for Incidence of Infection, Recurrent Infection, and Study Design. Smieszek T; White PJ.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Clinical Trial. Journal Article. Multicenter Study. Research Support, Non-U.S. Gov't]
UI: 26910762
Mycoplasma genitalium is a potentially major cause of urethritis, cervicitis, pelvic inflammatory disease, infertility, and increased HIV risk. A better understanding of its natural history is crucial to informing control policy. Two extensive cohort studies (students in London, UK; Ugandan sex workers) suggest very different clearance rates; we aimed to understand the reasons and obtain
improved estimates by making maximal use of the data from the studies. As M. genitalium is a sexually-transmitted infectious disease, we developed a model for time-to-event analysis that incorporates the processes of (re)infection and clearance, and fitted to data from the two cohort studies to estimate incidence and clearance rates under different scenarios of sexual partnership dynamics and study design (including sample handling and associated test sensitivity). In the London students, the estimated clearance rate is 0.80 p.a. (mean duration 15 months), with incidence 1.31%-3.93% p.a. Without adjusting for study design, corresponding estimates from the Ugandan data are 3.44 p.a. (mean duration 3.5 months) and 58% p.a. Apparent differences in clearance rates are probably mostly due to lower testing sensitivity in the Uganda study due to differences in sample handling, with 'true' clearance rates being similar, and adjusted incidence in Uganda being 28% p.a. Some differences are perhaps due to the sex workers having more-frequent antibiotic treatment, whilst reinfection within ongoing sexual partnerships might have caused some of the apparently-persistent infection in the London students. More information on partnership dynamics would inform more accurate estimates of natural-history parameters.

Detailed studies in men are also required.

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A Perspective on the Evolving Landscape in Male Reproductive Medicine.
Bhasin S.

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[Journal Article. Research Support, Non-U.S. Gov't]

UI: 26908110

CONTEXT: Men's health and aging are emerging as important areas of research opportunity because of advances in reproductive biology and the recognition of men's health as a unique and important aspect of public health.

EVIDENCE ACQUISITION: A perspective of the evolving landscape in male reproductive medicine.

EVIDENCE SYNTHESIS: Remarkable discoveries in reproductive biology have greatly advanced the treatment of erectile dysfunction, androgen deficiency, infertility, hormone sensitive cancers, and prostate diseases. Although the off-label use of testosterone in middle-aged and older men has grown, the management of androgen deficiency syndromes remains suboptimal. There is a pressing need for wider adoption of accurate testosterone assays and harmonized reference ranges and large randomized trials of testosterone's efficacy and cardiovascular and prostate safety. The transformation in idealized body image towards greater muscularity has contributed to increasing prevalence of body image disorders and the use of muscle building drugs in men. Therapeutic options for fertility regulation in men remain limited, the pathophysiologic basis of infertility in a vast majority of infertile men remains unknown, and assisted reproductive technologies remain inaccessible to many infertile men. Much of the dogma on testosterone's binding to its binding proteins remains inaccurate, and the role of free and albumin-bound testosterone poorly understood. The reproductive health of cancer survivors and the availability of wider contraceptive choices for men are other areas of unmet need. Suboptimal care of transgender persons has framed transgender medicine as an important healthcare disparities issue.

CONCLUSIONS: Transformative changes in societal attitudes towards men's sexual health, body image, and gender identity, and in the economics of reproductive healthcare services, offer extraordinary opportunities for translational science that is patient focused, mechanism based, and integrated with healthcare.
Gonadal steroid-dependent effects on bone turnover and bone mineral density in men.
Finkelstein JS; Lee H; Leder BZ; Burnett-Bowie SA; Goldstein DW; Hahn CW; Hirsch SC; Linker A; Perros N; Servais AB; Taylor AP; Webb ML; Youngner JM; Yu EW.
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[Journal Article. Randomized Controlled Trial. Research Support, Non-U.S. Gov't]
UI: 26901812

BACKGROUND: Severe gonadal steroid deficiency induces bone loss in adult men; however, the specific roles of androgen and estrogen deficiency in hypogonadal bone loss are unclear. Additionally, the threshold levels of testosterone and estradiol that initiate bone loss are uncertain.

METHODS: One hundred ninety-eight healthy men, ages 20-50, received goserelin acetate, which suppresses endogenous gonadal steroid production, and were randomized to treatment with 0, 1.25, 2.5, 5, or 10 grams of testosterone gel daily for 16 weeks. An additional cohort of 202 men was randomized to receive these treatments plus anastrozole, which suppresses conversion of androgens to estrogens. Thirty-seven men served as controls and received placebos for goserelin and testosterone. Changes in bone turnover markers, bone mineral
density (BMD) by dual-energy x-ray absorptiometry (DXA), and BMD by quantitative computed tomography (QCT) were assessed in all men. Bone microarchitecture was assessed in 100 men.

RESULTS: As testosterone dosage decreased, the percent change in C-telopeptide increased. These increases were considerably greater when aromatization of testosterone to estradiol was also suppressed, suggesting effects of both testosterone and estradiol deficiency. Decreases in DXA BMD were observed when aromatization was suppressed but were modest in most groups. QCT spine BMD fell substantially in all testosterone-dose groups in which aromatization was also suppressed, and this decline was independent of testosterone dose. Estradiol deficiency disrupted cortical microarchitecture at peripheral sites. Estradiol levels above 10 pg/ml and testosterone levels above 200 ng/dl were generally sufficient to prevent increases in bone resorption and decreases in BMD in men.

CONCLUSIONS: Estrogens primarily regulate bone homeostasis in adult men, and testosterone and estradiol levels must decline substantially to impact the skeleton.

TRIAL REGISTRATION: ClinicalTrials.gov, NCT00114114.

FUNDING: AbbVie Inc., AstraZeneca Pharmaceuticals LP, NIH.

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PMID
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4767351

BACKGROUND: Intra-uterine insemination (IUI) is a widely used fertility treatment for couples with unexplained subfertility. Although IUI is less invasive and less expensive than in vitro fertilisation (IVF), the safety of IUI in combination with ovarian hyperstimulation (OH) is debated. The main concern about IUI treatment with OH is the increase in multiple pregnancy rate. This is an update of a Cochrane review (Veltman-Verhulst 2012) originally published in 2006 and updated in 2012.

OBJECTIVES: To determine whether, for couples with unexplained subfertility, IUI improves the live birth rate compared with timed intercourse (TI), or expectant management, both with and without ovarian hyperstimulation (OH).

SEARCH METHODS: We searched the Cochrane Gynaecology and Fertility (formerly Cochrane Menstrual Disorders and Subfertility Group) Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library, inception to Issue 11, 2015), Ovid MEDLINE, Ovid EMBASE, PsycINFO and trial registers, all from inception to December 2015 and reference lists of articles. Authors of identified studies were contacted for missing or unpublished data. The evidence is current to December 2015.

SELECTION CRITERIA: Truly randomised controlled trial (RCT) comparisons of IUI versus TI, in natural or stimulated cycles. Only couples with unexplained subfertility were included.

DATA COLLECTION AND ANALYSIS: Two review authors independently performed study selection, quality assessment and data extraction. We extracted outcomes, and pooled data and, where possible, we carried out subgroup and sensitivity analyses.

MAIN RESULTS: We included 14 trials including 1867 women. IUI versus TI or expectant management both in natural cycleLive birth rate (all cycles)There was no evidence of a difference in cumulative live births between the two groups (Odds Ratio (OR) 1.60, 95% confidence interval (CI) 0.92 to 2.78; 1 RCT; n = 334; moderate quality evidence). The evidence suggested that if the chance of a live birth in TI was assumed to be 16%, that of IUI would be between 15% and 34%.Multiple pregnancy rateThere was no evidence of a difference in multiple pregnancy rate between the two treatment groups (OR 0.50, 95% CI 0.04 to 5.53; 1 RCT; n = 334; moderate quality evidence). IUI versus TI or expectant management both in stimulated cycleLive birth rate (all cycles)There was no evidence of a difference between the two treatment groups (OR 1.59, 95% CI 0.88 to 2.88; 2 RCTs; n = 208; I²(2) = 72%; moderate quality evidence). The evidence suggested that if the chance of achieving a live birth in TI was assumed to be 26%, the chance of
a live birth with IUI would be between 23% and 50%. Multiple pregnancy rate. There was no evidence of a difference in multiple pregnancy rates between the two treatment groups (OR 1.46, 95% CI 0.55 to 3.87; 4 RCTs, n = 316; I² = 0%; low quality evidence). IUI in a natural cycle versus IUI in a stimulated cycle Live birth rate (all cycles) An increase in live birth rate was found for women who were treated with IUI in a stimulated cycle compared with those who underwent IUI in natural cycle (OR 0.48, 95% CI 0.29 to 0.82; 4 RCTs, n = 396; I² = 0%; moderate quality evidence). The evidence suggested that if the chance of a live birth in IUI in a stimulated cycle was assumed to be 25%, the chance of a live birth in IUI in a natural cycle would be between 9% and 21%. Multiple pregnancy rate. There was no evidence of a difference in multiple pregnancy rate between the two treatment groups (OR 0.33, 95% CI 0.01 to 0.870; 2 RCTs; n = 65; low quality evidence). IUI in a stimulated cycle versus TI or expectant management in a natural cycle Live birth rate (all cycles) There was no evidence of a difference in live birth rate between the two treatment groups (OR 0.82, 95% CI 0.45 to 1.49; 1 RCT; n = 253; moderate quality evidence). The evidence suggested that if the chance of a live birth in TI or expectant management in a natural cycle was assumed to be 24%, the chance of a live birth in IUI in a stimulated cycle would be between 12% and 32%. Multiple pregnancy rate. There was no evidence of a difference in multiple pregnancy rate between the two treatment groups (OR 2.00, 95% CI 0.18 to 22.34; 2 RCTs; n = 304; moderate quality evidence). IUI in natural cycle versus TI or expectant management in stimulated cycle Live birth rate (all cycles) There was evidence of an increase in live births for IUI (OR 1.95, 95% CI 1.10 to 3.44; 1 RCT, n = 342; moderate quality evidence). The evidence suggested that if the chance of a live birth in TI in a stimulated cycle was assumed to be 13%, the chance of a live birth in IUI in a natural cycle would be between 14% and 34%. Multiple pregnancy rate. There was no evidence of a difference in multiple pregnancy rate between the groups (OR 1.05, 95% CI 0.07 to 16.90; 1 RCT; n = 342; moderate quality evidence). The quality of the evidence was assessed using GRADE methods. Quality ranged from low to moderate, the main limitation being imprecision in the findings for both live birth and multiple pregnancy.

AUTHORS' CONCLUSIONS: This systematic review did not find conclusive evidence of a difference in live birth or multiple pregnancy in most of the comparisons for couples with unexplained subfertility treated with intra-uterine insemination (IUI) when compared with timed intercourse (TI), both with and without ovarian hyperstimulation (OH). There were insufficient studies to allow for pooling of data on the important outcome measures for each of the comparisons.

Status
MEDLINE

Authors Full Name
Veltman-Verhulst, Susanne M; Hughes, Edward; Ayeleke, Reuben Olugbenga; Cohlen, Ben J.
Summary evidence on the effects of varicocele treatment to improve natural fertility in subfertile men. [Review]
Tiseo BC; Esteves SC; Cocuzza MS.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article. Review]
UI: 26806080
The objective of this review was to summarize the evidence concerning the benefit of varicocele treatment to improve natural fertility in subfertile males. We also analyzed the effect of varicocele treatment on conventional semen parameters and sperm functional tests. An electronic search to collect the data was performed using the PubMed/MEDLINE databases until July 2015. Data pooled from a variety of study designs indicate that varicocelectomy improves semen parameters in the majority of the treated men with clinical varicocele and abnormal semen parameters regardless of the chosen surgical method. Surgical varicocele repair was beneficial not only for alleviating oxidative stress-associated infertility but also to improve sperm nuclear DNA integrity. However, given the low magnitude of the effect size in sperm DNA integrity, further research is needed to elucidate its clinical significance. Conflicting results on the effect of varicocele treatment on natural fertility seem to be due to heterogeneous study designs and, more importantly, patient selection criteria. When these issues are controlled, current evidence indicates that treatment of subclinical varicocele is not warranted, as it does not seem to improve fertility. On the contrary, fair evidence indicates that varicocele treatment should be offered to infertile patients with palpable varicocele and abnormal semen parameters. This evidence supports the current guidelines issued by the American Urological Association and European
Association of Urology, which state that varicocele treatment should be offered to male partners of infertile couples presenting for evaluation with clinical varicocele and semen parameters alterations.

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386.
Six months of daily treatment with vardenafil improves parameters of endothelial inflammation and of hypogonadism in male patients with type 2 diabetes and erectile dysfunction: a randomized, double-blind, prospective trial.
Santi D; Granata AR; Guidi A; Pignatti E; Trenti T; Roli L; Bozic R; Zaza S; Pacchioni C; Romano S; Nofer JR; Rochira V; Carani C; Simoni M.

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[Journal Article. Randomized Controlled Trial. Research Support, Non-U.S. Gov't]

UI: 26792933

OBJECTIVE: Type 2 diabetes mellitus (T2DM) is associated with endothelial dysfunction, characterized by a reduction of nitric oxide (NO)-mediated relaxation. Phosphodiesterase type 5 inhibitors (PDE5i) improve NO levels. The aim of the study was to investigate whether long-term, chronic treatment with the PDE5i vardenafil improves systemic endothelial function in diabetic men.
DESIGN: A prospective, investigator-initiated, randomized, placebo-controlled, double-blind, clinical trial was conducted.

METHODS: In total, 54 male patients affected by T2DM, diagnosed within the last 5 years, and erectile dysfunction were enrolled, regardless of testosterone levels. In all, 26 and 28 patients were assigned to verum and placebo groups respectively. The study consisted of an enrollment phase, a treatment phase (24 weeks) (vardenafil/placebo 10 mg twice in a day) and a follow-up phase (24 weeks). Parameters evaluated were as follows: International Index of Erectile Function 15 (IIEF-15), flow-mediated dilation (FMD), serum interleukin 6 (IL6), endothelin 1 (ET-1), gonadotropins and testosterone (measured by liquid chromatography/tandem mass spectrometry).

RESULTS: IIEF-15 erectile function improved during the treatment (P<0.001). At the end of the treatment both FMD (P=0.040) and IL6 (P=0.019) significantly improved. FMD correlated with serum testosterone levels (R(2)=0.299; P<0.001). Testosterone increased significantly under vardenafil treatment and returned in the eugonadal range only in hypogonadal men (n=13), without changes in gonadotropins. Chronic vardenafil treatment did not result in relevant side effects.

CONCLUSION: This is the first double-blind, placebo-controlled clinical trial designed to evaluate the effects of chronic treatment of vardenafil on endothelial health-related parameters and sexual hormones in patients affected by a chronic disease. Chronically administered vardenafil is effective and improves endothelial parameters in T2DM patient. Moreover, chronic vardenafil therapy improves hypogonadism in diabetic, hypogonadal men.

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Comments

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Effect of varicocele on semen characteristics according to the new 2010 World Health Organization criteria: a systematic review and meta-analysis. [Review]
Agarwal A; Sharma R; Harlev A; Esteves SC.
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UI: 26780872
This study investigated the effects of varicocele on semen parameters in infertile men based on the new 2010 World Health Organization laboratory manual for the examination of human semen. Semen analysis results (volume, sperm count, motility, and morphology) were the primary outcomes. An electronic search to collect the data was conducted using the Medline/PubMed, SJU discover, and Google Scholar databases. We searched articles published from 2010 to August 2015, i.e., after the publication of the 2010 WHO manual. We included only those studies that reported the actual semen parameters of adult infertile men diagnosed with clinical varicocele and contained a control group of either fertile men or normozoospermic men who were not diagnosed with varicocele. Ten studies were included in the meta-analysis, involving 1232 men. Varicocele was associated with reduced sperm count (mean difference: -44.48 x 10^6 ml\(^{-1}\); 95% CI: -61.45, -27.51 x 10^6 ml\(^{-1}\); P < 0.001), motility (mean difference: -26.67%; 95% CI: -34.27, -19.08; P < 0.001), and morphology (mean difference: -19.68%; 95% CI: -29.28, -10.07; P < 0.001) but not semen volume (mean difference: -0.23 ml; 95% CI: -0.64, 0.17). Subgroup analyses indicated that the magnitude of effect was influenced by control subtype but not WHO laboratory manual edition used for semen assessment. We conclude that varicocele is a significant risk factor that negatively affects semen quality, but the observed pooled effect size on semen parameters does not seem to be affected by the WHO laboratory manual edition. Given most of the studies published after 2010 still utilized the 1999 manual for semen analysis, further research is required to fully understand the clinical implication of the 2010 WHO laboratory manual on the association between varicocele and semen parameters.
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An update on the role of medical treatment including antioxidant therapy in varicocele. [Review]
Garg H; Kumar R.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article. Review]
UI: 26763549

Varicocele-associated male infertility has classically been managed using surgery or assisted reproductive techniques. With increasing evidence of oxidative stress as a pathophysiological factor in varicocele-associated infertility, medical therapy especially antioxidants might become a treatment option with lower risks. We reviewed the existing literature on the role of various medical agents in the management of male infertility attributed to varicoceles. Medical therapy is typically evaluated in three different situations such as (a) comparison of two drugs or one drug with placebo, (b) comparison of drugs versus surgery, and (c) comparison of drugs as adjuvant therapy with surgery versus drug therapy alone. Due to heterogeneity of data and lack of well-conducted studies, there is insufficient data to recommend routine use of medical therapy for men with varicocele-associated infertility and surgery remains the treatment of choice. Pregnancy and live birth rates are usually not reported in most studies and mere improvement in sperm parameters or antioxidant capacity is insufficient to support its routine use. Antioxidant therapy is a potential option due to its theoretical benefit, data from preclinical studies, and lack of major side effects. Adjuvant therapy with antioxidants after surgical repair of varicocele may improve the outcome and is a potential area for further research.
Sperm Retrieval in Adolescents and Young Adults with Klinefelter Syndrome: A Prospective, Pilot Study.

Nahata L; Yu RN; Paltiel HJ; Chow JS; Logvinenko T; Rosoklija I; Cohen LE.

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present


[Clinical Trial. Journal Article. Research Support, Non-U.S. Gov't]

UI: 26746120

OBJECTIVE: To assess sperm retrieval rates in adolescents and young adults with Klinefelter syndrome, with the ultimate goal of improving fertility in this population. Secondary aims were to evaluate other clinical characteristics of the cohort and identify predictors of sperm retrieval.

STUDY DESIGN: Patients 12-25 years of age with Klinefelter syndrome (47,XXY) were recruited at the Boston Children's Hospital. Physical examination, biochemical evaluation, scrotal ultrasonography, and semen analysis were performed. Neurocognitive data were collected. Microdissection sperm extraction (unilateral micro-testicular sperm extraction) was offered to individuals with no sperm in their ejaculates. Given the small sample size, analysis was primarily descriptive.

RESULTS: Fifteen patients were enrolled. None had sperm in their ejaculates. Ten patients underwent unilateral micro-testicular sperm extraction. Sperm retrieval rate was 50%. From a neurocognitive standpoint, subjects reported problems with peers, conduct, and overall difficulties. Incidentally, one-third of the patients were found to have testicular microlithiasis and 17% of subjects with renal ultrasound imaging had bilateral renal medullary nephrocalcinosis.
CONCLUSIONS: This pilot study suggests that sperm retrieval rates in adolescents and young adults with Klinefelter syndrome are comparable with those reported in older men. However, larger studies are needed to confirm our findings. The clinical significance of the scrotal and renal ultrasound findings merits further investigation.

TRIAL REGISTRATION: ClinicalTrials.gov: NCT01817296.

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20160229

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Genetic evidence that lower circulating FSH levels lengthen menstrual cycle, increase age at menopause and impact female reproductive health.
Ruth KS; Beaumont RN; Tyrrell J; Jones SE; Tuke MA; Yaghoobkar H; Wood AR; Freathy RM; Weedon MN; Frayling TM; Murray A.

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
STUDY QUESTION: How does a genetic variant in the FSHB promoter, known to alter FSH levels, impact female reproductive health?

SUMMARY ANSWER: The T allele of the FSHB promoter polymorphism (rs10835638; c.-211G>T) results in longer menstrual cycles and later menopause and, while having detrimental effects on fertility, is protective against endometriosis.

WHAT IS KNOWN ALREADY: The FSHB promoter polymorphism (rs10835638; c.-211G>T) affects levels of FSHB transcription and, as a result, circulating levels of FSH. FSH is required for normal fertility and genetic variants at the FSHB locus are associated with age at menopause and polycystic ovary syndrome (PCOS).

STUDY DESIGN, SIZE, DURATION: We used cross-sectional data from the UK Biobank to look at associations between the FSHB promoter polymorphism and reproductive traits, and performed a genome-wide association study (GWAS) for length of menstrual cycle.

PARTICIPANTS/MATERIALS, SETTING, METHODS: We included white British individuals aged 40-69 years in 2006-2010, in the May 2015 release of genetic data from UK Biobank. We tested the FSH-lowering T allele of the FSHB promoter polymorphism (rs10835638; c.-211G>T) for associations with 29, mainly female, reproductive phenotypes in up to 63 350 women and 56 608 men. We conducted a GWAS in 9534 individuals to identify genetic variants associated with length of menstrual cycle.

MAIN RESULTS AND THE ROLE OF CHANCE: The FSH-lowering T allele of the FSHB promoter polymorphism (rs10835638; MAF 0.16) was associated with longer menstrual cycles [0.16 SD (c. 1 day) per minor allele; 95% confidence interval (CI) 0.12-0.20; P = 6 x 10(-16)], later age at menopause (0.13 years per minor allele; 95% CI 0.04-0.22; P = 5.7 x 10(-3)), greater female nulliparity [odds ratio (OR) = 1.06; 95% CI 1.02-1.11; P = 4.8 x 10(-3)] and lower risk of endometriosis (OR = 0.79; 95% CI 0.69-0.90; P = 4.1 x 10(-4)). The FSH-lowering T allele was not associated with other female reproductive illnesses or conditions in our study and we did not replicate associations with male infertility or PCOS. In the GWAS for menstrual cycle length, only variants near the FSHB gene reached genome-wide significance (P < 5 x 10(-9)).

LIMITATIONS, REASONS FOR CAUTION: The data included might be affected by recall bias. Cycle length was not available for 25% of women still cycling (1% did not answer, 6% did not know and for 18% cycle length was recorded as 'irregular'). Women with a cycle length recorded were aged over 40 and were approaching menopause; however, we did not find evidence that this affected the results. Many of the groups with illnesses had relatively small sample sizes and so the study may have been under-powered to detect an effect.
WIDER IMPLICATIONS OF THE FINDINGS: We found a strong novel association between a
genetic variant that lowers FSH levels and longer menstrual cycles, at a locus previously robustly
associated with age at menopause. The variant was also associated with nulliparity and
endometriosis risk. These findings should now be verified in a second independent group of
patients. We conclude that lifetime differences in circulating levels of FSH between individuals
can influence menstrual cycle length and a range of reproductive outcomes, including
menopause timing, infertility, endometriosis and PCOS.

STUDY FUNDING/COMPETING INTERESTS: None.

TRIAL REGISTRATION NUMBER: Not applicable.

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Varicoceles had been recognized in clinical practice for over a century. Originally, these procedures were utilized for the management of pain but, since 1952, the repairs had been mostly for the treatment of male infertility. However, the diagnosis and treatment of varicoceles were controversial, because the pathophysiology was not clear, the entry criteria of the studies varied among centers, and there were few randomized clinical trials. Nevertheless, clinicians continued developing techniques for the correction of varicoceles, basic scientists continued investigations on the pathophysiology of varicoceles, and new outcome data from prospective randomized trials have appeared in the world's literature. Therefore, this special edition of the Asian Journal of Andrology was proposed to report much of the new information related to varicoceles and, as a specific part of this project, the present article was developed as a comprehensive review of the evolution and refinements of the corrective procedures.
Prognostic factors for a favorable outcome after varicocele repair in adolescents and adults. [Review]
Samplaski MK; Jarvi KA.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article. Review]
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The effect of varicocele repair on male fertility remains controversial. It would be helpful to determined which men would benefit most from varicocele repair, and target repair efforts at those individuals. A detailed review of the literature on prognostic factors for varicocele repair was performed using the PubMed NLM database. We found that the best predictor of postvaricocelectomy semen parameters is the preoperative semen parameters. The greatest improvements in semen parameters were found in men with larger varicoceles. While there is controversy, higher testosterone, younger age and larger testis size, in some studies predict for improvements in semen parameters postvaricocelectomy. A nomogram has been developed to predict the postvaricocelectomy semen parameters based on the preoperative semen parameters, varicocele grade and the age of the man (www.fertilitytreatmentresults.com). Limited data consistently demonstrates the greatest improvements in DNA fragmentation rates in men with higher baseline DNA fragmentation rates. With respect to reproductive outcomes, higher baseline sperm density consistently predicts for natural pregnancy or assisted reproductive
technology (ART) pregnancy rates. In addition, varicocele repair does seem to reduce the need for more invasive modalities of ART. In conclusion, we can now start to use specific parameters such as baseline semen quality, varicocele grade and patient age to predict post-repair semen quality and fertility potential following varicocelectomy.

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393.
Presence of human papillomavirus in semen in relation to semen quality.
Luttmer R; Dijkstra MG; Snijders PJ; Hompes PG; Pronk DT; Hubeek I; Berkhof J; Heideman DA; Meijer CJ.
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STUDY QUESTION: Is the presence of human papillomavirus (HPV) in semen associated with impairment of semen quality?
SUMMARY ANSWER: In a large cohort of males seeking fertility evaluation, no associations were observed between seminal HPV presence and semen parameters.
WHAT IS KNOWN ALREADY: HPV is commonly detected in semen samples. Whether the presence of HPV is related to impairment of semen quality, remains unclear.
STUDY DESIGN, SIZE, DURATION: This cross-sectional study included a cohort of 430 males.
PARTICIPANTS/MATERIALS, SETTING, METHODS: Male partners in couples seeking fertility evaluation provided one semen sample per person. Semen samples were tested for HPV-DNA using GP5+/6+-PCR. Sperm concentration was counted and motility was assessed in a Makler counting chamber at a magnification of x200. The presence of antisperm antibodies was assessed by a mixed agglutination reaction (MAR)-test.

MAIN RESULTS AND THE ROLE OF CHANCE: Overall HPV was detected in 14.9% (64/430) of semen samples, including 2.1% (9/430) that contained both high-risk (hr) HPV and low-risk (lr) HPV types, 8.8% (38/430) with exclusively hrHPV types and 4.0% (17/430) with exclusively lrHPV types. The presence of HPV in semen was not associated with the age of the participants, seminal pH, semen volume, total sperm count, sperm concentration, progressive motility or the presence of antisperm antibodies.

LIMITATIONS, REASONS FOR CAUTION: This study did not observe an association between HPV presence in semen and impairment of semen quality. However, we cannot exclude an effect of seminal HPV on early embryo development and clinical reproductive outcomes.

WIDER IMPLICATIONS OF THE FINDINGS: As HPV is frequently present in semen, screening of donor semen for HPV should be considered to prevent iatrogenic cervical HPV infections in the recipient. However our findings do not support standardized HPV testing of semen in the diagnostic work-up of subfertile couples.

STUDY FUNDING/COMPETING INTERESTS: This study was sponsored by an unrestricted grant of Stichting Researchfonds Pathology Amsterdam, the Netherlands. P.J.F.S. has been on the speakers bureau of Roche, Gen-Probe, Abbott, Qiagen and Seegene and has been a consultant for Crucell B.V. J.B. has been on the speakers bureau of Qiagen and has been a consultant for Roche, DDL Diagnostic Laboratory, GlaxoSmithKline and Merck. D.A.M.H. has been member of the scientific advisory boards of Amgen and Pfizer, and has been on the speakers bureau of Hologic/Gen-Probe. C.J.L.M.M. has been on the speakers bureau of GlaxoSmithKline, Qiagen, Merck, Roche, Menarini and Seegene, has served occasionally on the scientific advisory board of GlaxoSmithKline, Qiagen, Merck, Roche and Gentecel, and has occasionally been a consultant for Qiagen. Formerly, C.J.L.M.M. was a minority shareholder of Delphi Biosciences, which bankrupted in 2014. C.J.L.M.M. is a minority shareholder of Diassay B.V. P.J.F.S., D.A.M.H. and C.J.L.M.M. have minority stake in Self-Screen B.V., a spin-off company of VU University Medical Center. R.L., M.G.D., P.G.A.H., D.T.M.P., and I.H. do not have any conflicts of interest to disclose.

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Status
The varicocele: diagnostic dilemmas, therapeutic challenges and future perspectives. [Review]
Chiba K; Ramasamy R; Lamb DJ; Lipshultz LI.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
A varicocele is defined as the abnormal dilation of the internal testicular vein and pampiniform venus plexus within the spermatic cord. If a semen analysis is not obtained from the adolescent male, in the absence of other symptoms, the main clinical indication used by many urologists to recommend repair is testicular atrophy. The varicocele may result in testicular damage in some males causing testicular atrophy with impaired sperm production and decreased Leydig cell function, while in other males the varicocele may seemingly cause no ill effects. In adult men, varicoceles are frequently present and surgically correctable, yet the measurable benefits of surgical repair are slight according to a Cochrane review. While occurring more commonly in infertile men than fertile men, only 20% of men with a documented varicocele will suffer from fertility problems. Most varicoceles found in adolescents are detected during a routine medical examination, and it is difficult to predict which adolescent presenting with a varicocele will ultimately show diminished testicular function in adolescence or adulthood. As in adults, the mainstay of treatment for varicocele in adolescents is surgical correction. However, unlike an adult varicocelectomy (the microsurgical approach is the most common), treatment for an adolescent varicocele is more often laparoscopic. Nevertheless, the goals of treatment are the same in the adolescent and adult patients. Controversy remains as to which patients to treat, when to initiate the treatment, and what type of treatment is the best. This review will present the current understanding of the etiology, diagnosis and treatment of the adolescent varicocele.
The objective of this systematic review was to evaluate the benefit of repairing clinical varicocele in infertile men with nonobstructive azoospermia (NOA). The surgically obtained sperm retrieval rate (SRR) and pregnancy rates following assisted reproductive technology (ART) with the use of retrieved testicular sperm were the primary outcomes. The secondary outcomes included the presence of viable sperm in postoperative ejaculate to avoid the testicular sperm retrieval and pregnancy rates (both assisted and unassisted) using postoperative ejaculated sperm. An electronic search to collect the data was performed using the MEDLINE and EMBASE databases until April 2015. Eighteen studies were included in this systematic review and accounted for 468 patients who were diagnosed with NOA and varicocele. These patients were subjected to either surgical varicocele repair or percutaneous embolization. Three controlled studies evaluating sperm retrieval outcomes indicated that in patients who underwent varicocelectomy, SRR increased compared to those without varicocele repair (OR: 2.65; 95% CI: 1.69-4.14; P< 0.001). Although pregnancy rates with the use of testicular sperm favored the varicocelectomy group, results were not statistically significant (clinical pregnancy rate OR: 2.07; 95% CI: 0.92-4.65; P= 0.08; live birth rate OR: 2.19; 95% CI: 0.99-4.83; P= 0.05). The remaining fifteen studies reported postoperative semen analysis results. In 43.9% of the patients (range: 20.8%-55.0%), sperm were found in postoperative ejaculates. Pregnancy rates for unassisted and assisted (after IVF/ICSI) were 13.6% and 18.9% in the group of men with sperm in postoperative ejaculates, respectively. Our findings indicate that varicocelectomy in patients with NOA and clinical varicocele is associated with improved SRR. In addition, approximately 44% of the treated men will have enough sperm in the ejaculate to avoid sperm retrieval. Limited data on pregnancy outcomes with both postoperative ejaculated sperm and harvested testicular sperm preclude any firm conclusion with regard to the possible increased fertility potential in treated individuals. In conclusion, the results of our study indicate that infertile men with NOA and clinical varicocele benefit from varicocelectomy. Given the low/moderate quality of evidence available, it is
advisable that doctors discuss with their patients with NOA the risks and benefits of varicocele repair.

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396.
The infertility trap: how defeat and entrapment affect depressive symptoms.
Galhardo A; Moura-Ramos M; Cunha M; Pinto-Gouveia J.
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STUDY QUESTION: Does the perception of failure without a solution or way forward of infertile couples have a mediator role between the importance couples attribute to parenthood and depressive symptoms?

SUMMARY ANSWER: The perception of failure without a solution or way forward, assessed by feelings of entrapment and defeat, mediates the effect of the importance of parenthood on depressive symptoms of infertile men and women.

WHAT IS KNOWN ALREADY: Research has documented that the heightened importance of parenthood affects infertile couples' adjustment to infertility and medical treatments. However, it remains unclear which psychological mechanisms and perceptions may underlie the association
between having parenthood as a nuclear aspect of life and presenting depressive symptoms related to difficulties in accomplishing that important life goal. Although these links have been scantly addressed in infertility, previous studies have pointed to the role that perceptions of defeat and entrapment have in several psychopathological conditions.

STUDY DESIGN, SIZE, DURATION: The study was cross-sectional. Couples pursuing medical treatment for their fertility problems were invited to participate by their doctors in several public and private clinics. Data collection took place between July 2009 and 2011.

PARTICIPANTS/MATERIALS, SETTING, METHODS: One hundred forty-seven infertile couples consented to participate in the study. Both couple members (147 women and 147 men) completed a set of self-report instruments for the assessment of depressive symptoms, perceptions of defeat and entrapment, importance of parenthood and rejection of a childfree lifestyle. Analyses were conducted through Structural Equation Modeling and followed a dyadic analysis strategy, allowing for controlling the interdependence of the data.

MAIN RESULTS AND THE ROLE OF CHANCE: The hypothesized tested model showed a very good fit to the data [(chi(2) = 68.45, P = 0.014, comparative fit index = 0.98, standardized root-mean-square residual = 0.06 and root mean square error of approximation = 0.06] and explained 67 and 58% of the variability in depressive symptoms in women and men, respectively. Results revealed that the importance of parenthood does not have a direct effect on depressive symptoms of infertile men and women, but an indirect effect, by affecting the perception of having failed and not being able to solve it or move forward [women: estimate for indirect effect: 0.38 (bias corrected (BC) 95% confidence interval (CI) = 0.25; 0.56; P < 0.001); men: estimate for indirect effect: 0.23 (BC 95% CI = 0.06; 0.40; P = 0.013)].

LIMITATIONS, REASONS FOR CAUTION: The study was cross-sectional, which does not allow for the establishment of causality. Another limitation is the heterogeneity of the sample, as participants were recruited at various stages of their fertility care. In addition, due to the specific nature of the variables, further studies are needed to establish exactly how the relationship between defeat and entrapment and depression operates, as the mechanism may be bidirectional.

WIDER IMPLICATIONS OF THE FINDINGS: This study emphasizes the role of perceptions of defeat and entrapment on the psychological adjustment to infertility and assisted reproduction. These emotional processes should be taken into consideration and targeted in psychological interventions of couples undergoing medical treatments for infertility. In fact, although parenthood may be perceived as a core purpose for many couples dealing with difficulties in conceiving, it is only when these difficulties are experienced as failures without a resolution and as inescapable, that couples are prone to develop depressive symptoms.
STUDY FUNDING/COMPETING INTERESTS: This research has been supported by the first author Ph.D. Grant (SFRH/BD/68392/2010), sponsored by the Portuguese Foundation for Science and Technology (FCT). The authors have no conflict of interests.

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397.
Insulin Resistance and Inflammation in Hypogonadotropic Hypogonadism and Their Reduction After Testosterone Replacement in Men With Type 2 Diabetes.

Dhindsa S; Ghanim H; Batra M; Kuhadiya ND; Abuaysheh S; Sandhu S; Green K; Makdissi A; Hejna J; Chaudhuri A; Punyanitya M; Dandona P.
OBJECTIVE: One-third of men with type 2 diabetes have hypogonadotropic hypogonadism (HH). We conducted a randomized placebo-controlled trial to evaluate the effect of testosterone replacement on insulin resistance in men with type 2 diabetes and HH.

RESEARCH DESIGN AND METHODS: A total of 94 men with type 2 diabetes were recruited into the study; 50 men were eugonadal, while 44 men had HH. Insulin sensitivity was calculated from the glucose infusion rate (GIR) during hyperinsulinemic-euglycemic clamp. Lean body mass and fat mass were measured by DEXA and MRI. Subcutaneous fat samples were taken to assess insulin signaling genes. Men with HH were randomized to receive intramuscular testosterone (250 mg) or placebo (1 mL saline) every 2 weeks for 24 weeks.

RESULTS: Men with HH had higher subcutaneous and visceral fat mass than eugonadal men. GIR was 36% lower in men with HH. GIR increased by 32% after 24 weeks of testosterone therapy but did not change after placebo (P = 0.03 for comparison). There was a decrease in subcutaneous fat mass (-3.3 kg) and increase in lean mass (3.4 kg) after testosterone treatment (P < 0.01) compared with placebo. Visceral and hepatic fat did not change. The expression of insulin signaling genes (IR-beta, IRS-1, AKT-2, and GLUT4) in adipose tissue was significantly lower in men with HH and was upregulated after testosterone treatment. Testosterone treatment also caused a significant fall in circulating concentrations of free fatty acids, C-reactive protein, interleukin-1beta, tumor necrosis factor-alpha, and leptin (P < 0.05 for all).

CONCLUSIONS: Testosterone treatment in men with type 2 diabetes and HH increases insulin sensitivity, increases lean mass, and decreases subcutaneous fat.

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398.
Critical appraisal of conventional semen analysis in the context of varicocele. [Review]
Kruger T.
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Varicocele is present in approximately 15% of men, and, although it is the most commonly diagnosed cause of male infertility, nearly two-thirds of men with varicoceles remain fertile. It was decided to make use of the current evidence obtained from the previous meta-analyses between 2004 and 2015 as well as available articles covering this field, preferably randomized controlled articles dealing with the topic of semen analysis before and after repair. Two important meta-analyses were discussed as well as other articles dealing with the topic of semen analysis before and after varicocelectomy. The evidence suggests that all semen parameters improve after varicocele repair. Based on the available evidence, it is clear that there is a benefit in treating men with a palpable varicocele. One can expect that all semen parameters will improve within 3 months after repair.

399.
EMAS position statement: Testosterone replacement therapy in the aging male. [Review]
Dimopoulou C; Ceausu I; Depypere H; Lambrinoudaki I; Mueck A; Perez-Lopez FR; Rees M; van der Schouw YT; Senturk LM; Simonsini T; Stevenson JC; Stute P; Goulis DG.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
INTRODUCTION: Late-onset hypogonadism (LOH) represents a common clinical entity in aging males, characterized by the presence of symptoms (most usually of a sexual nature, such as decreased libido, decreased spontaneous erections and erectile dysfunction) and signs, in combination with low serum testosterone concentrations. Whether testosterone replacement therapy (TRT) should be offered to those individuals is still under extensive debate.

AIMS: The aim of this position statement is to provide and critically appraise evidence on TRT in the aging male, focusing on pathophysiology and characteristics of LOH, indications for TRT, available therapeutic agents, monitoring and treatment-associated risks.

MATERIALS AND METHODS: Literature review and consensus of expert opinion.

RESULTS AND CONCLUSIONS: Diagnosis and treatment of LOH is justified, if a combination of symptoms of testosterone deficiency and low testosterone is present. Patients receiving TRT could profit with regard to obesity, metabolic syndrome, type 2 diabetes mellitus, sexual function and osteoporosis and should undergo scheduled testing for adverse events regularly. Potential adverse effects of TRT on cardiovascular disease, prostate cancer and sleep apnea are as yet unclear and remain to be investigated in large-scale prospective studies. Management of aging men with LOH should include individual evaluation of co-morbidities and careful risk versus benefit assessment.

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Development and validation of concurrent preimplantation genetic diagnosis for single gene disorders and comprehensive chromosomal aneuploidy screening without whole genome amplification.

Zimmerman RS; Jalas C; Tao X; Fedick AM; Kim JG; Pepe RJ; Northrop LE; Scott RT Jr; Treff NR.

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[Comparative Study. Journal Article. Validation Studies]
UI: 26602983
OBJECTIVE: To develop a novel and robust protocol for multifactorial preimplantation genetic testing of trophectoderm biopsies using quantitative polymerase chain reaction (qPCR).

DESIGN: Prospective and blinded.

SETTING: Not applicable.

PATIENT(S): Couples indicated for preimplantation genetic diagnosis (PGD).

INTERVENTION(S): None.

MAIN OUTCOME MEASURE(S): Allele dropout (ADO) and failed amplification rate, genotyping consistency, chromosome screening success rate, and clinical outcomes of qPCR-based screening.

RESULT(S): The ADO frequency on a single cell from a fibroblast cell line was 1.64% (18/1,096). When two or more cells were tested, the ADO frequency dropped to 0.02% (1/4,426). The rate of amplification failure was 1.38% (55/4,000) overall, with 2.5% (20/800) for single cells and 1.09% (35/3,200) for samples that had two or more cells. Among 152 embryos tested in 17 cases by qPCR-based PGD and CCS, 100% were successfully given a diagnosis, with 0% ADO or amplification failure. Genotyping consistency with reference laboratory results was >99%. Another 304 embryos from 43 cases were included in the clinical application of qPCR-based PGD and CCS, for which 99.7% (303/304) of the embryos were given a definitive diagnosis, with only 0.3% (1/304) having an inconclusive result owing to recombination. In patients receiving a transfer with follow-up, the pregnancy rate was 82% (27/33).

CONCLUSION(S): This study demonstrates that the use of qPCR for PGD testing delivers consistent and more reliable results than existing methods and that single gene disorder PGD can be run concurrently with CCS without the need for additional embryo biopsy or whole genome amplification.

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Comments

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401.
Proinflammatory Cytokine Infusion Attenuates LH's Feedforward on Testosterone Secretion: Modulation by Age.
Veldhuis J; Yang R; Roelfsema F; Takahashi P.
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[Journal Article. Randomized Controlled Trial. Research Support, N.I.H., Extramural]
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CONTEXT: In the experimental animal, inflammatory signals quench LH's feedforward drive of testosterone (T) secretion and appear to impair GnRH-LH output. The degree to which such suppressive effects operate in the human is not known.

OBJECTIVE: To test the hypothesis that IL-2 impairs LH's feedforward drive on T and T's feedback inhibition of LH secretion in healthy men.

SETTING: Mayo Center for Translational Science Activities.
PATIENTS OR OTHER PARTICIPANTS: A total of 35 healthy men, 17 young and 18 older.
INTERVENTIONS: Randomized prospective double-blind saline-controlled study of IL-2 infusion in 2 doses with concurrent 10-minute blood sampling for 24 hours.
MAIN OUTCOME MEASURES: Deconvolution analysis of LH and T secretion.
RESULTS: After saline injection, older compared with young men exhibited reduced LH feedforward drive on T secretion (P < .001), and decreased T feedback inhibition of LH secretion (P < .01). After IL-2 injection, LH's feedforward onto T secretion declined markedly especially in young subjects (P < .001). Concomitantly, IL-2 potentiated T's proportional feedback on LH secretion especially in older volunteers.
CONCLUSION: This investigation confirms combined feedforward and feedback deficits in older relative to young men given saline and demonstrates 1) joint mechanisms by which IL-2 enforces biochemical hypogonadism, viz, combined feedforward block and feedback amplification; and 2) unequal absolute inhibition of T and LH secretion by IL-2 in young and older men. These outcomes establish that the male gonadal axis is susceptible to dual-site suppression by a prototypic inflammatory mediator. Thus, we postulate that selected ILs might also enforce male hypogonadism in chronic systemic inflammation.

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PMID
The ICSI procedure from past to future: a systematic review of the more controversial aspects.

[Review]
Rubino P; Vigano P; Luddi A; Piomboni P.
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BACKGROUND: ICSI is currently the most commonly used assisted reproductive technology, accounting for 70-80% of the cycles performed. This extensive use, even excessive, is partly due to the high level of standardization reached by the procedure. There are, however, some aspects that deserve attention and can still be ameliorated. The aim of this systematic review was to evaluate the results of available publications dealing with the management of specific situations during ICSI in order to support embryologists in trying to offer the best laboratory individualized treatment.

METHODS: This systematic review is based on material obtained by searching PUBMED between January 1996 and March 2015. We included peer-reviewed, English-language journal articles that have evaluated ICSI outcomes in the case of (i) immature oocytes, (ii) oocyte degeneration, (iii) timing of the various phases, (iv) polar body position during injection, (v) zona-free oocytes, (vi) fertilization deficiency, (vii) round-headed sperm, (viii) immotile sperm and (ix) semen samples with high DNA fragmentation.

RESULTS: More than 1770 articles were obtained, from which only 90 were specifically related to the issues developed for female gametes and 55 for the issues developed for male gametes. The studies selected for this review were organized in order to provide a guide to overcome roadblocks. According to these studies, the injection of rescue metaphase I oocytes should be discouraged due to poor clinical outcomes and a high aneuploidy rates; laser-assisted ICSI
represents an efficient method to solve the high oocyte degeneration rate; the optimal ICSI timing and the best polar body position during the injection have not been clarified; injected zona-free oocytes, if handled carefully, can develop up to blastocyst stage and implant; efficient options can be offered to patients who suffered fertilization failure in previous conventional ICSI cycles. Most controversial and inconclusive are data on the best method to select a viable spermatozoa when only immotile spermatozoa are available for ICSI and, to date, there is no reliable approach to completely filter out spermatozoa with fragmented DNA from an ejaculate. However, most of the studies do not report essential clinical outcomes, such as live birth, miscarriage and fetal abnormality rate, which are essential to establish the safety of a procedure.

CONCLUSIONS: This review provides the current knowledge on some controversial technical aspects of the ICSI procedures in order to improve its efficacy in specific contexts. Notwithstanding that embryologists might benefit from the approaches presented herein in order to improve ICSI outcomes, this area of expertise still demands a greater number of well-designed studies, especially in order to solve open issues about the safety of these procedures.

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Tailored expectant management in couples with unexplained infertility does not influence their experiences with the quality of fertility care.

Kersten FA; Hermens RP; Braat DD; Tepe E; Sluijmer A; Kuchenbecker WK; Van den Boogaard N; Mol BW; Goddijn M; Nelen WL; Improvement study Group.

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STUDY QUESTION: Do couples who were eligible for tailored expectant management (TEM) and did not start treatment within 6 months after the fertility work-up, have different experiences with the quality of care than couples that were also eligible for TEM but started treatment right after the fertility work-up?

SUMMARY ANSWER: Tailored expectant management of at least 6 months in couples with unexplained infertility is not associated with the experiences with quality of care or trust in their physician.

WHAT IS KNOWN ALREADY: In couples with unexplained infertility and a good prognosis of natural conception within 1 year, expectant management for 6-12 months does not compromise ongoing birth rates and is equally as effective as starting medically assisted reproduction immediately. Therefore, TEM is recommended by various international clinical guidelines. Implementation of TEM is still not optimal because of existing barriers on both patient and professional level. An important barrier is the hesitance of professionals to counsel their patients for TEM because they fear that patients will be dissatisfied with care. However, if and how adherence to TEM actually affects the couples’ experience with care is unknown. Experiences with the quality care can be measured by evaluating the patient-centredness of care and the patients' trust in their physician.

STUDY DESIGN, SIZE, DURATION: This is a retrospective cross-sectional study. A survey with written questionnaires was performed among all couples who participated in the retrospective audit of guideline adherence on TEM in 25 Dutch clinics.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Couples were eligible to participate if they were diagnosed with unexplained infertility and had a good prognosis (>30%) of natural conception within 1 year based on the Hunault prediction model. We used patient's questionnaires to collect data on the couples’ experience with the quality of care and possible confounders for their experiences other than having undergone TEM or not. Multilevel regression
analyses were performed to investigate case-mix adjusted association of TEM with the patient-centredness of care (PCQ-Infertility) and the patients’ trust in their physician (Wake Forest Trust Scale).

MAIN RESULTS AND THE ROLE OF CHANCE: Couples who adhered to TEM experienced the quality of care on the same level as couples who were exposed to early treatment, i.e. started fertility treatment within 6 months after fertility work-up. There were no associations between adherence to TEM and the patient-centredness of care or the patients' trust in their physician.

LIMITATIONS, REASONS FOR CAUTION: Because this study is retrospective, recall bias might occur. Furthermore, we were unable to measure the difference in experience with care over time. Therefore, our results have to be interpreted carefully.

WIDER IMPLICATIONS OF THE FINDINGS: Prospective research on couples undergoing TEM have to be performed to provide more detailed insight in the patients' experiences with the decision making process and subsequently the expectant period. Tackling the barriers surrounding TEM, i.e. better counselling and more patient information material, could further improve patient experiences with the quality of care for couples who are advised TEM.

STUDY FUNDING/COMPETING INTERESTS: Supported by Netherlands Organisation for Health Research and Development (ZonMW). ZonMW had no role in designing the study, data collection, analysis and interpretation of data or writing of the report. Competing interests: none.

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Protozoan parasitic diseases are endemic in many countries worldwide, especially in developing countries, where infertility is a major burden. It has been reported that such infections may cause infertility through impairment in male and female reproductive systems. We searched Medline, PubMed, and Scopus databases and Google scholar to identify the potentially relevant studies on protozoan parasitic infections and their implications in human and animal model infertility. Literature described that some of the protozoan parasites such as Trichomonas vaginalis may cause deformities of the genital tract, cervical neoplasia, and tubal and atypical pelvic inflammations in women and also non-gonoccocal urethritis, asthenozoospermia, and
teratozoospermia in men. Toxoplasma gondii could cause endometritis, impaired folliculogenesis, ovarian and uterine atrophy, adrenal hypertrophy, vasculitis, and cessation of estrus cycling in female and also decrease in semen quality, concentration, and motility in male. Trypanosoma cruzi inhibits cell division in embryos and impairs normal implantation and development of placenta. Decrease in gestation rate, infection of hormone-producing glands, parasite invasion of the placenta, and overproduction of inflammatory cytokines in the oviducts and uterine horns are other possible mechanisms induced by Trypanosoma cruzi to infertility. Plasmodium spp. and Trypanosoma brucei spp. cause damage in pituitary gland, hormonal disorders, and decreased semen quality. Entamoeba histolytica infection leads to pelvic pain, salpingitis, tubo-ovarian abscess, and genital ulcers. Cutaneous and visceral leishmaniasis can induce genital lesion, testicular amyloidosis, inflammation of epididymis, prostatitis, and sperm abnormality in human and animals. In addition, some epidemiological studies have reported that rates of protozoan infections in infertile patients are higher than healthy controls. The current review indicates that protozoan parasitic infections may be an important cause of infertility. Given the widespread prevalence of parasitic protozoa diseases worldwide, we suggest further studies to better understanding of relationship between such infections and infertility.

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A number of studies have linked omeprazole, a commonly used acid reducer under the brand name Prilosec, with semen quality. This MiniReview systematically addresses and summarizes the effect of omeprazole on semen quality, and male infertility. We searched the MEDLINE electronic database for English-language articles using the keywords 'omeprazole' versus 'sperm' and 'testosterone' and the references from selected articles were reviewed, if relevant. In summary, omeprazole does not appear to change semen quality. This may be because, at least in part, it does not alter the basal levels of pituitary-gonadal hormones; in addition, it counteracts the damaging effect of reactive oxygen species. However, further research is still required to confirm this effect.
BACKGROUND: Data from prior studies have yielded inconsistent results on the association of serum testosterone levels with the risk for cardiovascular disease. There are no clinical trial data on the effects of testosterone replacement therapy on plaque progression.

OBJECTIVE: We designed a study to investigate the effect of testosterone therapy on coronary artery plaque progression using serial coronary computed tomographic angiography (CCTA). In this paper, we describe the study design, methods, and characteristics of the study population.

METHODS: The Cardiovascular Trial of the Testosterone Trials (TTrials; NCT00799617) is a double-blind, placebo-controlled trial of 1 year of testosterone therapy in men 65 years or older with clinical manifestations of androgen deficiency and unequivocally low serum testosterone concentrations (<275ng/dl). CCTA performed at baseline and after 12 months of therapy will determine the effects of testosterone on the progression of the total volume of noncalcified plaques. All scans are evaluated at a central reading center by an investigator blinded to treatment assignment.

RESULTS: A total of 165 men were enrolled. The average age is 71.1 years, and the average BMI is 30.7. About 9% of men had a history of myocardial infarction, 6% angina, and 10% coronary artery revascularization. A majority reported hypertension and/or high cholesterol; 31.8% reported diabetes. Total noncalcified plaque at baseline showed a slight but nonsignificant trend toward lower plaque volume with higher serum testosterone concentrations (P=0.12).

CONCLUSION: The Cardiovascular Trial will test the hypothesis that testosterone therapy inhibits coronary plaque progression, as assessed by serial CCTA.
Utility of a single serum testosterone measurement to determine response to topical testosterone replacement in hypogonadal men.

Muram D; Ni X.

OBJECTIVE: To evaluate the utility of single serum testosterone measurement in patients receiving transdermal testosterone therapy.
RESEARCH DESIGN AND METHODS: Data were from an open-label, 120 day, multi-center titration trial in androgen-deficient men receiving an initial daily dose of 60mg testosterone (testosterone topical solution 2%) applied to axillae (30mg/axilla). Average concentration (Cavg) of serum testosterone (TT) was determined on days 15, 60, and 120; doses were adjusted to maintain normal Cavg (300-1050ng/dL [10.4-36.4nmol/L]). Accuracy of single serum TT measurements (2, 4, 8, 12, 16, and 20 hours post-dose) was assessed in patients with Cavg TT within and below (<300ng/dL [<10.4nmol/L]) the normal range.

CLINICAL TRIAL REGISTRATION: Clinicaltrials.gov - NCT00702650.

MAIN OUTCOME MEASURE: Serum testosterone levels.

RESULTS: In patients with normal Cavg (n=85), 79% to 92% had serum testosterone levels within normal range 2, 4, 8, 12, 16, and 20 hours post-dose; significant effects of time post-dose for single testosterone measurement accuracy (P=0.01) were observed: testing accuracy peaked 4-8 hours post-dose and tapered ~16 hours post-dose. In 28/63 instances with low Cavg TT throughout the study a normal 2 hour serum TT level was observed. The average percentage (across all days) of discordant results between Cavg (<300ng/dL [<10.4nmol/L]) and single serum TT measurements (300-1050ng/dL [10.4-36.4nmol/L]) declined with increasing time from dose application (44% at 2 hours, 38% at 4 hours, 22% at 8 hours, 3% at 16 hours).

CONCLUSIONS: Reliance on a single serum testosterone measurement to determine the need for dose adjustment of testosterone topical solution 2% may lead clinicians to change the dose unnecessarily, or alternatively, not increase the dose when necessary. The results reported here are limited to testosterone topical solution 2% and may not be applicable to other topical agents.
OBJECTIVE: The role of testosterone (T) in regulating body composition is conflicting. Thus, our goal is to meta-analyse the effects of T supplementation (TS) on body composition and metabolic outcomes.

METHODS: All randomized controlled trials (RCTs) comparing the effect of TS on different endpoints were considered.

RESULTS: Overall, 59 trials were included in the study enrolling 3029 and 2049 patients in TS and control groups respectively. TS was associated with any significant modification in body weight, waist circumference and BMI. Conversely, TS was associated with a significant reduction in fat and with an increase in lean mass as well as with a reduction of fasting glycaemia and insulin resistance. The effect on fasting glycaemia was even higher in younger individuals and in those with metabolic diseases. When only RCTs enrolling hypogonadal (total T <12 mol/l) subjects were considered, a reduction of total cholesterol as well as triglyceride (TGs) levels were also detected. Conversely, an improvement in HDL cholesterol levels as well as in both systolic and diastolic blood pressure was not observed.

CONCLUSION: Our data suggest that TS is able to improve body composition and glycometabolic profile particularly in younger subjects and in those with metabolic disturbances. Specifically designed studies are urgently needed to confirm this point.

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Outcome of assisted reproductive technology in men with treated and untreated varicocele: systematic review and meta-analysis. [Review]
Esteves SC; Roque M; Agarwal A.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
UI: 26510504
Varicocele affects approximately 35%-40% of men presenting for an infertility evaluation. There is fair evidence indicating that surgical repair of clinical varicocele improves semen parameters, decreases seminal oxidative stress and sperm DNA fragmentation, and increases the chances of natural conception. However, it is unclear whether performing varicocelectomy in men with clinical varicocele prior to assisted reproductive technology (ART) improve treatment outcomes. The objective of this study was to evaluate the role of varicocelectomy on ART pregnancy outcomes in nonazoospermic infertile men with clinical varicocele. An electronic search was performed to collect all evidence that fitted our eligibility criteria using the MEDLINE and EMBASE databases until April 2015. Four retrospective studies were included, all of which involved intracytoplasmic sperm injection (ICSI), and accounted for 870 cycles (438 subjected to ICSI with prior varicocelectomy, and 432 without prior varicocelectomy). There was a significant increase in the clinical pregnancy rates (OR = 1.59, 95% CI: 1.19-2.12, I² = 25%) and live birth rates (OR = 2.17, 95% CI: 1.55-3.06, I² = 0%) in the varicocelectomy group compared to the group subjected to ICSI without previous varicocelectomy. Our results indicate that performing varicocelectomy in patients with clinical varicocele prior to ICSI is associated with improved pregnancy outcomes.
Status
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PMID
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4770495
Oral enclomiphene citrate raises testosterone and preserves sperm counts in obese hypogonadal men, unlike topical testosterone: restoration instead of replacement.
Kim ED; McCullough A; Kaminetsky J.

OBJECTIVES: To determine the effects of daily oral doses of enclomiphene citrate compared with topical testosterone gel treatment on serum total testosterone (TT), luteinising hormone (LH), follicle-stimulating hormone (FSH), and sperm counts in men with secondary hypogonadism.

PATIENTS AND METHODS: Two parallel randomised, double-blind, double-dummy, placebo-controlled, multicentre, phase III studies were undertaken to evaluate two doses of enclomiphene citrate vs testosterone gel (AndroGel() 1.62%) on TT, LH, FSH, and sperm counts in overweight men aged 18-60 years with secondary hypogonadism. Men were screened and enrolled in the trials (ZA-304 and ZA-305). All enrolled men had early morning serum TT levels in the low or low normal range (<300 ng/dL; <10.4 nmol/L) and had low or normal LH (<9.4 IU/L) levels measured on two separate occasions 2-10 days apart. Serum samples were obtained over the course of the study to determine relevant hormone levels at baseline and after 16 weeks of treatment. Men provided semen samples twice to enroll at the beginning and twice at the end of the study.

RESULTS: TT levels increased between baseline and after 16 weeks of treatment in all the treatment groups. FSH and LH levels increased in the enclomiphene citrate groups and decreased in the testosterone gel group at 16 weeks. Enclomiphene citrate maintained sperm concentration in the normal range over the treatment period, while there was a marked reduction in spermatogenesis in the testosterone gel group.

CONCLUSIONS: Enclomiphene citrate consistently increased serum TT, LH and FSH, restoring normal levels of serum TT. Enclomiphene citrate treatment maintained sperm concentrations in
the normal range. The effects on TT were also seen with testosterone replacement via testosterone gel but sperm counts were not maintained.

The Effects of Gonadotropin Replacement Therapy on Metabolic Parameters and Body Composition in Men with Idiopathic Hypogonadotrophic Hypogonadism.
Bayram F; Elbuken G; Korkmaz C; Aydogdu A; Karaca Z; Cakir I.

[Clinical Trial. Journal Article]
UI: 26485362

Testosterone replacement therapy (TRT) in idiopathic hypogonadotrophic hypogonadism (IHH) slows the process of metabolic syndrome (MetS), diabetes mellitus, and cardiovascular diseases by its inversing effects on insulin resistance, dyslipidemia, and blood pressure. Since there are not enough data regarding the effects of gonadotropin replacement therapy (GRT), we aimed to investigate the impact of GRT on MetS parameters in IHH patients. Sixteen patients with IHH and
20 age and body mass index (BDI)-matched healthy controls were enrolled into the study. Patients were evaluated at baseline and 6 months after the GRT. Sex hormones, insulin like growth factor-1, prolactin, insulin, C-reactive protein (CRP), homocysteine, and lipid levels were measured at baseline and after the treatment. Anthropometric measurements, including BMI, body fat ratio (BFR), fat free mass (FFM), waist circumference, and waist-to-hip ratio (WHR), were also performed. Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) index was calculated. Body fat ratio, triglyceride, HOMA-IR, and CRP levels were higher, whereas bone age, fat free mass, and creatinine levels were lower in the patients with hypogonadism. HOMA-IR indices and basal insulin levels decreased significantly after 6 months of GRT compared with baseline levels. Triglyceride levels, and BFRs diminished significantly by an accompanying decline in WHR. FFM of the patients increased following the GRT. No significant changes were detected in CRP, homocysteine, total and LDL-cholesterol levels. Similar to TRT, hCG treatment decreases HOMA-IR, triglyceride levels, BFR and WHRs, and increases FFM in patients with IHH.
Testosterone Replacement Therapy and Mortality in Older Men. [Review]
Hackett GI.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article. Review]
UI: 26482385
While US testosterone prescriptions have tripled in the last decade with lower trends in Europe, debate continues over the risks, benefits and appropriate use of testosterone replacement therapy (TRT). Several authors blame advertising and the availability of more convenient formulations, whilst others have pointed out that the routine testing of men with erectile dysfunction (ED) (a significant marker of cardiovascular risk) and those with diabetes would inevitably increase the diagnosis of hypogonadism and lead to an increase in totally appropriate prescribing. They commented that this was merely an appropriate correction of previous under-diagnosis and under-treatment in line with evidence based guidelines. It is unlikely that persuasive advertising or convenient formulations could grow a market over such a sustained period if the treatment was not effective. Urologists and primary care physicians are the most frequent initiators of TRT usually for ED. Benefits are clearly established for sexual function, increase in lean muscle mass and strength, mood and cognitive function, with a possible reduction in frailty and osteoporosis. There remains no evidence that TRT is associated with increased risk of prostate cancer or symptomatic benign prostatic hyperplasia, yet the decision to initiate and continue therapy is often decided by urologists. The cardiovascular issues associated with TRT have been clarified by recent studies showing that therapy associated with clear increases in serum testosterone levels to the normal range is associated with reduced all-cause mortality. Studies reporting to show increased risk have been subject to flawed designs with inadequate baseline diagnosis and follow-up testing. Effectively, they have compared non-treated patients with under-treated or non-compliant subjects involving a range of different therapy regimes. Recent evidence suggests long-acting injections may be associated with decreased cardiovascular risk, but the transdermal route may be associated with potentially relatively greater risk because of conversion to dihydrotestosterone by the effect of 5-alpha reductase in skin. The multiple effects of TRT may add up to a considerable benefit to the patient that might be underestimated by the physician primarily concerned with his own specialty. In a response to concerns about the possible risks associated with inappropriate prescribing expressed by Public
Citizen, the Food and Drug Administration (FDA) published a complete refutation of all the concerns, only to issue a subsequent bulletin of concern over inappropriate use, whilst confirming the benefits in treating men with established testosterone deficiency. No additional evidence was provided for this apparent change of opinion, but longer term safety data on testosterone products were strongly suggested. In contrast, the European Medicines Agency (EMA), in November 2014, concluded that "there is no consistent evidence of increased cardiovascular risk with testosterone products". This paper explores the most recent evidence surrounding the benefits and risks associated with TRT.

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Authors Full Name
Hackett, G I.
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2016

413.
Another look at human sperm morphology.
Auger J; Jouannet P; Eustache F.
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[Journal Article. Research Support, Non-U.S. Gov't]
UI: 26472152
STUDY QUESTION: Can a standardized assessment of abnormal human sperm morphology provide additional useful information by identifying men with more severe disturbances in different types of abnormalities?
SUMMARY ANSWER: Definition-based categorization of sperm head, midpiece and tail defects has shown how differently these abnormalities are distributed in fertile men and other groups of men, thus providing high and low thresholds, a starting point for diagnosis or research purposes.
WHAT IS KNOWN ALREADY: Several recent studies have reported indisputable genetic origins for various sperm defects. A few studies have also identified associations between environmental
factors and low percentages of morphologically normal spermatozoa. Nevertheless, with the exception of rare situations in which the vast majority of spermatozoa have specific, easily characterized defects, such as 'globozoospermia', little attention has been paid to the description and precise quantification of human sperm abnormalities. The lack of standardization in the phenotyping of sperm morphological defects by conventional microscopy is a limiting factor for diagnosis and for intra- or inter-observer or centre consistency in studies investigating the causal factors and possible functional consequences of the abnormalities detected. There are currently no baseline data for abnormalities of sperm morphology based on a standardized classification, in the general population, among fertile or other groups of men.

STUDY DESIGN, SIZE, DURATION: This study is based on detailed sperm abnormality datasets acquired by a standardized classification method, from several groups of men, over the same 5-year period.

PARTICIPANTS/MATERIALS, SETTING, METHODS: We studied cross-sectional data from fertile men (n = 926), male partners from infertile couples (n = 1747) and testicular cancer patients (n = 239). We used a standardized classification to analyse Shorr-stained slides, taking into account all the abnormalities encountered.

MAIN RESULTS AND THE ROLE OF CHANCE: Most sperm defects were significantly more frequent in infertile than in fertile men, with 20-30% of infertile men having frequencies of abnormalities above the 95th percentile in fertile men for 9 out of the 15 categories of abnormalities. Interestingly, several head abnormalities were significantly more frequent in patients with testicular cancer than in infertile men, highlighting the particular impact of this condition on sperm morphogenesis. We used the 95th percentile in fertile men as the lower threshold and the 99th percentile in infertile men as an extreme upper threshold, for the classification of morphological abnormality frequencies into three levels: low, intermediate and high. The assessment of several semen samples, with or without a genetic background, for abnormal sperm morphology, based on the percentage of normal spermatozoa, a teratozoospermia index, and the detailed profile of abnormalities categorized according to the three levels proposed, has highlighted the value of detailed phenotyping for diagnosis and research purposes.

LIMITATIONS, REASONS FOR CAUTION: The thresholds proposed for the various categories of sperm abnormality should be considered relative rather than absolute, owing to the known sampling error related to the limited number of spermatozoa assessed per sample, or when studying the general population or populations from regions other than Western Europe. The standardized assessment of abnormal sperm morphology requires time and experience. We therefore suggest that this assessment is carried out during a first andrological check-up or for epidemiological or research studies, rather than in the routine management of infertile couples for assisted reproductive technologies.
WIDER IMPLICATIONS OF THE FINDINGS: The study design used for the fertile group of men was similar to that previously used for the WHO reference values, providing a rationale for considering the 95th percentile in fertile men as the level below which abnormalities may be considered to occur at a frequency representing random background variations of a normal spermiogenesis process. The crude frequencies obtained, and the three levels of abnormality frequency proposed for each standardized category of sperm defect, provide baseline data useful for diagnosis and a starting point for future studies aiming to identify associations with genetic or environmental factors.

STUDY FUNDING/COMPETING INTERESTS: Part of this study was supported by contract BMH4-CT96-0314 from the European Union. The authors have no competing interests to declare.

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414.

Oocyte activation deficiency: a role for an oocyte contribution?. [Review]
Yeste M; Jones C; Amdani SN; Patel S; Coward K.
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[Journal Article. Research Support, Non-U.S. Gov't. Review]
UI: 26346057

BACKGROUND: Infertility affects between 10 and 16% of couples worldwide. Twenty to 30% of cases of infertility are due to a male factor, 20-35% to a female factor, and 25-40% are due to both male and female factors. In ~10-25% of cases, the precise underlying cause remains unclear. IVF or ICSI followed by embryo transfer can be very appropriate treatment options in cases of female tubal damage, ovulatory failure or male-factor infertility. While the use of IVF has been reported to be suitable for many infertile couples, normal IVF cycles can fail in some cases. While ICSI can represent a powerful alternative in cases of IVF failure, complete fertilization failure can still occur in 1-5% of ICSI cycles. This can be due to a variety of factors and while commonly attributed to deficiency of sperm factors, it is very likely that abnormalities in crucial oocyte factors could also play a key role.

METHODS: A critical literature review using PubMed was performed between April 2014 and July 2015 targeting studies concerning sperm and oocyte factors that could account for oocyte activation deficiency, and including studies of in vitro oocyte maturation in human oocytes, and animal models.

RESULTS: Accumulating evidence indicates that phospholipase C zeta (PLCzeta) is the sperm oocyte activation factor, although recent studies claim that another sperm protein known as post-acrosomal WWP-binding domain protein could also play a significant role in the activation of oocytes. The present review discusses our current understanding of these two proteins but emphasizes that defects in the molecular machinery within the oocyte that interacts with such sperm proteins may also represent an underlying cause of fertilization failure and infertility, especially in cases where there is no obvious indication for sperm deficiency. Abnormalities in such mechanisms are highly likely to exert influence over the pulsatile release of calcium within the ooplasm, the critical signal that controls oocyte activation events. These molecular targets within the oocyte are rarely, if ever, considered clinically. We therefore recommend that future diagnostic assays should be developed to consider the inositol triphosphate receptor, protein kinase C, proteins associated with stored operated calcium entry calcium/calmodulin-dependent protein kinase II and mitogen-activated protein kinase. Development of such assays would
represent a significant step forward in the diagnosis of oocyte activation deficiency and may identify a series of potential therapeutic targets.

CONCLUSIONS: The present review provides a general overview of how a combination of sperm and oocyte factors can underlie oocyte activation deficiency, but pays particular attention to the less appreciated role of the oocyte. Enhanced research within this realm is much warranted and may establish new approaches for the diagnosis and treatment of infertility.

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415.

Efficacy and safety of silodosin in the medical expulsion therapy for distal ureteral calculi: a systematic review and meta-analysis. [Review]

Huang W; Xue P; Zong H; Zhang Y.
AIMS: Using a selective alpha-adrenoceptor blocker for medical expulsive therapy (MET) is an effective treatment approach widely used for ureteral stones. The aim of the review was to assess the efficacy and safety of silodosin in medical expulsion therapy compared with placebo and tamsulosin.

METHODS: A systematic search was performed in PubMed, Cochrane Library and Embase to identify randomized controlled trials that compared silodosin with a placebo or tamsulosin for ureteral calculi.

RESULTS: Eight publications involving a total of 1048 patients were used in the analysis, which compared silodosin with placebo and tamsulosin. We found that silodosin was effective in treating ureteral calculi in our meta-analysis and was superior to tamsulosin in its efficacy. The expulsion rate of all ureteral stones (OR 1.59, 95% CI 1.08, 2.36, P = 0.02), the expulsion rate of distal ureteral stones (OR 2.82, 95% CI 1.70, 4.67, P < 0.0001) and the expulsion time (days) of distal ureteral stones (standard mean difference (SMD) -4.71, 95% CI -6.60, -2.83, P < 0.00001) indicated that silodosin was more effective than the placebo. Moreover, expulsion rate (OR 2.54, 95% CI 1.70, 3.78, P < 0.00001), expulsion time (days) (SMD -2.64, 95% CI -3.64, -1.64, P < 0.00001) and pain episodes (P < 0.00001) indicated that silodosin was more effective than the tamsulosin. Even though silodosin had a significant increase in abnormal ejaculation compared with tamsulosin, no significant differences were observed for complications (OR 1.00, 95% CI 0.58, 1.74, P = 1.00).

CONCLUSIONS: This meta-analysis indicated that silodosin was superior to placebo or tamsulosin in the efficacy for distal ureteral calculi with better control of pain. The safety profile of silodosin was similar to tamsulosin though retrograde ejaculation was worse for silodosin use. We conclude that silodosin might have potential as a MET for ureteral stones.

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416.
Testicular fine-needle aspiration for the assessment of intratesticular hormone concentrations.
Lee AP; Roth MY; Nya-Ngatchou JJ; Lin K; Walsh TJ; Page ST; Matsumoto AM; Bremner WJ; Amory JK; Anawalt BD.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present Asian Journal of Andrology. 18(1):21-4, 2016 Jan-Feb.
UI: 26208394
Measurement of intratesticular sex steroid concentrations in men informs both the development of male hormonal contraceptives and the understanding of male infertility. Given the challenges of using invasive techniques to measure testicular hormone physiology, our group has used a minimally-invasive fine-needle aspiration technique to measure intratesticular hormones in normal healthy men. Herein, we present a post-hoc analysis of the safety and efficacy of testicular fine-needle aspiration (FNA) completed as part of six clinical trials. From 2001 through 2011, a total of 404 procedures were conducted among 163 research volunteers, 85.9% of which were successful in obtaining sufficient fluid for the measurement of intratesticular steroid
concentrations. Pain was the most common side effect, with 36.8% of procedures associated with moderate procedural pain and 4.7% with severe procedural pain. Postprocedural pain was uncommon and abated within a few days. Mild local bruising occurred with 14.9% of procedures. Two serious adverse events (0.5%) required surgical intervention. The risk of an adverse event was not associated with age, body mass index, testicular size, or the volume of fluid aspirated. Testicular FNA to obtain fluid for measurement of intratesticular steroid concentrations frequently causes mild to moderate procedural pain, but serious adverse events occur rarely. Testicular FNA has been instrumental for defining human intratesticular hormone physiology and is a minimally-invasive, safe, effective method for obtaining fluid for research on testicular physiology and pathology.

Status
MEDLINE
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Lee, Ada P; Roth, Mara Y; Nya-Ngatchou, Jean-Jacques; Lin, Kat; Walsh, Thomas J; Page, Stephanie T; Matsumoto, Alvin M; Bremner, William J; Amory, John K; Anawalt, Bradley D.
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Year of Publication
2016

417.
Association of polymorphisms of A260G and A386G in DAZL gene with male infertility: a meta-analysis and systemic review. [Review]
Chen P; Wang X; Xu C; Xiao H; Zhang WH; Wang XH; Zhang XH.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
To investigate the association of single nucleotide polymorphism 260 and 386 (SNP260 and SNP386) gene with male infertility, an electronic search was performed to identify case-control studies evaluating the relationship of SNP260 or SNP386 of deleted in azoospermia-like (DAZL) and male infertility. Review Manager 5 was used to process the meta-analysis and other statistical analysis. A total of 139 records were retrieved, of which 13 case-control studies with total 2715 patients and 1835 normozoospermic men were included. SNP260 was found not to play a functional role in male oligo/azoospermia either for Caucasians or for Asians. But for SNP386, models of allele (A/G), dominant (AA/AG + GG), co-dominant (AA/AG) and super-dominant (AA + GG/AG) had a strong correlation to spermatogenic failure with related odds ratio being 0.15 (95% confidence interval [95% CI] 0.07 to 0.34, P < 0.00001), 0.16 (95% CI 0.07 to 0.35, P < 0.00001), 0.15 (95% CI 0.06 to 0.33, P < 0.00001) and 0.15 (95% CI 0.06 to 0.33, P < 0.00001), respectively. Moreover, this correlation was only found in the Chinese Han population (decreasing around 85% risk of oligo/azoospermia infertility) and not found in India, Japan, and Caucasian countries. Our analysis demonstrated that SNP260 of DAZL did not contribute to oligo/azoospermia while SNP386 was correlated to male infertility. However, this correlation was only found in China with a country-specific and ethnicity-specific manner.

Status
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Chen, Ping; Wang, Xiao; Xu, Chang; Xiao, He; Zhang, Wen-Hao; Wang, Xing-Huan; Zhang, Xin-Hua.
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PMID
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4736364
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20151229
Year of Publication
2016
Effects of long-term androgen replacement therapy on the physical and mental statuses of aging males with late-onset hypogonadism: a multicenter randomized controlled trial in Japan (EARTH Study).

Konaka H; Sugimoto K; Orikasa H; Iwamoto T; Takamura T; Takeda Y; Shigehara K; Iijima M; Koh E; Namiki M; EARTH study group.

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article. Multicenter Study. Randomized Controlled Trial]
UI: 25761833

Androgen replacement therapy (ART) efficacy on late-onset hypogonadism (LOH) has been widely investigated in Western countries; however, it remains controversial whether ART can improve health and prolong active lifestyles. We prospectively assessed long-term ART effects on the physical and mental statuses of aging men with LOH in Japan. The primary endpoint was health-related quality of life assessed by questionnaires. Secondary endpoints included glycemic control, lipid parameters, blood pressure, waist circumference, body composition, muscular strength, International Prostate Symptom Scores (IPSS), International Index of Erectile Function-5 (IIEF-5) scores, and serum prostate-specific antigen levels. Of the 1637 eligible volunteers, 334 patients > 40 years with LOH were randomly assigned to either the ART (n = 169) or control groups (n = 165). Fifty-two weeks after the initial treatment, ART significantly affected the role physical subdomain of the short form-36 health survey (SF-36) scale (P = 0.0318). ART was also associated with significant decreases in waist circumstance (P = 0.002) and serum triglyceride (TG) (P = 0.013) and with significant increases in whole-body and leg muscle mass volumes (P = 0.071 and 0.0108, respectively), serum hemoglobin (P < 0.001), IPSS voiding subscore (P = 0.0418), and the second question on IIEF-5 (P = 0.0049). There was no significant difference between the groups in terms of severe adverse events. In conclusion, in patients with LOH, long-term ART exerted beneficial effects on Role Physical subdomain of the SF-36 scale, serum TG, waist circumstance, muscle mass volume, voiding subscore of IPSS, and the second question of IIEF-5. We hope our study will contribute to the future development of this area.

Status
MEDLINE
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Konaka, Hiroyuki; Sugimoto, Kazuhiro; Orikasa, Hideki; Iwamoto, Teruaki; Takamura, Toshinari; Takeda, Yoshifu; Shigehara, Kazuyoshi; Iijima, Masashi; Koh, Eietsu; Namiki, Mikio; EARTH study group.
Institution
Zinc levels in seminal plasma and their correlation with male infertility: A systematic review and meta-analysis.
Embase Scientific reports. 6 (pp 22386), 2016. Date of Publication: 02 Mar 2016.
[Article]
AN: 616055525
Zinc is an essential trace mineral for the normal functioning of the male reproductive system. Current studies have investigated the relationship between seminal plasma zinc and male infertility but have shown inconsistent results. Hence, we systematically searched PubMed, EMBASE, Science Direct/Elsevier, CNKI and the Cochrane Library for studies that examined the relationship between seminal plasma zinc and male infertility, as well as the effects of zinc supplementation on sperm parameters. Twenty studies were identified, including 2,600 cases and 867 controls. Our meta-analysis results indicated that the seminal plasma zinc concentrations from infertile males were significantly lower than those from normal controls (SMD [standard mean differences] [95% CI] -0.64 [-1.01, -0.28]). Zinc supplementation was found to significantly increase the semen volume, sperm motility and the percentage of normal sperm morphology (SMD [95% CI]: -0.99 [-1.60, -0.38], -1.82 [-2.63, -1.01], and -0.75 [-1.37, -0.14], respectively). The present study showed that the zinc level in the seminal plasma of infertile males was significantly lower than that of normal males. Zinc supplementation could significantly increase
the sperm quality of infertile males. However, further studies are needed to better elucidate the correlation between seminal plasma zinc and male infertility.

PMID

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420.
Comparison of the effect of a combination of eight micronutrients versus a standard mono preparation on sperm parameters.
Lipovac M., Bodner F., Imhof M., Chedraui P.

Embase
Reproductive Biology and Endocrinology. 14 (1) (no pagination), 2016. Article Number: 84. Date of Publication: 09 Dec 2016.
[Article]
AN: 613586441

Background: There are reports showing that l-carnitine alone or in combination with other micronutrients improve sperm parameters. However, comparative studies are still lacking. This study was carried out to compare the short term effects of a combination of eight micronutrients including l-carnitine vs. a mono-substance (l-carnitine alone) on sperm parameters. Methods: This was a prospective, open-labelled, nonrandomized study that included male subjects (20 to 60 years) with at least 1 year of subfertility and at least one pathological semen analysis who received 3 months treatment with a mono-substance (500 mg l-carnitine/twice a day, n = 156) or a combined compound (440 mg l-carnitine + 250 mg l-arginine + 40 mg zinc + 120 mg vitamin E + 80 mg glutathione + 60 mug selenium + 15 mg coenzyme Q10 + 800 mug folic acid/once a day, n = 143) for the same time period. Sperm parameters were analyzed before and after treatment and groups comparisons performed. Results: Baseline characteristics were similar among studied groups (age and body mass indices). Semen parameters (volume, density, overall progressive
motility [including slow and fast motility]) and percentage of sperm with normal morphology improved after 3 months in both groups as compared to baseline. However, relative change (expressed as % increase of absolute values) for sperm density and overall progressive motility (including fast motility) was found to be higher for the combined micronutrient treatment group as compared to the mono-treatment using l-carnitine alone. Conclusion: Both analyzed groups displayed a positive short term effect on all sperm parameters; however effect on density and motility was significantly better for the combined formulation. There is need for more research in this matter that includes long term outcome data. Trial registration: Retrospectively registered at ISRCTN (7th October 2016). Study ID: ISRCTN48594239 Copyright © 2016 The Author(s). PMID 27938385 [http://www.ncbi.nlm.nih.gov/pubmed/?term=27938385] Status EMBASE Institution (Lipovac, Bodner, Imhof) IMI Fertility Center, Vienna, Austria (Lipovac, Bodner, Imhof) Karl Landsteiner Institute for cell-based therapy in Gynecology, Wiener Ring 3-5, Korneuburg 2100, Austria (Imhof) Medical University of Vienna, Vienna, Austria (Chedraui) Universidad Catolica de Santiago de Guayaquil, Institute of Biomedicine, Research Area for Women's Health, Facultad de Ciencias Medicas, Guayaquil, Ecuador Publisher BioMed Central Ltd. (E-mail: info@biomedcentral.com) Date Created 20170104 Year of Publication 2016

421. Efficacy and safety of antidepressants added to antipsychotics for schizophrenia: A systematic review and meta-analysis.

Helfer B., Samara M.T., Huhn M., Klupp E., Leucht C., Zhu Y., Engel R.R., Leucht S.

Embase

Objective: The authors examined the safety and efficacy of antidepressants added to antipsychotic drugs in the treatment of schizophrenia. Method: Multiple databases and previous publications were searched through June 2015 to identify all randomized controlled trials of any add-on antidepressants compared with placebo or no-treatment in schizophrenia. Depressive and negative symptoms (primary outcomes), overall symptoms, positive symptoms, side effects, exacerbation of psychosis, and responder rates were examined. Subgroup, meta-regression, and sensitivity analyses were performed, as well as investigations of publication bias and risk of bias.

Results: Eighty-two randomized controlled trials with a total of 3,608 participants were included. Add-on antidepressants appeared more efficacious than controls for depressive symptoms (standardized mean difference: -0.25, 95% CI = -0.38 to -0.12), negative symptoms (standardized mean difference: -0.30, 95% CI = -0.44 to -0.16), overall symptoms (standardized mean difference: -0.24, 95% CI = -0.39 to -0.09), positive symptoms (standardized mean difference: -0.17, 95% CI = -0.33 to -0.01), quality of life (standardized mean difference: -0.32, 95% CI = -0.57 to -0.06), and responder rate (risk ratio: 1.52, 95% CI = 1.29 to 1.78; number needed-to-treat-to-benefit: 5, 95% CI = 4 to 7). The effects on depressive and negative symptoms appeared more pronounced when minimum thresholds of these symptoms were inclusion criteria (standardized mean difference: -0.34, 95% CI = -0.58 to -0.09 and standardized mean difference: -0.58, 95% CI = -0.94 to -0.21, respectively). There were no significant differences between antidepressants and controls in terms of exacerbation of psychosis, premature discontinuation, and the number of participants with at least one adverse event. More patients taking add-on antidepressants suffered from abdominal pain, constipation, dizziness, and dry mouth. Conclusions: Analysis of primary outcomes (depressive and negative symptoms) suggests small, beneficial effects of adjunctive antidepressants. It would appear that this augmentation can be accomplished with a low risk of exacerbation of psychosis and adverse effects. However, secondary and subgroup analyses should be interpreted cautiously and considered exploratory.

422.
Testosterone supplementation and body composition: results from a meta-analysis of observational studies.
Corona G., Giagulli V.A., Maseroli E., Vignozzi L., Aversa A., Zitzmann M., Saad F., Mannucci E., Maggi M.
Embase
[Review]
AN: 611771589
Purpose: The concept of testosterone (T) supplementation (TS) as a new anti-obesity medication in men with testosterone deficiency syndrome (TDS) is emerging. Data from placebo-controlled trials are more conflicting. The aim of this study is to systematically review and meta-analyze available observational and register studies reporting data on body composition in studies on TS in TDS. Methods: An extensive MEDLINE, Embase, and Cochrane search was performed including the following words: "testosterone" and "body composition." All observational studies comparing the effect of TS on body weight and other body composition and metabolic endpoints were considered. Results: Out of 824 retrieved articles, 32 were included in the study enrolling 4513 patients (mean age 51.7 +/- 6.1 years). TS was associated with a time-dependent reduction in body weight and waist circumference (WC). The estimated weight loss and WC reduction at 24 months were -3.50 [-5.21; -1.80] kg and -6.23 [-7.94; -4.76] cm, respectively. TS was also associated with a significant reduction in fat and with an increase in lean mass as well as with a reduction in fasting glycemia and insulin resistance. In addition, an improvement of lipid profile (reduction in total cholesterol as well as of triglyceride levels and an improvement in HDL cholesterol levels) and in both systolic and diastolic blood pressure was observed. Conclusions: Present data support the view of a positive effect of TS on body composition and on glucose and lipid metabolism. In addition, a significant effect on body weight loss was observed, which should
be confirmed by a specifically designed RCT. Copyright © 2016, Italian Society of Endocrinology (SIE).

PMID

Status
EMBASE

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20160905

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2016

423.

Unmet needs of the patients with obsessive-compulsive disorder.

Embase


[Article]
BACKGROUND: Obsessive compulsive disorder (OCD) is a disabling mental disorder with the chronic and difficult course. The disorder is accompanied by numerous limitations in personal and interpersonal functioning. OCD decreases the quality of life and the chance to maintain relationships and professional status. The patients with OCD often experience a severe disabling course of the disorder. Even the individuals, who follow treatment advice, are often still highly symptomatic. In the last decade, the concept of the needs has been assessed as an extent of the traditional outcome evaluation in order to focus on the identification of the specific needs of the patients and their relatives, improve the patients’ overall mental condition and quality of life, and also to increase the treatment effectiveness of the mental disorders. The objective of the article was to review the current literature about unmet needs of the OCD patients and their caregivers.

METHOD: A computerized search of the literature published between January 2000 and June 2016 was conducted in MEDLINE, and additional papers were extracted using keywords "obsessive compulsive disorder", "needs", "pharmacotherapy", "CBT", and "family" in various combinations. Primary selection selected the total of 449 articles. According to the established criteria, 168 articles were chosen. After a detailed examination of the full texts, 53 articles remained. Secondary articles from the reference lists of primarily selected papers were read and evaluated for the eligibility and added to the final list of the articles (n = 107).

RESULTS: The needs of the OCD patients might differ at various stages and severity of the disorder. Four sets of the needs were identified: the needs connected with the symptoms, the treatment, the quality of life, and the family. The patients suffering from OCD often experience many limitations in the fulfillment of their fundamental human needs such as disturbed patients’ functioning in the common life, family, at work, in the ability to realize their goals, skills, potential, capacity to follow prescribed treatment, take medication, cooperate in addressing the root causes of their problems, reduce obsessive thoughts and compulsive behavior, as well as their willingness to realize exposures with the desire to resolve the situation.

CONCLUSION: Monitoring the patients’ needs may be relevant for the treatment of the individuals suffering from OCD. A bigger focus on the patients’ needs could be beneficial and should be targeted in the treatment.
The use of maca (Lepidium meyenii) to improve semen quality: A systematic review.

Lee M.S., Lee H.W., You S., Ha K.-T.

Embase
Maturitas. 92 (pp 64-69), 2016. Date of Publication: 01 Oct 2016.

[Review]
AN: 611441035

The aim of this review was to assess the evidence for the effectiveness of maca (Lepidium meyenii) in improving semen quality. We searched 11 databases from their inception to March 2016 and included all clinical trials on the improvement of semen quality parameters in infertile and healthy men, regardless of the study design or the type of maca. The risk of bias for each study was assessed using the Cochrane criteria. The selection of studies, data extraction, and validation were performed independently by the first two authors. Discrepancies were resolved through discussion by the same two authors. Five studies - 3 randomized clinical trials (RCTs) and 2 uncontrolled observational studies (UOSs) - met all of the inclusion criteria. One RCT found favorable effects of maca on sperm mobility in infertile men. The two other RCTs showed positive effects of maca on several semen quality parameters in healthy men. The two UOSs also suggested favorable effects of maca on semen quality. The results of our systematic review provide suggestive evidence for the effectiveness of maca in improving semen quality. However, the total number of trials, the total sample size, and the risk of bias of the included studies prevent the drawing firm conclusions. More rigorous studies are warranted. Copyright © 2016 Elsevier Ireland Ltd

PMID
425.
Multicolor detection of every chromosome as a means of detecting mosaicism and nuclear organization in human embryonic nuclei.
Turner K., Fowler K., Fonseka G., Griffin D., Ioannou D.
Embase
Panminerva medica. 58 (2) (pp 175-190), 2016. Date of Publication: 01 Jun 2016.
[Review]
AN: 615598968
Fluorescence in-situ hybridization (FISH) revolutionized cytogenetics using fluorescently labelled probes with high affinity with target (nuclear) DNA. By the early 1990s FISH was adopted as a means of preimplantation genetic diagnosis (PGD) sexing for couples at risk of transmitting X-linked disorders and later for detection of unbalanced translocations. Following a rise in popularity of PGD by FISH for sexing and the availability of multicolor probes (5-8 colors), the use of FISH was expanded to the detection of aneuploidy and selective implantation of embryos more likely to be euploid, the rationale being to increase pregnancy rates (referral categories were typically advanced maternal age, repeated IVF failure, repeated miscarriage or severe male factor infertility). Despite initial reports of an increase in implantation rates, reduction in trisomic
offspring and spontaneous abortions criticism centered around experimental design (including lack of randomization), inadequate control groups and lack of report on live births. Eleven randomized control trials (RCTs) (2004-2010) showed that preimplantation genetic screening (PGS) with FISH did not increase delivery rates with some demonstrating adverse outcomes. These RCTs, parallel improvements in culturing and cryopreservation and a shift to blastocyst biopsy essentially outdated FISH as a tool for PGS and it has now been replaced by newer technologies (array CGH, SNP arrays, qRT-PCR and NGS). Cell-by-cell follow up analysis of individual blastomeres in non-transferred embryos is however usually prohibitively expensive by these new approaches and thus FISH remains an invaluable resource for the study of mosaicism and nuclear organization. We thus developed the approach described herein for the FISH detection of chromosome copy number of all 24 human chromosomes. This approach involves 4 sequential layers of hybridization, each with 6 spectrally distinct fluorochromes and a bespoke capturing system. Here we report previously published studies and hitherto unreported data indicating that 24 chromosome FISH is a useful tool for studying chromosome mosaicism, one of the most hotly debated topics currently in preimplantation genetics. Our results suggest that mosaic embryo aneuploidy is not highly significantly correlated to maternal age, probably due, in part, to the large preponderance of post-zygotic (mitotic) errors. Chromosome loss (anaphase lag) appears to be the most common mechanism, followed by chromosome gain (endoreduplication), however 3:1 mitotic non-disjunction of chromosomes appears to be rare. Nuclear organization (i.e. the spatial and temporal topology of chromosomes or sub-chromosomal compartments) studies indicate that human morula or blastocyst embryos (days 4-5) appear to adopt a "chromocentric" pattern (i.e. almost all centromeric signals reside in the innermost regions of the nuclear volume). By the blastocyst stage however, a more ordered organization with spatial and temporal cues important for embryo development appears. We have however found no association between aneuploidy and nuclear organization using this approach despite our earlier studies. In conclusion, while FISH is mostly "dead and buried" for mainstream PGS, it still has a place for basic biology studies; the development of a 24 chromosome protocol extends the power of this analysis.

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Date Created 20170425
Year of Publication 2016
Denosumab is really effective in the treatment of osteoporosis secondary to hypogonadism in prostate carcinoma patients? A prospective randomized multicenter international study.
Doria C., Leali P.T., Solla F., Maestretti G., Balsano M., Scarpa R.M.
Embase
Clinical Cases in Mineral and Bone Metabolism. 13 (3) (pp 195-199), 2016. Date of Publication: 2016.
[Article]
AN: 615509207
Introduction: Osteoporosis is a complication of androgen deprivation therapy (ADT) in men with prostate carcinoma. The best defense against osteoporosis in prostate cancer is to identify patients with a high risk for fracture during the first clinical visit, select an effective anti-osteoporosis agent, and advise the patient to change his lifestyle and diet to prevent further bone loss. New agents include denosumab, a human monoclonal antibody that inhibits the RANK ligand (RANKL). RANKL promotes the formation, activity, and survival of osteoclasts and, thus, supports the breakdown of bone. Purpose: This is a multicenter, randomized, double-blind prospective study on use of denosumab versus alendronate in the therapy of secondary osteoporosis related to ADT in prostate cancer patients in three European countries (Italy, France, Switzerland). Patients and methods: In this 24-month observation study we enrolled 234 patients with diagnosis of osteoporosis underwent ADT for prostate cancer. All patients aged >55 years and had a dual-energy X-ray absorptiometry (DEXA) T-score <-1.0 (hip or spine, measured within last 2 years) and > 1 fragility fracture. Patients were randomly assigned 1:1 to receive denosumab 60 mg subcutaneously every 6 months or alendronate (70 mg weekly) for 2 years. All patient received supplemental Vitamin D (600 IU per day) and supplemental calcium to maintain a calcium intake of 1200 mg per day. Effectiveness of therapy in both groups (denosumab group and alendronate group) was assessed by changes in bone turnover markers (BTMs), Bone Mineral Density (BMD), fracture incidence, Visual Analogue Scale (VAS) score for back pain, and Short Form-8 (SF-8TM) health survey score for health-related quality of life (HRQoL). Percent changes from baseline in BTMs and BMD were assessed using the paired t test; a P-value 0.05). Mean changes in BMD at final follow-up differed significantly between two groups. BMD changes at the lumbar spine at 24 months were 5.6% with denosumab vs -1.1% with alendronate (P<0.001). New vertebral fractures developed in fewer patients in the denosumab group than in the alendronate group during the 24-month period, although this difference was not significant.
(P=0.10). Back pain significantly (P<0.001) improved from baseline at all time points during the study in both study groups. SF-8 health survey scores significantly improved following treatment with both drugs. Incidence of adverse drug reactions were similar in both groups. Conclusion: In our study denosumab and alendronate showed similar clinical efficacy in the therapy of ADT-related osteoporosis in men with prostate carcinoma; both drugs provided significant improvements in back pain and general health conditions. Denosumab showed significant increase of BTMs and BMD than alendronate with lower rate of new vertebral fractures.

Status
INPROCESS

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Publisher
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20170423

Year of Publication
2016

427.
Use of Iranian medicinal plants effective on male fertility indices.
Shirani M., Heidari-Soureshjani S., Yavangi M.

Embase

[Review]
AN: 615230100

This systematic review article was conducted to report medicinal plants that are effective on male fertility indices. To conduct this review, search terms fertility or pregnancy combined with medicinal plants, herb, and phyto were used to retrieve relevant publications indexed in ISI, PubMed, and Iranian scientific databases. Escanbil, Fumaria parviflora L., Apium graveolens L.,
Achillea millefolium inflorescence, Urtica dioica L., Withania somnifera L., Phaleria macrocarpa, Satureja khuzestanica, Achillea millefolium, Malva sylvestris, Humulus lupulus L., Allium cepa, Petroselinum crispum, Carthamus tinctorius, and Zingiber officinale were reported to be medicinal plants with fertility indices-promoting properties. Medicinal plants that are used in Iran affect hormonal compounds and other effective compounds on hormonal system as well as the proliferation and viability of sex cells due to their antioxidant properties, and therefore enhance fertility in human and animals. Copyright © 2009-2016, JGPT.

Status
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Journal of Global Pharma Technology (E-mail: globalpharmatechnology@gmail.com)
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428.
Medicinal plants used in Lesotho for treatment of reproductive and post reproductive problems. Moteetee A., Seleteng Kose L.
Embase
[Article]
AN: 613528882
Ethnopharmacological relevance Reproductive healthcare has been highlighted as a major challenge in Lesotho mainly due to the high prevalence of HIV/AIDS and sexually transmitted infections. As a result other reproductive ailments have not received much attention, particularly because healthcare facilities are already limited and many of them are inaccessible. For these
reasons, medicinal plants play a major role in primary healthcare system in the country, in addition the plants are easily accessible, more affordable, and their use forms part of the cultural heritage. However, documentation of medicinal plants used for reproductive ailments is scattered, more importantly the biological and pharmacological properties, as well as toxicity of many of these plants are not yet known. Aim of the study To document the plants used by both male and female Basotho (residing in Lesotho) for the treatment of reproductive ailments, to explore their recorded biological and pharmacological effects as well as their toxicity, and to establish if these plants are used for similar purposes in other southern African cultures. Materials and methods The results stem from published findings of recent interviews of traditional medicinal practitioners in the Maseru District of Lesotho, first author's own experiences and observations from the Qacha's Nek District as well as comprehensive literature survey including numerous books and unpublished data. Electronic databases such as Google, Google Scholar, PubMed, and ScienceDirect were also used to search for the chemical compounds, pharmacological activity, and toxicity of the plants. Results A total of 87 plant species are reported to be used for the treatment of several reproductive problems such as infertility, complications associated with pregnancy (twelve plants are used to treat conditions such as colic, heartburn, nausea, and constipation), cleansing and/or toning of the uterus (with a purpose either to induce pregnancy or to get rid of the placenta, for example Withania somnifera and Zantedeschia albomaculata), difficult childbirth, as well treatment of breast and cervical cancer, cysts, fibroids, and testicular tumours (e.g. Hypoxis hemerocallidea). For the toning of the uterus, it is common to use a combination of plants, e.g. Gunnera perpensa, Scabiosa columbaria, and Eriospermum ornithogaloides. Conclusions Of the 87 plants used for reproductive healthcare, the highest number (31) is used for the treatment of infertility (in both men and women). The pharmacological effects, active compounds, and toxicology of many of these plants are not yet known. Copyright © 2016 Elsevier Ireland Ltd


Status EMBASE

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Date Created 20161220

Year of Publication
Applying data mining techniques for increasing implantation rate by selecting best sperms for intra-cytoplasmic sperm injection treatment.

Mirroshandel S.A., Ghasemian F., Monji-Azad S.

Embase

Computer Methods and Programs in Biomedicine. 137 (pp 215-229), 2016. Date of Publication: 01 Dec 2016.

[Article]

AN: 612616751

Background and objective Aspiration of a good-quality sperm during intracytoplasmic sperm injection (ICSI) is one of the main concerns. Understanding the influence of individual sperm morphology on fertilization, embryo quality, and pregnancy probability is one of the most important subjects in male factor infertility. Embryologists need to decide the best sperm for injection in real time during ICSI cycle. Our objective is to predict the quality of zygote, embryo, and implantation outcome before injection of each sperm in an ICSI cycle for male factor infertility with the aim of providing a decision support system on the sperm selection. Methods The information was collected from 219 patients with male factor infertility at the infertility therapy center of Alzahra hospital in Rasht from 2012 through 2014. The prepared dataset included the quality of zygote, embryo, and implantation outcome of 1544 injected sperms into the related oocytes. In our study, embryo transfer was performed at day 3. Each sperm was represented with thirteen clinical features. Data preprocessing was the first step in the proposed data mining algorithm. After applying more than 30 classifiers, 9 successful classifiers were selected and evaluated by 10-fold cross validation technique using precision, recall, F1, and AUC measures. Another important experiment was measuring the effect of each feature in prediction process. Results In zygote and embryo quality prediction, IBK and RandomCommittee models provided 79.2% and 83.8% F1, respectively. In implantation outcome prediction, KStar model achieved 95.9% F1, which is even better than prediction of human experts. All these predictions can be done in real time. Conclusions A machine learning-based decision support system would be helpful in sperm selection phase of ICSI cycle to improve the success rate of ICSI treatment.

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PMID
Prevalence of Active Long-term Problems in Patients with Anorectal Malformations: A Systematic Review.

Rigueros Springford L., Connor M.J., Jones K., Kapetanakis V.V., Giuliani S.

Embase

Diseases of the Colon and Rectum. 59 (6) (pp 570-580), 2016. Date of Publication: 01 Jun 2016.

[Review]

AN: 610453503

BACKGROUND: Anorectal malformations are a spectrum of congenital anomalies of the rectum with high infantile survival rates and variable outcomes. Long-term (>10 years old) active problems associated with this condition have been poorly investigated. OBJECTIVE: The purpose of this review was to systematically define the prevalence of the most common active long-term problems in patients with a history of anorectal malformation repair. DATA SOURCES: MEDLINE, EMBASE, and the Cochrane Library were searched electronically using the OVID search platform. STUDY SELECTION: Original articles from August 1, 1994, to October 20, 2015, that included outcome data for patients aged >10 years with anorectal malformation. Cloaca was excluded from the study. INTERVENTIONS: Prevalence estimates of anorectal malformations were obtained from published articles. CIs were ascertained in the logit scale after transforming prevalence into log odds and were then transformed into the original scale. The same method
was used for subgroup analysis investigating high and low anorectal malformations. MAIN
OUTCOME MEASURES: The overall prevalences of fecal, urinary, and sexual dysfunction were
analyzed. RESULTS: Twelve studies including 455 patients with a history of anorectal
malformation repair were included for analysis. The range of reported prevalence of long-term
active problems was as follows: fecal incontinence, 16.7% to 76.7%; chronic constipation, 22.2%
to 86.7%; urinary incontinence, 1.7% to 30.5%; ejaculatory dysfunction, 15.6% to 41.2%; and
erectile dysfunction, 5.6% to 11.8%. LIMITATIONS: The study was limited by its retrospective,
small size; multiple complex associated anomalies often not reported; and heterogeneous
composition of patients with limited stratification analysis. CONCLUSIONS: There is an overall
high prevalence of active long-term issues in adolescents and young adults with anorectal
malformations. Additional multicenter research is needed to define characteristics and predictors
of long-term outcome, to implement effective follow-up, and to transition to adult health care.
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431.
Endocrine Society of Australia position statement on male hypogonadism (part 1): assessment
and indications for testosterone therapy.
INTRODUCTION: This article, Part 1 of the Endocrine Society of Australia's position statement on male hypogonadism, focuses on assessment of male hypogonadism, including the indications for testosterone therapy. (Part 2 will deal with treatment and therapeutic considerations.) MAIN RECOMMENDATIONS: Key points and recommendations are:

- Pathological hypogonadism arises due to diseases of the hypothalamus or pituitary gland (hypogonadotropic hypogonadism) or testes (hypergonadotropic hypogonadism). It is a clinical diagnosis with a pathological basis, confirmed by hormone assays.
- Hormonal assessment is based on measurement of circulating testosterone, luteinising hormone (LH) and follicle-stimulating hormone (FSH) concentrations. Measurement of sex hormone-binding globulin levels can be informative, but use of calculated free testosterone is not recommended for clinical decision making.
- Testosterone replacement therapy is warranted in men with pathological hypogonadism, regardless of age. Currently, there are limited data from high-quality randomised controlled trials with clinically meaningful outcomes to justify testosterone treatment in older men, usually with chronic disease, who have low circulating testosterone levels but without hypothalamic, pituitary or testicular disease. Obesity, metabolic syndrome and type 2 diabetes are associated with lowering of circulating testosterone level, but without elevation of LH and FSH levels. Whether these are non-specific consequences of non-reproductive disorders or a correctable deficiency state is unknown, but clear evidence for efficacy and safety of testosterone therapy in this setting is lacking. Glucocorticoid and opioid use is associated with possibly reversible reductions in circulating testosterone level, without elevation of LH and FSH levels. Where continuation of glucocorticoid or opioid therapy is necessary, review by an endocrinologist may be warranted.
- Changes in management as result of the position statement: Men with pathological hypogonadism should be identified and considered for testosterone therapy, while further research is needed to clarify whether there is a role for testosterone in these other settings.


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(McLachlan, Allan, Burger) Hudson Institute of Medical Research, Melbourne, VIC
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Prevalence of sexual dysfunction in men with chronic prostatitis/chronic pelvic pain syndrome: a meta-analysis.
Li H.-J., Kang D.-Y.
Embase
World journal of urology. 34 (7) (pp 1009-1017), 2016. Date of Publication: 01 Jul 2016.
[Article]
AN: 615393687
PURPOSE: This study aims to estimate the prevalence of sexual dysfunction in men with chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) by conducting a meta-analysis. METHODS: Relevant publications were searched using PubMed, Embase, CBM, China National Knowledge Infrastructure, VIP and Wanfang databases up to August 2015. Studies that reported the prevalence of erectile dysfunction, premature ejaculation and total sexual dysfunction in men with CP/CPPS were included.
RESULTS: A total of 24 studies involving 11,189 men were included. Overall prevalence of sexual dysfunction in men with CP/CPPS was 0.62 (95 % CI 0.48-0.75), while the prevalence of erectile dysfunction and premature ejaculation was 0.29 (95 % CI 0.24-0.33) and 0.40 (95 % CI 0.30-0.50), respectively. From 1999 to 2010, the prevalence of sexual dysfunction, erectile dysfunction and premature ejaculation was 0.65 (95 % CI 0.45-0.83), 0.27 (95 % CI 0.22-0.33) and 0.41 (95 % CI 0.27-0.55), respectively. From 2011 to 2014, the prevalence of sexual dysfunction, erectile dysfunction and premature ejaculation was 0.50 (95 % CI 0.22-0.75), 0.35 (95 % CI 0.29-0.40) and 0.39 (95 % CI 0.37-0.41), respectively.
CONCLUSION: The prevalence of sexual dysfunction in men with CP/CPPS was high, even though overall sexual dysfunction demonstrated a slightly decreasing trend. Furthermore, erectile dysfunction prevalence rate had an increasing trend in recent years. More prospective studies are needed to evaluate sexual dysfunction improvement with better management of CP/CPPS.
Abstracts of the 32nd Annual Meeting of the European Society of Human Reproduction and Embryology. Anonymous

Embase


AN: 615298340

The proceedings contain 1077 papers. The topics discussed include: human reproduction keynote lecture - modifiable and non-modifiable risk factors for poor sperm morphology; a prospective randomized controlled trial investigating embryonic development and clinical outcome after using Ca2+ ionophore in cases with previous fertilization arrest; late activation with calcium ionophore is associated with chromosome retention by the oocyte following completion of meiosis ii and extrusion of the second polar body; prospective randomized study comparing human embryo development in a microwell group culture dish (primo vision dish) or in a standard dish with individual droplet; shift in pH during transition to the embryonic genome impacts embryo development; shift in pH during transition to the embryonic genome impacts embryo development; do not disturb the embryos until day 5: preliminary results of a double blind prospective randomized controlled trial; prediction model for obtaining spermatozoa with TESE in men with non-obstructive azoospermia; prediction model for live birth in intracytoplasmic sperm injection
using testicular extracted sperm; meaning of DNA fragmentation in relation to the sperm source and ART outcome; genome-wide DNA methylation and mRNA expression profiling in eutopic endometrium, disease tissue and fat: implications for endometriosis research; choosing the appropriate insemination method according to sperm DNA fragmentation level; and regulation of angiogenesis-related prostaglandin F2alpha-induced VEGF and CXCL-8 factors in endometriosis.

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434.
Current and future alternative therapies for beta-thalassemia major.
de Dreuzy E., Bhukhai K., Leboulch P., Payen E.
Embase
Biomedical Journal. 39 (1) (pp 24-38), 2016. Date of Publication: 2016.
[Review]
AN: 611202306
Beta-thalassemia is a group of frequent genetic disorders resulting in the synthesis of little or no beta-globin chains. Novel approaches are being developed to correct the resulting alpha/beta-globin chain imbalance, in an effort to move beyond the palliative management of this disease and the complications of its treatment (e.g. life-long red blood cell transfusion, iron chelation, splenectomy), which impose high costs on healthcare systems. Three approaches are envisaged: fetal globin gene reactivation by pharmacological compounds injected into patients throughout their lives, allogeneic hematopoietic stem cell transplantation (HSCT), and gene therapy. HSCT is currently the only treatment shown to provide an effective, definitive cure for beta-thalassemia. However, this procedure remains risky and histocompatible donors are identified for only a small fraction of patients. New pharmacological compounds are being tested, but none has yet made it into common clinical practice for the treatment of beta-thalassemia major. Gene therapy is in the experimental phase. It is emerging as a powerful approach without the immunological
complications of HSCT, but with other possible drawbacks. Rapid progress is being made in this field, and long-term efficacy and safety studies are underway. Copyright © 2016 Chang Gung University

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435.

Impact of CAG repeat length in the androgen receptor gene on male infertility - a meta-analysis.

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[Review]
AN: 610219663

CAG repeats are polymorphic nucleotide repeats present in the androgen receptor gene. Many studies have estimated the association between CAG repeat length and male infertility, but the conclusions are controversial. Previous meta-analyses have come to different conclusions;
however, new studies have been published. An updated meta-analysis was conducted. PubMed, CBM, CNKI and Web of Science databases were systematically searched for studies published from 1 January 2000 to 1 October 2015. Case-control studies on the association between CAG repeat length and male infertility using appropriate methodology were included. Forty studies were selected, including 3858 cases and 3161 controls. Results showed statistically significantly longer CAG repeat length among cases compared with controls (SMD = 0.14; 95% CI, 0.02-0.26). Shorter repeat length was associated with a lower risk of male infertility compared with a longer repeat length in the overall analysis (OR = 0.79, 95% CI: 0.66-0.95). Moreover, CAG repeat length was associated with male infertility in Caucasian populations, but not Asian or Egyptian populations. Subgroup analysis revealed no significant difference in German populations, but CAG repeat length was associated with male infertility in China and the USA. There were no significant differences between cases and controls in azoospermia and severe oligozoospermia. Copyright © 2016 Reproductive Healthcare Ltd.
Improving ICSI: A review from the spermatozoon perspective.
Simopoulos M., Gkoles L., Bakas P., Giannelou P., Kalampokas T., Pantos K., Koutsilieris M.
Embase
[Review]
AN: 612277497

Intracytoplasmic sperm injection (ICSI) is the most frequently applied method for fertilization making the process of identifying the perfect spermatozoon fundamental. Herein we offer a critical and thorough presentation on the techniques reported regarding (i) handling and preparing semen samples, (ii) identifying and 'fishing' spermatoza, and (iii) improving key factors, such as motility for a successful ICSI practice. These approaches are suggested to make the process easier and more effective especially in atypical and challenging circumstances. Furthermore, we present an epigrammatic opinion—where appropriate—based upon our collective experience.

Techniques such as intracytoplasmic morphologically selected sperm injection, hyaluronic binding, polarized light microscopy, and annexin V agent identification for comparing sperm cells and their chromatin integrity are analyzed. Moreover, for the demanding cases of total sperm immotility the use of the hypoosmotic swelling test, methylxanthines, as well as the option of laser assisted immotile sperm selection are discussed. Finally, we refer to the employment of myo-inositol as a way to bioreactively improve ICSI outcome for oligoasthenoteratozoospermic men. The diversity and the constant development of novel promising techniques to improve ICSI from the spermatozoon perspective, is certainly worth pursuing. The majority of the techniques discussed are still a long way from being established in routine practices of the standard IVF laboratory. In most cases an experienced embryologist could yield the same results. Although some of the techniques show great benefits, there is a need for large scale multicenter randomized control studies to be conducted in order to specify their importance before suggesting horizontal application. Taking into consideration the a priori invasive nature of ICSI, when clinical application becomes a possibility we need to proceed with caution and ensure that in the pursuit for innovation we are not sacrificing safety and the balance of the physiological and biological pathways of the spermatozoon's dynamic. Abbreviations: ICSI: intracytoplasmic sperm injection; IVF: in vitro fertilization; PGD: reimplantation genetic diagnosis; IVM: in vitro maturation; HCV/HIV: hepatitis C virus/human immunodeficiency virus; IMSI: intracytoplasmic morphologically selected sperm injection; DGC: density gradient centrifugations; S-U: swim-up; ART: assisted reproduction technology; IUI: intrauterine insemination; PVP: polyvinylpyrrolidone;
437.
Endocrine Society of Australia position statement on male hypogonadism (Part 2): Treatment and therapeutic considerations.

Embase
Medical Journal of Australia. 205 (5) (pp 228-231), 2016. Date of Publication: 05 Sep 2016.
[Article]
AN: 612217418

Introduction: Part 1 of this position statement dealt with the assessment of male hypogonadism, including the indications for testosterone therapy. This article, Part 2, focuses on treatment and therapeutic considerations for male hypogonadism and identifies key questions for future
research. Main recommendations: Key points and recommendations are:

Excess cardiovascular events have been reported in some but not all studies of older men without pathological hypogonadism who were given testosterone treatment. Additional studies are needed to clarify whether testosterone therapy influences cardiovascular risk. Testosterone is the native hormone that should be replaced in men being treated for pathological hypogonadism. Convenient and cost-effective treatment modalities include depot intramuscular injection and transdermal administration (gel, cream or liquid formulations). Monitoring of testosterone therapy is recommended for efficacy and safety, focusing on ameliorating symptoms, restoring virilisation, avoiding polycythaemia and maintaining or improving bone mineral density. Treatment aims to relieve an individual's symptoms and signs of androgen deficiency by administering standard doses and maintaining circulating testosterone levels within the reference interval for eugonadal men. Evaluation for cardiovascular disease and prostate cancer risks should be undertaken as appropriate for eugonadal men of similar age. Nevertheless, when there is a reasonable possibility of substantive pre-existing prostate disease, digital rectal examination and prostate-specific antigen testing should be performed before commencing testosterone treatment.

Changes in management as result of the position statement: Treatment aims to relieve symptoms and signs of androgen deficiency, using convenient and effective formulations of testosterone. Therapy should be monitored for efficacy and safety.

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Publisher
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The impact of premature progesterone rise on the outcome of intrauterine insemination cycles with controlled ovarian hyperstimulation in unexplained infertility.
Mutlu M.F., Erdem M., Erdem A., Mutlu I., Guler I., Demirdag E.
Embase
Date of Publication: 01 Aug 2016.
[Article]
AN: 610473587
Objective To ascertain the incidence of premature progesterone P rise and its impact on outcomes in controlled ovarian hyperstimulation and intrauterine insemination (COH-IUI) cycles, and also to identify variables related with premature P rise. Study design Four hundred sixty cycles of 460 couples with unexplained infertility having COH-IUI treatment with a starting dose of 75 IU recombinant FSH enrolled in this prospective study. Serum P levels were determined on the day of hCG trigger. Premature P rise was defined as progesterone >1 ng/mL. The primary outcome measure was live birth per cycle with regard to P levels of >1 ng/mL and >1.5 ng/mL. Secondary outcome measures were cycle characteristics associated with P rise. Results The incidence of premature P rise was 22.0%. P levels on hCG day were significantly lower in cycles with live birth as compared to cycles without live birth 0.49 +/- 0.51 vs. 0.73 +/- 0.82 ng/mL. Live birth rates were significantly lower in cycles with hCG day P levels >1.0 ng/mL (%7.9 vs. %22.6) and >1.5 ng/mL (%6.4 vs. %20.8). Among age, number of dominant follicles, estradiol, LH and P levels on the day of hCG trigger, it was found that P levels was the only significant variable to predict live birth on multivariate analysis. The number of dominant follicles on hCG day and premature LH surge were the only significant variables related with premature P rise. Conclusion Premature P is a frequent feature of COH-IUI cycles and associated with decreased live birth rates. Copyright © 2016 Elsevier Ireland Ltd. All rights reserved.
PMID
Predicting low testosterone in aging men: A systematic review.


Embase


[Article]

AN: 612310541

Background: Physicians diagnose and treat suspected hypogonadism in older men by extrapolating from the defined clinical entity of hypogonadism found in younger men. We conducted a systematic review to estimate the accuracy of clinical symptoms and signs for predicting low testosterone among aging men. Methods: We searched the MEDLINE and Embase databases (January 1966 to July 2014) for studies that compared clinical features with a measurement of serum testosterone in men. Three of the authors independently reviewed articles for inclusion, assessed quality and extracted data. Results: Among 6053 articles identified, 40 met the inclusion criteria. The prevalence of low testosterone ranged between 2% and 77%. Threshold testosterone levels used for reference standards also varied substantially. The summary likelihood ratio associated with decreased libido was 1.6 (95% confidence interval [CI])
1.3-1.9), and the likelihood ratio for absence of this finding was 0.72 (95% CI 0.58-0.85). The likelihood ratio associated with the presence of erectile dysfunction was 1.5 (95% CI 1.3-1.8) and with absence of erectile dysfunction was 0.83 (95% CI 0.76-0.91). Of the multiple-item instruments, the ANDROTEST showed both the most favourable positive likelihood ratio (range 1.9-2.2) and the most favourable negative likelihood ratio (range 0.37-0.49). Interpretation: We found weak correlation between signs, symptoms and testosterone levels, uncertainty about what threshold testosterone levels should be considered low for aging men and wide variation in estimated prevalence of the condition. It is therefore difficult to extrapolate the method of diagnosing pathologic hypogonadism in younger men to clinical decisions regarding age-related testosterone decline in aging men. Copyright © 2016 Joule Inc. or its licensors.

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Publisher
Canadian Medical Association (1867 Alta Vista Drive, Ottawa KIG5W8, Canada)
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2016
Finding the balance between surgery and medically-assisted reproduction in women with deep infiltrating endometriosis.

Cohen J., Ballester M., Selleret L., Mathieu D'argent E., Antoine J.-M., Chabbert-Buffet N., Darai E.

Embase
Minerva Ginecologica. 68 (6) (pp 642-652), 2016. Date of Publication: December 2016.
[Review]
AN: 612769102

Deep infiltrating endometriosis (DIE) affects several anatomical locations including the bladder, torus uterinum, uterosacral ligament, rectovaginal septum and bowel. It is the most debilitating form of endometriosis and causes severe pain, digestive and urinary symptoms as well as infertility. Faced with an infertile woman suffering from DIE, the dilemma is whether to opt for first-line IVF treatment or for surgery. In the absence of high-level of evidence from randomized studies, several factors should be taken into account in the decision-making process. The main criterion is whether the patient wants in-vitro fertilization (IVF) treatment or not. Secondly, while previous reports have demonstrated the positive impact of surgery on pregnancy, they also underline the risk of severe complications requiring management in expert centers. Despite the availability of predictive models or scoring systems, the decision mainly boils down to the couple's characteristics. It seems logical to propose first-line IVF when spontaneous fertility is not possible due to associated male infertility or tubal obstruction; for women aged >35 years; or in women with diminished ovarian reserve. Conversely, first-line surgery could be the best option for women without these characteristics. However, this strategy is mainly based on low-level of evidence underlining the requiring of randomized trials. Copyright © 2016 EDIZIONI MINERVA MEDICA.


Embase
Introduction: Schizophrenia is a chronic and debilitating mental disorder that affects the patient's and their family's quality of life, as well as financial costs and health care settings. Despite the variety of available antipsychotics, optimal treatment outcomes are not always achieved. Novel drugs, such as iloperidone, can provide more effective, tolerable and safer strategies. Aim: To review the evidence for the clinical impact of iloperidone on the treatment of patients with schizophrenia. Evidence review: Clinical trials, observational studies and meta-Analyses reached a common consensus that iloperidone is as effective as haloperidol, risperidone and ziprasidone in reducing schizophrenia symptoms. Similar amounts of adverse events and discontinuations were observed with iloperidone compared to placebo and active treatments. Common adverse events are mild and include dizziness, hypotension, dry mouth and weight gain. Iloperidone can induce extension of QTc interval, and clinicians should be aware of its contraindications. In long-term trials, iloperidone also showed promising safety and tolerability profiles. The low propensity to cause akathisia, extrapyramidal symptoms (EPS), increased prolactin levels or changes to metabolic laboratory parameters support its use in practice. Results showed that iloperidone prevents relapse in stabilized patients, with a time to relapse superior to placebo and similar to haloperidol. Patients using a prior antipsychotic (e.g., risperidone and aripiprazole) can easily switch to iloperidone with no serious impact on safety or efficacy. However, the acquisition costs of iloperidone may hamper its use. Further evidence comparing iloperidone with other antipsychotics, and pharmacoeconomic studies would be welcome. Place in therapy: Considering just the clinical profile of iloperidone, it represents a promising drug for treating schizophrenia, particularly in patients who are intolerant to previous antipsychotics, as well as being suitable as...
first-line therapy. Cost-effectiveness comparisons are needed to justify its use in clinical practice.

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442.

Transitional Zone Index as a Predictor of the Efficacy of alpha-Blocker and 5alpha-Reductase Inhibitor Combination Therapy in Korean Patients with Benign Prostatic Hyperplasia.

Choi J.D., Kim J.H., Ahn S.H.

Embase

Urologia Internationalis. 96 (4) (pp 406-412), 2016. Date of Publication: 01 May 2016.

[Article]

AN: 607997950

Introduction: We investigated the value of the transitional zone index (TZI) for predicting treatment response to combination therapy involving alpha-blockers and 5alpha-reductase inhibitors for benign prostatic hyperplasia (BPH). Materials and Methods: Symptomatic BPH patients (n = 118) were randomized to receive 0.2 mg tamsulosin alone or with 0.5 mg dutasteride daily for 12 months. The TZI, International Prostate Symptom Scores, maximum urinary flow rates (Qmax), postvoid residual urine volumes, and prostate-specific antigen (PSA) were evaluated at baseline and after 12 months. The groups were subdivided according to a cut-
off TZI value of 0.5 to compare treatment-related changes. Results: After 12 months, the combination therapy group had significantly greater decreases in prostate volume (p < 0.001), TZ volume (p < 0.001) and PSA (p < 0.001) than the monotherapy group, regardless of TZI. However, combination therapy resulted in significantly greater Qmax increases (p < 0.001) only in patients with a TZI >0.5. Multivariate analysis determined that TZI was the strongest independent predictor of the Qmax increase at 12 months in the combination therapy group (beta = 13.7, p < 0.001). Conclusions: Greater Qmax improvement is expected with combination therapy comprising alpha-blockers and 5alpha-reductase inhibitors for patients with a TZI >0.5. The TZI may be useful for predicting the Qmax response to combination treatment for BPH. Copyright © 2016 S. Karger AG, Basel.

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Publisher
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20160614
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2016

443.
Risk of adverse pregnancy and perinatal outcomes after high technology infertility treatment: A comprehensive systematic review.
Palomba S., Homburg R., Santagni S., La Sala G.B., Orvieto R.
Embase
Reproductive Biology and Endocrinology. 14 (1) (no pagination), 2016. Article Number: 76. Date of Publication: 04 Nov 2016.
[Review]
AN: 613008770
In the literature, there is growing evidence that subfertile patients who conceived after infertility treatments have an increased risk of pregnancy and perinatal complications and this is particularly true for patients who conceived through use of high technology infertility treatments. Moreover, high technology infertility treatments include many concomitant clinical and biological risk factors. This review aims to summarize in a systematic fashion the current evidence regarding the relative effect of the different procedures for high technology infertility treatments on the risk of adverse pregnancy and perinatal outcome. A literature search up to August 2016 was performed in IBSS, SocINDEX, Institute for Scientific Information, PubMed, Web of Science and Google Scholar and an evidence-based hierarchy was used to determine which articles to include and analyze. Data on prepregnancy maternal factors, low technology interventions, specific procedures for male factor, ovarian tissue/ovary and uterus transplantation, and chromosomal abnormalities and malformations of the offspring were excluded. The available evidences were analyzed assessing the level and the quality of evidence according to the Oxford Centre for Evidence-Based Medicine guidelines and the Grading of Recommendations Assessment, Development, and Evaluation system, respectively. Current review highlights that every single procedure of high technology infertility treatments can play a crucial role in increasing the risk of pregnancy and perinatal complications. Due to the suboptimal level and quality of the current evidence, further well-designed studies are needed. 

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Publisher BioMed Central Ltd. (E-mail: info@biomedcentral.com)

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Year of Publication 2016
Clinical observation of effect of diosmin combined with Jinshuibao capsule treatment on improvement of semen quality in patients with varicocele.

Pan Z., Deng N., Zou Z.

Embase

Medical Science Technology. 57 (pp 42-46), 2016. Date of Publication: 2016.

[Article]

AN: 614907773

Background: Diosmin is widely used in clinical practice. Jinshuibao capsules are made from fermented Cordyceps sinensis bacteria powder, which is similar to Cordyceps sinensis. We aimed to observe the effect of Diosmin combined with Jinshuibao capsule treatment on improvement of semen quality in patients with varicocele (VC).

Material/Methods: We randomly divided 147 male infertility patients with VC into 3 groups. The Treatment Group consisted of 49 patients orally administered Diosmin (2 tablets twice a day), Jinshuibao capsule (3 tablets twice a day), and zinc selenium (2 pills twice a day). Control Group 1 consisted of 48 patients orally administered zinc selenium (2 pills twice a day). Control Group 2 consisted of 50 patients orally administered Jinshuibao (3 tablets twice a day and zinc selenium (2 pills twice a day). Each group received a 3-month course of treatment. Results: The survival rate of sperm and percentage of grade I sperm were obviously increased in the treatment group compared to the control groups after 3-month treatment (P<0.01). The fragmentation index of sperm DNA and rate of abnormal sperm nucleoprotein were significantly reduced in the treatment group. Conclusions: Diosmin combined with Jinshuibao capsule therapy improves semen quality in patients with VC and curative effect is superior to that of zinc selenium alone or combined with Jinshuibao.


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Date Created
Medical cannabis for pain in adolescence.
Knishkowy B.
Embase
[Review]
AN: 614439902
The use of medical cannabis for pain in adolescence is controversial. The purpose of this review is to summarize the literature regarding efficacy, adverse bio-psychosocial and neurodevelopmental effects, as well as legislation and utilization patterns of adolescents. Clinical trials demonstrating efficacy of cannabis for adolescent pain are essentially nonexistent. Adolescent marijuana use may result in a number of physical symptoms, has a strong association with schizophrenia, may affect neurocognitive development in the not fully mature adolescent brain, and may lead to school, relationship and work problems as well as motor vehicle accidents. The proportion of legal medical cannabis patients under the age of 18 years ranges from 0.04% to 0.36% in different US states with medical marijuana laws. Leading reasons for its being given are pain and epilepsy. Adolescents who use medical cannabis have an increased likelihood of displaying high-risk drug related behavior. Diversion of medical cannabis to other teenagers is not uncommon. There is a need for clinical trials of cannabis for pain control in different adolescent health conditions. Clinical guidelines should be prepared to aid physicians and legislators in determining when medical marijuana is justified in this age group, and in identifying adolescents likely to misuse the drug. Copyright © Nova Science Publishers, Inc.
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Date Created
The Urolift System for the Treatment of Lower Urinary Tract Symptoms Secondary to Benign Prostatic Hyperplasia: A NICE Medical Technology Guidance.
Embase
[Review]
AN: 608107495
As part of its Medical Technologies Evaluation Programme (MTEP), the National Institute for Health and Care Excellence (NICE) invited Neotract (manufacturer) to submit clinical and economic evidence for their prostatic urethral lift device, Urolift, for the relief of lower urinary tract symptoms secondary to benign prostatic hyperplasia (LUTS BPH). The Urolift System uses implants to retract the prostatic lobe away from the urethral lumen. The clinical evidence used in the manufacturer's submission shows that Urolift is effective for the treatment of BPH. Urolift delivers a weighted mean International Prostate Symptom Score (IPSS) improvement of between 9.22 and 11.82 points. These Urolift improvements are greater than a published 'marked improvement' in IPSS score of 8.80. Comparison with randomised controlled trials (RCTs) of TURP (Transurethral Resection of Prostate) and HoLEP (Holmium Laser Enucleation of Prostate) show that Urolift does not yield better clinical outcomes from baseline compared to TURP and HoLEP in terms of IPSS, QoL (Quality of Life) and Qmax (maximum urinary flow). However, Urolift appears to have the advantage in terms of minimal and mild complications, and this may be of interest to patients and urologists. The economic case for Urolift was made using a very detailed and thorough de novo cost model. The base case posed by the manufacturer placed Urolift at almost cost-neutral (3 cost incurring, based on 2014 prices) compared to TURP, and 418 cost incurring compared to HoLEP. In an additional scenario comparing day-case Urolift with in-patient TURP, the estimated per-patient savings with Urolift were 286 compared with monopolar TURP (mTURP) and 159 compared with bipolar TURP (BiTURP). NICE guidance
MTG26 recommends that the case for adoption of Urolift was supported by the evidence, when implemented in a day-case setting. Copyright © 2016, The Author(s).

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2016

447.
Serum testosterone and cognitive function in ageing male: Updating the evidence.
Giagulli V.A., Guastamacchia E., Licchelli B., Triggiani V.

Embase
Recent Patents on Endocrine, Metabolic and Immune Drug Discovery. 10 (1) (pp 22-30), 2016.

Date of Publication: 2016.

[Article]
AN: 613959872

Background: Testosterone (T) deficit, either in prepubertal or postpubertal form of hypogonadism, seems to play a key role in impairing cognitive function, including memory, attention, language and visuospatial abilities, especially in elderly men Objective: Several studies have recently showed the association between low serum T levels and important cognitive dysfunctions in ageing male as well as in subjects suffering from Alzheimer's disease (AD), mild cognitive impairment (MCI) and even depression, suggesting that T could exert an active neuro protective role. Methods: By searching PubMed and recent patents (ranging from 2010 to 2015), we identified several observational and intervention studies dealing with T and cognitive function in
adult and ageing men. Findings were reviewed, thoroughly examined and, finally, summarized herein. Results: Although a large number of studies have been carried out so far, conclusive evidence cannot be drawn, in particular, for cognitive disorders in males. Conversely, T supplementation has been suggested for depressive syndrome in young and ageing men. To date, no clinical data have been carried out on cognitive dysfunctions employing the quoted patents in men. Conclusions: Studies aiming to evaluate the role of serum T and its supplementation in adult and ageing men with T deficiency syndrome need to be encouraged, given that subjects affected by overt hypogonadism, either in prepubertal (i.e. Klinefelter syndrome) or postpubertal forms (chemical castration in subjects affected by prostate cancer), often complain of cognitive dysfunction, and seem to considerably benefit from T replacement therapy. Copyright © 2016 Bentham Science Publishers.


Identification of late-onset hypogonadism in middle-aged and elderly men from a community of China.

Embase
Asian Journal of Andrology. 18 (5) (pp 747-753), 2016. Date of Publication: September 2016. [Article]
In this study, we investigated the essential criteria for late-onset hypogonadism (LOH) syndrome based on the presence of symptoms associated with low testosterone levels in Han Chinese men. Blood tests for total testosterone (TT) and sex hormone-binding globulin (SHBG) were performed, and the aging male symptoms (AMS) questionnaire was conducted in a randomly selected cohort composed of 944 Chinese men aged 40 to 79 years from nine urban communities. Three sexual symptoms (decreased ability/frequency of sexual activity, decreased number of morning erections, and decreased libido) were confirmed to be related to the total and free testosterone levels. The thresholds for TT were approximately 12.55 nmol l\(^{-1}\) for a decreased ability/frequency to perform sex, 12.55 nmol l\(^{-1}\) for decreased frequency of morning erections, and 14.35 nmol l\(^{-1}\) for decreased sexual desire. The calculated free testosterone (CFT) thresholds for these three sexual symptoms were 281.14, 264.90, and 287.21 pmol l\(^{-1}\), respectively. TT <13.21 nmol l\(^{-1}\) (OR = 1.4, 95%CI: 1.0-1.9, P = 0.037) or CFT <268.89 pmol l\(^{-1}\) (OR = 1.5, 95%CI: 1.1-2.0, P = 0.020) was associated with an increase in the aforementioned three sexual symptoms. The prevalence of LOH was 9.1% under the criteria, including all three sexual symptoms with TT levels <13.21 nmol l\(^{-1}\) and CFT levels <268.89 pmol l\(^{-1}\). Our results may improve the diagnostic accuracy of LOH in older men.
Cystinosis: a new perspective.
Embse
[Article]
AN: 611018156
Cystinosis is a rare, autosomal recessive inherited lysosomal storage disease. It is the most frequent and potentially treatable cause of the inherited renal Fanconi syndrome. If left untreated, renal function rapidly deteriorates towards end-stage renal disease by the end of the first decade of life. Due to its rarity and non-specific presentation, the entity is often not promptly recognized resulting in delayed diagnosis. Two major milestones in cystinosis management, cystine-depleting therapy with cysteamine and renal allograft transplantation, have had a considerable impact on the natural history and prognosis of cystinosis patients. However, due to its significant side effects and a strict 6-hourly dosing regimen, non-adherence to the immediate release of cysteamine bitartrate formulation (Cystagon) is a major issue that might affect long-term outcome. Recently, a new twice-daily administered delayed-release enteric-coated formula of cysteamine bitartrate (ProcysbiTM) has been approved by the European Medical Agency for the treatment of cystinosis, and has been shown to be safe and effective. This delayed-release cysteamine has the potential to improve compliance and hence prognosis, through its better dosing regimen, positive impact on quality of life and possibly less side-effects, and is now tested in an ongoing long-term clinical trial. Longer survival of patients with cystinosis makes transition from pediatric to adult-oriented care another challenge in cystinosis management and requires an extended multidisciplinary approach. Copyright © 2016, © Acta Clinica Belgica 2016.
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The effect of epilepsy and antiepileptic drugs on sexual, reproductive and gonadal health of adults with epilepsy.

Hamed S.A.
Embase

[Review]
AN: 609209564

ABSTRACT: Epilepsy is a common chronic medical illness. Hyposexuality is the most frequent abnormality in men and women with epilepsy. In men with epilepsy, hypoandrogenimia, hypogonadism and sperm abnormalities are common. Testicular atrophy was also infrequently reported. In women with epilepsy, hyperandrogenism, polycystic ovaries (PCOs) and PCO syndrome are frequent. Decreased serum free testosterone, dehydroepiandrosterone levels, free androgen index and free testosterone/leutinizing hormone (LH) ratio and increased sex hormone binding globulin, estradiol, prolactin, LH, follicle stimulating hormone (FSH) levels and LH/FSH ratio are common with epilepsy. Disturbance of central and/or peripheral control of hypothalamic-pituitary-gonadal axis and alteration of central neurotrasmitters (GABA, glutamate and serotonin) by epileptic discharges or antiepileptic drugs (AEDs), direct gonadal toxicity by AEDs and psychiatric/psychosocial factors are all incriminated in sexual, reproductive and gonadal abnormalities associated with epilepsy. Patients may benefit from multidisciplinary evaluation, tight seizure control, change the AED, androgen therapy, genital vasodilators, L-carnitine supplementation and psychotherapy. Copyright © 2016 Informa UK Limited, trading as Taylor & Francis Group.

451.
Genetic counseling for men with recurrent pregnancy loss or recurrent implantation failure due to abnormal sperm chromosomal aneuploidy.
Kohn T.P., Kohn J.R., Darilek S., Ramasamy R., Lipshultz L.
Embase
[Review]
AN: 609300149
Purpose: The purpose of this study is to review recurrent pregnancy loss (RPL) due to sperm chromosomal abnormalities and discuss the genetic counseling that is required for men with sperm chromosomal abnormalities. Method: The literature was reviewed, and a genetic counselor lends her expertise as to how couples with RPL and sperm chromosomal abnormalities ought to be counseled. The review of the literature was performed using MEDLINE. Results: Sperm fluorescence in situ hybridization (FISH) can be used to determine if disomy or unbalanced chromosomal translocations are present. In men with aneuploidy in sperm or who carry a chromosomal translocation, pre-implantation genetic screening (PGS) combined with in vitro fertilization (IVF) and intra-cytoplasmic sperm injection (ICSI) can increase chances of live birth. In men with abnormal sperm FISH results, the degree of increased risk of abnormal pregnancy remains unclear. Genetic counselors can provide information to couples about the risk for potential trisomies and sex chromosome aneuploidies and discuss their reproductive and testing options such as PGS, use of donor sperm, and adoption. The provision of genetic counseling also
allows a couple to be educated about recommended prenatal testing since pregnancies conceived with a partner who has had abnormal sperm FISH are considered to be at increased risk for aneuploidy. Conclusion: We review the literature and discuss genetic counseling for couples with RPL or recurrent implantation failure due to increased sperm aneuploidy. Copyright © 2016, Springer Science+Business Media New York.

PMID

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Publisher
Springer New York LLC (E-mail: barbara.b.bertram@gsk.com)

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2016

452.
Efficacy and Safety of Hexanic Lipidosterolic Extract of Serenoa repens (Permixon) in the Treatment of Lower Urinary Tract Symptoms Due to Benign Prostatic Hyperplasia: Systematic Review and Meta-analysis of Randomized Controlled Trials.
Embase
European Urology Focus. 2 (5) (pp 553-561), 2016. Date of Publication: 01 Dec 2016.
[Review]
AN: 614513455
Context A recent Cochrane Collaboration meta-analysis of randomized controlled trials (RCTs) evaluating the efficacy of different extracts of Serenoa repens in relieving lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH) concluded that these extracts were no more effective than placebo. However, among all Serenoa repens extracts, Permixon (Pierre Fabre Medicament, Paris, France) has the highest activity and the most accurate standards of drug preparation and extraction. Objective To evaluate the efficacy and safety of Permixon in the treatment of LUTS/BPH. Evidence acquisition A systematic review and meta-analysis of the literature was performed in January 2016 using the Medline, Scopus, and Web of Science databases, searching for the term Serenoa repens in all fields of the records. Only RCTs reporting on efficacy and safety of Permixon in the treatment of LUTS/BPH were selected. Evidence synthesis The systematic search identified 12 RCTs: 7 compared Permixon with placebo; 2 compared Permixon with tamsulosin; 2 compared Permixon plus tamsulosin with, respectively, placebo plus tamsulosin and tamsulosin alone; and 1 compared Permixon with finasteride. Permixon was significantly more effective than placebo in reducing the number of nocturnal voids (weighted mean difference [WMD] -0.31; p = 0.03) and increasing maximum flow rate (Qmax; WMD 3.37; p < 0.0001). The rates of overall adverse events (odds ratio [OR] 1.12; p = 0.92) and withdrawal (OR 1.52; p = 0.60) were similar for Permixon and placebo. Permixon was as effective as tamsulosin monotherapy and short-term therapy with finasteride in improving International Prostate Symptom Score (WMD 1.15; 95% confidence interval [CI], -1.11 to 3.40; p = 0.32) and Qmax (WMD -0.16; 95% CI, -0.60 to 0.28; p = 0.48). The combination of Permixon and tamsulosin was more effective than Permixon alone for relieving LUTS (WMD 0.31; 95% CI, 0.13-0.48; p < 0.01) but not for improving Qmax (WMD 0.10; 95% CI -0.02 to 0.21; p = 0.10). Permixon had a favorable safety profile, with a very limited impact with regard to ejaculatory dysfunction compared with tamsulosin (0.5% vs 4%; p = 0.007) and with regard to decreased libido and impotence compared with short-term finasteride (2.2% and 1.5% vs 3% and 2.8%, respectively). Conclusions The conclusions of the recent Cochrane meta-analysis on Serenoa repens in the treatment of LUTS/BPH apparently do not apply to Permixon. Our meta-analysis showed that Permixon decreased nocturnal voids and Qmax compared with placebo and had efficacy in relieving LUTS similar to tamsulosin and short-term finasteride. Moreover, Permixon had a favorable safety profile with a very limited impact on sexual function, which is significantly affected by all other drugs used to treat LUTS/BPH. Patient summary A systematic review of the literature showed that Permixon was effective for relieving urinary symptoms due to prostate enlargement and improving urinary flow compared with placebo. Permixon had efficacy similar to tamsulosin and short-term finasteride in relieving urinary symptoms. Permixon was well tolerated and had a very limited impact on sexual function. Copyright © 2016 European Association of Urology

Status
Single versus double intrauterine insemination in controlled ovarian hyperstimulation cycles: A randomized trial.

Zahiri Sorour Z., Rashid Shomali R., Pourmarzi D.

Embase

Archives of Iranian Medicine. 19 (7) (pp 465-469), 2016. Date of Publication: July 2016.

[Article]

AN: 610950067

BACKGROUND: There are many factors that affect intrauterine insemination (IUI) success rate and identifying those factors can be helpful. This study aimed to investigate the single versus double IUI in controlled ovarian hyperstimulation cycles. METHODS: This is a randomized clinical trial with equal randomization (1:1) conducted on 580 women who underwent IUI in a private
infertility clinic from May 2013 to November 2014 in Rasht, Iran. Women were randomly assigned to single (n = 290) or double (n = 290) IUI groups. Women in the single group underwent IUI performed 36 h after human chorionic gonadotropin (HCG) administration. Women in the double group underwent two IUIs performed 18 and 40 h after HCG administration. The main outcome was clinical pregnancy confirmed by evidence of fetal cardiac activity. Data were analyzed by SPSS software. Comparisons of frequencies were done using the Fisher exact test and chi-square test. For comparing means between the two groups, the independent t-test was used. The P-value < 0.05 was considered to indicate statistical significance. RESULTS: Pregnancy rate was 11.7% (34/290) in the single IUI group and 13.4% (39/290) in the double IUI group. The difference between the two groups was not statistically significant (P = 0.617, OR = 1.17, 95% CI: 0.72 - 1.91). Also, we could not show significant difference between single and double IUI groups in different cause of infertility groups regarding the success rate. CONCLUSION: Based on findings, double versus single IUI did not increase the pregnancy rate of IUI and further investigations are recommended. Copyright © 2016, Academy of Medical Sciences of I.R. Iran.


Status EMBASE

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Publisher Academy of Medical Sciences of I.R. Iran

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Year of Publication 2016

454.
Serenoa repens, selenium and lycopene to manage lower urinary tract symptoms suggestive for benign prostatic hyperplasia.
Introduction: Benign prostatic hyperplasia (BPH) is a disease affecting most of the elderly male. alpha1-blockers and 5-alpha reductase inhibitors are currently used to target lower urinary tract symptoms (LUTS). Moreover phytotherapeutic agents, including Serenoa Repens (SeR), have shown to have a role in ameliorating BPH/LUTS alone or in combination of other elements like Selenium (Se) and Lycopene (Ly). Areas covered: A literature review was performed using data from articles assessing the role of SeR+Se+Ly in the management of LUTS secondary to BPH. Diverging evidence on SeR’s efficacy is available. On one hand several studies have shown SeR efficacy in treating BPH/LUTS. SeR is effective in reducing prostate size, urinary frequency, dysuria, nocturia and in improving maximum urine flow-rate. On the other hand two long-term trials reported that SeR did not improve prostate size or urinary flow. SeR+Se+Ly in combination with tamsulosin is more effective than single therapies in improving IPSS and increasing maximal urinary flow-rate in patients affected by LUTS/BPH. Expert opinion: Despite great amount of preclinical and clinical studies, the use of SeR in BPH/LUTS is not sustained by clear evidence for a therapeutic efficacy but current data hint higher efficacy of SeR+Se+Ly compared to SeR alone. Copyright © 2016 Informa UK Limited, trading as Taylor & Francis Group.

Controversial effects of exogenous testosterone on cardiovascular diseases.

Al-Khazaali A., Arora R., Muttar S.

Embase
American Journal of Therapeutics. 23 (6) (pp e1504-e1513), 2016. Date of Publication: 28 Nov 2016.
[Article]
AN: 613333906

The use of testosterone (T) among men aged 40 years or older was increased more than 3 times from 0.81% in 2001 to 2.91% in 2011. Until recently, the majority of the studies did not show any increased cardiovascular (CV) risk by using T in male patients with hypogonadism. What is more, some studies had observed a protective effect of using T against CV diseases. However, in 2010, a randomized clinical trial (RCT) was intended to study the advantage of T gel in older men with limitations in mobility; the study was stopped due to unexpected high prevalence of CV adverse outcome. These findings were confirmed by 2 other studies published in November of 2013 and January of 2014. Consequently, the Food and Drug Administration (FDA) had announced in January 2014 that it will reassess the safety of those treatments. Meanwhile, the agency had not reached to a definitive conclusion that FDA-approved testosterone therapy raises the risk of stroke, heart attack, or death. A report released in the broadcast of the NBC Nightly News in September of this year that the FDA says there’s little evidence that T boosting drugs taken by millions of American men are actually effective. NBC notes that the agency also pointed out that it was not convinced that they carry serious risk either. The condition has been marketed as low ‘T’, and the medications are offered to help with low sex drive and fatigue among some men, notes NBC. The European Medicines Agency EMA’s Pharmacovigilance Risk Assessment Committee has also responded to the concern of potential CV adverse outcomes associated with the use of T, and they have concluded in their October meeting of this year that the use of T in men who do not produce enough T raises the risk of heart diseases. In our review, we highlighted the association between exogenous T and major adverse CV outcomes. Additionally, we focused on the interplay between exogenous T and some endocrine abnormalities such as diabetes mellitus type 2, metabolic syndrome, dyslipidemia, and obesity. 

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456.
Preliminary MALDI-TOF-MS analysis of seminal plasma N-glycome of infertile men.
Embass
[Article]
AN: 612328543
Glycosylation pattern within reproductive tract is now suggested to be involved in providing female immune tolerance for allograft sperm and developing embryo, but the information whether impaired glycosylation may influence male fertility potential is still limited. We have analyzed seminal plasma N-glycome in pooled samples derived from fertile and infertile men by means of MALDI-TOF/TOF tandem mass spectrometry. Among infertile subjects, normozoospermic, oligozoospermic, asthenozoospermic and oligoasthenozoospermic samples were obtained. Eighty-six oligosaccharides were identified in all the analyzed samples. Differences in the content of unique glycans: high mannose and hybrid type, lacking terminal sialic acid and highly fucosylated were found when samples derived from infertile subjects with different semen
patterns were compared to the fertile control. The content of highly branched glycans was 3-fold elevated in normozoospermic infertile men, while the expression of highly fucosylated oligosaccharides was increased in asthenozoospermic, oligozoospermic and oligoasthenozoospermic samples. Sialylation of oligosaccharides was decreased in oligozoospermic, oligoasthenozoospermic and especially asthenozoospermic samples, but increased in infertile normozoospermic subjects. Altered glycosylation observed in seminal plasma may reflect similar changes in sperm surface glycoproteins, and may disturb sperm interaction with female immune system. We suggest that at least some cases of unexplained male infertility may be associated with impaired glycosylation. Copyright © 2016 Elsevier Ltd


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457.

Exercise improves the effects of testosterone replacement therapy and the durability of response after cessation of treatment: A pilot randomized controlled trial.


Embase
The effects of the combination of exercise and TRT on symptoms of late-onset hypogonadism (LOH) and the durability of response after cessation of TRT were investigated. A total of fifty patients with erectile dysfunction (ED) who had a sedentary lifestyle and low serum total testosterone (T) levels were enrolled and followed for 20 weeks. Patients were randomly divided into two groups; all of them received T gel for 12 weeks and it was discontinued for 8 weeks. Patients assigned to Group II were offered a supervised exercise program for 20 weeks. Measurement of serological testing was performed and self-assessment questionnaires and Global Assessment Question (GAQ) were asked. Baseline characteristics and the initial symptom scores showed no significant difference between the two groups. Serum total T levels and the symptom scores were increased at 12 weeks in both groups, and Group II showed better results with statistical significance. There was a decrease in T levels and worsening of symptom scores at week 20 compared to week 12 in both groups, and Group II showed better results with statistical significance. On the GAQ, Group II showed higher ratio of "yes" at week 12 and the same tendency was sustained at week 20 with significant difference between two groups. The combination of exercise and TRT showed significant improvements in serum T levels and LOH symptoms compared to TRT alone. In addition, these improvements were maintained in the combination group with continuous exercise, even after cessation of TRT. Copyright © 2016 AJA, SIMM & SJTU. All rights reserved.
458.
Enclomiphene citrate for the treatment of secondary male hypogonadism.
Rodriguez K.M., Pastuszak A.W., Lipshultz L.I.
Embase
[Article]
AN: 611100168
ABSTRACT: Introduction: Hypogonadism is a growing concern in an aging male population. Historically treated using exogenous testosterone, concerns about possible adverse effects of testosterone have led physicians to seek alternative treatment approaches. Areas covered: Enclomiphene citrate is the trans isomer of clomiphene citrate, a non-steroidal estrogen receptor antagonist that is FDA-approved for the treatment of ovarian dysfunction in women. Clomiphene citrate has also been used off-label for many years to treat secondary male hypogonadism, particularly in the setting of male infertility. Here we review the literature examining the efficacy and safety of enclomiphene citrate in the setting of androgen deficiency. Expert opinion: Initial results support the conclusion that enclomiphene citrate increases serum testosterone levels by raising luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels, without negatively impacting semen parameters. The ability to treat testosterone deficiency in men while maintaining fertility supports a role for enclomiphene citrate in the treatment of men in whom testosterone therapy is not a suitable option. Copyright © 2016 Informa UK Limited, trading as Taylor & Francis Group.
PMID
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(Rodriguez) Baylor College of Medicine, Houston, TX, United States  (Pastuszak, Lipshultz) Center for Reproductive Medicine, Baylor College of Medicine, Houston, TX, United States (Pastuszak, Lipshultz) Scott Department of Urology, Baylor College of Medicine, Houston, TX, United States
Publisher
459.
Effects of Korean red ginseng on semen parameters in male infertility patients: A randomized, placebo-controlled, double-blind clinical study.
Park H.J., Choe S., Park N.C.
Embase
Chinese Journal of Integrative Medicine. 22 (7) (pp 490-495), 2016. Date of Publication: 01 Jul 2016.
[Article]
AN: 604433455
Objective: To investigate the effects of Korean red ginseng (KRG) on semen parameters in male infertility patients in a randomized, double-blind, placebo-controlled study. Methods: A total of 80 male infertility patients with varicocele were recruited from April 2011 to February 2012. The subjects were then divided into the following four groups: non-varicocelectomy (V)+placebo (P) group, V+P group, non-V+KRG group (1.5-g KRG daily), and V+KGR group (1.5-g KRG daily). Semen analysis was performed and hormonal levels were measured in each treatment arm after 12 weeks. Results: All groups but not the non-V+P group, showed significant improvements in sperm concentrations, motility, morphology, and viability at the end of the study. However, there were no significant differences in serum follicle-stimulating hormone, luteinizing hormone, and testosterone among groups. The incidence of adverse events was low, and all events were assumed to be unrelated to the treatments administered. Conclusions: Although the exact mechanism by which KRG improves spermatogenesis remains unclear, KRG may be a useful agent for the treatment of male infertility. Nevertheless, additional studies to evaluate the optimal dose and duration of treatment are needed.  Copyright © 2015, Chinese Association of the Integration of Traditional and Western Medicine and Springer-Verlag Berlin Heidelberg.
PMID
Status
460.
Hypogonadotropic Hypogonadism in Non-Functioning Pituitary Adenomas: Impact of Intervention:
Monteiro D.M., Freitas P., Vieira R., Carvalho D.
Embase
[Article In Press]
AN: 614484451
Purpose To determine the prevalence of hypogonadotropic hypogonadism (HH) among patients with non-functioning pituitary adenomas (NFPA) and the post-surgery outcome on pituitary gonadotropins secretion (PGS); to determine the prevalence of erectile dysfunction (ED) on male patients with NFPA, to evaluate the impact of testosterone replacement therapy (TRT) in those with HH. Methods Retrospective evaluation of gonadal function in 109 NFPA patients (45 males), with a mean age of 51.8 years, diagnosed on the last 10 years. ED questionnaire applied to 34 male patients. Results Male patients with NFPA were significantly older (males 58.1 +/- 15.8 vs. females 47.4 +/- 16.94; p=0.001). Most patients had macroadenomas (67%; p=0.001) and only a minority were incidentalomas (19%; p<0.001). Prevalence of HH was 40% (60% on males, 25% on females; p<0.001). Surgery was performed in 54% of all patients (71% of males, 42% of
females; p<0.003). After intervention, 14% became HH, 69% maintained previous function and 17% improved. On the questionnaire, 76% reported having ED, 54% of which had HH and 21% were under TRT. Of the patients under TRT, 79% still had ED. Median age of patients with ED was significantly higher (with ED 65 vs. without 49 years; p=0.012). There was no BMI difference between patients with or without TRT (28.0 vs. 27.4 Kg/m2). Conclusions NFPA was more frequent in older rather than younger patients. Males were older, had more HH and surgery. There was no significant improvement of pituitary function with surgery (17%) and 13% became iatrogenic HH. TRT had a low efficacy to improve ED in these patients. Copyright © 2016, Georg Thieme Verlag KG. All rights reserved.
Background: Pregnancy failure and placenta mediated pregnancy complications affect > 25% of pregnancies. Although there is biological plausibility for a procoagulant mechanism underlying some of these events, antithrombotic intervention trials demonstrate limited benefit, possibly through lack of stratification in heterogeneous patient groups. The ANXA5 M2 haplotype is a possible procoagulant biomarker and was tested pragmatically to determine whether this screening and LMWH treatment normalized the outcome for ANXA5 M2 positive couples. This was a pragmatic study that aimed to measure the effectiveness of a testing (for the M2 haplotype) and treatment (LMWH) pathway in routine clinical practice where there is variation between patients. Such a study in couples with fertility problems can inform choices between treatments; it is then the management protocol which is the subject of the investigation, not the individual treatments.

Methods: Couples (N = 77) with one or both partners ANXA5 M2 positive demonstrated association of this haplotype with adverse IVF outcome. A pragmatic, multicenter, prospective cohort study of ANXA5 M2 haplotype screening, and LMWH treatment following embryo transfer (ET) in 103 IVF couples positive for ANXA5 M2 was performed. They were compared with a group of 1000 contemporaneous randomly selected unscreened and untreated couples undergoing assisted conception, from which 103 matched control couples were derived. The primary outcome measure was live birth incidence. Secondary outcomes were results following embryo transfer (ET) and live birth outcome by gender and M2 carriage, and allelic dose influence. Findings: The tested and treated cohort of ANXA5 M2 carriers achieved a similar live birth rate (37.9%) per ET cycle compared to both the more fertile comparison group (38.5%), and to the 103 matched controls (33.0%). Significantly more treated male carrier only couples had a live birth versus female M2 only (47.7% vs. 25.0% p = 0.045). Interpretation: Pragmatic ANXA5 M5 screening and treatment with LMWH in couples undergoing IVF is associated with similar outcome to couples with more favorable prognostic factors. The difference in live birth outcome for treated male only carrier couples may be consistent with an additional maternal thrombophilic factor that may adversely affect pregnancy, although other mechanisms are possible. This study suggests that LMWH treatment should be started prior to clinical pregnancy. Copyright © 2016 The Authors.

Randomised clinical trial of comparing effects of acupuncture and varicocelectomy on sperm parameters in infertile varicocele patients.

Kucuk E.V., Bindayi A., Boylu U., Onol F.F., Gumus E.

Andrologia. 48 (10) (pp 1080-1085), 2016. Date of Publication: 01 Dec 2016.

The aim of the study was to evaluate the effect of the acupuncture treatment on sperm parameters and pregnancy rates in patients with primary infertility. Between January 2008 and May 2010, 30 men with the primary infertility (one year of unprotected intercourse, healthy wife) and varicocele with normal hormone levels and abnormal semen analysis were randomised into two groups. Group 1 underwent subinguinal microscopic varicocelectomy, and Group 2 underwent acupuncture treatment twice a week for 2 months. Both groups were evaluated with
semen analysis at 6 months after the treatment. Patients in both groups evaluated with telephone calls and e-mail in terms of pregnancy. The mean age of the patients was 27.2, and groups were comparable regarding the age (P = 0.542). The pre-treatment sperm concentration, motility and morphological characteristics were similar in both groups. Sperm concentration and motility improved significantly in both groups after the treatment. Increase in sperm concentration was higher in the acupuncture group compared to the varicocelectomy group (P = 0.039). The average follow-up was 42 months, and pregnancy rates were emphasised 33% in both groups. Acupuncture treatment in primary infertile varicocele patients with semen abnormalities seems to be effective and has comparable results with the varicocelectomy treatment. Copyright © 2016 Blackwell Verlag GmbH

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463.
SEOM Clinical Guideline of fertility preservation and reproduction in cancer patients (2016).
Munoz M., Santaballa A., Segui M.A., Beato C., de la Cruz S., Espinosa J., Fonseca P.J., Perez J., Quintanar T., Blasco A.

Embase
Clinical and Translational Oncology. 18 (12) (pp 1229-1236), 2016. Date of Publication: 01 Dec 2016.
[Article]
AN: 613478273
Chemotherapy and radiotherapy often result in reduced fertility in cancer patients. With increasing survival rates, fertility is an important quality-of-life concern for many young cancer patients. Around 70-75% of young cancer survivors are interested in parenthood but the numbers of patients who access fertility preservation techniques prior to treatment are significantly lower. Moreover, despite existing guidelines, healthcare professionals do not address fertility preservation issues adequately. There is a critical need for improvements in clinical care to ensure patients are well informed about infertility risks and fertility preservation options and to support them in their reproductive decision-making prior to cancer treatment. Copyright © 2016, The Author(s).


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Year of Publication 2016
Durgam S., Gommoll C., Forero G., Nunez R., Tang X., Mathews M., Sheehan D.V.
Embase
[Article]
AN: 613958141
Objective: To evaluate the efficacy, safety, and tolerability of vilazodone as an acute treatment for generalized anxiety disorder (GAD). Vilazodone is a selective serotonin reuptake inhibitor and 5-HT1A receptor partial agonist approved for the treatment of major depressive disorder in adults.
Methods: This was a randomized, placebo-controlled, parallel-group, multicenter, flexible-dose study conducted from May 2013-March 2014. Adult patients (18-70 years, inclusive) who met DSM-IV-TR criteria for GAD were randomized (1:1) to placebo or vilazodone 20-40 mg/d for 8 weeks of double-blind treatment. Primary and secondary efficacy parameters were change from baseline to week 8 in the Hamilton Anxiety Rating Scale (HARS) total score and in the Sheehan Disability Scale (SDS) total score, respectively, analyzed using a mixed-effects model for repeated measures approach on a modified intent-To-Treat population. Safety outcomes were summarized descriptively.
Results: Efficacy analyses were based on 400 patients (placebo = 200, vilazodone = 200); 76% completed the study (placebo = 81%, vilazodone = 71%). The least squares mean difference (95% CI) in total score change from baseline to week 8 was statistically significant for vilazodone versus placebo on the HARS (-2.20 [-3.72 to -0.68]; P = .0048) and on the SDS (-1.89 [-3.52 to -0.26]; P = .0236). Treatment-emergent adverse events reported in > 5% of vilazodone patients and at least twice the rate of placebo were nausea, diarrhea, dizziness, fatigue, delayed ejaculation, and erectile dysfunction. Conclusion: Statistically significant differences in favor of vilazodone 20-40 mg/d versus placebo were seen on all measures of anxiety and functional impairment in patients with GAD. Vilazodone was generally well tolerated, and no new safety concerns were noted. © Copyright 2016 Physicians Postgraduate Press, Inc.
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Publisher
Physicians Postgraduate Press Inc.
Date Created
Factors affecting clinical pregnancy rates after IUI for the treatment of unexplained infertility and mild male subfertility.
Atasever M., Kalem M.N., Hatirnaz S., Hatirnaz E., Kalem Z., Kalaylioglu Z.
Embase
Journal of the Turkish-German Gynecological Association. 17 (3) (pp 134-138), 2016. Date of Publication: 2016.
[Article]
AN: 614224014
Objective: The aim of the present retrospective study was to evaluate intrauterine insemination (IUI) clinical experiences and to define the variables for predicting success.
Methods: The present study was an observational trial performed in a private IVF center on subfertile couples who had applied for treatment between 2002 and 2012, in which the data of 503 IUI cases were retrospectively reviewed. Couples who had been diagnosed with unexplained and mild male subfertility were included. The primary outcome measure was the clinical pregnancy rate in an attempt to form a predictive model for the odds of a clinical pregnancy.
Results: Utilizing univariate logistic regression analysis, clinical pregnancy was positively associated with the duration of infertility (OR=1.09, p=0.089), secondary infertility (OR=1.77, p=0.050), and +4 sperm motility after preparation (OR=1.03, p=0.091). Following an adjustment analysis involving a multivariate logistic regression, clinical pregnancy was still found to positively associate with secondary infertility (OR=2.51, p=0.008). Conclusion: IUI success in secondary infertile couples who were in the unexplained infertility and mild male subfertility groups was higher than that in primary infertile couples, and the chances of pregnancy increased as sperm numbers with +4 motility increased. It is difficult to concomitantly evaluate all these parameters and to determine a predictive parameter in IUI independent from other factors. Copyright © 2016 by the Turkish-German Gynecological Education and Research Foundation.
Status
INPROCESS
Prevalence and Etiology of Hypogonadism in Young Men With Chronic Spinal Cord Injury: A Cross-Sectional Analysis From Two University-Based Rehabilitation Centers.

Sullivan S.D., Nash M.S., Tefera E., Tinsley E., Blackman M.R., Groah S.

Embase

PM and R. (no pagination), 2016. Date of Publication: April 21, 2016.

[Article In Press]

AN: 614103027

Background: Spinal cord injury (SCI) triggers an accelerated aging process that may include development of hypogonadism, even among younger men with SCI; however, few studies have investigated the prevalence or etiology of hypogonadism in men with SCI. Young men with SCI also are at increased risk for developing metabolic dysfunction after injury, which may be exacerbated by concomitant testosterone (T) deficiency, thus identifying the prevalence and risk factors for T deficiency in men with SCI is important for their long-term health. Objective: To investigate the prevalence, risk factors, and etiology of T deficiency (hypogonadism) in otherwise-healthy men with chronic, motor complete SCI. Design: Secondary cross-sectional analysis.

Setting: Rehabilitation research centers in Washington, DC, and Miami, Florida. Participants: Men (n = 58) aged 18-45 years with chronic (>1 year), motor complete SCI without comorbidities or use of testosterone therapy. Methods: Plasma concentrations of hormones were measured with
standardized assays. Body composition was assessed with dual-energy x-ray absorptiometry scan. Main Outcome Measurements: Serum total T and calculated free T. Results: T deficiency was more common in men after SCI than in a matched cohort of similarly-aged men without SCI (25%, SCI versus 6.7%, non-SCI, \( P < .001 \)). The risk of hypogonadism appeared to be increased in men with more extensive injury and with higher percent body fat. The majority of men with SCI with low T had low serum LH levels, suggesting that central suppression of the hypothalamic-pituitary-gonadal axis may be the most common etiology of hypogonadism after SCI. Conclusions: Hypogonadism is more common in young men with SCI than in similarly aged men without SCI, suggesting that SCI should be identified as a risk factor for T deficiency and that routine screening for hypogonadism should be performed in the SCI population. Level of Evidence: To be determined. Copyright © 2016 American Academy of Physical Medicine and Rehabilitation.

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ARTICLE IN PRESS

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2016
Complications and cancer rates in spine fusion with recombinant human bone morphogenetic protein-2 (rhBMP-2).

Vavken J., Mameghani A., Vavken P., Schaeren S.

Embase

European Spine Journal. 25 (12) (pp 3979-3989), 2016. Date of Publication: 01 Dec 2016.

[Article]

Purpose: To quantitatively synthesize the available best evidence for general complications, heterotopic ossification (HO), retrograde ejaculation, cervical swelling, and cancer rates with the use of rhBMP-2 in lumbar and cervical spine fusion. Methods: We conducted an online search for relevant controlled trials and extracted data on the abovementioned endpoints. Studies were eligible for inclusion if they reported on spinal fusion with rhBMP-2 in humans. Publication bias and heterogeneity were assessed mathematically. These data were synthesized in a meta-analysis using DerSimonian-Laird random effects modeling to calculate pooled odds ratios.

Results: We identified 26 studies reporting on a total of 184,324 patients (28,815 experimental, 155,509 controls) with a mean age of 51.1 +/- 1.8 years. There was a significantly higher risk of general complications with rhBMP-2 compared to iliac crest bone graft (ICBG) with an odds ratio (OR) of 1.78 (95 %CI 1.20-2.63), (p = 0.004). The odds ratio for HO was 5.57 (95 %CI 1.90-16.36), (p = 0.002), for retrograde ejaculation 3.31 (95 %CI 1.20-9.09), (p = 0.020), and for cervical swelling 4.72 (95 %CI 1.42-15.67), (p = 0.011), all significantly higher in the rhBMP-2 group. The pooled odds ratio for new onset of tumor was 1.35 (95 %CI 0.93-1.96), which represents no statistically significant difference between the groups (p = 0.111). Conclusion: rhBMP-2 is associated with a higher rate of general complications as well as retrograde ejaculation, HO, and cervical tissue swelling in spine fusion. There is a slightly increased risk of new onset of tumors, however, without statistical significance.

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BMP-2 with anterior lumbar interbody fusion: Clinical usage and recent controversies. Makanji H.S., Bhalla A., Bono C.M.

Seminars in Spine Surgery. 28 (4) (pp 233-238), 2016. Date of Publication: 01 Dec 2016.

AN: 613760372

BMP-2 in the spine was first introduced as an adjunct to anterior lumbar interbody fusion (ALIF). The best available evidence suggests increased fusion rates with BMP-2, which has led many to view it as a replacement for iliac crest autograft. It may also be beneficial in patients who are at higher risk for pseudarthrosis. In either case, only a few studies have shown a favorable cost-benefit ratio. The complication profile of BMP-2 has come under recent scrutiny, dependent not only on its biologic properties but also the dosage, carrier properties, surgical approach, and graft containment technique. Recently highlighted issues such as retrograde ejaculation, heterotopic ossification, and radiculitis have been associated with its use in the lumbar spine. An understanding of the benefits, risks, and costs of BMP-2 use in ALIF can help identify patients who are most likely to benefit from it and promote informed decision-making. Copyright © 2016 Elsevier Inc.

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Invasive alien plant species used for the treatment of various diseases in Limpopo province, South Africa.
Maema L.P., Potgieter M., Mahlo S.M.

Embase

[Article]
AN: 613664668

Background: Invasive alien plant species (IAPs) are plants that have migrated from one geographical region to non-native region either intentional or unintentional. The general view of IAPs in environment is regarded as destructive to the ecosystem and they pose threat to native vegetation and species. However, some of these IAPS are utilized by local inhabitants as a substitute for scarce indigenous plants. The aim of the study is to conduct ethnobotanical survey on medicinal usage of invasive plant species in Waterberg District, Limpopo Province, South Africa. Materials and methods: An ethnobotanical survey on invasive plant species was conducted to distinguish species used for the treatment of various ailments in the Waterberg, District in the area dominated by Bapedi traditional healers. About thirty Bapedi traditional healers (30) were randomly selected via the snowball method. A guided field work by traditional healers and a semistructured questionnaire was used to gather information from the traditional healers. The questionnaire was designed to gather information on the local name of plants, plant parts used and methods of preparation which is administered by the traditional healers. Results: The study revealed that Schinus molle L., Catharanthus roseus (L.), Datura stramonium L., Opuntia stricta (Haw.) Haw., Opuntia ficus-indica, Sambucus canadensis L., Ricinus communis L., Melia azedarch L., Argemone ochroleuca and Eriobotrya japonica are used for treatment of various diseases such as chest complaint, blood purification, asthma, hypertension and infertility. The
most plant parts that were used are 57.6% leaves, followed by 33.3% roots, and whole plant, seeds and bark at 3% each. Noticeably, most of these plants are cultivated (38%), followed by 28% that are common to the study area, 20% abundant, 12% wild, and 3% occasionally. Schinus molle is the most frequently used plant species for the treatment of various ailments in the study area. National Environmental Management Biodiversity Act (NEMBA) (10/2004) and Conservation of Agricultural Resource Act (CARA) were consulted to confirm the invaders status. Only eight plants (60%) are regulated by CARA (10/2004). Of 10 IAPs, 80% (8 species) are listed in both NEMBA and CARA legislation. Only 20% (2 species) are listed in NEMBA alone. Conclusion: Invasive alien plants are utilized by communities to combat various ailments in humans and these plants can help to reduce pressure on heavily harvested indigenous plant. Copyright © 2016, African Ethnomedicines Network. All rights reserved.

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African Ethnomedicines Network (E-mail: editor@africanethnomedicines.net)

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20170111

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2016

470.
Efficacy and safety of an injectable combination hormonal contraceptive for men.

Embase

[Article]
Context: The development of a safe and effective reversible method of male contraception is still an unmet need. Objective: Evaluation of suppression of spermatogenesis and contraceptive protection by coadministered im injections of progestogen and testosterone. Design: Prospective multicentre study. Setting: Ten study centers. Participants: Healthy men, aged 18-45 years, and their 18- to 38-year-old female partners, both without known fertility problems. Intervention: Intramuscular injections of 200-mg norethisterone enanthate combined with 1000-mg testosterone undecanoate, administered every 8 weeks. Main Outcomes Measures: Suppression of spermatogenesis by ejaculate analysis, contraceptive protection by pregnancy rate. Results: Of the 320 participants, 95.9 of 100 continuing users (95% confidence interval [CI], 92.8- 97.9) suppressed to a sperm concentration less than or equal to 1 million/mL within 24 weeks (Kaplan-Meier method). During the efficacy phase of up to 56 weeks, 4 pregnancies occurred among the partners of the 266 male participants, with the rate of 1.57 per 100 continuing users (95% CI, 0.59-4.14). The cumulative reversibility of suppression of spermatogenesis after 52 weeks of recovery was 94.8 per 100 continuing users (95% CI, 91.5-97.1). The most common adverse events were acne, injection site pain, increased libido, and mood disorders. Following the recommendation of an external safety review committee the recruitment and hormone injections were terminated early. Conclusions: The study regimen led to near-complete and reversible suppression of spermatogenesis. The contraceptive efficacy was relatively good compared with other reversible methods available for men. The frequencies of mild to moderate mood disorders were relatively high. Copyright © 2016 by the Endocrine Society.

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Antioxidant supplements and semen parameters: An evidence based review.
Ahmadip S., Bashirip R., Ghadiri-Anarip A., Nadjarzadehp A.
Embase
[Review]
AN: 613941802
Many studies have focused on male infertility. There is limited evidence about the influence of nutrition on quality of semen. Approximately, 30-80% of infertility cases are caused by oxidative stress and decreased level of seminal total antioxidant capacity. This study was aimed to review the effects of oral antioxidant supplements on improving major semen parameters such as sperm concentration, motility, morphology, DNA damage, and fertility rate. Data were extracted from PubMed and Google scholar database by using the terms "antioxidant", "multivitamin", "carnitine", "CoQ10", "vitamin C", "vitamin E", "zinc", "folic acid", "N-acetyl cysteine" and "selenium" combined with "male infertility", "semen", and "sperm" to generate a set of relevant citations. Supplements such as CoQ10 and alpha-tocopherol significantly improve sperm count. Also, carnitine has positive effects on sperm motility and morphology. Simultaneous
administration of vitamin E and vitamin C reduces the sperm DNA damage. However, in some studies, one or more factors have not changed substantially. In most of the studies, antioxidant supplementation improved the number, motility, morphology and sometimes DNA integrity of sperm. The present study showed that antioxidant supplements, especially a combination of antioxidants such as vitamin C, vitamin E, and CoQ10 intake can effectively improve semen parameters in infertile men. Copyright © 2016, Research and Clinical Center for Infertility. All rights reserved.

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Publisher
Research and Clinical Center for Infertility (E-mail: IJRM@yazdivf.org)

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Year of Publication
2016

472.
Coenzyme Q10 Intake From Food and Semen Parameters in a Subfertile Population.
Tiseo B.C., Gaskins A.J., Hauser R., Chavarro J.E., Tanrikut C.

Embase
Urology. (no pagination), 2016. Date of Publication: July 13, 2016.
[Article In Press]
AN: 613994417

Objective: To assess the association between coenzyme Q10 (CoQ10) intake from food sources and semen quality. We assessed this association in a prospective cohort of men attending a fertility clinic. CoQ10 supplementation has been associated with improvements in semen parameters. However, the impact of CoQ10 intake from food sources on semen quality has not been investigated. Materials and Methods: Subfertile couples seeking fertility evaluation at the
Massachusetts General Hospital Fertility Center were invited to participate in an ongoing study of environmental factors and fertility. In total, 211 male participants completed a validated food frequency questionnaire and provided 476 semen samples. Multivariable linear mixed models were used to examine the relation between CoQ10 intake from food and semen parameters while adjusting for potential confounders and accounting for within-person correlations. Results: Mean dietary CoQ10 intake was 19.2 mg/day (2.4-247.2 mg/day). No subjects were taking CoQ10 supplements. There were no associations between dietary CoQ10 intake from food and conventional semen parameters. The adjusted mean difference (95% confidence interval) comparing men in the top and bottom quartiles of CoQ10 intake from food were -3.1 mil/mL (95% confidence interval -29.5, 38.8 mil/mL) for sperm concentration, -4.5% (-15.1%, 6.0%) for total motility, -1.3% for progressive motility (-8.4%, 5.7%), and 0.3% (-1.4%, 2.0%) for sperm morphology. Conclusion: CoQ10 intake from food was not related to semen parameters among subfertile men. Mean dietary intake of CoQ10 in this study was 10-fold lower than the supplemental dose used in clinical trials showing improved sperm motility. CoQ10 intake from food alone may be insufficient to optimize semen parameters. Copyright © 2016 Elsevier Inc.
Effects of tadalafil treatment combined with physical activity in patients with low onset hypogonadism: results from a not-randomized single arm phase 2 study.
Embase
Aging Male. 19 (3) (pp 155-160), 2016. Date of Publication: 02 Jul 2016.
[Article]
AN: 610258606
Purpose: To investigate a possible relation between penile Doppler ultrasound examination (PDUE) parameters and efficacy of chronic therapy with tadalafil (TAD) combined with a protocol of aerobic physical activity (PA) in patients with late onset hypogonadism (LOH). Methods: The study evaluated 30 patients consecutively enrolled with LOH and erectile dysfunction which present contraindication to hormonal replacement therapy for concomitant prostate disease. These patients were subjected to a combined protocol with phosphodiesterase V selective inhibitors (TAD 5 mg daily) and aerobic PA. Results: After three months, we observed significant improvements in erectile function [IIEF-5, median (IQR) = 13.0 (7.0-18.0) versus 6.0 (5.0-6.75); p < 0.01] and of the main metabolic [homeostatic model assessment index, median (IQR) = 2.5 (1.62-3.37) versus 3.0 (2.0-3.75); p < 0.01; body mass index, median (IQR) = 27.0 (24.0-28.75) versus 27.5 (24.0-29.5)] and vascular parameters [peak systolic velocity, median (IQR) = 29.5 (24.25-31.0) versus 28.0 (23.0-24.25); acceleration time, median (IQR) = 114 (105.25-134.0) versus 115.0 (106.5-134.0)], assessed by PDUE. Conclusion: PA in association with phosphodiesterase V inhibitors could compensate the effects of hypogonadism on erectile function and facilitate the clinical response to these drugs even in the absence of adequate serum concentrations of total testosterone. Copyright © 2016 Informa UK Limited, trading as Taylor & Francis Group.
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Publisher
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Date Created
Depression, anxiety and stress among female patients of infertility; A case control study.
Yusuf L.
Embase
Pakistan Journal of Medical Sciences. 32 (6) (pp 1340-1343), 2016. Date of Publication: November-December 2016.
[Article]
AN: 613866425
Objectives: Infertility, in many ways, is a very distressing condition that can have its impact on social and marital life of a couple. Depression, anxiety and stress associated with infertility may affect treatment and outcomes for such couples. The purpose of this study was to find out prevalence of depression, anxiety and stress among females suffering from infertility. Methods: One hundred females suffering from infertility as study subjects and 100 females accompanying them as controls were randomly selected from infertility clinic at Arif Memorial Teaching Hospital, Lahore, Pakistan. Females with diagnosed mental health issues and those from couples having male factor infertility were not included. Validated Urdu version of Depression, anxiety, stress scale (DASS) was used for assessment of depression, anxiety and stress scores. Results from both groups were compared and independent sample t-test was used to analyze the results. Results: There was high prevalence of depression, anxiety and stress among females suffering from infertility compared to females in control group (p < 0.05). Level of education did not appear to have any positive effect on these scores. Similarly, results did not appear to change when occupations of infertile females were used for stratified analysis. Conclusion: Depression, anxiety and stress are very common among females suffering from infertility. Healthcare professionals should consider psychological counseling, and psychiatric help if required, when they offer fertility treatment for such females. Copyright © 2016, Professional Medical Publications. All rights reserved.
Barragan-Arteaga I., Reyes-Vallejo L.
Embase
Revista Mexicana de Urologia. 76 (6) (pp 360-369), 2016. Date of Publication: 01 Nov 2016.
[Short Survey]
AN: 613363319
Recent interest in the coadministration of approved pharmaceutical agents has resulted in a wealth of emerging data on the safety and efficacy of dual pharmacological treatment for lower urinary tract symptoms (LUTS). Much evidence supports the coadministration of alpha-blockers with 5-alpha-reductase inhibitors (5-ARIs) in patients at risk for clinical progression. The use of phosphodiesterase-5 inhibitors (PDE5Is) in combination with 5-ARIs has also demonstrated a good safety and efficacy profile, providing early symptomatic relief and reduction of sexual side effects associated with 5-ARI use, although longer-term studies are needed. Studies investigating the combination of PDE5Is with alpha-blockers have shown additive effects on each of the individual agents with respect to the International Prostate Symptom Score (IPSS) and the International Index of Erectile Function (IIEF), which holds promise for patients who have shown a poor response to monotherapy. The coadministration of alpha-blockers and antimuscarinic agents provides an alternative for treatment of storage symptoms in patients who have failed to respond to monotherapy. This review aims to summarize and comment on available evidence regarding the safety and efficacy of combination treatment for LUTS. Copyright © 2016
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Introduction Testosterone deficiency (TD), also known as hypogonadism, is a condition affecting a substantial proportion of men as they age. The diagnosis and management of TD can be challenging and clinicians should be aware of the current literature on this condition. Aim To review the available literature concerning the diagnosis and management of TD and to provide clinically relevant recommendations from the Fourth International Consultation for Sexual Medicine (ICSM) meeting. Methods A literature search was performed using the PubMed database for English-language original and review articles published or e-published up to January 2016. Main Outcome Measures Levels of evidence (LoEs) and grades of recommendations are provided based on a thorough analysis of the literature and committee consensus. Results Recommendations were given for 12 categories of TD: definition, clinical diagnosis, routine measurement, screening questionnaires, laboratory diagnosis, threshold levels for the biochemical diagnosis of TD, prostate cancer, cardiovascular disease, fertility, testosterone (T) formulations, alternatives to T therapy, and adverse events and monitoring. A total of 42 recommendations were made: of these, 16 were unchanged from the Third ICSM and 26 new recommendations were made during this Fourth ICSM. Most of these recommendations were
supported by LoEs 2 and 3. Several key new recommendations include the following: (i) the clinical manifestations of TD occur as a result of decreased serum androgen concentrations or activity, regardless of whether there is an identified underlying etiology [LoE = 1, Grade = A]; (ii) symptomatic men with total T levels lower than 12 nmol/L or 350 ng/dL should be treated with T therapy [LoE = 1, Grade = C]; (iii) a trial of T therapy in symptomatic men with total T levels higher than 12 nmol/L or 350 ng/dL can be considered based on clinical presentation [LoE = 3, Grade = C]; (iv) there is no compelling evidence that T treatment increases the risk of developing prostate cancer or that its use is associated with prostate cancer progression [LoE = 1, Grade = C]; and (v) the weight of evidence indicates that T therapy is not associated with increased cardiovascular risk [LoE = 2, Grade = B]. Conclusion TD is an important condition that can profoundly affect the sexual health of men. We provide guidance regarding its diagnosis and management. Men with TD who receive treatment often experience resolution or improvement in their sexual symptoms and non-sexual health benefits. Copyright © 2016 International Society for Sexual Medicine

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Cardiovascular health, growth and gonadal function in children and adolescents with congenital adrenal hyperplasia.


Embase

Archives of Disease in Childhood. (no pagination), 2016. Date of Publication: December 14, 2016.

[Article In Press]

AN: 613865684

After the introduction of replacement therapy with glucocorticoids and mineralocorticoids in the 1950s, congenital adrenal hyperplasia (CAH) is no longer a lifelimiting condition. However, due to the successful introduction of medical steroid hormone replacement, CAH has become a chronic condition, with associated comorbidities and long-term health implications. The aim of treatment is the replacement of mineralocorticoids and glucocorticoids and the normalisation of elevated androgen concentrations. Long-term consequences of the condition and current treatment regimens include unfavourable changes in the cardiovascular risk profile, impaired growth, testicular adrenal rest tumours (TART) in male and subfertility in both male and female patients with CAH. Optimising replacement therapy in patients with CAH remains challenging. On one hand, treatment with supraphysiological doses of glucocorticoids might be required to normalise androgen concentrations and decrease size or presence of TARTs. On the other hand, treatment with supraphysiological doses of glucocorticoids is associated with an increased prevalence of unfavourable cardiovascular and metabolic risk profiles as well as impaired longitudinal growth and gonadal function. Therefore, treatment of children and adults with CAH requires an individualised approach. Careful monitoring for early signs of complications is already warranted during paediatric healthcare provision to prevent and reduce the impact of comorbidities in later life.

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Purpose Sexual dysfunction and impaired quality of life due to fecal incontinence are common after classic operations for anorectal malformations. We hypothesized that modern repairs may result in improved outcomes. Materials and Methods Following ethical approval for this single institution cross-sectional study, all patients 16 years or older treated for rectourethral, vestibular or perineal fistula from 1983 onward were sent detailed postal questionnaires on sexual function and quality of life. Each respondent was age and gender matched to 3 controls randomly selected from the general population. Penoscrotal/gynecologic abnormalities were obtained from the records. Results A total of 41 patients (62%) with a median age of 22 years participated in the study. Of the patients 20 were males with rectourethral fistula (prostatic in 60%), 10 were females with vestibular/perineal fistula and 11 were males with low malformations. Although experience of sexual relationships and orgasmic function were reported in comparable proportions to controls, age at coital debut was significantly delayed in all groups of patients (p <0.046). Erectile function was preserved after sagittal repair but absent ejaculations or azoospermia affected 3 males with rectourethral fistula (15%). Penoscrotal/gynecologic abnormalities affected 12% of patients. Overall quality of life scores were comparable to controls but a trend was found for lower scores.
on emotional items in males with rectourethral fistula (p = 0.06) and for a negative effect on sexual life in females (p = 0.03). Conclusions While erectile and orgasmic function appear preserved after sagittal repair, further evaluation of fertility issues in males with rectourethral fistula is indicated. Larger multicenter studies are needed to confirm our findings. Copyright © 2016 American Urological Association Education and Research, Inc.

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479.
Testosterone Therapy in Patients with Treated and Untreated Prostate Cancer: Impact on Oncologic Outcomes.
Ory J., Flannigan R., Lundeen C., Huang J.G., Pommerville P., Goldenberg S.L.
Embase
[Article]
AN: 612996997
Purpose Testosterone deficiency and prostate cancer have an increasing prevalence with age. However, because of the relationship between prostate cancer and androgen receptor activation, testosterone therapy among patients with known prostate cancer has been approached with caution. Materials and Methods We identified a cohort of 82 hypogonadal men with prostate cancer who were treated with testosterone therapy. They included 50 men treated with radiation therapy, 22 treated with radical prostatectomy, 8 on active surveillance, 1 treated with cryotherapy and 1 who underwent high intensity focused ultrasound. We monitored prostate specific antigen, testosterone, hemoglobin, biochemical recurrence and prostate specific antigen
velocity. Results Median patient age was 75.5 years and median followup was 41 months. We found an increase in testosterone (p <0.001) and prostate specific antigen (p = 0.001) in the entire cohort. Prostate specific antigen increased in patients on active surveillance. However, no patients were upgraded to higher Gleason score on subsequent biopsies and none have yet gone on to definitive treatment. We did not note any biochemical recurrence among patients treated with radical prostatectomy but 3 (6%) treated with radiation therapy experienced biochemical recurrence. It is unclear whether these cases were related to testosterone therapy or reflected the natural biology of the disease. We calculated mean prostate specific antigen velocity as 0.001, 0.12 and 1.1 mug/l per year in the radical prostatectomy, radiation therapy and active surveillance groups, respectively. Conclusions In the absence of randomized, placebo controlled trials our study supports the hypothesis that testosterone therapy may be oncologically safe in hypogonadal men after definitive treatment or in those on active surveillance for prostate cancer. Copyright © 2016 American Urological Association Education and Research, Inc.

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Date Created
20161227
Year of Publication
2016

Gentamicin versus ceftriaxone for the treatment of gonorrhoea (G-TOG trial): Study protocol for a randomised trial.
Background: Gonorrhoea is a common sexually transmitted infection which causes genital pain and discomfort; in women it can also lead to pelvic inflammatory disease and infertility, and in men to epididymo-orchitis. Current treatment is with ceftriaxone, but there is increasing evidence of antimicrobial resistance which is reducing its effectiveness against gonorrhoea. A small, but increasing, number of patients have already been found to have highly resistant strains of gonorrhoea which has been associated with clinical failure. This trial aims to determine whether gentamicin is not clinically worse than ceftriaxone in the treatment of gonorrhoea.

Methods/design: This is a blinded, two-arm, multicentre, noninferiority randomised trial. Patients are eligible if they are aged 16-70 years with a diagnosis of genital, pharyngeal and/or rectal gonorrhoea. Exclusion criteria are: known concurrent sexually transmitted infection(s) (excluding chlamydia); bacterial vaginosis and/or Trichomonas vaginalis infection; contraindications or an allergy to gentamicin, ceftriaxone, azithromycin or lidocaine; pregnancy or breastfeeding; complicated gonorrhoeal infection; weight under 40 kg; use of ceftriaxone, gentamicin or azithromycin within the preceding 28 days. Randomisation is to receive a single intramuscular injection of either gentamicin or ceftriaxone, all participants receive 1 g oral azithromycin as standard treatment. The estimated sample size is 720 participants (noninferiority limit 5%). The primary outcome is clearance of Neisseria gonorrhoeae at all infected sites by a negative Nucleic Acid Amplification Test, 2 weeks post treatment. Secondary outcomes include clinical resolution of symptoms, frequency of adverse events, tolerability of therapy, relationship between clinical effectiveness and antibiotic minimum inhibitory concentration for N. gonorrhoeae, and cost-effectiveness. Discussion: The options for future treatment of gonorrhoea are limited. Results from this randomised trial will demonstrate whether gentamicin is not clinically worse than ceftriaxone for the treatment of gonorrhoea. This will inform clinical practice and policy for the treatment of gonorrhoea when current therapy with cephalosporins is no longer effective, or is contraindicated. Trial registration: International Standard Randomised Controlled Trial Number - ISRCTN51783227, Registered on 18 September 2014. Current protocol version 2.0 17 June 2015. 

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481.
Clinical utility of sperm DNA fragmentation testing: Practice recommendations based on clinical scenarios.
Agarwal A., Majzoub A., Esteves S.C., Ko E., Ramasamy R., Zini A.
Embase
Translational Andrology and Urology. 5 (6) (pp 935-950), 2016. Date of Publication: 2016.
[Article]
AN: 613769258
Sperm DNA fragmentation (SDF) has been generally acknowledged as a valuable tool for male fertility evaluation. While its detrimental implications on sperm function were extensively investigated, little is known about the actual indications for performing SDF analysis. This review delivers practice based recommendations on commonly encountered scenarios in the clinic. An illustrative description of the different SDF measurement techniques is presented. SDF testing is recommended in patients with clinical varicocele and borderline to normal semen parameters as it can better select varicocelectomy candidates. High SDF is also linked with recurrent spontaneous abortion (RSA) and can influence outcomes of different assisted reproductive techniques. Several studies have shown some benefit in using testicular sperm rather than ejaculated sperm in men with high SDF, oligozoospermia or recurrent in vitro fertilization (IVF) failure. Infertile men with evidence of exposure to pollutants can benefit from sperm DNA testing as it can help reinforce the importance of lifestyle modification (e.g., cessation of cigarette smoking, antioxidant therapy), predict fertility and monitor the patient's response to intervention. Copyright © Translational Andrology and Urology. All rights reserved.
Status
EMBASE
Testosterone therapy and prostate cancer.
Pastuszak A.W., Rodriguez K.M., Nguyen T.M., Khera M.

Testosterone therapy (TTh) is used to treat hypogonadism in men with a history of prostate cancer (CaP) and in men without a history of CaP. The safety of TTh in men with a history of CaP is controversial due to fears of cancer recurrence or progression. Recent studies have examined the safety of TTh in men with a history of CaP and in men with low-risk CaP. TTh results in improvements in quality of life, and there is little evidence of biochemical recurrence or progression in men with a history of CaP or low-risk CaP. In men with high-risk CaP, limited data suggest that TTh may be safe, but these findings remain inconclusive. Despite the historic avoidance of TTh in men with a history of CaP, the use of TTh in men with a history of CaP remains controversial.
existing body of evidence largely supports the safe and effective use of testosterone in these men, although additional study is needed before unequivocal safety can be demonstrated. 

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483.
Testosterone replacement therapy and voiding dysfunction.
Baas W., Kohler T.S.

Embase
Translational Andrology and Urology. 5 (6) (pp 890-897), 2016. Date of Publication: 2016.

[Review]
AN: 613769226

Testosterone replacement therapy (TRT) represents an increasing popular treatment option for men with late-onset hypogonadism (LOH). Because of unsubstantiated beliefs of testosterone's effect on the prostate, the FDA has recently placed a warning on testosterone products, stating that TRT may worsen benign prostatic hyperplasia (BPH). Within this review article we have demonstrated the current understanding of the physiology of testosterone and its relationship with prostatic and lower urinary tract physiology. The current evidence suggests that not only does TRT not worsen lower urinary tract symptoms (LUTS), but that hypogonadism itself is an important risk factor for LUTS/BPH. Copyright © Translational Andrology and Urology. All rights reserved.
484.
Effects of varicocelectomy on serum testosterone.
Whelan P., Levine L.
Embase
Translational Andrology and Urology. 5 (6) (pp 866-876), 2016. Date of Publication: 2016.
[Review]
AN: 613769211
Varicocele is most often surgically repaired due to male infertility, however, has recently been linked to low serum testosterone. This paper serves to review the current literature regarding varicocele and its subsequent repair on serum testosterone. Twenty-eight human studies were identified with fifteen showing improved serum testosterone after repair. The majority of the studies that demonstrated improvement had preoperative testosterone levels that were low or below normal. Additionally, multiple well-designed studies with control groups not undergoing surgical repair demonstrated significant difference between groups. This improvement was less observed in studies with normal preoperative serum testosterone. A majority of these patients studied were presenting for infertility. It remains to be determined if these findings can be reproduced in men without infertility. The findings suggest that microsurgical varicocele repair can improve serum testosterone in men with low levels preoperatively in appropriately counseled men. It remains to be seen whether varicocele repair can help prevent the development of low testosterone in the future or which patients are at risk of developing low testosterone due to varicocele. Copyright © Translational Andrology and Urology. All rights reserved.
Hypogonadism is a common clinical condition affecting men of different age groups. In addition to its sexual consequences, it has several implications posing significant concerns for a man's health and well-being. Recent advances in testosterone (T) supplementation have facilitated hypogonadism treatment. Despite that, patients complaining of infertility or seeking conception are still hindered by the unfavorable effects supplemental T has on testicular function. Consequently, alternative approaches that can stimulate endogenous T production are favored. Selective estrogen receptor modulators, gonadotropins and aromatase inhibitors (AIs) can be successful in restoring serum T levels, preserving fertility, and providing symptomatic relief.
The incidence of hypogonadism has been steadily increasing over the last few years. Exogenous testosterone has been the standard treatment for hypogonadal men, but is associated with suppression of spermatogenesis as well as other possible adverse effects. There are other medications, currently considered "off label" for androgen replenishment, that exert their effect through modulation of the hypothalamic-gonadal axis. These medications increase endogenous testosterone levels and offer a different therapeutic approach. This review will focus on these alternative (off-label) therapies for androgen replacement in men.
Pharmacology of testosterone replacement therapy preparations.
Embase
Translational Andrology and Urology. 5 (6) (pp 834-843), 2016. Date of Publication: 2016.
[Review]
AN: 613769182
The goal of testosterone replacement therapy (TRT) is to return serum testosterone levels to within physiologic range and improve symptoms in hypogonadal men. Some of the symptoms aimed to improve upon include decreased libido, erectile dysfunction, infertility, hot flashes, depressed mood, and loss of muscle mass or hair. Clinical use of testosterone for replacement therapy began approximately 70 years ago. Over the decades, numerous preparations and formulations have been developed primarily focusing on different routes of delivery and thus pharmacokinetics (PKs). Currently the routes of delivery approved for use by the United States Food and Drug Administration encompasses buccal, nasal, subdermal, transdermal, and intramuscular (IM). Many factors must be considered when a clinician is choosing the most correct formulation for a patient. As this decision depends highly on the patient, active patient participation is important for effective selection. The aim of this review is to describe and compare all testosterone preparations currently available and approved by the United States Food and Drug Administration. Areas of focus will include pharmacology, PKs, adverse effects, and specifics related to individual delivery routes. Copyright © Translational Andrology and Urology. All rights reserved.
Testosterone deficiency (TD) has become a growing concern in the field of men's sexual health, with an increasing number of men presenting for evaluation of this condition. Given the increasing demand for testosterone replacement therapy (TRT), a panel of experts met in August of 2015 to discuss the treatment of men who present for evaluation in the setting of low or normal gonadotropin levels and the associated signs and symptoms of hypogonadism. This constellation of factors can be associated with elements of both primary and secondary hypogonadism. Because this syndrome commonly occurs in men who are middle-aged and older, it was termed adult-onset hypogonadism (AOH). AOH can be defined by the following elements: low levels of testosterone, associated signs and symptoms of hypogonadism, and low or normal gonadotropin levels. Although there are significant benefits of TRT for patients with AOH, candidates also need to understand the potential risks. Patients undergoing TRT will need to be monitored regularly because there are potential complications that can develop with long-term use. This review is aimed at providing a deeper understanding of AOH, discussing the benefits and risks of TRT, and outlining each modality of TRT in use for AOH.
Cryopreservation of testicular tissue or testicular cell suspensions: A pivotal step in fertility preservation.

Onofre J., Baert Y., Faes K., Goossens E.

Embase
Human Reproduction Update. 22 (6) (pp 744-761), 2016. Date of Publication: 01 Nov 2016.

[Article]

AN: 613479597

BACKGROUND: Germ cell depletion caused by chemical or physical toxicity, disease or genetic predisposition can occur at any age. Although semen cryopreservation is the first reflex for preserving male fertility, this cannot help out prepubertal boys. Yet, these boys do have spermatogonial stem cells (SSCs) that able to produce sperm at the start of puberty, which allows them to safeguard their fertility through testicular tissue (TT) cryopreservation. SSC transplantation (SSCT), TT grafting and recent advances in in vitro spermatogenesis have opened new possibilities to restore fertility in humans. However, these techniques are still at a research stage and their efficiency depends on the amount of SSCs available for fertility restoration. Therefore, maintaining the number of SSCs is a critical step in human fertility preservation. Standardizing a successful cryopreservation method for TT and testicular cell suspensions (TCSs) is most important before any clinical application of fertility restoration could be successful. OBJECTIVE AND RATIONALE: This review gives an overview of existing cryopreservation protocols used in different animal models and humans. Cell recovery, cell viability, tissue integrity and functional assays are taken into account. Additionally, biosafety and current perspectives in male fertility preservation are discussed. SEARCH METHODS: An extensive PubMed and MEDline database search was conducted. Relevant studies linked to the topic were identified by the search terms: cryopreservation, male fertility preservation, (immature)testicular tissue, testicular cell suspension, spermatogonial stem cell, gonadotoxicity, radiotherapy and chemotherapy. OUTCOMES: The feasibility of fertility restoration techniques using frozen-thawed TT and TCS has been proven in animal models. Efficient protocols for cryopreserving human TT exist and are currently applied in the clinic. For TCSs, the highest post-thaw viability reported after vitrification is 55.6 +/- 23.8%. Yet, functional proof of fertility
restoration in the human is lacking. In addition, few to no data are available on the safety aspects inherent to offspring generation with gametes derived from frozen-thawed TT or TCSs. Moreover, clarification is needed on whether it is better to cryopreserve TT or TCS. WIDER IMPLICATIONS: Fertility restoration techniques are very promising and expected to be implemented in the clinic in the near future. However, inter-center variability needs to be overcome and the gametes produced for reproduction purposes need to be subjected to safety studies. With the perspective of a future clinical application, there is a dire need to optimize and standardize cryopreservation and safety testing before using frozen-thawed TT of TCSs for fertility restoration. Copyright © The Author 2016.

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490.
Relationship between waist circumference and insulin resistance and its impact on sperm parameters. <Relacion circunferencia abdominal e insulinorresistencia y su impacto en parametros seminales.>
Aguilar-Roa P., Echavarria-Sanchez M.
Embase
Perinatologia y Reproduccion Humana. 30 (2) (pp 75-81), 2016. Date of Publication: 2016.
[Short Survey]
AN: 613516293
Infertility affects between 8-15% of general population of reproductive age. The term refers to the inability of couples to achieve pregnancy after one year of unprotected sexual activity. The male
factor is solely responsible in 20%, and 30-40% with the couple. The initial evaluation of the male reproductive situation is the seminogram, which is considered as a key assessment tool. Several conditions may be associated with infertility in men, such as endocrine-metabolic diseases such as hypogonadism, hyperprolactinaemia, dysthyroidism, dyslipidaemia, alterations glucose and insulin alteration, central obesity, or to the group of parameters called metabolic syndrome (MS). Obesity contributes to development of hypertension, dyslipidaemia and insulin resistance. The aim of our review was to find documents that showed the impact of the association between waist circumference and insulin resistance in semen parameters as a possible origin of male infertility. The search for information was conducted in Medline, ScienceDirect, and Scopus. The terms used for the basic search were: obesity, abdominal circumference, insulin resistance, male infertility, semen, semen parameters. There are studies documenting the deleterious effect of obesity and insulin resistance in female fertility. Some performed in men suggest harmful effects on their reproductive potential. Semen anomalies are found in obese men with insulin resistance, but still require further studied to assess the association between them. The literature reports semen anomalies associated with obesity that are still to be elucidated. Copyright © 2016 Instituto Nacional de Perinatologia Isidro Espinosa de los Reyes

491.
Fertility in disorders of sex development: A review.
Van Batavia J.P., Kolon T.F.
Embase
Introduction Disorders of sex development (DSD) are a heterogeneous group of complex conditions that can affect chromosomal, gonadal, and/or phenotypical sex. In addition to impacts on internal and external genitalia, these conditions can affect fertility potential to various degrees. In this review we discuss fertility issues including gonadal preservation and reproductive outcomes based on specific DSD conditions.

Methods and Materials A systematic literature review was performed on EmbaseTM, PubMed, and Google ScholarTM for disorders of sex development and infertility. Original research articles and relevant reviews were examined and a synopsis of these data was generated for a comprehensive review of fertility potential in disorders of sex development. Results While patients with some DSDs may have functioning gonads with viable germ cells but an inability to achieve natural fertility secondary to incongruent internal or external genitalia, other patients may have phenotypically normal genitalia but infertility due to abnormal gonad development. Fertility rates in females with congenital adrenal hyperplasia (CAH) depend on phenotype and are inversely proportional to the severity of the disease. Men with classic CAH have reduced fertility and due to the presence of testicular adrenal rest tumors and to suppression of the hypothalamic-pituitary-gonadal axis by high systemic levels of androgens. Infertility is seen in complete androgen insensitivity and subfertility is common in partial cases. Fertility is rare in pure or mixed gonadal dysgenesis, ovotesticular disorder, Klinefelter syndrome, and XX males. Conclusion Fertility potential appears to be the highest in patients with XX or XY CAH, especially non-classic forms. Advancements in assisted reproduction techniques has in rare cases produced offspring in some diagnoses thought to be universally infertile. Discussion of fertility issues with the patient and family is essential to the optimal treatment of each patient and an important part of the multi-disciplinary approach to evaluating and counseling these families.

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Management of undescended testes: European Association of Urology/European Society for Paediatric Urology Guidelines.

Radmayr C., Dogan H.S., Hoebeke P., Kocvara R., Nijman R., Stein R., Undre S., Tekgul S.

Embase

[Review]
AN: 613309287

Context Undescended testis is the most common endocrinological disease in the male newborn period. Incidence varies between 1.0% and 4.6% in full-term neonates, with rates as high as 45% in preterm neonates. Failure or delay of treatment can result in reduced fertility and/or increased testicular cancer risk in adulthood. Objective To provide recommendations for the diagnosis and treatment of boys with undescended testes which reduce the risk of impaired fertility and testicular cancer in adulthood. Evidence acquisition Embase and Pubmed were searched for all relevant publications, from 1990 to 2015 limited to English language. Data were narratively synthesized in light of methodological and clinical heterogeneity. The risk of bias of each included study was assessed. Evidence synthesis There is consensus that early treatment, by 18 months at the latest, for undescended testes is mandatory to avoid possible sequelae regarding fertility potential and cancer risk. The current standard therapy is orchidopexy, while hormonal therapy is still under debate. However, in some individuals the successful scrotal placement of previously undescended testes may not prevent potential negative long-term outcomes regarding fertility and testicular malignancy. Conclusions There is good evidence for early placement of undescended testes in the scrotal position to prevent potential impairment of fertility and reduce the risk of testicular malignancy. No consensus exists on the various forms of hormonal treatment, which are assessed on an individual basis. Copyright © 2016 Journal of Pediatric Urology Company

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Institution
Patients with Acromegaly Presenting with Colon Cancer: A Case Series.
Gordon M.B., Nakhle S., Ludlam W.H.
Embase
[Article]
AN: 613671934
Introduction. Frequent colonoscopy screenings are critical for early diagnosis of colon cancer in patients with acromegaly. Case Presentations. We performed a retrospective analysis of the incidental diagnoses of colon cancer from the ACCESS trial (ClinicalTrials.gov identifier: NCT01995734). Colon cancer was identified in 2 patients (4.5%). Case 1 patient was a 36-year-old male with acromegaly who underwent transsphenoidal surgery to remove the pituitary adenoma. After surgery, the patient underwent routine colonoscopy screening, which revealed a
40 mm tubular adenoma in the descending colon. A T1N1a carcinoma was surgically removed, and 1 of 22 lymph nodes was positive for metastatic disease, leading to a diagnosis of stage 3 colon cancer. Case 2 patient was a 50-year-old male with acromegaly who underwent transsphenoidal surgery to remove a 2 cm pituitary adenoma. The patient reported severe cramping and lower abdominal pain, and an invasive 8.1 cm3 grade 2 adenocarcinoma with signet rings was identified in the ascending colon and removed. Of the 37 lymph nodes, 34 were positive for the presence of tumor cells, and stage 3c colon cancer was confirmed. Conclusion. Current guidelines for colonoscopy screening at the time of diagnosis of acromegaly and at appropriate follow-up intervals should be followed. Copyright © 2016 Murray B. Gordon et al. Status EMBASE Author NameID Gordon, Murray B.; ORCID: http://orcid.org/0000-0001-9185-9424 Institution (Gordon) Allegheny Neuroendocrinology Center, Departments of Medicine and Neurosurgery, Allegheny General Hospital, 320 East North Avenue, Pittsburgh, PA 15212, United States (Nakhle) Palm Research Center, 9280 West Sunset Road, Las Vegas, NV 89148, United States (Ludlam) Novartis Pharmaceuticals, 1 Health Plaza, East Hanover, NJ 07936, United States Publisher Hindawi Publishing Corporation (410 Park Avenue, 15th Floor, 287 pmb, New York NY 10022, United States) Date Created 20161223 Year of Publication 2016

Male reproductive issues are frequently overlooked in patients of chronic myeloid leukemia (CML) on imatinib therapy. Current article describes a young man with CML on imatinib mesylate since 13 years who presented to us with painful left sided breast swelling. Mammography and fine needle aspiration cytology confirmed the diagnosis of gynaecomastia and hormone profile revealed low testosterone levels. Gynaecomastia was attributed to imatinib related hypogonadism. Gynaecomastia improved after hormone replacement therapy. Need for long term monitoring of reproductive hormones in patients of CML on imatinib therapy is emphasized in this report. Copyright © 2016 Indian Society of Haematology & Transfusion Medicine


AN: 613367239
STUDY QUESTION Have ART live birth rates improved in Australia over the last 12 years?
SUMMARY ANSWER There were striking improvements in per-cycle live birth rates observed for frozen/thaw embryo transfers, blastocyst transfer and single embryo transfer (SET), while live birth rates following ICSI were lower than IVF for non-male factor infertility in most years. WHAT
IS ALREADY KNOWN ART and associated techniques have become the predominant treatment of infertility over the past 30 years in most developed countries. However, there are differences in ART laboratory and clinical practices, and success rates worldwide. Australia has one of the highest ART utilization rates and lowest multiple birth rates in the world, thus providing a unique setting to investigate the contribution of common ART strategies in an unrestricted population of patients to ART success rates. STUDY DESIGN, SIZE, DURATION A retrospective cohort study of 585,065 ART treatment cycles performed in Australia between 2002 and 2013 using the Australian and New Zealand Assisted Reproduction Database (ANZARD). PARTICIPANTS MATERIALS, SETTING, METHOD An unrestricted population of all women who underwent autologous ART treatment between 2002 and 2013. Visual descriptive analysis was used to assess the trends in ART procedures by the calendar years. Adjusted odds ratios (aORs) of a live birth for four common ART techniques were calculated after controlling for important confounders including female age, infertility diagnosis, stage of the embryo (blastocyst versus cleavage stage), type of embryo (fresh versus thawed), fertilization method (IVF versus ICSI) and number of embryos transferred (SET versus multiple embryos). MAIN RESULTS AND THE ROLE OF CHANCE The overall live birth rate per embryo transfer increased from 19.2% in 2002 to 23.3% in 2013 (21.9-24.3% for fresh embryo transfers and 14.6-23.3% for frozen/thaw embryo transfers). This occurred concurrently with an increase in SET from 29.7% to 78.9%, and an increase in the average age of women undergoing treatment from 35.0 to 35.9 years. Individuals who had a frozen/thaw embryo transfer cycle in 2002 had 43% (aOR: 0.57, 95% CI: 0.53-0.61) reduced odds of a live birth compared with a fresh embryo transfer cycle. This contrasted with 16% (aOR: 0.84, 95% CI: 0.80-0.98) reduced odds of a live birth from frozen/thaw embryo transfer cycles in 2013. In 2013, the odds of blastocyst transfer resulting in a live birth were more than twice as great as for cleavage stage transfer (aOR 2.01, 95% CI: 1.92-2.11). The adjusted odds of live birth per SET compared with multiple embryo transfer increased significantly over the last 12 years, from a 38% reduced odds of a live birth follow SET in 2002 (aOR: 0.62, 95% CI: 0.57-0.67) compared to an 8% reduced odds in 2013 (aOR: 0.92, 95% CI: 0.87-0.98). The aOR of a live birth using ICSI compared to IVF in non-male factor patients was lower in most years bringing into question its widespread use. LIMITATION, REASONS FOR CAUTION This is a retrospective cohort analysis and cannot confirm causality. High-level evidence on the effectiveness of particular ART techniques, particularly ICSI and blastocyst culture, requires prospective randomized controlled trials or detailed statistical analysis using large-scale data that counts for fertilization failure, embryo loss, prognostic factors and cycle characteristics. WIDER IMPLICATION OF THE FINDINGS The most striking improvements in ART success rates in Australia have been observed for frozen/thaw embryo transfers, blastocyst transfer and SET. Further studies of the role of ICSI in non-male factor infertility and blastocyst transfer success rates that take into account embryo loss are needed. STUDY FUNDING/COMPETING
INTEREST(S) No funding was received to undertake this study. The authors declare that they do not have competing interests with this study. TRIAL REGISTRATION NUMBER NA. Copyright © 2016 The Author 2016. Published by Oxford University Press on behalf of the European Society of Human Reproduction and Embryology. All rights reserved.

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496.
Effects of 8-Year Treatment of Long-Acting Testosterone Undecanoate on Metabolic Parameters, Urinary Symptoms, Bone Mineral Density, and Sexual Function in Men With Late-Onset Hypogonadism.
Permpongkosol S., Khupulsup K., Leelaphiwat S., Pavavattanunusorn S., Thongpradit S., Petchthong T.
Introduction The long-term effects of long-acting testosterone undecanoate (TU) and androgen receptor CAG repeat lengths in Thai men with late-onset hypogonadism (LOH) have not been reported. Aim To analyze the 8-year follow-up effects of intramuscular TU therapy on metabolic parameters, urinary symptoms, bone mineral density, and sexual function and investigate CAG repeat lengths in men with LOH. Methods We reviewed the medical records of 428 men with LOH who had been treated with TU and 5 patients were diagnosed with prostate cancer during TU therapy. There were 120 patients (mean age = 65.6 +/- 8.9 years) who had 5 to 8 years of continuous TU supplementation and sufficiently completed records for analysis. Genomic DNA was extracted from peripheral blood and the CAG repeat region was amplified by polymerase chain reaction. Fragment analysis, sequencing, electropherography, and chromatography were performed. Main Outcome Measures The main outcome measure was dynamic parameter changes during testosterone supplementation. Results TU did not improve all obesity parameters. A statistically significant decrease was found in waist circumference, percentage of body fat, glycated hemoglobin, cholesterol, low-density lipoprotein, and International Prostate Symptom Score (P < .05). TU did not produce differences in body mass index, high-density lipoprotein, triglyceride, or the Aging Male Symptoms score from baseline. However, a statistically significant increase was found in the level of testosterone, prostate-specific antigen, hematocrit, International Index of Erectile Function score, and vertebral and femoral bone mineral density (P < .05). No major adverse cardiovascular events or prostate cancer occurred during this study. The CAG repeat length was 14 to 28 and the median CAG length was 22. There was no association between CAG repeat length and any of the anthropometric measurements. Conclusion Long-term TU treatment in men with LOH for up to 8 years appears to be safe, tolerable, and effective in correcting obesity parameters. Copyright © 2016 International Society for Sexual Medicine
Purpose We examined first (incident) reports of selected adverse experiences associated with medical therapy in men with lower urinary tract symptoms secondary to benign prostatic hyperplasia. Materials and Methods We studied the 6 most common adverse experiences, including nonsexual function related experiences (dizziness, orthostatic hypotension and weakness) and sexual function related experiences (impotence, decreased libido and abnormal ejaculation) reported in the MTOPS (Medical Therapy of Prostatic Symptoms) Study. A total of 3,047 men were randomized to placebo, doxazosin, finasteride or combination therapy and followed for a mean duration of 4.5 years. We compared the incidence rates of adverse experiences at year 1 to the rates thereafter. Results For each assigned treatment group, the incidence rates were significantly higher for all 6 adverse experiences examined at year 1 compared with the rates thereafter. Men assigned to combination therapy experienced the highest rates at year 1 with rates 3.4-fold to 10.6-fold higher than rates after year 1. The incidence rates for orthostatic hypotension and dizziness were significantly higher in the doxazosin and combination therapy groups compared with the placebo group at year 1. The incidence rates of the 3 examined sexual function related adverse experiences were significantly higher in the finasteride and combination therapy groups than in the placebo group at year 1.
Conclusions Rates of the first report of sexual function related and other adverse experiences associated with doxazosin, finasteride and combination therapy were greatest during year 1 of treatment. These patterns should be considered by patients and physicians when treatment for lower urinary tract function is initiated with these drugs. Copyright © 2016 American Urological Association Education and Research, Inc.

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498.
Possible influence of vitamin D on male reproduction.
Boisen I.M., Bollehus Hansen L., Mortensen L.J., Lanske B., Juul A., Blomberg Jensen M.

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AN: 613545146
Vitamin D is a versatile signaling molecule with an established role in the regulation of calcium homeostasis and bone health. In recent years the spectrum of vitamin D target organs has expanded and a reproductive role is supported by the presence of the vitamin D receptor (VDR) and the vitamin D metabolizing enzymes in the gonads, reproductive tract, and human
spermatozoa. Interestingly, expression levels of VDR and the vitamin D inactivating enzyme CYP24A1 in human spermatozoa serve as positive predictive markers of semen quality and are higher expressed in spermatozoa from normal than infertile men. VDR mediates a non-genomic increase in intracellular calcium concentration, sperm motility, and induces the acrosome reaction. Furthermore, functional animal model studies have shown that vitamin D is important for sex steroid production, estrogen signaling, and semen quality. Cross-sectional clinical studies have supported the notion of a positive association between serum 25-hydroxyvitamin D (25-OHD) level and semen quality in both fertile and infertile men. However, it remains to be determined whether this association reflects a causal effect. The VDR is ubiquitously expressed and activated vitamin D is a regulator of insulin, aromatase, and osteocalcin. Hence, it is plausible that the influence of vitamin D on gonadal function may be mediated indirectly through other vitamin D regulated endocrine factors. Recent studies have indicated that vitamin D supplementation may be beneficial for couples in need of assisted reproductive techniques as high serum vitamin D levels were found to be associated with a higher chance of achieving pregnancy. Randomized clinical trials are needed to determine whether systemic changes in vitamin D metabolites can influence semen quality, fertility, and sex steroid production in infertile men. In this review known and possible future implications of vitamin D in human male reproduction function will be discussed. Copyright © 2016.

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Clomiphene Citrate versus Letrozole for Ovarian Stimulation in Therapeutic Donor Sperm Insemination.

El Hachem H., Antaki R., Sylvestre C., Kadoch I.-J., Lapensee L., Bouet P.E.

Embase
[Article In Press]
AN: 613339703

Aim: To compare clomiphene citrate (CC) and letrozole for ovarian stimulation (OS) in therapeutic donor sperm insemination (TDI) cycles. Methods: Retrospective cohort study between January 2011 and June 2014 at a University-affiliated private IVF clinic in Montreal, Canada. 257 normo-ovulatory women <40 years of age with no history of infertility undergoing 590 TDI cycles in the absence of a male partner (single women and same-sex couples) or azoospermia were included. Patients received 100 mg CC daily (145 women, 321 cycles) or letrozole 5 mg daily (112 women, 269 cycles), from days 3 to 7. Only the first 3 cycles were included per patient. Our main outcome measure was cumulative live birth rates (LBR). Results: Baseline characteristics were comparable between the 2 groups. There were no differences in LBR per cycle (16.5% (53/321) vs. 11.5% (31/269), p = 0.08) and cumulative LBR (36.6% (53/145) vs. 27.7% (31/112), p = 0.13), between CC and letrozole, respectively. Multiple pregnancy rate (11.6% (8/69) vs. 8.7% (4/46), p = 0.6) and miscarriage rate (21.7 vs. 21.7%, p = 1) were also comparable between CC and letrozole, respectively. Conclusion: In normo-ovulatory women undergoing TDI, OS with CC or letrozole resulted in similar live birth and twin pregnancy rates.  Copyright © 2016 S. Karger AG, Basel

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Fatty acids profiling reveals potential candidate markers of semen quality.


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Previous reports showed altered fatty acid content in subjects with altered sperm parameters compared to normozoospermic individuals. However, these studies focused on a limited number of fatty acids, included a short number of subjects and results varied widely. We conducted a case-control study involving 155 patients allocated into four groups, including normozoospermia (n = 33), oligoasthenoteratozoospermia (n = 32), asthenozoospermia (n = 25), and varicocele (n = 44). Fatty acid profiling, including 30 species, was analyzed by a validated gas chromatography (GC) method on the whole seminal fluid sample. Multinomial logistic regression modeling was used to identify the associations between fatty acids and the four groups. Specimens from 15 normozoospermic subjects were also analyzed for fatty acids content in the seminal plasma and spermatozoa to study the distribution in the two compartments. Fatty acids lipidome varied markedly between the four groups. Multinomial logistic regression modeling revealed that high levels of palmitic acid, behenic acid, oleic acid, and docosahexaenoic acid (DHA) confer a low risk to stay out of the normozoospermic group. In the whole population, seminal fluid stearic acid was negatively correlated (r = -0.53), and DHA was positively correlated (r = 0.65) with sperm motility. Some fatty acids were preferentially accumulated in spermatozoa and the highest difference was observed for DHA, which was 6.2 times higher in spermatozoa than in seminal plasma. The results of this study highlight complete fatty acids profile in patients with different semen parameters. Given the easy-to-follow and rapid method of analysis, fatty acid profiling by GC method can be used for therapeutic purposes and to measure compliance in infertility trials using fatty acids supplements. Copyright © 2016 American Society of Andrology and European Academy of Andrology.

Status

ARTICLE IN PRESS

Institution
501.
The psychosocial experiences of women with breast cancer across the lifespan: A systematic review.
Campbell-Enns H.J., Woodgate R.L.
Embase
Psycho-Oncology. (no pagination), 2016. Date of Publication: 2016.
[Article In Press]
AN: 613228579
Objective: To summarize the psychosocial experience of women with breast cancer from a lifespan perspective by examining the findings of qualitative studies. Methods: A meta-aggregate review of 24 qualitative studies was undertaken. To be included, studies must include women with a breast cancer diagnosis and focus on younger or older women (as defined by the study), or compare a psychosocial issue across the lifespan. Eight databases were searched systematically. Results: Study participants ranged in age from 26 to 91 years. Sixteen studies focused on younger women, six focused on older women, and two included women across the lifespan. A total of 155 findings were extracted from the studies and were aggregated into 11 categories. These were synthesized into four synthesized findings: (a) dealing with cancer, (b) the
importance of caring, (c) the aftermath of cancer, and (d) fertility and infertility. Conclusions: Further research is required to explore these findings, and to examine the needs of older women in particular. Delineating the similarities and differences in the needs of women across the lifespan will inform the development of psychosocial interventions for all women with breast cancer. Copyright © 2016 John Wiley & Sons, Ltd.

Status
ARTICLE IN PRESS

Institution
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2016

502.
Total antioxidant status and lipid peroxidation with and without in vitro zinc supplementation in infertile men.
Ajina T., Sallem A., Haouas Z., Mehdi M.

Embase
Andrologia. (no pagination), 2016. Date of Publication: 2016.
[Article In Press]
AN: 613223262

The aim of this study was to assess the total antioxidant capacity (TAC) and malondialdehyde (MDA) level in infertile men with asthenozoospermia and asthenoteratozoospermia compared to fertile donors, and to examine the effect of zinc on sperm lipid peroxidation and antioxidant status in infertile and fertile men. Semen samples provided by infertile men (n = 38) and fertile donors (controls; n = 12) were exposed to 6 mmol/L of zinc for 2 hr at 37° C. After semen analysis,
lipid peroxidation was detected by MDA assay and seminal TAC was assessed by colorimetric method using TAS (total antioxidant status) Kit. TAC was significantly lower in infertile group compared to controls ($p = .037$). However, lipid peroxidation did not alter in infertile patients compared to controls ($p > .05$). After in vitro incubation of samples with zinc, a significant increase in TAC level was found only in infertile men ($p < .001$). Meanwhile, zinc had no effect on sperm lipid peroxidation in both fertile and infertile men ($p > .05$). Our data indicate that antioxidant treatment based on zinc in vitro supplementation may be helpful to enhance the rate of seminal antioxidant status in infertile men; however, it does not prevent sperm lipid peroxidation. Copyright © 2016 Blackwell Verlag GmbH.
from Shanghai, China. The Aging Male Symptoms (AMS) questionnaire and the Androgen Deficiency in Aging Male (ADAM) questionnaire were completed by the subjects. Testosterone (T), sex hormone-binding globulin (SHBG), albumin, and other blood biochemical indexes were measured in 332 males. The corresponding cFT was obtained using the Vermeulen formula and the correlations between T and cFT were analyzed by SPSS statistical software. Results: Among the 332 males who underwent biochemical evaluation, 289 males (87.0%) was positively screened by the ADAM questionnaire and 232 males (69.9%) by the AMS questionnaire. As suggested by linear regression, cFT exhibited a negative correlation with age in both ADAM+ and AMS+ group, whereas T did not appear to have significant correlation with age. Besides, there were statistically significant differences in cFT (P<.001) in the AMS questionnaire. Conclusions: Calculated free testosterone levels are more reliable than T levels for diagnosing LOH in middle-aged and elderly males. Copyright © 2016 Wiley Periodicals, Inc.

504. Anterior Lumbar Interbody Fusion (ALIF) with and without an "Access Surgeon": A Systematic Review and Meta-analysis.
Phan K., Xu J., Scherman D.B., Rao P.J., Mobbs R.J.
Embase
[Article In Press]
AN: 612362766
STUDY DESIGN.: A systematic review and meta-analysis OBJECTIVE.: To investigate the outcomes of anterior lumbar interbody fusion (ALIF) with and without an "access surgeon".

SUMMARY OF BACKGROUND DATA.: Anterior approaches for spine operations have become increasingly popular but may often involve unfamiliar anatomy and territory for spine surgeons, potentially placing the patient at risk to a greater proportion of approach-related complications. Thus many spine surgeons require or prefer the assistance of an "access surgeon" to perform the exposure. However there has been much debate about the necessity of an "access surgeon".

METHODS.: A systematic search of six databases from inception to April 2016 was performed by two independent reviewers. Meta-analysis was used to pool overall rates, and compare the outcomes of ALIF with an access surgeon and without. RESULTS.: A total of 58 (8028 patients) studies were included in this meta-analysis. The overall intraoperative complications were similar with and without an "access surgeon". The overall pooled rate of arterial injuries (no access 0.44% vs access 1.16%, OR 2.67, P<0.001), retrograde ejaculation (0.41% vs 0.96%, OR 2.34, P=0.005) and ileus (1.93% vs 2.26%, OR 2.45, P<0.001) was higher with an "access surgeon". However the overall pooled rates of peritoneal injury (0.44% vs 0.16%, OR 0.36, P=0.034) and neurological injury (0.99% vs 0.11%, OR 0.11, P<0.001) were lower with an "access surgeon". Total postoperative complications (5.95% vs 4.08%, OR 0.67, P<0.001) were lower with an "access surgeon" along with prosthesis complications (1.59% vs 0.89%, OR 0.56, P<0.001) and reoperation rates (2.28% vs 1.31%, OR 0.57, P<0.001).

CONCLUSIONS.: Compared to no access surgeon, the use of an access surgeon was associated with similar intraoperative complication rates, higher arterial injuries, retrograde ejaculation, ileus, and lower prosthesis complications, reoperation rates and postoperative complications. In cases where exposure may be difficult, support from an "access surgeon" should be available.

Level of Evidence: 1   Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.

Status
ARTICLE IN PRESS
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Publisher
Lippincott Williams and Wilkins (E-mail: kathiest.clai@apta.org)
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2016
Beneficial effects of microsurgical varicocelectomy on sperm maturation, DNA fragmentation, and nuclear sulfhydryl groups: A prospective trial.
Alhathal N., San Gabriel M., Zini A.
Embase
Andrology. (no pagination), 2016. Date of Publication: 2016.
[Article In Press]
AN: 611872934
There is evidence to show that varicocele repair can improve conventional sperm parameters but the effects on sperm chromatin integrity have not been fully elucidated. We sought to examine the effects of varicocelectomy on sperm maturation, nuclear chromatin integrity and nuclear sulfhydryl groups. We conducted a prospective study of consecutive infertile men (n=29) that underwent a microsurgical sub-inguinal varicocelectomy for treatment of a clinically palpable varicocele and abnormal semen parameters. Six healthy sperm donors served as controls. We evaluated conventional sperm parameters and markers of sperm chromatin and DNA integrity (aniline blue (AB) staining, iodoacetamide fluorescein (IAF) fluorescence and, % DNA fragmentation index (%DFI) and percent high DNA stainability (%HDS) by sperm chromatin structure assay) before and 6 months after surgery. The sperm %DFI, %HDS, % 5-IAF staining (diffuse head staining) and % AB staining (dark blue) were all significantly lower in the control group compared to infertile men with varicocele (8 vs. 20%, 4.0 vs. 9.6%, 1.7 vs. 16.3%, and 2.5 vs. 13.5% respectively). The %HDS and %DFI decreased significantly after surgery (from 10% to 6% and from 20% to 13%, respectively). Similarly, the %5-IAF and %AB staining also decreased significantly after surgery (from 16.3% to 5.4%, and from 13.5% to 5.4%, respectively). We observed significant inversely relationships between sperm progressive motility and both %IAF staining and %DFI (r=-0.44 and -0.43, respectively). The data show that varicocelectomy is associated with an improvement in sperm DNA integrity and chromatin compaction using three different assays of sperm chromatin integrity. Copyright © 2016 American Society of Andrology and European Academy of Andrology.
Status
ARTICLE IN PRESS
Institution
(Alhathal, San Gabriel, Zini) McGill University Montreal, QC Canada
Publisher
Introduction: Evidence from well-designed studies documenting the benefit of testosterone replacement therapy as a function of patient demographic and clinical characteristics is lacking.

Aim: To determine demographic and clinical predictors of treatment outcomes in hypogonadal men with low sex drive, low energy, and/or erectile dysfunction. Methods: Post hoc analysis of a randomized, multicenter, double-blinded, placebo-controlled, 16-week study of 715 hypogonadal men (mean age = 55.3 years, age range = 19-92 years) presenting with low sex drive and/or low energy who received placebo or testosterone solution 2% for 12 weeks. Main Outcomes and Measures: Two levels defined patient-reported improvement (PRI) in sex drive or energy: level 1 was at least "a little better" and level 2 was at least "much better" in energy or sex drive on the Patient Global Impression of Improvement at study end point. PRI in erectile function was stratified by erectile dysfunction severity at baseline as measured by the erectile function domain of the International Index for Erectile Function: mild at baseline (change of 2), moderate at baseline (change of 5), and severe at baseline (change of 7). Associations of demographic and clinical characteristics with PRI were calculated with stepwise forward multiple logistic regression analysis. Odds ratios represented the likelihood of PRI in symptoms among variable categories.

Results: Higher levels of end-point testosterone were associated with higher rates of PRI (at levels 1 and 2) in sex drive and energy (P < .001 for the two comparisons). Lower baseline testosterone levels were associated with higher rates of level 1 PRI in sex drive (P = .028); and classic hypogonadism (vs non-classic hypogonadism) was associated with higher rates of level 2
PRI in sex drive (P = .005) and energy (P = .006). Conclusion: When assessing the potential for improvements in men with testosterone deficiency using patient-reported outcome questionnaires, possible predictors of treatment outcomes to consider include the etiology of hypogonadism and testosterone levels (baseline and end point). Copyright © 2016.

Status
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507.
The impact of sperm protamine deficiency and sperm DNA damage on human male fertility: A systematic review and meta-analysis.
Ni K., Spiess A.-N., Schuppe H.-C., Steger K.
Embase
Andrology. (no pagination), 2016. Date of Publication: 2016.
[Article In Press]
AN: 610573645

Existing literature suggests evidence that protamine deficiency is related to DNA damage and male fertility. In this meta-analysis, we analyzed the relationship between the ratio of protamine-1 and protamine-2 with male fertility and the association of protamine deficiency with sperm DNA damage. Quality of available cohort studies was evaluated using the Newcastle-Ottawa Scale checklist. Summary effect estimates with 95% confidence intervals (CI) were derived using a random effects model. The effect of the protamine ratio on male fertility was analyzed in nine studies demonstrating a significantly higher value of the protamine ratio in subfertile men (n =
633) when compared with controls (n = 453, SMD = 0.46, 95% CI 0.25-0.66, Z = 4.42, p < 0.00001). Both protamine mRNA (SMD = 0.45, 95% CI 0.11-0.79, Z = 2.63, p = 0.009) and protein ratio (SMD = 0.46, 95% CI 0.25-0.68, Z = 4.22, p < 0.0001) showed significantly increased values in subfertile patients. The association between protamine deficiency and DNA damage was analyzed in 12 studies (n = 845) exhibiting a combined overall correlation coefficient (COR) of 0.53 (95% CI 0.28-0.71, Z = 3.87, p < 0.001). Protamine deficiency measured by CMA3 staining was significantly associated with sperm DNA damage (COR = 0.71, 95% CI 0.48-0.85, Z = 4.87, p < 0.001), whereas the P1/P2 ratio was not (COR = 0.17, 95% CI -0.16 to 0.46, Z = 0.99, p = 0.33). It is concluded that the protamine ratio represents a suitable biomarker for the assessment of sperm quality and protamine deficiency is closely related with sperm DNA damage. Copyright © 2016 American Society of Andrology and European Academy of Andrology.

Status
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508.

Effects of Testosterone Replacement Therapy on Lower Urinary Tract Symptoms: A Systematic Review and Meta-analysis.
Kohn T.P., Mata D.A., Ramasamy R., Lipshultz L.I.

Embase
European Urology. 69 (6) (pp 1083-1090), 2016. Date of Publication: 01 Jun 2016. [Review]
AN: 610582563
Context There is a potential risk that testosterone replacement therapy (TRT) may exacerbate lower urinary tract symptoms (LUTS) among aging men with late-onset hypogonadism (LOH) because of testosterone’s growth-promoting effects on the prostate. Objective To compare the change in LUTS severity as assessed using the International Prostate Symptom Score (IPSS) between men receiving TRT versus placebo for the treatment of LOH. Evidence acquisition Systematic search of MEDLINE, Embase, ClinicalTrials.gov, and The Cochrane Library for randomized controlled trials of TRT for LOH published between January 1992 and September 2015. Studies were eligible for inclusion if they were a randomized control trial, used TRT, and assessed LUTS outcomes using the IPSS. Estimates were pooled using random effects meta-analysis. Differences by study-level characteristics were estimated using meta-regression.

Evidence synthesis Data were extracted from 14 trials involving 2029 participants. The average age was 64.5 yr and the average follow-up was 34.4 mo. Seven studies used topical, five used injectable, and two used oral testosterone. There was no statistically significant difference in pooled changes in IPSS from baseline to follow up in men treated with TRT compared with those receiving placebo (-0.41 points [95% confidence interval: -0.89 to 0.07; I2 = 0%, p = 0.28] vs. 0.12 points [95% confidence interval: -0.32 to 0.55; I2 = 0%, p = 0.81], between-group difference p > 0.05). No between-group differences were noted in subanalyses that controlled for potential confounders such as type of testosterone, change in testosterone, aging Male symptom scale, or prostate-specific antigen levels (p > 0.05 for all comparisons). Conclusions In this meta-analysis of 14 clinical trials of TRT for LOH, the change in IPSS was similar among men receiving TRT versus placebo, suggesting that TRT treatment does not worsen LUTS among men with LOH.

Patient summary In this analysis of 14 clinical trials, testosterone replacement therapy did not worsen lower urinary tract symptoms among men being treated for late-onset hypogonadism.

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Status
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Publisher
Elsevier
Date Created
20160609
Holmium Laser vs Monopolar Electrocautery Bladder Neck Incision for Prostates Less Than 30 Grams: A Prospective Randomized Trial.
Bansal A., Sankhwar S., Kumar M., Jhanwar A., Purkait B., Aeron R., Goel S.

Urology. 93 (pp 158-163), 2016. Date of Publication: 01 Jul 2016.

Objective To compare the efficacy and results of bladder neck incision (BNI) in bladder outlet obstruction (BOO) in men with a small prostate using holmium laser vs conventional monopolar electrocautery technique. Materials and Methods This study included 140 patients of BOO (prostate size < 30 cc, American Urological Association (AUA) score > 8, Qmax < 15 mL/sec, and Schafer grade > 2) who were randomly assigned to holmium laser BNI (HoBNI) or conventional BNI (C-BNI). AUA score and Qmax were assessed preoperatively and postoperatively at 3, 6, and 12 months. At 6 months, detrusor pressure at Qmax, Schafer grade, and postvoid residual were assessed. Results The incidence of postoperative hematuria and blood transfusion in the C-BNI group were 4.2% and 2.8%, respectively. No patient in the HoBNI group developed hematuria or required blood transfusion. Qmax and AUA score at each follow-up, and Pdet Qmax, Schafer grade, and postvoid residual at 6 months were comparable between two groups but showed significant improvement when compared to baseline in both the groups. At 6 months, 2.9% patients in the HoBNI group developed urodynamically and underwent reoperation (P > .05). The incidence of retrograde ejaculation was significantly higher in HoBNI (22.9% vs 6.1%, P < .02) Conclusion Both procedures are equally efficient in relieving BOO in patients with prostate size < 30 cc and have similar success rates. The risk of postoperative hematuria is less with HoBNI because of its better hemostatic properties, but its use must be counterbalanced with significant increase in incidence of retrograde ejaculation. Copyright © 2016 Elsevier Inc.
Efficacy and safety of tamsulosin oral-controlled absorption system, solifenacin, and combined therapy for the management of ureteric stent-related symptoms.


Objectives To evaluate the efficacy of solifenacin, tamsulosin oral-controlled absorption system (OCAS), and the combination of both drugs on JJ stent-related symptoms using the validated Arabic version of the ureteric stent symptom questionnaire (USSQ). Patients and methods In all, 260 patients who had undergone JJ stenting of the ureter for different endoscopic urological procedures were postoperatively randomly assigned into four equal groups. Patients in Group I received no treatment and served as the control group, Group II patients received tamsulosin OCAS 0.4 mg daily, Group III patients received solifenacin 5 mg daily, and Group IV patients received a combination of both drugs. Before stent removal, all patients completed the Arabic version of the USSQ. Results In all, 234 patients completed the study, comprised of 56 in Group I, 59 in Group II, 58 in Group III, and 61 in Group IV. Baseline characteristics and indications for JJ stenting were comparable in the four groups. There were highly significant differences in all items of the USSQ between the treatment groups and the controls, while Group II and III were comparable. Crossing of the distal curl of the stent to the midline had a significant positive correlation with the severity of the urinary symptoms, body pain, general health, and work performance in the medicated groups. Conclusions Combined therapy with tamsulosin OCAS 0.4 mg daily and solifenacin 5 mg daily is
a safe and well-tolerated management for stent-related symptoms. However, stent position remains a significant factor affecting response to medical therapy and patients' health-related quality of life. Copyright © 2016 Arab Association of Urology. Production and hosting by Elsevier B.V.

Status
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(Al Azab) International Medical Center, Jeddah, Saudi Arabia
Publisher
Arab Association of Urology (E-mail: araburo@yahoo.com)
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20160611
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2016

511.
Diagnosis and treatment of infertility-related male hormonal dysfunction.
Kathrins M., Niederberger C.
Embase
[Review]
AN: 610055787
Treatment of infertility-related hormonal dysfunction in men requires an understanding of the hormonal basis of spermatogenesis. The best method for accurately determining male androgenization status remains elusive. Treatment of hormonal dysfunction can fall into two categories-empirical and targeted. Empirical therapy refers to experience-based treatment approaches in the absence of an identifiable aetiology. Targeted therapy refers to the correction of a specific underlying hormonal abnormality. However, the tools available for inferring the intratesticular hormonal environment are unreliable. Thus, understanding the limitations of serum hormonal assays is very important for determining male androgen status. Furthermore, bulk
seminal parameters are notoriously variable and consequently unreliable for measuring responses to hormonal therapy. In the setting of azoospermia owing to spermatogenic dysfunction, hormonal therapy-relying on truly objective parameters including the return of sperm to the ejaculate or successful surgical sperm retrieval-is a promising treatment. This approach to the treatment of fertility-related hormonal dysfunction in men contrasts with the current state of its counterpart in female reproductive endocrinology. Treatment of male hormonal dysfunction has long emphasized empirical therapy, whereas treatment of the corollary female dysfunction has been directed at specific deficits. Copyright © 2016 Macmillan Publishers Limited.

512.

Management of beta-thalassemia-associated osteoporosis.
Giusti A., Pinto V., Forni G.L., Pilotto A.

Embase
[Article]
AN: 609899619

Beta-Thalassemia-associated osteoporosis is a multifactorial and complex condition. Different acquired and genetic factors are involved in its pathogenesis. These factors produce an imbalance in bone remodeling by inhibiting osteoblast activity and increasing osteoclast function, leading to bone loss and increased fracture risk. The management of patients presenting with
thalassemia-associated osteoporosis should consist of the implementation of general measures and the prescription of a specific pharmacological agent, with the aim of reducing fracture risk and preventing disability and deterioration of quality of life. General measures include control of anemia, adequate chelation therapy, healthy nutrition and lifestyle, regular exercise, adequate management of comorbid conditions, hormone replacement therapy in patients with hypogonadism, and vitamin D supplementation/therapy. Among the pharmacological agents currently available for the management of osteoporosis in postmenopausal women and men, bisphosphonates have been shown to improve bone mineral density, to reduce bone turnover, and to decrease bone/back pain in patients with thalassemia-associated osteoporosis, with a good profile of safety and tolerability. On the other hand, there are limited experiences with other pharmacological agents (e.g., denosumab or teriparatide). The complexity of this condition presents diagnostic and therapeutic challenges and underscores the importance of a comprehensive and multidisciplinary approach. Copyright © 2016 The New York Academy of Sciences.

Predictors of pregnancy and live-birth in couples with unexplained infertility after ovarian stimulation-intrauterine insemination.

Objective To identify baseline characteristics of couples that are likely to predict conception, clinical pregnancy, and live birth after up to four cycles of ovarian stimulation with IUI in couples with unexplained infertility. Design Secondary analyses of data from a prospective, randomized, multicenter clinical trial investigating pregnancy, live birth, and multiple pregnancy rates after ovarian stimulation-IUI with clomiphene citrate, letrozole, or gonadotropins. Setting Outpatient clinical units. Patient(s) Nine-hundred couples with unexplained infertility who participated in the Assessment of Multiple Intrauterine Gestations from Ovarian Stimulation clinical trial. Intervention(s) As part of the clinical trial, treatment was randomized equally to one of three arms and continued for up to four cycles or until pregnancy was achieved. Main Outcome Measure(s) Conception, clinical pregnancy, and live-birth rates. Result(s) In a multivariable logistic regression analysis, after adjustment for other covariates, age, waist circumference, income level, duration of infertility, and a history of prior pregnancy loss were significantly associated with at least one pregnancy outcome. Other baseline demographic and lifestyle characteristics including smoking, alcohol use, and serum levels of antimullerian hormone were not significantly associated with pregnancy outcomes. Conclusion(s) While age and duration of infertility were significant predictors of all pregnancy outcomes, many other baseline characteristics were not. The identification of level of income as a significant predictor of outcomes independent of race and education may reflect differences in the underlying etiologies of unexplained infertility or could reveal disparities in access to fertility and/or obstetrical care. Clinical Trial Registration NCT01044862. Copyright © 2016 American Society for Reproductive Medicine Status EMBASE Author NameID Wild, Robert A.; ORCID: http://orcid.org/0000-0002-1298-265X Alvero, Ruben; ORCID: http://orcid.org/0000-0001-6542-710X Institution (Hansen, Wild) Department of Obstetrics and Gynecology, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, United States (He, Huang, Zhang) Department of Biostatistics, Yale University School of Public Health, New Haven, Connecticut, United States (Styer) Department of Obstetrics, Gynecology, and Reproductive Biology, Massachusetts General Hospital/Harvard Medical School, Boston, Massachusetts, United States (Butts, Coutifaris) Department of Obstetrics and Gynecology, University of Pennsylvania, Philadelphia, Pennsylvania, United States
Testicular microlithiasis and testicular cancer: review of the literature.

Pedersen M.R., Rafaelsen S.R., Moller H., Vedsted P., Osther P.J.  

Embase  
International Urology and Nephrology. 48 (7) (pp 1079-1086), 2016. Date of Publication: 01 Jul 2016.  
[Review]  
AN: 609239077  
Purpose: To perform a systematic literature review to assess whether the occurrence of testicular microlithiasis (TML) in conjunction with other risk factors is associated with testicular cancer.
Methods: A systematic literature search was performed of original articles in English published 1998 to 2015. Relevant studies were selected by reading the title and abstract by two of the authors. Studies were included if TML was diagnosed by ultrasonography and a risk condition was reported. Studies were only eligible if the particular risk condition was reported in more than one article. Results: In total, 282 abstracts in were identified. Based on title and abstract the eligibility was assessed and 31 studies were included. Five conditions in relation to TML and testicular cancer emerged: Down syndrome, McCune-Albright syndrome, cryptorchidism, infertility and familial disposition of testicular cancer. Conclusion: Data support the conclusion that TML is not an independent risk factor for testicular cancer but associated with testicular cancer through other conditions. In male infertility, TML appears to be related to an increased risk of testicular cancer possibly as part of a testicular dysgenesis syndrome. Copyright © 2016, Springer Science+Business Media Dordrecht.

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2016
515.
Salvage hormonal therapy after failed microdissection testicular sperm extraction: A multi-institutional prospective study.
Shiraishi K., Ishikawa T., Watanabe N., Iwamoto T., Matsuyama H.
Embase
International Journal of Urology. 23 (6) (pp 496-500), 2016. Date of Publication: 01 Jun 2016.
[Article]
AN: 609152612
Objective: To validate the efficacy of salvage hormonal therapy in men with non-obstructive azoospermia at their second microdissection testicular sperm extraction. Methods: This was a multi-institutional study registered at the Japanese University Hospital Medical Information Network clinical trial center. After 1 month of human chorionic gonadotropin therapy (5000 IU, three times a week), patients were treated with recombinant human follicle-stimulating hormone (150 IU, three times a week) and human chorionic gonadotropin for the next 3 months. Three testicular samples were obtained randomly from both testes, and sent for pathological diagnosis at the first and second microdissection testicular sperm extraction. Results: A total of 21 men, excluding those with chromosomal abnormalities, azoospermia factor a or b deletions, extremely small testes (<2 mL), or prior hormonal therapy, were eligible to participate based on our inclusion criteria. At the first microdissection testicular sperm extraction, 13 and six patients had Sertoli cells only and an early maturation arrest, respectively. With the second microdissection testicular sperm extraction, sperm were successfully obtained from two patients (10%). Patient age, testicular volume and hormone profiles were not associated with the results of the second microdissection testicular sperm extraction. However, the testicular histology of the two successful patients were late maturation arrest and hypospermatogenesis. Conclusions: Effectiveness of human chorionic gonadotropin-based salvage hormonal therapy preceding a second microdissection testicular sperm extraction seems to be limited. Non-obstructive azoospermia men who have differentiated cells in their testes are likely to respond to hormonal stimulation. Copyright © 2016 The Japanese Urological Association.
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Publisher
516.
Evaluation of intrauterine insemination practices: a 1-year prospective study in seven French assisted reproduction technology centers.
Monraisin O., Chansel-Debordeaux L., Chiron A., Floret S., Cens S., Bourrinet S., Paulhac S., Jimenez C., Parinaud J., Leandri R.
Embase
Fertility and Sterility. 105 (6) (pp 1589-1593), 2016. Date of Publication: 01 Jun 2016.
[Article]
AN: 609130424
Objective To determine the best practices of intrauterine insemination with the partner's fresh sperm. Design Prospective multicenter observational study. Setting Assisted reproduction technology (ART) centers. Patient(s) Seven hundred and seven patients entering the program, regardless of age or cause of infertility. Intervention(s) Intrauterine insemination by standard procedures. Main Outcome Measure(s) Effect of patient characteristics (duration of infertility, indications, age, parity, body mass index, semen parameters) as well as IUI parameters on delivery rates per couple or per attempt. Result(s) The overall live birth rate was 11.4% per cycle, varying from 8.4% to 17.6% between centers. The main differences in practice that had a statistically significant impact on the delivery rate were the use of gonadotropin-releasing hormone (GnRH) antagonists (15.2% with versus 9.4% without) and the number of mature recruited follicles (9.4% for one versus 15.2% for two). Conclusion(s) Our results indicate that the use of GnRH antagonists has a positive effect on the delivery rate, especially in the multifollicular stimulations that are required when women are older than 27 years.  Copyright © 2016 American Society for Reproductive Medicine
Status
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Institution
Who receives a medical evaluation for infertility in the United States?


Embase
Fertility and Sterility. 105 (5) (pp 1274-1280), 2016. Date of Publication: 01 May 2016.

[Article]
AN: 607967174

Objective To investigate characteristics of receiving a medical evaluation for infertility among infertile women. Design Prospective cohort. Setting Academic institution. Patient(s) A total of 7,422 women who reported incident infertility between 1989 and 2009 in the Nurses’ Health Study II. Intervention(s) None. Main Outcome Measure(s) Report of receiving a medical evaluation for infertility. Result(s) Approximately 65% of women who reported infertility had a medical evaluation for infertility. Infertile women who were parous (relative risk [RR] = 0.81, 95% confidence interval [CI] 0.78-0.84), older, current smokers (RR = 0.89, 95% CI 0.83-0.96), or who had a higher body
mass index (BMI) were less likely to report receiving a medical infertility evaluation. Infertile women who exercised frequently, took multivitamins (RR = 1.03, 95% CI 1.00-1.07), lived in states with comprehensive insurance coverage (RR = 1.09, 95% CI 1.00-1.19), had a high household income, or who had a recent physical examination (RR = 1.15, 95% CI 1.06-1.24) were more likely to report receiving a medical infertility evaluation. Conclusion(s) These findings highlight demographic, lifestyle, and access barriers to receiving medical infertility care. Historically, the discussion of barriers to infertility care has centered on financial access, geographic access, and socioeconomic status. Our findings build off literature by supporting previously reported associations and showcasing the importance of demographic and lifestyle factors in accessing care.  Copyright © 2016 American Society for Reproductive Medicine, Published by Elsevier Inc.
Association of anti-sperm antibodies with chronic prostatitis: A systematic review and meta-analysis.

Jiang Y., Cui D., Du Y., Lu J., Yang L., Li J., Zhang J., Bai X.

Embase

Journal of Reproductive Immunology. 118 (pp 85-91), 2016. Date of Publication: 01 Nov 2016.

[Article]

AN: 612630756

Chronic prostatitis is a risk factor for impaired male fertility potential, and anti-sperm antibodies (ASAs) cause the autoimmune disease immune infertility, which has a negative effect on semen parameters. Current studies have investigated the ASA-positive relationship between chronic prostatitis versus normal controls, but have shown inconsistent results. Hence, we systematically searched the PubMed, EMBASE, Science Direct/Elsevier, Medline, and the Cochrane Library up to October 2015 for case-control studies that involved the ASA-positive relationship between chronic prostatitis patients versus normal controls. The meta-analysis was performed with Review Manager and Stata software. After literature search, six studies were identified, including 721 cases of chronic prostatitis and 160 normal controls. Our results illustrated a significant correlation of the ASA-positive relationship between chronic prostatitis patients versus normal controls. The combined odds ratio of the ASA-positive rate in chronic prostatitis patients and normal controls was 3.26 (1.86-5.71). There was also a significant correlation of the ASA-positive relationship between National Institutes of Health (NIH) III versus normal controls, and the combined OR was 2.46 (1.10-5.51). However, there was no significant correlation of the ASA-positive relationship between National Institutes of Health (NIH) II versus normal controls. The present study illustrates that the positive rate of ASAs in chronic prostatitis patients was significantly higher than in the control group, suggesting that chronic prostatitis has a negative effect on male reproductive function. However, studies with larger samples are needed to better illustrate the correlation between ASAs and chronic prostatitis. Copyright © 2016 Elsevier Ireland Ltd

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519.
Medical Expulsive Therapy Following Shock Wave Lithotripsy in Ureteral Calculi: An Effective Approach for the Improvement of Health-Related Quality of Life.
Eryildirim B., Sahin C., Tuncer M., Sabuncu K., Tarhan F., Sarica K.
Embase
Urologia Internationalis. 97 (3) (pp 260-265), 2016. Date of Publication: 01 Oct 2016.
[Article]
AN: 610082686
Objective: To evaluate the possible effects of medical expulsive therapy (MET) on the health-related quality of life (HRQOL) of patients undergoing shock wave lithotripsy (SWL) for ureteric stones. Methods: Eighty patients treated with SWL for ureteric stones were included in this study. Patients were divided into 2 groups; Group 1 received medical therapy only for colic pain and Group 2 received MET in addition to medical therapy. Patients requiring DJ stenting and auxiliary measures after SWL procedure were excluded. The remaining 54 patients were further evaluated (Group 1: n = 26, Group 2: n = 28) and followed up during the 4-week period for analgesic requirement, number of renal colic attacks, emergency department (ED) visits and the HRQOL scores by using EQ-5D index and EQ-5D visual analogue scale (VAS) values. Results: During the 4-week follow-up period, cases undergoing SWL only required significantly higher amount of analgesics. In addition to the lower number of renal colic attacks and ED visits, EQ-5D index and EQ-5D VAS values also demonstrated higher mean values in patients undergoing SWL + MET. Conclusion: In addition to the increased spontaneous stone passage rates, MET following SWL for ureteral calculi could increase the HRQOL scores by lowering the number of both renal colic attacks and ED visits along with decreased analgesic need. Copyright © 2016 S. Karger AG, Basel.
Status
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Tamsulosin or silodosin adjuvant treatment is ineffective in improving shockwave lithotripsy outcome: A short-term follow-up randomized, placebo-controlled study.


Embase

Journal of Endourology. 30 (7) (pp 817-821), 2016. Date of Publication: 01 Jul 2016.

AN: 611252034

Introduction: The role of alpha-blockers after shockwave lithotripsy (SWL) is controversial. The aim of our study was to evaluate the effect of tamsulosin and silodosin after SWL for kidney stones. Methods: From 2012 onward, a consecutive series of patients undergoing SWL were prospectively enrolled and randomized by closed envelopes in three groups receiving tamsulosin 0.4 mg (A), silodosin 8 mg (B), and placebo (C) daily for 21 days after SWL. Anthropometrics, stone size, and location were recorded before SWL. Visual analogue scale (VAS) score was collected at 6, 12, and 24 hours after treatment to evaluate patients’ discomfort. Stone-free rate was assessed 1 and 3 weeks postoperatively. Complications and medical treatment-related adverse events (AEs) were recorded. Differences in VAS score, stone-free rate, and complications were compared among the groups. Results: Overall, 60 patients were enrolled. Mean stone sizes were 10.28 +/- 2.46 mm, 10.45 +/- 1.73 mm, and 9.23 +/- 2.04 mm in groups A, B, and C, respectively (p = 0.474). There was no significant difference between the three groups with regard to stone location. Comparable energy was used to treat patients from the three groups. The overall 3-week stone-free rate was 53%: 58% in the tamsulosin group, 47% in the silodosin group, and 55% in the placebo group (p = 0.399). No significant differences were observed in the VAS scores reported by the groups at 6 hours (p = 1.254), 12 hours (p = 0.075),
and 24 hours (p = 0.490). Overall, 12 complications were reported: 11 patients (7 in group C and 4 in group B) needed analgesics for colic, and 1 patient (group B) was surgically treated for Steinstrasse. Tamsulosin was superior to placebo (p = 0.008) and silodosin (p = 0.021) in preventing complications; no difference between silodosin and placebo (p = 0.629) was noted. Conclusions: Tamsulosin and silodosin are ineffective in increasing stone-free rate as well as early patients' discomfort after extracorporeal lithotripsy. Copyright © Mary Ann Liebert, Inc. 2016.

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Mary Ann Liebert Inc. (E-mail: info@liebertpub.com)
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20160720
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2016

521.
To evaluate the efficacy of combination antioxidant therapy on oxidative stress parameters in seminal plasma in the male infertility.
Singh A., Jahan N., Radhakrishnan G., Banerjee B.D.
Embase
[Article]
AN: 611220619
Introduction: Infertility is defined as inability to conceive after 1 year of unprotected intercourse and it affects 7% of male population and 8-10% of couples. According to estimates WHO, 13-19 million couples in India are infertile. Oxidative stress is the causative factor in 25% of infertile males. Aim: To study the efficacy of antioxidant therapy on oxidative stress parameters in seminal plasma of infertile male. Materials and Methods: Forty patients of male infertility were enrolled in
study after two abnormal semen analyses reports at 2-3 weeks interval, of oligozoospermia and/or asthenozoospermia, as per WHO guide line 1999. First semen sample was collected at a time of enrollment of study and second semen sample was collected three months after combined antioxidant therapy. Semen samples from the infertile male (the second confirmatory sample of oligoasthenozoospermia) were taken and after liquefaction semen sample were utilized for various analyses, 0.5 ml of sample for standard semen analysis, 1.2 ml sample for separation of seminal plasma to evaluate Oxidative stress (OS) parameters like Malondialdehyde (MDA), Protein Carbonyl (PC) and antioxidant capacity by Glutathione (GSH). We followed the patient for three months after completion of the treatment. Results: Semen parameters - Out of 40 patients recruited in the study group 7 patients had only oligospermia (1 to 20 million/ml) and 31 patients had oligoasthenozoospermia (motility range 0-50%) and 2 patients had oligoasthenoteratozoospermia. There was no patient with asthenospermia alone as abnormal semen parameters. After the three months treatment with combined antioxidants the semen parameters like count (mean SD =-1.70+/−1.44) and motility (mean +SD=−9.56+/−9.05) were significantly increased (p-value=0.000). Oxidative Stress Assessment - The level of MDA which is a marker of oxidative stress is significantly lower after the three months therapy of antioxidants (p-value=0.002) whereas another marker which is denoted by PC is also lower after the treatment but not statistically significant (p-value=0.584). The level of antioxidants GSH also significantly increased after the treatment (p-value=0.000). After the treatment out of 40, five patients were conceived (16.7%). Conclusion: As we have seen through this study antioxidant dramatically reduced the oxidative stress markers and enhancing the antioxidant enzymes, it also observed in multiple studies. So antioxidant should be used on routine basis in case of male factor infertility.
Human chorionic gonadotropin stimulation gives evidence of differences in testicular steroidogenesis in Klinefelter syndrome, as assessed by liquid chromatography-tandem mass spectrometry.

Belli S., Santi D., Leoni E., Dall'Olio E., Fanelli F., Mezzullo M., Pelusi C., Roli L., Tagliavini S., Trenti T., Granata A.R., Pagotto U., Pasquali R., Rochira V., Carani C., Simoni M.

Embase

AN: 611184259

Background: Men with Klinefelter syndrome (KS) show hypergonadotropic hypogonadism, but the pathogenesis of hypotestosteronemia remains unclear. Testicular steroidogenesis in KS men was evaluated over three decades ago after human chorionic gonadotropin (hCG) stimulation, but inconclusive results were obtained. Intriguingly, some recent studies show increased intratesticular testosterone concentrations in men with KS. Objective: To analyze serum steroid profile, as a proxy of testicular steroidogenesis, after hCG stimulation in KS compared with control men. Design: A prospective, longitudinal, case-control, clinical trial. Methods: Thirteen KS patients (36 +/- 9 years) not receiving testosterone (TS) replacement therapy and 12 eugonadic controls (32 +/- 8 years) were enrolled. Serum steroids were measured by liquid chromatography-tandem mass spectrometry (LC-MS/MS) at baseline and for five consecutive days after intramuscular injection of 5000 IU hCG. Results: Progesterone (P), 17-hydroxyprogesterone (17OHP), TS, and estradiol (E2) showed a significant increase (P < 0.001) after hCG stimulation in both groups. On the contrary, androstenedione (AS) and dehydroepiandrosterone did not increase after hCG stimulation. The 17OHP/P ratio increased in both groups (P < 0.001), the TS/AS ratio (17beta-hydroxysteroid dehydrogenase type 3 (17betaHSD3) activity) did not increase after hCG in any group, and the E2/TS ratio (aromatase activity) increased significantly in both groups (P = 0.009 in KS and P < 0.001 in controls). Luteinizing hormone decreased after hCG in both groups (P = 0.014 in KS and P < 0.001 in controls), whereas follicle-stimulating hormone decreased only in control men (P < 0.001). Conclusion: This study demonstrates for the first time using LC-MS/MS that Leydig cells of KS men are able to respond to hCG stimulation and that the first steps of steroidogenesis are fully functional. However, the TS production in KS men is impaired, possibly related to reduced hydroxysteroid dehydrogenase activity due to an
unfavorable intratesticular metabolic state. Copyright © 2016 European Society of Endocrinology.

523.

Montorsi F., Gandaglia G., Chapple C., Cruz F., Desgrandchamps F., Llorente C.

International Journal of Urology. 23 (7) (pp 572-579), 2016. Date of Publication: 01 Jul 2016.
[Article]
AN: 611168924
Objectives: To assess the benefit-risk balance of silodosin in a real-life setting of benign prostatic hyperplasia patients with lower urinary tract symptoms. Methods: A phase IV trial including men...
aged >60 years with a clinical diagnosis of benign prostatic hyperplasia with an International Prostate Symptom Score >12 was carried out. Patients received silodosin 8 mg for 24 weeks. The primary end-point was a decrease >25% in the total International Prostate Symptom Score. Secondary end-points were: changes in total, storage and voiding, and quality of life International Prostate Symptom Scores; changes in the International Continence Society-male questionnaire; changes in the frequency/volume chart; and satisfaction according to the Patient Perception of Study Medication questionnaire. Treatment-emergent adverse events were recorded. Results: Overall, 1036 patients were enrolled. Of these, 766 patients (77.1%) had a decrease >25% in the total International Prostate Symptom Score. The mean total International Prostate Symptom Score, and storage and voiding symptoms subscores decreased from 18.9, 8.1 and 10.8 to 10.6, 4.9 and 5.7. Nocturia decreased from 85.7% to 52.4%. The mean International Prostate Symptom Score quality of life score decreased from 4.0 to 2.2. Half of the patients reported an improvement in the frequency and bothersomeness of the most frequent symptoms reported at baseline (all P < 0.001). A reduction in the number of voids was documented by the frequency/volume chart data. The most common treatment-emergent adverse event was ejaculation failure (185 patients; 17.9%), which led to study discontinuation in 2.4% of patients. Overall, 74.2% of patients were satisfied with the medication. Conclusions: Silodosin improved lower urinary tract symptoms in three out of four patients, including diurnal voiding and storage symptoms, nocturia, and quality of life. This treatment showed a favorable safety profile in this setting. Copyright © 2016 The Japanese Urological Association

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Publisher
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Date Created
Psychometric testing of two new patient-reported outcome instruments for the evaluation of treatment for hypogonadism.

Hayes R.P., Ni X., Heiselman D.E., Kinchen K.

Embase

International Journal of Clinical Practice. 70 (7) (pp 587-595), 2016. Date of Publication: 01 Jul 2016.

[Article]

AN: 611156087

Aim: The aim of this study was to perform psychometric testing and estimate minimal important change (MIC) of two new patient-reported outcome (PRO) instruments - Sexual Arousal, Interest and Drive Scale (SAID) and Hypogonadism Energy Diary (HED).

Methods: New PRO instruments were administered immediately after screening (Time 1, test-retest subset only) and immediately prior to both randomisation (Time 2) and end-point (Time 3) to men participating in a randomised clinical trial comparing the effect of testosterone solution 2% (TS) and placebo on serum total testosterone. Psychometric analyses included reliability, validity and responsiveness. Total scores for both PRO instruments were transformed to a 0-100 scale.

Results: Study participants (n = 694) were 80% age < 65 years, 79% White, with mean baseline testosterone = 202 ng/dl. Clinicians identified 86% subjects as having low sex drive, 86% with low energy and 76% with both symptoms. Reliability analyses for SAID and HED yielded reliability coefficients > 0.70. SAID scores discriminated between men having low sex drive (n = 553) and those who did not (n = 80) (34.5 vs. 42.8, p < 0.001). HED scores discriminated between men having low energy (n = 541) and those who did not (n = 64) (48.9 vs. 60.2, p < 0.001). In the men randomised to TS (vs. placebo), SAID and HED detected effect sizes of 0.61 (vs. 0.39) and 0.68 (vs. 0.48), respectively. MIC estimates for SAID and HED were approximately 10 and 8, respectively.

Conclusions: This study provided evidence of the reliability, validity and responsiveness of SAID and HED as measures of sex drive and energy, respectively, making them potentially useful for evaluation of hypogonadal treatment. Copyright © 2016 Eli Lilly & Company. International Journal of Clinical Practice Published by John Wiley & Sons Ltd.
Neutral alpha-1,4-glucosidase and fructose levels contribute to discriminating obstructive and nonobstructive azoospermia in Chinese men with azoospermia.


Andrologia. 48 (6) (pp 670-675), 2016. Date of Publication: 01 Aug 2016.

Nowadays, whether neutral alpha-1,4-glucosidase (NAG) and fructose levels are contributed to discriminating obstructive and nonobstructive azoospermia in Chinese azoospermic patients remains unclear. In this study, we retrospectively analysed the levels of NAG and fructose in 229 patients with obstructive azoospermia and 415 patients with nonobstructive azoospermia from three different medical central. Results indicated that NAG and fructose levels in patients with nonobstructive azoospermia were significantly higher compared with those with obstructive azoospermia (P < 0.05). According to the reference value of NAG and fructose defined by the World Health Organization (WHO, 2010), decreased level of NAG was observed in 77.3% of patients with obstructive azoospermia, which was significantly higher than those with nonobstructive azoospermia (55.2%, P < 0.0001). Low level of fructose was observed in 48.0% of patients with obstructive azoospermia, which is also obviously higher than those with
nonobstructive azoospermia (31.8%, P < 0.0001). Moreover, the decrease of both NAG and fructose was only recorded in 3.7% of patients with SCO syndrome, 5.0% of patients with severe hypospermatogenesis and 18.2% of patients with maturation arrest. Therefore, our results indicated that NAG and fructose levels are contributed to discriminating obstructive and nonobstructive azoospermia in Chinese patients based on the histological types of testes.

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2016

Clinical significance of subclinical varicocelectomy in male infertility: systematic review and meta-analysis.

Embase
Andrologia. 48 (6) (pp 654-661), 2016. Date of Publication: 01 Aug 2016.

[Review]
AN: 611150701
Recent meta-analysis by the Cochrane collaboration concluded that treatment of varicocele may improve an infertile couple's chance of pregnancy. However, there has been no consensus on the
management of subclinical varicocele. Therefore, we determine the impact of varicocele
treatment on semen parameters and pregnancy rate in men with subclinical varicocele. The
randomised controlled trials that assessed the presence and/or treatment of subclinical varicocele
were included for systematic review and meta-analysis. Random effect model was used to
calculate the weighted mean difference of semen parameters and odds ratio of pregnancy rates.
Seven trials with 548 participants, 276 in subclinical varicocelectomy and 272 in no-treatment or
clophiphene citrate subjects, were included. Although there was also no statistically significant
difference in pregnancy rate (OR 1.29, 95% CI 0.99-1.67), surgical treatment resulted in
statistically significant improvements on forward progressive sperm motility (MD 3.94, 95% CI
1.24-6.65). However, the evidence is not enough to allow final conclusions because the quality of
included studies is very low and further research is needed. Copyright © 2015 Blackwell Verlag
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2016
Zinc is proposed to have an important role in the morphology, viability and motility of spermatozoa. There are inconsistent reports on the association between seminal plasma zinc concentration and male infertility. For this purpose, papers reporting the level of seminal zinc among asthenozoospermic groups were selected and used for further analysis. This meta-analysis of previous published studies was performed to obtain more precise information on the association between seminal plasma zinc and asthenozoospermia. Relevant studies for inclusion were identified after preliminary investigation of research papers published on electronic databases up to February 2015. Eight reports and 475 subjects were finally included in the meta-analysis. In the overall analysis, a statistically significant reduction in seminal plasma zinc concentrations was observed in asthenozoospermic infertile men. Random-effects method was used to evaluate the summary effect size due to the presence of significant heterogeneity. The effect of zinc on asthenozoospermia was significant (Hedge's G effect size = -0.506, 95% confidence interval (95% CI): -0.998 to -0.014, P = 0.044). Taken together, despite of significant statistical heterogeneity between studies, our findings were indicative of significant association between zinc concentration and asthenozoospermia. In conclusion, the meta-analysis suggests that seminal plasma zinc concentration is negatively associated with male infertility. Copyright © 2015 Blackwell Verlag GmbH

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Date Created
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The efficacy, bioavailability and safety of a novel hydroalcoholic testosterone gel 2% in hypogonadal men: results from phase II open-label studies.
Efros M., Carrara D., Neijber A.
Embase
Andrologia. 48 (6) (pp 637-645), 2016. Date of Publication: 01 Aug 2016.
[Article]
AN: 611150692
Pharmacokinetics, pharmacodynamics and safety of a novel hydroalcoholic testosterone gel 2% (TG) were evaluated in phase II sequential dose escalation studies using 3 application sites (thigh, abdomen and shoulder/upper arm) and 2 application methods. Hypogonadal men (n = 40), 18-75 years, with serum testosterone <300 ng dl-1 were included in both studies. Study 1 evaluated hand-applied multiple doses of TG 1.25, 2.50 and 3.75 ml (23, 46 and 70 mg of testosterone, respectively), once daily for 10 days to shoulder/upper arm. Study 2 evaluated applicator-applied (TG 1.25, 2.50 and 3.75 ml) versus hand-applied (TG 2.5 ml) doses, once daily for 7 days to shoulder/upper arm. Primary endpoint for both studies was responder rate (Cave testosterone levels between 298 and 1050 ng dl-1). In Study 1 following multiple applications, >70% participants in each group were responders. Dose-dependent increase was observed in PK values for total testosterone, free testosterone and DHT. In Study 2, responder rate was dose proportional: 16.7%, 50.0% and 77.8% responders in TG 1.25, 2.50 and 3.75 ml groups respectively. The bioavailability was highest for the shoulder application. There was a significant improvement in almost all the domains of sexual functioning. Applicator-application was preferred over hand-application by majority of the participants. TG was found to be safe and well tolerated in hypogonadal men. Copyright © 2015 Blackwell Verlag GmbH
Long-term use of everolimus in patients with tuberous sclerosis complex: Final results from the EXIST-1 study.
Embase
[Article]
AN: 611145074
Background Everolimus, a mammalian target of rapamycin (mTOR) inhibitor, has demonstrated efficacy in treating subependymal giant cell astrocytomas (SEGAs) and other manifestations of tuberous sclerosis complex (TSC). However, long-term use of mTOR inhibitors might be necessary. This analysis explored long-term efficacy and safety of everolimus from the conclusion of the EXIST-1 study (NCT00789828). Methods and Findings EXIST-1 was an international, prospective, double-blind, placebo-controlled phase 3 trial examining everolimus in patients with new or growing TSC-related SEGAs. After a doubleblind core phase, all remaining patients could receive everolimus in a long-term, open-label extension. Everolimus was initiated at a dose (4.5 mg/m2/day) titrated to a target blood trough of 5-15 ng/mL. SEGAs with at least one of the following characteristics were included: (a) had new or growing TSC-related SEGAs, (b) had stable SEGAs for at least 6 months, or (c) were intolerant of or had a contraindication to recent anti-SEGAs treatment. End points included long-term efficacy and safety of everolimus. Results Of 111 patients included in the study, 86 (77.7%) achieved confirmed >50% reduction in the sum volume of target SEGAs from baseline in the absence of worsening nontarget SEGAs, new target SEGAs, or worsening hydrocephalus. Of 111 patients
(median age, 9.5 years) who received >1 dose of everolimus (median duration, 47.1 months), 57.7%(95% confidence interval [CI], 47.9-67.0) achieved SEGA response. Of 41 patients with target renal angiomyolipomas at baseline, 30 (73.2%) achieved renal angiomyolipoma response. In 105 patients with >1 skin lesion at baseline, skin lesion response rate was 58.1%. Incidence of adverse events (AEs) was comparable with that of previous reports, and occurrence of emergent AEs generally decreased over time. The most common AEs (>30% incidence) suspected to be treatment-related were stomatitis (43.2%) and mouth ulceration (32.4%). Conclusions Everolimus use led to sustained reduction in tumor volume, and new responses were observed for SEGA and renal angiomyolipoma from the blinded core phase of the study. These findings support the hypothesis that everolimus can safely reverse multisystem manifestations of TSC in a significant proportion of patients. Copyright © 2016 Franz et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.
Relationship between damage clustering and mortality in systemic lupus erythematosus in early and late stages of the disease: Cluster analyses in a large cohort from the Spanish Society of Rheumatology Lupus Registry.


[Article]

AN: 611124157

Objectives. To identify patterns (clusters) of damage manifestations within a large cohort of SLE patients and evaluate the potential association of these clusters with a higher risk of mortality.

Methods. This is a multicentre, descriptive, cross-sectional study of a cohort of 3656 SLE patients from the Spanish Society of Rheumatology Lupus Registry. Organ damage was ascertained using the Systemic Lupus International Collaborating Clinics Damage Index. Using cluster
analysis, groups of patients with similar patterns of damage manifestations were identified. Then, overall clusters were compared as well as the subgroup of patients within every cluster with disease duration shorter than 5 years. Results. Three damage clusters were identified. Cluster 1 (80.6% of patients) presented a lower amount of individuals with damage (23.2 vs 100% in clusters 2 and 3, P < 0.001). Cluster 2 (11.4% of patients) was characterized by musculoskeletal damage in all patients. Cluster 3 (8.0% of patients) was the only group with cardiovascular damage, and this was present in all patients. The overall mortality rate of patients in clusters 2 and 3 was higher than that in cluster 1 (P < 0.001 for both comparisons) and in patients with disease duration shorter than 5 years as well. Conclusion. In a large cohort of SLE patients, cardiovascular and musculoskeletal damage manifestations were the two dominant forms of damage to sort patients into clinically meaningful clusters. Both in early and late stages of the disease, there was a significant association of these clusters with an increased risk of mortality. Physicians should pay special attention to the early prevention of damage in these two systems.

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531.
Swain J.P., Shukla H.K., Nigam P.
Embase
Indian Journal of Public Health Research and Development. 7 (3) (pp 91-94), 2016. Date of Publication: July-September 2016.
[Article]
AN: 611118947
Background and Aims: Treatment of collagen vascular diseases like systemic sclerosis, dermatomyositis, systemic lupus erythematosus (SLE) has been generally discouraging. Methylprednisolone pulse therapy has been used for various connective tissue disorders since long. The success of dexamethasone-cyclophosphamide pulse (DCP) therapy in pemphigus has prompted many a dermatologist to try it in other autoimmune diseases. We used intravenous dexamethasone cyclophosphamide pulse therapy to treat SLE. Materials and Method: Eleven patients (9 females and 2 males) of SLE between the ages of 20-48 years with classical clinical criteria laid by American Rheumatism Association criteria were treated by Dexamethasone-Cyclophosphamide pulse (DCP) therapy at our center for six to nine pulses. Results: The treatment resulted overall 75% improvement in SLE. In most of the patients, there was complete clinical remission with DCP therapy leading a better quality of life after 4 pulses. The side effects commonly observed with conventional daily dose regimen of corticosteroids were virtually absent, rather bacterial and candidal infections of the skin and oral mucosa were found due to continuous immune suppression in most cases. Conclusions: We conclude that DCP is relatively safe and effective as compared to methylprednisolone pulse and side effects are also less compared to
daily regimen of steroids. Majority of patients had good response after 3-4 pulses to allow them a normal life style. We also observed that patients who reported early and put on pulse early responded better. Copyright © 2016, Indian Journal of Public Health Research and Development. All rights reserved.

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2016

532.
Male psychological adaptation to unsuccessful medically assisted reproduction treatments: A systematic review.
Martins M.V., Basto-Pereira M., Pedro J., Peterson B., Almeida V., Schmidt L., Costa M.E.
Embase
[Article]
AN: 611023403
Background: Similarly to women, men suffer from engaging in fertility treatments, both physically and psychologically. Although there is avast body of evidence on the emotional adjustment of women to infertility, there are no systematic reviews focusing on men's psychological adaptation to infertility and related treatments. Objective and Rationale: The main research questions addressed in this review were 'Does male psychological adaptation to unsuccessful medically assisted reproduction (MAR) treatment vary over time?' and 'Which psychosocial variables act as protective or riskfactors for psychological maladaptation?' Search
Methods: A literature search was conducted from inception to September 2015 on five databases using combinations of MeSH terms and keywords. Eligible studies had to present quantitative prospective designs and samples including men who did not achieve pregnancy or parenthood at follow-up. A narrative synthesis approach was used to conduct the review. Outcomes: Twelve studies from three continents were eligible from 2534 records identified in the search. The results revealed that psychological symptoms of maladjustment significantly increased in men 1 year after the first fertility evaluation. No significant differences were found two or more years after the initial consultation. Evidence was found for anxiety, depression, active-avoidance coping, catastrophizing, difficulties in partner communication and the use of avoidance or religious coping from the wife as risk factors for psychological maladjustment. Protective factors were related to the use of coping strategies that involve seeking information and attribution of a positive meaning to infertility, having the support of others and of one's spouse, and engaging in open communication about the infertility problem. Wider Implications: Our findings recommend an active involvement of men during the treatment process by health care professionals, and the inclusion of coping skills training and couple communication enhancement interventions in counselling. Further prospective large studies with high-quality design and power are warranted.

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Investigating psychosocial attitudes, motivations and experiences of oocyte donors, recipients and egg sharers: A systematic review.
Embase
[Article]
AN: 611023402
Introduction: The donation of oocytes has been made feasible as a result of in vitro fertilization (IVF). This treatment offers an answer for infertile women with ovarian conditions, such as primary ovarian insufficiency. Demand for oocyte donors has been on the rise globally, with infertile couples, as well as gay men, increasingly using it as a means to found their families. With an acute shortage of oocyte donors globally, the psychosocial aspects behind oocyte donation are important for fertility clinics to understand. This paper aims primarily to provide an up-to-date systematic review of the psychosocial aspects of oocyte donation from the point of view of oocyte donors and recipients and egg sharers. Its secondary aims are to explore the motives and experiences of donors as well as attitudes towards donor anonymity and disclosure. An emphasis has been placed on the analysis of donors in the UK. No review has analysed together the aforementioned donor groups along with recipient group. Methods: A systematic search of English peer-reviewed journals of four computerized databases was undertaken, with no time restriction set for publications. Results: There were 62 studies which met the inclusion criteria and were included in the systematic review. Attitudes towards donation were positive from both a donor oocyte and recipient point of view, with medical procedures being well tolerated and excellent post-donation satisfaction among all donor groups. There were distinct differences between the different donor groups and recipients in motivation for oocyte donation and decisions for disclosure. Attitudes towards anonymity issues were reassuring with a significant proportion of donors of all types willing to donate as identifiable donors. However, there were methodological limitations identified in the studies reviewed. Conclusion: This review successfully explored the important psychosocial aspects of oocyte donation. In general terms the attitudes and feeling of patients involved from all sides of the donation process were extremely positive. A number of key and consistent issues emerged which demonstrated differences and similarities between the different donor groups, as well as a greater understanding of the recipient. With regard to psychosocial well-being, the results were reassuring throughout all donor groups, especially the
egg share donors. Although it seems the 2005 legislative changes in the UK have not caused the anticipated dramatic decrease in gamete donation, oocyte donation still falls far short of demand. The UK has an increasing population of patients from different ethnic backgrounds and same sex relationships seeking oocyte donation, with very few studies including these groups of patients. An increased number of well-designed studies looking into the psychological issues surrounding gamete donation of different patient groups, could allow more directed assessment and counselling of oocyte donors and recipients, with a resulting increase in donor recruitment.

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534.

Salacia sps.: A source of herbal drug for several human diseases and disorders.
Ramakrishna D., Tidke S.A., Shinomol George K., Kiran S., Ravishankar G.A.

Embase
Salacia sps is prominent plant in the domain of medicinal plant with varied benefits for several ailments. Salacia sps contains abundant range of phytochemicals (secondary metabolites) like Salacinol, Katnanol, Mangiferin, Poly phenolic, Tannins and many more Salacia sps possess Antimicrobial, Antifungal, Antimalarial, Anticancer, Antiobesity, Antidiabetic properties etc. Salacia sps has been found to offer high potency of biological owing to the bioavailability and safety. These properties are helpful in the formulation of drug and also potentially offer significant nutritional and dietary benefits. This review focuses on the biodiversity, plant characteristics, phytochemicals, ethno pharmacological properties, in vitro and clinical trials including the product developments as well as manufacture. Further research would lead to validation of the claims which will have far reaching benefits to mankind.

Detecting diseases of neglected seminal vesicles using imaging modalities: A review of current literature.
Dagur G., Warren K., Suh Y., Singh N., Khan S.A.
Embase
Seminal vesicles (SVs) are sex accessory organs and part of male genitourinary system. They play a critical role in male fertility. Diseases of the SVs, usually results in infertility. Diseases of the SVs are extremely rare and are infrequently reported in the literature. We address the current literature of SV pathologies, symptoms, diagnosis, and treatment options. We review the clinical importance of SVs from PubMed. The current imaging modalities and instrumentation that help diagnose SV diseases are reviewed. Common pathologies including, infection, cysts, tumors, and congenital diseases of the SVs are addressed. Many times symptoms of hematospermia, pain, irritative and obstructive lower urinary tract symptoms, and infertility are presented in patients with SV diseases. Copyright © 2016, Research and Clinical Center for Infertility. All Rights Reserved.
Subfertility is defined as the condition of being less than normally fertile though still capable of effecting fertilization. When these subfertile couples seek assistance for conception, a thorough evaluation of male endocrine function is often overlooked. Spermatogenesis is a complex process where even subtle alterations in this process can lead to subfertility or infertility. Male endocrine abnormalities may suggest a specific diagnosis contributing to subfertility; however, in many patients, the underlying etiology is still unknown. Optimizing underlying endocrine abnormalities may improve spermatogenesis and fertility. This manuscript reviews reproductive endocrine abnormalities and hormone-based treatments. Copyright © 2016, Springer Science+Business Media New York.

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537.
Taste and smell function in testicular cancer survivors treated with cisplatin-based chemotherapy in relation to dietary intake, food preference, and body composition.
Embase
Appetite. 105 (pp 392-399), 2016. Date of Publication: 01 Oct 2016.
[Article]
AN: 610899683
Background Chemotherapy can affect taste and smell function. This may contribute to the high prevalence of overweight and metabolic syndrome in testicular cancer survivors (TCS). Aims of the study were to evaluate taste and smell function and possible consequences for dietary intake,
food preference, and body composition in TCS treated with cisplatin-based chemotherapy. Methods Fifty TCS, 1-7 years post-chemotherapy, and 50 age-matched healthy men participated. Taste and smell function were measured using taste strips and ‘Sniffin’ Sticks’, respectively. Dietary intake was assessed using a food frequency questionnaire. Food preference was assessed using food pictures varying in taste (sweet/savoury) and fat or protein content. Dual-Energy X-ray Absorptiometry was performed to measure body composition. Presence of metabolic syndrome and hypogonadism were assessed. Results TCS had a lower total taste function, a higher bitter taste threshold, higher Body Mass Index (BMI), and more (abdominal) fat than controls (p < 0.05). No differences in smell function and dietary intake were found. Testosterone level was an important determinant of body composition in TCS (p = 0.016). Conclusion Although taste function was impaired in TCS, this was not related to a different dietary intake compared to controls. Lower testosterone levels were associated with a higher BMI, fat mass, and abdominal fat distribution in TCS. Copyright © 2016 Elsevier Ltd Status EMBASE Institution (Ijpma, Renken, Mensink, Ter Horst, Reyners) Top Institute Food and Nutrition, Wageningen, Netherlands (Ijpma, Renken, Ter Horst) Neuroimaging Center Groningen, University of Groningen, University Medical Center Groningen, Groningen, Netherlands (Ijpma, Gietema, Reyners) Department of Medical Oncology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands (Slart) Medical Imaging Center, Department of Nuclear Medicine and Molecular Imaging, University of Groningen, University Medical Center Groningen, Groningen, Netherlands (Slart) Faculty of Science and Technology, Biomedical Photonic Imaging, University of Twente, Netherlands (Mensink) Food & Biobased Research, Wageningen UR, Wageningen, Netherlands (Lefrandt) Department of Internal Medicine, University of Groningen, University Medical Center Groningen, Groningen, Netherlands Publisher Academic Press Date Created 20160713 Year of Publication 2016
Comparative efficacy of tadalafil versus tamsulosin as the medical expulsive therapy in lower ureteric stone: A prospective randomized trial.

Puvvada S., Mylarappa P., Aggarwal K., Patil A., Joshi P., Desigowda R.

Embase

Central European Journal of Urology. 69 (2) (pp 178-182), 2016. Date of Publication: 2016.

Introduction In recent years, medical expulsive therapy has been used in the management of distal ureteric stones as a supplement to conservative treatment. Therefore, we conducted a prospective randomized study to evaluate the possible role of tadalafil individually in comparison with proven tamsulosin therapy in ureteric stone expulsion. The aim of this study is to compare the safety and efficacy of a phosphodiesterase-5 inhibitor (tadalafil) and an alpha-1 blocker (tamsulosin) as medical expulsive therapy for distal ureteric calculi.

Material and methods

Between August 2014 and October 2015, 207 patients who presented with distal ureteric stones of size 5-10 mm were randomly divided into two groups: tadalafil (Group A) and tamsulosin (Group B). Therapy was given for a maximum of 4 weeks. Stone expulsion rate, time to stone expulsion, analgesic use, number of hospital visits for pain, follow-up, endoscopic treatment and adverse effects of drugs were noted. Both groups were compared for normally distributed data by percentage, analysis of variance, and T-test. All the classified and categorical data were analyzed for both groups using the chi-square test. Results A statistically significant expulsion rate of 84.0% in Group A compared with 68.0% in Group B (P value = 0.0130), and shorter stone expulsion time in Group A (14.7 +/- 3.8) in comparison to Group B (16.8 +/- 4.5) was observed. Statistically significant differences were noted in renal colic episodes and analgesic requirement in Group A than Group B. No serious adverse effects were noted. Conclusions Tadalafil is safe, efficacious, and well tolerated as medical expulsive therapy for distal ureteric stones. This study showed that tadalafil increases ureteric stone expulsion quite significantly along with better control of pain and significantly lower analgesic requirement. Copyright © 2016, Polish Urological Association. All rights reserved.

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539.
Pilot initiative in India to explore the gonadal function and fertility outcomes of a cohort of childhood cancer survivors.
Arora P.R., Misra R., Mehrotra S., Mittal C., Sharma S., Bagai P., Arora R.S.
Embase
Journal of Human Reproductive Sciences. 9 (2) (pp 90-93), 2016. Date of Publication: April-June 2016.
[Article]
AN: 610874813
CONTEXT: Steady improvement in childhood cancer outcomes has led to a growing number of survivors, many of who develop long-term sequelae. There is limited data about these sequelae (including those related to fertility) on childhood cancer survivors from India. AIMS: We undertook a prospective pilot study on childhood cancer survivors from India to assess their gonadal function and fertility. SUBJECTS AND METHODS: A pediatric oncologist and a reproductive medicine specialist assessed 21 childhood cancer survivors. The risk of infertility was established using disease and treatment variables. Current status of puberty, sexuality, and fertility were assessed using clinical and biochemical parameters. Outcomes were correlated with risk group of infertility. Information was also ascertained on counseling with regards to risk of infertility.
RESULTS: The cohort included 21 survivors (71% males) with a median age of 18 years who were off treatment for a median age of 7 years. Ten (48%) survivors were at low risk for infertility, 9 (43%) at medium risk and 2 (9%) at high risk. Gonadal dysfunction was seen in 3 (14%) survivors: 0/10 (0%) low risk, 1/9 (11%) medium risk, and 2/2 (100%) high risk. None of the survivors, who are at high risk or medium risk of infertility, received any counseling before treatment. CONCLUSIONS: This prospective pilot study of a cohort of childhood cancer survivors from India demonstrates a deficiency in the information provided and counseling of patients/families at the time of diagnosis with regards to the risk of infertility. Fertility outcomes of
childhood cancer survivors were congruent with recognized risk groups for infertility. Future action points have been identified. Copyright © 2016 Journal of Human Reproductive Sciences Published by Wolters Kluwer - Medknow 63.

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540.
Characterizing sexual function in patients with generalized anxiety disorder: A pooled analysis of three vilazodone studies.
Clayton A.H., Durgam S., Tang X., Chen C., Ruth A., Gommoll C.
Embase
Neuropsychiatric Disease and Treatment. 12 (pp 1467-1476), 2016. Date of Publication: 21 Jun 2016.
[Article]
AN: 610866861
Background: Vilazodone has been shown to reduce core symptoms of generalized anxiety disorder (GAD) in three randomized, double-blind, placebo-controlled trials. Since sexual dysfunction (SD) is not well characterized in GAD, a post hoc analysis of these trials was conducted to evaluate the effects of vilazodone on sexual functioning in GAD patients. Materials and methods: Data were pooled from one fixed-dose trial of vilazodone 20 and 40 mg/day (NCT01629966) and two flexible-dose studies of vilazodone 20-40 mg/day (NCT01766401,
NCT01844115) in adults with GAD. Sexual functioning was assessed using the Changes in Sexual Functioning Questionnaire (CSFQ). Outcomes included mean change from baseline to end of treatment (EOT) in CSFQ total score and percentage of patients shifting from SD at baseline (CSFQ total score <47 for males, <41 for females) to normal functioning at EOT. Treatment-emergent adverse events related to sexual functioning were also analyzed. Results: A total of 1,373 patients were included in the analyses. SD at baseline was more common in females (placebo, 46.4%; vilazodone, 49%) than in males (placebo, 35.1%; vilazodone, 40.9%). CSFQ total score improvement was found in both females (placebo, +1.2; vilazodone, +1.6) and males (placebo, +2.1; vilazodone, +1.0), with no statistically significant differences between treatment groups. The percentage of patients who shifted from SD at baseline to normal sexual functioning at EOT was higher in males (placebo, 40.6%; vilazodone, 35.7%) than in females (placebo, 24.9%; vilazodone, 34.9%); no statistical testing was performed. Except for erectile dysfunction and delayed ejaculation in vilazodone-treated males (2.4% and 2.1%, respectively), no treatment-emergent adverse events related to sexual functioning occurred in $2% of patients in either treatment group. Conclusion: Approximately 35%-50% of patients in the vilazodone GAD studies had SD at baseline. Vilazodone and placebo had similar effects on CSFQ outcomes in both females and males, indicating a limited adverse impact on sexual functioning with vilazodone. Copyright © 2016 Clayton et al.
Introduction: Changes in the magnitude of efficacy throughout 26 weeks of atomoxetine treatment, along with impact of dosing, were evaluated in adults with ADHD from two randomized, double-blind, placebo-controlled studies. Aims: Pooled placebo (n = 485) and atomoxetine (n = 518) patients, dosed 25, 40, 60, 80 (target dose), or 100 mg daily, were assessed. Change from baseline in Conners’ Adult ADHD Rating Scale-Investigator Rated Scale: Screening Version (CAARS) total ADHD symptoms score and Adult ADHD Investigator Symptom Rating Scale (AISRS) total score were analyzed using mixed-model repeated measures, with least squares mean change, effect size, and response rate calculated at 1, 2, 4, 8, 12, 16, 22, and 26 weeks. Results: Decreases on CAARS for atomoxetine- versus placebo-treated patients were consistently statistically significantly greater at every time point beginning at one week (P < 0.006, 0.28 effect size). By 4 weeks, comparison was -13.19 compared with -8.84 (P < 0.0001, 0.45 effect size). By 26 weeks, mean change was -15.42 versus -9.71 (0.52 effect size); increase in effect size over time was most pronounced in the 80 mg group (0.82 effect size). AISRS demonstrated similar results. Atomoxetine response rate (CAARS 50% decrease) continued to increase throughout 26 weeks. Conclusions: Atomoxetine treatment in adults with ADHD was associated with small effect sizes after 4 weeks and moderate effect sizes by 6 months of treatment. The data support increased effect size and response rate over time during longer-term treatment at target dose. Copyright © 2016 Eli Lilly and Company. CNS Neuroscience & Therapeutics published by John Wiley & Sons Ltd.

Ejaculatory disorders lie along a conceptual continuum with premature ejaculation anchoring one end, normal ejaculation in the center, and difficulties with delayed or anejaculation at the opposite end. Retrograde ejaculation, painful ejaculation, and postorgasmic illness syndrome can occur at any point on the continuum. This manuscript defines the ejaculatory dysfunctions, reviews the anatomy and physiology of orgasm and ejaculation, and summarizes the pharmacological, psychological, and combined treatment approaches to ejaculatory dysfunctions.

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Introduction: Phosphodiesterase type 5 (PDE-5) hydrolyzes cyclic guanylate monophosphate (cGMP) specifically to 5' GMP, promoting successful corporeal vascular relaxation and penile erection during sexual stimulation. Oral PDE-5 inhibitors such as sildenafil, vardenafil, tadalafil, and avanafil have provided noninvasive, effective, well-tolerated treatment for erectile dysfunction (ED) patients and, at the same time, stimulated both academic and clinical interests. Lately, some oral PDE-5 inhibitors were released as low-dose preparations with the concept of potential daily administration and long-term use. Aim: To highlight the possible potential implications of low-dose long-term use of PDE-5 inhibitors. Method: A systematic review was carried out until December 2015 based on a search of all concerned articles in MEDLINE, medical subjects heading (MeSH) databases, Scopus, The Cochrane Library, EMBASE, and CINAHL databases without language restriction. Key words used to assess the outcome and estimates for concerned associations were: PDE-5 inhibitors; erectile dysfunction; low-dose; long-term; sildenafil; tadalafil; vardenafil; avanafil. Main Outcome Measures: Demonstrating different implications for low-dose long-term use of PDE-5 inhibitors. Results: Low-dose and/or long-term use of PDE-5 inhibitors was shown to put forth beneficial sound effects in different medical implications with potentials that could be extended for different utilities. These implications included sexual, urogenital, cardiovascular, pulmonary, cutaneous, gastrointestinal, and reproductive, as well as neurological disorders. However, it is evident that most potential appliances were carried out experimentally on preclinical studies with off-label indications. Conclusion: Making use of and exploring low-dose and/or long-term use of several PDE-5 inhibitors for their possible implications seem to be valuable in different medical disorders. Increased knowledge of the drug characteristics, comparative treatment regimens, optimal prescribing patterns, and well-designed clinical trials are
Introduction: Tramadol exhibits an effect profile similar to that of opioid agonists, and tramadol abuse seems to be a problem for a number of countries. The relationship between tramadol and sexual function appears to be controversial. Men with premature ejaculation (PE) may benefit from taking tramadol off label; however, these patients live "on a knife's edge" and are exquisitely sensitive to develop other sexual dysfunctions. Aim: To review the literature regarding the problem of tramadol abuse and its relationship with sexual function. Methods: We searched electronic databases from 1977 to September 2015, including PubMed MEDLINE, EMBASE, EBSCO Academic Search Complete, Cochrane Systematic Reviews Database, and GoogleScholar using the following key words: tramadol, sexual functions, and sexual dysfunction. Main Outcome Measure: To define the supposed benefits and the potential risks of tramadol on different sexual functions including ejaculation, orgasm, erection, desire, and testosterone levels. Results: Although tramadol is thought to have low abuse and dependence potentials worldwide,
its abuse has become a serious problem in many countries, particularly in the Middle East, Africa, and West Asia. The benefit of tramadol in PE was reported in 11 clinical trials, evaluated by 6 systematic reviews, 3 of which pooled data in a meta-analysis. The evidence base on erectile dysfunction, decreased libido, hypogonadism, anorgasmia, and risky sexual behaviors in patients abusing tramadol is inadequate. Conclusions: Tramadol may offer a useful intervention for treating PE. As all primary studies had suffered from selection, allocation, performance, or assessment bias, additional rigorous well-designed controlled trials are warranted to further investigate the potential long-term risks of tramadol and to determine the safe and the effective minimum daily dose. Clinical research on drug abuse and sexual dysfunction is an emerging field. To date, small numbers of studies have been performed and further studies are warranted. Copyright © 2016 International Society for Sexual Medicine.

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545.
Challenges in Testosterone Measurement, Data Interpretation, and Methodological Appraisal of Intervventional Trials.
Trost L.W., Mulhall J.P.
Embase
Introduction: Male hypogonadism is a common condition, with an increasing body of literature on diagnosis, implications, and management. Given the significant variability in testosterone (T) from a physiologic and assay perspective, a thorough understanding of factors affecting T values and study methodology is essential to interpret reported study outcomes appropriately. However, despite the large number of publications on T, there are no reference materials consolidating all relevant and potentially confounding factors necessary to interpret T studies appropriately. Aims: To create a resource document that reviews sources of T variability, free vs total T, assay techniques and questionnaires, and study methodology relevant to interpreting outcomes.

Methods: A PubMed search was performed of all the T literature published on T variability, assay techniques, and T-specific questionnaires. Results were summarized in the context of their impact on interpreting T literature outcomes and methodology. Main Outcome Measures: Effect of various factors on T variability and their relevance to study methodology and outcomes. Results: Several factors affect measured T levels, including aging, circadian rhythms, geography, genetics, lifestyle choices, comorbid conditions, and intraindividual daily variability. The utility of free T over total T is debatable and must be compared using appropriate threshold levels. Among various assay techniques, mass spectrometry and equilibrium dialysis are gold standards. Calculated empirical estimates of free T also are commonly used and accepted. Hypogonadism-specific questionnaires have limited utility in screening for hypogonadism, and their role as objective end points for quantifying symptoms remains unclear. Numerous aspects of study methodology can directly or indirectly affect reported outcomes, including design (randomized, prospective, retrospective), duration, populations studied (age, comorbid conditions), low T threshold, therapeutic agent used, objective measurements and end points selected, and statistical interpretation. Conclusion: Critical appraisal of the T literature requires an understanding of numerous factors resulting in T variability, study design and methodology, and limitations of assay techniques and objective measurement scales. Copyright © 2016.
Sex and gender differences in risk, pathophysiology and complications of type 2 diabetes mellitus.

Kautzky-Willer A., Harreiter J., Pacini G.

Embase
Endocrine Reviews. 37 (3) (pp 278-316), 2016. Date of Publication: 01 Jun 2016.

[Review]
AN: 610800369

The steep rise of type 2 diabetes mellitus (T2DM) and associated complications along with mounting evidence of clinically important sex and gender differences. T2DM is more frequently diagnosed at lower age and body mass index in men; however, the most prominent risk factor, which is obesity, is more common in women. Generally, large sex-ratio differences across countries are observed. Diversities in biology, culture, lifestyle, environment, and socioeconomic status impact differences between males and females in predisposition, development, and clinical presentation. Genetic effects and epigenetic mechanisms, nutritional factors and sedentary lifestyle affect risk and complications differently in both sexes. Furthermore, sex hormones have a great impact on energy metabolism, body composition, vascular function, and inflammatory responses. Thus, endocrine imbalances relate to unfavorable cardiometabolic traits, observable in women with androgen excess or men with hypogonadism. Both biological and psychosocial factors are responsible for sex and gender differences in diabetes risk and outcome. Overall, psychosocial stress appears to have greater impact on women rather than on men. In addition, women have greater increases of cardiovascular risk, myocardial infarction, and stroke mortality than men, compared with nondiabetic subjects. However, when dialysis therapy is initiated, mortality is comparable in both males and females. Diabetes appears to attenuate the protective effect of the female sex in the development of cardiac diseases and nephropathy. Endocrine and behavioral factors are involved in gender inequalities and affect the outcome. More research regarding sex-dimorphic pathophysiological mechanisms of T2DM and its complications could contribute to more personalized diabetes care in the future and would thus promote more awareness in terms of sex- and gender-specific risk factors. Copyright © 2016 by the Endocrine Society.

Status
Sequential versus Monophasic Media Impact Trial (SuMMIT): A paired randomized controlled trial comparing a sequential media system to a monophasic medium.


Embase
Fertility and Sterility. 105 (5) (pp 1215-1221), 2016. Date of Publication: 01 May 2016.

Objective To determine whether sequential or monophasic media is the more optimal formulation for blastocyst development and sustained implantation rates (SIR) in IVF. Design Paired randomized controlled trials. Setting Academic. Patient(s) Infertile couples (N = 192) with female partner <42 years old and normal ovarian reserve. Intervention(s) Fertilized zygotes from each patient were randomly divided into two groups: [1] cultured in sequential media and [2] cultured in monophasic medium. Sequential media consisted of Quinn's Advantage Cleavage Medium (SAGE) followed by Blast Assist (Origio). The monophasic medium used was Continuous Single Culture (Irvine Scientific). Paired ETs were accomplished by transferring the best euploid blastocyst from each media group. DNA fingerprinting was used to link outcomes. Main Outcome Measure(s) The primary outcome measure was the proportion of blastocysts suitable for clinical use. Secondary outcome measures included timing of blastulation, aneuploidy rates, and SIR. Sustained implantation rate is defined as the number fetal heart beats at 8-9 weeks of gestation,
divided by the number of embryos transferred. Result(s) A total of 192 patients had their 2PN embryos (N = 2,257) randomized to each culture system. Sequential media had higher blastulation rate than monophasic medium (55.2% vs. 46.9%). No differences were found in the day of blastulation or aneuploidy rate. Of the 168 patients who had euploid blastocysts suitable for transfer, 126 completed a paired ET. Among the double ETs, there was no difference in implantation between groups. Conclusion(s) This is the first randomized controlled trial to examine paired euploid transfers of sibling zygotes cultured in sequential versus monophasic media. This study demonstrates that the usable blastocyst rate is greatest after culture in the sequential media tested in comparison with the monophasic formulation selected for study. However, no difference exists in timing of blastulation, aneuploidy, or SIR. Whether these observations are generalizable to other media systems remains to be determined. Copyright © 2016 American Society for Reproductive Medicine, Published by Elsevier Inc.

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548.
Antioxidants in the treatment of male infertility.
Sotoudeh M., Arbabisarjou A.

Embase
Der Pharmacia Lettre. 8 (8) (pp 167-172), 2016. Date of Publication: 2016.
By affecting the process of spermatogenesis, several genetic, environmental, physiological and nutritional factors can reduce sperm quality and quantity and cause male infertility. The present study aimed to summarize studies conducted on the epidemiological and pathophysiological causes of male infertility, the effects of oxidative stress on poor sperm function and the role of antioxidants in the treatment of male infertility. In the present meta-analysis, the following key words were searched on PubMed, Google scholar, Scopus and Web of Science (1993-2013): male reproductive, male infertility, treatment for male infertility, antioxidant, role of antioxidant therapy, oxidative stress, antioxidant treatment in male fertility, oxidative stress and male infertility and effects of oral antioxidants on sperm quality. Oxidative stress is created by Reactive Oxygen Species (ROS) or free radicals. Although small amounts of ROS are required for sperm functioning, high levels of ROS can affect semen quality which is responsible for %25 of male infertility cases. However, there are antioxidants that have control over the production of ROS and the process of lipid peroxidation by collecting ROS and balancing useful oxidants creating oxidative stress. Thus, using these antioxidants has been recommended for the treatment of male infertility. the administration of L-Carnitine, Selenium, Vitamin E, Vitamin C, Glutathione and coenzyme Q10, as antioxidants, has been proven effective for improving sperm parameters.

Randomized trial of a lifestyle program in obese infertile women.
BACKGROUND: Small lifestyle-intervention studies suggest that modest weight loss increases the chance of conception and may improve perinatal outcomes, but large randomized, controlled trials are lacking. METHODS: We randomly assigned infertile women with a body-mass index (the weight in kilograms divided by the square of the height in meters) of 29 or higher to a 6-month lifestyle intervention preceding treatment for infertility or to prompt treatment for infertility. The primary outcome was the vaginal birth of a healthy singleton at term within 24 months after randomization. RESULTS: We assigned women who did not conceive naturally to one of two treatment strategies: 290 women were assigned to a 6-month lifestyle-intervention program preceding 18 months of infertility treatment (intervention group) and 287 were assigned to prompt infertility treatment for 24 months (control group). A total of 3 women withdrew consent, so 289 women in the intervention group and 285 women in the control group were included in the analysis. The discontinuation rate in the intervention group was 21.8%. In intention-to-treat analyses, the mean weight loss was 4.4 kg in the intervention group and 1.1 kg in the control group (P=0.001). The primary outcome occurred in 27.1% of the women in the intervention group and 35.2% of those in the control group (rate ratio in the intervention group, 0.77; 95% confidence interval, 0.60 to 0.99). CONCLUSIONS: In obese infertile women, a lifestyle intervention preceding infertility treatment, as compared with prompt infertility treatment, did not result in higher rates of a vaginal birth of a healthy singleton at term within 24 months after randomization.
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Niedzielski J.K., Oszukowska E., Slowikowska-Hilczer J.

Embase
Archives of Medical Science. 12 (3) (pp 667-677), 2016. Date of Publication: 2016.

[Review]
AN: 610734693

The best mode of undescended testis (UDT) treatment remains controversial. However, knowledge gained from randomized controlled studies and meta-analyses allowed different groups of researchers to set out guidelines on management of patients with UDT. The authors reviewed recent literature and came to the following conclusions: (1) Hormonal treatment is not recommended, considering both the immediate results (only 15–20% of retained testes descend) and the possible long-term adverse effects on spermatogenesis. (2) Surgery is the treatment of choice; orchiopexy is successful in about 95% of UDT, with a low rate of complications (about
Infertility in the light of new scientific reports - Focus on male factor.
Szkodziak P., Wozniak S., Czuczwar P., Wozniakowska E., Milart P., Mroczkowski A., Paszkowski T.
Embase
[Review]
AN: 610667826
Epidemiological data indicate that infertility is a problem of global proportions, affecting one-fifth of couples trying to conceive worldwide (60-80 mln). According to the trends observed, the problem is predicted to increase by another two million cases annually. In Poland, infertility-related issues are found in about 19% of couples, including 4% with infertility and 15% with limited fertility. Inability to conceive occurs equally in men and women (50%), irrespective of the direct cause. Although it is generally thought that reproductive issues concern women, infertility affects men and women equally. This study is an attempted to systematize knowledge about the
role of the male factor in infertility, particularly current knowledge concerning the environmental factors of infertility. For this purpose, the Medline and CINAHL databases and the Cochrane Library was searched for articles published in English during the last 10 years, using the following keywords: infertility, male factor, semen examination and environmental factor of infertility.

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Publisher
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552.
Zeta sperm selection improves pregnancy rate and alters sex ratio in male factor infertility patients: A double-blind, randomized clinical trial.

Esfahani M.H.N., Deemeh M.R., Tavalaee M., Sekhavati M.H., Gourabi H.

Embase
International Journal of Fertility and Sterility. 10 (2) (pp 253-260), 2016. Date of Publication: July-September 2016.

[Article]
AN: 610663444

Background: Selection of sperm for intra-cytoplasmic sperm injection (ICSI) is usually considered as the ultimate technique to alleviate male-factor infertility. In routine ICSI, selection is based on morphology and viability which does not necessarily preclude the chance injection of DNA-damaged or apoptotic sperm into the oocyte. Sperm with high negative surface electrical charge, named "Zeta potential", are mature and more likely to have intact chromatin. In addition, X-bearing spermatozoa carry more negative charge. Therefore, we aimed to compare the clinical
outcomes of Zeta procedure with routine sperm selection in infertile men candidate for ICSI.

Materials and Methods: From a total of 203 ICSI cycles studied, 101 cycles were allocated to density gradient centrifugation (DGC)/Zeta group and the remaining 102 were included in the DGC group in this prospective study. Clinical outcomes were compared between the two groups. The ratios of X- and Y bearing sperm were assessed by fluorescence in situ hybridization (FISH) and quantitative polymerase chain reaction (qPCR) methods in 17 independent semen samples. Results: In the present double-blind randomized clinical trial, a significant increase in top quality embryos and pregnancy rate were observed in DGC/Zeta group compared to DGC group. Moreover, sex ratio (XY/XX) at birth significantly was lower in the DGC/Zeta group compared to DGC group despite similar ratio of X/Y bearings spermatozoa following Zeta selection. Conclusion: Zeta method not only improves the percentage of top embryo quality and pregnancy outcome but also alters the sex ratio compared to the conventional DGC method, despite no significant change in the ratio of X- and Y- bearing sperm population (Registration number: IRCT201108047223N1). Copyright © 2016, Royan Institute (ACECR). All Rights Reserved.
Effects of vitrification on outcomes of in vivo-mature, in vitro-mature and immature human oocytes.


Embase

Cellular Physiology and Biochemistry. 38 (5) (pp 2053-2062), 2016. Date of Publication: 2016.

[Article]

AN: 610654048

Background/Aims: To observe the effects of vitrification on spindle, zona pellucida, embryonic aneuploidy and DNA injury in in vivo-matured, in vitro-mature and immature human oocytes.

Methods: Between January 2009 and February 2015, 223 immature oocytes from 450 infertile patients, and 31 in vivo-mature oocytes from 3 infertile couples were collected. Of the 223 immature oocytes, 113 were used for in vitro culture before vitrification. Some oocytes were randomly divided into in vivo-mature group (group A, n = 15), in vitro-mature group (group B, n = 88) and immature group (group C, n = 85), and then the oocytes with spindle in these three groups after freezing-thawing were selected to use for Polscope imaging, embryonic aneuploidy screening and embryo development evaluation. Other oocytes were randomly divided into group A (n = 16), group B (n = 25) and group C (n = 25) for detecting DNA injury. Results: After thawing, spindle occurrence rate, spindle Retardance value, and cleavage rate were significantly higher in groups A and B than in group C (all P < 0.05), but there were no statistical differences in fertility rate, high-quality embryo rate, blastulation rate and aneuploidy rate amongst the three groups (all P > 0.05). Zona pellucida density (ZPD) was significantly lower in group A than in groups B and C both before and after vitrification (all P < 0.05). ZPD was significantly higher after thawing than before vitrification (all P < 0.05), but zona pellucida thickness (ZPT) was not significantly changed in all the three groups (all P > 0.05). Rate of comet cells was significantly lower in group A than in groups B and C (all P < 0.01). Comet tail was significantly longer in group C than in groups B and A (all P < 0.05). Conclusion: In vivo- and in vitro-mature human oocytes are more suitable to vitrification than immature human oocytes. Spindle Retardance value has more predictive value for embryonic development potential than ZPD and ZPT.

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Predictive value of GGN and CAG repeat polymorphisms of androgen receptors in testicular cancer: A meta-analysis.


Embase
Oncotarget. 7 (12) (pp 13754-13764), 2016. Date of Publication: 22 Mar 2016.

The risk of testicular cancer (TC) is markedly increased in subjects with androgen insensitivity, and previous studies have proposed that GGN and CAG repeats in androgen receptors (AR) could be related to the risk of TC. To evaluate the association between the length of GGN and CAG repeats in AR and TC, a meta-analysis involving 3255 TC cases and 2804 controls was performed. The results suggested that long GGN repeats are associated with an increased risk of TC compared with those < 23 [odds ratio (OR) = 1.22, 95% confidence interval (CI) = 1.05-1.41]; similarly, a subgroup analysis revealed that this association occurred in studies with case sizes > 200, and in the mid-latitude, and seminoma subgroups. The subgroup analysis based on populations, high-latitude, and seminomas/non-seminomas suggested that AR CAG repeat polymorphisms with > 25 and < 21 + > 25 repeats might confer a protective effect to the patients with TC (in the high-latitude subgroup analysis, for > 25 vs. 21-25: OR = 0.54, 95% CI = 0.41-0.70). In contrast, an increased risk of TC was observed for AR CAG repeat polymorphisms with > 25 and < 21 + > 25 repeats in the mid-latitude subgroup (for > 25 vs. 21-25: OR = 1.65, 95% CI = 1.09-2.50). In addition, no associations between the remaining subgroups and male infertility were observed. In short, this meta-analysis suggested that AR GGN and CAG repeat polymorphisms may be involved in the etiology of TC.

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Background: To evaluate the efficacy and safety of silodosin as a medical expulsive therapy for ureteral stones by means of a systematic review and meta-analysis. Methods: We searched MEDLINE, EMBASE and the Cochrane Controlled Trials Register to identify randomized controlled trials (RCTs) of silodosin in the treatment of ureteral stones. The reference lists of retrieved studies were also investigated. Results: Six RCTs, including 916 participants and comparing silodosin with controls, were used in the meta-analysis. Silodosin was superior to controls in terms of stone expulsion rate, the primary efficacy end point in all six RCTs (odds ratio [OR] for expulsion 2.16, 95 % confidence interval [CI] 1.62 to 2.86, p <0.00001). Silodosin was also more effective for secondary efficacy end points; the stone expulsion time (standardized mean difference [SMD] -3.66, 95 % CI -6.61 to -0.71; p =0.01) and analgesic requirements (SMD -0.89, 95 % CI -1.19 to -0.60; p < 0.00001) were significantly reduced compared with those of controls. Other than the incidence of abnormal ejaculation, which was higher in the silodosin groups (OR 2.84, 95 % CI 1.56 to 5.16, p =0.0006), few adverse effects were observed.
Conclusion: This meta-analysis indicates silodosin is an effective and safe treatment option for ureteral stones with a low occurrence of side effects. Copyright © 2016 Yang et al.


Dimitropoulos K., Gravas S.

Embase Research and Reports in Urology. 8 (pp 51-59), 2016. Date of Publication: 26 Apr 2016. [Review]

AN: 610066147

Male lower urinary tract symptoms (LUTS) are prevalent in the general population, especially in those of advanced age, and are characterized by notable diversity in etiology and presentation, and have been proven to cause various degrees of impairment on quality of life. The prostate has traditionally been regarded as the core cause of male LUTS. As a result, medical treatment aims to provide symptomatic relief and effective management of progression of male LUTS due to benign prostatic enlargement. In this context, alpha1-blockers, phosphodiesterase-5 inhibitors, and 5alpha-reductase inhibitors have long been used as monotherapies or in combination treatment to control voiding LUTS. There is accumulating evidence, however, that highlights the role of the bladder in the pathogenesis of male LUTS. Current research interests have shifted to bladder disorders, and medical management is aimed at the bladder. Muscarinic receptor antagonists and the newly approved beta3-adrenergic agonist mirabegron aim to alleviate the most bothersome storage LUTS and thus improve quality of life. As voiding and storage LUTS
frequently coexist, combination therapeutic strategies with alpha1-blockers and antimuscarinics or beta3-agonists have been introduced to manage symptoms effectively. Anti-inflammatory agents, vitamin D3-receptor analogs, and cannabinoids represent treatment modalities currently under investigation for use in LUTS patients. Furthermore, luteinizing hormone-releasing hormone antagonists, transient receptor-potential channel blockers, purinergic neurotransmission antagonists, Rho-kinase inhibitors, and inhibitors of endothelin-converting enzymes could have therapeutic potential in LUTS management, but still remain in the experimental setting. This article reviews new strategies for the medical treatment of male LUTS, which are dictated by the potential role of the bladder and the risk of benign prostatic hyperplasia progression. Moreover, combination treatments and therapies currently under investigation are also presented.

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557.
Bone morphogenetic protein use in spine surgery-complications and outcomes: a systematic review.
Faundez A., Tournier C., Garcia M., Aunoble S., Le Huec J.-C.
Embase
[Review]
AN: 608939245
Purpose: Because of significant complications related to the use of autologous bone grafts in spinal fusion surgery, bone substitutes and growth factors such as bone morphogenetic protein
(BMP) have been developed. One of them, recombinant human (rh) BMP-2, has been approved by the Food and Drug Administration (FDA) for use under precise conditions. However, rhBMP-2-related side effects have been reported, used in FDA-approved procedures, but also in off-label use. A systematic review of clinical data was conducted to analyse the rhBMP-2-related adverse events (AEs), in order to assess their prevalence and the associated surgery practices. Methods: Medline search with keywords "bone morphogenetic protein 2", "lumbar spine", "anterolateral interbody fusion" (ALIF) and the filter "clinical trial". FDA published reports were also included. Study assessment was made by authors (experienced spine surgeons), based on quality of study designs and level of evidence. Results: Extensive review of randomised controlled trials (RCTs) and controlled series published up to the present point, reveal no evidence of a significant increase of AEs related to rhBMP-2 use during ALIF surgeries, provided that it is used following FDA guidelines. Two additional RCTs performed with rhBMP-2 in combination with allogenic bone dowels reported increased bone remodelling in BMP-treated patients. This AE was transient and had no consequence on the clinical outcome of the patients. No other BMP-related AEs were reported in these studies. Conclusions: This literature review confirms that the use of rhBMP-2 following FDA-approved recommendations (i.e. one-level ALIF surgery with an LT-cage) is safe. The rate of complications is low and the AEs had been identified by the FDA during the pre-marketing clinical trials. The clinical efficiency of rhBMP-2 is equal or superior to that of allogenic or autologous bone graft in respect to fusion rate, low back pain disability, patient satisfaction and rate of re-operations. For all other off-label use, the safety and effectiveness of rhBMP-2 have not been established, and further RCTs with high level of evidence are required. Copyright © 2016, SICOT aisbl.

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Evaluation of the relation between preapoptotic sperm rate in ejaculate and intrauterine insemination success rate in patients with unexplained infertility.

Boyraz G., Selcuk I., Sokmensuer L.K., Bozdag G., Menkveld R., Gunalp S.

Embase

The parameters measured in the standard semen analysis may be insufficient for exact differentiation between fertile and infertile men. Therefore, we assume that the high rate of apoptotic sperm in ejaculate may play a role on the aetiology of unexplained infertility. Couples with unexplained infertility treated by ovulation induction and intrauterine insemination were consecutively enrolled (n = 94). To determine the proapoptotic sperm rate, the ejaculate from patients was stained with annexin V. Thirteen of the 94 couples (13.8%) conceived after intrauterine insemination. The annexin V-positive sperm rate was found to be 20.0% in the whole group. In women failing to conceive, the annexin V-positive sperm rate was 20.8% compared to 15.7% in patients who achieved pregnancy. Although there is a trend towards higher preapoptotic sperm rate in couples failing to get pregnant with insemination, the difference did not reach statistical significance.

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Effect of Testosterone Solution 2% on Testosterone Concentration, Sex Drive and Energy in Hypogonadal Men: Results of a Placebo Controlled Study.


Embase

Purpose We determined the effect of testosterone solution 2% on total testosterone level and the 2 symptoms of hypogonadism, sex drive and energy level. Materials and Methods This was a randomized, multicenter, double-blind, placebo controlled, 16-week study to compare the effect of testosterone and placebo on the proportion of men with a testosterone level within the normal range (300 to 1,050 ng/dl) upon treatment completion. We also assessed the impact of testosterone on sex drive and energy level measured using SAID (Sexual Arousal, Interest and Drive scale) and HED (Hypogonadism Energy Diary), respectively. A total of 715 males 18 years old or older with total testosterone less than 300 ng/dl and at least 1 symptom of testosterone deficiency (decreased energy and/or decreased sexual drive) were randomized to 60 mg topical testosterone solution 2% or placebo once daily. Results Of study completers 73% in the testosterone vs 15% in the placebo group had a testosterone level within the normal range at study end point (p <0.001). Participants assigned to testosterone showed greater baseline to end point improvement in SAID scores (low sex drive subset p <0.001 vs placebo) and HED scores (low energy subset p = 0.02 vs placebo, not significant at prespecified p <0.01). No major adverse cardiovascular or venous thrombotic events were reported in the testosterone group. The incidence of increased hematocrit was higher with testosterone vs placebo (p = 0.04). Conclusions Once daily testosterone solution 2% for 12 weeks was efficacious in restoring normal testosterone levels and improving sexual drive in hypogonadal men. Improvement was also seen in energy levels on HED though not at the prespecified p <0.01. No new safety signals were identified. Copyright © 2016 American Urological Association Education and Research, Inc.
560.

Testosterone therapy in men with testosterone deficiency: Are we beyond the point of no return?.

Traish A.

Embase

Investigative and Clinical Urology. 57 (6) (pp 384-400), 2016. Date of Publication: November 2016.

[Article]

AN: 613238821

Although testosterone therapy in men with testosterone deficiency was introduced in the early 1940s, utilization of this effective treatment approach in hypogonadal men is met with considerable skepticism and resistance. Indeed, for decades, the fear that testosterone may cause prostate cancer has hampered clinical progress in this field. Nevertheless, even after
considerable knowledge was acquired that this fear is unsubstantiated, many in the medical community remain hesitant to utilize this therapeutic approach to treat men with hypogonadism. As the fears concerning prostate cancer have subsided, a new controversy regarding use of testosterone therapy and increase in cardiovascular disease was introduced. Although the new controversy was based on one ill-fated clinical trial, one meta-analysis with studies that utilized unapproved formulation in men with liver cirrhosis, and two retrospective studies with suspect or nonvalidated statistical methodologies and database contaminations, the flames of such controversy were fanned by the lay press and academics alike. In this review we discuss the adverse effect of testosterone deficiency and highlight the numerous proven benefits of testosterone therapy on men's health and debunk the myth that testosterone therapy increases cardiovascular risk. Ultimately, we believe that there is considerable scientific and clinical evidence to suggest that testosterone therapy is safe and effective with restoration of physiological levels in men with testosterone deficiency, irrespective of its etiology.

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561.
The human epididymis: Its function in sperm maturation.
Sullivan R., Mieusset R.
Embase
[Article]
BACKGROUND: Spermatozoa acquire their fertilizing ability and forward motility properties during epididymal transit. Our knowledge of gamete physiology is based on studies conducted in laboratory and domestic species; our knowledge of these processes in humans is limited. Medical indications for assisted reproductive technologies (ART) have progressed to include male infertility. Surgical procedures allow collection of spermatozoa from all along the human excurrent ducts, and the former have been used with some success in reproductive medicine. This has raised questions over the role of the epididymis in human sperm physiology.

OBJECTIVE AND RATIONALE: To reanalyze what we now know about epididymal physiology in humans and to assess the relevance of laboratory animal models for understanding human physiology and the pathophysiology of the epididymis.

SEARCH METHODS: A systematic bibliographic search of PubMed for articles published in English before May 2015 was carried out using the search terms 'epididymis' and 'sperm maturation'. Literature on the consequences of vasectomy on the epididymis was also searched.

OUTCOMES: Whereas the proximal epididymis is almost exclusively occupied by efferent ducts, the sperm reservoir capacity is poorly developed in humans. At the molecular level, the human transcriptome and proteome show some segment specificity; conflicting results persist with regard to secretome variation along the tubule. The number of genes regulated along the excurrent ducts in men is lower when compared to rodent species, but remains significant. It is challenging to reconcile biochemical and physiological studies with clinical data obtained from men undergoing reanastomosis of the vas deferens at different points along the excurrent duct. We propose that vasectomy/vasovasostomy is a model to understand the consequences of obstruction on epididymis function in humans.

WIDER IMPLICATIONS: Despite the scarcity of biological material available, the interspecies variability of the male reproductive tract urges us to use modern molecular and cellular biology tools to better understand human epididymis physiology in order to apply ART in a more responsible manner.
BACKGROUND: Subfertility affects approximately 15% of all couples, and a severe male factor is identified in 17% of these couples. While the etiology of a severe male factor remains largely unknown, prior gonadotoxic treatment and genomic aberrations have been associated with this type of subfertility. Couples with a severe male factor can resort to ICSI, with either ejaculated spermatozoa (in case of oligozoospermia) or surgically retrieved testicular spermatozoa (in case of azoospermia) to generate their own biological children. Currently there is no direct treatment for azoospermia or oligozoospermia. Spermatogonial stem cell (SSC) autotransplantation (SSCT) is a promising novel clinical application currently under development to restore fertility in sterile childhood cancer survivors. Meanwhile, recent advances in genomic editing, especially the clustered regulatory interspaced short palindromic repeats-associated protein 9 (CRISPR-Cas9) system, are likely to enable genomic rectification of human SSCs in the near future.

OBJECTIVE AND RATIONALE: The objective of this review is to provide insights into the prospects of the potential clinical application of SSCT with or without genomic editing to cure spermatogenic failure and to prevent transmission of genetic diseases.

SEARCH METHODS: We performed a narrative review using the literature available on PubMed not restricted to any publishing year on topics of subfertility, fertility treatments, (molecular regulation of) spermatogenesis and SSCT, inherited (genetic) disorders, prenatal screening methods, genomic editing and germline editing. For germline editing, we focussed on the novel CRISPR-Cas9 system. We included papers
written in English only. OUTCOMES: Current techniques allow propagation of human SSCs in vitro, which is indispensable to successful transplantation. This technique is currently being developed in a preclinical setting for childhood cancer survivors who have stored a testis biopsy prior to cancer treatment. Similarly, SSCT could be used to restore fertility in sterile adult cancer survivors. In vitro propagation of SSCs might also be employed to enhance spermatogenesis in oligozoospermic men and in azoospermic men who still have functional SSCs albeit in insufficient numbers. The combination of SSCT with genomic editing techniques could potentially rectify defects in spermatogenesis caused by genomic mutations or, more broadly, prevent transmission of genomic diseases to the offspring. In spite of the promising prospects, SSCT and germline genomic editing are not yet clinically applicable and both techniques require optimization at various levels. WIDER IMPLICATIONS: SSCT with or without genomic editing could potentially be used to restore fertility in cancer survivors to treat couples with a severe male factor and to prevent the paternal transmission of diseases. This will potentially allow these couples to have their own biological children. Technical development is progressing rapidly, and ethical reflection and societal debate on the use of SSCT with or without genomic editing is pressing. Copyright © The Author 2016. Published by Oxford University Press on behalf of the European Society of Human Reproduction and Embryology.

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563.
Safety and tolerability of long-acting injectable versus oral antipsychotics: A meta-analysis of randomized controlled studies comparing the same antipsychotics.
Objective We aimed to assess whether long-acting injectable antipsychotics (LAIs), which are initiated in a loading strategy or overlapping with oral antipsychotics (OAPs) and which cannot be stopped immediately, are associated with greater safety/tolerability issues than OAPs. Method Systematic review and meta-analysis of randomized controlled trials (RCTs) comparing LAIs and OAPs, including only LAI-OAP pairs of the same OAP (allowing oral risperidone and paliperidone as comparators for either risperidone or paliperidone LAI). Primary outcome was treatment discontinuation due to adverse events. Secondary outcomes included serious adverse events, death, > 1 adverse event and individual adverse event rates. Results Across 16 RCTs (n = 4902, mean age = 36.4 years, males = 65.8%, schizophrenia = 99.1%) reporting on 119 adverse event outcomes, 55 (46.2%) adverse events were reported by > 2 studies allowing a formal meta-analysis. Out of all 119 reported adverse events, LAIs and OAPs did not differ significantly regarding 115 (96.6%). LAIs were similar to OAPs regarding the frequency of treatment discontinuation due to adverse events, serious adverse events, all-cause death and death for reasons excluding accident or suicide. Compared to OAPs, LAIs were associated with significantly more akinesia, low-density lipoprotein cholesterol change and anxiety. Conversely, LAIs were associated with significantly lower prolactin change. Conclusion LAIs and OAPs did not differ on all serious and > 90% of individual adverse events. However, more studies focusing on adverse event frequencies, severity and time course associated with LAI vs OAP formulations of the same antipsychotic are needed. Additionally, adverse events data for LAIs after stopping overlapping oral antipsychotic treatment are needed. Copyright © 2016 Elsevier B.V.
The control of male fertility by spermatid-specific factors: Searching for contraceptive targets from spermatozoon's head to tail.


Cell Death and Disease. 7 (11) (no pagination), 2016. Article Number: e2472. Date of Publication: 10 Nov 2016.

Male infertility due to abnormal spermatozoa has been reported in both animals and humans, but its pathogenic causes, including genetic abnormalities, remain largely unknown. On the other hand, contraceptive options for men are limited, and a specific, reversible and safe method of male contraception has been a long-standing quest in medicine. Some progress has recently been made in exploring the effects of spermatid-specific genetic factors in controlling male fertility. A comprehensive search of PubMed for articles and reviews published in English before July 2016 was carried out using the search terms 'spermiogenesis failure', 'globozoospermia', 'spermatid-specific', 'acrosome', 'infertile', 'manchette', 'sperm connecting piece', 'sperm annulus', 'sperm ADAMs', 'flagellar abnormalities', 'sperm motility loss', 'sperm ion exchanger' and 'contraceptive targets'. Importantly, we have opted to focus on articles regarding spermatid-specific factors. Genetic studies to define the structure and physiology of sperm have shown that spermatozoa appear to be one of the most promising contraceptive targets. Here we summarize how these spermatid-specific factors regulate spermiogenesis and categorize them according to their localization and function from spermatid head to tail (e.g., acrosome, manchette, head-tail conjunction, annulus, principal piece of tail). In addition, we emphatically introduce small-molecule contraceptives, such as BRDT and PPP3CC/PPP3R2, which are currently being developed to target spermatogenic-specific proteins. We suggest that blocking the differentiation
of haploid germ cells, which rarely affects early spermatogenic cell types and the testicular microenvironment, is a better choice than spermatogenic-specific proteins. The studies described here provide valuable information regarding the genetic and molecular defects causing male mouse infertility to improve our understanding of the importance of spermatid-specific factors in controlling fertility. Although a male contraceptive 'pill' is still many years away, research into the production of new small-molecule contraceptives targeting spermatid-specific proteins is the right avenue. Copyright © The Author(s) 2016.

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Publisher
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Date Created
20161207

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2016

565.
Intracytoplasmic sperm injection outcomes with freshly ejaculated sperms and testicular or epididymal sperm extraction in patients with idiopathic cryptozoospermia.
Ketabchi A.A.

Embase


[Article]
Background: Cryptozoospermia (CO) is a situation in which spermatozoa cannot be observed in a fresh semen sample unless an extended centrifugation and microscopic search are performed. CO patients are suggested to use only intracytoplasmic sperm injection (ICSI) as infertility treatment. But still there is debate about the choice of sperm source in cryptozoospermic candidate for ICSI. Objectives: This study was conducted to evaluate fertility outcomes in men with idiopathic cryptozoospermia who were treated using ICSI with freshly ejaculated sperm and testis sperm extraction (TESE) or percutaneous epididymal sperm aspiration (PESA). Methods: In this prospective cohort study carried out in an academic institution, 83 out of 92 couples with cryptozoospermia undergoing their first ICSI cycle were recruited. These patients were randomly allocated to two groups: group one (n = 42) who produced freshly ejaculated sperm and, group two (n = 41) who produced a sample by TESE or PESA. The groups were analyzed and compared in terms of fertilization rate, cleavage rate, embryo quality, implantation rate, and clinical pregnancy rate. Results: There was a significant difference in fertilization rate, embryo quality, implantation rate, and pregnancy rates between the group of surgically extracted sperm and those of naturally ejaculated sperm using conventional ICSI (P < 0.05). Conclusions: Sperm quality extracted by percutaneous PESA and TESE procedures increases fertility outcomes compared to naturally ejaculated sperm in men with idiopathic CO. More specifically, embryo quality, which is most relevant to fertility outcome, improved when surgically extracted sperm was used for ICSI. Copyright © 2016, Nephrology and Urology Research Center.
Sexually Transmitted Disease and Male Infertility: A Systematic Review.
Fode M., Fusco F., Lipshultz L., Weidner W.

Embase
European Urology Focus. 2 (4) (pp 383-393), 2016. Date of Publication: 01 Oct 2016.

[Review]

AN: 613084251

Context Theoretically, sexually transmitted diseases (STDs) have the potential to disrupt male fertility; however, the topic remains controversial. Objective To describe the possible association between STDs and male infertility and to explore possible pathophysiologic mechanisms.

Evidence acquisition We performed a systematic literature review in accordance with the PRISMA guidelines. PubMed, Embase, and the Cochrane Library were searched for articles published before January 1, 2016, using the MeSH terms for a variety of STDs and infertility. The search was restricted to human studies performed in men and published in English. Studies were included if they contained original data on a possible association or a cause-and-effect relationship between STD and male infertility. Studies were considered only if they included an appropriate control group and/or comprehensive laboratory data. Due to heterogeneity in the literature, a qualitative analysis was performed. Evidence synthesis Relevant studies on Chlamydia trachomatis, genital mycoplasmas, Neisseria gonorrhoeae, Trichomonas vaginalis, and viral infections were identified. For all pathogens, the studies were contradictory and generally of limited quality. In studies confirming an association, there was a tendency for authors to perform multiple analyses without appropriate corrections and to subsequently focus solely on outcomes that seemed to suggest a positive association; however, the body of literature that does not confirm an association between STDs and male infertility is also of inadequate quality. The data regarding possible pathophysiologic mechanisms are inconclusive. Conclusions There may be an association between STDs and male infertility of unknown genesis and possibly with different pathogenic mechanisms for different pathogens. Alternatively, some STDs may cause male infertility, whereas others may not; however, there is hardly a strong correlation. High-quality studies of the subject are needed. Patient summary Sexually transmitted diseases may cause male infertility through unknown mechanisms; however, from the available research, we cannot be sure that there is an association, and more studies are needed. Copyright © 2016 European Association of Urology

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Impact of Testosterone Solution 2% on Ejaculatory Dysfunction in Hypogonadal Men.

Maggi M., Heiselman D., Knorr J., Iyengar S., Paduch D.A., Donatucci C.F.

Introduction Hypogonadism is defined as decreased testosterone levels in men. Hypogonadism can be accompanied by erectile, orgasmic, and ejaculatory dysfunction. Aims To evaluate whether treatment with testosterone solution 2% (testosterone) could improve ejaculatory function in a cohort of hypogonadal men. Methods Sexually active, hypogonadal men at least 18 years old (total testosterone < 300 ng/dL) were randomized to receive testosterone or placebo for 12 weeks. Main Outcome Measures Effects of testosterone on primary outcomes were evaluated using the International Index of Erectile Function (IIEF) and the Men's Sexual Health Questionnaire, Ejaculatory Dysfunction, Short Form (MSHQ-EjD-SF) questionnaires. Treatment differences were calculated using analysis of covariance. Results In total, 715 men (mean age = 55 years) were randomized to placebo (n = 357) or testosterone (n = 358). Most sexually active men who reported IIEF scores had some degree of erectile dysfunction (IIEF erectile function score < 26). Although ejaculatory function score (MSHQ-EjD-SF) improved in the testosterone group compared with placebo (P < .001), improvement on the "bother" item did not reach statistical significance. Treatment-related adverse events in the testosterone group affecting at
least 1% of patients were increased hematocrit, upper respiratory tract infection, arthralgia, burning sensation, fatigue, increased prostate-specific antigen, erythema, and cough. Few patients in either treatment group developed at least one adverse event leading to discontinuation (testosterone = 1.98% vs placebo = 3.09%; P = .475). Conclusion Hypogonadal men receiving testosterone solution 2% therapy experience significantly greater improvement in ejaculatory function, compared with placebo, as assessed by the MSHQ-EjD-SF. However, improvement in "bother" was not statistically different between the two groups. Testosterone therapy was generally well tolerated. Copyright © 2016 International Society for Sexual Medicine Status
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568.
Prolactin related symptoms during risperidone maintenance treatment: Results from a prospective, multicenter study of schizophrenia.
Bo Q., Dong F., Li X., Wang Z., Ma X., Wang C.
Embase
BMC Psychiatry. 16 (1) (no pagination), 2016. Article Number: 386. Date of Publication: 09 Nov 2016.
[Article]
AN: 613170298
Background: This study aimed to investigate prolactin related symptoms (PRS) in individuals with schizophrenia during risperidone maintenance treatment for one year, as well as to identify the risk factors for PRS. Methods: In a multicenter, randomized, controlled, longitudinal study,
clinically stabilized schizophrenia patients (N = 374) were randomized to a no-dose-reduction group (N = 129) and 4-week (N = 125) and 26-week (N = 120) reduction groups, in which the original dose was followed by a 50% reduction over 8 weeks and subsequently maintained. PRS were assessed via a scale of prolactin related adverse events, which included 16 items: menstrual cycle, menstrual period, menstrual volume, menstrual irregularities, amenorrhea, dysmenorrhea, postpartum lactation, gynecomastia, breast tenderness, sexual dysfunction, decreased sexual desire, erectile dysfunction, ejaculatory dysfunction, impotence, increased body hair, and acne. The occurrence of PRS was assessed at baseline and monthly for six months, followed by every two months. A mixed model was used. Results: PRS at baseline were reported in 18.4, 15.0, and 14.0% of the 4-week, 26-week, and no-dose-reduction groups, respectively. Female gender, younger age at onset, and the Positive and Negative Syndrome Scale (PANSS) total scores at entry predicted the development of PRS. The mixed model indicated that PRS were more severe in females and at a high dose. In the 237 patients who remained in the study after one year, the incidence of PRS decreased to 9.6, 11.1, and 7.6% in the 4-week, 26-week, and no-dose-reduction groups, respectively. Conclusion: These findings indicate that the PRS severity was alleviated during the one year treatment period because of the dose reduction. Attention should focus on the side effects of hyperprolactinemia during long-term treatment, especially with a high dose, females, younger age at onset, and more severe patients. Trial registration: ClinicalTrials.gov identifier: NCT00848432. Registered February 19, 2009.
Which way is infertility treatment heading? - A review on the latest techniques in assisted reproductive technology.
Govindaiah P., Jyothi J., Gunasheela D.
Embase
Perinatology. 17 (2) (pp 31-43), 2016. Date of Publication: July-September 2016.
[Review]
AN: 613184188
Across the world, among millions of couples who fail to conceive, some seek medical help and undergo treatment, some resign to their fate, while others resort to adoption. The incidence of infertility in India is estimated to be between 10% and 15%. The birth of the world's first baby through the in vitro fertilization (IVF) technique opened up a new horizon in the management of infertility. The purpose of this review article is to provide information on latest techniques and advances in assisted reproductive technology (ART); Preimplantation genetic screening and fertility preservation are the current burning issues in ART. A systematic search of MEDLINE, Cochrane Library, PubMed, and reference list of articles on ART was conducted and is summarized in this article. The techniques used in IVF continue to evolve as we strive to improve success rates while minimizing multiple pregnancies. However, we should all remain cognizant that currently, live birth rates generally do not exceed 50% per stimulated IVF cycle, even in young women with good prognosis, and in older women, success rates are dramatically lower.
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Effect of time interval between human chorionic gonadotropin injection and intrauterine insemination on pregnancy rate.

Soliman B.S.

Embase

Middle East Fertility Society Journal. 21 (4) (pp 222-227), 2016. Date of Publication: 01 Dec 2016.

[Article]

AN: 609666380

Background Controlled ovarian stimulation with intrauterine insemination (COS/IUI) is an established tool in infertility treatment. There has been debate regarding the optimum time at which IUI can be done to yield the peak pregnancy rate. Objective To compare the effect of postponing IUI 48 h after hCG injection with current practice protocol, on pregnancy rate. Study design: A randomized. controlled study. Setting was at Cytogenetic and Endoscopy Unit, Zagazig University Hospital. Material and methods This study included one hundred and forty-one infertile couples that had been scheduled for artificial insemination by husband semen. Women were divided into 2 groups: the study group, including seventy women in whom IUI was performed 48 h after hCG injection and the control group, including seventy-one women in whom IUI was done 36 h after hCG injection. Results The total and clinical pregnancy rate was significantly higher in the study group compared to the control group (25% vs. 10.6% p = 0.03 and 20.31% vs. 7.57% p = 0.03 respectively). Conclusion This study showed a statistically significant increase in pregnancy rate in women with delaying IUI 48 h after hCG trigger, compared to the pregnancy rate in the women having the standard procedure. 

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Middle East Fertility Society

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Year of Publication
The role of Silodosin as a new medical expulsive therapy for ureteral stones: a meta-analysis.

Hui D., Ning Z., Yu D., Shang P., Yang L.

Embase

[Review]
AN: 613127544

To evaluate the efficacy of Silodosin as a medical expulsive therapy of ureteral stones, we searched PubMed, EMBASE, the Cochrane Library, and CBM up to June 2015. All randomized controlled trials (RCTs) were identified in which patients were randomized to receive Silodosin versus placebo or other therapies for ureteral stones. Outcome measures assessed were overall stone expulsion rate (primary) and expulsion time, analgesics times, and the incidence of additional treatment and regarding treatment complications (secondary). Two authors independently assessed study quality and extracted data. All data were analyzed using RevMan 5.3. Seven RCTs with a total of 1035 patients met the inclusion criteria. The pooled meta-analysis showed a significant improvement in stone clearance with Silodosin (Silodosin versus placebo, OR =1.69, 95% CI [1.19-2.40], p = 0.003; Silodosin versus tamsulosin, OR =2.82, 95% CI [1.79-4.44], p < 0.00001). According to the size and location of ureteral stone, the pooling effects of Silodosin were analyzed, with a meaningful expulsion rate in distal ureteral stone when the size was 5-10 mm. In addition, a shorter expulsion time, fewer analgesics times, and additional treatments were observed. The common side effect was retrograde ejaculation. In summary, Silodosin appears to be more effective than either placebo or tamsulosin. Within the limits of available data, high-quality multicenter RCTs are needed to thoroughly evaluate the outcome in the future. Copyright © 2016 Informa UK Limited, trading as Taylor & Francis Group.
Undergoing varicocele repair before assisted reproduction improves pregnancy rate and live birth rate in azoospermic and oligospermic men with a varicocele: a systematic review and meta-analysis.

Kirby E.W., Wiener L.E., Rajanahally S., Crowell K., Coward R.M.

Embase
Fertility and Sterility. 106 (6) (pp 1338-1343), 2016. Date of Publication: 01 Nov 2016.

Objective To evaluate how varicocele repair (VR) impacts pregnancy (PRs) and live birth rates in infertile couples undergoing assisted reproduction wherein the male partner has oligospermia or azoospermia and a history of varicocele. Design Systematic review and meta-analysis. Setting Not applicable. Patient(s) Azoospermic and oligospermic males with varicoceles and in couples undergoing assisted reproductive technology (ART) with IUI, IVF, or testicular sperm extraction (TESE) with IVF and intracytoplasmic sperm injection (ICSI). Intervention(s) Measurement of PRs, live birth, and sperm extraction rates. Main Outcome Measure(s) Odds ratios for the impact of VR on PRs, live birth, and sperm extraction rates for couples undergoing ART. Result(s) Seven articles involving a total of 1,241 patients were included. Meta-analysis showed that VR improved live birth rates for the oligospermic (odds ratio [OR] = 1.699) and combined oligospermic/azoospermic groups (OR = 1.761). Pregnancy rates were higher in the azoospermic group (OR = 2.336) and combined oligospermic/azoospermic groups (OR = 1.760). Live birth rates were higher for patients undergoing IUI after VR (OR = 8.360). Sperm retrieval rates were higher in persistently azoospermic men after VR (OR = 2.509). Conclusion(s) Oligospermic and azoospermic patients with clinical varicocele who undergo VR experience improved live birth rates and PRs with IVF or IVF/ICSI. For persistently azoospermic men after VR requiring TESE for IVF/ICSI, VR improves sperm retrieval rates. Therefore, VR should be considered to have substantial benefits for couples with a clinical varicocele even if oligospermia or azoospermia
Prevalence of chromosomal abnormalities and y chromosome microdeletion among men with severe semen abnormalities and its correlation with successful sperm retrieval.

Mascarenhas M., Thomas S., Kamath M.S., Ramalingam R., Kongari A.M., Yuvarani S., Srivastava V.M., George K.

Embase
Journal of Human Reproductive Sciences. 9 (3) (pp 187-193), 2016. Date of Publication: July-September 2016.

[Article]
AN: 613096464
AIM: To estimate the prevalence of chromosomal abnormalities and Y chromosome microdeletion among men with azoospermia and severe oligozoospermia and its correlation with successful
surgical sperm retrieval. SETTING AND DESIGN: A prospective study in a tertiary level infertility unit. MATERIALS AND METHODS: In a prospective observation study, men with azoospermia and severe oligozoospermia (concentration <5 million/ml) attending the infertility center underwent genetic screening. Peripheral blood karyotype was done by Giemsa banding. Y chromosome microdeletion study was performed by a multiplex polymerase chain reaction. RESULTS: The study group consisted of 220 men, 133 of whom had azoospermia and 87 had severe oligozoospermia. Overall, 21/220 (9.5%) men had chromosomal abnormalities and 13/220 (5.9%) men had Y chromosome microdeletions. Chromosomal abnormalities were seen in 14.3% (19/133) of azoospermic men and Y chromosome microdeletions in 8.3% (11/133). Of the 87 men with severe oligozoospermia, chromosomal abnormalities and Y chromosome microdeletions were each seen in 2.3% (2/87). Testicular sperm aspiration was done in 13 men and was successful in only one, who had a deletion of azoospermia factor c. CONCLUSIONS: Our study found a fairly high prevalence of genetic abnormality in men with severe semen abnormalities and a correlation of genetic abnormalities with surgical sperm retrieval outcomes. These findings support the need for genetic screening of these men prior to embarking on surgical sperm retrieval and assisted reproductive technology intracytoplasmic sperm injection. Copyright © 2016 Journal of Human Reproductive Sciences
Published by Wolters Kluwer. Medknow.

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Tribulus terrestris: Chemistry and pharmacological properties.
Miraj S.
Embase
Der Pharma Chemica. 8 (17) (pp 142-147), 2016. Date of Publication: 2016.
[Article]
AN: 612993379
Tribulus terrestris is an annual plant in the caltrop family (Zygophyllaceae) widely distributed around the world, that is adapted to grow in dry climate locations in which few other plants can survive. While this plant has lots of properties, the aim of this study is to overview its therapeutic effects than its nutritive and industrial effects. This review article was carried out by searching studies in PubMed, Medline, Web of Science, and IranMedex databases from 1994 to 2016. totally, of 100 found articles, 47 articles were included. The search terms were "Tribulus terrestris", "therapeutic", "pharmacological", Various studies have shown that Tribulus terrestris Possess Antiinfertility, Diabetes Heart disease, Anti-inflammatory effects, Antibacterial activity, Liver disease, Supplemental activity, Kidney disease, Anti-oxidant properties, Anti-cancer, Aphrodisiac activity, Anti-stress Oxidative stress, Liver and kidney, Hyperplasia, Antioxidant and metal chelator activity and Hepatoprotective activity, Anti- Androgenic Activity, Supplemental Sport, Pro-sexual androgen enhancing effects, Aphrodisiac properties. Tribulus terrestris not likely to become an important alternative to standard medical therapies unless there are changes to the regulation, standardization, and funding for research of these products.
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Year of Publication
2016
Efficacy and safety of multiple doses of levomilnacipran extended-release for the treatment of major depressive disorder.

Huang Q., Zhong X., Yun Y., Yu B., Huang Y.

Embase

Neuropsychiatric Disease and Treatment. 12 (pp 2707-2714), 2016. Date of Publication: 25 Oct 2016.

[Article]

AN: 612916005

Objective: The aim of this meta-analysis was to evaluate the efficacy and safety of levomilnacipran extended-release (ER) in the treatment of major depressive disorder (MDD).

Methods: Randomized controlled trials were searched by electronic databases. Unpublished data were also searched by the relevant websites. Weighted mean difference (WMD) and risk ratio (RR) with 95% confidence interval (CI) were calculated and pooled using fixed-effects model or random-effects model. Results: Five randomized placebo-controlled trials including 2,637 patients were analyzed. Compared with placebo, levomilnacipran ER had a greater reduction in the Montgomery-Asberg Depression Rating Scale (MADRS) total score and Sheehan Disability Scale (SDS) total score (MADRS: WMD -3.49 [95% CI -4.28, -2.70; P<0.00001]; SDS: WMD -2.41 [95% CI -3.05, -1.77; P<0.00001]). Significantly more patients in levomilnacipran ER achieved MADRS response rate (RR 1.35 [95% CI 1.23, 1.47; P<0.00001]) and MADRS remission rate (RR 1.30 [95% CI 1.06, 1.59; P=0.01]). In terms of safety, more patients discontinued due to adverse events (AEs) in levomilnacipran ER compared with placebo (RR 3.15 [95% CI 2.26, 4.39; P<0.00001]), but it was generally well tolerated in each eligible trial. The most common AEs were nausea, delay in ejaculation, erectile dysfunction, tachycardia, headache and increase in heart rate. Conclusion: Levomilnacipran ER is a safe and effective short-term treatment for MDD (<10 weeks). Long-term and head-to-head trials comparing levomilnacipran ER with other antidepressants are needed to confirm the conclusion. Copyright © 2016 Huang et al.
Current evidence supports the use of testosterone replacement in men with the clinical-biochemical syndrome of hypogonadism, defined as low testosterone serum levels and symptoms such as fatigue, exercise intolerance, erectile dysfunction, low libido, or depression. Although the evidence consistently shows that hypogonadism is associated with elevated cardiovascular risk, evidence is mixed regarding whether testosterone (T) replacement provides cardiovascular (CV) benefit or harm. For a man with symptomatic hypogonadism in the setting of CV disease, clinical heart failure, and/or traditional CV risk factors (hypertension, diabetes, and hyperlipidemia), a balanced approach would be to counsel him that overall, the evidence should not dissuade him from utilizing T replacement for non-cardiac symptom relief but that more data are needed before a definitive recommendation can be made about T replacement for CV benefit. The preponderance of available evidence, reviewed in this article, suggests that T replacement, at appropriate doses and with monitored response, is likely to be safe for men with CV disease or CV risk factors and may even reduce major adverse cardiovascular events (MACE). The 2015 American Association of Clinical Endocrinologists and American College of Endocrinology position statement supports this stance and calls for improved prospective data. There is a clear need for a large, prospective randomized trial evaluating the impact of T replacement on MACE, for men both with and without CV disease or CV risk factors. Clinicians should be aware that all
men who elect to take T replacement therapy require regular follow-up with the prescribing physician to include both clinical assessment and surveillance laboratory assessment of total T level, complete blood count, and prostate specific antigen. Copyright © 2016, Springer Science+Business Media New York.

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2016

577.
Usefulness of magnetic activated cell sorting processing of sperm samples in intrauterine insemination. <Utilidad de la separacion magnetica mediante columnas de anexina V en el procesado de muestras seminales para inseminacion intrauterina.> Ballester M., Boada M., Mateo S., Buxaderas R., Vendrell J.M., Coroleu B., Veiga A. Embase Medicina Reproductiva y Embriologia Clinica. 3 (3) (pp 113-118), 2016. Date of Publication: 01 Dec 2016.
[Article]
AN: 611499962
Infertile men show a higher proportion of apoptotic spermatozoa in ejaculate, and have a negative impact on the assisted reproduction techniques (ART) results. An adequate sperm selection which eliminates the apoptotic spermatozoa could improve the results. The objective of the study was to evaluate the effect of eliminating apoptotic spermatozoa in the ejaculate by density gradient (DG) and Magnetic Activated Cell Sorting (MACS) processing of sperm on the
pregnancy rate (PR) and new born rate (NBR) after intrauterine insemination (IUI). A prospective observational and analytical study was performed on 566 cycles of IUI in 326 couples, from June 2012 to March 2014 in the Reproductive Medicine Service of Dexeus Women's Health comparing a study group (MACS) and a control group (Non-MACS). The preparation of the semen sample in both groups was by DG, and in the MACS group, the post capacitation fraction was processed using annexin V columns. The PR and NBR obtained in MACS group were 16.2% and 12.9%, respectively versus 17.7% and 15.3% in Non-MACS group. No significant differences were observed. Our results suggest that MACS used in IUI without a clinical indication does not improve the results in either the pregnancy rate or new born rate. The use of annexin V columns in other techniques, or specific indications cannot be ruled out. Further prospective randomised studies are needed in order to determine the advantages of MACS in ART. Copyright © 2016 Asociacion para el Estudio de la Biologia de la Reproduccion y Sociedad Espanola de Fertilidad Status
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578.
Fertility-related quality of life from two RCT cohorts with infertility: Unexplained infertility and polycystic ovary syndrome.
Embase
Human Reproduction. 31 (10) (pp 2268-2279), 2016. Date of Publication: 01 Oct 2016.
STUDY QUESTION Does fertility-related quality of life (FertiQOL) differ by infertility diagnosis between women with polycystic ovary syndrome (PCOS) and their partners, compared with couples with unexplained infertility (UI)?

SUMMARY ANSWER Women with PCOS report lower QOL than those with UI, whereas males with UI report lower QOL than males with PCOS partners.

WHAT IS KNOWN ALREADY The fertility-specific QOL survey, FertiQOL, has been used to examine fertility-related QOL in a number of worldwide cohorts. Few data have addressed fertility-related QOL as a function of infertility diagnosis. Overall, men report better QOL than women with infertility, and there is variation in FertiQOL scores across different samples from different countries.

STUDY DESIGN, SIZE, DURATION This was a prospective, cohort study derived from two concurrent, randomized clinical trials, and designed to examine QOL in infertile females with PCOS and UI at the time of enrollment compared with each other and their male partners; to compare concordance FertiQOL scores in this study across other worldwide cohorts; and to determine if baseline FertiQOL was associated with pregnancy outcome.

PARTICIPANTS/MATERIALS, SETTING, METHODS Women with PCOS and their partners (n = 733 and n = 641, respectively), and couples with UI (n = 865 women and 849 men) completed a validated fertility-specific QOL survey (FertiQOL) at the time of the study screening visit. PCOS women were randomized to either clomiphene citrate or letrozole treatment; couples with UI were randomized to clomiphene citrate, letrozole or gonadotrophin plus IUI. FertiQOL results were compiled by diagnosis (PCOS or UI) and compared by diagnosis and sex using Wilcoxon Rank-Sum testing. Relationships between baseline FertiQOL and pregnancy outcomes were examined using logistic regression. Multivariable models were performed to assess the association between FertiQOL scores and key participant characteristics.

MAIN RESULTS AND THE ROLE OF CHANCE Women with PCOS had lower total FertiQOL scores (72.3 +/- 14.8) than those with UI (77.1 +/- 12.8; P < 0.001); this was true for each domain (except Relational). These differences were largely explained by variation in BMI, hirsutism, household income and age. Women had lower overall FertiQOL scores than their male partners. Males with PCOS partners had higher scores than males with UI (84.9 +/- 10.2 versus 83.3 +/- 10.8; P = 0.003). Scores were not consistently associated with conception or pregnancy outcome.

LIMITATIONS, REASONS FOR CAUTION The use of multiple tests of association may have resulted in spurious statistically significant findings. Inherent sociodemographic differences between women with PCOS and those with UI largely account for the lower QOL in women with PCOS. Our study was unable to assess if changes in QOL affected pregnancy outcome as FertiQOL data were collected prior to treatment. Finally, the participants for both studies represent their local communities, but are not a population-based sample and thus firm conclusions about how representative these couples are to the general population must be made with caution.
IMPLICATIONS OF THE FINDINGS  Women with PCOS with elevated BMI and hirsutism scores and with lower socioeconomic status may require more, targeted psychosocial support than those with other diagnoses. Possible attribution of infertility to the male partner appears to result in a lower QOL. There appears to be substantial national variation in FertiQOL scores, with US-based cohorts reporting overall higher QOL. STUDY FUNDING/COMPETING INTEREST(S) This work was supported by National Institutes of Health (NIH)/Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Grants U10 HD39005 (to M.D.), U10 HD38992 (to R.S.L.), (to C.C.), U10 HD38998 (to R.A.), U10 HD055942 (to R.D.R.), HD055944 (to P.C.), U10 HD055936 (to G.C.), U10 HD055925 (to H.Z.); and U10 U54-HD29834 (to the University of Virginia Center for Research in Reproduction Ligand Assay and Analysis Core of the Specialized Cooperative Centers Program in Reproduction and Infertility Research). Most importantly, this research was made possible by the funding by American Recovery and Reinvestment Act. N.S., E.E., J.C.T., C.G., H.H., R.A., P.C., G.C., C.C., M.D., S.J., W.D.S. and H.Z. report no conflicts of interests/disclosures. L.B.C. reports research support from Ferring Pharmaceuticals and Roche Diagnostics; R.S.L. reports receipt of consulting fees from AstraZeneca, Euroscreen, Sprout Pharmaceuticals, Taken, Kindex, Clarus and Bayer, Inc., and research support from AstraZeneca and Ferring Pharmaceuticals. R.D.R. reports research support from AbbVie. TRIAL REGISTRATION NUMBER Pregnancy in Polycystic Ovary Syndrome II (PPCOS II), NCT00719186; Assessment of Multiple Intrauterine Gestations in Ovulation Stimulation (AMIGOS) NCT01044862, clinicaltrials.gov. TRIAL REGISTRATION DATE PPCOS II 17 July 2008; AMIGOS 7 January 2010. DATE OF FIRST PATIENT'S ENROLMENT PPCOS II 19 February 2009; AMIGOS 2 August 2010. Copyright © 2016 Published by Oxford University Press on behalf of the European Society of Human Reproduction and Embryology 2016. This work is written by (a) US Government employee(s) and is in the public domain in the US. Status EMBASE Institution (Santoro, Alvero) Department of Obstetrics and Gynecology, University of Colorado School of Medicine, 12631 E 17th Avenue AO1 Room 4010, Aurora, CO 80045, United States (Eisenberg) Fertility and Infertility Branch, NICHD, NIH, Bethesda, MD 20892, United States (Trussell) Department of Urology, State University of New York Upstate Medical University, 750 E Adams St, Syracuse, NY 13210, United States (Craig) Department of Obstetrics and Gynecology, University of Oklahoma Health Sciences Center, PO Box 26901, WP 2410, Oklahoma City, OK 73126, United States (Gracia, Coutifaris) Department of Obstetrics and Gynecology, University of Pennsylvania Penn Fertility Center, 3701 Market Street, Philadelphia, PA 19104, United States
Introduction Hypogonadism in men is often associated with poor libido, erectile dysfunction, irritability, fatigue, and psychological and relationship problems. Many of these symptoms can be
best assessed through patient report. The 28-item Hypogonadism Impact of Symptoms Questionnaire (HIS-Q) was developed to evaluate hypogonadism symptoms in men with low testosterone in the context of clinical trials. Aim To develop a briefer version of the HIS-Q that could be practical for use in treatment settings. Methods Participants with low testosterone levels and symptoms consistent with hypogonadism were recruited through clinical sites. Focus groups and interviews were conducted to elicit symptom concepts and identify those that were most relevant to patients, including changes as a consequence of treatment. Main Outcome Measures Systematic analysis of the qualitative data and expert clinician input were used to develop the HIS-Q short form (HIS-Q-SF). One-on-one cognitive interviews were conducted to confirm the content validity of the HIS-Q-SF. Results Thirty-five men participated in this qualitative research. Concept elicitation was conducted through focus group discussions (n = 18) and telephone interviews (n = 2); then, the draft HIS-Q-SF was evaluated through cognitive interviews (n = 15). The mean age of total sample was 53.2 +/- 6.8 years, and the mean serum total testosterone level was 184.9 +/- 55.2 ng/dL. Results suggest that the HIS-Q-SF has demonstrated content validity, including the content coverage, comprehensibility, and the appropriateness of the response options and recall period. The final version of the HIS-Q-SF includes 17 items and is aligned with the original longer version of the instrument. Conclusion The HIS-Q-SF is a comprehensive measurement of hypogonadism symptom severity in men. Content coverage and content validity were confirmed. The instrument will be evaluated further to establish the psychometric characteristics and to assess the utility of the measurement in clinical treatment settings. Copyright © 2016 The Authors
Introduction The Hypogonadism Impact of Symptoms Questionnaire (HIS-Q) is a patient-reported outcome measurement designed to comprehensively evaluate the symptoms of hypogonadism and to detect changes in these symptoms in response to treatment. Aim To conduct item analysis and reduction, evaluate the psychometric properties of the HIS-Q, and provide guidance on interpreting the instrument score. Methods A 12-week observational, longitudinal study of hypogonadal men was conducted. Participants completed the HIS-Q every 2 weeks. Blood samples were collected to evaluate testosterone levels. Participants also completed the Aging Male's Symptoms Scale, the International Index of Erectile Function, the Short Form-12 Health Survey, and the Patient-Reported Outcomes Measurement Information System Sexual Activity, Satisfaction with Sex Life, Sleep Disturbance, and Applied Cognition Scales (at baseline and weeks 6 and 12). Clinicians completed the Clinical Global Impression of Severity and Change measurements and a clinical form. Main Outcome Measures Individual item performance was evaluated using descriptive statistics and Rasch analyses. Reliability (internal consistency and test-retest), validity (concurrent and know groups), and responsiveness were assessed. Results In total, 177 men participated in the study (mean age = 54.1 years, range = 23-83). The original 53-item draft HIS-Q was reduced to 28 items; the final instrument included five domains (sexual, energy, sleep, cognition, and mood) with two sexual subdomains (libido and sexual function). For all domains, test-retest reliability was acceptable (intraclass correlation coefficients > 0.70), construct validity was good (r > 0.30 for all comparisons). Known-groups validity was demonstrated for all HIS-Q domain scores, subdomain scores, and the total score as measured by the Clinical Global Impression of Severity, and total testosterone level at baseline (P < .05 for all comparisons). All domains and subdomains were responsive to change based on patient-rated anchor questions (P < .05 for all comparisons). Conclusion The final 28-item HIS-Q is reliable, valid, and responsive. The HIS-Q is suitable for inclusion in future clinical trials to help characterize the effects of testosterone replacement therapy.

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Holmium laser enucleation of the prostate: Patient selection and perspectives.
Marien T., Kadihasanoglu M., Miller N.L.

Embase
[Review]
AN: 612915874

Background: Multiple endoscopic surgical options exist to treat benign prostatic hyperplasia (BPH), including holmium laser enucleation of the prostate (HoLEP). HoLEP alleviates obstructive prostatic tissue via enucleation, both bluntly with a resectoscope and by cutting tissue with the holmium laser, and removal of adenoma via morcellation. This article reviews patient selection for HoLEP in order to optimize outcomes, costs, and patient satisfaction. Methods: A literature review of all studies on HoLEP was conducted. Studies that focused on outcomes in regard to patient and procedural factors were closely reviewed and discussed. Results: Various studies found that men with large or small prostates, on antithrombotic therapy, in urinary retention, with bladder hypocontractility, with prostate cancer, undergoing retreatment for BPH, or in need of concomitant
surgery for bladder stones and other pathologies do well with HoLEP, as demonstrated by excellent functional and symptomatic outcomes as well as low complication rates. There is a 74-78% rate of retrograde ejaculation following HoLEP. Techniques to preserve ejaculatory function following enucleative techniques have not been able to demonstrate a significant improvement.

Conclusion: Patient selection for HoLEP can include most men with bothersome BPH who have evidence of bladder outlet obstruction and are healthy enough to undergo surgery. The ability to safely perform concomitant surgery with HoLEP benefits the patient by sparing them an additional anesthetic and also decreases costs. Patients should be made aware of the risk of retrograde ejaculation following HoLEP and counseled on treatment alternatives if maintaining ejaculatory function is desired.

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582.
"Is late-onset hypogonadotropic hypogonadism a specific age-dependent disease, or merely an epiphenomenon caused" by accumulating disease-burden?.
Embase
Minerva Endocrinologica. 41 (2) (pp 196-210), 2016. Date of Publication: June 2016.
[Review]
AN: 612971385
BACKGROUND: The aim of this paper is to summarize the available evidence supporting the link between late onset hypogonadism (LOH) and associated common clinical illnesses, focusing on
metabolic diseases. The possible benefits or risks related to testosterone replacement therapy (TRT) in these conditions will also be analyzed. METHODS: An extensive Medline search was performed. RESULTS: LOH is closely associated with a worse metabolic profile and a higher cardiovascular risk. The relationship between hypogonadism obesity and insulin resistance is complex and bidirectional. Emerging evidence suggests a positive role of TRT in improving body composition and metabolic outcomes in subjects with LOH. CONCLUSIONS: Despite the aforementioned data, it is not completely known whether reduced testosterone levels in elderly males might play a direct pathogenetic role in these conditions or whether low T and associated morbidities are concomitant conditions, both associated with the aging process. Further and longer studies are advisable to confirm the preliminary results. Copyright © 2016 EDIZIONI MINERVA MEDICA.

583.
Testosterone undecanoate improves sexual function in men with type 2 diabetes and severe hypogonadism: results from a 30-week randomized placebo-controlled study.
Hackett G., Cole N., Saghir A., Jones P., Strange R.C., Ramachandran S.

BJU International. 118 (5) (pp 804-813), 2016. Date of Publication: 01 Nov 2016.

[Article]
AN: 610573189

Objective: To evaluate the sexual function response to 30 weeks' treatment with long-acting testosterone undecanoate (TU) or placebo in 199 men with type 2 diabetes and either severe or mild hypogonadism (HG). Patients and Methods: Men with HG were identified from seven primary care type 2 diabetes registers. A 30-week randomized placebo-controlled study of TU was carried out in 199 of these men (placebo, n = 107, TU, n = 92). The patient-reported outcome measure was the 15-item International Index of Erectile Function score. Men completing the study (n=189) were stratified, firstly, by baseline total testosterone (TT) or free testosterone (FT) into mild HG (TT 8.1-12 nmol/L or FT 0.18-0.25 nmol/L) and severe HG groups (TT <8 nmol/L and FT <0.18 nmol/L), and secondly, by intervention (placebo or TU), thereby creating four groups: mild HG/placebo; mild HG/TU; severe HG/placebo and severe HG/TU. Statistical Analysis: Changes in sexual function score (a secondary outcome of the study) at each visit within group (from baseline) and between groups (TU vs placebo) at each assessment (6, 18 and 30 weeks) were compared using a Wilcoxon signed-rank and Wilcoxon rank-sum test, respectively. Results: Significant improvement in erectile function was evident only in the severe HG group after 30 weeks of TU treatment; this finding persisted when TU was compared with placebo. Intercourse satisfaction and sexual desire scores were also improved at 6, 18 and 30 weeks in the severe HG group after TU treatment; this increase in scores was also evident when compared with placebo. TU did not appear to alter orgasmic function significantly in any of the patient groups. Conclusions: The present study suggests that benefit in sexual symptoms after TU treatment is evident principally in patients with HG with TT levels <8 nmol/L and FT levels <0.18 nmol/L. We also suggest that 30 weeks of treatment is necessary before evaluating improvement in erectile function.

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Many monotherapies are currently available to clinically treat and alleviate symptoms of lower urinary tract symptoms secondary to benign prostatic hyperplasia: alpha-blockers, 5ARIs, PDE5Is, beta3-andrenoceptor agonists, and anticholinergic agents. Current studies have evaluated the effectiveness of these treatments in comparison to other groups or in combination therapies. The current review evaluates the effectiveness of class formulations. Based on the findings, alpha-blockers, specifically doxazosin and terazosin, were most effective in reducing IPSS scores and peak urinary flow rate, while being most cost-effective. However, further clinical investigations are required to evaluate the clinical implications of different formulations.
585.

Testosterone and the Prostate: Artifacts and Truths.
DeLay K.J., Kohler T.S.

Embase
Urologic Clinics of North America. 43 (3) (pp 405-412), 2016. Date of Publication: 01 Aug 2016.
[Review]
AN: 612852891

Despite a lack of evidence, there have been stated concerns that testosterone replacement therapy (TRT) can pose a risk to men suffering with lower urinary tract symptoms (LUTS)/benign prostatic hyperplasia (BPH). TRT may improve components of the metabolic syndrome, which is associated with worsening LUTS. Furthermore, the evidence suggests that TRT may decrease prostatic inflammation, which is also associated with worsening LUTS. The data on the relationship between TRT and LUTS have never shown worsening of LUTS, often show no change in LUTS, and occasionally show improvement.  Copyright © 2016 Elsevier Inc.

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W.B. Saunders

Date Created
20161024
Sexual Side Effects of Medical and Surgical Benign Prostatic Hyperplasia Treatments.
Welliver C., Essa A.

Treatments for lower urinary tract symptoms due to benign prostatic hyperplasia can be evaluated by multiple metrics. A balance within the confines of patient expectations is key to determining the ideal treatment. A troubling adverse event for some patients is sexual dysfunction. Because the cohort of men who seek treatment of sexual dysfunction and lower urinary tract symptoms is essentially identical, these disease processes frequently overlap. This article considers potential pathophysiologic causes of dysfunction with treatment and attempts to critically review the available data to assess the true incidence of sexual adverse events with treatment. Copyright © 2016

Publisher
W.B. Saunders
587.

Alpha-blockers for the Treatment of Benign Prostatic Hyperplasia.
Lepor H.
Embase
Urologic Clinics of North America. 43 (3) (pp 311-323), 2016. Date of Publication: 01 Aug 2016.
[Review]
AN: 612852885
Over the last 2 decades the evolution of alpha-blockers for lower urinary tract symptoms (LUTS)/benign prostatic hyperplasia (BPH) has been to preserve effectiveness, improve tolerability, and eliminate dose titration. Today, alpha-blockers represent the first-line treatment of most men with BPH whereby the primary objective is relief from bothersome LUTS. Copyright © 2016 Elsevier Inc.
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20161024
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2016
Bipolar, Monopolar, Photovaporization of the Prostate, or Holmium Laser Enucleation of the Prostate: How to Choose What's Best?.
Cornu J.-N.
Embase
[Review]
AN: 612852879
Endoscopic management of benign prostatic obstruction is based on resection, vaporization, or enucleation. Enucleation provides the best efficacy and long-term outcome. Lasers have advantages in patients at high risk of bleeding. Holmium enucleation is the best evaluated technique, but has a steep learning curve. Greenlight photovaporization is a safe alternative to transurethral resection of the prostate (TURP) in prostates of less than 100 mL, especially in patients at high risk of bleeding. Bipolar devices can be used for resection, vaporization, and enucleation and provides efficacy results similar to TURP in the short term with better safety.
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589.
5-Alpha-Reductase Inhibitors and Combination Therapy.
Fullhase C., Schneider M.P.
Embase
By inhibiting the conversion from testosterone to dihydrotestosterone 5-Alpha reductase inhibitors (5ARIs) are able to hinder prostatic growth, shrink prostate volumes, and improve BPH-related LUTS. 5ARIs are particularly beneficial for patients with larger prostates (>30-40ml). Generally the side effects of 5ARI treatment are mild, and according to the FORTA classification 5ARIs are suitable for frail elderly. 5ARI / alpha-blocker (AB) combination therapy showed the best symptomatic outcome and risk reduction for clinical progression. Combining Phosphodiesteaserase type 5 inhibitors (PDE5Is) with 5ARIs counteracts the negative androgenic sexual side effects of 5ARIs, and simultaneously combines their synergistic effects on LUTS.  

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Embase

Mayo Clinic Proceedings. 91 (7) (pp 881-896), 2016. Date of Publication: 01 Jul 2016.
To address widespread concerns regarding the medical condition of testosterone (T) deficiency (TD) (male hypogonadism) and its treatment with T therapy, an international expert consensus conference was convened in Prague, Czech Republic, on October 1, 2015. Experts included a broad range of medical specialties including urology, endocrinology, diabetology, internal medicine, and basic science research. A representative from the European Medicines Agency participated in a nonvoting capacity. Nine resolutions were debated, with unanimous approval: (1) TD is a well-established, clinically significant medical condition that negatively affects male sexuality, reproduction, general health, and quality of life; (2) symptoms and signs of TD occur as a result of low levels of T and may benefit from treatment regardless of whether there is an identified underlying etiology; (3) TD is a global public health concern; (4) T therapy for men with TD is effective, rational, and evidence based; (5) there is no T concentration threshold that reliably distinguishes those who will respond to treatment from those who will not; (6) there is no scientific basis for any age-specific recommendations against the use of T therapy in men; (7) the evidence does not support increased risks of cardiovascular events with T therapy; (8) the evidence does not support increased risk of prostate cancer with T therapy; and (9) the evidence supports a major research initiative to explore possible benefits of T therapy for cardiometabolic disease, including diabetes. These resolutions may be considered points of agreement by a broad range of experts based on the best available scientific evidence.
Sexual Dysfunction Due to Psychotropic Medications.
Clayton A.H., Alkis A.R., Parikh N.B., Votta J.G.
Embase
[Review]
AN: 612748392
Sexual functioning is important to assess in patients with psychiatric illness as both the condition and associated treatment may contribute to sexual dysfunction (SD). Antidepressant medications, mood stabilizers, antipsychotics, and antianxiety agents may be associated with SD related to drug mechanism of action. Sexual adverse effects may be related to genetic risk factors, impact on neurotransmitters and hormones, and psychological elements. Effective strategies to manage medication-induced sexual dysfunction are initial choice of a drug unlikely to cause SD, switching
to a different medication, and adding an antidote to reverse SD. Appropriate interventions should be determined on a clinical case-by-case basis. Copyright © 2016

Adverse Effects of Psychotropic Medications: A Call to Action.
Mago R.
Embase
[Review]
AN: 612748389
Adverse effects are common, bothersome, and a leading cause of discontinuation of treatment. The methodology for evaluating adverse effects of medications has been greatly neglected, however, especially in comparison to the methodology for assessment of efficacy of medications. Existing methods for assessment and reporting of adverse effects have important limitations leading to lack of much-needed data related to adverse effects. Lastly, there is little systematic research into management of most adverse effects. A series of recommendations are made in this article about how to improve identification, assessment, reporting, and management of adverse effects. Copyright © 2016 Elsevier Inc.
593.
9-Month Efficacy and Safety Study of Testosterone Solution 2% for Sex Drive and Energy in Hypogonadal Men.
Brock G., Heiselman D., Knorr J., Ni X., Kinchen K.
Embase
[Article]
AN: 612934766
Purpose We evaluated the continued safety and efficacy of testosterone solution 2% (T-sol) in a 6-month open label extension study following a 3-month, double-blind, placebo controlled study in which T-sol was safe and efficacious for sex drive in men with androgen deficiency. Materials and Methods A total of 558 hypogonadal participants with a mean (SD) age of 55 (11) years entered the open label treatment study. Of these patients 275 had previously received placebo (formerly placebo group) and 283 had received active treatment with T-sol (continuing active group) during the double-blind phase. Outcome measures were the proportion of men with total testosterone levels within the normal range; assessment of treatment induced change in sex drive measured using the Sexual Arousal, Interest, and Drive scale; and assessment of treatment induced change in energy measured using the Hypogonadism Energy Diary. Results At the completion of the open label phase 60% and 66% of the participants had total testosterone levels within the normal range in the formerly placebo and continuing active groups, respectively. Participants assigned to both groups showed baseline to end point improvement in Sexual Arousal, Interest, and Drive score (both p <0.001) and Hypogonadism Energy Diary score (both p <0.001) during the open label phase. No new safety concerns were reported. Conclusions Once daily T-sol administered for 6 months in an open label study did not indicate new safety concerns, and the outcomes of
Developmental origins of male subfertility: role of infection, inflammation, and environmental factors.

Schagdarsurengin U., Western P., Steger K., Meinhardt A.


[Review]

AN: 610883834

Male gamete development begins with the specification of primordial cells in the epiblast of the early embryo and is not complete until spermatozoa mature in the epididymis of adult males. This protracted developmental process involves extensive alteration of the paternal germline epigenome. Initially, epigenetic reprogramming in fetal germ cells results in removal of most DNA methylation, including parent-specific epigenetic information. The germ cells then establish sex-specific epigenetic information through de novo methylation and undergo spermatogenesis. Chromatin in haploid germ cells is repackaged into protamines during spermiogenesis, providing further widespread epigenetic reorganization. Finally, after fertilization, epigenetic reprogramming in the preimplantation embryo is necessary for regaining totipotency. These events provide substantial windows during which epigenetic errors either may be corrected or may occur in the germline. There is now increasing evidence that environmental factors such as exposure to
toxicants, the parents’ and individual's diet, and even infectious and inflammatory events in the male reproductive tract may influence epigenetic reprogramming. This, together with other damage inflicted on the germline chromatin, may result in negative consequences for fertility and health. Large epidemiological birth cohort studies have yielded insight into possible causative environmental factors. Together with experimental animal studies, a clearer view of environmental impacts on fetal development and their intergenerational and even transgenerational effects on reproductive health has emerged and is reviewed in this article.

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20161021
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2016

Study of male sex hormone levels in male Egyptian children with beta-thalassemia: Correlation with Iron load.
Hagag A.A., Badraia I.M., Elfarargy M.S., Abo El-Enein A.M.

Embase
Endocrine, Metabolic and Immune Disorders - Drug Targets. 16 (2) (pp 124-130), 2016. Date of Publication: 2016.
[Article]
AN: 612788993
Background: Beta thalassemia is an inherited hemoglobin disorder resulting in chronic hemolytic anemia. RBCs hemolysis and repeated blood transfusions are the major causes of secondary iron overload which leads to deposition of iron in different endocrine glands. Delayed puberty and hypogonadism are the most obvious clinical consequences of iron overload. The aim of this study was to evaluate male sex hormone levels in male children with beta- thalassemia major in correlation with iron overload. Material and Methods: The present study was conducted on 60 male children with beta- thalassemia major with serum ferritin of more than 1000 ng/ml with their age ranging from 11-18 years and mean age value of 14.16+/-.48 (Group I) and 60 male children with beta- thalassemia major of matched age with no iron overload (Group II). For all children in both groups the following were done: Complete blood count, Hb electrophoresis, serum ferritin, serum iron, TIBC, serum testosterone levels and assessment of testicular volume by ultrasound and Orchidometer. Results: Serum iron and ferritin were significantly higher while TIBC, serum testosterone levels and testicular volume were significantly lower in Group I than Group II (Mean serum iron was 221.70+/-.46.76 in group I versus 122.45+/-.14.32 in group II with p value of 0.001, mean serum ferritin was 2595.06+/-.903.43 in group I versus 373.75+/-.6.82 in group II with p value of 0.001, mean serum TIBC was 210.93+/-.18.17 in group I versus 311.40+/-.13.57 in group II with p value of 0.001, mean serum testosterone was 1.01+/-.1.61 in group I versus 2.73+/-.2.66 in group II with p value of 0.006, mean testicular volume was 4.45+/-.7.08 in group I versus 8.66+/-.7.08 in group II with p value of 0.016). There was significant negative correlation between serum ferritin and serum testosterone and between serum ferritin and testicular volume in studied patients in group I (r = -0.457 and p value = 0.011 for correlation between ferritin and testosterone and r = -0.908 and p value = 0.001 for correlation between ferritin and testicular volume). Conclusion: Male sex hormone and testicular volume were significantly lower in thalassemic patients with iron overload, significant negative correlation and serum ferritin. Recommendations: Regular follow up for thalassemia patients for early detection of iron overload with regular assessment of puberty as thalassemic patients are vulnerable to develop hypogonadism and may require sex hormone replacement therapy. Copyright © 2016 Bentham Science Publishers.

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Long-term follow-up of fertility and pregnancy in autoimmune diseases after autologous haematopoietic stem cell transplantation.
Massenkeil G., Alexander T., Rosen O., Dorken B., Burmester G., Radbruch A., Hiepe F., Arnold R.
Embase
Rheumatology International. 36 (11) (pp 1563-1568), 2016. Date of Publication: 01 Nov 2016.
[Article]
AN: 611708650
Issues of fertility and pregnancy require special attention in the long-term care of patients with autoimmune diseases (AD), who are candidates for haematopoietic stem cell transplantation (HSCT). In this single-centre observational study, we report fertility status and pregnancy outcomes in 15 patients (11 female and 4 male) after immunoablation with cyclophosphamide, antithymocyte globulin and autologous CD34+-selected HSCT for severe, refractory AD. The median follow-up after HSCT was 12 years (range 2-16 years). Impaired fertility was observed in six patients (five females and one male) before HSCT based on sexual hormone measurements. Higher age and cumulative cyclophosphamide dosage before HSCT correlated with fertility impairment. Median serum level of follicle-stimulating hormone (FSH) was significantly higher in female patients at 1 year after HSCT compared to baseline values, but premature ovarian failure developed in only one patient. Four women had five pregnancies and six healthy offsprings during follow-up, and no miscarriages were observed. The mothers were in treatment-free remissions during conception. No peripartal flare of their AD occurred. Although AD patients undergoing HSCT are at risk of developing infertility, pre-HSCT treatment and patients’ age seem to have higher impact on long-term fertility status than HSCT itself. HSCT offers the opportunity to conceive during treatment-free remissions with favourable pregnancy outcomes. Copyright © 2016, Springer-Verlag Berlin Heidelberg.
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Effect of testosterone on hepcidin, ferroportin, ferritin and iron binding capacity in patients with hypogonadotropic hypogonadism and type 2 diabetes.

Dhindsa S., Ghanim H., Batra M., Kuhadiya N.D., Abuaysheh S., Green K., Makdissi A., Chaudhuri A., Dandona P.

Context: As the syndrome of hypogonadotropic hypogonadism (HH) is associated with anaemia and the administration of testosterone restores haematocrit to normal, we investigated the potential underlying mechanisms. Design: Randomized, double-blind, placebo-controlled trial.

Methods: We measured basal serum concentrations of erythropoietin, iron, iron binding capacity, transferrin (saturated and unsaturated), ferritin and hepcidin and the expression of ferroportin and transferrin receptor (TR) in peripheral blood mononuclear cells (MNC) of 94 men with type 2 diabetes. Forty-four men had HH (defined as subnormal free testosterone along with low or normal LH concentrations) while 50 were eugonadal. Men with HH were randomized to testosterone or placebo treatment every 2 weeks for 15 weeks. Blood samples were collected at baseline, 3 and 15 weeks after starting treatment. Twenty men in testosterone group and 14 men in placebo group completed the study. Results: Haematocrit levels were lower in men with HH.
(41.1 +/- 3.9% vs 43.8 +/- 3.4%, P = 0.001). There were no differences in plasma concentrations of hepcidin, ferritin, erythropoietin, transferrin or iron, or in the expression of ferroportin or TR in MNC among HH and eugonadal men. Haematocrit increased to 45.3 +/- 4.5%, hepcidin decreased by 28 +/- 7% and erythropoietin increased by 21 +/- 7% after testosterone therapy (P < 0.05). There was no significant change in ferritin concentrations, but transferrin concentration increased while transferrin saturation and iron concentrations decreased (P < 0.05). Ferroportin and TR mRNA expression in MNC increased by 70 +/- 13% and 43 +/- 10%, respectively (P < 0.01), after testosterone therapy. Conclusions: The increase in haematocrit following testosterone therapy is associated with an increase in erythropoietin, the suppression of hepcidin, and an increase in the expression of ferroportin and TR. Copyright © 2016 John Wiley & Sons Ltd


Status EMBASE
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Publisher Blackwell Publishing Ltd (E-mail: customerservices@oxonblackwellpublishing.com)
Date Created 20161019
Year of Publication 2016

Frequency of y chromosome microdeletions among Iranian infertile men with azoospermia and severe oligozoospermia: A meta-analysis.
Yousefi-Razin E., Nasiri M.J., Omrani M.D.

Embase
Background: While multiple factors can contribute to male infertility, genetic factors, such as chromosomal disorders or Y-chromosome microdeletion, are responsible for about 10% of male infertility. Considering the role of Y-chromosome microdeletions in men with oligozoospermia who volunteer for in vitro fertilization (IVF), the prevalence of such microdeletions in each particular community needs to be exactly determined. Hence, the present study attempted to analyze the available literature on the frequency of chromosome microdeletion among Iranian infertile men.

Methods: In the first stage, a systematic search was performed on international and Iranian databases including PubMed, Scopus, Web of Science, IranMedex, MEDLIB, and Scientific Information Database in order to extract all relevant studies published until December 1, 2014.

Results: According to the literature review and meta-analysis process, Y chromosome microdeletions were present in about 12.1% (95% CI, 6.5-21.5) of Iranian infertile men with azoospermia and severe oligozoospermia. Conclusion: Because of the presence of Y-chromosome microdeletion in at least 12% of Iranian infertile men, it is necessary all the IVF centers, implement this Y-chromosome microdeletion screening tests in the work-up of male infertility.
Changes in Testosterone Levels and Sex Hormone-Binding Globulin Levels in Extremely Obese Men after Bariatric Surgery.

Boonchaya-Anant P., Laichuthai N., Suwannasrisuk P., Houngngam N., Udomsawaengsup S., Snabboon T.

Embase
Date of Publication: 2016.
[Article]
AN: 612579258

Objective. Obesity is a risk factor for hypogonadotropic hypogonadism in men. Weight loss has been shown to improve hypogonadism in obese men. This study evaluated the early changes in sex hormones profile after bariatric surgery. Methods. This is a prospective study including 29 morbidly obese men. Main outcomes were changes in serum levels of total testosterone (TT), free testosterone (cFT), SHBG, estradiol, adiponectin, and leptin at 1 and 6 months after surgery. Results. The mean age of patients was 31 +/- 8 years and the mean BMI was 56.8 +/- 11.7 kg/m2. Fifteen patients underwent Roux-en-Y gastric bypass and 14 patients underwent sleeve gastrectomy. At baseline, 22 patients (75.9%) had either low TT levels (<10.4 nmol/L) or low cFT levels (<225 pmol/L). Total testosterone and SHBG levels increased significantly at 1 month after surgery (p < 0.001). At 6 months after surgery, TT and cFT increased significantly (p < 0.001) and 22 patients (75.9%) had normalized TT and cFT levels. There were no changes in estradiol levels at either 1 month or 6 months after surgery. Conclusions. Increases in TT and SHBG levels occurred early at 1 month after bariatric surgery while improvements in cFT levels were observed at 6 months after bariatric surgery. Copyright © 2016 Patchaya Boonchaya-anant et al.

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Outdoor air pollution and sperm quality.
Lafuente R., García-Blaquez N., Jacquemin B., Checa M.A.
Embase
Fertility and Sterility. 106 (4) (pp 880-896), 2016. Date of Publication: 15 Sep 2016.
[Review]
AN: 612579964
Exposure to air pollution has been clearly associated with a range of adverse health effects, including reproductive toxicity, but its effects on male semen quality are still unclear. We performed a systematic review (up to June 2016) to assess the impact of air pollutants on sperm quality. We included 17 semi-ecological, panel, and cohort studies, assessing outdoor air pollutants, such as PM2.5, PM10, NOx, SO2, and O3, and their effects on DNA fragmentation, sperm count, sperm motility, and sperm morphology. Thirteen studies assessed air pollution exposure measured environmentally, and six used biomarkers of air pollution exposure (two did both). We rated the studies using the Newcastle-Ottawa Scale and assessed with the exposure method. Taking into account these factors and the number of studies finding significant results (positive or negative), the evidence supporting an effect of air pollution on DNA fragmentation is weak but suggestive, on sperm motility is limited and probably inexistent, on lower sperm count is inconclusive, and on sperm morphology is very suggestive. Because of the diversity of air pollutants and sperm parameters, and the studies' designs, we were unable to perform a meta-analysis. In summary, most studies concluded that outdoor air pollution affects at least one of the four semen quality parameters included in the review. However, results lack consistency, and furthermore, studies were not comparable. Studies using standardized air pollution and semen
measures are required to obtain more reliable conclusions. PROSPERO Registration Number CRD42015007175. Copyright © 2016 American Society for Reproductive Medicine

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601.
Have the Testosterone Trials demonstrated the effectiveness of testosterone therapy in older men without classical hypogonadism?
Gan E.H., Quinton R.
Embase
[Article]
AN: 612600736
The ‘Testosterone Trials’ (TTT) are an interlinked and coordinated series of seven US National Institutes of Health (NIH)-sponsored, double-blinded, placebo controlled studies examining the potential benefits of testosterone therapy in a hyper-selected cohort of older men.1 TTT aimed to evaluate the impact of testosterone therapy on symptoms commonly associated with male ageing and also postulated to relate to testosterone deficiency, but were not powered to detect adverse outcomes. Findings from the three lead studies, focusing on vitality, sexual and physical function, were recently published.1 These three lead studies comprised 790 men (having screened 51,085 applicants) aged 65 years and older, with an average serum total testosterone concentration less than 275 ng/dl (9.5 nmol/l), from morning venepuncture on two separate days. Participants received either testosterone or placebo gel for 1 year. Each man could participate in one or more of the three trials, depending on their reported symptoms in relation to impairment of sexual function, physical function and/or vitality. In order to evaluate efficacy, assessments were made every three months from baseline to end-of-study at 12 months. Testogel (Androgel 1%) was initiated at 5 g daily and the dose titrated so as to achieve serum total testosterone concentrations in what would be the mid normal range for men aged between 19 and 40. A statistically significant improvement in sexual activity from baseline was observed in the treatment arm, as ascertained by the Psychosexual Daily Questionnaire score; this emerged from the Sexual Function Trial itself and also when data from all three trials were combined: OR 0.58 (p < 0.001) and 0.62 (p < 0.001), respectively. A better response was associated with a greater increase in testosterone level. Sexual desire and erectile function also improved with a treatment effect of 2.93 (p < 0.001) and 2.64 (p < 0.001), respectively. However, the magnitude of these responses began to decline in a linear manner from 9 months until observations ceased at the study end-point of 12 months. The Physical Function Trial examined the percentage of men whose 6-min walking distance increased by at least 50 m over the course of the study, and failed to identify any benefit from testosterone therapy, although a small but significant improvement was noted when data from all three studies were pooled (20.5% in T arm vs 12.6% receiving placebo: OR 1.75; p = 0.003). The Vitality Trial likewise failed to identify any significant improvements in this domain for the testosterone arm, although there was a statistically significant difference in PANAS (positive and negative affect schedule) scores compared with the
placebo arm when data from all three studies were pooled, suggesting slightly better mood and lower severity of depressive symptoms with testosterone treatment. Overall, testosterone therapy increased levels of free testosterone, estradiol and dihydrotestosterone, but unsurprisingly did not increase levels of sex hormone binding globulin. No significant adverse effects were observed in the treatment arms and no significant between-group differences were observed in cardiac adverse events in the 12-month study period. However, the study was a priori underpowered for evaluation of safety. Copyright © 2016 Royal College of Physicians of Edinburgh.

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Year of Publication
2016

602.
Cigarette Smoking and Semen Quality: A New Meta-analysis Examining the Effect of the 2010 World Health Organization Laboratory Methods for the Examination of Human Semen.
Embase
European Urology. 70 (4) (pp 635-645), 2016. Date of Publication: 01 Oct 2016.
[Review]
AN: 610052992
Objective Approximately 37% of men of reproductive age smoke cigarettes, with Europe having the highest tobacco use among all the World Health Organization (WHO) regions. Toxins from tobacco smoking can potentially affect sperm development and function, with a negative effect on semen parameters. Given the high prevalence of smoking and recent changes in the WHO laboratory methods for the examination of human semen, the role of this exposure in face of new
WHO methods needs to be clarified. Evidence acquisition We conducted a systematic review, followed by a meta-analysis, to determine whether cigarette smoking affects human semen parameters. PubMed, Saint Joseph's University Discover, and Google Scholar were used to identify relevant studies published after release of the latest WHO methods for laboratory evaluation of human semen. Participants were from fertility/urologic clinics and andrology laboratories. The outcome measures were semen volume, sperm concentration, motility, and morphology, the parameters usually used in clinical settings to assess fertility. Evidence synthesis Twenty studies with 5865 participants were included in the meta-analysis. Exposure to cigarette smoking was associated with reduced sperm count (mean difference [MD]: -9.72 x 106/ml; 95% confidence interval [CI], -13.32 to -6.12), motility (MD: -3.48%; 95% CI, -5.53 to -1.44), and morphology (MD: -1.37%; 95% CI, -2.63 to -0.11). Subgroup analyses indicated that effect size was higher in infertile men than in the general population and in moderate/heavy smokers than in mild smokers. The overall effect size on semen volume, sperm count, and motility remained similar when 2010 and earlier WHO manuals were used for semen analysis but was lower with regard to sperm morphology. Conclusions Our results suggest that cigarette smoking has an overall negative effect on semen parameters. The latest WHO laboratory methods for the examination of human semen had a minimal impact on the magnitude of effect size, thus confirming the observed negative effect of smoking on conventional semen parameters. Patient summary A new systematic review and meta-analysis comprising 5865 men shows that cigarette smoking is associated with reduced sperm count and motility. Deterioration of semen quality is more pronounced in moderate and heavy smokers. Copyright © 2016 European Association of Urology Status EMBASE Institution (Sharma) Department of Health Services, Saint Joseph's University, Philadelphia, PA, United States (Harlev) Fertility and IVF Unit, Soroka University Medical Center, Ben Gurion University of the Negev, Beer Sheva, Israel (Harlev, Agarwal) American Center for Reproductive Medicine, Cleveland Clinic, Cleveland, OH, United States (Esteves) ANDROFERT, Andrology and Human Reproduction Clinic, Referral Center for Male Reproduction, Campinas, SP, Brazil Publisher Elsevier B.V. Date Created 20161012 Year of Publication
Epigenetics in male reproduction: Effect of paternal diet on sperm quality and offspring health. Schagdarsurengin U., Steger K.

Embase

[Review]
AN: 611990525

Epigenetic inheritance and its underlying molecular mechanisms are among the most intriguing areas of current biological and medical research. To date, studies have shown that both female and male germline development follow distinct paths of epigenetic events and both oocyte and sperm possess their own unique epigenomes. Fertilizing male and female germ cells deliver not only their haploid genomes but also their epigenomes, which contain the code for preimplantation and postimplantation reprogramming and embryonal development. For example, in spermatozoa, DNA methylation profile, DNA-associated proteins, protamine 1:protamine 2 ratio, nucleosome distribution pattern, histone modifications and other properties make up a unique epigenetic landscape. However, epigenetic factors and mechanisms possess certain plasticity and are affected by environmental conditions. Paternal and maternal lifestyle, including physical activity, nutrition and exposure to hazardous substances, can alter the epigenome and, moreover, can affect the health of their children. In male reproductive health, data are emerging on epigenetically mediated effects of a man's diet on sperm quality, for example through phytochemicals, minerals and vitamins, and nutritional support for subfertile men is already being used. In addition, studies in animal models and human epidemiological data point toward a transgenerational effect of the paternally contributed sperm epigenome on offspring health.

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Publisher
Nature Publishing Group (Houndmills, Basingstoke, Hampshire RG21 6XS, United Kingdom)
The effect of compound herbal remedy used in male infertility on spermatogenesis and pregnancy rate.

Ouladsahebmadarek E., Giasi G.S., Khaki A., Ahmadi Y., Farzadi L., Ghasemzadeh A., Hajizade K.

Embase

AN: 612379011

Objectives: Nowadays, male infertility is one of the most common issues in the medical field and the main reason for it is impaired sperm production. Assisted Reproductive Techniques (ARTs) used for treatment of infertile couples are too costly. Currently, using herbal medicine due to lower side effects and cost has gained special significance. In this study, the effect of combination of several plants was evaluated on male infertility and pregnancy rate.

Materials and Methods: In this clinical trial, 40 infertile men referring to Alzahra hospital were randomly selected to take a combination of 7 plants including Allium cepa, Zingiber officinale, Ocimum basilicum, Cinnamomum verum, Citrus sinensis' peel, Citrullus lanatus'seeds and Daucus carota' seeds in a form of 700 mg capsule, once daily for 6 months. Before and after treatment, the patients' blood and semen samples were collected and analyzed.

Results: The number of sperms (P = 0.001), overall motility (P = 0.002), forward movement (P = 0.002), and normal morphology of sperms (P = 0.006) after treatment showed significant improvement. Also patients' blood glucose levels meaningfully reduced after treatment (P = 0.036). The total volume of semen, total cholesterol, testosterone, and LH levels did not significantly differ with use of the compound herbal medicine. Seven couples during the study and after six months of receiving medication got pregnant.

Conclusion: Consumption of compound herbal medicine with the lowest risk and cost, significantly improves sperm parameters. It seems that the mechanism of action is through counteracting the effects of oxidative stress. Copyright © 2016 The Author(s).
The effect of seasonal variation on sexual behaviors in males and its correlation with hormone levels: A prospective clinical trial.

Demir A., Uslu M., Arslan O.E.

Embase


Introduction

We examined the effect of seasonal variation on sexual behavior and its relationship with testosterone levels. The existence of the inhibiting effect of cold stress on sexual behavior and testosterone levels was our hypothesis.

Material and methods

A total of 80 cases, aged between 20 and 35 years old, were enrolled. Blood samples for testosterone, FSH, LH, and prolactin were obtained twice from each participant at the same time of day (before 10 am). The first samples were taken in January and February, the months which have the average lowest heat days (-15.9°C and -14.6°C, respectively) in our region. The second samples were taken in July and August, which has the average highest heat days (25.4°C and 26.1°C, respectively) in our region. Two times IIEFs (International Index of Erectile Function) were fulfilled at the same day of taking blood samples. The frequency of sexual thoughts and ejaculation were questioned by asking "How many times did you imagine having sex?" and "How many times did you ejaculate in a week?". The body mass index of the participants in the study
was calculated in the winter and in the summer. Results There were significant differences in terms of IIEF scores, frequency of sexual thoughts and ejaculations, BMI (Body mass index), and both testosterone and FSH levels between the winter and summer measurements. We did not find any significant differences with regards to prolactin and LH levels. Conclusions Although testosterone levels are within normal limits in both seasons, its level in cold months is less than in hot months. Testosterone levels can change according to the season. The impact of cold seasons in particular should be taken into account when evaluating testosterone levels and sexual status, as well as the other influences (social, cultural).   Copyright © 2016 Polish Urological Association. All rights reserved.

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20161012
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2016

Comparison of quality of life, sexual satisfaction and marital satisfaction between fertile and infertile couples.
Masoumi S.Z., Garousian M., Khani S., Oliaei S.R., Shayan A.
Embase
International Journal of Fertility and Sterility. 10 (3) (pp 290-296), 2016. Date of Publication: October-December 2016.
[Article]
AN: 612377271
Background: Fertility plays an important role in sexual and psychological function in families. Infertility can result in major emotional, social, and mental disorders, including a reduction in satisfaction with marital life and quality of life. The present study aimed to compare the quality of life and marital satisfaction and sexual satisfaction between fertile and infertile couples. Materials
and Methods: This analytical cross-sectional study was conducted on 250 couples at the Fatemiyeh Educational Research Center affiliated to Hamadan University of Medical Sciences, Hamadan, Iran, from May to August in 2014. The subjects were randomly selected from the patients referred to this center using a table of random numbers. They were then allocated into two groups of infertile group (n=125) and fertile group (n=125). The study participants completed World Health Organization Quality of Life-BREF (WHOQOL-BREF) questionnaire, Linda Berg's Sexual Satisfaction Scale, and Enrich Marital Satisfaction Scale. Then, the data were entered into the SPSS version16 for statistical analysis. The Chi-square and Mann-Whitney tests were also applied to compare the data between the groups. Results: The results revealed no significant difference between the two groups regarding demographic and general health variables. The mean scores of sexual satisfaction were 63.67 +/- 13.13 and 46.37 +/- 7.72 in the fertile and infertile couples, respectively. Furthermore, the mean scores of marital satisfaction were also 44.03 +/- 9.36 and 36.20 +/- 4.03 in the fertile and infertile groups, respectively. Our finding demonstrated that the fertile couples obtained significantly higher mean scores of quality of life as well as lower mean scores of sexual satisfaction and marital satisfaction as compared to the infertile ones (P<0.001). Conclusion: According to the results, the fertile couples obtained significantly higher quality of life and lower sexual satisfaction and marital satisfaction as compared to the infertile ones. Therefore, holding consultation programs and conducting more studies are necessary for improving the quality of life and promoting sexual and marital satisfaction in infertile couples. Copyright © 2016, Royan Institute (ACECR). All Rights Reserved.

Background: Few studies have been conducted on the infertility problems in Iran. This study aimed to investigate the prevalence of infertility problems and related factors in Iranian infertile patients. Materials and Methods: In this cross sectional study, 405 infertile patients referred to Royan Institute, Tehran, Iran, between 2014 and 2015, were selected by simple random sampling. Participants completed the Fertility Problem Inventory (FPI) including 46 questions in five domains (social concern, sexual concern, relationship concern, rejection of parenthood, and need for parenthood). Mean difference between male and female was verified using independent samples Student's t test. A generalized linear model (GLM) was also used for testing the effect of variables on the fertility problems. Data was analyzed using Stata software version 13. Results: The mean age (SD) of participants was 31.28 (5.42). Our results showed that 160 infertile men (95.23%) were classified as very high prevalence of infertility problems. Among infertile women, 83 patients (35.02%) were as very high prevalence of infertility problems, and 154 patients (64.98%) were as high prevalence. Age (P<0.001), sex (P<0.001), a history of abortion (P=0.009), failure of previous treatment (P<0.001), and education (P=0.014) had a significant relationship with FPI scores. Conclusion: Bases on the results of current study, an younger male with lower education level, history of abortion and history of previous treatments failure experienced more infertility problems. Copyright © 2016 Royan Institute (ACECR). All rights reserved.
Male infertility during antihypertensive therapy: Are we addressing correctly the problem?.
Lagana A.S., Vitale S.G., Iaconianni P., Gatti S., Padula F.
Embase
International Journal of Fertility and Sterility. 10 (3) (pp 267-269), 2016. Date of Publication:
October-December 2016.
[Article]
AN: 612377260
Male fertility significantly decreased in the last 50 years, as showed in several studies reporting a reduction of sperm counts per ml in the seminal fluid. Several "acute" pharmacological treatments, as antibiotics, could cause subclinical and temporary reduction of male fertility; conversely, long-term medical treatment may severely affect male fertility, although this effect could be considered transient in most of the cases. Thus, nowadays, several long-term pharmacological treatments may represent a clinical challenge. The association between several kind of antihypertensive drugs and reduction of male fertility has been showed in the mouse model, although the modification(s) which may alter this fine-regulated machinery are still far to be elucidated. Furthermore, well-designed observational studies and randomized controlled trials are needed to accurately define this association in human model, meaning a narrative overview synthesizing the findings of literature retrieved from searches of computerized databases. We strongly solicit future human studies (both observational and randomized clinical trials) on large cohorts with adequate statistical power which may clarify this possible association and the effects (reversible or permanent) of each drug. Furthermore, we suggest a close collaboration between general practitioners, cardiologists, and andrologists in order to choose the most appropriate
antihypertensive therapy considering also patient's reproductive desire and possible risk for his fertility. Copyright © 2016 Royan Institute (ACECR). All rights reserved.

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609.
Effects of testosterone and estradiol deficiency on vasomotor symptoms in hypogonadal men.
Embase
[Article]
AN: 612434710
Context: The hormonal basis of vasomotor symptoms (VMS) in hypogonadal men is incompletely understood. Objective: To determine the contributions of testosterone and estradiol deficiency to VMS in hypogonadal men. Design: Two randomized trials were conducted sequentially between September 2004 and April 2011. Controls were recruited separately. Setting: A single-site academic medical center. Participants: Healthy men ages 20-50, with normal serum testosterone levels. Intervention: Cohort 1 (n = 198, 81% completion) received goserelin acetate every 4 weeks to suppress gonadal steroids and were randomized to placebo or 1.25, 2.5, 5, or 10 g of testosterone gel daily for 16 weeks. Cohort 2 (n = 202, 78% completion) received the same
regimen as cohort 1 plus anastrozole to block aromatization of testosterone. Controls (n = 37, 89% completion) received placebos for goserelin acetate and testosterone. Main Outcome Measures: Incidence of visits with VMS. This was a preplanned secondary analysis. Results: VMS were reported at 26% of visits in cohort 1, and 35% of visits in cohort 2 (P = .02), demonstrating an effect of estradiol deficiency. When adjacent estradiol level groups in cohort 1 were compared, the largest difference in VMS incidence was observed between the 5-9.9 and 10-14.9 pg/mL groups (38% vs 16%, P < .001). In cohort 2, the 10-g testosterone group differed significantly from placebo (16% vs 43%, P = .048) after adjustment for small differences in estradiol levels, indicating that high testosterone levels may suppress VMS. Conclusions: Estradiol deficiency is the key mediator of VMS in hypogonadal men. At high levels, testosterone may have a suppressive effect.
An evidence-based approach to medicinal plants for the treatment of sperm abnormalities in traditional Persian medicine.

Tahvilzadeh M., Hajimahmoodi M., Toliyat T., Karimi M., Rahimi R.

Andrologia. 48 (8) (pp 860-879), 2016. Date of Publication: 01 Oct 2016.

Infertility is defined as inability of a sexually active couple to conceive after 1 year of regular intercourse without contraception. Male factors account for 20%-50% of cases of infertility. The aim of this study was to review medicinal plants that proposed to improve sperm abnormalities in traditional Persian medicine. For this purpose, PubMed, Scopus, GoogleScholar and Cochrane library were explored for medicinal plants used in traditional Persian medicine for sperm abnormalities to obtain studies giving any evidence for their efficacy and pharmacological mechanisms related to male infertility. Data were collected for the years 1966 to March 2015. For some of them, including Chlorophytum borivilianum, Crocus sativus, Nigella sativa, Sesamum indicum, Tribulus terrestris, Mucuna pruriens and Withania somnifera, more reliable evidence was found. The mechanisms involved in the beneficial effects of medicinal plants in sperm abnormalities are antioxidant, anti-inflammatory, anti-oedematous and venotonic activity as well as containing precursors for sperm production and increasing blood testosterone level. Various phytochemical categories including saponins, phytosterols, carotenoids, oxygenated volatile compounds, phenolic compounds and alkaloids seem to be responsible for these beneficial effects. Further studies are recommended for obtaining more conclusive results about the efficacy and safety of the mentioned medicinal plants. Copyright © 2016 Blackwell Verlag GmbH

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The fertility quality of life questionnaire (FertiQoL) relational subscale: Psychometric properties and discriminant validity across gender.

Donarelli Z., Lo Coco G., Gullo S., Salerno L., Marino A., Sammartano F., Allegra A.

Embase Human Reproduction. 31 (9) (pp 2061-2071), 2016. Date of Publication: 2016.

[Article]

AN: 612436270

Study question: Is the Fertility Quality of Life Questionnaire (FertiQoL)-Relational Scale a valid measure to assess the relational domain regarding quality of life in women and men undergoing infertility treatment? summary answer: The FertiQoL-Relational scale (FertiQoL-REL) showed good psychometric properties and captured core aspects of couple relationships. what is known already: FertiQoL has become a gold standard for the assessment of infertility-related quality of life in patients undergoing assisted reproduction treatment (ART). Despite its growing importance, no previous studies have examined the convergent validity of the FertiQoL-REL and its discriminant validity across gender. study design, size, duration: Baseline cross-sectional data as part of a longitudinal study of infertile couples undergoing an ART between February 2013 and January 2015. participants/materials, setting, methods: Five hundred and eighty-nine patients (301 females and 288 males), prior to starting an ART in a private clinic, filled in the Fertility Quality of Life Questionnaire (FertiQoL) and several measures of the marital relationship (Dyadic Adjustment Scale, Marital Commitment Inventory, and ENRICH Marital Satisfaction Scale) and infertility-related distress (Fertility Problem Inventory). main results and the role of chance:
Confirmatory factor analysis showed that the FertiQoL four-factor solution provided a good fit for the observed data. Reliability of the FertiQoL-REL was higher for women than men. Significant correlations between the FertiQoL-REL scores and all the other measures of marital relationship were found for both women and men. FertiQoL-REL scores did not differ significantly in women and men. The FertiQoL-REL was able to differentiate subjects as regards the Dyadic Adjustment Scale and ENRICH Marital Satisfaction Scale threshold. Limitations, reasons for caution: Findings are limited because the data were obtained from only one Italian private clinic. Wider implications of the findings: FertiQoL-REL threshold scores are useful for identifying those patients undergoing ART who are more likely to report poor or good relationship quality. Clinicians should tailor their counselling strategies to the positive qualities in a couple's relationship, so as to reinforce the overall quality of life, especially among women, and to support patients in tackling the psychological burden, so that they can either continue treatment or choose discontinuation.

Study funding/competing interest(s): This research was supported by funds provided by Centro Andros S.r.l., Palermo, Italy. The authors declare no financial or commercial conflicts of interest in this study. Trial registration number: Not necessary. Copyright © The Author 2016.

Embase

[Article]

AN: 612436225

Study question: Does the sperm DNA fragmentation index (DFI) improve depending on the FSH receptor (FSHR) genotype as assessed by the nonsynonymous polymorphisms rs6166 (p.N680S) after 3 months of recombinant FSH treatment in men with idiopathic infertility?

Summary answer: FSH treatment significantly improves sperm DFI only in idiopathic infertile men with the p.N680S homozygous N FSHR. What is known already: FSH, fundamental for spermatogenesis, is empirically used to treat male idiopathic infertility and several studies suggest that DFI could be a candidate predictor of response to FSH treatment, in terms of probability to conceive. Furthermore, it is known that the FSHR single nucleotide polymorphism (SNP) rs6166 (p.N680S) influences ovarian response in women and testicular volume in men.

Study design, size and duration: A multicenter, longitudinal, prospective, open-label, two-arm clinical trial was performed. Subjects enrolled were idiopathic infertile men who received 150 IU recombinant human FSH s.c. every other day for 12 weeks and were followed-up for a further 12 weeks after FSH withdrawal. Patients were evaluated at baseline, at the end of treatment and at the end of follow-up.

Participants/materials, setting, methods: Eighty-nine men with idiopathic infertility carrier of the FSHR p.N680S homozygous N or S genotype, FSH < 8 IU/l and DFI > 15%, were enrolled. A total of 66 patients had DFI analysis completed on at least two visits. DFI was evaluated in one laboratory by TUNEL/PI (propidium iodide) assay coupled to flow cytometry, resolving two different fractions of sperm, namely the 'brighter' and 'dimmer' sperm DFI fractions. Main results and the role of chance: Thirty-eight men (57.6%) were carriers of the p.N680S homozygous N and 28 (42.4%) of the homozygous S FSHR. Sperm concentration/number was highly heterogeneous and both groups included men ranging from severe oligozoospermia to normozoospermia. Total DFI was significantly lower at the end of the study in homozygous carriers of the p.N680S homozygous N versus p.N680S S allele (P = 0.008). Total DFI decreased significantly from baseline to the end of the study (P = 0.021) only in carriers of the p.N680S homozygous N polymorphism, and this decrease involved the sperm population containing vital sperm (i.e. brighter sperm) (P = 0.008). The dimmer sperm DFI fraction, including only nonvital sperm, was significantly larger in p.N680S S homozygous patients than in...
homozygous N men (P = 0.018). Total DFI was inversely related to total sperm number (P = 0.020) and progressive sperm motility (P = 0.014). When patients were further stratified according to sperm concentration (normozoospermic versus oligozoospermic) or -211G>T polymorphism in the FSHB gene (rs10835638) (homozygous G versus others), the significant improvement of sperm DFI in FSHR p.N680S homozygous N men was independent of sperm concentration and associated with the homozygous FSHB -211G>T homozygous G genotype. Limitations, reasons for caution: The statistical power of the study is 86.9% with alpha error 0.05. This is the first pharmacogenetic study suggesting that FSH treatment induces a significant improvement of total DFI in men carriers of the p.N680S homozygous FSHR; however, the results need to be confirmed in larger studies using a personalized FSH dosage and treatment duration. Wider implications of the findings: The evaluation of sperm DFI as a surrogate marker of sperm quality, and of the FSHR SNP rs6166 (p.N680S), might be useful to predict the response to FSH treatment in men with idiopathic infertility. Study funding/competing interest(s): The study was supported by an unrestricted grant to M.S. and H.M.B. from Merck Serono that provided the drug used in the study. MS received additional grants from Merck Serono and IBSA as well as honoraria from Merck Serono. The remaining authors declare that no conflicts of interest are present. Trial registration number: EudraCT number 2010-020240-35. Copyright © The Author 2016.

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613.
Klinefelter syndrome and fertility: Sperm preservation should not be offered to children with Klinefelter syndrome.
Embase
[Review]
AN: 612436207
Study question: Should fertility preservation be offered to children with Klinefelter syndrome (KS)?
summaryanswer: Current evidence shows that fertility preservation should not be offered to adolescents with KS younger than 16 years because of lower retrieval rates for germ cells by testicular sperm extraction (TESE) compared with retrieval rates for adolescents and adults between 16 and 30 years. what is known already: KS, the most common chromosomal disorder in men leading to non-obstructive azoospermia, is caused by the presence of at least one additional X chromosome. The onset of puberty in adolescents with KS leads to progressive degeneration of the testicular environment. The impact of the subsequent tissue degeneration on fertility potential of patients with KS is unknown, but in previous literature it has been suggested that fertility preservation should be started in adolescents as early as possible. However spermatozoa can be found by TESE in about 50% of adults with KS despite severe testicular degeneration. This review discusses the current evidence for fertility preservation in children and adolescents and possible prognostic markers for fertility treatment in KS. study design, size, duration: An extensive literature search was conducted, searching Pubmed, Embase, Cinahl and Web of Science from origin until April 2016 for 'Klinefelter syndrome' and 'fertility' and various
participants/materials, setting, methods: In total 76 studies were found to be eligible for inclusion in this review. Information from the papers was extracted separately by two authors. main results and the role of chance: Various studies have shown that pre-pubertal children with KS already have a reduced number of germ cells despite a normal hormonal profile during childhood. The presence of spermatozoa in the ejaculate of adolescents with KS is extremely rare. Using TESE, the retrieval rates of spermatozoa for adolescents younger than 16 years old are much lower (0-20%) compared with those for adolescents and young adults between 16 and 30 years old (40-70%). Although spermatogonia can be found by TESE in about half of the peri-pubertal adolescents, there are currently no clinically functional techniques for their future use. Children and adolescents need to be informed that early fertility preservation before the age of 16 cannot guarantee fertility later in life and may even reduce the chances for offspring by removing functional immature germ cells which may possibly develop into spermatozoa after puberty. Furthermore, except for the age of patients with KS, there are no identified factors that can reliably be used as a predictive marker for fertility preservation.

limitations, reasons for caution: Most of the evidence presented in this review is based on studies including a small number of adolescents with KS. Therefore, the studies may have been underpowered to detect clinically significant differences for their various outcomes, especially for potential predictive factors for fertility preservation, such as hormone levels. Furthermore, the population of patients with KS diagnosed during childhood might be different from the adult population with KS where the diagnosis is based on infertility. Results based on comparisons between the two groups must be interpreted with caution.

wider implications of the findings: Despite the limitations, this review summarizes the current evidence for managing fertility preservation in patients with KS to provide optimal health care.

study funding/competing interests: There was no funding for this study. S.F., Y.H., K.D., W.L.M.N., D.S., H.L.C.-v.d.G. and L.R. declare to have no conflicts of interests. D.D.M.B. reports grants from Merck Serono, grants from Ferring and grants from MSD, outside the submitted work. K.F. reports personal fees from MSD (commercial sponsor), personal fees from Ferring (commercial sponsor), grants from Merck-Serono (commercial sponsor), grants from Ferring (commercial sponsor) and grants from MSD (commercial sponsor), outside the submitted work.

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614.
Prediction model for live birth in ICSI using testicular extracted sperm.
Meijerink A.M., Cissen M., Mochtar M.H., Fleischer K., Thoonen I., De Melker A.A., Meissner A.,
Repping S., Braat D.D.M., VanWely M., Ramos L.
Embase
[Article]
AN: 612436199
Study question: Which parameters have a predictive value for live birth in couples undergoing
ICSI after successful testicular sperm extraction (TESE-ICSI)? summaryanswer: Female age, a
first or subsequent started TESE-ICSI cycle, male LH, male testosterone, motility of the
spermatozoa during the ICSI procedure and the initial male diagnosis before performing TESE
were identified as relevant and independent parameters for live birth after TESE-ICSI. what is
known already: In reproductive medicine prediction models are used frequently to predict
treatment success, but no prediction model currently exists for live birth after TESE-ICSI.
study
design, size, duration: Aretrospective cohort studybetween 2007 and 2015 in two academic
hospitals including 1559 TESEICSI cycles. The prediction model was developed using data from
one centre and validation was performed with data from the second centre. participants/materials,
setting, methods: We included couples undergoing ICSI treatment with surgically retrieved sperm
from the testis for the first time. In the development set we included 526 couples undergoing 1006
TESE-ICSI cycles. In the validation set we included 289 couples undergoing 553 TESE-ICSI
cycles. Multivariable logistic regression models were constructed in a stepwise fashion (P < 0.2
for entry). The external validation was based on discrimination and calibration. main results and
the role of chance: We included 224 couples (22.3%) with a live birth in the development set. The
occurrence of a live birth was associated with lower female age, first TESE-ICSI cycle, lower male LH, higher male testosterone, the use of motile spermatozoa for ICSI and having obstructive azoospermia as an initial suspected diagnosis. The area under the receiver operating characteristic (ROC) curve was 0.62. From validation data, the model had moderate discriminative capacity (c-statistic 0.67, 95% confidence interval: 0.62-0.72) but calibrated well, with a range from 0.06 to 0.56 in calculated probabilities. limitations, reasons for caution: We had a lack of data about the motility of spermatozoa during TESE, therefore, we used motility of the spermatozoa used for ICSI after freeze-thawing, information which is only available during treatment. We had to exclude data on paternal BMI in the model because too many missing values in the validation data hindered testing. We did not include a histologic diagnosis, which would have made our data set less heterogeneous and, finally, our model may not be applicable in centres which have a different policy for the indication for performing sperm extraction. The prognostic value of the model is limited because of a low 'area under the curve'. wider implications of the findings: This model enables the differentiation between couples with a lower high chance to reach a live birth using TESE-ICSI. As such it can aid in the counselling of patients and in clinical decision-making. study funding/competing interest(s): This study was partly supported by an unconditional grant from Merck Serono (to D.D.M.B. and K.F.) and by the Department of Obstetrics and Gynaecology of Radboud University Medical Center, Nijmegen, The Netherlands, The Department of Obstetrics and Gynaecology, Jeroen Bosch Hospital, Den Bosch, The Netherlands, and the Department of Obstetrics and Gynaecology, Academic Medical Center, Amsterdam, The Netherlands. Merck Serono had no influence in concept, design, nor elaboration of this study. trial registration number: Not applicable. Copyright © The Author 2016.
Prediction model for obtaining spermatozoa with testicular sperm extraction in men with non-obstructive azoospermia.


Embase

Human Reproduction. 31 (9) (pp 1934-1941), 2016. Date of Publication: 2016.

[Article]

AN: 612436188

Study question: Can an externally validated model, based on biological variables, be developed to predict successful sperm retrieval with testicular sperm extraction (TESE) in men with non-obstructive azoospermia (NOA) using a large nationwide cohort? summary answer: Our prediction model including six variables was able to make a good distinction between men with a good chance and men with a poor chance of obtaining spermatozoa with TESE. what is known already: Using ICSI in combination with TESE even men suffering from NOA are able to father their own biological child. Only in approximately half of the patients with NOA can testicular sperm be retrieved successfully. The few models that have been developed to predict the chance of obtaining spermatozoa with TESE were based on small datasets and none of them have been validated externally. study design, size, duration: We performed a retrospective nationwide cohort study. Data from 1371 TESE procedures were collected between June 2007 and June 2015 in the two fertility centres. participants/materials, setting, methods: All men with NOA undergoing their first TESE procedure as part of a fertility treatment were included. The primary end-point was the presence of one or more spermatozoa (regardless of their motility) in the testicular biopsies. We constructed a model for the prediction of successful sperm retrieval, using univariable and multivariable binary logistic regression analysis and the dataset from one centre. This model was then validated using the dataset from the other centre. The area under the receiver-operating characteristic curve (AUC) was calculated and model calibration was assessed. main results and the role of chance: There were 599 (43.7%) successful sperm retrievals after a first TESE procedure. The prediction model, built after multivariable logistic regression analysis,
demonstrated that higher male age, higher levels of serum testosterone and lower levels of FSH and LH were predictive for successful sperm retrieval. Diagnosis of idiopathic NOA and the presence of an azoospermia factor c gene deletion were predictive for unsuccessful sperm retrieval. The AUC was 0.69 (95% confidence interval (CI): 0.66-0.72). The difference between the mean observed chance and the mean predicted chance was <2.0% in all groups, indicating good calibration. In validation, the model had moderate discriminative capacity (AUC 0.65, 95% CI: 0.62-0.72) and moderate calibration: the predicted probability never differed by more than 9.2% of the mean observed probability. Limitations, reasons for caution: The percentage of men with Klinefelter syndrome among men diagnosed with NOA is expected to be higher than in our study population, which is a potential selection bias. The ability of the sperm retrieved to fertilize an oocyte and produce a live birth was not tested. Wider implications of the findings: This model can help in clinical decision-making in men with NOA by reliably predicting the chance of obtaining spermatozoa with TESE. Study funding/competing interest: This study was partly supported by an unconditional grant from Merck Serono (to D.D.M.B. and K.F.) and by the Department of Obstetrics and Gynaecology of Radboud University Medical Center, Nijmegen, The Netherlands, the Department of Obstetrics and Gynaecology, Jeroen Bosch Hospital, Den Bosch, The Netherlands, and the Department of Obstetrics and Gynaecology, Academic Medical Center, Amsterdam, The Netherlands. Merck Serono had no influence in concept, design nor elaboration of this study. Trial registration number: Not applicable. Copyright © The Author 2016.

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Perfluoroalkyl and polyfluoroalkyl substances and measures of human fertility: a systematic review.
Bach C.C., Vested A., Jorgensen K.T., Bonde J.P.E., Henriksen T.B., Toft G.

Critical Reviews in Toxicology. 46 (9) (pp 735-755), 2016. Date of Publication: 20 Oct 2016.

Perfluoroalkyl and polyfluoroalkyl substances (PFASs) are found widespread in the environment and humans. The relation of PFASs to fertility has now been examined in a relatively large number of epidemiologic studies and a synthesis is in order. The aim of this study was to assess the current human epidemiologic evidence on the association between exposure to PFASs and measures of human fertility, with particular emphasis on perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA). Systematic literature searches were initially conducted in MEDLINE and EMBASE and subsequently in references and citations of included papers. Studies were included if they assessed exposure to PFASs in biological samples in relation to reproductive hormones, semen characteristics, or time to pregnancy (TTP). Study characteristics and results were abstracted to predefined forms, and the studies were assessed for the risk of bias and confounding. Sixteen studies investigated the association between PFAS exposure in men and semen parameters, reproductive hormone levels, or TTP. There was a lack of consistent results among the numerous investigated exposure-outcome combinations. However, subtle associations between higher PFOS and lower testosterone or abnormal semen morphology cannot be excluded. Eleven studies assessed the association between PFAS exposure in women and TTP or reproductive hormones levels. Four of eight studies found prolonged TTP with higher PFOS or PFOA, but only one study found an association when restricting to nulliparous women. In men, there is little evidence of an association between PFAS exposure and semen quality or levels of reproductive hormones. For PFOS and PFOA, the literature indicates an association with female fecundability in parous women, which is most likely not causal. Copyright © 2016 Informa UK Limited, trading as Taylor & Francis Group.

Status
Screening for genital chlamydia infection.
Low N., Redmond S., Uuskula A., van Bergen J., Ward H., Andersen B., Gotz H.

Embase
Cochrane Database of Systematic Reviews. 2016 (9) (no pagination), 2016. Article Number: CD010866. Date of Publication: 13 Sep 2016.

[Review]
AN: 612125729

Background: Genital infections caused by Chlamydia trachomatis are the most prevalent bacterial sexually transmitted infection worldwide. Screening of sexually active young adults to detect and treat asymptomatic infections might reduce chlamydia transmission and prevent reproductive tract morbidity, particularly pelvic inflammatory disease (PID) in women, which can cause tubal infertility and ectopic pregnancy. Objectives: To assess the effects and safety of chlamydia screening versus standard care on chlamydia transmission and infection complications in
pregnant and non-pregnant women and in men. Search methods: We searched the Cochrane Sexually Transmitted Infections Group Specialised Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, LILACS, CINAHL, DARE, PsycINFO and Web of Science electronic databases up to 14 February 2016, together with World Health Organization International Clinical Trials Registry (ICTRP) and ClinicalTrials.gov. We also handsearched conference proceedings, contacted trial authors and reviewed the reference lists of retrieved studies. Selection criteria: Randomised controlled trials (RCTs) in adult women (non-pregnant and pregnant) and men comparing a chlamydia screening intervention with usual care and reporting on a primary outcome (C. trachomatis prevalence, PID in women, epididymitis in men or incidence of preterm delivery). We included non-randomised controlled clinical trials if there were no RCTs for a primary outcome. Data collection and analysis: Two review authors independently assessed trials for inclusion, extracted data and assessed the risk of bias. We resolved disagreements by consensus or adjudication by a third reviewer. We described results in forest plots and conducted meta-analysis where appropriate using a fixed-effect model to estimate risk ratios (RR with 95% confidence intervals, CI) in intervention vs control groups. We conducted a pre-specified sensitivity analysis of the primary outcome, PID incidence, according to the risks of selection and detection bias. Main results: We included six trials involving 359,078 adult women and men. One trial was at low risk of bias in all six specific domains assessed. Two trials examined the effect of multiple rounds of chlamydia screening on C. trachomatis transmission. A cluster-controlled trial in women and men in the general population in the Netherlands found no change in chlamydia test positivity after three yearly invitations (intervention 4.1% vs control 4.3%, RR 0.96, 95% CI 0.84 to 1.09, 1 trial, 317,304 participants at first screening invitation, low quality evidence). Uptake of the intervention was low (maximum 16%). A cluster-randomised trial in female sex workers in Peru found a reduction in chlamydia prevalence after four years (adjusted RR 0.72, 95% CI 0.54 to 0.98, 1 trial, 4465 participants, low quality evidence). Four RCTs examined the effect of chlamydia screening on PID in women 12 months after a single screening offer. In analysis of four trials according to the intention-to-treat principle, the risk of PID was lower in women in intervention than control groups, with little evidence of between-trial heterogeneity (RR 0.68, 95% CI 0.49 to 0.94, I2 7%, 4 trials, 21,686 participants, moderate quality evidence). In a sensitivity analysis, the estimated effect of chlamydia screening in two RCTs at low risk of detection bias (RR 0.80, 95% CI 0.55 to 1.17) was compatible with no effect and was lower than in two RCTs at high or unclear risk of detection bias (RR 0.42, 95% CI 0.22 to 0.83). The risk of epididymitis in men invited for screening, 12 months after a single screening offer, was 20% lower risk for epididymitis than in those not invited; the confidence interval was wide and compatible with no effect (RR 0.80, 95% CI 0.45 to 1.42, 1 trial, 14,980 participants, very low quality evidence). We found no RCTs of the effects of chlamydia screening in pregnancy and no trials that measured the harms of chlamydia screening. Authors’
conclusions: Evidence about the effects of screening on C. trachomatis transmission is of low quality because of directness and risk of bias. There is moderate quality evidence that detection and treatment of chlamydia infection can reduce the risk of PID in women at individual level. There is an absence of RCT evidence about the effects of chlamydia screening in pregnancy. Future RCTs of chlamydia screening interventions should determine the effects of chlamydia screening in pregnancy, of repeated rounds of screening on the incidence of chlamydia-associated PID and chlamydia reinfection in general and high risk populations. Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

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2016

618.
Endometrial Injury May Increase the Pregnancy Rate in Patients Undergoing Intrauterine Insemination.
Objective: This study aimed to investigate the effect of endometrial injury using Pipelle catheter in the follicular phase (cycle day 5, 6, or 7) of the stimulation cycle on pregnancy rates in patients undergoing intrauterine insemination. Methods: This prospective randomized controlled study was carried out in the Assisted Reproductive Technology Unit of Ain Shams University Maternity Hospital, Cairo, Egypt, from July 1, 2013 to August 31, 2015. Three hundred sixty women, 20 to 35 years of age, with patent fallopian tubes, mild male factor infertility, or unexplained infertility were recruited. Participants were allocated randomly into 2 groups: experimental arm and control arm. Women in the experimental arm underwent endometrial biopsy using a Pipelle catheter on day 5, 6, or 7 of the stimulation cycle combined with intrauterine insemination. Women in the control group underwent intrauterine insemination with no endometrial biopsy done. The primary outcomes were the clinical and chemical pregnancy rates. Results: Data of 344 participants were statistically analyzed. The chemical pregnancy rate was 23.66% in the experimental arm and 10.85% in the control arm (P = .002). The clinical pregnancy rate was 18.93% in the experimental arm and 7.42% in the control arm (P = .003). Conclusion: Endometrial injury using a Pipelle catheter in the stimulation cycle may improve pregnancy rates in women undergoing intrauterine insemination. Copyright © Society for Gynecologic Investigation.
Association Between Infertility and Sexual Dysfunction in Men and Women.
Berger M.H., Messore M., Pastuszak A.W., Ramasamy R.

Embase
[Review]
AN: 612207162

Introduction
The relation between infertility and sexual dysfunction can be reciprocal. Causes of sexual dysfunction that affect fertility include erectile dysfunction, Peyronie's disease (abnormal penile curvature), low libido, ejaculatory disorders in men, and genito-pelvic pain/penetration disorder (GPPPD) and low sexual desire in women. Aim To review the association between infertility and sexual dysfunction and discuss current management strategies to address sexual disorders in couples with infertility. Methods Peer-reviewed publications from PubMed published from 1980 through February 2016 were identified that related to sexual dysfunction and infertility in men and women. Main Outcome Measures Pathophysiology and management approach of erectile dysfunction, Peyronie's disease, low libido, ejaculatory disorders in men, and GPPPD and low sexual desire in women and how each etiology contributes to sexual dysfunction and infertility in the couple. Results Treating the infertile couple with sexual dysfunction involves addressing underlying conditions such as psychogenic erectile dysfunction, low testosterone, Peyronie's disease in men, and GPPPD and low sexual desire in women. Psychogenic erectile dysfunction can be successfully treated with phosphodiesterase inhibitors. Low testosterone is often identified in men with infertility, but testosterone therapy is contraindicated in men attempting conception. Men with Peyronie's disease have a new treatment option to address their penile curvature-collagenase Clostridium histolyticum injection directly into the penile plaque. GPPPD is a broad disorder that includes vulvodynia and vaginismus and can be treated with topical lubricants and moisturizers. We must address psychosocial factors in women with low sexual desire. Flibanserin and transdermal testosterone (off-label) are novel therapies for women with low sexual desire. Conclusion Sexual dysfunction in a couple with infertility is a complex issue. Management of infertility and sexual dysfunction should involve appropriate medical therapy and addressing the psychosocial concerns of the couple. Copyright © 2016 International Society for Sexual Medicine

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The Varicocele: Clinical Presentation, Evaluation, and Surgical Management. 
Lomboy J.R., Coward R.M.

Seminars in Interventional Radiology. 33 (3) (pp 163-169), 2016. Date of Publication: 01 Sep 2016.

A varicocele is an abnormal dilatation and tortuosity of the veins of the spermatic cord. Although varicoceles are common in the general population and are frequently found on routine physical examinations, they represent the most common correctable cause of male factor infertility. Varicoceles are also often incidental findings on imaging studies, particularly scrotal ultrasound. Importantly, not all varicoceles should be treated equally (or at all), and basic guidelines on the evaluation and indications for treatment of adult varicoceles should be reviewed before counseling and treatment. A semen analysis should be obtained for any male patient of reproductive age considering intervention. The adolescent varicocele is managed much differently than the adult varicocele and remains a source of controversy. This review describes the clinical presentation and the evaluation of adult and pediatric varicoceles, and provides guidance on their diagnosis and workup. It also describes options for surgical repair and the
success and complication rates associated with each surgical approach, ultimately supporting microsurgical subinguinal varicocele repair as the current surgical standard.

Aims: To evaluate the effect of testosterone replacement therapy (TRT) on body composition, insulin sensitivity, oxidative metabolism and glycaemic control in aging men with lowered bioavailable testosterone (BioT) levels and type 2 diabetes mellitus (T2D) controlled on metformin monotherapy. Materials and methods: We conducted a randomized, double-blind, placebo-controlled study in 39 men aged 50-70 years with BioT levels <7.3 nmol/L and T2D treated with metformin monotherapy. Patients were randomized to testosterone gel (TRT, n = 20) or placebo (n = 19) for 24 weeks. Lean body mass (LBM), total and regional fat mass were measured using whole-body dual-energy X-ray absorptiometry scans. Whole-body peripheral insulin sensitivity, endogenous glucose production (EGP) and substrate oxidation were assessed by euglycaemic-
hyperinsulinaemic clamp with glucose tracer and combined with indirect calorimetry. Coefficients (beta) represent the placebo-controlled mean effect of intervention. Results: LBM (beta = 1.9 kg, p = 0.001) increased after TRT, while total fat mass (beta = -1.3 kg, p = 0.009), fat mass trunk (beta = -0.7 kg, p = 0.043), fat mass legs (beta = -0.7 kg, p = 0.025), fat mass arms (beta = -0.3 kg, p = 0.001), and HDL cholesterol (beta = -0.11 mmol/L, p = 0.009) decreased after TRT compared with placebo. Insulin-stimulated glucose disposal rates did not change in response to TRT compared with placebo (p = 0.18). Moreover, glycated haemoglobin, and basal and insulin-stimulated rates of EGP, lipid- and glucose-oxidation were unaltered after TRT. Conclusion: TRT in aging men with lowered BioT levels and T2D controlled on metformin monotherapy improved body composition; however, glycaemic control, peripheral insulin sensitivity, EGP and substrate metabolism were unchanged. Copyright © 2016 John Wiley & Sons Ltd

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In the adult male, testosterone (T) deficiency (TD) also known as male hypogonadism, is a well-established medical condition, which has been recognized for more than a century. T therapy in men with TD was introduced as early as 1940s and was reported to improve overall health with no concomitant serious adverse effects. A wealth of recent studies demonstrated that T therapy in men with TD is associated with increased lean body mass, reduced fat mass and waist circumference, improvement in glycemic control, and reduced obesity. T therapy is also associated with improvements in lipid profiles, amelioration of metabolic syndrome (Met S) components, reduced inflammatory biomarkers, reduced systolic and diastolic blood pressure, and improvements in sexual function. More importantly, T therapy is associated with amelioration of diabetes and reduced mortality. However, few studies, marred with serious methodological and analytical flaws reported between 2010 and 2014, suggested that T therapy is associated with increased cardiovascular (CV) risk. As summarized in this review, a thorough and critical analysis of these studies showed that the risks purported are unsubstantiated and such studies lacked credible scientific and clinical evidence. Moreover, recent observational, registry studies, clinical trials, and meta-analyses, all revealed no increase in CV risks in men receiving T therapy. In this review, the benefits of T therapy in adult men with TD and the lack of credible evidence suggesting that T therapy is linked to increased CV risks are discussed. It should be noted that the literature is replete with studies demonstrating beneficial effects of T therapy on CV and overall health. Copyright © 2016 the American Physiological Society.
Emerging medication for the treatment of male hypogonadism.

Aydogdu A., Swerdloff R.S.

Expert Opinion on Emerging Drugs. 21 (3) (pp 255-266), 2016. Date of Publication: 02 Jul 2016. [Review]

AN: 612023889

Introduction: Male hypogonadism is characterized by inadequate production of Testosterone (T) (hypoandrogenism) and deficiencies in spermatogenesis. The main treatment of male hypogonadism is T replacement therapy (TRT), but for some of the patients, alternative drugs may be more suitable. Areas covered: The available literature of T and alternative treatments for male hypogonadism are discussed. Expert opinion: Transdermal application of T gels are the most commonly used route of T administration. Some oral T formulations are either associated with hepatic toxicity (i.e. methyltestosterone) or short half-lives that require multiple doses per day (i.e. oral testosterone undecanoate). Short acting, injectable T formulations are also available. If the patient prefers not to use daily drugs or short acting injectable formulations, depot formulations such as injectable testosterone undecanoate (TU) may be a good alternative. If the patient has hypogonadotropic hypogonadism and desires fertility or if he is adolescent, instead of TRT, gonadotropins can be started to stimulate testicular growth and spermatogenesis. In obese patients or for the patients having high risks for TRT, off label aromatase inhibitors (AI) and clomiphene citrate (CC), may be considered to stimulate LH, FSH and T levels. In patients with high prostate disease risk, selective androgen receptor modulators may be an alternative treatment but these latter treatments have not had high level evidence. Copyright © 2016 Informa UK Limited, trading as Taylor & Francis Group.
Long-term safety and efficacy of dutasteride in the treatment of male patients with androgenetic alopecia.

Tsunemi Y., Irisawa R., Yoshiie H., Brotherton B., Ito H., Tsuboi R., Kawashima M., Manyak M. 

Embase Journal of Dermatology. 43 (9) (pp 1051-1058), 2016. Date of Publication: 01 Sep 2016. 
[Article] 
AN: 612040048 

Androgenetic alopecia is an androgen-induced pattern of progressive hair loss, which occurs in genetically predisposed people. This study aimed to determine long-term safety, tolerability and efficacy of dutasteride 0.5 mg, an inhibitor of 5-alpha-reductase, in Japanese male patients with androgenetic alopecia. This was a multicenter, open-label, prospective outpatient study (clinicaltrials.gov NCT01831791, GSK identifier ARII14264) in which patients took dutasteride 0.5 mg p.o. once daily for 52 weeks. Primary end-points included adverse event assessment, incidence of drug-related adverse event and premature discontinuations. Secondary end-points included hair growth, hair restoration and global improvement in hair. A total of 120 patients were enrolled, of whom 110 completed 52 weeks of treatment. Nasopharyngitis, erectile dysfunction and decreased libido were the most frequently reported adverse events and most adverse events were mild. Drug-related adverse events were reported with an incidence of 17%, none of which led to study withdrawal. Hair growth (mean target area hair count at week 52), hair restoration (mean target area hair width at week 52) and global appearance of hair (mean of the median score at week 52) improved from baseline during the study. As a potential future treatment option for male androgenetic alopecia, dutasteride 0.5 mg exhibited long-term safety, tolerability and efficacy within this study population. 

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Retrograde ejaculation, painful ejaculation and hematospermia.

Parnham A., Serefoglu E.C.

Embase

Translational Andrology and Urology. 5 (4) (pp 592-601), 2016. Date of Publication: 01 Aug 2016.
[Review]

AN: 611873963

Although there has been an increased interest on premature ejaculation in the recent years, our understanding regarding the disorders of retrograde ejaculation, painful ejaculation and hematospermia remain limited. All three of these conditions require a keen clinical acumen and willingness to engage in thinking outside of the standard established treatment paradigm. The development of novel investigational techniques and treatments has led to progress in the management of these conditions symptoms; however, the literature almost uniformly is limited to small series and rare randomised trials. Further investigation and randomised controlled trials are needed for progress in these often challenging cases. Copyright © Translational Andrology and Urology.

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The drug treatment of delayed ejaculation.
Abdel-Hamid I.A., Elsaied M.A., Mostafa T.

Delayed ejaculation (DE) is an uncommon and a challenging disorder to treat. It is often quite concerning to patients and it can affect psychosocial well-being. Here we reviewed how DE is treated pharmacologically. We also highlighted specific settings where drugs could be introduced to medical practice. Electronic databases were searched from 1966 to February 2016, including PubMed MEDLINE, EMBASE, EBCSO Academic Search Complete, Cochrane Systematic Reviews Database, and Google Scholar using key words; delayed ejaculation, retarded ejaculation, inhibited ejaculation, drugs, treatment, or pharmacology. To achieve the maximum sensitivity of the search strategy and to identify all studies, we combined "delayed ejaculation" as Medical Subject Headings (MeSH) terms or keywords with each of "testosterone" or "cabergoline" or "bupropion" or "amantadine" or "cyproheptadine" or "midodrine" or "imipramine" or "ephedrine" or "pseudoephedrine" or "yohimbine" or "buspirone" or "oxytocin" or "bethanechol" as MeSH terms or keywords. There are a number of drugs to treat patients with DE including: Testosterone, cabergoline, bupropion, amantadine, cyproheptadine, midodrine, imipramine, ephedrine, pseudoephedrine, yohimbine, buspirone, oxytocin, and bethanechol. Although there are many pharmacological treatment options, the evidence is still limited to small trials, case series or case reports. Review of literature showed that evidence level 1 (Double blind randomized clinical trial) studies were performed with testosterone, oxytocin, buspirone or bethanechol treatment. It is concluded that successful drug treatment of DE is still in its infancy. The clinicians need to be aware of the pathogenesis of DE and the pharmacological basis
underlying the use of different drugs to extend better care for these patients. Various drugs are available to address such problem, however their evidence of efficacy is still limited and their choice needs to be individualized to each specific case. Copyright © Translational Andrology and Urology.

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Publisher
AME Publishing Company (E-mail: info@amepc.org)

Epidemiology of delayed ejaculation.
Di Sante S., Mollaioli D., Gravina G.L., Ciocca G., Limoncin E., Carosa E., Lenzi A., Jannini E.A.
Embase
Translational Andrology and Urology. 5 (4) (pp 541-548), 2016. Date of Publication: 01 Aug 2016.

A large body of literature on diminished ejaculatory disorders has been generated without the use of a clear diagnostic definition. Many studies have not distinguished between the orgasm and ejaculation disorders leading to doubtful results. Delayed ejaculation (DE) is one of the diminished ejaculatory disorders, which range from varying delays in ejaculatory latency to a complete inability to ejaculate. The present review is aimed at providing a comprehensive overview of the current knowledge on the definition and epidemiology of diminished ejaculatory disorders. We focus on the acquired diseases, such as benign prostatic hyperplasia (BPH) and specific drug regimens that may cause an iatrogenic form of ejaculatory disorder. In addition, the impact of aging is discussed since the prevalence of DE appears to be moderately but positively
related to age. Finally, we also focus on the importance of the hormonal milieu on male ejaculation. To date, evidence on the endocrine control of ejaculation is derived from small clinical trials, but the evidence suggests that hormones modulate the ejaculatory process by altering its overall latency. Copyright © Translational Andrology and Urology.

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628.
The office management of ejaculatory disorders.
Jiann B.-P.
Embase
Translational Andrology and Urology. 5 (4) (pp 526-540), 2016. Date of Publication: 01 Aug 2016. [Review]
AN: 611873958
Premature ejaculation (PE), delayed ejaculation (DE), anejaculation (AE) and retrograde ejaculation (RE) are four main ejaculatory disorders (EjDs) observed in clinical practice. Despite their high prevalence, EjDs remain underdiagnosed and undertreated. Primary care physicians should incorporate the discussion of sexual health topics into routine visits to facilitate EjD diagnosis and treatment. Because the causes of EjDs are multifactorial, the management of EjDs is etiology-specific and may require a holistic approach. Dapoxetine, a selective serotonin reuptake inhibitor, is the only drug approved for on-demand treatment of lifelong and acquired
PE. In clinical practice, scheduled follow-up visits, risk factor treatment, appropriate dose escalation, adequate sexual attempts, patient education, and partner involvement are critical factors responsible for optimal overall management of PE and dapoxetine treatment outcomes.

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629.
Ejaculatory dysfunction in the treatment of lower urinary tract symptoms.
DeLay K.J., Nutt M., McVary K.T.
Embase
Translational Andrology and Urology. 5 (4) (pp 450-459), 2016. Date of Publication: 01 Aug 2016.
[Review]
AN: 611873950
The link between lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) and sexual dysfunction is well established. Sexual dysfunction can encompass both ejaculatory dysfunction (EjD) and erectile dysfunction (ED). Ejaculatory dysfunction can consist of premature ejaculation, delayed ejaculation, retrograde ejaculation, anejaculation, decreased force of ejaculation and pain upon ejaculation. The impact of different medical and surgical therapies on ejaculatory function will be reviewed. We reviewed the various categories of LUTS treatment including the canonical epidemiology and pathophysiology as well as the surgical and medical treatments for LUTS/BPH. We note that most surgeries and several medical treatments have a certain but ill-defined negative impact on ejaculatory function. Several MISTs and selected
medical therapies appear to have little impact on EjD. Both EjD and BPH are very common disorders in men under the care of an urologist. It is well documented that there is a clinical association between these two entities. Unfortunately many of the medical treatments and almost all surgical treatment impact the ejaculatory function of the patient. The surgical treatment of BPH often leads to retrograde ejaculation while medical treatment leads to anejaculation. Copyright © Translational Andrology and Urology.

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630.

The influence of ginger (Zingiber officinale) on human sperm quality and DNA fragmentation: A double-blind randomized clinical trial.
Hosseini J., Mamaghani A.M., Hosseinifar H., Gilani M.A.S., Dadkhah F., Sepidarkish M.
Embase
[Article]
AN: 611876283

Background: Although the effectiveness of ginger as an antioxidant agent has been exploited, little human research has been conducted on its activity on male reproductive functions.
Objective: This study was designed to investigate the effects of ginger (Zingiber officinale) on sperm DNA fragmentation (SDF) in infertile men. Materials and Methods: This randomized double-blind, placebo-controlled trial with a 1:1 allocation was performed on 100 infertility treatment candidates who were admitted to Royan Institute for Reproductive Biomedicine,
Tehran, Iran. Patients were randomly assigned to receive one of two treatments: ginger and placebo. Patients were given a 3-month oral treatment (members received capsules containing 250 mg of ginger powder twice a day in ginger and a placebo in other group). Before and after treatment, standardized semen samples were obtained to determine sperm concentration, motility, and SDF according to World Health Organization. Results: There was no significant difference between two groups regarding SDF at baseline (53.48, 95%CI: 37.95-69.02) in cases and (56.75, 95%CI: 40.01-73.5) in controls. The average positive percentage of SDF in patients receiving ginger (17.77, 95%CI: 6.16-29.39) was lower compared with placebo (40.54, 95%CI: 23.94-57.13) after three month of treatment (p=0.02). In multivariate analysis, SDF was significantly lower in patients receiving ginger compared with placebo (mean difference: 3.21, 95%CI: 0.78-5.63, p=0.009). There were no significant differences between two groups regarding to semen parameters. Conclusion: The present study has demonstrated that ginger in a controlled study of efficacy was effective in decreasing SDF in infertile men. Copyright © 2016, Research and Clinical Center for Infertility. All rights reserved.
Novel Uses for the Anabolic Androgenic Steroids Nandrolone and Oxandrolone in the Management of Male Health.

Wu C., Kovac J.R.

Embase

Current Urology Reports. 17 (10) (no pagination), 2016. Article Number: 72. Date of Publication: 01 Oct 2016.

[Review]

AN: 611711667

There has recently been renewed interest in novel clinical applications of the anabolic-androgenic steroid (AAS) testosterone and its synthetic derivatives, particularly given with the rising popularity of testosterone supplementation therapy (TST) for the treatment of male hypogonadism. In this manuscript, we provide a brief review of the history of AAS and discuss clinical applications of two of the more well-known AAS: nandrolone and oxandrolone. Both agents exhibit favorable myotrophic/androgenic ratios and have been investigated for effectiveness in numerous disease states. We also provide a brief synopsis of selective androgen receptor modulators (SARMs) and postulate how these orally active, non-aromatizing, tissue-selective agents might be used in contemporary andrology. Currently, the applications of testosterone alternatives in hypogonadism are limited. However, it is tempting to speculate that these agents may one day become accepted as alternatives, or adjuncts, to the treatment of male hypogonadism. Copyright © 2016, Springer Science+Business Media New York.

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Vitamin D deficiency and low ionized calcium are linked with semen quality and sex steroid levels in infertile men.


Human Reproduction. 31 (8) (pp 1875-1885), 2016. Date of Publication: 01 Aug 2016.

[Article]

AN: 611633716

STUDY QUESTION Are low vitamin D levels linked with semen quality and sex steroids in infertile men? SUMMARY ANSWER Infertile men with vitamin D deficiency had lower sperm motility, total numbers of motile sperm, Inhibin B, sex-hormone-binding-globulin (SHBG) and testosterone/estradiol ratio, but higher levels of free sex steroids, than infertile men with normal vitamin D levels. WHAT IS KNOWN ALREADY Low vitamin D levels have been associated with decreased sperm motility in healthy men, but a relationship between vitamin D and calcium with semen quality and especially sex steroids has not been sufficiently described in infertile men.

STUDY DESIGN, SIZE, DURATION This study comprises baseline characteristics of 1427 infertile men screened from 2011 to 2014 for inclusion in a randomized clinical trial, the Copenhagen-Bone-Gonadal Study. PARTICIPANTS/MATERIALS, SETTING, METHODS In total 1427 infertile men, consecutively referred to our tertiary andrological centre for fertility workup, underwent a physical examination and had semen quality assessed based on two samples and blood analysed for serum testosterone, SHBG, estradiol, inhibin B, luteinizing hormone, follicle-stimulating hormone (FSH), 25-hydroxyvitamin D (25-OHD), ionized calcium (Ca2+) and karyotype. There were 179 men excluded due to serious comorbidities or anabolic steroid usage, leaving 1248 patients for analyses. MAIN RESULTS AND THE ROLE OF CHANCE Men with 25-OHD >75 nmol/l had higher sperm motility and 66 and 111% higher total numbers of motile spermatozoa after 45 and 262 min, respectively, than men with 25-OHD <25 nmol/l (all P < 0.05). SHBG levels and testosterone/estradiol ratios were 15 and 14% lower, respectively, while free testosterone and estradiol ratios were 6 and 13% higher, respectively, in men with 25-OHD <25 nmol/l (all P < 0.05). Men with lower Ca2+ levels had higher progressive sperm motility and inhibin B/FSH ratio but lower testosterone/estradiol ratio (all P < 0.05). LIMITATIONS, REASONS FOR CAUTION All outcomes presented are predefined end-points but inferral of causality is compromised by the descriptive study design. It remains to be shown whether the links between vitamin D, calcium, semen quality and sex steroids in infertile men are causal. WIDER IMPLICATIONS OF THE FINDINGS The associations between vitamin D deficiency and low
calcium with semen quality and sex steroids support the existence of a cross-link between regulators of calcium homeostasis and gonadal function in infertile men. STUDY FUNDING/COMPETING INTERESTS This study was supported by the Danish Agency for Science, Technology and Innovation, Horslev Fonden, Danish Cancer Society and Novo Nordisk Foundation. There are no conflicts of interest. Copyright © 2016 The Author.

633.
Study Question Would couples diagnosed with non-obstructive azoospermia (NOA) consider two future treatments with artificial gametes (AGs) as alternatives for testicular sperm extraction followed by ICSI (TESE-ICSI)?

Summary Answer Most couples with NOA (89%) would opt for treatment with AGs before attempting TESE-ICSI and/or after failed TESE-ICSI. What is Known Already Couples with NOA who undergo TESE-ICSI have a 25% chance of conceiving a child. Two future treatments that are being developed are 'ICSI with artificial sperm formed from somatic cells' (ICSI with AGs) and 'natural conception after autotransplantation of in vitro proliferated spermatogonial stem cells' (natural conception with AGs). It is unknown what treatment preferences patients have. Study Design, Size, Duration A cross-sectional survey conducted in 2012-2013, addressing all 921 couples diagnosed with NOA and treated with TESE-ICSI in Dutch fertility clinics between 2007 and 2012. The coded questionnaires were sent by mail and followed up with two reminders. Participants/Materials, Setting, Methods We developed the questionnaire based on a literature review and previous qualitative interviews, and included treatment preference and the valuation of nine treatment characteristics. We assessed reliability of the questionnaires and calculated mean importance scores (MISs: 0-10) of each treatment characteristic. We assessed which patient and treatment characteristics were associated with a couple's hypothetical treatment preference using binominal regression. Main Results and the Role of Chance The vast majority (89%) of the 494 responding couples (response rate: 54%) would potentially opt for AGs as a first and/or a last resort treatment option. More specifically, as a first treatment couples were likely (67%) to prefer natural conception with AGs over TESE-ICSI and less likely to prefer ICSI with AGs over TESE-ICSI (34%). After failed TESE-ICSI, the majority of couples (75%) would want to attempt ICSI with AGs as a last resort option. The most important characteristics of treatment were safety for children (MIS: 8.2), pregnancy rates (MIS: 7.7) and curing infertility (MIS: 6.8). Costs, burden, naturalness and technological sophistication were of about equal importance (MIS: 3.1-4.0). The majority of patients rated conception at home and moral acceptability as not important (MIS: 1.7 and 0.8, respectively), but the importance attributed to these variables did still affect patients' likeliness to opt for AGs. LIMITATIONS AND REASONS FOR CAUTION Couples with NOA not opting for TESE-ICSI were not included and might have other perspectives. Couples' hypothetical choices for AGs might differ from their actual choices once data on the costs, safety and pregnancy rates become available from these new treatment options. Wider Implications of the Findings The interest of couples with NOA in potential future treatments with AGs encourages further pre-clinical research. Priority setting for research and future decision-making on clinical application of AGs should take all characteristics important to patients into account. STUDY FUNDING/COMPETING INTEREST(S) The authors report no financial or other conflict of interest relevant to the subject of this article. Copyright © 2016 The Author.

Status
Autophagy: controlling cell fate in rheumatic diseases.
Rockel J.S., Kapoor M.
Embase
Nature Reviews Rheumatology. 12 (9) (pp 517-531), 2016. Date of Publication: 01 Sep 2016.
[Review]
AN: 610941584
Autophagy, an endogenous process necessary for the turnover of organelles, maintains cellular homeostasis and directs cell fate. Alterations to the regulation of autophagy contribute to the progression of various rheumatic diseases, including systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), osteoarthritis (OA) and systemic sclerosis (SSc). Implicit in the progression of these diseases are cell-type-specific responses to surrounding factors that alter autophagy: chondrocytes within articular cartilage show decreased autophagy in OA, leading to rapid cell death and cartilage degeneration; fibroblasts from patients with SSc have restricted autophagy, similar to that seen in aged dermal fibroblasts; fibroblast-like synoviocytes from RA joints show altered autophagy, which contributes to synovial hyperplasia; and dysregulation of autophagy in haematopoietic lineage cells alters their function and maturation in SLE. Various upstream mechanisms also contribute to these diseases by regulating autophagy as part of their
signalling cascades. In this Review, we discuss the links between autophagy, immune responses, fibrosis and cellular fates as they relate to pathologies associated with rheumatic diseases. Therapies in clinical use, and in preclinical or clinical development, are also discussed in relation to their effects on autophagy in rheumatic diseases. Copyright © 2016 Macmillan Publishers Limited, part of Springer Nature.

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635.
Uropathogenic Escherichia coli causes fibrotic remodelling of the epididymis.

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Despite antibiotic treatment, up to 40% of patients have impaired fertility after epididymitis due to serovars of Escherichia coli, a frequent pathogen. The reasons for infertility are unclear, but it may result from epididymal duct obstruction. To determine whether E. coli infection of the epididymis causes obstruction due to fibrosis, and to identify the key mediators, tissues from
patients with epididymitis were assessed. Additionally, epididymitis was induced with uropathogenic E. coli (UPEC) or commensal serovars in wild-type and MyD88-/- mice, which are relatively unresponsive to bacterial pathogens. Epididymal organ cultures were treated with activin A and bacteria and their histology and levels of cytokines and fibrosis markers were analysed. Patients with epididymitis showed severe fibrosis of the epididymal duct. In mice, UPEC infection also caused fibrosis and ductal obstruction in the cauda epididymis. Levels of mRNA for fibrotic markers (alpha-smooth muscle actin, fibronectin) and cytokines (activin A, TNFalpha, IL-1alpha, IL-1beta, IL-6) and total collagen levels were significantly elevated. This fibrotic response was blunted by the loss of MyD88. Activin A induced fibrosis in cultured epididymis, which was inhibited by the activin-binding protein follistatin. In summary, bacterial epididymitis causes fibrosis and obstruction. The milder tissue damage in Myd88-/- UPEC epididymitis highlights the importance of the host response to infection in causing epididymal damage. Elevated levels of activin A in vivo and fibrotic remodelling elicited by activin A in vitro indicate that this cytokine is a potential target for supplementary treatment to antibiotic therapy.

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636.
Long-term administration of escitalopram in patients with social anxiety disorder in Japan.
Asakura S., Hayano T., Hagino A., Koyama T.
Embase
Neuropsychiatric Disease and Treatment. 12 (pp 1817-1825), 2016. Date of Publication: 22 Jul 2016.
[Article]
AN: 611326087
Purpose: To investigate the safety, tolerability, and effectiveness of escitalopram in patients with social anxiety disorder in Japan. Methods: A 52-week, open-label study was conducted in Japanese patients with social anxiety disorder with a total score >60 on the Liebowitz Social Anxiety Scale-Japanese Version (LSAS-J) and >4 on the Clinical Global Impression-Severity Scale. Escitalopram 10 mg/day was administered for the first week and could be increased to 20 mg/day. Results: The study included 158 patients: 81.0% (128/158) completed 52 weeks of escitalopram treatment, 68.4% (108/158) increased their dose to 20 mg/day, and 56.3% (89/158) remained on 20 mg/day. Adverse drug reactions were reported by 57.6% (91/158) of patients. The most common (incidence >10%) were somnolence and nausea. The incidence of adverse drug reactions was similar in extensive and poor metabolizers of cytochrome P450 2C19. No adverse drug reactions increased in incidence by >5% after week 12. The incidence of serious adverse events was 1.3% (2/158). No deaths occurred. The LSAS-J total scores improved until week 52. The LSAS-J response rate (>30% improvement in LSAS-J) was 69.0%, the Clinical Global Impression-Improvement Scale response rate (<2) was 73.0%, and the LSAS-J remission rate (>30) was 27.0%. Conclusion: In this first 52-week clinical study of social anxiety disorder, escitalopram 10-20 mg/day was safe, well tolerated, and effective in Japanese patients.
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637.
The impact of vitamin E supplementation on semen parameters and pregnancy rates after varicocelectomy: a randomised controlled study.
Ener K., Aldemir M., Isik E., Okulu E., Ozcan M.F., Ugurlu M., Tangal S., Ozayar A.
Embase
Andrologia. 48 (7) (pp 829-834), 2016. Date of Publication: 01 Sep 2016.
[Article]
AN: 611569768
In this study, we aimed to investigate the impact of vitamin E supplementation on semen parameters and pregnancy after varicocelectomy. Forty-five infertile male patients who were diagnosed with varicocele and underwent subinguinal varicocelectomy were included in the study. After performing subinguinal varicocelectomy, the patients were randomised into two groups: 22 receiving vitamin E for 12 months, and 23 as the control group without receiving any supplementation. The pre-operative parameters of semen analyses and pregnancy rates of both groups were compared with those of post-operative parameters. There were no statistically significant differences between the groups in terms of sperm count and motile sperm percentage, in pre-operative, post-operative 3rd month, post-operative 6th month and post-operative 12th month periods. Repeated-measures anova was performed, and sperm count, percentage of change in sperm count, motile sperm count and percentage of change in motile sperm count of the groups were compared. The administration of vitamin E increased all of these parameters; however, they were not found to be statistically significant. In conclusion, vitamin E supplementation might improve the sperm parameters after varicocelectomy; however, further
Testosterone therapy, association with age, initiation and mode of therapy with cardiovascular events: a systematic review.
Albert S.G., Morley J.E.
Embase
Clinical Endocrinology. 85 (3) (pp 436-443), 2016. Date of Publication: 01 Sep 2016.
[Article]
AN: 611711252
Background: Although male hypogonadism is associated with increased cardiovascular events (CVE), recent concerns are that testosterone supplementation may increase CVE. The purpose was to determine associations with age, initiation or mode of therapy to explain these discrepancies. Data synthesis: Meta-analyses were supplemented through Scopus and PubMed with search terms 'testosterone', 'random' and 'trial'. CVE, defined before data extraction, were death, myocardial infarction, acute coronary syndrome, percutaneous coronary intervention, coronary bypass, syncope, arrhythmia, hospital admission for congestive heart failure or
cerebrovascular event. Results: There were 45 trials with 5328 subjects evaluated, with a mean age of 63.3 (SD +/- 7.9) years, followed for mean study duration of 10.6 (+/- 8.6) months. Overall, testosterone supplementation was not associated with increased CVE risk ratio (rr = 1.10 (95% CI 0.86; 1.41, P = 0.45)). However, there was an increase event rate during the first 12 months (rr = 1.79 (1.13;2.83, P = 0.012)), predominantly in those >65 years, (rr = 2.90 (1.35;6.21, P = 0.006)). Within studies with lipid data, CVE were associated with fall in HDL, P = 0.002. Intramuscular testosterone appeared neutral for CVE (rr = 0.96 (0.46;1.98, P = 0.91)) compared with oral testosterone (rr = 2.28 (95% CI 2.28;8.59, P = 0.22)) and transdermal testosterone (rr = 2.80 (1.38;5.68, P = 0.004)). Intramuscular testosterone had the least effect of lowering HDL and non-HDL cholesterol (both P < 0.001). Conclusions: Testosterone supplementation may be associated with increased CVE in those >65 years especially during the first year. Biological actions may differ depending upon mode of testosterone administration with intramuscular testosterone having less cardiovascular risk. Copyright © 2016 John Wiley & Sons Ltd


Status EMBASE
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639.
The impact of sperm protamine deficiency and sperm DNA damage on human male fertility: a systematic review and meta-analysis.
Ni K., Spiess A.-N., Schuppe H.-C., Steger K.
Existing literature suggests evidence that protamine deficiency is related to DNA damage and male fertility. In this meta-analysis, we analyzed the relationship between the ratio of protamine-1 and protamine-2 with male fertility and the association of protamine deficiency with sperm DNA damage. Quality of available cohort studies was evaluated using the Newcastle-Ottawa Scale checklist. Summary effect estimates with 95% confidence intervals (CI) were derived using a random effects model. The effect of the protamine ratio on male fertility was analyzed in nine studies demonstrating a significantly higher value of the protamine ratio in subfertile men (n = 633) when compared with controls (n = 453, SMD = 0.46, 95% CI 0.25-0.66, Z = 4.42, p < 0.00001). Both protamine mRNA (SMD = 0.45, 95% CI 0.11-0.79, Z = 2.63, p = 0.009) and protein ratio (SMD = 0.46, 95% CI 0.25-0.68, Z = 4.22, p < 0.0001) showed significantly increased values in subfertile patients. The association between protamine deficiency and DNA damage was analyzed in 12 studies (n = 845) exhibiting a combined overall correlation coefficient (COR) of 0.53 (95% CI 0.28-0.71, Z = 3.87, p < 0.001). Protamine deficiency measured by CMA3 staining was significantly associated with sperm DNA damage (COR = 0.71, 95% CI 0.48-0.85, Z = 4.87, p < 0.001), whereas the P1/P2 ratio was not (COR = 0.17, 95% CI -0.16 to 0.46, Z = 0.99, p = 0.33). It is concluded that the protamine ratio represents a suitable biomarker for the assessment of sperm quality and protamine deficiency is closely related with sperm DNA damage. Copyright © 2016 American Society of Andrology and European Academy of Andrology

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Tamoxifen in men: a review of adverse events.
Wibowo E., Pollock P.A., Hollis N., Wassersug R.J.
Embase
Andrology. 4 (5) (pp 776-788), 2016. Date of Publication: 01 Sep 2016.
[Review]
AN: 611710414
Tamoxifen is an off-label option to treat men for breast cancer, infertility, and idiopathic gynecomastia. Lately, tamoxifen has been proposed as a treatment to prevent gynecomastia in prostate cancer patients receiving antiandrogen therapy. We reviewed the adverse events (AEs) reported in studies of men prescribed tamoxifen for these conditions to better understand its side-effect profile. We searched PubMed for randomized controlled trials (RCTs) that included safety data of tamoxifen treatment in men with prostate cancer, breast cancer, infertility, and idiopathic gynecomastia. Non-RCTs were also reviewed. The results demonstrate that the AE profile in tamoxifen-treated male populations varied. Excluding breast events, gastrointestinal, and cardiovascular problems were the most commonly reported AEs in prostate cancer patients, whereas more psychiatric disorders were reported in male breast cancer patients. Few AEs have been documented in men receiving tamoxifen for infertility and idiopathic gynecomastia. Less than 5% of men withdrew from tamoxifen therapy because of toxicity. This suggests that for most men, tamoxifen is well-tolerated. Of those who discontinued tamoxifen, the majority were male breast cancer patients, and cardiovascular events were the most common reason for stopping tamoxifen treatment. Unfortunately, in many cases, the reasons for withdrawing tamoxifen were unspecified. Based on the available evidence, tamoxifen's AE profile appears to vary depending upon which male population is treated. Also, the frequency at which AEs occur varies - less AEs in men with infertility and idiopathic gynecomastia compared to men with prostate cancer or breast cancer. Long-term studies that rigorously document the side-effect profile of tamoxifen in men are lacking. Copyright © 2016 American Society of Andrology and European Academy of Andrology
PMID
A Review of the Clinical Side Effects of Bone Morphogenetic Protein-2.
James A.W., LaChaud G., Shen J., Asatrian G., Nguyen V., Zhang X., Ting K., Soo C.

Bone morphogenetic protein-2 (BMP-2) is currently the only Food and Drug Administration (FDA)-approved osteoinductive growth factor used as a bone graft substitute. However, with increasing clinical use of BMP-2, a growing and well-documented side effect profile has emerged. This includes postoperative inflammation and associated adverse effects, ectopic bone formation, osteoclast-mediated bone resorption, and inappropriate adipogenesis. Several large-scale studies have confirmed the relative frequency of adverse events associated with the clinical use of BMP-2, including life-threatening cervical spine swelling. In fact, the FDA has issued a warning of the potential life-threatening complications of BMP-2. This review summarizes the known adverse effects of BMP-2, including controversial areas such as tumorigenesis. Next, select animal models that replicate BMP-2's adverse clinical effects are discussed. Finally, potential
molecules to mitigate the adverse effects of BMP-2 are reviewed. In summary, BMP-2 is a potent osteoinductive cytokine that has indeed revolutionized the bone graft substitute market; however, it simultaneously has accrued a worrisome side effect profile. Better understanding of these adverse effects among both translational scientists and clinicians will help determine the most appropriate and safe use of BMP-2 in the clinical setting. Copyright © 2016 Mary Ann Liebert, Inc.

642.


Embase


[Review]
Objective: Insulin resistance and diabetes mellitus (DM) are well defined causes of female infertility. Animal studies present evidence for decreased sperm quality, but conflicting results have been presented in clinically-orientated studies. We sought to evaluate whether DM affects functional sperm characteristics.

Study design: We searched the Medline, Scopus, ClinicalTrials.gov, and Cochrane Central Register of Controlled Trials databases.

Results: DM seems to decrease the seminal volume (MD -0.66 ml, 95% CI -1.10, -0.22) and the percentage of motile cells (MD -14.29%, 95% CI -22.76, -5.82) and increase the FSH values (MD 0.47 mIU/ml, 95% CI 0.01, 0.93) of men who were screened for infertility. It does not, however, influence the total sperm count (MD 13.16 106 cells, 95% CI -22.75, 49.07), the percentage of normal sperm morphology (-3.06%, 95% CI -6.25, 0.14), or LH (MD 0.65 mIU/ml, 95% CI -0.84, 2.13 Supp. Fig. 2) and testosterone values (MD -0.18 ng/ml, 95% CI -0.60, 0.24).

Conclusion: Current evidence suggests that the presence of DM seems to influence functional sperm characteristics. Firm results are, however, precluded due to the significant heterogeneity of the included studies. Future prospective studies will clarify whether the DM affects semen quality and IVF outcome. Copyright © 2016 Elsevier Inc.
Adverse effects and safety of 5-alpha reductase inhibitors (finasteride, dutasteride): A systematic review.

Hirshburg J.M., Kelsey P.A., Therrien C.A., Gavino A.C., Reichenberg J.S.

Embase

[Review]

AN: 611411371

Finasteride and dutasteride, both 5-alpha reductase inhibitors, are considered first-line treatment for androgenetic hair loss in men and used increasingly in women. In each case, patients are expected to take the medications indefinitely despite the lack of research regarding long-term adverse effects. Concerns regarding the adverse effects of these medications has led the United States National Institutes of Health to add a link for post-finasteride syndrome to its Genetic and Rare Disease Information Center. Herein, the authors report the results of a literature search reviewing adverse events of 5-alpha reductase inhibitors as they relate to prostate cancer, psychological effects, sexual health, and use in women. Several large studies found no increase in incidence of prostate cancer, a possible increase of high-grade cancer when detected, and no change in survival rate with 5-alpha reductase inhibitor use. Currently, there is no direct link between 5-alpha reductase inhibitor use and depression; however, several small studies have led to depression being listed as a side effect on the medication packaging. Sexual effects including erectile dysfunction and decreased libido and ejaculate were reported in as many as 3.4 to 15.8 percent of men. To date, there are very few studies evaluating 5-alpha reductase inhibitor use in women. Risks include birth defects in male fetuses if used in pregnancy, decreased libido, headache, gastrointestinal discomfort, and isolated reports of changes in menstruation, acne, and dizziness. Overall, 5-alpha reductase inhibitors were well-tolerated in both men and women, but not without risk, highlighting the importance of patient education prior to treatment.

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Brachytherapy and fertility.

Abstract: Fertility is a major part of the global care of patients treated for cancer. A new discipline known as oncofertility has emerged in some countries. Although the relationship between chemotherapy and external radiotherapy and fertility has been studied and reported, there is only scarce data available on brachytherapy. This systematic review aims to report available knowledge on the impact of brachytherapy on fertility. Specific consultations should be considered before brachytherapy to inform patients about their fertility preservation options.

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Favorable outcome of primary mediastinal large B-cell lymphoma patients treated with sequential RCHOP-RICE regimen without radiotherapy.

Goldschmidt N., Kleinstern G., Orevi M., Paltiel O., Ben-Yehuda D., Gural A., Libster D., Lavie D., Gatt M.E.

Embase Cancer Chemotherapy and Pharmacology. 77 (5) (pp 1053-1060), 2016. Date of Publication: 07 Apr 2016.

[Article]

AN: 609711614

Purpose Outcomes in primary mediastinal B cell lymphoma (PMBL) improved with the introduction of dose intense treatments, consolidation radiotherapy and rituximab. DA-EPOCH-R, which omits radiotherapy has been adopted with worldwide enthusiasm, despite lack of proven superiority in randomized trials. We aimed to evaluate the course and outcome of PMBL using an alternative intensive rituximabcontaining regimen, RCHOP-RICE. We also evaluated the prognostic value of 18FDG-PET-CT (PET-CT). Methods We reviewed the clinical, laboratory and imaging data of PMBL patients receiving 1st-line treatment in Hadassah Medical Center between 8/2002 and 10/2014. Results Of 47 PMBL patients, 24 (51%) were treated with RCHOP-RICE and 23 (49%) with other protocols. Overall, the 5-year progression-free survival was 93% and the overall survival was 98% (87 and 100%, respectively, for the RCHOP-RICE regimen). Patient characteristics and treatment toxicities were balanced among protocols. A mean of 11.1 +/- 1.3 hospitalization days/patient were needed to administer RCHOP-RICE regimen compared to 37 +/- 2 days/patient for DA-EPOCH-R (n = 2). Radiotherapy was given to 3 patients (12%) treated with RCHOPRICE compared to 18 patients (78%) treated with other protocols (p < 0.01). For patients followed with interim and end of treatment (EOT) PET-CT, we observed a significant reduction in the uptake between the two (p < 0.0001). Using a Deauville score cutoff of 3, the negative and positive predictive values (NPV and PPV) of EOT PET-CT were 94 and 33%, respectively. Conclusions The RCHOP-RICE protocol results in excellent survival outcomes, generally permits omission of RT and is simpler to administer than DA-EPOCH-R. Interim PET-
CT in PMBL may be unjustified; however, EOT Deauville scores <3 predicts a favorable outcome.

American Urological Association (AUA) - 111th annual meeting (May 6-10, 2016 - San Diego, California, USA).

Croasdell G.

Embase

Drugs of Today. 52 (5) (pp 313-315), 2016. Date of Publication: May 2016.

[Conference Paper]

AN: 611403025

The 111th Annual Meeting of the American Urological Association (AUA) brought together a wide range of researchers in the field of urology to share knowledge and set standards in urological research. The meeting consisted of plenary, podium and moderated poster sessions, in which the latest research and advances in urologic medicine were presented. This report will highlight some of the presentations on therapeutic developments for a range of urological conditions. Copyright © 2016 Prous Science, S.A.U. or its licensors. All rights reserved.
Association of Chlamydia trachomatis with infertility and clinical manifestations: a systematic review and meta-analysis of case-control studies.
Ahmadi M.H., Mirsalehian A., Bahador A.
Embase
Infectious Diseases. 48 (7) (pp 517-523), 2016. Date of Publication: 02 Jul 2016.
[Article]
AN: 611313582

Background Chlamydia trachomatis is one of the sexually transmitted pathogens causing reproductive health-threatening diseases worldwide. However, its role in infertility, particularly in asymptomatic individuals, is not yet definitely determined. Methods For the study, electronic databases were searched using the following keywords; 'Chlamydia trachomatis', 'prevalence', 'frequency', 'fertile', 'infertile', 'case', 'control', 'symptomatic' and 'asymptomatic'. Finally, after some exclusions, 34 studies (19 fertile-infertile and 15 symptomatic-asymptomatic) from different countries were included in the study and meta-analysis was performed on the data collected.

Results Odds ratios (ORs) for urogenital C. trachomatis prevalence in males in the fertile-infertile group, for infertile and fertile individuals, ranged from 1.3-3.7 and in females from 1.04-4.8, and the overall OR for both genders was 2.2 (95% CI). In the symptomatic-asymptomatic group, the overall OR in males and females was 4.9 (95% CI = 1.1-21.7) and 3.3 (95% CI = 1.7-6.3), respectively. In all of the analyses, there were high levels of heterogeneity (I² >50%, p-value <0.05) and, except for the females in the symptomatic-asymptomatic group, neither Egger's tests nor Begg's tests were statistically significant for publication bias.

Conclusions C. trachomatis can impact on the potential for fertility and cause clinical manifestations and complications in both
males and females. Thus, national programmes for adequate diagnosis, screening and treatment of infected individuals, particularly asymptomatic ones, seem to be necessary.

648.

Stable intraprostatic dihydrotestosterone in healthy medically castrate men treated with exogenous testosterone.


Embase


[Article]

AN: 611271915

Context: Concern exists that T replacement therapy (TRT) might increase the risk of prostate disease. There are limited data regarding the impact of TRT on prostate androgen concentrations. Objective: Determine the dose-dependent effects of exogenous T administration on intraprostatic androgen concentrations. Design: Twelve-week, double-blinded, randomized, placebo-controlled trial. Setting: Academic medical center. Participants: Sixty-two healthy eugonadal men, aged 25-55 years. Interventions: Subjects were randomly assigned to receive injections of acyline, a GnRH antagonist (used to achieve medical castration), every 2 weeks plus transdermal T gel (1.25 g, 2.5 g, 5.0 g, 10 g, or 15 g daily), or placebo injections and transdermal
gel for 12 weeks. Main Outcomes: Serum T and dihydrotestosterone (DHT) were measured at baseline and every 2 weeks during treatment. Intraprostatic T and DHT concentrations were assessed from tissue obtained through ultrasound-guided prostate needle biopsies at week 12. Androgens were quantified by liquid chromatography-tandem mass spectrometry. Results: 51 men completed the study and were included in the analysis. There were no significant adverse events. Exogenous T resulted in a dose-dependent increase in serum T and DHT concentrations (190-770 and 60-180 ng/dL, respectively). Although intraprostatic T differed among dose groups (P <.01), intraprostatic DHT was comparable regardless of T dose (P <.11) and was 10-to 20-fold greater than intraprostatic T. Conclusions: In healthy, medically castrate men receiving exogenous T, the total intraprostatic androgen concentration (predominantly DHT) remained stable across serum T concentrations within the physiological range. These findings further our knowledge of the relationship between serum and intraprostatic androgens and suggest that physiological serum T achieved by TRT is unlikely to alter the prostate hormonal milieu.

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Comparative efficacy of density gradient and swim-up methods of semen preparation in intrauterine insemination cycles.

Butt F., Chohan M.A.

Embase

[Article]

AN: 611204524

Objective: To see the efficacy of different methods of intrauterine insemination preparation for sperm recovery and conception rate. Methods: This prospective observational study was carried out at Chohan Reproduction and Assisted Fertility Treatment Centre, Lahore, Pakistan, from January 2014 to July 2014, and comprised infertile couples undergoing intrauterine insemination cycles. Method of sperm preparation for intrauterine insemination during super-ovulation was randomly assigned for swim-up and density gradient techniques. Total sperm count, percentage recovery of motile sperm count, conception rate and cycle fecundity (live births, miscarriages, ectopic pregnancy) were measured. Mean percentages of sperm recovery and motility were compared. SPSS 21 was used for data analysis. Results: Of the 220 couples who underwent 440 cycles, 138(62.7%) suffered from primary infertility and 82(37.27%) from secondary infertility. The mean age of women was 31.75+/-5.47 years, while that of men was 35.78+/-5.27 years. Mean duration of infertility in these couples was 5.50+/-3.51 years. Intrauterine insemination was performed at the first attempt in 180(81.8%) couples, at the second attempt in 37(16.8%) and at the third attempt in 3(1.3%) couples. Mean percentage of sperm motility in post-preparation of density gradient procedure was 83.88+/-15.02 (day 1) and 84.02+/-18.51 (day 2) while in swim-up procedure it was 91.02+/-11.85 (day 1) and 92.28+/-9.89 (day 2). Mean percentage of sperm concentration after processing in density gradient procedure was higher than swim-up (p=0.368 day 1; p=0.225 day 2) but mean percentage of sperm motility in post-preparation of density gradient procedure was less than swim-up procedure (p=0.000 day 1; p=0.000 day 2). Recovery rates in density gradient were 50.89% on day 1 and 50.13% on day 2compared to 36.69% on day 1 and 37.5%on day 2in swim-up technique (p=0.02). Conception rate was 15%. Conclusion: Despite the difference in percentage recovery of motile sperms in different techniques, cycle fecundity remained the same. Copyright © 2016, Pakistan Medical Association. All rights reserved.

Status
The reciprocal links between synaptophysin serum levels and the prevalence of metabolic syndrome according to selected low-grade inflammation indices and age-related androgen serum level changes in men.

Herman W.A., Wojcicka M., Kolodziejczak B., Losy J., Lacka K.

UNLABELLED: The correlations between synaptophysin (SYP) plasma levels and the brain neurotransmission activity are still not strictly identified. However, the efficiency of neurotransmission depends, inter alia, on the age, hormonal status, and coexistence of a low-grade systemic inflammation (LGSI) which is regarded as a pathogenic link with obesity and insulin resistance, atherogenesis and aging per se. AIM: The aim of this study was to investigate the associations between synaptophysin serum levels and age, LGSI indices, homocysteine and selected hormonal parameters (dehydroepiandrosterone and its sulfate, free-testosterone, SHBG) and the prevalence of metabolic syndrome (MS) in men over the age of 40.

MATERIALS AND METHODS: After randomization, 157 male volunteers aged 40-80 years were included in a retrospective study. MS was diagnosed according to the International Diabetes...
Federation criteria. For the diagnosis of late-onset hypogonadism (LOH) we adopted the criteria proposed by the European Male Aging Study (EMAS).

RESULTS: Synaptophysin plasma concentrations in respondents decreased with age, but only between the ages of 40 to 70 years. There were no differences in SYP plasma concentrations in men suffering from MS compared to healthy subjects (p=0.845). Men suffering from MS demonstrated while higher hs-CRP (high sensitive C-reactive protein) levels than healthy (p=0.019), contrary to the alpha1-antichymotrypsin and transferrin. A positive monotonic correlation between synaptophysin and hs-CRP was demonstrated (r=0.235; p=0.003). No statistically significant relationships between SYP and homocysteine plasma levels were presented (r=0.047; p=0.562), although in men diagnosed with MS higher homocysteine levels compared to healthy subjects were demonstrated. No correlations between synaptophysin and free testosterone (r=-0.036; p=0.651), DHEA (r=-0.122; p=0.128) and its sulphate (r=-0.024; p=0.764) as well as SHBG (r=-0.088; p=0.288) were demonstrated.

CONCLUSIONS: Although the correlations between synaptophysin plasma levels and age as well as strong LGSI indicator (hs-CRP) have been demonstrated, the usefulness of determining SYP serum concentration as a marker of age-related studied diseases (MS, LOH) seems to be significantly limited.

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Development of male sterile Eruca sativa carrying a Raphanus sativus/Brassica oleracea cybrid cytoplasm.
Nothnagel T., Klocke E., Schrader O., Linke B., Budahn H.
Embase
TAG. Theoretical and applied genetics. Theoretische und angewandte Genetik. 129 (2) (pp 331-344), 2016. Date of Publication: 01 Feb 2016.
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AN: 610747801
KEY MESSAGE: Alloplasmic male sterile breeding lines of Eruca sativa were developed by intergeneric hybridization with CMS-Brassica oleracea, followed by recurrent backcrosses and determination of the breeding value.
ABSTRACT: Male sterile breeding lines of rocket salad (Eruca sativa) were developed by intergeneric hybridization with cytoplasmic male sterile (CMS) cauliflower (Brassica oleracea) followed by recurrent backcrosses. Five amphidiploid F1 plants (2n = 2x = 20, CE), achieved by manual crosses and embryo rescue, showed an intermediate habit. The plants were completely male sterile and lacked seed set after pollination with the Eruca parent. Allotetraploid F1 hybrid plants (4n = 4x = 40, CCEE) obtained after colchicine treatment were backcrossed six times with pollen of the Eruca parent to select alloplasmic diploid E. sativa lines. The hybrid status and the nucleo-cytoplasmic constellation were continuously controlled by RAPD and Southern analysis during subsequent backcrosses. The ploidy level was investigated by flow cytometry and chromosome analysis. Premeiotic (sporophytic) and postmeiotic (pollen abortive) defects during the anther development were observed in the alloplasmic E. sativus plants in comparison to the CMS-cauliflower donor. No further incompatibilities were noticed between the CMS-inducing cybrid cytoplasm and the E. sativa nuclear genome. The final alloplasmic E. sativa lines were diploid with 2n = 2x = 22 chromosomes and revealed complete male sterility and restored female fertility. Plant vigor and yield potential of the CMS-E. sativa BC5 lines were comparable to the parental E. sativa line. In conclusion, the employed cybrid-cytoplasm has been proven as a vital source of CMS for E. sativa. The developed lines are directly applicable for hybrid breeding of rocket salad.
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Osteoporosis and Low Bone Mineral Density in Men with Testosterone Deficiency Syndrome.
Gaffney CD; Pagano MJ; Kuker AP; Stember DS; Stahl PJ.
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[Journal Article]
UI: 27784602
INTRODUCTION: Testosterone deficiency syndrome (TDS) is a risk factor for low bone mineral density (BMD) and osteoporosis. Knowledge of the relationship between TDS and bone health, as well as the practical aspects of how to diagnose and treat low BMD, is therefore of practical importance to sexual medicine practitioners.
AIM: The aim of this study was to review the physiologic basis and clinical evidence of the relationship between TDS and bone health; and to provide a practical, evidence-based algorithm for the diagnosis and management of low BMD in men with TDS.
METHODS: Method used was a review of relevant publications in PubMed.
MAIN OUTCOME MEASURES: Pathophysiology of low BMD in TDS, morbidity, and mortality of osteoporosis in men, association between TDS and osteoporosis, indications for dual X-ray
absorptiometry (DXA) scanning in TDS, evidence for testosterone replacement therapy (TRT) in men with osteoporosis, treatment for osteoporosis in the setting of TDS.

RESULTS: Sex hormones play a pleomorphic role in maintenance of BMD. TDS is associated with increased risk of osteoporosis and osteopenia, both of which contribute to morbidity and mortality in men. DXA scanning is indicated in men older than 50 years with TDS, and in younger men with longstanding TDS. Men with TDS and osteoporosis should be treated with anti-osteoporotic agents and TRT should be highly considered. Men with osteopenia should be stratified by fracture risk. Those at high risk should be treated with anti-osteoporotic agents with strong consideration of TRT; while those at low risk should be strongly considered for TRT, which has a beneficial effect on BMD.

CONCLUSION: Low BMD is a prevalent and treatable cause of morbidity and mortality in men with TDS. Utilization of a practical, evidence-based approach to diagnosis and treatment of low BMD in men with TDS enables sexual medicine practitioners to make a meaningful impact on patient quality of life and longevity. Gaffney CD, Pagano MJ, Kuker AP, Stember DS, and Stahl PJ. Osteoporosis and low bone mineral density in men with testosterone deficiency syndrome. Copyright © 2015 International Society for Sexual Medicine. Published by Elsevier Inc. All rights reserved.

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Testosterone and Cardiovascular Health: Safety of Treatment of Hypogonadism. [Review]
Kloner RA.
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[Review. Journal Article]
UI: 27784573

INTRODUCTION: Controversy has arisen over the issue of the cardiovascular safety of testosterone.

AIM: The aim of this article is to examine the evidence as to the cardiovascular safety involved with the administration of testosterone.

METHODS: A literature review was performed with regard to cardiovascular safety of testosterone.

MAIN OUTCOME MEASURE: The main outcome measure was to evaluate the available evidence as to cardiovascular safety and risk of testosterone.

RESULTS: A handful of recently published and widely discussed manuscripts have suggested that administration of testosterone replacement therapy increases the frequency of adverse cardiovascular events. In contrast, there have been recent clinical reports suggesting that testosterone is either safe or actually reduces cardiovascular events and mortality. All of these studies—both those suggesting that testosterone has adverse effects, as well as those suggesting it has positive effects on the cardiovascular system—have limitations.

CONCLUSION: What is missing is a large, long-term, prospective, placebo controlled, double blind trial in which hypogonadal men receive either testosterone or placebo, testosterone levels are carefully monitored, and the primary outcomes are well-defined major adverse cardiovascular/cerebrovascular events. Kloner RA. Testosterone and cardiovascular health: Safety of treatment of hypogonadism. Sex Med Rev 2015;3:56-62.

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INTRODUCTION: Testosterone replacement therapy (TRT) is a common treatment for hypogonadism in aging males. Men with low to low-normal levels of testosterone have documented benefit from hormone replacement. Recent meta-analyses have revealed that increases in hemoglobin (Hb) and hematocrit (Hct) are the variants most commonly encountered. Clinically, this response is described as erythrocytosis or polycythemia secondary to TRT. However, the recent Food and Drug Administration warning regarding the risk for venothromboembolism (VTE) has made the increases in Hb and Hct of more pertinent concern. The risks associated with androgen replacement need further examination.

AIM: To review the available literature on erythrocytosis and polycythemia secondary to TRT. To discuss potential etiologies for this response, the role it plays in risk for VTE, and recommendations for considering treatment in at-risk populations.

METHODS: A literature review was performed through PubMed regarding TRT and erythrocytosis and polycythemia.

MAIN OUTCOME MEASURES: To assess the mechanisms of TRT-induced erythrocytosis and polycythemia with regard to basic science, pharmacologic preparation, and route of delivery. To
review Hct and risk for thrombotic events. To offer clinical suggestions for therapy in patients at risk for veno-thrombotic events.

RESULTS: Men undergoing TRT have a 315% greater risk for developing erythrocytosis (defined as Hct>0.52) when compared with control. Mechanisms involving iron bioavailability, erythropoietin production, and bone marrow stimulation have been postulated to explain the erythrogenic effect of TRT. The association between TRT-induced erythrocytosis and subsequent risk for VTE remains inconclusive.

CONCLUSIONS: All TRT formulations cause increases in Hb and Hct, but injectables tend to produce the greatest effect. The evidence regarding the risk for VTE with increased Hct is inconclusive. For patients with risk factors for veno-thrombotic events, formulations that provide the smallest effect on blood parameters hypothetically provide the safest option. Further trials are needed to fully evaluate the hematological side effects associated with TRT. Jones SD Jr, Dukovac T, Sangkum P, Yafi FA, and Hellstrom WJG. Erythrocytosis and polycythemia secondary to testosterone replacement therapy in the aging male. Sex Med Rev 2015;3:101-112. Copyright © 2015 International Society for Sexual Medicine. Published by Elsevier Inc. All rights reserved.
Annexin V-MACS in infertile couples as method for separation of sperm without DNA fragmentation.

Troya J; Zorrilla I.

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present


[Journal Article]

UI: 27206090

OBJECTIVE: To determine the effect of using MACS technology on clinical pregnancy, as a method for separation of damaged sperm in infertile patients.

METHODS: 136 infertile men having normal semen parameters in accordance with WHO 2010 criterion, undergoing ICSI cycle were enrolled during the course of the study. The patients were prospectively randomized and enrolled after oocyte retrieval and were assigned to the ICSI group, PICSI group or MACS group. Embryo development and clinical pregnancy were assessed. In 17 randomized MACS patients, sperm DNA fragmentation was tested in the presumptive apoptotic and no apoptotic spermatozoa fractions.

RESULTS: Similar results were obtained between groups for the following parameters: fertilization rates of 78.97% (95% confidence interval [CI]:74.37-83.57), 70.15 % (95% CI:63.98-76.33) and 80.28% (95% CI:73.74-86.81) for ICSI, PICSI and MACS group, respectively; Number of Day-3 embryos was 5.04 (95% CI:4.09-5.98), 5.17(95% CI:4.24-6.10) and 5.59(95% CI:4.31-6.87) for ICSI, PICSI and MACS group, respectively; number of freezing embryos in blastocyst stage was 0.78 (95% CI:0.25-1.31), 0.70(95% CI:0.27-1.14) and 1 (95% CI:0.37-1.6) for ICSI, PICSI and MACS group, respectively. However, clinical pregnancy rates of 58.1% for MACS group versus 40.4% and 27.3% for PICSI and ICSI group, respectively, were showed statistical difference (P=0.019). DNA fragmentation index for the two sperm MACS fraction showed statistical differences (P=0.000), MACS reduced the D.F.I of the sperm sample.

CONCLUSIONS: The use of MACS technology improves the clinical pregnancy on infertile couples and can be applied as a method for sperm separation, discriminating sperm with high DNA fragmentation.

Status
PubMed-not-MEDLINE

Authors Full Name
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Institution
Evaluation of subacute bisphenol - A toxicity on male reproductive system.

Karnam SS; Ghosh RC; Mondal S; Mondal M.

AIM: The aim was to evaluate the effect of multiple oral administration of bisphenol A (BPA) for 28 days on seminal characteristic on mammal using Wistar rat as a model.

MATERIALS AND METHODS: Rats were randomly divided into five different groups having 6 male rats in each group. The doses chosen were 50, 200, and 600 mg/kg body weight for Groups III, IV and V, respectively, based on preliminary dose range finding study and Group II served as vehicle control and Group I was negative control.

RESULTS: Reproductive study in the BPA-treated rats on day 28 revealed that there was significant (p<0.05) reduction in the epididymal sperm count of rats of Group IV and significant (p<0.01) decrease in Group V. Sperm motility percentage, dead count percentage, head and tail abnormality percentage were found to be significantly (p<0.01) increased in rats of BPA-treated groups as compared to rats of control groups. Testes showed necrosis of germinal layer and spermatogonial cells in the seminiferous tubules. Hematological examination revealed significant (p<0.01) decrease in the mean values of total erythrocyte count (TEC), total leukocyte count (TLC), hemoglobin, packed cell volume, and there was also significant (p<0.05) lymphocytopenia in treated animals.

CONCLUSION: It can be concluded from this study that subacute toxicity of BPA caused a reduction in the epididymal sperm count, sperm motility, dead count, head and tail abnormality, as well as hematological indices such as TLC, TEC etc. Hence, it appears that BPA affects the
germ cells leading to impairment in the spermatogenesis, and thus having its property as reproductive toxicant and it also suppresses bone marrow functioning, which leads to normocytic hypochromic anemia in rats.

Status
PubMed-not-MEDLINE

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657.
The effect of preprocedure anxiety levels on postprocedure pain scores in women undergoing hysterosalpingography.
Tokmak A; Kokanali MK; Guzel AI; Tasdemir U; Akselim B; Yilmaz N.
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[Journal Article. Randomized Controlled Trial]
UI: 26143387
BACKGROUND: Hysterosalpingography (HSG) is an invasive, uncomfortable, and painful procedure. Patients often experience considerable anxiety and stress before the procedure. In this study, we aimed to evaluate the effect of preprocedure anxiety on postprocedure pain scores and clinical outcomes in women undergoing HSG.

METHODS: This study was designed as a prospective randomized study. Women undergoing HSG were asked to complete the Beck Anxiety Inventory before the procedure. Patients were classified into two groups according to the anxiety score (Group 1: anxiety score < 25; n = 84 and Group 2: anxiety score > 25, n = 25). All of the patients were asked to state the severity of their pain during the procedure using a visual analogue scale immediately after the procedure. Then, postprocedure pain scores and clinical features were evaluated. Data analyzed were: age, gravidity, parity, durations of marriage and infertility, body mass index, procedure time, amount of contrast media used, operator sex, history of surgery, educational level, and HSG results.

RESULTS: A total of 109 women were enrolled into this prospective study. There was no statistically significant difference between the groups in terms of age, body mass index, durations of marriage and infertility, procedure time, amount of contrast media used, operator sex, history of surgery, educational level, and patency of the one and/or two fallopian tubes (p > 0.05). The median parity and pain scores after the procedure were lower in Group 1 (p < 0.05). There was also a positive correlation between anxiety scores and postprocedure pain scores (r = 0.289, p = 0.002). Receiver operator characteristics curve analysis demonstrated that operator sex was an important risk factor for postprocedure pain in patients with a preprocedure Beck Anxiety Inventory > 25. Logistic regression method demonstrated that higher parity, preprocedure anxiety score > 25, and male operator were risk factors for increased postprocedure visual analogue scale scores.

CONCLUSION: According to this study, preprocedure anxiety levels have an effect on postoperative pain scores in women undergoing HSG procedure. Multiparity, male operator, and higher preprocedure anxiety scores also may have an effect on postoperative pain scores.

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Status
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Objectives

OBJECTIVE: The aim of this study was to evaluate the efficacy of treatment with FSH in Chinese infertility population. Design: Prospective, randomized, double-blind, placebo-controlled clinical study. Patients: A total of 354 men affected by idiopathic oligozoospermia from three medical centres. Measurements: This study contained three parts: (i) treatment with different doses of rhFSH (50 IU, 100 IU, 200 IU and 300 IU); (ii) the efficacy of rhFSH at different periods (2, 3, 4, 5 months); (iii) FSH treatment in patients with different levels of inhibin B (normal-level group, low-
level group and high-level group). Semen parameters were evaluated in all subjects. The patients who had not reached spontaneous pregnancy underwent assisted reproductive techniques.

RESULTS: Sperm number was significantly increased after treatment with FSH at doses of at least 200 IU, and the improvement was observed beginning at the third month. The significant improvement in both morphology and forward motility was observed beginning at the fifth month. Moreover, 300 IU rhFSH administration for 5 months could significantly improve the spontaneous pregnancy rate (12/40) and ART pregnancy rate (14/28), while the rates for placebo group were two of twenty-nine and five of twenty-seven, respectively. The seminal parameters (total sperm count, sperm concentration, forward motility and morphology) were significantly improved in the normal- and low-level inhibin B groups, but no significant variation was observed in the high-level group at the end of the study.

CONCLUSIONS: The efficacy of FSH treatment was associated with the dose of FSH and duration of treatment, and FSH therapy was more effective in patients with normal level and low level of inhibin B.

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Male infertility and its genetic causes. [Review]
Miyamoto T; Minase G; Okabe K; Ueda H; Sengoku K.
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[Journal Article. Research Support, Non-U.S. Gov't. Review]
UI: 26178295

AIM: Infertility is a serious social problem in advanced nations, with male factor infertility accounting for approximately half of all cases of infertility. Here, we aim to discuss our laboratory results in the context of recent literature on critical genes residing on the Y chromosome or autosomes that play important roles in human spermatogenesis.

METHODS: The PubMed database was systematically searched using the following keywords: 'genetics of male factor infertility'; 'male infertility genes', 'genetics of spermatogenesis' to retrieve information for this review.

RESULTS: Striking progress has recently been made in the elucidation of mechanisms of spermatogenesis using knockout mouse models. This information has, in many cases, not been directly translatable to humans. Nevertheless, mutations in several critical genes have been shown to cause male infertility. We discuss here the contribution to male factor infertility of a number of genes identified in the azoospermia factor (AZF) region on the Y chromosome, as well as the autosomally located genes: SYKP3, KLHL10, AURKC and SPATA16.

CONCLUSIONS: Non-obstructive azoospermia is the most severe form of azoospermia. However, the presence of spermatozoa can only be confirmed through procedures, which may prove to be unnecessary. Elucidation of the genes underlying male factor infertility, and thereby a better understanding of the mechanisms that cause it, will result in more tailored, evidence-based decisions in treatment of patients.

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Status
MEDLINE
Authors Full Name
Miyamoto, Toshinobu; Minase, Gaku; Okabe, Kimika; Ueda, Hiroto; Sengoku, Kazuo.
A 12-Week, Open Label, Multi-Center Study to Evaluate the Clinical Efficacy and Safety of Silodosin on Voiding Dysfunction in Patients with Neurogenic Bladder.
Moon KH; Park CH; Jung HC; Oh TH; Kim JS; Kim DY.
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[Clinical Trial. Journal Article. Multicenter Study. Research Support, Non-U.S. Gov't]
UI: 26663648
OBJECTIVES: The purpose of this study is to evaluate clinical effect and safety of alpha1A-adrenoceptor blocker, silodosin, in patients with voiding dysfunction caused by neurogenic bladder.
METHODS: From April 2011 to January 2012, patients who were diagnosed as potential voiding dysfunction associated with neurogenic bladder, aged≥20 years were enrolled. Silodosin (8mg/day) was administered once daily in the morning with food. The efficacy was assessed at the baseline and after 12 weeks of the treatment having following parameters of international prostate symptom score and other measures including the maximum flow rate and the postvoid residual urine volume.
RESULTS: A total of 97 patients were screened and 95 were enrolled. Of these 95 patients, 82 patients were completed and included in analysis. After 12-weeks of treatment, mean total international prostate symptom score decreased significantly from 22.23+/-6.80 to 14.98+/-9.48 (P=0.0002). Voiding symptoms and storage symptoms were also improved by decreasing in international prostate symptom score-QoL from 4.62+/-0.92 to 3.48+/-1.63 (P<0.0001). Maximum flow rate increased significantly from 10.72+/-2.66 to 15.14+/-6.63 (P<0.0001). The main adverse event was ejaculation disorder. No serious adverse events related to silodosin were noted. CONCLUSIONS: This study indicates that silodosin was significantly effective, well tolerated and safe in patients who have voiding dysfunction associated with neurogenic bladder.

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Status
MEDLINE

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20151215

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2015

661.
Is Any Press Good Press? The Impact of Media Portrayals of Infertility on Young Adults' Perceptions of Infertility.
OBJECTIVE: Infertility is an issue of current concern across North America. The Society of Obstetricians and Gynaecologists of Canada advocates for public education regarding infertility issues. Public education is supposed to be a fundamental objective of news media. However, it is uncertain whether the media are acting as good partners to the medical profession in this objective of educating the public, and young women in particular. Recent findings suggest that print news tends to present infertility using high-alarm framing strategies; however, the impact of this framing on news consumers is unknown. The purpose of this study was to understand the effects of high- versus low-alarm frames on consumers of infertility-related news.

METHODS: In this experiment, 131 undergraduate students were randomly assigned to read infertility-focused news articles judged to employ either high- or low-alarm framing strategies in presenting infertility. Participants subsequently completed various psychological, emotional, and knowledge measures to gauge the impact of the news exposure.

RESULTS: The participants exposed to the high-alarm framing showed higher levels of perceived personal susceptibility to infertility, marginally higher levels of worry about infertility, and significantly lower levels of infertility-related knowledge than those exposed to the low-alarm framing.

CONCLUSION: The manner in which the news media report on infertility has repercussions on how individuals think and feel about infertility. The findings of this study can inform health care providers about how the media are shaping perceptions of infertility, and can assist professional bodies interested in undertaking public education initiatives.
la sensibilisation du public constitue, en principe, l'un des objectifs fondamentaux des médias d'information, la question de savoir si ces derniers collaborent de façon efficace avec la profession médicale à cet égard (et plus particulièrement en ce qui concerne la sensibilisation des jeunes femmes) demeure trouble. De récentes études semblent indiquer que la presse écrite tend à utiliser des stratégies grandement alarmistes en ce qui concerne la communication des nouvelles traitant de l'infertilité ; cependant, les effets de ces stratégies sur le public demeurent inconnus. Cette étude avait pour objectif de comparer et de comprendre les effets des stratégies de communication grandement alarmistes et peu alarmistes sur le public visé par les nouvelles traitant de l'infertilité. Méthodes : Dans le cadre de cette expérience, 131 étudiants de premier cycle ont été affectés au hasard à un groupe devant lire des articles de journaux qui, à notre avis, utilisaient des stratégies de communication grandement alarmistes pour aborder le sujet de l'infertilité ou à un groupe devant lire des articles de journaux qui, à notre avis, utilisaient des stratégies peu alarmistes pour aborder ce sujet. Les participants ont par la suite rempli un questionnaire mesurant divers paramètres psychologiques, affectifs et liés aux connaissances, et ce, pour nous permettre d'évaluer les effets de l'exposition à chacun de ces types de nouvelles. Résultats : Les participants qui ont été exposés à des stratégies de communication grandement alarmistes ont présenté des taux accrus de sensibilité personnelle perçue à l'infertilité, des taux légèrement accrus d'inquiétude envers l'infertilité et des niveaux considérablement moindres de connaissances à l'égard de l'infertilité, par comparaison avec les participants ayant été exposés à des stratégies de communication peu alarmistes. Conclusion : La façon dont les médias d'information traitent de la question de l'infertilité exerce une influence sur la façon dont les gens perçoivent les renseignements qui leur sont fournis à ce sujet. Les résultats de cette étude pourraient renseigner les fournisseurs de soins de santé quant à la façon dont les médias influencent les perceptions en ce qui concerne l'infertilité et pourraient s'avérer utiles pour les organismes professionnels qui souhaitent mettre en œuvre des initiatives d'éducation publique.

Language: French

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20151205

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2015
BACKGROUND: Semen represents a reservoir for human papillomavirus (HPV), rising concern in couples eligible for assisted reproduction techniques (ART). Humoral immunity against HPV is considered to protect from reinfection. We investigated the impact of vaccination on virus clearance in a cohort of infertile male patients showing HPV semen infection.

METHODS: 179 out of 619 infertile patients, showing HPV-DNA detection in semen by FISH analysis, were enrolled. Subjects were split into 91 vaccine-sensitive (VSPs) and 88 nonvaccine-sensitive patients (NVSPs) by INNO-LiPA. 19 VSPs showed vaccine-type specific seroconversion at recruitment. All patients underwent specific counselling. 42 seronegative VSPs were randomly assigned to receive quadrivalent vaccination in 6 months, whilst 49 VSPs, 19 seroconverted and 30 seronegative, served as controls. The prevalence of HPV-DNA semen infection and serology was studied in a follow-up of 24 months.

RESULTS: Compared to seronegative patients, VSP seroconverted at recruitment showed absence of multiple infections and reduced prevalence of HPV semen infection at 12 (P = 0.039), 18 (P = 0.034) and 24 months (P = 0.034) of follow-up. Vaccinated VSP showed improved healing (P = 0.001 at 6 months and P < 0.001 at 12 months vs seroconverted VSP), achieving clearance in 12 months.

DISCUSSION: Humoral immunity has a major role in healing from HPV infection. Elder ART patients with HPV semen infection may benefit by the union of both specific counselling and available prophylactic vaccination.
We evaluated whether seroconversion in males influences HPV semen infection. Naturally seroconverted patients showed reduced prevalence of HPV semen infection. Naturally seroconverted patients also showed virtual absence of HPV multiple infection. Prophylactic HPV vaccination induced clearance within 12 months from recruitment. Seroconversion represents a key process involved in the clearance of the HPV. Available prophylactic vaccinations are considered of protective value for genital condyloma and precancerous lesions in female, but cost-effectiveness of the use of HPV vaccine in males is largely underinvestigated. HPV detection in semen is also an emerging problem in couples eligible for assisted reproduction techniques, since persistent infections are not compatible with repeated 6-months counselling-cycles to allow any spontaneous clearance of the virus in older infertile couples. In this study, we provide evidence that the development of seroconversion in human males affected by HPV infection in the genito-urinary tract, detected by HPV-DNA presence in the semen, has beneficial effects on the clearance of a viral load. Moreover, administration of prophylactic vaccination to HPV infected-seronegative patients induced seroconversion within 6 months from the first dosage administration, achieving 10 folds-higher antibody titre compared to natural seroconversion. If vaccine administration ameliorates the clearance of HPV semen infection, this could be a potential benefit to overcome fertility problems related to persistent HPV infections in males, after an obvious cost-effectiveness analysis.

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20160309
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2015

663.
Efficacy of Antimicrobial Therapy for Mycoplasma genitalium Infections. [Review]
Manhart LE; Jensen JS; Bradshaw CS; Golden MR; Martin DH.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Clinical Infectious Diseases. 61 Suppl 8:S802-17, 2015 Dec 15.
[Journal Article. Review]
UI: 26602619
Mycoplasma genitalium has been causally linked with nongonococcal urethritis in men and cervicitis, pelvic inflammatory disease, preterm birth, spontaneous abortion, and infertility in women, yet treatment has proven challenging. To inform treatment recommendations, we reviewed English-language studies describing antimicrobial susceptibility, resistance-associated mutations, and clinical efficacy of antibiotic therapy, identified via a systematic search of PubMed supplemented by expert referral. Minimum inhibitory concentrations (MICs) from some contemporary isolates exhibited high-level susceptibility to most macrolides and quinolones, and moderate susceptibility to most tetracyclines, whereas other contemporary isolates had high MICs to the same antibiotics. Randomized trials demonstrated poor efficacy of doxycycline and better, but declining, efficacy of single-dose azithromycin therapy. Treatment failures after extended doses of azithromycin similarly increased, and circulating macrolide resistance was present in high levels in several areas. Moxifloxacin remains the most effective therapy, but treatment failures and quinolone resistance are emerging. Surveillance of M. genitalium prevalence and antimicrobial resistance patterns is urgently needed.

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2015
Varicocele Repair Improves Testicular Histology in Men with Nonobstructive Azoospermia.
Ustuner M; Yilmaz H; Yavuz U; Ciftci S; Saribacak A; Aynur BS; Yasar H; Culha MM.

OBJECTIVE: To determine the histopathological differences after varicocele repair in testicular tissue in males with nonobstructive azoospermia.

METHODS: Between 2009 and 2014, 45 men with complete azoospermia and palpable varicocele, presenting with primary infertility of at least 1 year, undergoing varicocele repair at our institution were selected for the study. A standard systematic testicular 6-core Tru-Cut biopsy was performed during varicocele repair. Other biopsies were obtained from each testicle of all patients at the time of microscopic sperm extraction procedure.

RESULTS: Nineteen patients were selected for the study. Testicular biopsy specimens were classified as Sertoli cell only on preoperative histopathological analysis in 14 patients. After varicocele repair, focal spermatogenesis (n = 3) and late maturation arrest (n = 2) were found in these patients. Average Johnsen score was significantly increased after varicocelectomy (P = 0.003). Motile sperm was found in one patient on postoperative semen analyses and in 10 more patients in the microscopic sperm extraction procedure. Preoperative high serum follicle stimulating hormone level and venous reflux were significantly and negatively correlated with the increase in average Johnsen score (P < 0.05).

CONCLUSIONS: Our findings suggest significant improvement in testicular histology after varicocele repair.

Status
MEDLINE
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Ustuner, Murat; Yilmaz, Hasan; Yavuz, Ufuk; Ciftci, Seyfettin; Saribacak, Ali; Aynur, Bahri Serkan; Yasar, Hikmet; Culha, Mustafa Melih.
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Hypotestosteronaemia in the aging male: should we treat it?. [Review]

Christe N; Meier CA.

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[Journal Article. Review]

UI: 26599486

The term male hypogonadism is defined as the failure to maintain physiological concentrations of testosterone, a physiological quantity of sperm or the combination of both. Aetiologically, androgen deficiency can originate from the testes (primary hypogonadism) or from the hypothalamic-pituitary regulation of the testicular function (secondary hypogonadism). The causes of hypogonadism are very diverse and may be genetically determined (e.g. Klinefelter's syndrome) or acquired (tumours, infections, haemochromatosis). Classical hypogonadism linked to an underlying disease, such as a pituitary tumour, is a distinct indication for androgen substitution. But how about the aging male? It is known that there is a highly variable age-related
decline in testosterone levels; whether this represents a variation of normality or has a true disease value requiring therapy has been disputed over more than a decade. The key questions surrounding this debate concern not only the age-dependent threshold for serum testosterone but, more importantly, the risks and benefits of testosterone replacement therapy in the aging male. We searched the literature for randomised controlled trials of testosterone administration in aging males with a size of at least 100 patients and a follow-up of at least 6 months, and identified eight studies. These studies mostly tried to evaluate the effect of testosterone on bone density, muscle strength and body composition, rather than clinically meaningful endpoints. Moreover, these trials have provided evidence for relevant cardiovascular adverse events in elderly men. This supports the need for further studies to define the treatment threshold for testosterone levels in the aging male, as well as with regard to the long-term risks and relevant benefits of testosterone therapy in this population. Until we have more solid data in aging males, testing for testosterone deficiency and testosterone replacement should remain reserved for patients with predisposing conditions, symptoms and signs of bona fide hypogonadism.

Correction of Retrograde Ejaculation in Patients with Diabetes Mellitus Using Endourethral Collagen Injection: Preliminary Results.
Kurbatov D; Russo GI; Galstyan GR; Rozhivanov R; Lepetukhin A; Dubsky S; Shwartz YG; Cimino S; Morgia G; Sansalone S.
INTRODUCTION: Diabetic neuropathy secondary to diabetes mellitus type 1 (DM1) is responsible for retrograde ejaculation (RE) in 5-18% of cases. Medical treatment of RE is based either on increasing the sympathetic tone of the bladder or on decreasing the parasympathetic activity. However, the onset of side effects and the lack of response should be considered.

AIMS: The aim of this study was to analyze long-term outcome of endourethral injection of volume-forming material (VFM) of collagen type 2 into bladder neck submucosa in patients with RE secondary to DM1.

METHODS: Twenty-four patients with complete RE refractory to imipramine and DM1 were included in the study. Patients were single-blinded randomized according to a computer-generated random sequence with a 1:1 ratio in two treatment groups, namely group A (endourethral collagen type 2 injection) and group B (endourethral saline water injection). New technique includes an endoscopic injection of VFM such as collagen (Correcting MIT, Ltd. minimally invasive technologies, Moscow, Russia) into bladder neck submucosa. Primary endpoint of the study was the reduction of semen antegrade volume (mL). Secondary endpoints were considered as the changes of antegrade count (millions/mL), antegrade total motility (%), antegrade progressive motility (%), State-Trait Anxiety Inventory, Beck Depression Questionnaire and International Index of Erectile Function (IIEF-5). Pregnancy rate was calculated in each group.

RESULTS: Twenty-three patients completed the study. In group A, significant differences from baseline to 12 months were observed relative to antegrade volume (mL) (mean difference: 0.71, P < 0.05), antegrade count (millions/mL) (mean difference: 45.6, P < 0.05), antegrade total motility (%) (mean difference: 15.4, P < 0.05) and antegrade progressive motility (%) (mean difference: 8.4, P < 0.05). In group A, we observed significant differences in terms State-Trait Anxiety Inventory (mean difference: -20.5, P < 0.05) and Beck Depression Inventory (mean difference: -8.4, P < 0.05) with significant differences compared with group B. We observed significant improvements in group A vs. group B when considering primary and secondary endpoints of the study, but not for the IIEF-5.

CONCLUSION: Correction of RE in DM1 patients could be achieved with endourethral injection of collagen type 2.

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Status

MEDLINE
667.
Interplay Between Premature Ejaculation and Erectile Dysfunction: A Systematic Review and Meta-Analysis. [Review]
Corona G; Rastrelli G; Limoncin E; Sforza A; Jannini EA; Maggi M.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
INTRODUCTION: The specific determinants and underlying factors linking erectile dysfunction (ED) and premature ejaculation (PE) have yet to be clearly identified.

AIM: The aim of this study was to review and meta-analyze all available data regarding the link between ED and PE.

METHODS: An extensive Medline Embase and Cochrane search was performed including the following words: "premature ejaculation" and "erectile dysfunction".

MAIN OUTCOME MEASURES: All observational trials comparing the risk of ED in relation to PE were included. Data extraction was performed independently by two of the authors (G.R, G.C.), and conflicts resolved by the third investigator (M.M.).

RESULTS: Out of 474 retrieved articles, 18 were included in the study for a total of 57,229 patients, of which 12,144 (21.2%) had PE. The presence of PE, however defined, was associated with a significant increase in ED risk (odds ratio: 3.68[2.61;5.18]; P<0.0001). Meta-regression analysis showed that the risk of ED in PE subjects was higher in older individuals as well as in those with a lower level of education and in those who reported a stable relationship less frequently. In addition, subjects with PE and ED more often reported anxiety and depressive symptoms and a lower prevalence of organic associated morbidities, including diabetes mellitus, hypertension and dyslipidemia. All the latter associations were confirmed even after adjustment for age. Finally the risk of PE-related ED increased with the increased proportion of acquired ejaculatory problems (adj r=0.414; P<0.0001 after the adjustment for age).

CONCLUSIONS: In conclusion, the present data showed that ED and PE are not distinctly separate entities, but should be considered from a dimensional point of view. Understanding this dimensional perspective might help sexual health care professionals in providing the most appropriate therapeutic approach to realistically increase patient related outcomes in sexual medicine.

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Status

MEDLINE

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Corona, Giovanni; Rastrelli, Giulia; Limoncin, Erika; Sforza, Alessandra; Jannini, Emmanuele A; Maggi, Mario.

Institution
Clinical and Demographic Correlates of Ejaculatory Dysfunctions Other Than Premature Ejaculation: A Prospective, Observational Study.

Paduch DA; Polzer P; Morgentaler A; Althof S; Donatucci C; Ni X; Patel AB; Basaria S.

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

[Journal Article. Observational Study. Research Support, Non-U.S. Gov't]
UI: 26511106

INTRODUCTION: Ejaculatory dysfunctions other than premature ejaculation are commonly encountered in specialized clinics; however, their characterization in community-dwelling men is lacking.
AIM: The aim of this study was to evaluate the prevalence, severity, and associated distress of four ejaculatory dysfunctions: delayed ejaculation (DE), anejaculation (AE), perceived ejaculate volume reduction (PEVR) and/or decreased force of ejaculation (DFE) as a function of demographic and clinical characteristics in men.

METHODS: Observational analysis of 988 subjects presenting with one or more types of ejaculatory dysfunctions other than premature ejaculation who screened for a randomized clinical trial assessing the efficacy of testosterone replacement on ejaculatory dysfunction. Demographic and clinical characteristics were assessed as potential risk factors using regression analysis.

MAIN OUTCOME MEASURES: The main outcome measures used were ejaculatory dysfunction prevalence and scores (3-item Men's Sexual Health Questionnaire Ejaculatory Dysfunction-Short Form [MSHQ-EjD-SF]), and bother (MSHQ-EjD-SF Bother item) and sexual satisfaction/enjoyment (International Index of Erectile Function Questionnaire Q7, Q8) as a function of subject's age, race, body mass index (BMI) and serum testosterone levels (measured by liquid chromatography tandem mass spectrometry).

RESULTS: Mean (standard deviation [SD]) age of the participants was 52 years (11). Eighty-eight percent of the men experienced more than one type of ejaculatory dysfunction and 68% considered their symptoms to be bothersome. Prevalence of the ejaculatory dysfunctions was substantial across a range of age, race, BMI, and serum testosterone categories. Prevalence of PEVR and DFE were positively associated with age (<40 years vs. 60-70 years: PEVR: odds ratio [OR], 3.05; 95% confidence interval [CI], 1.32-7.06; DFE: OR, 2.78; 95% CI, 1.46-5.28) while DFE was associated with BMI (>30kg/m(2) vs.<25kg/m(2) : OR, 1.80; 95% CI, 1.062-3.05). All ejaculatory dysfunctions were more prevalent in black men.

CONCLUSION: The majority of the participants experienced multiple ejaculatory dysfunctions and found them to be highly bothersome. Ejaculatory dysfunctions were prevalent across a wide range of demographic and clinical characteristics.

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Status
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Comments
Comment in: J Sex Med. 2015 Dec;12(12):2287-8; discussion 2289-90; PMID: 26608798

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20151223

Year of Publication
2015

669.
Adjudin—A Male Contraceptive with Other Biological Activities. [Review]
Cheng YH; Xia W; Wong EW; Xie QR; Shao J; Liu T; Quan Y; Zhang T; Yang X; Geng K; Silvestrini B; Cheng CY.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Recent Patents on Endocrine, Metabolic & Immune Drug Discovery. 9(2):63-73, 2015.
UI: 26510796

BACKGROUND: Adjudin has been explored as a male contraceptive for the last 15 years since its initial synthesis in the late 1990s. More than 50 papers have been published and listed in PubMed in which its mechanism that induces exfoliation of germ cells from the seminiferous epithelium, such as its effects on actin microfilaments at the apical ES (ectoplasmic specialization, a testis-specific actin-rich anchoring junction) has been delineated.

OBJECTIVE: Recent studies have demonstrated that, besides its activity to induce germ cell exfoliation from the seminiferous epithelium to cause reversible infertility in male rodents, adjudin possesses other biological activities, which include anti-cancer, anti-inflammation in the brain, and anti-ototoxicity induced by gentamicin in rodents. Results of these findings likely spark the interest of investigators to explore other medical use of this and other indazole-based compounds, possibly mediated by the signaling pathway(s) in the mitochondria of mammalian cells following treatment with adjudin. In this review, we carefully evaluate these recent findings.
METHODS: Papers published and listed at www.pubmed.org and patents pertinent to adjudin and its related compounds were searched. Findings were reviewed and critically evaluated, and summarized herein.

RESULTS: Adjudin is a novel compound that possesses anti-spermatogenetic activity. Furthermore, it possesses anti-cancer, anti-inflammation, anti-neurodegeneration, and anti-ototoxicity activities based on studies using different in vitro and in vivo models.

CONCLUSION: Studies on adjudin should be expanded to better understand its biological activities so that it can become a useful drug for treatment of other ailments besides serving as a male contraceptive.

Status
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Cheng, Yan-Ho; Xia, Weiliang; Wong, Elissa W P; Xie, Qian R; Shao, Jiaxiang; Liu, Tengyuan; Quan, Yizhou; Zhang, Tingting; Yang, Xiao; Geng, Keyi; Silvestrini, Bruno; Cheng, Chuen-Yan.

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670.
FSHB -211G>T stratification for follicle-stimulating hormone treatment of male infertility patients: making the case for a pharmacogenetic approach in genetic functional secondary hypogonadism. Busch AS; Kliesch S; Tuttelmann F; Gromoll J.

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present Andrology. 3(6):1050-3, 2015 Nov.

[Journal Article. Research Support, Non-U.S. Gov't]
UI: 26445243
Male infertility contributes to a substantial share to couple infertility. Despite scientific efforts, most cases of male infertility remain 'idiopathic' and male-specific therapeutic options are sparse. Given the crucial role of the follicle-stimulating hormone (FSH) for spermatogenesis, FSH is used empirically to improve semen parameters. Furthermore, a recently updated Cochrane review points to a beneficial effect of FSH treatment in idiopathic infertile men on spontaneous pregnancy rates. However, since response to FSH varies strongly even in selected patients and given the lack of powerful evidence of FSH treatment regimens, intra-cytoplasmic spermatozoa injection (ICSI) is widely used in idiopathic male infertility, though the treatment burden is high for the couple and it entails considerable costs and some risks. Single nucleotide polymorphisms (SNPs) within FSH ligand/receptor genes (FSHB/FSHR), significantly influencing reproductive parameters in men, represent promising candidates to serve as pharmacogenetic markers to improve prediction of response to FSH. However, there is an evident lack of information which patients should be treated and how many patients in an andrological outpatient clinic would be eligible for such a treatment, a crucial decision criterion for clinicians and also pharmaceutical industry to start such a pharmacogenetic intervention therapy. After screening our andrological patient cohort, we present a realistic scenario and a basis for further prospective studies using FSH in idiopathic infertile men.

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20160115
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2015
Infertility affects approximately 15% of couples in reproductive age. Male infertility is estimated to represent about 20% of the etiologies. Among them, a rare type of teratozoospermia known as globozoospermia leads to disappointing pregnancy outcomes. Morphological, physiological and genetic aspects of this severe disorder have been described. We undertook a complete review of the available data on the reproductive outcomes in globozoospermic patients. To this end, a literature review in both English and French, over a 20-year time period using PubMed/Medline, ScienceDirect, and Scopus was performed. A total of 45 publications describing 172 attempts of treatment with assisted reproduction techniques (ICSI or IMSI with or without oocyte activation) were identified. We reviewed 28 deliveries and 34 children. However, for these patients, the fertilization rate after ICSI remained low. The present review suggests that oocyte activation (in particular with calcium ionophore) could improve the pregnancy rate significantly when dealing with globozoospermia. Once the exact pathogenesis of human globozoospermia is clearly identified, it is likely that other treatments such as recombinant phospholipase C zeta (PLC zeta, PLCzeta), which seems to be a promising biological tool, would be developed.

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Autoimmune reactions against the sperm cells play an ambiguous role in fertility impairment. The objective of this study was to characterize functional deficit of sperm conditioned by antisperm immune response in normozoospermic men. This was a multi-centric, cross-sectional, case-control study. The study subjects were 1060 infertile normozoospermic men and 107 fertile men. The main outcome measures were clinical examination, semen analysis including MAR test for antisperm antibodies (ASA), computer-aided sperm analysis, acrosome reaction (AR) detected with flow cytometry, DNA fragmentation measured with sperm chromatin dispersion, reactive oxygen species (ROS) assessed using the luminol-dependent chemiluminescence method. 2% of the fertile men had MAR-IgG > 50%, but all subjects with MAR-IgG>12% were outliers; 16% infertile men had MAR-IgG > 50% (p<0.0001). There was a direct correlation between the infertility duration and MAR-IgG (R=0.3; p<0.0001). The ASA-positive infertile men had AR disorders 2.1 times more frequently (p<0.02), predominantly inductivity disorders. We found signs of hyperactivation proportionate to the ASA level (p<0.001). DNA fragmentation was more highly expressed and was 1.6 and 1.3 times more frequent compared with the fertile and the ASA-negative patients, respectively (p<0.001 and p<0.05). We found signs of oxidative stress (OS): ROS generation by washed ASA-positive spermatozoa was 3.7 times higher than in the fertile men (p<0.00001) and depended on the ASA levels (R=0.5; p<0.0001). The ASA correlation with ROS generation in native sperm was weak (R=0.2; p<0.001). We concluded that autoimmune reactions against spermatozoa are accompanied by a fertility decrease in normozoospermia. This
results from AR and capacitation disorders and DNA fragmentation. The pathogenesis of sperm abnormalities in immune infertility is associated with the OS of spermatozoa.

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20151109

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2015
MTHFR-Ala222Val and male infertility: a study in Iranian men, an updated meta-analysis and an in silico-analysis.

Nikzad H; Karimian M; Sareban K; Khoshkokhan M; Hosseinzadeh Colagar A.

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Reproductive Biomedicine Online. 31(5):668-80, 2015 Nov.
[Journal Article. Meta-Analysis]
UI: 26380869

Methylenetetrahydrofolate reductase (MTHFR) functions as a main regulatory enzyme in folate metabolism. The association of MTHFR gene Ala222Val polymorphism with male infertility in an Iranian population was investigated by undertaking a meta-analysis and in-silico approach. A genetic association study included 497 men; 242 had unexplained infertility and 255 were healthy controls. Polymerase chain reaction restriction fragment length polymorphism was used for genotyping MTHFR-Ala222Val. OpenMeta[Analyst] software was used to conduct the analysis; 22 studies were identified by searching PubMed and the currently reported genetic association study. A novel in-silico approach was used to analyse the effects of Ala222Val substitution on the structure of mRNA and protein. Genetic association study revealed a significant association of MTHFR-222Val/Val genotype with oligozoospermia (OR 2.32; 95% CI, 1.12 to 4.78; \( P = 0.0451 \)) and azoospermia (OR 2.59; 95% CI 1.09 to 6.17; \( P = 0.0314 \)). Meta-analysis for allelic, dominant and codominant models showed a significant association between Ala222Val polymorphism and the risk of male infertility (\( P < 0.001 \)). In silico-analysis showed MTHFR-Ala222Val affects enzyme structure and could also change the mRNA properties (\( P = 0.1641 \); \( P < 0.2 \) is significant). The meta-analysis suggested significant association of MTHFR-Ala222Val with risk of male infertility, especially in Asian populations.

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674.
Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. [Review]
Campbell JM; Lane M; Owens JA; Bakos HW.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Reproductive Biomedicine Online. 31(5):593-604, 2015 Nov.
UI: 26380863
This systematic review investigated the effect of paternal obesity on reproductive potential. Databases searched were Pubmed, Ovid, Web of Science, Scopus, Cinahl and Embase. Papers were critically appraised by two reviewers, and data were extracted using a standardized tool. Outcomes were: likelihood of infertility, embryo development, clinical pregnancy, live birth, pregnancy viability, infant development, sperm; concentration, morphology, motility, volume, DNA fragmentation, chromatin condensation, mitochondrial membrane potential (MMP), and seminal plasma factors. Thirty papers were included, with a total participant number of 115,158. Obese men were more likely to experience infertility (OR = 1.66, 95% CI 1.53-1.79), their rate of live birth per cycle of assisted reproduction technology (ART) was reduced (OR = 0.65, 95% CI 0.44-0.97) and they had a 10% absolute risk increase of pregnancy non-viability. Additionally, obese men had an increased percentage of sperm with low MMP, DNA fragmentation, and abnormal morphology. Clinically significant differences were not found for conventional semen parameters.
From these findings it can be concluded that male obesity is associated with reduced reproductive potential. Furthermore, it may be informative to incorporate DNA fragmentation analysis and MMP assessment into semen testing, especially for obese men whose results suggest they should have normal fertility.

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675.
Prevalence of genital Chlamydia trachomatis in Iran: a systematic review and meta-analysis.
[Review]
Ahmadi MH; Mirsalehian A; Bahador A.
UI: 26343285
OBJECTIVE: To determine the overall prevalence of Chlamydia trachomatis in Iranian males and females and to find out the effect of this bacterium on fertility potential and its association with urogenital symptoms.

METHODS: We searched both English and Persian electronic databases using keywords 'Chlamydia', 'Chlamydia trachomatis', 'prevalence', 'incidence', 'frequency', 'epidemiology' and 'Iran'. Finally, after some exclusion, 34 studies from different regions of Iran were included in our study, and a meta-analysis was performed to determine pooled prevalence estimates for each group.

RESULTS: C. trachomatis prevalence for women and men was high and ranged from 0 to 32.7% and 0 to 23.3%, respectively (95% CI). The pooled prevalence of the bacterium in the female population was 12.3% (95% CI: 10.6-14.2%) and in men was 10.9% (95% CI: 7.6-15.4%). A high level of heterogeneity was seen for both men (I(2) = 77.4%; P < 0.001) and women (I(2) = 77.5%; P < 0.001); but in men and not in women, some evidence for publication bias was observed [Egger's test (two-tailed P = 0.013); Begg's test (two-tailed P = 0.025)]. In females analysis of symptomatic/infertile group with asymptomatic/fertile group in females, the overall OR was above 1 and the overall P-value was below zero.

CONCLUSIONS: This bacterium may play a role in female infertility or be associated with clinical manifestations; thus, planning national programmes for adequate diagnosis of genital infections caused by this pathogen is necessary. Furthermore, screening strategies, particularly for asymptomatic individuals, and treatment of infected people can reduce consequent complications.

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PMID
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4727584
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Mycoplasma and ureaplasma infection and male infertility: a systematic review and meta-analysis. [Review]
Huang C; Zhu HL; Xu KR; Wang SY; Fan LQ; Zhu WB.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
UI: 26311339
The relationship between mycoplasma and ureaplasma infection and male infertility has been studied widely; however, results remain controversial. This meta-analysis investigated the association between genital ureaplasmas (Ureaplasma urealyticum, Ureaplasma parvum) and mycoplasmas (Mycoplasma hominis, Mycoplasma genitalium), and risk of male infertility. Differences in prevalence of ureaplasma and mycoplasma infection between China and the rest of the world were also compared. Study data were collected from PubMed, Embase and the China National Knowledge Infrastructure. Summary odds ratio (OR) with 95% confidence interval (CI) was applied to assess the relationship. Heterogeneity testing and publication bias testing were also performed. A total of 14 studies were used: five case-control studies with 611 infertile cases and 506 controls featuring U. urealyticum infection, and nine case-control studies with 2410 cases and 1223 controls concerning M. hominis infection. Two other infection (U. parvum and M. genitalium) were featured in five and three studies, respectively. The meta-analysis results indicated that U. parvum and M. genitalium are not associated with male infertility. However, a significant relationship existed between U. urealyticum and M. hominis and male infertility. Comparing the global average with China, a significantly higher positive rate of U. urealyticum, but a significantly lower positive rate of M. hominis, was observed in both the infertile and control groups in China.
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Intracytoplasmic morphologically selected sperm injection versus conventional intracytoplasmic sperm injection: a randomized controlled trial.
La Sala GB; Nicoli A; Fornaciari E; Falbo A; Rondini I; Morini D; Valli B; Villani MT; Palomba S. OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Comparative Study. Journal Article. Randomized Controlled Trial]
UI: 26307050
BACKGROUND: Intracytoplasmic morphologically selected sperm injection (IMSI) is still proposed and employed in the clinical practice to improve the reproductive outcome in infertile couples scheduled for conventional intracytoplasmic sperm injection (cICSI). The aim of the current randomized controlled trial (RCT) was to test the hypothesis that IMSI gives a better live birth delivery rate than cICSI.
METHODS: Infertile couples scheduled for their first cICSI cycle for male factor were allocated using a simple randomization procedure. All available biological and clinical data were recorded and analyzed in a triple-blind fashion.
RESULTS: Our final analysis involved the first 121 patients (48 and 73 subjects for IMSI and cICSI arm, respectively) because the trial was stopped prematurely on the advice of the data safety and monitoring Committee because of concerns about IMSI efficacy at the first interim
analysis. No significant difference between arms was detected in rates of clinical pregnancy per embryo transferred [11/34 (32.3%) vs. 15/64 (23.4%); odds ratio (OR) 1.56, 95% (confidence interval) CI 0.62-3.93, P=0.343] and of live birth delivery [9/48 (18.8%) vs. 11/73 (15.1%); OR 1.30, 95% CI 0.49-3.42, P=0.594).

CONCLUSION: Current data did not support the routine use of IMSI in the clinical practice for improving cICSI results in unselected infertile couples with male factor.
Implication of sperm chromosomal abnormalities in recurrent abortion and multiple implantation failure. [Review]
Caseiro AL; Regalo A; Pereira E; Esteves T; Fernandes F; Carvalho J.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article. Review]
UI: 26299791
Currently, some infertility treatment centres provide sperm karyotype analysis, although the impact of sperm chromosomal abnormalities on fertility is not yet fully understood. Several studies using fluorescence in-situ hybridization (FISH) to analyse sperm chromosomal constitution discovered that the incidence of aneuploidy is increased in individuals with a history of repeated abortion or implantation failure and is even higher in cases of oligoasthenoteratozoospermia (OAT), abnormal somatic karyotype or in spermatozoa retrieved directly from the testis or epididymis, showing that the application of FISH in these cases may be of some benefit for improving the reproductive outcome. This article presents the results of clinical trials of FISH analysis on spermatozoa, the medical indications for performing this examination, its results in infertile patients and the advantages when performing genetic counselling prior to treatment. Also discussed is the possibility of applying the latest techniques of genetic analysis in these cases and the potential benefits for improving the prognosis of male infertility.
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Outcomes of Microscopic Subinguinal Varicocelectomy With and Without the Assistance of Doppler Ultrasound: A Randomized Clinical Trial.

Guo L; Sun W; Shao G; Song H; Ge N; Zhao S; Liu Y; Zhang X; Xiao Z; Yuan M.

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present


[Comparative Study. Journal Article. Randomized Controlled Trial. Research Support, Non-U.S. Gov't]

UI: 26278823

OBJECTIVE: To compare the surgical outcomes and complications between microscopic subinguinal varicocelectomy (MV) and intraoperative vascular Doppler ultrasound-assisted microscopic subinguinal varicocelectomy (IVDU-MV) for infertile patients with varicoceles.

MATERIALS AND METHODS: One hundred seventy-two infertile patients with varicoceles were randomly divided into IVDU-MV group (n = 85) and MV group (n = 87). We assessed patients' operative and postoperative parameters, semen parameters, and the pregnancy rate. The mean follow-up period was 21 months (range, 13-34 months).
RESULTS: The operative time was significantly shorter in the IVDU-MV group than MV group (41.9 +/- 13.6 vs 52.7 +/- 14.1 minutes, P <.05). The number of intraoperative arteries spared was significantly greater in the IVDU-MV group than the MV group (1.9 +/- 0.8 vs 1.3 +/- 0.7, P <.05). In addition, the average number of spermatic veins ligated was significantly greater in the IVDU-MV group (7.8 +/- 2.1 vs 7.0 +/- 1.9, P <.05). Lymphatic spared showed no significant difference (P >.05). The postoperative hospital stay showed no significant difference. Sperm concentration, sperm motility, and the percentage of grade a+b sperm were significantly increased in both groups at 3, 6, and 12 months after surgery (P <.05), and the sperm motility was higher in IVDU-MV than MV group (43.98 +/- 7.64 vs 36.98 +/- 5.10, P <.05) in 12 months after surgery. Sperm morphology was comparable between the 2 groups. The pregnancy rate showed no significant difference (36.8% of the MV vs 34.1% of the IVDU-MV, P >.05).

CONCLUSION: Our study demonstrated that both MV and IVDU-MV are effective methods for the improvement of semen parameters in infertile men with varicocele, with a natural conception rate of 35% over a mean follow-up of 21 months. Compared with MV, IVDU-MV is superior in shortening operative time, increasing the number of spermatic arteries spared, spermatic veins ligated, and sperm motility after surgery. IVDU should be routinely used as an effective tool to improve outcomes and safety of varicocelectomy.

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Status
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680.
Differential effects of strength training and testosterone treatment on soluble CD36 in aging men: Possible relation to changes in body composition.
Glintborg D; Christensen LL; Kvorning T; Larsen R; Hojlund K; Brixen K; Hougaard DM; Handberg A; Andersen M.

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[Comparative Study. Journal Article. Randomized Controlled Trial. Research Support, Non-U.S. Gov't]
UI: 26264425
PURPOSE: We measured soluble CD36 (sCD36) and body composition to determine the effects of testosterone treatment (TT) and/or strength training (ST) on cardiovascular risk in men with low normal testosterone levels.
METHODS: Double-blinded, placebo-controlled study in 54 men aged 60-78 years with bioavailable testosterone < 7.3 nmol/L and waist > 94 cm randomized to TT (gel, 50-100 mg/day,
n = 20), placebo (n = 18) or ST (n = 16) for 6 months. Moreover, the ST group was randomized to
TT (ST + TT, n = 7) or placebo (ST + placebo, n = 9) after 3 months.

OUTCOMES: sCD36, total and regional fat mass were established by Dual X-ray absorptiometry
and magnetic resonance imaging. Data are presented as median (quartiles). Kruskal-Wallis and
Mann-Whitney tests were performed on delta values at 0, 3 and 6 months.

RESULTS: ST + placebo decreased sCD36 levels by 21% [from 0.80 (0.68-1.22) to 0.63 (0.51-
0.73) rel. units] vs. TT and vs. placebo (p < 0.05). ST + placebo did not change bioavailable
testosterone and lean body mass. Fat mass measures significantly improved during ST +
placebo, ST + TT, and TT vs. placebo. During ST + placebo, delta sCD36 was associated with
delta total fat mass (r = 0.81) and delta central fat mass (r = 0.84).

CONCLUSIONS: Compared to testosterone treatment, six months of strength training reduced
sCD36 levels suggesting decreased cardiovascular risk, possibly due to a reduction in central fat
mass.

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20151002
A systematic review of recent clinical practice guidelines and best practice statements for the evaluation of the infertile male. [Review]
Esteves SC; Chan P.
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[Journal Article. Review]
UI: 26238943
PURPOSE: We systematically identified and reviewed the methods and consistency of recommendations of recently developed clinical practice guidelines (CPG) and best practice statements (BPS) on the evaluation of the infertile male.
METHODS: MEDLINE and related engines as well as guidelines' Web sites were searched for CPG and BPS written in English on the general evaluation of male infertility published between January 2008 and April 2015.
RESULTS: Four guidelines were identified, all of which reported to have been recently updated. Systematic review was not consistently used in the BPS despite being reported in the CPG. Only one of them reported having a patient representative in its development team. The CPG issued by the European Association of Urology (EAU) graded some recommendations and related that to levels (but not quality) of evidence. Overall, the BPS issued respectively by the American Urological Association and American Society for Reproductive Medicine concurred with each other, but both differed from the EAU guidelines with regard to methods of collection, extraction and interpretation of data. None of the guidelines incorporated health economics. Important specific limitations of conventional semen analysis results were ignored by all guidelines. Besides variation in the methodological quality, implementation strategies were not reported in two out of four guidelines.
CONCLUSIONS: While the various panels of experts who contributed to the development of the CPG and BPS reviewed should be commended on their tremendous efforts aiming to establish a clinical standard in both the evaluation and management of male infertility, we recognized inconsistencies in the methodology of their synthesis and in the contents of their final
recommendations. These discrepancies pose a barrier in the general implementation of these guidelines and may limit their utility in standardizing clinical practice or improving health-related outcomes. Continuous efforts are needed to generate high-quality evidence to allow further development of these important guidelines for the evaluation and management of males suffering from infertility.

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682.
Combination of vitamin E and clomiphene citrate in treating patients with idiopathic oligoasthenozoospermia: A prospective, randomized trial.
ElSheikh MG; Hosny MB; Elshenoufy A; Elghamrawi H; Fayad A; Abdelrahman S.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Comparative Study. Journal Article. Randomized Controlled Trial]
UI: 26235968
The most common cause of male infertility is idiopathic oligoasthenozoospermia. Empirical medical treatment for idiopathic male infertility is still a controversial issue. The aim of this study was to evaluate any possible effects of combining vitamin E as antioxidant and clomiphene citrate as antiestrogen on spermatozoa concentration and motility in comparison to give either of medications alone in patients with idiopathic oligoasthenozoospermia. This is a comparative prospective randomized study. Ninety patients with idiopathic oligoasthenozoospermia were randomized into equally three groups: Group A: received vitamin E (400 mg/day) for 6 months.
Group B: received clomiphene citrate (25 mg daily) for 6 months. Group C: received combination of both drugs in the same doses for 6 months. All patients were subjected to the following: history taking, general and genital examination, semen analysis, serum FSH, total testosterone, and scrotal duplex. Semen examination was performed according to the guidelines of (WHO, 2010), at the start of treatment and was repeated after 3 months and after 6 months of treatment. Regarding vitamin E group, there was insignificant increase in mean sperm concentration after 6 months of treatment in comparison to baseline. On the other hand, there was a significant improvement of mean sperm concentration in the other two groups after 6 months of treatment, with more significance in combination therapy group ($p = 0.001$). The mean total sperm motility has improved in all patients groups, in comparison to baseline, with more significance in combination therapy group. In vitamin E group, it was 28.07 +/- 9.65% ($p = 0.000$). For those in clomiphene citrate group, was 33.33 +/- 14.10% ($p = 0.003$) and 40.50 +/- 17.54% ($p = 0.000$) in combination therapy group. Combining antioxidant and anti-estrogen therapy is a valid option for the treatment of a selected group of men with unexplained isolated oligoasthenozoospermia.

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20150827
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2015
Diagnostic accuracy of sperm DNA degradation index (DDSi) as a potential noninvasive biomarker to identify men with varicocele-associated infertility.

Esteves SC; Gosalvez J; Lopez-Fernandez C; Nunez-Calonge R; Caballero P; Agarwal A; Fernandez JL.

[Clinical Trial. Journal Article. Research Support, Non-U.S. Gov't]
UI: 26228577

PURPOSE: Varicocele is a frequent cause of impaired testicular function that has been associated with increased levels of sperm DNA fragmentation (SDF). Sperm with degraded DNA (DDS), as observed using the sperm chromatin dispersion (SCD) test, represent a subpopulation of spermatozoa with extensive DNA and nuclear protein damage. The aim of this work was to determine the usefulness of sperm DNA degradation index (DDSi) as a novel noninvasive biomarker to identify infertile men with varicocele.

METHODS: A total of 593 semen samples obtained from men attending infertility clinics were analyzed for SDF and DDS with the SCD test. These samples were classified as: (1) fertile donors; (2) infertile patients with least two failed assisted reproduction cycles; (3) leukocytospermia; (4) Chlamydia trachomatis infection; (5) testicular cancer, and (6) infertile men with varicocele. The DDSi was obtained by determining the proportion of DDS in the whole sperm population presenting with fragmented DNA. The diagnostic accuracy of DDSi was evaluated by correlation coefficient and receiver operating characteristics analyses.

RESULTS: A positive correlation (r > 0.52) was observed between the SDF and the frequency of degraded sperm in all patient groups. The sperm DNA degradation index (DDSi) was at least twice as higher in infertile men with varicocele (mean: 0.54) compared with other clinical conditions and fertile donors (means ranging from 0.02 to 0.21; P < 0.0001). A DDSi > 0.33 identified patients with varicocele with 94 % accuracy.

CONCLUSION: Although DDS is not pathognomonic of varicocele, the DDSi is a useful noninvasive biomarker to identify infertile individuals with varicocele when examining sperm DNA damage during a routine semen analysis. This finding may alert practitioners and laboratories performing semen analysis that in the presence of an abnormal DDSi it is likely that a given patient has varicocele. It is therefore strongly recommended that such patients be referred to urologists in order to undergo a full andrological examination and be properly counseled.

Status
MEDLINE
Authors Full Name
Tamoxifen is a potent antioxidant modulator for sperm quality in patients with idiopathic oligoasthenospermia.

Guo L; Jing J; Feng YM; Yao B.

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[Journal Article. Randomized Controlled Trial. Research Support, Non-U.S. Gov't]
UI: 26216675

OBJECTIVE: To explore the new mechanisms of tamoxifen (TAM) in the treatment for patients with idiopathic oligoasthenospermia.

METHODS: In a prospective, randomized, controlled clinical trial, 120 cases of idiopathic oligoasthenospermia were enrolled and randomly assigned to the indomethacin group (n = 60) treated with indomethacin (25 mg, bid) and TAM group (n = 60) treated with TAM (10 mg, bid) for 3 months. Before and after treatment, we evaluated semen parameters, serum malondialdehyde (MDA) and total antioxidant capacity (TAC), seminal plasma MDA and TAC, spermatozoa intracellular reactive oxygen species (ROS), sperm succinate dehydrogenase (SDH) activity, sperm mitochondrial membrane potential (MMP), and sperm adenosine triphosphate (ATP) content. The independent t test and one-way repeated measures analysis of variance were used to compare the variables between and within two groups.

RESULTS: In the indomethacin group, the percentage of progressive motile sperms, total motility, sperm MMP, and ATP content were increased significantly after 3-month treatment (P < 0.05). In the TAM group, total sperm count, sperm concentration, the percentage of progressive motile...
sperms, total motility, serum and seminal plasma TAC, sperm MMP, and ATP content were significantly improved or increased (P < 0.05), while spermatozoa intracellular ROS was significantly decreased (P < 0.05). Compared to the indomethacin group, TAM treatment showed better improvement in total sperm count, sperm concentration, serum TAC, seminal plasma TAC, spermatozoa intracellular ROS, and sperm SDH activity.

CONCLUSIONS: TAM treatment can significantly improve sperm quality, which is achieved through alleviating oxidative stress, improving sperm mitochondrial functionality, and subsequently increasing sperm motility.

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685.
Stem cells in reproductive medicine: ready for the patient?. [Review]
Vassena R; Eguizabal C; Heindryckx B; Sermon K; Simon C; van Pelt AM; Veiga A; Zambelli F; ESHRE special interest group Stem Cells.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article. Research Support, Non-U.S. Gov't. Review]
UI: 26202914

STUDY QUESTION: Are there effective and clinically validated stem cell-based therapies for reproductive diseases?

SUMMARY ANSWER: At the moment, clinically validated stem cell treatments for reproductive diseases and alterations are not available.
WHAT IS KNOWN ALREADY: Research in stem cells and regenerative medicine is growing in scope, and its translation to the clinic is heralded by the recent initiation of controlled clinical trials with pluripotent derived cells. Unfortunately, stem cell 'treatments' are currently offered to patients outside of the controlled framework of scientifically sound research and regulated clinical trials. Both physicians and patients in reproductive medicine are often unsure about stem cells therapeutic options.

STUDY DESIGN, SIZE, DURATION: An international working group was assembled to review critically the available scientific literature in both the human species and animal models.

PARTICIPANTS/MATERIALS, SETTING, METHODS: This review includes work published in English until December 2014, and available through Pubmed.

MAIN RESULTS AND THE ROLE OF CHANCE: A few areas of research in stem cell and reproductive medicine were identified: in vitro gamete production, endometrial regeneration, erectile dysfunction amelioration, vaginal reconstruction. The stem cells studied range from pluripotent (embryonic stem cells and induced pluripotent stem cells) to monopotent stem cells, such as spermatogonial stem cells or mesenchymal stem cells. The vast majority of studies have been carried out in animal models, with data that are preliminary at best.

LIMITATIONS, REASONS FOR CAUTION: This review was not conducted in a systematic fashion, and reports in publications not indexed in Pubmed were not analyzed.

WIDER IMPLICATIONS OF THE FINDINGS: A much broader clinical knowledge will have to be acquired before translation to the clinic of stem cell therapies in reproductive medicine; patients and physicians should be wary of unfounded claims of improvement of existing medical conditions; at the moment, effective stem cell treatment for reproductive diseases and alterations is not available.

STUDY FUNDING/COMPETING INTERESTS: None.

TRIAL REGISTRATION NUMBER: NA.

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Impact of sperm genome decay on Day-3 embryo chromosomal abnormalities from advanced-maternal-age patients.

Kaarouch I; Bouamoud N; Louanjli N; Madkour A; Copin H; Benkhalifa M; Sefrioui O.

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[Journal Article. Randomized Controlled Trial. Research Support, Non-U.S. Gov't]

UI: 26191648

Infertile male patients often exhibit unconventional semen parameters, including DNA fragmentation, chromatin dispersion, and aneuploidy—collectively referred to as sperm genome decay (SGD). We investigated the correlation of SGD to embryo chromosomal abnormalities and its effect on clinical pregnancy rates in patients with advanced maternal age (AMA) (>40 years) who were undergoing intracytoplasmic sperm injection-preimplantation genetic screening (ICSI-PGS). Three groups were assessed: patients with AMA and male partners with normal sperm
AMA-N); AMA patients and male partners presenting with SGD (AMA-SGD); and young fertile female patients and male partners with SGD (Y-SGD). We found a significant increase in embryonic chromosomal abnormalities-polyploidy, nullisomy, mosaicism, and chaotic anomaly rates-when semen parameters are altered (76% vs. 67% and 66% in AMA-SGD vs. AMA-N and Y-SGD groups, respectively). Statistical analysis showed a correlation between SGD and aneuploidies of embryonic chromosomes 13, 16, 21, X, and Y, as well as negative clinical outcomes. Incorporation of molecular sperm analyses should therefore significantly minimize the risk of transmission of chromosomal anomalies from spermatozoa to embryos, and may provide better predictors of pregnancy than conventional sperm analyses. We also demonstrated that an ICSI-PGS program should be implemented for SGD patients in order to limit transmission of chromosomal paternal anomalies and to improve clinical outcome.

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Obesity and late-onset hypogonadism. [Review]
Corona G; Vignozzi L; Sforza A; Mannucci E; Maggi M.
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MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article. Review]
UI: 26143633
Obesity and male hypogonadism (HG) are often associated, as demonstrated in all cross-sectional studies. Prospective studies have indicated that i) having HG at baseline increases the risk of visceral obesity (and metabolic syndrome) and that ii) obesity induces incident HG. Hence, there is a bidirectional relationship between the two conditions. This is the main topic of this review, along with some pathogenic considerations. Meta-analysis of intervention studies indicates that treating obesity is a very efficient treatment for obesity-induced HG. The mechanism by which obesity induces HG has not yet been completely understood, but dietary-induced hypothalamic inflammation, along with a decreased GnRH release, is plausible. Among patients seeking medical care for obesity, the proportion of HG is relatively high. The prevalence of obesity among patients referring for sexual dysfunction is also elevated. Hence, in symptomatic, obese, hypogonadal subjects, testosterone supplementation (TS) can be considered. Whereas long-term uncontrolled register studies suggest that TS could decrease weight, analysis of controlled studies only support a parallel increase in lean mass and decrease in fat mass, with a resulting null effect on weight. Considering that T induces an increase in muscle mass, it is conceivable that the amount of activity obese people can undertake after TS will increase, allowing a closer adherence to physical exercise programs. Some studies, here meta-analyzed, support this concept.
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FSHR gene Thr307Ala and Asn680Ser polymorphisms in infertile men: an association study in North China and meta-analysis.

Wu XQ; Xu SM; Wang YQ; Li Q; Wang ZQ; Zhang CL; Shen Y.

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[Journal Article. Meta-Analysis. Research Support, Non-U.S. Gov't]

UI: 26125757

Male infertility is a complex multifactorial and polygenic disease, and genetic factors play an important role in its formation and development. Recently, the association between follicle stimulating hormone receptor (FSHR) gene polymorphisms and male infertility risk has attracted widespread attention due to the unique biological functions of FSH. The aim of this study was to further explore the associations between the Thr307Ala and Asn680Ser polymorphisms of the FSHR gene and male infertility. A case-control study of 212 infertile and 164 fertile men from North China was performed. FSHR polymorphism genotypes were obtained through direct DNA sequencing. A meta-analysis was also performed. In the single-site association analysis, no significant associations were identified between FSHR Thr307Ala and Asn680Ser polymorphisms and male infertility (P > 0.05). However, we found that the combined genotypic frequency of
Thr/Ala + Asn/Asn was higher in infertile patients than in controls (6.6 vs 1.8%; odds ratio (OR) = 3.795; 95% confidence interval (CI): 1.072-13.434, P = 0.027). In the meta-analysis, there was also no evidence of FSHR polymorphism (rs 6165 and rs 6168) association with male infertility (P > 0.05). However, we found that the combined genotypes Thr/Thr + Asn/Asn had an increased risk of male infertility (OR = 1.238; 95%CI: 1.001-1.537, P = 0.049). Our studies further confirmed reports that there were no significant associations between the FSHR Thr307Ala and Asn680Ser polymorphisms and male infertility risk. However, a combined FSHR genotype showed significant association with male infertility.

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689.
Direct comparison of the effects of intravenous kisspeptin-10, kisspeptin-54 and GnRH on
gonadotrophin secretion in healthy men.
Jayasena CN; Abbara A; Narayanaswamy S; Comninos AN; Ratnasabapathy R; Bassett P;
Mogford JT; Malik Z; Calley J; Ghatei MA; Bloom SR; Dhillo WS.
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UI: 26089302
STUDY QUESTION: How potently does the novel hypothalamic stimulator of reproduction,
kisspeptin, increase gonadotrophin secretion when compared with GnRH in healthy men?
SUMMARY ANSWER: At the doses tested, intravenous administration of either of two major
kisspeptin isoforms, kisspeptin-10 and -54, was associated with similar levels of gonadotrophin
secretion in healthy men; however, GnRH was more potent when compared with either kisspeptin
isoform.
WHAT IS KNOWN ALREADY: Kisspeptin-10 and -54 are naturally occurring hormones in the
kisspeptin peptide family which potently stimulates endogenous GnRH secretion from the
hypothalamus, so have the potential to treat patients with reproductive disorders. Rodent studies
suggest that kisspeptin-54 is more potent when compared with kisspeptin-10; however, their
effects have not previously been directly compared in humans, or compared with direct pituitary
stimulation of gonadotrophin secretion using GnRH.
STUDY DESIGN, SIZE AND DURATION: A single-blinded placebo controlled physiological study
was performed from January to December 2013. Local ethical approval was granted, and five
participants were recruited to each dosing group.
PARTICIPANTS/MATERIALS, SETTING, METHODS: Healthy men were administered vehicle,
kisspeptin-10, kisspeptin-54 and GnRH intravenously for 3 h on different study days. Each
hormone was administered at 0.1, 0.3 and 1.0 nmol/kg/h doses (n = 5 subjects per group).
Regular blood sampling was conducted throughout the study to measure LH and FSH. Study
visits were conducted at least a week apart.
MAIN RESULTS AND THE ROLE OF CHANCE: Serum LH and FSH levels were ~3-fold higher
during GnRH infusion when compared with kisspeptin-10 and ~2-fold higher when compared with
kisspeptin-54 [mean area under the curve serum LH during infusion (in hours times international
units per litre, h.IU/l): 10.81 +/- 1.73, 1.0 nmol/kg/h kisspeptin-10; 14.43 +/- 1.27, 1.0 nmol/kg/h
kisspeptin-54; 34.06 +/- 5.18, 1.0 nmol/kg/h GnRH, P < 0.001 versus kisspeptin-10, P < 0.01
versus kisspeptin-54].
LIMITATIONS, REASONS FOR CAUTION: This study had a small sample size.
WIDER IMPLICATIONS OF THE FINDINGS: Kisspeptin offers a novel means of stimulating the reproductive axis. Our data suggest that kisspeptin stimulates gonadotrophin secretion less potently when compared with GnRH; however, kisspeptin may stimulate gonadotrophins in a more physiological manner when compared with current therapies. Kisspeptin is emerging as a future therapeutic agent, so it is important to establish which kisspeptin hormones could be used to treat patients with infertility. Results of this study suggest that either isoform has similar effects on reproductive hormone secretion in healthy men when administered intravenously.

STUDY FUNDING/COMPETING INTERESTS: This work is funded by grants from the MRC and NIHR and is supported by the NIHR Imperial Biomedical Research Centre Funding Scheme. C.N.J. is supported by an NIHR Clinical Lectureship. A.A. is supported by Wellcome Trust Research Training Fellowships. A.N.C. is supported by Wellcome Trust Translational Medicine Training Fellowship. W.S.D. is supported by an NIHR Career Development Fellowship.

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Varicocele is associated with varicose veins: A population-based case-control study.
Lai YW; Hsueh TY; Hu HY; Chiu YC; Chen SS; Chiu AW.
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[Journal Article. Research Support, Non-U.S. Gov't]
UI: 26088019
OBJECTIVE: To analyze the association between patients with varicocele and varicose veins in Taiwan.
METHODS: Between 2001 and 2010, comprehensive data were analyzed on the characteristics of patients with varicocele and varicose veins in Taiwan through a retrospective, nationwide, population-based study. Data were obtained from the Taiwan National Health Insurance Research Database. A total of 2727 cases with varicose veins and 10,908 randomly selected controls were included in this study. Conditional logistic regression analyses were used to examine the association between varicose veins and varicocele.
RESULTS: The prevalence of varicocele was 1.3% and 0.3% for cases (with varicose veins) and controls (without varicose vein), respectively (P < 0.001). Conditional logistic regression analysis showed that the odds ratio of being previously diagnosed with varicose veins for cases was 4.71 (95% confidence interval 2.87-7.89) when compared with controls after adjusting for age,
diabetes, heart disease, chronic obstructive pulmonary disease, liver and kidney disease, and edema. Furthermore, the odds ratio was 5.96 (95% confidence interval 2.90-12.24), 4.76 (95% confidence interval 1.68-13.48) and 1.69 (95% confidence interval 0.30-9.55) in patients aged <50 years, 51-65 years and >65 years, respectively. In addition, the prevalence of male infertility was 15.1% for patients with varicocele and varicose veins, and 14.5% for patients with varicocele only, but no significant difference was observed.

CONCLUSION: Our findings suggest an association between both varicocele and varicose veins. In addition, this association is higher in patients aged younger than 50 years. Evaluation of male patients with varicose veins for varicocele should be recommended.

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Effects of testosterone replacement therapy on nocturia and quality of life in men with hypogonadism: a subanalysis of a previous prospective randomized controlled study in Japan. Shigehara K; Konaka H; Koh E; Izumi K; Kitagawa Y; Mizokami A; Nakashima T; Shimamura M; Iwamoto T; Namiki M.

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present Aging Male. 18(3):169-74, 2015. [Journal Article. Randomized Controlled Trial]

UI: 26075538

OBJECTIVE: We investigated the effects of testosterone replacement therapy (TRT) on nocturia and general health among men with hypogonadism and nocturia.

METHODS: From our previous EARTH study population, 64 patients with a clinical diagnosis of nocturia (two or more times per one night) and hypogonadism, comprising the TRT group (n=31) and controls (n=33), were included in this analysis. The TRT group was administered 250mg of testosterone enanthate as an intramuscular injection every 4 weeks for 6 months. All patients responded to the following questionnaires: International Prostatic Symptoms Score (IPSS), Aging Male Symptoms (AMS) score and Short Form-36 health survey at baseline and 6-month visit. These categories were compared based on changes from baseline to the 6-month visit between TRT and control groups.

RESULTS: At the 6-month visit, the TRT group had a significant decrease in IPSS question no. 7 and AMS question no. 4, whereas no significant changes were observed in the control group. Additionally, role limitation because of health program, vitality and mental health domains were significantly improved in the TRT group.

CONCLUSIONS: Six-month TRT may improve nocturia, sleep conditions and quality of life among men with hypogonadism and nocturia.
Effects of long-term testosterone replacement therapy, with a temporary intermission, on glycemic control of nine hypogonadal men with type 1 diabetes mellitus - a series of case reports. 

Saad F; Yassin A; Almehmadi Y; Doros G; Gooren L.
Type 2 diabetes mellitus (T2DM) is often associated with obesity and subnormal serum testosterone (T) levels. Until 5 years ago there was no indication that men with type 1 diabetes mellitus (T1DM) had subnormal serum T. But recent studies indicate that about 10% of men with T1DM suffer from hypogonadism, as a rule aged men and men with obesity. While hypogonadal men with T2DM benefit from normalization of their serum T, this has not been investigated in men with T1DM. Nine men with T1DM, erectile dysfunction and hypogonadism (total testosterone<12nmol/L) received testosterone replacement therapy (TRT). In seven men TRT was intermittently: one man with prostate malignancy and six men because of problems of reimbursement. Incidentally, this provided an opportunity to monitor the effects of withdrawal and of the reinstatement of TRT. In all men, glycemic control (serum glucose and HbA1c), weight, waist circumference, lipid profiles and erectile function improved upon TRT. The seven men whose TRT was intermittently showed a deterioration which improved again upon reinstatement of TRT. The data suggest that aging and obese men with T1DM might have subnormal T levels and that their glycemic control, lipid profiles and erectile function might benefit from TRT.
Association of serum levels of typical organic pollutants with polycystic ovary syndrome (PCOS): a case-control study.

Yang Q; Zhao Y; Qiu X; Zhang C; Li R; Qiao J.

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[Journal Article. Research Support, Non-U.S. Gov't]
UI: 26040477

STUDY QUESTION: Is polycystic ovary syndrome (PCOS) associated with increased serum levels of typical organic pollutants?

SUMMARY ANSWER: PCOS in Han females from Northern China was significantly associated with elevated serum levels of pollutants, including polychlorinated biphenyls (PCBs), organochlorine pesticides and polycyclic aromatic hydrocarbons (PAHs).

WHAT IS KNOWN ALREADY: PCOS is arguably the most common endocrinopathy in females of reproductive age. The etiology of PCOS is thought to be multifactorial.

STUDY DESIGN, SIZE, DURATION: This was a preliminary case-control study undertaken at the Division of Reproductive Center, Peking University Third Hospital. Fifty participants affected by PCOS and 30 normal controls were recruited between August and October 2012 from Northern China. All participants were Han women.

PARTICIPANTS/MATERIALS, SETTING, METHODS: PCOS participants were diagnosed according to the 2003 Rotterdam criteria. The control participants were non-pregnant females unable to conceive solely due to male azoospermia. Serum levels of a wide range of organic pollutants, including PCBs, organochlorine pesticides, PAHs and more than 20 phenolic pollutants, were analyzed using gas chromatographic mass spectrometry.

MAIN RESULTS AND THE ROLE OF CHANCE: Serum levels of PCBs, pesticides and PAHs were significantly higher in the PCOS group than the control group. Concentrations of PCBs, p,p'-dichlorodiphenyldichloroethylene (p,p'-DDE) and PAHs in serum above median levels were associated with PCOS with odds ratios of 3.81 [95% confidence interval (CI), 1.45-10.0], 4.89 (95% CI, 1.81-13.2) and 2.39 (95% CI, 0.94-6.05), respectively. Partial least-squares-discriminant analysis (PLS-DA) confirmed that serum levels of organic pollutants were associated with PCOS, especially for p,p'-DDE and PCBs.
LIMITATIONS, REASONS FOR CAUTION: Some other possible covariates (e.g. dietary and income) were missed in this study, although education and occupation have been considered as an indicator of personal income. The PLS-DA model allowed a quasi-exposome analysis with over 60 kinds of typical organic pollutants; however, the possibility of other pollutants involved in the PCOS still could not be excluded.

WIDER IMPLICATIONS OF THE FINDINGS: Our study identified that bodily retention of environmental organic pollutants-including PCBs, pesticides (especially p,p'-DDE) and PAHs-was associated with PCOS.

STUDY FUNDING/COMPETING INTERESTS: This research was supported by the Ministry of Science and Technology of China Grants (973 program; 2014CB943203 and 2015CB553401), National Natural Science Foundation of China (21322705, 21190051, 41121004 and 81170538), National Key Technology R&D Program in the Twelve Five-Year Plan (2012BAI32B01) and the Collaborative Innovation Center for Regional Environmental Quality. There are no conflicts of interest to declare.

TRIAL REGISTRATION NUMBER: None. This is not a clinical trial.

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Erectile dysfunction is a prognostic indicator of comorbidities in men with late onset hypogonadism.

Almehmadi Y; Yassin DJ; Yassin AA.

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[Journal Article]
UI: 26030350

INTRODUCTION: The role of testosterone deficiency in erectile dysfunction (ED) is increasingly recognized; however, there is a need to clarify the nature of the relationship between ED and late onset hypogonadism (LOH).

AIM: In this study, we sought to determine the correlators of ED severity amongst men with LOH.

METHODS: 130 patients diagnosed with LOH fulfilling the criteria of total testosterone <3.5ng/ml (<12nmol/l) and with an erectile function domain score <21 on the International Index of Erectile Function questionnaire (IIEF questions 1-5) were enrolled for a subsequent trial of Testosterone Undecanoate. Demographic data were recorded at baseline.

MAIN OUTCOME MEASURES: Subjects completed three standardised questionnaires to assess sexual health including International Prostate Symptom Score (IPSS), Aging Males Symptoms (AMS) and IIEF Sexual Health Inventory for Men (SHIM). Patients were stratified by ED severity
with SHIM scores of 1-7 considered severe ED, 8-11 moderate ED and 12-16 mild to moderate.

Serum testosterone, sex hormone binding globulin (SHBG) and lipids (total cholesterol, triglycerides, high-density lipoprotein and low-density lipoprotein) were assessed along with plasma fasting glucose and HbA1c. Weight, BMI and waist circumference were also recorded.

RESULTS: A significant association was observed between severity of ED and mean weight (p=0.000), waist circumference (p=0.000), triglycerides (p=0.009), total cholesterol (p=0.027), HbA1c (p=0.000), fasting glucose (p=0.003) and AMS scores (p=0.043). No significant differences were seen in testosterone fractions and SHBG levels between ED subgroups. A positive correlation existed between the prevalence of diabetes mellitus (type 1 and type 2) and ED severity in this cohort (p=0.018).

CONCLUSIONS: The descriptive data of our cohort show that increased severity of ED within LOH patients correlated with an increased waist circumference, hyperglycemia, hypertriglyceridemia, hyperlipidemia and a history of diabetes mellitus. Severe ED functions as a prognostic indicator of co-morbidities in men with LOH.
BACKGROUND: There has been a longstanding question as to whether testosterone therapy could precipitate or worsen urinary symptoms in aging men. We investigated the effects of 1-year oral testosterone undecanoate (TU) therapy on urinary symptoms in aging, hypogonadal men.

METHODS: A total of 322 men >50 years with symptomatic testosterone deficiency participated in a 1-year, randomized, multicenter, double-blind trial. Patients received placebo or oral TU 80mg/day, 160mg/day, or 240mg/day.

RESULTS AND LIMITATIONS: Compared with placebo, treatment with oral TU at doses of 80mg/day and 160mg/day resulted in no significant change in IPSS urinary symptoms or quality of life (QoL) scores. Treatment with oral TU 240mg/day led to a statistically significant, but clinically insignificant, improvement in IPSS total score and a significant improvement in IPSS QoL score. None of the TU doses tested had a significant effect on PSA or PV.

CONCLUSIONS: Long-term oral TU therapy had no deleterious effects on IPSS total score and did not change PV and PSA in aging, hypogonadal men. Oral TU therapy at a dose of 240mg/day may even improve IPSS QoL score.
Altered segregation pattern and numerical chromosome abnormalities interrelate in spermatozoa from Robertsonian translocation carriers.

Godo A; Blanco J; Vidal F; Sandalinas M; Garcia-Guixe E; Anton E.

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[Journal Article. Research Support, Non-U.S. Gov't]
UI: 25985997

The aim of this study was to assess whether there is a relationship between numerical chromosome abnormalities and certain segregation modes in spermatozoa from Robertsonian translocation carriers. A sequential fluorescence in-situ hybridization protocol based on two successive hybridization rounds was performed on sperm samples from one t(13;22) and ten t(13;14) carriers. Patient inclusion criteria included the presence of a positive interchromosomal effect (ICE). In the first round, numerical abnormalities for chromosomes 15/22, 18, 21, X and Y were analysed. In the second round, the segregation outcome of the rearranged chromosomes was evaluated in the numerically abnormal spermatozoa detected in the first round, as well as in randomly assessed spermatozoa. Aneuploid spermatozoa showed statistical differences in all segregation modes when compared with randomly assessed spermatozoa: alternate (50.7% versus 84.3%), adjacent (36.6% versus 14.6%) and 3:0 (10.2% versus 1%). Diploid/multiple disomic spermatozoa showed differences in alternate (3.7% versus 84.3%) and 3:0 (67.6% versus 1%). We concluded that in Robertsonian translocation carriers that exhibit ICE, numerically abnormal spermatozoa preferentially contain unbalanced segregation products. This might be explained by heterosynapsis acting as a rescue mechanism that would lead to aberrant recombination, which is a predisposing factor for non-disjunction events.
Cost-effectiveness of assisted conception for male subfertility.

Moolenaar LM; Cissen M; de Bruin JP; Hompes PG; Repping S; van der Veen F; Mol BW.

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[Journal Article]

UI: 25900905
Intrauterine insemination (IUI), with or without ovarian stimulation, IVF and intracytoplasmatic sperm injection (ICSI) are frequently used treatments for couples with male subfertility. No consensus has been reached on specific cut-off values for semen parameters, at which IVF would be advocated over IUI and ICSI over IVF. The aim of this study was to evaluate the cost-effectiveness of interventions for male subfertility according to total motile sperm count (TMSC). A computer-simulated cohort of subfertile women aged 30 years with a partner was analysed with a pre-wash TMSC of 0 to 10 million. Three treatments were evaluated: IUI with and without controlled ovarian stimulation; IVF; and ICSI. Main outcome was expected live birth; secondary outcomes were cost per couple and the incremental cost-effectiveness ratio. The choice of IVF over IUI with ovarian stimulation and ICSI over IVF depends on the willingness to pay for an extra live birth. If only cost per live birth is considered for each treatment, above a pre-wash TMSC of 3 million, IUI is less costly than IVF and, below a pre-wash, TMSC of 3 million ICSI is less costly. Effectiveness needs to be confirmed in a large randomized controlled trial.

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A novel surgical management for male infertility secondary to midline prostatic cyst.

Cheng G; Liu B; Song Z; Xu A; Song N; Wang Z.

BACKGROUND: To summary the procedure and experience of a novel surgical management for male infertility secondary to midline prostatic cyst (MPC).

METHODS: From February 2012 to February 2014, 12 patients were diagnosed with PMC by semen analysis, seminal plasma biochemical analysis, transrectal ultrasonography (TRUS), and pelvic magnetic resonance imaging (MRI). All patients underwent the transurethral unroofing of MPC using resectoscope, the dilation of ejaculatory duct, and the irrigation of seminal vesicle using seminal vesiculoscope. All patients were followed up at least 3 months after operation.

RESULTS: Preoperative semen analyses of 12 patients showed oligoasthenozoospermia (5/12) or azoospermia (7/12), low semen volume (0-1.9 mL), and low pH level (5.5-7.0). Preoperative seminal plasma biochemical analyses showed reduced semen fructose. TURS and MRI revealed a cyst lesion located in the midline of prostatic. After 3 months follow up, the semen quality of 80% patients (4/5) with oligoasthenozoospermia improved obviously. The spermatozoa were present in the semen in 5 of 7 cases with azoospermia. In one patient, the spermatozoa occurred in the urine after ejaculation.

CONCLUSIONS: Surgical management using transurethral resectoscopy and seminal vesiculoscopy is effective, minimally invasive, and safe for male infertility secondary to MPC.
Testosterone replacement therapy and the risk of prostate cancer. [Review]
Warburton D; Hobaugh C; Wang G; Lin H; Wang R.
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[Journal Article. Review]
UI: 25865848
Understanding the role of testosterone replacement therapy (TRT) in the development and progression of prostate cancer is an important concept in treating patients with symptoms of hypogonadism. This article revealed a small number of mostly retrospective, observational studies describing the use of TRT in the general population, in men with prostatic intraepithelial neoplasia (PIN), in men with a history of treated prostate cancer, and in men on active surveillance for prostate cancer. The current literature does not report a statistically significant increase in the development or progression of prostate cancer in men receiving testosterone replacement for symptomatic hypogonadism, and the prostate saturation theory provides a model explaining the basis for these results. The use of TRT in men with a history of prostate cancer is considered experimental, but future results from randomized controlled trials could lead to a change in our current treatment approach.

Status
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Year of Publication
2015

700.
The influence of hormonal treatment with beta-human chorionic gonadotropin for cryptorchidism on future fertility in rats.
Yilmaz O; Akyol I; Ozyurt M; Ates F; Soydan H; Malkoc E.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid
MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Comparative Study. Journal Article]
INTRODUCTION: There have been two treatment modalities for cryptorchidism such that surgical and hormonal; the latter being highly controversial. While some authors suggest that hormonal treatment increases the number and maturation of germ cells in cryptorchid testes, others believe just the opposite.

OBJECTIVE: We aimed to find out the sperm counts and testicular index; briefly fertility potential of the normally descended contralateral testes in adulthood period in rats treated with Beta-HCG in early period of their lives.

MATERIALS AND METHODS: Three groups, each including 10 rats aged 22 days old, in which delactation and normal feeding can be started, were formed to be Group 1: Sham operated, Group 2: Experimental cryptorchidism (EC) and Group 3: Hormone-treated after experimental cryptorchidism was performed (HT-EC). Left testis was placed in the abdomen in group 2 and 3. In group 1, a sham operation was performed. The rats in EC-HT group received subcutaneous injections of 50 IU/kg Beta-HCG daily for 7 days. Right orchidectomy was performed when they reached reproductive period to evaluate fertility potential with sperm counts and testicular index. Testicular index was calculated according to the formula "testicular length x width/weight of rat". Epididymal sperm count was made with hemocytometer.

RESULTS:

DISCUSSION: We evaluated the physical characteristics and fertility potential (sperm counts) of contralateral normal testes during adulthood in rats that underwent experimental unilateral cryptorchidism during infancy. A relationship between testis weight and sperm counts were also investigated. We could not find any direct correlation of sperm count with either testicular weight or testicular index in our study. Although the rats had normal testes at birth, we found decreased sperm counts in contralateral normal testes in EC group. This suggests that unilateral cryptorchidism may cause some systemic effects that reach the other testis. Hormone treatment was not beneficial. This is comparable to Nambirajan et al. who reported histological changes and decreased spermatogenic cell count in contralateral scrotal testes in experimentally induced unilateral cryptorchidism in early period of life in rats. Heiskanen et al. reported that treatment with Beta-HCG leads to decreased total sperm counts in the future due to increased germ cell apoptosis caused by hormonal withdrawal after treatment. Cortes et al. also reported decreased number of germ cells in 1-3 year-old boys who underwent surgery after unsuccessful Beta-HCG treatment. The reasons could be delayed testicular descent or adverse effect of hormone treatment though. Our results concurred with them. Apparently, our model has failed to mimic the pathophysiologic mechanisms of congenital cryptorchidism in humans. Furthermore, we applied hormone treatment in normal rats with normally descended testes. Therefore, the "by-product" information of our study is that, unnecessary use of Beta-HCG during infancy may impair future fertility.
CONCLUSION: Our study suggests that Beta-HCG treatment may decrease sperm counts and decrease the future fertility potential. We could not find any direct correlation of sperm count with either testicular weight or testicular index.

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701.
Stress Experienced by Obstetrics and Gynecology Residents during Planned Laparoscopy: A Prospective, Multicentric, Observational, Blinded, and Comparative Study.
Ducarme G; Bricou A; Chanelles O; Sifer C; Poncelet C.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
AIMS: To describe heart rate (HR) variations in surgical residents during laparoscopy and to assess their intraoperative stress.

METHODS: We performed a prospective, multicentric, observational, blinded, and comparative analysis of the HR in 75 obstetrics and gynecology residents during planned laparoscopy for infertility in five teaching hospitals with assisted reproductive technology centers. The surgical residents had neither heart disease nor were under medical treatment or using tobacco or drugs. We describe HR variations at 9 preselected operative steps using real-time noninvasive measures of the HR during laparoscopy.

RESULTS: Residents performed 124 laparoscopies for unexplained infertility. Their HR increased significantly during the introduction of the Palmer needle, umbilical port and second port, and during abdominopelvic exploration and dye test compared to the baseline HR, the HR after hand washing, at the end of surgery and during skin suture (91.6 +/- 1.9, 104.8 +/- 2.3, 95.3 +/- 2.2, 93.7 +/- 2.5, 90.7 +/- 1.7 vs. 83.2 +/- 1.6, 88.6 +/- 1.9, 87.4 +/- 2.1, 88.2 +/- 1.9 bpm, respectively, p < 0.02).

CONCLUSION: Our results point to a potential stress for the surgeon assessed by HR variations during planned laparoscopy compared to the baseline HR before surgery. This 'static' stress can be repeated on the same day.

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Although numerous randomized studies have shown that testosterone replacement therapy (TRT) improves intermediate outcomes in patients at risk and in those with proven cardiovascular disease (CVD), results derived mainly from registries and observational studies have suggested an increased cardiovascular risk in elderly men receiving often supra-therapeutic doses of testosterone. Recent meta-analyses have shown that when testosterone has been used in patients with pre-existing cardiovascular conditions, the effect on the disease has been either beneficial or neutral. Similar results have been reported in hypo- and eugonadal men. Contrasting results have been reported by two trials of testosterone treatment in frail elderly men. Reports from poorly analyzed databases have reported an increased risk of cardiovascular events with testosterone use. More recently, a population-based study showed no increased cardiovascular risk of testosterone replacement in hypogonadal men. Available data from controlled clinical trials suggest that the use of testosterone in elderly men does not increase cardiovascular risk nor the risk of events. Studies in men with CVD, angina, or heart failure report a benefit from testosterone replacement in men with or without hypogonadism. Therefore, at present, the cardiovascular benefits of TRT in elderly men outweigh the risks. This is particularly evident in those men with pre-existing CVD.
No association of TP53 codon 72 SNP with male infertility: a study in a Chinese population and a meta-analysis.

Chan Y; Jiang H; Ma L; Chen J; Li D; Meng Y; Luo Y; Tang W.

[Journal Article. Meta-Analysis. Research Support, Non-U.S. Gov't]
UI: 25747431

Genetic polymorphisms may affect human male fertility. Even though TP53 plays a role in spermatogenesis we know little about the association of the functional polymorphism at codon 72 of TP53 with respect to susceptibility to male infertility. We conducted a case-control study to investigate this association in a Chinese population and performed a meta-analysis in different populations to clarify this association. The single nucleotide polymorphism (SNP) of TP53 codon 72 (rs1042522 G>C) was genotyped by PCR-RFLP in 83 Chinese male infertility patients and 401 healthy controls. Meta-analysis was performed using the data from four currently available studies. The data from our study were overlayed using the v.9.0 STATA software package. We observed no association between the TP53 codon 72 polymorphism and male infertility (p=0.84, OR=1.04, 95% CI, 0.74-1.45). Meta-analysis confirmed the case-control result that there was no significant association between the codon 72 polymorphism of TP53 and male infertility (Pro vs. Arg; p=0.31, OR=0.86, 95% CI, 0.65-1.15; Pro/Pro vs. Arg-carriers; p=0.65, OR=0.91, 95% CI, 0.61-1.36; Pro-carriers vs. Arg/Arg: p=0.15, OR=0.75, 95% CI, 0.51-1.11). The data presented in this communication supports the view that the codon 72 polymorphism of TP53 may not contribute to male infertility susceptibility in the Chinese population.

Status
MEDLINE

Wicki A; Ritschard R; Loesch U; Deuster S; Rochlitz C; Mamot C.

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present


[Journal Article. Research Support, Non-U.S. Gov't]

UI: 25701632

We describe the large-scale, GMP-compliant production process of doxorubicin-loaded and anti-EGFR-coated immunoliposomes (anti-EGFR-ILs-dox) used in a first-in-man, dose escalation clinical trial. 10 batches of this nanoparticle have been produced in clean room facilities. Stability data from the pre-GMP and the GMP batch indicate that the anti-EGFR-ILs-dox nanoparticle was stable for at least 18 months after release. Release criteria included visual inspection, sterility testing, as well as measurements of pH (pH 5.0-7.0), doxorubicin HCl concentration (0.45-0.55 mg/ml), endotoxin concentration (<1.21 IU/ml), leakage (<10%), particle size (Z-average of Caelyx +/- 20 nm), and particle uptake (uptake absolute: >0.50 ng doxorubicin/mug protein; uptake relatively to PLD: >5 fold). All batches fulfilled the defined release criteria, indicating a high reproducibility as well as batch-to-batch uniformity of the main physico-chemical features of the nanoparticles in the setting of the large-scale GMP process. In the clinical trial, 29 patients were treated with this nanoparticle between 2007 and 2010. Pharmacokinetic data of anti-EGFR-ILs-dox collected during the clinical study revealed stability of the nanocarrier in vivo. Thus, reliable
and GMP-compliant production of anti-EGFR-targeted nanoparticles for clinical application is feasible.

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Status
MEDLINE

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20150321

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2015

705.

Discovery of CLC transport proteins: cloning, structure, function and pathophysiology. [Review] Jentsch TJ.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present Journal of Physiology. 593(18):4091-109, 2015 Sep 15.
[Journal Article. Review]
UI: 25590607
After providing a personal description of the convoluted path leading 25 years ago to the molecular identification of the Torpedo Cl(-) channel CIC-0 and the discovery of the CLC gene family, I succinctly describe the general structural and functional features of these ion transporters before giving a short overview of mammalian CLCs. These can be categorized into plasma membrane Cl(-) channels and vesicular Cl(-)/H(+) -exchangers. They are involved in the regulation of membrane excitability, transepithelial transport, extracellular ion homeostasis, endocytosis and lysosomal function. Diseases caused by CLC dysfunction include myotonia, neurodegeneration, deafness, blindness, leukodystrophy, male infertility, renal salt loss, kidney stones and osteopetrosis, revealing a surprisingly broad spectrum of biological roles for chloride transport that was unsuspected when I set out to clone the first voltage-gated chloride channel.

CONTEXT: The effects of testosterone treatment on glucose metabolism and other outcomes in men with type 2 diabetes (T2D) and/or the metabolic syndrome are controversial.

OBJECTIVE: To perform a systematic review and meta-analysis of placebo-controlled double-blind randomized controlled clinical trials (RCT) of testosterone treatment in men with T2D and/or the metabolic syndrome.

DATA SOURCES: A systematic search of RCTs was conducted using Medline, Embase and the Cochrane Register of controlled trials from inception to July 2014 followed by a manual review of the literature.

STUDY SELECTION: Eligible studies were published placebo-controlled double-blind RCTs published in English.

DATA EXTRACTION: Two reviewers independently selected studies, determined study quality and extracted outcome and descriptive data.

DATA SYNTHESIS: Of the 112 identified studies, seven RCTs including 833 men were eligible for the meta-analysis. In studies using a simple linear equation to calculate the homeostatic model assessment of insulin resistance (HOMA1), testosterone treatment modestly improved insulin resistance, compared to placebo, pooled mean difference (MD) -1.58 [-2.25, -0.91], P < 0.001. The treatment effect was nonsignificant for RCTs using a more stringent computer-based equation (HOMA2), MD -0.19 [-0.86, 0.49], P = 0.58). Testosterone treatment did not improve glycaemic (HbA1c) control, MD -0.15 [-0.39, 0.10], P = 0.25, or constitutional symptoms, Aging Male Symptom score, MD -2.49 [-5.81, 0.83], P = 0.14).

CONCLUSIONS: This meta-analysis does not support the routine use of testosterone treatment in men with T2D and/or the metabolic syndrome without classical hypogonadism. Additional studies are needed to determine whether hormonal interventions are warranted in selected men with T2D and/or the metabolic syndrome.

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Status
MEDLINE
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Grossmann, Mathis; Hoermann, Rudolf; Wittert, Gary; Yeap, Bu B.
Institution
OBJECTIVE: We developed clinical practice guidelines to assess the individual risk-benefit profile of androgen replacement therapy in adult male hypogonadism (HG), defined by the presence of specific signs and symptoms and serum testosterone (T) below 12 nmol/L.

PARTICIPANTS: The task force consisted of eight clinicians experienced in treating HG, selected by the Italian Society of Endocrinology (SIE). The authors received no corporate funding or remuneration.

CONSENSUS PROCESS: Consensus was guided by a systematic review of controlled trials conducted on men with a mean T < 12 nmol/L and by interactive discussions. The guidelines were reviewed and sequentially approved by the SIE Guidelines Commission and Executive Committee.

CONCLUSIONS: We recommend T supplementation (TS) for adult men with severely reduced T levels (T < 8 nmol/L) to improve body composition and sexual function. We suggest that TS be offered to subjects with T < 12 nmol/L to improve glycaemic control, lipid profile, sexual function,
bone mineral density, muscle mass and depressive symptoms, once major contraindications have been ruled out. We suggest that lifestyle changes and other available interventions (e.g. for erectile dysfunction) be suggested prior to TS. We suggest that TS should be combined with currently available treatments for individuals at high risk for complications, such as those with osteoporosis and/or metabolic disorders. We recommend against using TS to improve cardiac outcome and limited mobility. We recommend against using TS in men with prostate cancer, unstable cardiovascular conditions or elevated haematocrit. The task force places a high value on the timely treatment of younger and middle-aged subjects to prevent the long-term consequences of hypoandrogenism.

Status
MEDLINE

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PMID
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4282686

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20150807

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2015
Effect of metformin therapy and dietary supplements on semen parameters in hyperinsulinaemic males.

Bosman E; Esterhuizen AD; Rodrigues FA; Becker PJ; Hoffmann WA.

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Andrologia. 47(9):974-9, 2015 Nov.
[Clinical Trial. Journal Article]
UI: 25359661

Previous reports indicated that hyperinsulinaemic men may exhibit a higher percentage of poorly compacted DNA in their spermatozoa and less success in an IVF programme (Andrologia, 45, 2003, 18; Andrologia, 2014, doi: 10.1111/and.12227). The aim of this study was to investigate the effect of metformin (Glucophage) and antioxidant treatment (StaminoGro) on the semen parameters of hyperinsulinaemic men. Nineteen hyperinsulinaemic male patients were treated for 3 months with metformin alone (Group A), and fifteen patients used metformin in combination with the nutritional supplement (Group B). Combined data of the two groups (pre- and post-treatment) differ significantly regarding sperm morphology (P = 0.0003) and CMA3 (P < 0.0001) values. The improvement in sperm morphology after treatment was similar for the two respective groups (P < 0.05). The morphological normal sperm forms increased from the mean percentage of 3.9 to 5.5% and from 4.2 to 5.5% for Group A and B respectively. Where a combination of metformin and the supplement were used (Group B), the combination treatment proved to be superior in obtaining enhanced chromatin packaging quality although not statistically significant (P = 0.5929) when compared with the metformin (Group A) group. The chromatin packaging quality in Group B improved with 10% while the improvement in Group A was approximately 8.3%. Therefore, infertile hyperinsulinaemic men can benefit from metformin treatment and should be advised on the use of nutritional supplements with antioxidant properties.

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Status
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Rodrigues, F A. Medfem Clinic, Bryanston, South Africa.
709.
Sperm aneuploidy in infertile male patients: a systematic review of the literature. [Review]
Chatziparasidou A; Christoforidis N; Samolada G; Nijs M.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid
MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article. Review]
UI: 25352353
Males with abnormal karyotypes and subgroups of fertile and infertile males with normal
karyotypes may be at risk of producing unbalanced or aneuploid spermatozoa. Biological, clinical,
environmental and other factors may also cause additional sperm aneuploidy. However,
increased risk of sperm aneuploidy is directly related to chromosomally abnormal embryo
production and hence to poor reproductive potential. This systemic literature review focuses on
the identification of these males because this is an essential step in the context of assisted
reproduction. This research may allow for a more personalised and, hence, more accurate
estimation of the risk involved in each case, which in turn will aid genetic counselling for affected
couples and help with informed decision-making.
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Magnetic activated cell sorting: an effective method for reduction of sperm DNA fragmentation in varicocele men prior to assisted reproductive techniques.

Degheidy T; Abdelfattah H; Seif A; Albuz FK; Gazi S; Abbas S.

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present


[Clinical Trial. Journal Article]

UI: 25209213

Semen parameters of varicocele men have been usually suspected to exhibit higher levels of abnormalities including DNA fragmentation, reactive oxygen species (ROS) and apoptotic markers. Negative correlation between increased level of DNA fragmentation and assisted reproductive techniques (ART) outcome has been studied by several authors. In the current study, we aim to evaluate the possible value of magnetic activated cell sorting (MACs) technology in reduction of DNA fragmentation in infertile varicocele patients prior to ART. Semen samples, collected from 36 varicocele patients, were prepared by density gradient centrifugation (DGC). Every sample was subsequently divided into two aliquots. One aliquot was kept untouched as pre-MACs control while the other aliquot was subjected to MACs technique, for depletion of apoptotic spermatozoa, and serves as post-MACs test. Sperm count, motility and DNA fragmentations were evaluated for both control and test samples. Post-MACs samples showed no deleterious reduction in total sperm motility (80.64 +/- 6.97%) compared with control samples.
(80.97 +/- 7.74%) while sperm DNA fragmentations were significantly reduced in post-MACs samples (9.61 +/- 5.62%) compared with pre-MACs controls (12.43 +/- 6.29%) (P < 0.05). It can be concluded that MACs technique is a simple, noninvasive, technique that can efficiently reduce DNA fragmentation in infertile varicocele patients prior to ART.

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Leduc BE; Fournier C; Jacquemin G; Lepage Y; Vinet B; Hetu PO; Chagnon M.

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present


[Journal Article. Randomized Controlled Trial. Research Support, Non-U.S. Gov't]

UI: 24969635
OBJECTIVE: The objective of this study is to evaluate the efficacy of midodrine in the treatment of anejaculation in men with spinal cord injury (SCI).

STUDY DESIGN: Prospective, double-blind, randomized, placebo-controlled pilot study.

METHOD: Men with anejaculation associated with SCI (level of injury above T10) of more than 1 year in duration were approached. Those with no ejaculatory response to one penile vibratory stimulation (PVS) trial were assigned in a double-blind manner to one of the two following interventions once a week for a maximum of 3 weeks or until ejaculation occurred: oral administration of flexible midodrine (7.5-22.5 mg max) followed by PVS (group M), or oral administration of flexible sham-midodrine (placebo) followed by PVS (group P). Sociodemographic data, medical characteristics, and plasma desglymidodrine concentration were collected for all participants.

OUTCOME MEASURE: Ejaculation success rate in each group.

RESULTS: Among the 78 men approached, 23 participants (level of SCI: C4-T9) were randomized. Three participants abandoned the study and 20 completed the study; 10 were assigned to group M, 10 to group P. Ejaculation was reached for one participant of group M and for two participants of group P. Autonomic dysreflexia associated to PVS occurred in three patients.

CONCLUSION: In this small sample study, treatment of anejaculation after SCI with midodrine and PVS did not result in a better rate of antegrade ejaculation in 10 men than in 10 men treated with a placebo and PVS.

Status
MEDLINE
Authors Full Name
Leduc, Bernard E; Fournier, Christine; Jacquemin, Geraldine; Lepage, Yves; Vinet, Bernard; Hetu, Pierre-Olivier; Chagnon, Miguel.
PMID
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Date Created
20150114
Year of Publication
2015
Lean tissue mass and energy expenditure are retained in hypogonadal men with spinal cord injury after discontinuation of testosterone replacement therapy.

Bauman WA; La Fountaine MF; Cirnigliaro CM; Kirshblum SC; Spungen AM.

OBJECTIVE: To determine whether favorable changes to lean tissue mass (LTM), resting energy expenditure (REE), and testosterone (T) that occurred with 12 months of physiological testosterone replacement therapy (TRT) were retained 6 months after discontinuing treatment.

DESIGN: Prospective, open-label, controlled drug intervention trial.

SETTING: Metropolitan area hospitals.

SUBJECTS: Eugonadal (n = 11) and hypogonadal (n = 13) men with chronic spinal cord injury (SCI).

INTERVENTIONS: Hypogonadal subjects received a 5 or 10 mg transdermal T patch daily for 12 months, with adjustment of the dose to normalize the serum T concentration; TRT was discontinued after 12 months (TRT-12M) and subjects were followed for an additional 6 months and re-evaluated (Post-TRT). Total body dual energy X-ray absorptiometry and blood draws were performed at baseline (BL) prior to TRT, TRT-12M, and Post-TRT. Eugonadal subjects did not receive treatment and were evaluated at comparable time points.

RESULTS: There were no significant differences between groups prior to TRT at BL for any of the study endpoints. In the hypogonadal group, a significant increase in LTM was observed from BL to TRT-12M (50.2 +/- 7.4 vs. 52.9 +/- 6.8 kg, P < 0.01), which persisted Post-TRT compared to BL (52.2 +/- 7.8 kg, P < 0.05). The increase in REE from BL to TRT-12M (1283 +/- 246 vs. 1410 +/- 250 kcal/day) was also retained at Post-TRT (1393 +/- 220 kcal/day). These sustained improvements in LTM and REE after termination of anabolic hormonal therapy may be associated with persistent beneficial effects on health and physical function of hypogonadal men with chronic SCI.

Status
MEDLINE
Authors Full Name
Bauman, William A; La Fountaine, Michael F; Cirnigliaro, Christopher M; Kirshblum, Steven C; Spungen, Ann M.

PMID
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4293532

Date Created
OBJECTIVES: Non-small cell lung cancer (NSCLC) is a heterogeneous group of disorders that can be subclassified based upon molecular characterization. Anaplastic lymphoma kinase translocation and MET aberrations occur in a subset of NSCLC. Anaplastic lymphoma kinase/MET have been shown to be inhibited by the small molecule tyrosine kinase inhibitor crizotinib. Recently, crizotinib was shown to decrease testosterone in males. Herein, we describe the effects of crizotinib on multiple hormonal axes.

MATERIALS AND METHODS: Seven consecutive patients with NSCLC who were receiving crizotinib as part of their standard care were evaluated for hormonal disruptions.

RESULTS: Primary hypogonadism was detected in 4/5 of males, whereas mildly elevated prolactin was observed in 4/7 patients. Hypocalcemia was observed in 3/7 patients. Interestingly, 5/7 patients had elevated levels of insulin-like growth factor-1 (IGF-1) levels, and the remaining 2 individuals had levels that were near the upper limits of the normal range.

CONCLUSIONS: Because of cellular cross-talk between MET and IGF-1 signaling, elevated IGF-1 levels induced by crizotinib treatment may have implications for long-term drug efficacy. Furthermore, this finding suggests a potential avenue of therapeutic synergy, namely coordinate inhibition of the MET and IGF-1 signaling pathways. Finally, as crizotinib has been recently approved, it is prudent to check hormone and calcium biomarkers and correct noted deficiencies for improved outcomes and quality of life.
Prospective comparison of ligation and bipolar cautery technique in non-scalpel vasectomy.

Altok M., Sahin A.F., Divrik R.T., Yildirim U., Zorlu F.

Embase

[Article]
AN: 616004846

OBJECTIVES: There is no trial comparing bipolar cautery and ligation for occlusion of vas in non-scalpel vasectomy. This study aimed to compare the effectiveness of these vasectomy occlusion techniques. MATERIALS AND METHODS: Between January 2002-June 2009, patients were allocated in alternate order. We recruited 100 cases in cautery group and 100 cases in ligation group. Non-scalpel approach was performed during vasectomy and fascial interposition was performed in all cases. First semen analysis was done 3 months after vasectomy. Vasectomy success was defined as azoospermia or non-motile sperm lower than 100,000/mL.

RESULTS: Four patients from the cautery group were switched to the ligation group due to technical problem of cautery device. Thus, data of 96 patients as cautery group and 104 patients as ligation group were evaluated. After vasectomy, semen analyses were obtained from 59 of 96
(61.5%) patients in cautery group and to 66 of 104 (63.5%) patients in ligation group. There was no statistical significant difference between the two groups in terms of the success of vasectomy (p=0.863).

CONCLUSION: Although bipolar cautery technique is safe, effective and feasible in non-scalpel vasectomy, it has no superiority to ligation. There was no statistically significant difference in terms of the success and complications between the two groups.


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Date Created 20170510
Year of Publication 2015

715.
Mutational landscape of the human Y chromosome-linked genes and loci in patients with hypogonadism.
Pathak D., Yadav S.K., Rawal L., Ali S.
Embase
Journal of genetics. 94 (4) (pp 677-687), 2015. Date of Publication: 01 Dec 2015.
[Article]
AN: 615963766

Sex chromosome-related anomalies engender plethora of conditions leading to male infertility. Hypogonadotropic hypogonadism (HH) is a rare but well-known cause of male infertility. Present study was conducted to ascertain possible consensus on the alterations of the Y-linked genes and loci in males representing hypogonadism (H), which in turn culminate in reproductive dysfunction. A total of nineteen 46, XY males, clinically diagnosed with H (11 representative HH adults and eight prepubertal boys suspected of having HH) were included in the study. Sequence-tagged site screening, SRY gene sequencing, fluorescence in situ hybridization
mapping (FISH), copy number and relative expression studies by real-time PCR were conducted to uncover the altered status of the Y chromosome in the patients. The result showed random microdeletions within the AZFa (73%)/b (78%) and c(26%) regions. Sequencing of the SRY gene showed nucleotide variations within and outside of the HMG box in four males (21%). FISH uncovered mosaicism for SRY, AMELY, DAZ genes and DYZ1 arrays, structural rearrangement for AMELY (31%) and duplication of DAZ (57%) genes. Copy number variation for seven Y-linked genes (2-8 rounds of duplication), DYZ1 arrays (495-6201 copies) and differential expression of SRY, UTY and VCY in the patients' blood were observed. Present work demonstrates the organizational vulnerability of several Y-linked genes in H males. These results are envisaged to be useful during routine diagnosis of H patients.


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Date Created 20170509
Year of Publication 2015

716.
A Study of Couple Burnout in Infertile Couples.
Ghavi F., Jamale S., Mosalanejad L., Mosallanezhad Z.
Embase
Global journal of health science. 8 (4) (pp 158-165), 2015. Date of Publication: 06 Aug 2015.
[Article]
AN: 615896701

INTRODUCTION: Infertility is a major crisis that can cause psychological problems and emotionally distressing experiences, and eventually affect a couples' relationship. The objective of this study is to investigate couple burnout in infertile couples who were undergoing treatment at the Infertility Clinic of Yazd, Iran. METHOD: The present study is a cross-sectional descriptive one on 98 infertile couples referring to the Infertility Center of Yazd, Iran, who were chosen on a simple random sampling basis. The measuring tools consisted of the Couple Burnout Measure
(CBM) and a demographic questionnaire. The collected data were analyzed using SPSS 16 and the statistical tests of ANOVA and t-test. P-values less than 0.05 were considered as significant.

RESULTS: The results show that infertile women experience higher levels of couple burnout than their husbands (p<0.001). Also, a comparison of the scales of couple burnout—psychological burnout (p<0.01), somatic burnout (p<0.01), and emotional burnout (p<0.001)—between wives and husbands show that women are at greater risk.

CONCLUSION: Infertile couples’ emotional, mental, and sexual problems need to be addressed as part of the infertility treatment programs, and psychotherapists should be included in the medical team.

PMID

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Date Created
20170506

Year of Publication
2015

717.

Role of genetic mutations in folate-related enzyme genes on Male Infertility.

Embase
Scientific reports. 5 (pp 15548), 2015. Date of Publication: 09 Nov 2015.

[Article]
AN: 615902001

Several studies showed that the genetic mutations in the folate-related enzyme genes might be associated with male infertility; however, the results were still inconsistent. We performed a meta-analysis with trial sequential analysis to investigate the associations between the MTHFR C677T, MTHFR A1298C, MTR A2756G, MTRR A66G mutations and the MTHFR haplotype with the risk of male infertility. Overall, a total of 37 studies were selected. Our meta-analysis showed that the MTHFR C677T mutation was a risk factor for male infertility in both azoospermia and oligoasthenoteroatozoospermia patients, especially in Asian population. Men carrying the MTHFR TC haplotype were most liable to suffer infertility while those with CC haplotype had lowest risk.
On the other hand, the MTHFR A1298C mutation was not related to male infertility. MTR A2756G and MTRR A66G were potential candidates in the pathogenesis of male infertility, but more case-control studies were required to avoid false-positive outcomes. All of these results were confirmed by the trial sequential analysis. Finally, our meta-analysis with trial sequential analysis proved that the genetic mutations in the folate-related enzyme genes played a significant role in male infertility.

PMID

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Date Created
20170506

Year of Publication
2015

Polymorphisms in Protamine 1 and Protamine 2 predict the risk of male infertility: a meta-analysis.


Embase
Scientific reports. 5 (pp 15300), 2015. Date of Publication: 16 Oct 2015.

[Article]
AN: 615875758

Several studies have investigated the association between polymorphisms in protamine 1 and 2 genes and male infertility risk, with inconsistent results to date. This meta-analysis based on the 13 published case-control studies, including 7350 cases and 6167 controls, was performed to further establish the potential association between the 6 common single nucleotide polymorphisms (rs35576928, rs737008, rs35262993, rs2301365, rs1646022, rs2070923) in protamines 1 and 2 and male infertility. The -190C>A (rs2301365) polymorphism was identified as a risk factor for male infertility under all models. Interestingly, rs1646022 and rs737008 polymorphisms exerted protective effects against male sterility in Asian and population-based
under some models. No associations between the remaining SNPs and male sterility were observed.

PMID

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Date Created
20170505

Year of Publication
2015

719.
Infertility etiologies are genetically and clinically linked with other diseases in single meta-diseases.

Tarin J.J., García-Perez M.A., Hamatani T., Cano A.

Embase

[Review]
AN: 615656446
The present review aims to ascertain whether different infertility etiologies share particular genes and/or molecular pathways with other pathologies and are associated with distinct and particular risks of later-life morbidity and mortality. In order to reach this aim, we use two different sources of information: (1) a public web server named DiseaseConnect (http://disease-connect.org) focused on the analysis of common genes and molecular mechanisms shared by diseases by integrating comprehensive omics and literature data; and (2) a literature search directed to find clinical comorbid relationships of infertility etiologies with only those diseases appearing after infertility is manifested. This literature search is performed because DiseaseConnect web server does not discriminate between pathologies emerging before, concomitantly or after infertility is manifested. Data show that different infertility etiologies not only share particular genes and/or
molecular pathways with other pathologies but they have distinct clinical relationships with other diseases appearing after infertility is manifested. In particular, (1) testicular and high-grade prostate cancer in male infertility; (2) non-fatal stroke and endometrial cancer, and likely non-fatal coronary heart disease and ovarian cancer in polycystic ovary syndrome; (3) osteoporosis, psychosexual dysfunction, mood disorders and dementia in premature ovarian failure; (4) breast and ovarian cancer in carriers of BRCA1/2 mutations in diminished ovarian reserve; (5) clear cell and endometrioid histologic subtypes of invasive ovarian cancer, and likely low-grade serous invasive ovarian cancer, melanoma and non-Hodgkin lymphoma in endometriosis; and (6) endometrial and ovarian cancer in idiopathic infertility. The present data endorse the principle that the occurrence of a disease (in our case infertility) is non-random in the population and suggest that different infertility etiologies are genetically and clinically linked with other diseases in single meta-diseases. This finding opens new insights for clinicians and reproductive biologists to treat infertility problems using a phenomic approach instead of considering infertility as an isolated and exclusive disease of the reproductive system/hypothalamic-pituitary-gonadal axis. In agreement with a previous validation analysis of the utility of DiseaseConnect web server, the present study does not show a univocal correspondence between common gene expression and clinical comorbid relationship. Further work is needed to untangle the potential genetic, epigenetic and phenotypic relationships that may be present among different infertility etiologies, morbid conditions and physical/cognitive traits.

PMID

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20170427
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2015
Effects of increased paternal age on sperm quality, reproductive outcome and associated epigenetic risks to offspring.

Embase
[Review]
AN: 615643330

Over the last decade, there has been a significant increase in average paternal age when the first child is conceived, either due to increased life expectancy, widespread use of contraception, late marriages and other factors. While the effect of maternal ageing on fertilization and reproduction is well known and several studies have shown that women over 35 years have a higher risk of infertility, pregnancy complications, spontaneous abortion, congenital anomalies, and perinatal complications. The effect of paternal age on semen quality and reproductive function is controversial for several reasons. First, there is no universal definition for advanced paternal ageing. Secondly, the literature is full of studies with conflicting results, especially for the most common parameters tested. Advancing paternal age also has been associated with increased risk of genetic disease. Our exhaustive literature review has demonstrated negative effects on sperm quality and testicular functions with increasing paternal age. Epigenetics changes, DNA mutations along with chromosomal aneuploidies have been associated with increasing paternal age. In addition to increased risk of male infertility, paternal age has also been demonstrated to impact reproductive and fertility outcomes including a decrease in IVF/ICSI success rate and increasing rate of preterm birth. Increasing paternal age has shown to increase the incidence of different types of disorders like autism, schizophrenia, bipolar disorders, and childhood leukemia in the progeny. It is thereby essential to educate the infertile couples on the disturbing links between increased paternal age and rising disorders in their offspring, to better counsel them during their reproductive years.

PMID

Institution
Human papillomavirus infection and fertility alteration: a systematic review.
Souho T., Benlemlih M., Bennani B.
Embase
PloS one. 10 (5) (pp e0126936), 2015. Date of Publication: 2015.
[Article]
AN: 615661732

BACKGROUND: HPV is the most prevalent sexually transmitted infection and its effect in cancer induction is well documented. HPV infections are mostly asymptomatic, but it is unclear whether HPV infections can result in alterations of reproductive health. OBJECTIVE: To determine the relationship between human papillomavirus infections and reproductive health in both men and women.

METHODS: A systematic literature review was performed in PubMed and ScienceDirect data bases from January 1994 through August 2014.
RESULTS: HPV infections are shown to be significantly associated to many adverse effects in the reproductive function. These adverse effects were reported in different levels from cells production to pregnancy and may be related to the infecting genotype.

CONCLUSIONS: It appears from this study that HPV detection and genotyping could be of great value in infertility diagnosis at least in idiopathic infertility cases. Like for the risk of carcinogenesis, another classification of HPV regarding the risk of fertility alteration may be considered after deep investigations.


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Date Created
20170427

Year of Publication
2015

722.

Diagnosis and Treatment of Low Testosterone among Patients with End-Stage Renal Disease.
Bao Y., Johansen K.L.
Embase
Seminars in dialysis. 28 (3) (pp 259-265), 2015. Date of Publication: 01 May 2015.
[Review]
AN: 615313623
The prevalence of low testosterone level is particularly high among patients with end-stage renal disease (ESRD) and has been associated with mortality. In populations without ESRD, low testosterone level has also been associated with a number of morbidities including cardiovascular disease, diabetes mellitus, low muscle mass, low bone mass, low physical performance, and frailty. However, there is controversy regarding what constitutes low testosterone level in the aging population and at what level replacement therapy with testosterone is indicated. There are no randomized controlled trials investigating long-term outcomes of testosterone replacement therapy in populations with or without ESRD. Available trial results suggest equivocal improvements in sexual function. Muscle mass and bone mineral density appear to improve, but results in physical function and performance are mixed and there are no data on fracture prevention. Some recent data suggest harm when testosterone was given to men with limited mobility. Finally, there is little evidence that testosterone adds to existing erythropoietin agents in the treatment of anemia in ESRD. Due to lack of evidence supporting long-term use of testosterone, the authors recommend against the routine use of testosterone in ESRD patients with low testosterone levels. Testosterone treatment can be considered in those with low bone mass and total testosterone level <200 ng/dl, or in younger patients with sexual complaints with total testosterone level lower than the reference range. It is important to engage patients in discussion of risks and benefits before initiating testosterone therapy; testosterone therapy should be discontinued if the intended treatment effect is not observed after short-term use. Copyright © 2014 Wiley Periodicals, Inc.

PMID

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20170414

Year of Publication
2015
AIM: The study's purpose was to examine the effects of providing a partnership support program. It was designed to improve Japanese couples' partnership, maintain quality of life, decrease psychological distress, and improve marital relationship satisfaction while they underwent infertility treatment that included the possibility of using assisted reproductive technology.

METHODS: This quasi-experimental study with a two-group pretest-post-test design used purposive sampling and non-random assignment of 318 consenting Japanese patients from previous phases of assisted reproductive technology fertility treatment who were patients from a fertility clinic in Tokyo, Japan. The intervention group of 152 patients (76 couples) participated in the partnership support program. The comparison group of 166 patients (83 couples) received usual care. Recruitment was age matched. The program provided information and used a participatory-interactive approach to enhance understanding and cooperation in couples undergoing fertility treatment. The main outcome measures were: "partnership", FertiQoL, Quality Marriage Index, and "psychological distress".

RESULTS: There were 311 participants (intervention group n=148; comparison group, n=163). The intervention group showed significant improvement in the couples' partnerships and a significant decrease in women's psychological distress using subgroup analysis.

CONCLUSION: The partnership support program provided effective improvement in partnership for the couples, and reduced psychological distress for the women; however, it had less impact for the men. The program was not effective in improving couples' overall quality of life (QOL); however, it was effective in improving the "mind-body" aspects of the QOL subscale.


Copy number variations in spermatogenic failure patients with chromosomal abnormalities and unexplained azoospermia.


Embase
Genetics and Molecular Research. 14 (4) (pp 16041-16049), 2015. Date of Publication: 07 Dec 2015.

[Article]
AN: 611418582

Male infertility is mostly caused by spermatogenic failure. Currently, routine genetic analyses of unexplained azoospermia or oligozoospermia are limited to the investigation of Y chromosomal microdeletions and chromosome karyotype analyses. The aim of this study was to find spermatogenic failure genes in patients with chromosomal abnormalities and unexplained azoospermia caused by copy number variations in order to provide a theoretical basis for further research. Spermatogenic failure patients consisting of 13 males with chromosomal abnormalities and 20 with unexplained azoospermia were enrolled. The subjects underwent high-throughput genome-wide sequencing to find copy number variants (CNVs), and the results were analyzed using the Database of Genomic Variants, Online Mendelian Inheritance in Man database, and PubMed. The results showed that 16 CNVs were detected in 11 patients with chromosome abnormalities, and 26 CNVs were found in 16 males with azoospermia. Our data showed CNV-involved loci including: three times on 11p11.12 and 14q11.2 and twice on 6p21.32, 13q11, 15q11.11, 16p12.2, and 21q22.3. Some CNVs may involve changes in genetic structure and function or gene mutations, which may affect gene expression in testicular tissues and lead to spermatogenic failure. The involved genes include EDDM3A, EDDM3B, HLA-DRB1, HLA-DQA1, POTEB, GOLGA8C, DNMT3L, ALF, NPHP1, NRG1, RID2, ADAMTS20, TWF1, COX10, MAK, and DNEL1. By applying high throughput genome-wide sequencing to determine CNVs, we provide a number of candidate genes possibly contributing to spermatogenic failure.
Importance of measuring testosterone in enzyme-inhibited plasma for oral testosterone undecanoate androgen replacement therapy clinical trials.
Lachance S., Dhingra O., Bernstein J., Gagnon S., Savard C., Pelletier N., Boudreau N., Levesque A.
Embase
Future Science OA. 1 (4) (no pagination), 2015. Article Number: FSO55. Date of Publication: November 2015.
[Article]
AN: 614411718
Aim: Testosterone undecanoate (TU) is metabolized by nonspecific esterases in blood to testosterone (T). Typical clinical practice has been to analyze testosterone in human serum. The degradation of TU to testosterone was evaluated in conditions typically used in clinical studies.
Methods & Results: Freshly collected whole blood was fortified with TU at known concentration. Serum was prepared and T concentration was determined by LC-MS/MS. It was observed that TU degrades extensively to T in human blood under conditions typical of harvesting serum causing overestimation of T concentration of up to 243%. These results were confirmed in a clinical study in which serum and plasma samples were compared. Conclusion: It was demonstrated that T must be analyzed in enzyme-inhibited plasma when TU is the administered medication. Testosterone undecanoate (TU) is metabolized into testosterone. Its degradation in whole blood into testosterone was studied in conditions typically used in clinical trials. It was observed that TU degrades extensively to testosterone in human blood under conditions typical of harvesting serum, causing overestimation of testosterone concentration. It was demonstrated that testosterone must be analyzed in enzyme-inhibited plasma when TU is the administered medication.
medication. Using serum for testosterone quantitation in a clinical trial for androgen replacement therapy would bias the conclusions on formulations adjustment and use.Copyright © 2015 inVentiv Health clinical.

Status
EMBASE
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(Lachance, Gagnon, Savard, Pelletier, Boudreau, Levesque) InVentiv Health Clinical, QC, Canada (Dhingra, Bernstein) SOV Therapeutics, Morrisville, NC, United States
Publisher
Future Medicine Ltd. (E-mail: info@future-science.com)
Date Created
20170221
Year of Publication
2015

726.
Dietary nutrients and male infertility: Review of current evidence.
Hosseini B., Djafarian K.
Embase
[Article]
AN: 614203917
Lifestyle factors and nutritional status are regarded as critical determinants of normal reproductive function. Hence, the role of dietary nutrients has attracted the attention of researchers to the extent that some studies have addressed the effects of diet on the risk of male infertility. This study aimed to summarize the literature regarding the association between various dietary factors and male infertility. Literature searching for studies on male infertility and nutrition, published between January 1982 and May 2015, was performed using PubMed and Scopus databases. The bibliographies of included studies were also searched for additional references. About 65 articles were identified and after the elimination of irrelevant studies, 35 related studies available for review were examined. Studies have indicated that in men with idiopathic infertility, omega-3 intervention resulted in significant improvement in total sperm count as well as sperm cell density. Moreover, several studies have shown that higher intake of poultry, cereals, fruit and vegetables
may play a beneficial role in male infertility; although, some studies have not attained such results. Taken as a whole, studies demonstrated that food consumption may play a major role in preventing or facilitating male infertility. Further studies are needed to clarify this association.

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20170218

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2015

727.
Assessment on the adverse effects of aminoglycosides and flouroquinolone on sperm parameters and male reproductive tissue: A systematic review.
Khaki A.

Embase
[Review]
AN: 610950892

Background: Antibiotic therapies used in treatment of many diseases have adverse effects on fertility. This review analyzes previous comparative studies that surveyed the effects of two common groups of antibiotics on male fertility. Objective: To evaluate histo-pathological effects of flouroquinolones and aminoglycosides on sperm parameters and male reproductive tissue.

Materials and Methods: Articles about the effects of aminoglycosides and flouroquinolones on male infertility, sperm parameters, male reproductive tissue, and spermatogenesis in English and Persian languages published on Google Scholar and PubMed databases from January 2000 to
December 2013 were assessed. Randomized controlled trials (RCTs) assessing the effects of aminoglycosides or fluoroquinolones on sperm parameters, artificial insemination, and male reproductive tract or RCTs comparing aminoglycosides vs. fluoroquinolones were eligible for inclusion. For ascertaining the reliability of study, data were extracted independently and in duplicate by two investigators. Results: Sperm viability was decreased significantly with streptomycin, gentamicin, and neomycin (p<0.001). Sperm motility was decreased significantly with gentamicin and neomycin (p<0.05). Total sperm count was significantly decreased with ofloxacin, gentamicin, streptomycin, and neomycin (p<0.022). There was significant decrease in post-thawing motility with low dose and high dose of ciprofloxacin. Testis weight was decreased with gentamicin and ofloxacin significantly (p<0.011). There was significant decrease in seminal vesicle weight with gentamicin, neomycin, and ofloxacin (p<0.022). Furthermore, changes in epididymis weight, percentage of total apoptotic cells, and diameter of seminiferous tubule were significant with all drugs including streptomycin, gentamicin, neomycin, and ofloxacin (p<0.05). Conclusion: Streptomycin has less negative effects on cell’s apoptosis and sperm parameters as compared to other drugs. Gentamicin has more detrimental effects so lesser dosage and duration is recommended. Fluoroquinolones showed negative effects on testis tissue and sperm parameters. Ciprofloxacin has less adverse effects than gentamicin in artificial insemination.

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Date Created
20160709
Year of Publication
2015

728.
Gonadal dysfunction and fertility preservation in Hodgkin lymphoma patients.
Behringer K., von Wolff M.
Osteoporotic fractures in patients with untreated hyperprolactinemia vs. those taking dopamine agonists: A systematic review and meta-analysis.
D'sylva C., Khan T., Uum S.V., Fraser L.-A.

Embase
[Review]
AN: 610483049
OBJECTIVE: Hyperprolactinemia is associated with bone fragility. Traditionally attributed to prolactin-induced hypogonadism, recent studies have identified increased fracture rates independent of gonadal function. METHODS: We performed a systematic review to identify studies assessing fracture risk in patients with untreated hyperprolactinemia compared to those on dopamine agonists. MEDLINE, EMBASE, Cochrane, Web of Science and BIOSIS Previews databases were searched from inception to December 2013 for studies of hyperprolactinemia with fractures as an outcome. Two authors independently performed title and abstract searches,
full-text searches, data abstraction, and quality assessment. A summary odds ratio (OR) was calculated using a random effects model. RESULTS: Of the 197 articles identified, 2 met inclusion criteria. Both cross-sectional studies examined cabergoline use (or non-use) in patients with prolactin-secreting adenomas, with vertebral fractures as the primary outcome. For women, vertebral fractures were identified in 46% of untreated patients, vs. 20% of patients on cabergoline (OR: 0.29, 95% CI: 0.10-0.78). For men, the results were 67% in untreated, vs. 26% in cabergoline treated patients (OR: 0.18, CI: 0.03-0.94), with no difference between gonadal and hypogonadal men (p=0.8). Combining studies gave a summary odds ratio of 0.25 (CI: 0.11-0.59), I²=0%. CONCLUSIONS: In the limited studies available, fracture prevalence was increased in patients with untreated hyperprolactinemia compared to those on treatment, independent of gonadal function. Further studies are needed to clarify if postmenopausal women, or high-risk men, with no other indication for treatment, should be on dopamine agonists to decrease fracture risk. Copyright © 2015 Neuroendocrinology Letters.

PMID

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Publisher
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20160607

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730.
Testosterone replacement and cardiovascular disease risk: What do endocrinologists need to know?.
Gonzalez J.R., Goldstein I.
Embase
Testosterone deficiency (or hypogonadism) affects millions of men worldwide. Consensus regarding an appropriate biochemical cutoff for the definition and treatment of hypogonadism has been challenging. Several recent, well-publicized studies have called into question the long recognized benefits of testosterone replacement therapy. The aim of the current article is to review the data on testosterone treatment, paying specific attention to the potential cardiovascular effects of this increasingly common therapy. We examine some of the most common cardiovascular diseases including hypertension, metabolic syndrome, coronary artery disease, atherosclerosis, congestive heart failure, myocardial infarction, and stroke. This review will also investigate the potential effect of testosterone replacement therapy on cardiovascular and all-cause mortality and address a growing fear among the medical community about the safety of testosterone replacement.
Over the past decade there has been an increase in awareness of the clinical syndrome of male hypogonadism and its association with comorbid conditions. This article reviews studies focusing on recent trials of testosterone replacement therapy on cardiovascular risk. Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.

The term male hypogonadism is defined as the failure to maintain physiological concentrations of testosterone, a physiological quantity of sperm or the combination of both. Aetiologically, androgen deficiency can originate from the testes (primary hypogonadism) or from the hypothalamic-pituitary regulation of the testicular function (secondary hypogonadism). The causes of hypogonadism are very diverse and may be genetically determined (e.g. Klinefelter's syndrome) or acquired (tumours, infections, haemochromatosis). Classical hypogonadism linked to an underlying disease, such as a pituitary tumour, is a distinct indication for androgen
substitution. But how about the aging male? It is known that there is a highly variable age-related decline in testosterone levels; whether this represents a variation of normality or has a true disease value requiring therapy has been disputed over more than a decade. The key questions surrounding this debate concern not only the age-dependent threshold for serum testosterone but, more importantly, the risks and benefits of testosterone replacement therapy in the aging male. We searched the literature for randomised controlled trials of testosterone administration in aging males with a size of at least 100 patients and a follow-up of at least 6 months, and identified eight studies. These studies mostly tried to evaluate the effect of testosterone on bone density, muscle strength and body composition, rather than clinically meaningful endpoints. Moreover, these trials have provided evidence for relevant cardiovascular adverse events in elderly men. This supports the need for further studies to define the treatment threshold for testosterone levels in the aging male, as well as with regard to the long-term risks and relevant benefits of testosterone therapy in this population. Until we have more solid data in aging males, testing for testosterone deficiency and testosterone replacement should remain reserved for patients with predisposing conditions, symptoms and signs of bona fide hypogonadism.

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Status EMBASE
Institution (Christe, Meier) Dept. of Internal Medicine and Specialities, Triemli Hospital, Birmensdorferstrasse 497, Zurich CH-8063, Switzerland
Publisher EMH Swiss Medical Publishers Ltd. (E-mail: verlag@emh.ch)
Date Created 20160812
Year of Publication 2015

733.
Recurrence of prostate cancer in patients receiving testosterone supplementation for hypogonadism.
Purpose. The relationship between recurrent prostate cancer risk and testosterone replacement therapy (TRT) for hypogonadal men is explored. Summary. The medical literature was searched to identify articles evaluating the use of TRT in symptomatic hypogonadal men with a history of prostate cancer. Eight English-language articles investigating TRT use in hypogonadal men with a history of prostate cancer were analyzed. For evaluative purposes, the normal ranges used for prostate-specific antigen (PSA) and total testosterone levels were less than 4.0 ng/mL and 300-1000 ng/dL, respectively. Most trials were small and involved patients with localized prostate cancer treated with radical prostatectomy or radiotherapy, though patients with metastatic disease or a Gleason score of =8 were included in a few studies. TRT was administered in a variety of dosages and dosage forms for up to nine years to manage hypogonadal symptoms. Testosterone concentrations increased, as expected, after TRT, but serum PSA levels remained below 0.1 ng/mL in the majority of patients. PSA levels were found to increase in select patients with high-risk and metastatic disease, but these elevations were not accompanied by disease progression. These studies have suggested a potential benefit for TRT use in select symptomatic hypogonadal men with a history of prostate cancer. Data were limited, however, by the retrospective nature of most studies, the lack of control groups, small sample sizes, and short follow-up periods. Conclusion. There is insufficient evidence to withhold TRT in certain populations of men with a history of prostate cancer. Am J Health-Syst Pharm. 2015; 72:536-41
The relationship between serum hormone levels (follicle-stimulating hormone, luteinizing hormone, total testosterone) and semen parameters.


Embase
Archivio Italiano di Urologia e Andrologia. 87 (3) (pp 194-197), 2015. Date of Publication: 2015.

Objective: The aim of this study was to investigate the effect of serum gonadotropin and total testosterone levels on semen parameters. Materials and Methods: Three hundred and eighty-two patients that applied to a male infertility polyclinic were included in our study. Serum gonadotropin and total testosterone levels and semen parameters of the patients were analyzed during the first visit to the clinic. The reference FSH value was 1.5-12.4 mIU/mL, that of LH was 1.7-8.6 mIU/mL and the reference value for total testosterone was 249-836 ng/dL. Results: While there was no statistically significant difference between the patients with low gonadotropin levels and the controls regarding any of the semen parameters (p > 0.05), there was a strong statistically significant difference between the patients with high gonadotropin levels and the controls regarding sperm concentration (p = 0.000), total motility (p = 0.000), progressive motility (p = 0.000), and morphology (p = 0.000). There was a strong statistically significant difference between the patients with low testosterone levels and the controls regarding total motility (p = 0.012) and progressive motility (p = 0.010), and a weak statistically significant difference in morphology (p = 0.042). There was no statistically significant difference in semen volume or sperm concentration (p > 0.05). There was no statistically significant difference in any of the semen parameters between the patients with high testosterone levels and the controls (p > 0.05).

Conclusions: Our findings especially regarding LH and T levels are not in agreement with previous reports. In this regard, there is a need for larger-scale and randomized trials to resolve this discrepancy.

PMID

Status
EMBASE
Improvement of seminal quality and sexual function of men with oligoasthenoteratozoospermia syndrome following supplementation with L-Arginine and Pycnogenol.


Embase
Archivio Italiano di Urologia e Andrologia. 87 (3) (pp 190-193), 2015. Date of Publication: 2015.

[Article]
AN: 611311236

We evaluated the effectiveness of antioxidant co-supplementation therapy using L-arginine and Pycnogenol in Japanese men with oligoasthenozoospermia and mild erectile dysfunction (ED). A total of forty-seven adult males with oligoasthenoteratozoospermia syndrome (OAT) were eligible for enrollment. The effectiveness of supplementation with a combination of L-Arginine 690 mg and French maritime pine bark extract (Pycnogenol) 60mg for OAT and ED was investigated. The sperm concentration was enhanced significantly after treatment 2 and 4 months (11.79 +/- 9.86 to 21.22 +/- 28.17 and 20.15 +/- 23.99 x 106/ml). Significant improvements in the International Index of Erectile Function (IIEF) were observed in the total score of IIEF (57.69 +/- 11.04 to 59.43 +/- 12.57) and domain of Orgasmic Function (9.01 +/- 1.92 to 9.34 +/- 1.66) after 4 months of treatment. L-Arginine acts to increase the production of nitric oxide and Pycnogenol activates the endothelial nitric oxide synthase and it is a potent antioxidant and inhibitor of inducible nitric oxide synthase. This study suggests that the combination of Pycnogenol and L-Arginine (Edicare) is
helpful for infertile men to ameliorate simultaneously quality of sperms as well as erectile functions.

PMID

Status
EMBASE

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2015

736.
Effect of Palm Pollen on Sperm Parameters of Infertile Man.
Rasekh A., Jashni H.K., Rahmanian K., Jahromi A.S.
Embase
Pakistan journal of biological sciences : PJBS. 18 (4) (pp 196-199), 2015. Date of Publication: 01 Apr 2015.
[Article]
AN: 613678491

There is a rapidly growing trend in the consumption of herbal remedies in the developing countries. The aim of this study was to determine the effects of orally administered Date Palm Pollen (DPP) on the results of semen analysis in adult infertile men. Forty infertile men participated in our study. They were treated by Pollen powder 120 mg kg(-1) in gelatinous capsules every other day, for two months. Before and at the end of therapy, the semen was collected after masturbation and sperm numbers, motility and morphology were determined. Our findings revealed that consumption of DPP improved the sperm count. The treatment was
significantly increased sperm motility, morphology and forward progressive motility. Date palm pollen seems to cure male infertility by improving the quality of sperm parameters.  


737.

Review of the Different Treatments and Management for Prostate Cancer and Fertility.
Tran S., Boissier R., Perrin J., Karsenty G., Lechevallier E.

Embase
Urology. 86 (5) (pp 936-941), 2015. Date of Publication: 01 Nov 2015.
[Article]
AN: 611847781

OBJECTIVE: To compare the options available for prostate cancer management and their consequences on fertility for men, in order to best advise these men to choose their treatment, especially if they are young, with no child with their current partner. METHODS: A literature review on prostate cancer and fertility over the last 26 years was carried out on PubMed database. The literature was based on evidence and practical considerations. Twenty-nine articles were selected according to their relevance.

RESULTS: After prostatectomy, there is an obstructive infertility in 100% of the cases. In external radiotherapy, doses more than 15 cGy induced reduction in sperm count. Direct irradiation between 15 and 35 cGy caused oligozoospermia and doses between 35 and 50 cGy caused reversible azoospermia. The calculated projected doses on testicles were 196 cGy (+/- 145 cGy). The brachytherapy effects on fertility seems to be less harmful. The irradiation dose received by testicles is less important (less than 20 cGy) after brachytherapy than after external radiotherapy. Infertility induced by hormonal therapy alone should be reversible. Fertility and focal therapy have not been well evaluated yet. Active surveillance is the management of prostate cancer which allows to keep at best men's fertility.

CONCLUSION: Urologists should consider approaching the topic of infertility when discussing the pros and cons of various prostate cancer management with their younger patients. If a patient
with prostate cancer expresses interest in future fertility, a semen analysis should be performed. Cryopreservation represents the only preemptive accompanying possibility to preserve fertility in young cancer patients.

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PMID

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Date Created
20160830

Year of Publication
2015

738.
AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY POSITION STATEMENT ON THE ASSOCIATION OF TESTOSTERONE AND CARDIOVASCULAR RISK.
Goodman N., Guay A., Dandona P., Dhindsa S., Faiman C., Cunningham G.R.
Embase
Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists. 21 (9) (pp 1066-1073), 2015. Date of Publication: 01 Sep 2015.
[Article]
This document represents the official position of the American Association of Clinical Endocrinologists and the American College of Endocrinology. Where there were no randomized controlled trials or specific U.S. FDA labeling for issues in clinical practice, the participating clinical experts utilized their judgment and experience. Every effort was made to achieve consensus among the committee members. Position statements are meant to provide guidance, but they are not to be considered prescriptive for any individual patient and cannot replace the judgment of a clinician.

PMID

Date Created
20160820

Year of Publication
2015

739.
The Impact of Infertility on the Psychological Well-Being, Marital Relationships, Sexual Relationships, and Quality of Life of Couples: A Systematic Review.
Luk B.H.-K., Loke A.Y.
Embase
Journal of sex & marital therapy. 41 (6) (pp 610-625), 2015. Date of Publication: 2015. [Review]
AN: 611460876

The purpose of this systematic review was to identify, with supporting evidence, the effect of infertility on couples. MEDLINE, PsycINFO, and CINHAL Plus articles were searched for relevant studies (2000-2014) published in English. Twenty articles were included in this review. The results showed that infertility affected couples in the following four aspects of their life: psychological well-being, marital relationships, sexual relationships, and quality of life. There is evidence that infertility has a negative effect on the psychological well-being and sexual relationships of couples, but the evidence is inconclusive for the effect on marital relationships and quality of life.
PMID
Gender differences in experiences with and adjustments to infertility: A literature review.
Ying L.Y., Wu L.H., Loke A.Y.
Embase
[Review]
AN: 610974884
BACKGROUND: It has been widely recognized that infertility and its treatment affects a couple as a dyad. Given biomedical differences and differences in socialization processes and gender-role expectations, it is reasonable to suspect that females and males may experience and respond to infertility in different ways. OBJECTIVE: To explore gender differences among infertile couples with regard to experiences with and adjustments to infertility.
DESIGN: A literature review.
DATA SOURCES: A literature search was performed using the following databases: PubMed, CINAHL, PsycInfo, Web of Science, Scopus, and the China Academic Journal Full-text Database.
REVIEW METHODS: The studies that were included were those published in English or Chinese from the years 2000 to 2014. The references of all of the studies selected for this review were also searched. An author search was also performed to retrieve relevant articles. Experiences with and adjustments to infertility were explored from the perspective of gender.
RESULTS: A total of 33 studies were included in this review. The experiences with infertility can be grouped under the five domains of the biopsychosocial theory, namely: existential stressors, physical stressors, emotional stressors, interpersonal stressors, and the moderators of stress. In general, females had more negative experiences with infertility than men in most of the domains, including lower levels of identity, self-esteem, and physical health; and higher levels of depression, stress, anxiety, stigma, and shame. Infertile couples experienced stress in their
married life, although there were no gender differences in the areas of marital adjustment, marital satisfaction, and sexual satisfaction. Females were likely to perceive themselves as being less confident than their partners in coping with infertility. For both men and women, partner support was found to be negatively related to stress due to infertility.

CONCLUSIONS: This review revealed that while there were gender differences in the experience with infertility in many realms, both men and women were subject to a stressful married life. Partner support was an important element of coping with infertility. Therefore, a supportive intervention, focusing on enhancing a sense of partnership among infertile couples is a way of helping them to cope.

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741.
Comparison between Microsurgical Subinguinal Varicocelectomy with and without Testicular Delivery for Infertile Men: Is Testicular Delivery an Unnecessary Procedure.
Hou Y., Zhang Y., Huo W., Li H.

Embase
Urology journal. 12 (4) (pp 2261-2266), 2015. Date of Publication: 01 Jul 2015.
[Article]
AN: 610927405
PURPOSE: Controversy still exists as to whether testicular delivery during microsurgical subinguinal varicocelecto-my (MSV) provides benefit to the patient or not. This study specifically
compared the therapeutic effect of MSV with and without testicular delivery for the treatment of varicocele in a cohort of infertile men. MATERIALS AND METHODS: We conducted a prospective, randomized, controlled study to evaluate the therapeutic efficacy of MSV with and without testicular delivery for the treatment of varicocele in infertile men. A total of 100 patients were specifically recruited using strict inclusion criteria to undergo MSV with testicular delivery (group 1, n = 50) or MSV without testicular delivery (group 2, n = 50). All patients were followed-up at 3, 6 and 12 months following surgery. Semen parameters, pregnancy and recurrence rates, and complications were monitored.

RESULTS: Mean surgical time for group 1 was significantly longer than group 2 (90.50 +/- 15.60 min vs. 84.30 +/- 15.58 min; P = .001). Sperm count and motility were significantly improved at the 12-month follow-up appointment in both groups compared with pre-operative values, but were not significantly different at 3, 6, and 12 months when compared between the two treatment groups. The incidence of scrotal edema, and spermatic/testicular engorgement were higher in group 1 (both P = .001), although natural pregnancy rate was not significantly different between the two groups at the 12 month follow-up appointment (46% vs. 42%) (P = .817).

CONCLUSION: MSV with testicular delivery did not reduce the risk of recurrence and led to improved semen quality compared with MSV without testicular delivery. However, there was a higher risk of complication with this technique, which must be borne in mind when considering the clinical implications of our dataset.

Clinical Use of Aromatase Inhibitors in Adult Males. [Review]
Tan RB; Guay AT; Hellstrom WJ.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Review. Journal Article]
UI: 27784593

INTRODUCTION: There is a growing interest in the treatment of late-onset hypogonadism, another name for the study of testosterone deficiency in an older age group. Initial attempts at testosterone replacement have also brought attention to the possible adverse effects on the patients' cardiovascular risk factors and their prostate health. The "female" hormone estradiol is no longer considered as the feminizing hormone, as it has been identified to have an effect on the sexual and general well-being of adult males. Urologists and endocrinologists alike have started to pay attention to the serum T/E2 (testosterone:estradiol) ratio that appears to be more important than the respective individual hormonal levels. Therein lies the possible role of aromatase inhibitors (AIs) in restoring the normal balance of serum testosterone and estradiol levels for the adequate treatment of late-onset hypogonadism, while limiting the potential adverse effects. Currently, other established clinical indications of AIs include the treatment of breast cancer in female patients and developmental growth problems in pediatric patients.

AIM: This review evaluates the role of AIs as a treatment option for late-onset hypogonadism and the evidence for its other clinical uses in men, including its possible adverse effects.

METHODS: A literature review was performed with regards to the use of aromatase inhibitors in adult males, the role of estrogens in adult males, as well as adverse effect of AIs on bone health in adult males.

MAIN OUTCOME MEASURES: To evaluate the evidence for the use of AIs in adult males to treat late-onset hypogonadism, obesity-related hypogonadotropic hypogonadism, gynecomastia, and male subfertility. To evaluate the evidence for the possible adverse effects on the bone health of adult males with the use of AIs.

RESULTS: Currently there is no literature to recommend the use of AIs in adult males to treat late-onset hypogonadism, obesity-related hypogonadotropic hypogonadism, gynecomastia, or male subfertility, although some positive effects have been reported. The adverse effects on bone health seen in females treated with AIs are not seen in males.
CONCLUSIONS: With the better understanding of the T/E2 ratio in adult males, the lack of scientific data to show that bone health is adversely affected by AI usage in adult males, the positive effects of AIs on the treatment of conditions like late-onset hypogonadism and male subfertility encourages conducting large-scale, multicenter, randomized controlled trials for the clinical use of AIs in adult males. Tan RBW, Guay AT, and Hellstrom WJG. Clinical use of aromatase inhibitors in adult males. Sex Med Rev 2014;2:79-90. Copyright © 2014 International Society for Sexual Medicine. Published by Elsevier Inc. All rights reserved.

743.
The Evaluation and Treatment of Delayed Ejaculation. [Review]
Shin DH; Spitz A.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Review. Journal Article]
UI: 27784563
INTRODUCTION: Delayed ejaculation is a small but important subsection of ejaculatory dysfunction, with prevalence estimated at 1-4%. It is most commonly defined by DSM-IV-TR
criteria, as "a persistent delay in, or absence of, orgasm in a male following a normal sexual excitement phase during sexual activity that the clinician, taking into account the person's age, judges to be adequate in focus, intensity, and duration." The pathophysiology of delayed ejaculation is related to disruptions in ejaculatory apparatus, nervous transmission, hormonal or neurochemical ejaculatory control, or psychosocial factors.

AIM: To update the clinician on the evaluation and treatment of delayed ejaculation.

METHODS: The keywords "delayed ejaculation" and "retarded ejaculation" were utilized to search Pubmed for relevant publications.

MAIN OUTCOME MEASURES: 319 results were generated from the search, and those publications judged relevant to the pathophysiology, epidemiology, evaluation, and treatment of delayed ejaculation were included in the review.

RESULT: 110 articles were ultimately selected for inclusion in this review.

CONCLUSION: The evaluation of this condition requires a focused history and physical, which includes a detailed sexual history, examination of the genitalia, and inquiry into the status of the partner. Laboratory tests are aimed at the detection of abnormalities in the blood count, glucose level, hormone levels, or kidney function. If a correctable etiology is discovered, treatment is directed towards the reversal of this condition. In some cases, the delayed ejaculation may be a lifelong problem. Also, in some cases the etiology of the delayed ejaculation may be irreversible, such as in the case of age-related sensation loss or diabetes-related neuropathy. In these instances treatment may require a combination of behavioral modification, sexual therapy, or perhaps pharmaceutical drugs. Participation of the partner in therapy may sometimes be necessary. Future investigations will continue to elucidate the complex biological and psychosocial factors which contribute to delayed ejaculation, leading to more effective treatments.


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744.
Testosterone and the Prostate. [Review]
Tan RB; Silberstein JL; Hellstrom WJ.
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MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Review. Journal Article]
UI: 27784562
INTRODUCTION: Late-onset hypogonadism, lower urinary tract symptoms (LUTS) due to benign prostatic enlargement (BPE), and prostate cancer commonly coexist in the aging male. Due to a better understanding of the physiology and impact of testosterone on benign and malignant diseases of the prostate, the view toward testosterone replacement therapy (TRT) in these individuals has changed dramatically over time.
AIM: This communication evaluates the effects of testosterone on benign prostatic growth and prostate cancer and reviews the evidence for TRT for men with BPE and prostate cancer.
METHODS: A literature review was performed with regards to TRT in men with prostate cancer as well as the effect of testosterone on the growth of benign prostate tissue and prostate cancer carcinogenesis.
MAIN OUTCOME MEASURE: To evaluate the evidence for an effect of testosterone on the growth of benign prostate tissue and the development of prostate cancer and TRT in men with prostate cancer.
RESULTS: TRT does not exacerbate LUTS. Current evidence is lacking but suggests that TRT may not increase the risk of subsequent diagnosis of prostate cancer, and is unlikely to impact recurrence or progression for men with treated prostate cancer, but longer follow-up is needed.
CONCLUSIONS: There is no evidence to suggest that TRT is contraindicated in men with BPE or effectively treated prostate cancer. Tan RBW, Silberstein JL, and Hellstrom WJG. Testosterone and the prostate. Sex Med Rev 2014;2:112-120.
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Status
Contraceptive vaccines have been proposed for controlling the growing human population and wildlife population management. Multiple targets such as gonadotropin releasing hormone (GnRH), luteinizing hormone, follicle stimulating hormone, gonadotropin receptors, sperm-specific proteins and zona pellucida glycoproteins have been exploited to develop contraceptive vaccine and their efficacy investigated and shown in various experimental animal models. Vaccines based on GnRH have found application in immuno-castration of male pigs for prevention of boar-taint. Vaccines based on zona pellucida glycoproteins have shown promising results for population management of wild horses and white-tailed deer. Phase II clinical trials in women with beta-human chorionic gonadotropin (beta-hCG)-based contraceptive vaccine established proof of principle that these can be developed for human application. Block in fertility by beta-hCG contraceptive vaccine was reversible. Further research inputs are required to establish the safety
of contraceptive vaccines, improve their immunogenicity and to develop novel vaccine delivery platforms for providing long lasting immunity.

Status
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746.
Prospective randomized controlled trial of the stabilis Stand Alone Cage (SAC) versus Bagby and Kuslich (BAK) implants for anterior lumbar interbody fusion.

Lavelle W., McLain R.F., Rufo-Smith C., Gurd D.P.

Embase

[Article]
AN: 610846489

Background Degenerative disc disease is common and debilitating for many patients. If conservative extensive care fails, anterior lumbar interbody fusion has proven to be an alternative form of surgical management. The Stabilis Stand Alone Cage(SAC) was introduced as a method to obtain stability and fusion. The purpose of this study was to determine whether the Stabilis Stand Alone Cage (SAC) is comparable in safety and efficacy to the Bagby and Kuslich (BAK) device. Methods As part of a prospective, randomized, controlled FDA trial, 73 patients underwent anterior interbody fusion using either the SAC(56%) or the BAK device (44%). Results Background characteristics were similar between the two groups. There was no significant
difference between the SAC and BAK groups in mean operative time or mean blood loss during surgery. Adverse event rates did not differ between the groups. Assessment of plain radiographs could not confirm solid fusion in 63% of control and 71% of study patients. Functional scores from Owestry and SF-36 improved in both groups by the two-year follow-up. There were no significant differences between the SAC and BAK patients with respect to outcome. Conclusions Both the Stabilis Stand Alone Cage and the BAK Cage provided satisfactory improvement in function and pain relief, despite less than expected radiographic fusion rates. The apparent incongruency between fusion rates and functional outcomes suggests that either radiographs underestimate the true incidence of fusion, or that patients are obtaining good pain relief and improved function despite a lower rate of fusion than previously reported. This was a Level III study. Copyright © 2014 ISASS - International Society for the Advancement of Spine Surgery.

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2014

Do children make you happier? Sustained child-wish and mental health in women 11-17 years after fertility treatment.
Gameiro S., Van Den Belt-Dusebout A.W., Bleiker E., Braat D., Van Leeuwen F.E., Verhaak C.M.
Embase
[Article]
AN: 612062594
STUDY QUESTION: Are fertility treatment-related factors, parenthood status and sustained child-wish associated with women's long-term mental health? summary answer: Sustaining a child-
wish is more strongly associated with women's long-term mental health than fertility treatment-related factors and parenthood status. WHAT IS KNOWN ALREADY: About one-third of the couples starting fertility treatment do not achieve parenthood and have to adjust to an unfulfilled child-wish. In women, remaining childless after treatment is associated with less favourable mental health. It is unclear if this is only related to their childlessness or if adjustment after unsuccessful treatment is affected by other variables. These include diagnostic and treatment-related factors (cause of fertility problems, age at first consultation, type and number of treatments) and the psychological ability to come to terms with the unfulfilled child-wish. Differentiating the relative contribution of these factors to women's long-term mental health will provide useful knowledge to support patients adjusting to negative treatment outcomes.

STUDY DESIGN, SIZE, DURATION: Across-sectional study with a nationally representative sample of 7148 women who started fertility treatment at any of the 12 IVF hospitals in the Netherlands from 1995 through 2000. Of 16 482 women who were invited to participate, 7148 (43.4%) provided psychological data. PARTICIPANTS/MATERIALS, SETTING, METHODS: The average age of women was 47 years and the average age at first fertility consultation was 30 years. Fifty-one percent of women did IUI and 85% did IVF/ICSI. Ninety percent of women were married/cohabiting, 20.9% remained childless and 5.9% had a child-wish. Women completed a questionnaire assessing diagnostic and treatment factors (retrospective data), parenthood status, sustained child-wish and mental health. MAIN RESULTS AND THE ROLE OF CHANCE: A multiple regression analysis controlling for background variables showed that, first, male factor (P < 0.05) and/or idiopathic infertility (P < 0.001) were associated with better mental health. Secondly, starting fertility treatment at an older age was associated with better mental health (P < 0.01). Thirdly, the interaction between parenthood status and sustained child-wish was significant (P < 0.01). Having a child-wish was associated with worse mental health for women with (beta=-0.058, P < 0.01) and without children (beta = -0.136, P < 0.001), but associations were stronger for the latter. Predictive factors accounted for <5% of the variation in mental health status in the study population. LIMITATIONS, REASONS FOR CAUTION: The sample was large and nationally representative. Response rate was in line with other studies but women without psychological data were less likely to have biological children and 15.9% of non-responders considered the questionnaire to be too confronting or to elicit too emotional memories. This could reflect an underestimation of the proportion of women with a sustained child-wish. WIDER IMPLICATIONS OF THE FINDINGS: Sustaining a child-wish is a more important risk for long-term adjustment problems than parenthood status. Women adjust better when they start treatment at older ages and know they were not responsible for the cause of the fertility problem. Fertility staff can play an important role in preparing patients for the possibility of treatment failure and the associated grief process. They can also inform patients about the positive effect of refocusing their life goals. STUDY FUNDING/COMPETING INTEREST(S): This study was
Human sperm sex chromosome disomy and sperm DNA damage assessed by the neutral comet assay.
McAuliffe M.E., Williams P.L., Korrick S.A., Dadd R., Marchetti F., Martenies S.E., Perry M.J.
Embase
[Article]
AN: 612062577
STUDY QUESTION: Is there an association between human sperm sex chromosome disomy and sperm DNA damage? SUMMARY ANSWER: An increase in human sperm XY disomy was
associated with higher comet extent; however, there was no other consistent association of sex chromosome disomies with DNA damage. WHAT IS KNOWN ALREADY: There is limited published research on the association between sex chromosome disomy and sperm DNA damage and the findings are not consistent across studies. study design, size, and duration: We conducted a cross-sectional study of 190 men (25% ever smoker, 75% never smoker) from subfertile couples presenting at the Massachusetts General Hospital Fertility Clinic from January 2000 to May 2003. participants/materials, setting, methods: Multiprobe fluorescence in situ hybridization for chromosomes X,Y and 18 was used to determine XX, YY, XY and total sex chromosome disomy in sperm nuclei using an automated scoring method. The neutral comet assay was used to measure sperm DNA damage, as reflected by comet extent, percentage DNA in the comet tail, and tail distributed moment. Univariate and multiple linear regression models were constructed with sex chromosome disomy (separate models for each of the four disomic conditions) as the independent variable, and DNA damage parameters (separate models for each measure of DNA damage) as the dependent variable. MAIN RESULTS AND THE ROLE OF CHANCE: Men with current or past smoking history had significantly greater comet extent (xm: regression coefficients with 95% CI) [XX18:15.17 (1.98,28.36); YY18:14.68 (1.50,27.86); XY 18:15.41 (2.37, 28.45); Total Sex Chromosome Disomy: 15.23 (2.09, 28.38)], and tail distributed moment [XX18:3.01 (0.30, 5.72); YY18:2.95 (0.24, 5.67); XY 18:3.04 (0.36, 5.72); Total Sex Chromosome Disomy: 3.10(0.31,5.71)] than men who had never smoked. In regression models adjusted for age and smoking, there was a positive association between XY disomy and comet extent. For an increase in XY disomy from 0.56 to 1.47% (representing the 25th to 75th percentile), there was a mean increase of 5.08 mum in comet extent. No other statistically significant findings were observed. LIMITATIONS, REASONS FOR CAUTION: A potential limitation of this study is that it is cross-sectional. Cross-sectional analyses by nature do not lend themselves to inference about directionality for any observed associations; therefore we cannot determine which variable is the cause and which one is the effect. A small sample size may be a further limitation. Comparison of these findings to other studies is limited due to methodological differences. WIDER IMPLICATIONS OF THE FINDINGS: Although consistent associations across sex chromosome disomies or DNA damage measures were not observed, this study highlights the need to explore etiologies of sperm DNA damage and sex chromosome disomy to better understand the potential mechanistic overlaps between the two. STUDY FUNDING/COMPETING INTEREST(S): This work was supported by NIOSH Grant T42 OH008416, and NIH/NIEHS Grants ES 009718, ES 000002, and R01 ES017457. During the study M.E.M. was affiliated with the Department of Environmental Health at the Harvard School of Public Health. trial registration number: N/A. Copyright © The Author 2014. Published by Oxford University Press on behalf of the European Society of Human Reproduction and Embryology. All rights reserved.
749.
Improving the reporting of Clinical trials of infertility treatments (IMPRINT): Modifying the
CONSORT statement.
Legro R.S., Wu X., Barnhart K.T., Farquhar C., Fauser B.C.J.M., Mol B.
Embase
[Article]
AN: 612062571
Clinical trials testing infertility treatments often do not report on the major outcomes of interest to patients and clinicians and the public (such as live birth) nor on the harms, including maternal risks during pregnancy and fetal anomalies. This is complicated by the multiple participants in infertility trials which may include a woman (mother), a man (father), and result in a third individual if successful, their offspring (child), whois also the desired outcome of treatment. The primary outcome of interest many adverse events occur after cessation of infertility treatment and during pregnancy and the puerperium, which create a unique burden of follow-up for clinical trial investigators and participants. In 2013, because of the inconsistencies in trial reporting and the unique aspects of infertility trials not adequately addressed by existing Consolidated Standards of Reporting Trials (CONSORT) statements, we convened a consensus conference in Harbin, China, with the aim of planning modifications to the CONSORT checklist to improve the quality of reporting of clinical trials testing infertility treatment. The consensus group recommended that the preferred primary outcome of all infertility trials is live birth (defined as any delivery of a live infant >20 weeks gestations) or cumulative live birth, defined as the live birth per women over a defined time period (or number of treatment cycles). In addition, harms to all participants should be systematically collected and reported, including during the intervention, any resulting pregnancy, and during the neonatal period. Routine information should be collected and reported on both male and female participants in the trial. We propose to track the change in quality that these guidelines may produce in published trials testing infertility treatments. Our ultimate goal is to increase the transparency of benefits and risks of infertility treatments to provide better medical care to affected individuals and couples.

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Clinically relevant enhancement of humanspermmotilityusingcompounds with reported phosphodiesterase inhibitor activity.
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STUDYQUESTION: Can we identify compound(s) with reported phosphodiesterase inhibitor (PDEI) activity that could be added to human spermatozoa in vitro to enhance their motility without compromising other sperm functions? SUMMARYANSWER: We have identified several compounds that produce robust and effective stimulation of sperm motility and, importantly, have a positive response on patient samples. WHAT IS KNOWN ALREADY: For 20 years, the use of non-selective PDEIs, such as pentoxifylline, has been known to influence the motility of human spermatozoa; however, conflicting results have been obtained. It is now clear that human sperm express several different phosphodiesterases and these are compartmentalized at different regions of the cells. By using type-specific PDEIs, differential modulation of sperm motility may be achieved without adversely affecting other functions such as the acrosome reaction (AR). STUDY DESIGN, SIZE, DURATION: This was a basic medical research study examining sperm samples from normozoospermic donors and subfertile patients attending the Assisted Conception Unit (ACU), Ninewells Hospital Dundee for diagnostic semen analysis, IVF and ICSI. Phase 1 screened 43 commercially available compounds with reported PDEI activity to identify lead compounds that stimulate sperm motility. Samples were exposed (20 min) to three concentrations (1, 10 and 100 mM) of compound, and selected candidates (n = 6) progressed to Phase 2, which provided a more comprehensive assessment using a battery of in vitro sperm function tests. PARTICIPANTS/MATERIALS, SETTING, METHODS: All healthy donors and subfertile patients were recruited at the Medical Research Institute, University of Dundee and ACU, Ninewells Hospital Dundee (ethical approval 08/S1402/6). In Phase 1, poor motility cells recovered from the 40% interface of the discontinuous density gradient were used as surrogates for patient samples. Pooled samples from three to four different donors were utilized in order to reduce variability and increase the number of cells available for simultaneous examination of multiple compounds. During Phase 2 testing, semen samples from 23 patients attending for either routine diagnostic
andrology assessment or IVF/ICSI were prepared and exposed to selected compounds. Additionally, 48 aliquots of prepared samples, surplus to clinical use, were examined from IVF (n = 32) and ICSI (n = 16) patients to further determine the effects of selected compounds under clinical conditions of treatment. Effects of compounds on sperm motility were assessed by computer-assisted sperm analysis. A modified Kremer test using methyl cellulose was used to assess sperm functional ability to penetrate into viscous media. Sperm acrosome integrity and induction of apoptosis were assessed using the acrosomal content marker PSA-FITC and annexin V kit, respectively.

**MAIN RESULTS AND THE ROLE OF CHANCE:** In Phase 1, six compounds were found to have a strong effect on poor motility samples with a magnitude of response of >60% increase in percentage total motility. Under capacitating and non-capacitating conditions, these compounds significantly (P < 0.05) increased the percentage of total and progressive motility. Furthermore, these compounds enhanced penetration into a cervical mucus substitute (P < 0.05). Finally, the AR was not significantly induced and these compounds did not significantly increase the externalization of phosphatidylserine (P = 0.6, respectively). In general, the six compounds maintained the stimulation of motility over long periods of time (180 min) and their effects were still observed after their removal. In examinations of clinical samples, there was a general observation of a more significant stimulation of sperm motility in samples with lower baseline motility. In ICSI samples, compounds #26, #37 and #38 were the most effective at significantly increasing total motility (88, 81 and 79% of samples, respectively) and progressive motility (94, 93 and 81% of samples, respectively). In conclusion, using a two-phased drug discovery screening approach including the examination of clinical samples, 3/43 compounds were identified as promising candidates for further study.

**LIMITATIONS, REASONS FOR CAUTION:** This is an in vitro study and caution must be taken when extrapolating the results. Data for patients were from one assessment and thus the robustness of responses needs to be established. The n values for ICSI samples were relatively small.

**WIDER IMPLICATIONS OF THE FINDINGS:** We have systematically screened and identified several compounds that have robust and effective stimulation (i.e. functional significance with longevity and no toxicity) of total and progressive motility under clinical conditions of treatment. These compounds could be clinical candidates with possibilities in terms of assisted reproductive technology options for current or future patients affected by asthenozoospermia or oligoasthenozoospermia.

**STUDY FUNDING/COMPETING INTEREST(S):** This study was funded primarily by the MRC (DPFS) but with additional funding from the Wellcome Trust, Tenovus (Scotland), University of Dundee, NHS Tayside and Scottish Enterprise. The authors have no competing interests. A patent (#WO2013054111A1) has been published containing some of the information presented in this manuscript. Copyright © The Author 2014. Published by Oxford University Press on behalf of the European Society of Human Reproduction and Embryology.
Fernando S., Rombauts L.
Embase
[Review]
AN: 612353219
In recent years, the negative impact of oxidative stress on fertility has become widely recognised. Several studies have demonstrated its negative effect on the number and quality of retrieved oocytes and embryos following in-vitro fertilisation (IVF). Melatonin, a pineal hormone that regulates circadian rhythms, has also been shown to exhibit unique oxygen scavenging abilities.
Some studies have suggested a role for melatonin in gamete biology. Clinical studies also suggest that melatonin supplementation in IVF may lead to better pregnancy rates. Here we present a critical review and summary of the current literature and provide suggestions for future well designed clinical trials. Copyright © 2014 Fernando and Rombauts.

PMID

Utility of antioxidants during assisted reproductive techniques: An evidence based review.
Agarwal A., Durairajanayagam D., du Plessis S.S.

Embase
[Review]
AN: 612243854

Assisted reproductive technology (ART) is a common treatment of choice for many couples facing infertility issues, be it due to male or female factor, or idiopathic. Employment of ART techniques, however, come with its own challenges as the in vitro environment is not nearly as ideal as the in vivo environment, where reactive oxygen species (ROS) build-up leading to oxidative stress is kept in check by the endogenous antioxidants system. While physiological amounts of ROS are
necessary for normal reproductive function in vivo, in vitro manipulation of gametes and embryos exposes these cells to excessive ROS production either by endogenous or exogenous environmental factors. In this review, we discuss the sources of ROS in an in vitro clinical setting and the influence of oxidative stress on gamete/embryo quality and the outcome of IVF/ICSI. Sources of ROS and different strategies of overcoming the excessive generation of ROS in vitro are also highlighted. Endogenously, the gametes and the developing embryo become sources of ROS. Multiple exogenous factors act as potential sources of ROS, including exposure to visible light, composition of culture media, pH and temperature, oxygen concentration, centrifugation during spermatozoa preparation, ART technique involving handling of gamete/embryo and cryopreservation technique (freeze/thawing process). Finally, the use of antioxidants as agents to minimize ROS generation in the in vitro environment and as oral therapy is highlighted. Both enzymatic and non-enzymatic antioxidants are discussed and the outcome of studies using these antioxidants as oral therapy in the male or female or its use in vitro in media is presented. While results of studies using certain antioxidant agents are promising, the current body of evidence as a whole suggests the need for further well-designed and larger scale randomized controlled studies, as well as research to minimize oxidative stress conditions in the clinical ART setting.

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2014
INTRODUCTION: Testosterone treatment for hypogonadism is detrimental for men in reproductive age as it impairs spermatogenesis, and therefore affects fertility. It is, therefore, not indicated in men with hypogonadism and infertility.

AIM: The aim of this review is to analyze current data regarding options of treatment for men with hypogonadism and infertility.

MAIN OUTCOMES MEASURES: A comprehensive review of the current literature on management of infertility among hypogonadal men.

METHODS: A literature search using PubMed from 1980 to 2012 was done on articles published in the English language. The following medical subject heading terms were used: "infertility," "infertile," "hypogonadism;" "testosterone deficiency" and "men" or "male;" and "treatment" or "management."

RESULTS: The options for hypogonadal testicular failure are limited. Hormonal treatment is by and large ineffective. For secondary hypogonadism (hypogonadotrophic/normogonadotrophic hypogonadism), the options include gonadotropin-releasing hormone, human chorionic gonadotropin (hCG), human menopausal gonadotropin (hMG), follicle-stimulating hormone (FSH), and anti-estrogens and aromatase inhibitors. Dopamine antagonist is indicated for prolactinoma. Artificial reproductive technique is indicated for primary testicular failure and also when medical therapy fails.

CONCLUSION: The most suitable option with the current data available is hCG with or without hMG/FSH. Testosterone supplementation should be avoided, but if they are already on it, it is still possible for a return of normal sperm production within 1 year after discontinuing testosterone. Ho CCK and Tan HM. Treatment of the hypogonadal infertile male-A review. Sex Med Rev 2013;1:42-49.

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Status
PubMed-not-MEDLINE
INTRODUCTION: Testosterone is increasingly being recognized as an important hormone in maintaining proper health in aging males. Testosterone replacement therapy in older men with decreased or low-normal testosterone levels has been recognized to improve sexual function, increase lean body mass and decrease fat mass, improve exercise-induced coronary ischemia, and elevate mood, among other benefits. Prostate cancer remains the most common non-skin malignancy in men in the United States, and as hypogonadism is being recognized and treated more, a dilemma has arisen: treating hypogonadism in men previously treated for prostate cancer. While testosterone replacement has traditionally been felt to be contraindicated in men with prostate cancer, recent studies have challenged this notion.

AIM: This review highlights the origins of this concern as well as newer data that suggest that testosterone replacement in men with prostate cancer is safe.
METHODS: A literature search on testosterone replacement therapy in men with prostate cancer was performed.

MAIN OUTCOME MEASURE: We sought to highlight the data supporting the use of testosterone in men with prostate cancer.

RESULTS: While no randomized controlled trials have been able to confirm this theory, data from multiple studies suggest that testosterone replacement is safe in selected men treated for prostate cancer.

CONCLUSION: Long-term data and more studies are needed to conclusively change the paradigm regarding testosterone and prostate cancer growth, but based on the current data and on our experience, we feel it is safe to prescribe testosterone replacement therapy to men treated for prostate cancer with favorable pathology. Selph JP and Carson CC. Testosterone replacement therapy in men with prostate cancer: What is the evidence? Sex Med Rev 2013;1:135-142.

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Patrick Selph, J; Carson, Culley C.

Fertility Preservation in Young Men Treated for Malignancies: Options for Precancer Treatment. [Review]

Coward RM; Kovac JR; Smith RP; Lipshultz LI.
INTRODUCTION: Fertility preservation (FP) is an essential component of treatment for young men with a new cancer diagnosis.

AIM: To discuss the barriers and recommendations for FP along with the impacts of cancer and cancer treatment on fertility, and to present the various options for FP in young men prior to cancer treatment.

METHODS: Literature Review.

MAIN OUTCOME MEASURE: To evaluate the options for FP in young men, including novel and experimental options for pre-pubertal boys.

RESULTS: With the advent of assisted reproductive technologies, fertility can be successfully preserved in the majority of post-pubertal patients with sperm cryopreservation, neurostimulatory methods of ejaculation, or surgical sperm retrieval procedures.

CONCLUSIONS: All men with a new diagnosis of cancer, including adolescents and children, should be offered FP prior to undergoing treatment. Sperm cryopreservation, the mainstay of FP, should be encouraged regardless of the treatment plan. Even without significant abnormalities on semen analysis, prompt referral to a male fertility specialist is recommended. Coward RM, Kovac JR, Smith RP, and Lipshultz LI. Fertility preservation in young men treated for malignancies: Options for precancer treatment. Sex Med Rev 2013;1:123-134.

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Status
PubMed-not-MEDLINE

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Year of Publication
Selenium (Se) is an essential element involved in normal gonadal development, gametogenesis, and fertilization. Molecular studies show that the gonads actively take up and store Se, most of which is incorporated in the glutathione peroxidase enzymes. We provide a systematic review of the original molecular studies, prospective observational data and randomized controlled trials on the role of Se in reproductive function conducted in the past 30 years. A critical appraisal of these findings suggests that Se supplementation produces a bell-shaped response curve, with negative effects observed for both low and high concentrations. The few available clinical trials support the use of Se supplementation (<200 mug/d) to improve male infertility, although their pre-treatment assessment of Se levels in enrolled subjects is inconsistent and their quality and size are insufficient to enable general recommendations. In females, a putative role in oocyte maturation and fertilization is suggested, but no large controlled trials have yet been performed. The role of Se supplementation on pregnancy outcomes is promising, and ongoing studies and meta-analysis should soon enable proper recommendations to be suggested. How best to assess Se in terms of cut-off value, sample type (serum, semen, other fluids) and the specific outcome of interest remains to be clarified. In the meantime, assessment of serum Se levels followed by low-dose replacement therapy when necessary is a reasonable approach to improve male idiopathic infertility and gestational outcome. Copyright © 2013, Editrice Kurtis.
Comparison of different starting gonadotropin doses (50, 75 and 100 IU daily) for ovulation induction combined with intrauterine insemination.

Streda R., Mardesic T., Sobotka V., Koryntova D., Hybnerova L., Jindra M.

Embase

[Article]
AN: 52070126

Purpose To prevent multiple pregnancies the goal of ovulation induction by gonadotropins is to achieve only mono-follicular development. The most important issue is therefore to determine the starting dose. The aim of this study is to compare three different starting doses of follitropin beta to assess the lowest effective dose. Methods We evaluated 92 cycles with ovarian stimulation for patients with unexplained infertility, anovulatory disorder or mild male factor. We prospectively divided patients into 50, 75 and 100 IU groups based on patients' response to clomiphene citrate treatment. Results We performed 87 intrauterine inseminations (95 % of cycles with ovulation induction). Five cycles were cancelled. We achieved 15 pregnancies; total pregnancy rate was 18 %. Pregnancy rate was 22, 10 and 28 % in 50, 75 and 100 IU follitropin beta groups. The average number of follicles was 2.0 +/- 0.8, 2.2 +/- 1.1 and 2.5 +/- 1.8 (ns), total dose of gonadotropins (IU) 483 +/- 192, 600 +/- 151 and 830 +/- 268 (p<0.001), respectively. We observed one case of twins in 75 and 100 IU treatment group, as well (25 % risk). Conclusions This study suggests that based on the dose which was chosen according to clomiphene citrate response, all treatment regimes were effective for ovulation induction. 50 IU of follitropin beta daily is the appropriate starting dose to support ovulation for clomiphene citratesensitive women. The disadvantage may be an increased risk of cycle cancellation due to low ovarian response. Daily doses 75 or 100 IU of rFSH increase total consumption of gonadotropins. Copyright © The Author(s) 2012.

PMID
Delayed Child-Bearing.


Objective: To provide an overview of delayed child-bearing and to describe the implications for women and health care providers. Options: Delayed child-bearing, which has increased greatly in recent decades, is associated with an increased risk of infertility, pregnancy complications, and adverse pregnancy outcome. This guideline provides information that will optimize the counselling and care of Canadian women with respect to their reproductive choices. Outcomes: Maternal age is the most important determinant of fertility, and obstetric and perinatal risks increase with maternal age. Many women are unaware of the success rates or limitations of assisted reproductive technology and of the increased medical risks of delayed child-bearing, including...
multiple births, preterm delivery, stillbirth, and Caesarean section. This guideline provides a framework to address these issues. Evidence: Studies published between 2000 and August 2010 were retrieved through searches of PubMed and the Cochrane Library using appropriate key words (delayed child-bearing, deferred pregnancy, maternal age, assisted reproductive technology, infertility, and multiple births) and MeSH terms (maternal age, reproductive behaviour, fertility). The Internet was also searched using similar key words, and national and international medical specialty societies were searched for clinical practice guidelines and position statements. Data were extracted based on the aims, sample, authors, year, and results. Values: The quality of evidence was rated using the criteria described in the Report of the Canadian Task Force on Preventive Health Care (Table 1). Sponsor: The Society of Obstetricians and Gynaecologists of Canada. Recommendations 1. Women who delay child-bearing are at increased risk of infertility. Prospective parents, especially women, should know that their fecundity and fertility begin to decline significantly after 32 years of age. Prospective parents should know that assisted reproductive technologies cannot guarantee a live birth or completely compensate for age-related decline in fertility. (II-2A) 2. A fertility evaluation should be initiated after 6 months of unprotected intercourse without conception in women 35 to 37 years of age, and earlier in women > 37 years of age. (II-2A) 3. Prospective parents should be informed that semen quality and male fertility deteriorate with advancing age and that the risk of genetic disorders in offspring increases. (II-2A). 4. Women = 35 years of age should be offered screening for fetal aneuploidy and undergo a detailed second trimester ultrasound examination to look for significant fetal birth defects (particularly cardiac defects). (II-1A) 5. Delayed child-bearing is associated with increased obstetrical and perinatal complications. Care providers need to be aware of these complications and adjust obstetrical management protocols to ensure optimal maternal and perinatal outcomes. (II-2A) 6. All adults of reproductive age should be aware of the obstetrical and perinatal risks of advanced maternal age so they can make informed decisions about the timing of child-bearing. (II-2A) 7. Strategies to improve informed decision-making by prospective parents should be designed, implemented, and evaluated. These strategies should provide opportunity for adults to understand the potential medical, social, and economic consequences of childbearing throughout the reproductive years. (III-B) 8. Barriers to healthy reproduction, including workplace policies, should be reviewed to optimize the likelihood of healthy pregnancies. (III-C)  Copyright © 2012 Society of Obstetricians and Gynaecologists of Canada.

PMID
Status  
EMBASE  
Institution
Familial Mediterranean fever (FMF) is a hereditary disorder characterised by recurrent attacks of fever with peritonitis or pleuritis, arthritis, myalgia or erysipelas-like skin lesions. The continuous inflammation in FMF is associated with increased serum amyloid A (SAA) protein which may lead to secondary amyloidosis and deposition of this insoluble protein in the kidney, gut, spleen, liver, heart etc. Therefore, treatment of patients with FMF is beneficial not only for the prevention of the acute attacks but also for improving their prognosis. In the present review we summarise the medical literature concerning FMF treatment, including new therapeutic agents and management of colchicine-resistant patients. Three electronic databases (MEDLINE, EMBASE, and the Cochrane Library) were searched from 1 January 1960 to 28 February 2010 for any therapeutic approach to FMF, with MeSH headings and text words (Familial Mediterranean Fever, FMF treatment, colchicine, infliximab, anakinra, SSRI). In conclusion, colchicine remains the mainstay therapeutic option in FMF. It is effective in various manifestations of the disease such as fever, peritonitis and pleuritis. It prevents the development of amyloidosis. It is safe in humans regarding
fertility, and can be used during pregnancy and nursing. Dose adjustment should be made in patients with renal or hepatic failure. It is less effective in arthritis or myalgia, requiring additional treatment with NSAIDs and steroids. In the few cases where FMF is resistant to colchicine other measures, including corticosteroids, non-biological and biological DMARDs, interferon alpha and SSRIs should be employed. Copyright © Clinical And Experimental Rheumatology 2011.

Advanced Reproductive Age and Fertility.

Embase
Objective: To improve awareness of the natural age-related decline in female and male fertility with respect to natural fertility and assisted reproductive technologies (ART) and provide recommendations for their management, and to review investigations in the assessment of ovarian aging. Options: This guideline reviews options for the assessment of ovarian reserve and fertility treatments using ART with women of advanced reproductive age presenting with infertility. Outcomes: The outcomes measured are the predictive value of ovarian reserve testing and pregnancy rates with natural and assisted fertility. Evidence: Published literature was retrieved through searches of PubMed or Medline, CINAHL, and The Cochrane Library in June 2010, using appropriate key words (ovarian aging, ovarian reserve, advanced maternal age, advanced paternal age, ART). Results were restricted to systematic reviews, randomized controlled trials/controlled clinical trials, and observational studies. There were no date or language restrictions. Searches were updated on a regular basis and incorporated into the guideline to December 2010. Values: The quality of evidence was rated using the criteria described in the Report of the Canadian Task Force on Preventive Health Care. Recommendations for practice were ranked according to the method described in that report (Table). Benefits, harms, and costs: Primary and specialist health care providers and women will be better informed about ovarian aging and the age-related decline in natural fertility and about options for assisted reproductive technology. Recommendations: 1. Women in their 20s and 30s should be counselled about the agerelated risk of infertility when other reproductive health issues, such as sexual health or contraception, are addressed as part of their primary well-woman care. Reproductive-age women should be aware that natural fertility and assisted reproductive technology success (except with egg donation) is significantly lower for women in their late 30s and 40s. (II-2A) 2. Because of the decline in fertility and the increased time to conception that occurs after the age of 35, women>35 years of age should be referred for infertility work-up after 6 months of trying to conceive. (III-B) 3. Ovarian reserve testing may be considered for women>35 years of age or for women<35 years of age with risk factors for decreased ovarian reserve, such as a single ovary, previous ovarian surgery, poor response to follicle-stimulating hormone, previous exposure to chemotherapy or radiation, or unexplained infertility. (III-B) 4. Ovarian reserve testing prior to assisted reproductive technology treatment may be used for counselling but has a poor predictive value for non-pregnancy and should be used to exclude women from treatment only if levels are significantly abnormal. (II-2A) 5. Pregnancy rates for controlled ovarian hyperstimulation are low for women>40 years of age. Women>40 years should consider IVF if they do not conceive within 1 to 2 cycles of controlled ovarian hyperstimulation. (II-2B) 6. The only effective treatment for ovarian aging is oocyte donation. A woman with decreased ovarian reserve should be offered oocyte donation as an option, as pregnancy rates associated with this treatment are significantly higher.
than those associated with controlled ovarian hyperstimulation or in vitro fertilization with a woman's own eggs. (II-2B)

Women should be informed that the risk of spontaneous pregnancy loss and chromosomal abnormalities increases with age. Women should be counselled about and offered appropriate prenatal screening once pregnancy is established. (II-2A)

Pre-conception counselling regarding the risks of pregnancy with advanced maternal age, promotion of optimal health and weight, and screening for concurrent medical conditions such as hypertension and diabetes should be considered for women>age 40. (III-B)

Advanced paternal age appears to be associated with an increased risk of spontaneous abortion and increased frequency of some autosomal dominant conditions, autism spectrum disorders, and schizophrenia. Men>age 40 and their partners should be counselled about these potential risks when they are seeking pregnancy, although the risks remain small. (II-2C)

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The use of methotrexate in children with rheumatic diseases.
Gutierrez-Suarez R., Burgos-Vargas R.

Embase
[Article]
AN: 615860931

Methotrexate (MTX) is one of the most useful drugs for the treatment of various rheumatic diseases in children, mainly juvenile idiopathic arthritis (JIA), juvenile dermatomyositis (JDM), and localised scleroderma. MTX is considered the standard treatment of JIA, particularly of those subgroups with polyarticular course. JIA response and remission rates to MTX are the standard for comparison with other drug modifying anti-rheumatic drug (DMARD) and biologic agents in clinical trials. On the other hand, short and long-term data suggest that MTX is a safety drug in the paediatric population with rheumatic diseases. Not surprisingly, MTX is the DMARD of choice in JIA either as monotherapeutic drug or in combination with biologic agents.

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Status
EMBASE

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2010

Varicocele. [Review]
Biyani CS; Cartledge J; Janetschek G.
INTRODUCTION: Varicocele is estimated to affect 10-15% of men and adolescent boys. It usually occurs only on the left side, and is often asymptomatic. There is little evidence that varicocele reduces male fertility, although it is found in 12% of male partners of couples presenting with infertility, and in 25% of men with abnormal semen analysis.

METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical question: What are the effects of treatments in men with varicocele? We searched: Medline, Embase, The Cochrane Library, and other important databases up to May 2008 (Clinical Evidence reviews are updated periodically, please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA).

RESULTS: We found 11 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions.

CONCLUSIONS: In this systematic review we present information relating to the effectiveness and safety of the following interventions: embolisation, expectant management, sclerotherapy, and surgical ligation.

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PMID
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2907779
Effects of aromatase inhibition in hypogonadal older men: a randomized, double-blind, placebo-controlled trial.
Burnett-Bowie SA; Roupenian KC; Dere ME; Lee H; Leder BZ.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
[Journal Article. Randomized Controlled Trial. Research Support, N.I.H., Extramural. Research Support, Non-U.S. Gov't]
UI: 18616708
OBJECTIVE: To assess the effects of sustained aromatase inhibition in older hypogonadal men.
DESIGN AND PATIENTS: In a 1-year randomized, double-blind, placebo-controlled trial, 88 men, aged 60 and older with testosterone levels between 5.2 and 10.4 nmol/L on a single measure or between 10.4 and 12.1 nmol/L on two consecutive measures, and symptoms of hypogonadism were recruited. Subjects received either anastrozole 1 mg daily or placebo.
MEASUREMENTS: Changes in gonadal steroid hormone levels, body composition (by computerized tomography (CT) and dual x-ray absorptiometry (DXA)), strength, prostate specific antigen (PSA), symptoms of benign prostatic hypertrophy (BPH), hematocrit and lipid levels were assessed.
RESULTS: Testosterone levels increased from 11.2 +/- 3.3 nmol/L at baseline to 18.2 +/- 4.8 nmol/L at month 3 (p < 0.0001 vs. placebo) while bioavailable testosterone levels increased from 2.7 +/- 0.8 nmol/L at baseline to 5.4 +/- 1.7 nmol/L at month 3 (p < 0.0001 vs. placebo). Testosterone and biotestosterone levels peaked at month 3 and then declined by month 12 (though they remained significantly higher than baseline and greater than placebo). Estradiol levels decreased from 55.8 +/- 15.4 pmol/L at baseline to 42.2 +/- 13.6 pmol/L at month 3 and then remained stable (p < 0.0001). Body composition and strength did not change, nor did PSA, BPH symptoms, hematocrit or lipid levels.
CONCLUSIONS: Anastrozole administration normalized androgen production in older hypogonadal men and decreased estradiol production modestly. These alterations did not improve body composition or strength.
Status
MEDLINE
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Burnett-Bowie, Sherri-Ann M; Roupenian, Kristen C; Dere, Melissa E; Lee, Hang; Leder, Benjamin Z.
Institution
Gonadotrophins for idiopathic male factor subfertility.
Attia A.M., Al-Inany H.G., Farquhar C., Proctor M.
Embase
[Article]
AN: 612761548
BACKGROUND: Male factor infertility accounts for 50% of all infertility. The treatment of idiopathic male infertility is empirical. Urinary, purified, and recombinant gonadotrophins have been used to improve sperm parameters in idiopathic male infertility with the goal of increasing pregnancy rates. Research addressing pregnancy rates in partners of men treated with gonadotrophins has had conflicting results and needs to be analysed. OBJECTIVES: To determine the effectiveness of gonadotrophin administration in men with idiopathic subfertility in improving spontaneous pregnancy rate and in assisted reproductive technique cycles.
SEARCH STRATEGY: We searched the Cochrane Menstrual Disorders and Subfertility Group trials register (31 May 2007), the Cochrane Central Register of Controlled Trials (The Cochrane Library, issue 2, 2007), MEDLINE (1966 to May 2007), EMBASE and Biological Abstracts (1980 to Week 21 2007). Searches were not limited by language. The bibliographies of included, excluded trials and abstracts of major meetings were searched for additional trials. Authors and pharmaceutical companies were contacted for missing and unpublished data.
SELECTION CRITERIA: Truly randomised controlled trials where gonadotrophins were administered for the treatment of idiopathic male subfertility with reporting of pregnancy rates were included in the review.
DATA COLLECTION AND ANALYSIS: Two reviewers independently assessed trial quality and extracted data. Study authors were contacted for additional information. Adverse effects
information was collected from the trials. We analysed data regarding pregnancy occurring within three months after gonadotrophin therapy.

MAIN RESULTS: Four RCTs with 278 participants were included in the analysis. None of the studies had an adequate sample size and they had variable follow-up periods. None of the studies reported live birth or miscarriage rates. Compared to placebo or no treatment, gonadotrophins showed a significantly higher pregnancy rate per couple randomized within three months of completing therapy (OR 4.17, 95% CI 1.30 to 7.09).

AUTHORS' CONCLUSIONS: The number of trials and participants is insufficient to draw final conclusions. A large multicenter study with adequate power is needed.


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765.
Intra-uterine insemination for male subfertility.
Bensdorp A.J., Cohlen B.J., Heineman M.J., Vandekerckhove P.

Embase

[Article]
AN: 612761528

BACKGROUND: Intra-uterine insemination (IUI) is one of the most frequently used fertility treatments for couples with male subfertility. Its use, especially when combined with ovarian hyperstimulation (OH) has been subject of discussion. Although the treatment itself is less invasive and expensive than others, its efficacy has not been proven. Furthermore, the adverse effects of OH such as ovarian hyperstimulation syndrome (OHSS ) and multiple pregnancy are a concern. OBJECTIVES: The aim of this review was to determine whether for couples with male
subfertility, IUI improves the live birth rates or ongoing pregnancy rates compared with timed intercourse (TI), with or without OH.

SEARCH STRATEGY: We searched the Cochrane Menstrual and Disorders Subfertility Group Trials Special Register, the Cochrane Central Register of Controlled Trials (the Cochrane Library, 2006, issue 3), MEDLINE (1966 to May 2006), EMBASE (1980 to May 2006), SCIsearch and the reference lists of articles. We hand searched abstracts of the American Society for Reproductive Medicine, the European Society for Human Reproduction and Embryology. Authors of identified articles were contacted for unpublished data.

SELECTION CRITERIA: Randomised controlled trials (RCT’s) with at least one of the following comparisons were included: 1) IUI versus TI or expectant management both in natural cycles 2) IUI versus TI both in cycles with OH 3) IUI in natural cycles versus TI + OH 4) IUI + OH versus TI in natural cycles 5) IUI in natural cycles versus IUI + OH. Couples with abnormal sperm parameters only were included.

DATA COLLECTION AND ANALYSIS: Two co-reviewers independently performed quality assessment and data extraction. Where possible data were pooled, and a meta-analysis was performed. Sensitivity and subgroup analyses were carried out where possible and appropriate.

MAIN RESULTS: Three trials of parallel design, and five trials of cross-over design with pre-cross-over data were included in the meta-analysis. Three compared IUI with TI both in stimulated cycles. The remaining four of these studies compared IUI versus IUI + OH. Three studies reported on our main outcome of interest live birth rate per couple. For the comparison IUI versus TI both in natural cycles no evidence of difference between the probabilities of pregnancy rates per woman after IUI compared with TI was found (Peto OR 5.3, 95% CI 0.42 to 67). No statistically significant of difference between pregnancy rates (PR) per couple for IUI + OH versus IUI could be found (Peto OR 1.47, 95% CI 0.92 to 2.37). For the comparison IUI versus TI both in stimulated cycles there was no evidence of statistically significant difference in pregnancy rates per couple either (Peto OR 1.67, 95% CI 0.83 to 3.37). There were insufficient data available for adverse outcomes such as OHSS, multiple pregnancy, miscarriage rate and ectopic pregnancy to perform a statistical analysis. For the other two comparisons no RCT’s were found which reported pregnancy rates per couple. A further 10 studies which included one of the comparisons of interests were found. Since these studies reported pregnancy rates per cycle only these data could not be included in the meta-analysis.

AUTHORS’ CONCLUSIONS: There was insufficient evidence of effectiveness to recommend or advise against IUI with or without OH above TI, or vice versa. Large, high quality randomised controlled trials, comparing IUI with or without OH with pregnancy rate per couple as the main outcome of interest are lacking. There is a need for such trials since firm conclusions cannot be drawn yet.

PMID
Combination therapy with venlafaxine and carbamazepine in depressive patients not responding to venlafaxine: Pharmacokinetic and clinical aspects.

Ciusani E., Zullino D.F., Eap C.B., Brawand-Amey M., Brocard M., Baumann P.

Embase


[Article]

AN: 610946515

The chiral antidepressant venlafaxine (VEN) is both a serotonin and a norepinephrine uptake inhibitor. CYP2D6 and CYP3A4 contribute to its metabolism, which has been shown to be stereoselective. Ten CYP2D6 genotyped and depressive (F32x and F33x, ICD-10) patients participated in an open study on the pharmacokinetic and pharmacodynamic consequences of a carbamazepine augmentation in VEN non-responders. After an initial 4-week treatment with VEN (195 +/- 52 mg/day), the only poor metabolizer out of 10 depressive patients had the highest plasma concentrations of S-VEN and R-VEN, respectively, whereas those of R-O-demethyl-VEN were lowest. Five non-responders completed the second 4-week study period, during which they were submitted to a combined VEN-carbamazepine treatment. In the only non-responder to this combined treatment, there was a dramatic decrease of both enantiomers of VEN, O-demethylvenlafaxine, N-desmethylenlafaxine and N,O-didesmethylenlafaxine in plasma, which suggests non-compliance, although metabolic induction by carbamazepine cannot entirely be excluded. The administration of carbamazepine [mean +/- SD, range: 360 +/- 89 (200-400) mg/day] over 4 weeks did not result in a significant modification of the plasma concentrations of the enantiomers of VEN and its O- and N-demethylated metabolites in the other patients. In
conclusion, these preliminary observations suggest that the combination of VEN and carbamazepine represents an interesting augmentation strategy by its efficacy, tolerance and absence of pharmacokinetic modifications. However, these findings should be verified in a more comprehensive study. Copyright © British Association for Psychopharmacology.

PMID

Status
EMBASE

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767.
The Resurgence of Chlamydia trachomatis.

Steben M.

Embase


[Article]

AN: 610557082

The objective of the review is to alert reproductive-care providers to the unexpected resurgence of Chlamydia infections and to new findings related to complications associated with Chlamydia infection. Data sources consisted of national and local guidelines and literature searches of MEDLINE with the heading Chlamydia infections 2002 and 2003. The complications of Chlamydia infections are considered to be longterm, and may include debilitating pain, infertility, tubal pregnancy, cancer, and HIV infection. Only a strong disease-management response from
reproductive-care providers, using new diagnostic techniques and simpler treatment regimens, as well as a strong public health reaction, will be effective to limit the scourges of Chlamydia infection in the female population. Copyright © 2004.

PMID

Status
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768.
Alfuzosin: a clinically uroselective alpha1-blocker.
Hofner K; Jonas U.
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

[Journal Article]
UI: 28386660

A once-daily (o.d.) formulation of alfuzosin has recently been developed in order to improve the convenience of dosing and to provide optimal pharmacokinetic coverage over a 24-h period. The results of two double-blind, placebo-controlled phase III studies of similar design that included 983 patients with LUTS that suggested BPH have confirmed that alfuzosin 10 mg o.d. is a 24-h effective treatment for both symptoms and flow rates, and that there is no additional benefit in using a higher dosage. In addition, alfuzosin is the only alpha1-blocker that has demonstrated a significant decrease in post-void residual urine, a known risk factor for acute urinary retention, as
well as the incidence of acute urinary retention in comparison with a placebo. Administered without an initial dose titration, alfuzosin 10 mg o.d. is well tolerated, with a low incidence of postural hypotension (<1%) and no significant changes in blood pressure compared with a placebo, even in elderly and hypertensive patients. Ejaculation disorders were rarely reported and did not show an evident causal relationship to treatment. Alfuzosin 10 mg o.d. also exhibits an excellent sexual side-effect profile, with no deleterious impact on this important aspect of quality of life for BPH patients.


Male erectile dysfunction is common and frustrating after the age of forty years. Erectile dysfunction is a cause of misery, relationship difficulties, and significantly reduced quality of life. Sildenafil citrate (Viagra) has shown promising results in recently published clinical trials. Sildenafil is a potent and competitive inhibitor of cGMP specific phosphodiesterase-5, predominant isoenzyme in the human corpus cavernosum. It is effective in erectile dysfunction of
diverse origin, however it requires a patent vascular system to be effective. It is not effective in patients with endocrinal impotence, loss of libido, premature ejaculation or infertility. Its main adverse effects are headache, flushing, dyspepsia, diarrhoea, nasal congestion, indigestion, visual disturbances, dizziness and rash. Ventricular tachycardia and acute myocardial infraction have been reported in patients of ischaemic heart disease after consumption of sildenafil. Six deaths have been reported in patients taking nitrates. In India it is likely to be prescribed by a primary care physician without complete evaluation of patient on complaint of impotence. Hence the ethical question of who should prescribe this drug should be addressed by medical fraternity and proper guidelines formulated to avoid misuse of sildenafil. Phosphodiesterase is distributed in nerve, central nervous system, and systemic vasculature, hence long-term effects of drug on these tissues has to be ascertained. It should be made mandatory to report all adverse drug reactions to ADR monitoring centres. It is a wonder for those who require it, but has potentially dangerous adverse effects and drug interactions and hence is and not a wonder pill for all kinds of impotence.

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770.
Fertilization rate and preimplantation development after intracytoplasmic sperm injection.
Schroder A.K., Diedrich K., Ludwig M.

Embase
Intracytoplasmic sperm injection (ICSI) is the treatment of choice in cases of male factor infertility. In the present review, all data from the literature regarding early fertilization and preimplantation embryo development are analysed. ICSI seems to offer better fertilization rates than conventional IVF, even in the absence of a male factor and in prospective, randomized studies on sibling oocytes. Blastocyst formation is lower in ICSI than in IVF. This may be due to sublethal disturbances in oocyte architecture and function. Implantation and pregnancy rates, however, are similar in ICSI and conventional IVF. Therefore, it can be concluded that ICSI offers a safe approach, as far as is known to date, for the treatment of male factor infertility. Embryo selection in cases of sublethal damage to oocytes seems to take place in the early preimplantation stages. Nor does the risk of monozygotic twinning, which was also proposed to be higher in ICSI compared with conventional IVF, seem to increase with this procedure. Copyright © 2001 Reproductive Healthcare Ltd, Duck End Farm, Dry Drayton, Cambridge CB23 8DB, UK

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771.
Progestogen-androgen combination: Results of Indonesian clinical trials.
Arsyad K.M.
Embase
[Article]
AN: 614019978
This article summarizes the results of two recent WHO supported clinical studies in Indonesia to assess the potential of progestogen-androgen combinations as a male method of fertility regulation and identifies some areas for future research and development. The first study was carried out with a combination of DMPA plus TE given by intramuscular injection at monthly intervals and at two dose levels: 100 mg DMPA plus 100 mg TE; 200 mg DMPA plus 250 mg TE. The second study is a multicentre study which is earned out in Indonesia, in which male volunteers received either a combination of DMPA and TE or a combination of DMPA plus 19-NT. In both cases, 250 mg DMPA was injected IM at week 0, 6, 12, and 18, and 200 mg TE or 200 mg 19-NT was given weekly for the first seven weekls and then at 3-weekly intervals until week 24. The encouraging results obtained in these two studies offer a good prospect for developing a safe and effective hormonal contraceptive methods suitable for use by Indonesian men. However, the frequency of injection and the high levels of hormones that needed to be injected would make the development of such a method difficult with the currently available compounds. Copyright © 1997, Faculty of Medicine, Universitas Indonesia. All rights reserved.

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772.
Polyester sling scrotal cover induces oligozoospermia in normal indonesian men.
Moeloek N.
Embase
[Article]
The objective of this study is to ascertain the effects of polyester sling scrotal cover on sperm production in healthy Indonesian men. This prospective study consisted of 2 phases, i.e., a control phase and treatment phase trial. Ten normal healthy volunteers used polyester sling scrotal cover all day and night for 24 weeks. Semen was analyzed at a 3-week interval, and clinical chemistry and hematology were monitored at a 12-week interval. The results showed that within 24 weeks sperm concentration, percentage of normal sperm morphology, and sperm velocity decreased to below normal range in all subjects. We concluded that polyester sling scrotal cover can suppress sperm production to oligospermia in Indonesian men. Not a single subject achieved azoospermia, as compared with in Egypt study that showed 100% azoospermia in 14 men. Copyright © 1995 Faculty of Medicine, Universitas Indonesia. All rights reserved.

773.
Interventions for preventing silent cerebral infarcts in people with sickle cell disease
Institution Lise J Estcourt.
TI Interventions for preventing silent cerebral infarcts in people with sickle cell disease.
EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 5, 2017.
[Systematic Review]
AN: 00075320-100000000-10783
Background
Sickle cell disease (SCD) is one of the commonest severe monogenic disorders in the world, due to the inheritance of two abnormal haemoglobin (beta globin) genes. SCD can cause severe pain, significant end-organ damage, pulmonary complications, and premature death. Silent cerebral infarcts are the commonest neurological complication in children and probably adults with SCD. Silent cerebral infarcts also affect academic performance, increase cognitive deficits and may lower intelligence quotient.

Objectives
To assess the effectiveness of interventions to reduce or prevent silent cerebral infarcts in people with SCD.

Search methods
We searched for relevant trials in the Cochrane Library, MEDLINE (from 1946), Embase (from 1974), the Transfusion Evidence Library (from 1980), and ongoing trial databases; all searches current to 19 September 2016. We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group Trials Register: 06 October 2016.

Selection criteria
Randomised controlled trials comparing interventions to prevent silent cerebral infarcts in people with SCD. There were no restrictions by outcomes examined, language or publication status.

Data collection and analysis
We used standard Cochrane methodological procedures.

Main results
We included five trials (660 children or adolescents) published between 1998 and 2016. Four of the five trials were terminated early. The vast majority of participants had the haemoglobin (Hb)SS form of SCD. One trial focused on preventing silent cerebral infarcts or stroke; three trials were for primary stroke prevention and one trial dealt with secondary stroke prevention.

Authors’ conclusions
We identified no trials for preventing silent cerebral infarcts in adults, or in children who do not have HbSS SCD.
Background
Surgery remains an acceptable treatment modality for tubal infertility despite the rise in usage of in vitro fertilisation (IVF). Estimated livebirth rates after surgery range from 9% for women with severe tubal disease to 69% for those with mild disease; however, the effectiveness of surgery has not been rigorously evaluated in comparison with other treatments such as IVF and expectant management (no treatment). Livebirth rates have not been adequately assessed in relation to the severity of tubal damage. It is important to determine the effectiveness of surgery against other treatment options in women with tubal infertility because of concerns about adverse outcomes, intraoperative complications and costs associated with tubal surgery, as well as alternative treatments, mainly IVF.

Objectives
The aim of this review was to determine the effectiveness and safety of surgery compared with expectant management or IVF in improving the probability of livebirth in the context of tubal infertility (regardless of grade of severity).

Search methods
We searched the following databases in October 2016: the Cochrane Gynaecology and Fertility (CGF) Group trials register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, the Cumulative Index to Nursing and Allied Health Literature (CINAHL) and PsycINFO; as well as clinical trials registries, sources of unpublished literature and reference lists of included trials and related systematic reviews.

Selection criteria
We considered only randomised controlled trials to be eligible for inclusion, with livebirth rate per participant as the primary outcome of interest.

Data collection and analysis
We planned that two review authors would independently assess trial eligibility and risk of bias and would extract study data. The primary review outcome was cumulative livebirth rate. Pregnancy rate and adverse outcomes, including miscarriage rate, rate of ectopic pregnancy and rate of procedure-related complications, were secondary outcomes. We planned to combine data to calculate pooled odds ratios (ORs) and 95% confidence intervals (CIs). We planned to assess statistical heterogeneity using the I² statistic and to assess the overall quality of evidence for the main comparisons using GRADE methods.

Main results
We identified no suitable randomised controlled trials.

Authors’ conclusions
The effectiveness of tubal surgery relative to expectant management and IVF in terms of livebirth rates for women with tubal infertility remains unknown. Large trials with adequate power are warranted to establish the effectiveness of surgery in these women. Future trials should not only report livebirth rates per patient but should compare adverse effects and costs of treatment over a longer time. Factors that have a major effect on these outcomes, such as fertility treatment, female partner's age, duration of infertility and previous pregnancy history, should be considered. Researchers should report livebirth rates in relation to severity of tubal damage and different techniques used for tubal repair, including microsurgery and laparoscopic methods.

775.
Pharmacological and non-pharmacological strategies for obese women with subfertility
EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 4, 2017.
[Protocol]
AN: 00075320-100000000-11056
This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:
To assess the effectiveness and safety of pharmacological and non-pharmacological strategies compared with each other, placebo or no treatment, for obese women with subfertility.

776.
Interim PET for prognosis in adults with Hodgkin lymphoma: a prognostic factor exemplar review
EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 4, 2017.
Primary objective

The objective of this systematic review is to identify all studies evaluating interim PET scan results as a prognostic factor, describe the characteristics and risk of bias of included studies and if possible, meta-analyse results on the association between PET scan results and overall or progression-free survival and adverse events.

Chemotherapy alone versus chemotherapy plus radiotherapy for adults with early stage Hodgkin lymphoma
EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 4, 2017.
[Systematic Review]
AN: 00075320-100000000-05715

Background

Combined modality treatment consisting of chemotherapy followed by localised radiotherapy is the standard treatment for patients with early stage Hodgkin lymphoma (HL). However, due to long-term adverse effects such as secondary malignancies the role of radiotherapy has been questioned recently and some clinical study groups advocate chemotherapy only for this indication.

Objectives

To assess the effects of chemotherapy alone compared to chemotherapy plus radiotherapy in adults with early stage HL.

Search methods

For the original version of this review, we searched MEDLINE, Embase and CENTRAL as well as conference proceedings (American Society of Hematology, American Society of Clinical Oncology and International Symposium of Hodgkin Lymphoma) from January 1980 to November 2010 for randomised controlled trials (RCTs) comparing chemotherapy alone versus
chemotherapy regimens plus radiotherapy. For the updated review we searched MEDLINE, CENTRAL and conference proceedings to December 2016.

Selection criteria
We included RCTs comparing chemotherapy alone with chemotherapy plus radiotherapy in patients with early stage HL. We excluded trials with more than 20% of patients in advanced stage. As the value of radiotherapy in addition to chemotherapy is still not clear, we also compared to more cycles of chemotherapy in the control arm. In this updated review, we also included a second comparison evaluating trials with varying numbers of cycles of chemotherapy between intervention and control arms, same chemotherapy regimen in both arms assumed. We excluded trials evaluating children only, therefore only trials involving adults are included in this updated review.

Data collection and analysis
Two review authors independently extracted data and assessed the quality of trials. We contacted study authors to obtain missing information. As effect measures we used hazard ratios (HR) for overall survival (OS) and progression-free survival (PFS) and risk ratios (RR) for response rates. Since not all trials reported PFS according to our definitions, we evaluated all similar outcomes (e.g. event-free survival) as PFS/tumour control.

Main results
Our search led to 5518 potentially relevant references. From these, we included seven RCTs in the analyses involving 2564 patients. In contrast to the first version of this review including five trials, we excluded trials randomising children. As a result, we excluded one trial from the former analyses and we identified three new trials.

Authors' conclusions
This systematic review compared the effects of chemotherapy alone and chemotherapy plus radiotherapy in adults with early stage HL.

Ataluren and similar compounds (specific therapies for premature termination codon class I mutations) for cystic fibrosis
Aslam, Aisha A. Higgins, Colin. Sinha, Ian P. Southern, Kevin W.Institution Kevin W Southern .TI Ataluren and similar compounds (specific therapies for premature termination codon class I mutations) for cystic fibrosis.
EBM Reviews - Cochrane Database of Systematic Reviews
Background
Cystic fibrosis is a common life-shortening genetic disorder in the Caucasian population (less common in other ethnic groups) caused by the mutation of a single gene that codes for the production of the cystic fibrosis transmembrane conductance regulator protein. This protein coordinates the transport of salt (and bicarbonate) across cell surfaces and the mutation most notably affects the airways. In the lungs of people with cystic fibrosis, defective protein results in a dehydrated surface liquid and compromised mucociliary clearance. The resulting thick mucus makes the airway prone to chronic infection and inflammation, which consequently damages the structure of the airways, eventually leading to respiratory failure. Additionally, abnormalities in the cystic fibrosis transmembrane conductance regulator protein lead to other systemic complications including malnutrition, diabetes and subfertility.

Objectives
To evaluate the benefits and harms of ataluren and similar compounds on clinically important outcomes in people with cystic fibrosis with class I mutations (premature termination codons).

Search methods
We searched the Cochrane Cystic Fibrosis Trials Register which is compiled from electronic database searches and handsearching of journals and conference abstract books. We also searched the reference lists of relevant articles. Last search of Group's register: 24 October 2016.

Selection criteria
Randomised controlled trials of parallel design comparing ataluren and similar compounds (specific therapies for class I mutations) with placebo in people with cystic fibrosis who have at least one class I mutation. Cross-over trials were reviewed individually to evaluate whether data from the first treatment arm could be included. We excluded trials that combined therapies for premature termination codon class I mutations with other mutation-specific therapies.

Data collection and analysis
The authors independently assessed the risk of bias and extracted data from the included trial; they contacted trial authors for additional data.

Main results
Our searches identified 28 references to eight trials; five trials were excluded (three were cross-over and one was not randomised and one did not have relevant outcomes), one cross-over trial is awaiting classification pending provision of data and one trial is ongoing. The included parallel randomised controlled trial compared ataluren to placebo for a duration of 48 weeks in 238 participants (age range 6 to 53 years) with cystic fibrosis who had at least one nonsense mutation (a type of class I mutation).
Authors’ conclusions

There is currently insufficient evidence to determine the effect of ataluren as a therapy for people with cystic fibrosis with class I mutations. Future trials should carefully assess for adverse events, notably renal impairment and consider the possibility of drug interactions. Cross-over trials should be avoided given the potential for the treatment to change the natural history of cystic fibrosis.

779.
Hydroxyurea (hydroxycarbamide) for sickle cell disease
Nevitt, Sarah J.  Jones, Ashley P.  Howard, Jo.Institution Sarah J Nevitt .TI Hydroxyurea (hydroxycarbamide) for sickle cell disease.
EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 4, 2017.
[Systematic Review]
AN: 00075320-100000000-01685

Background
Sickle cell disease (SCD) is one of the most common inherited diseases worldwide. It is associated with lifelong morbidity and a reduced life expectancy. Hydroxyurea (hydroxycarbamide), an oral chemotherapeutic drug, ameliorates some of the clinical problems of SCD, in particular that of pain, by raising fetal haemoglobin. This is an update of a previously published Cochrane Review.

Objectives
To assess the effects of hydroxyurea therapy in people with SCD (all genotypes), of any age, regardless of setting.

Search methods
We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group Haemoglobinopathies Register, comprising of references identified from comprehensive electronic database searches and handsearches of relevant journals and abstract books of conference proceedings. We also searched online trial registries.

Selection criteria
Randomised and quasi-randomised controlled trials, of one month or longer, comparing hydroxyurea with placebo, standard therapy or other interventions for people with SCD.

Data collection and analysis
Authors independently assessed studies for inclusion, carried out data extraction and assessed the risk of bias.

Main results
Seventeen studies were identified in the searches; eight randomised controlled trials were included, recruiting 899 adults and children with SCD (haemoglobin SS (HbSS), haemoglobin SC (HbSC) or haemoglobin S beta thalassaemia (HbS beta thal) genotypes). Studies lasted from six to 30 months.

Authors’ conclusions
There is evidence to suggest that hydroxyurea is effective in decreasing the frequency of pain episodes and other acute complications in adults and children with sickle cell anaemia of HbSS or HbS beta thal genotypes and in preventing life-threatening neurological events in those with sickle cell anaemia at risk of primary stroke by maintaining transcranial doppler velocities. However, there is still insufficient evidence on the long-term benefits of hydroxyurea, particularly in preventing chronic complications of SCD, recommending a standard dose or dose escalation to maximum tolerated dose. There is also insufficient evidence about the long-term risks of hydroxyurea, including its effects on fertility and reproduction. Evidence is also limited on the effects of hydroxyurea on individuals with HbSC genotype. Future studies should be designed to address such uncertainties.

780.
Chlorpromazine dose for people with schizophrenia
EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 4, 2017.
[Systematic Review]
AN: 00075320-100000000-06382

Background
The World Health Organization (WHO) Model Lists of Essential Medicines lists chlorpromazine as one of its five medicines used in psychotic disorders.

Objectives
To determine chlorpromazine dose response and dose side-effect relationships for schizophrenia and schizophrenia-like psychoses.
Search methods
We searched the Cochrane Schizophrenia Group's Study-Based Register of Trials (December 2008; 2 October 2014; 19 December 2016).

Selection criteria
All relevant randomised controlled trials (RCTs) comparing low doses of chlorpromazine (≤ 400 mg/day), medium dose (401 mg/day to 800 mg/day) or higher doses (> 800 mg/day) for people with schizophrenia, and which reported clinical outcomes.

Data collection and analysis
We included studies meeting review criteria and providing useable data. Review authors extracted data independently. For dichotomous data, we calculated fixed-effect risk ratios (RR) and their 95% confidence intervals (CIs). For continuous data, we calculated mean differences (MD) and their 95% CIs based on a fixed-effect model. We assessed risk of bias for included studies and graded trial quality using GRADE (Grading of Recommendations Assessment, Development and Evaluation).

Main results
As a result of searches undertaken in 2014, we found one new study and in 2016 more data for already included studies. Five relevant studies with 1132 participants (585 are relevant to this review) are now included. All are hospital-based trials and, despite over 60 years of chlorpromazine use, have durations of less than six months and all are at least at moderate risk of bias. We found only data on low-dose (≤ 400 mg/day) versus medium-dose chlorpromazine (401 mg/day to 800 mg/day) and low-dose versus high-dose chlorpromazine (> 800 mg/day).

Authors’ conclusions
The dosage of chlorpromazine has changed drastically over the past 50 years with lower doses now being the preferred of choice. However, this change was gradual and arose not due to trial-based evidence, but due to clinical experience and consensus. Chlorpromazine is one of the most widely used antipsychotic drugs yet appropriate use of lower levels has come about after many years of trial and error with much higher doses. In the absence of high-grade evaluative studies, clinicians have had no alternative but to learn from experience. However, such an approach can lack scientific rigor and does not allow for proper dissemination of information that would assist clinicians find the optimum treatment dosage for their patients. In the future, data for recently released medication should be available from high-quality trials and studies to provide optimum treatment to patients in the shortest amount of time.
Silodosin for the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia
EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 3, 2017.
[Protocol]
AN: 00075320-100000000-11022
This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:
To assess the effectiveness and adverse effects of silodosin compared to placebo or other medical treatments in men with LUTS suggestive of BPH.

Risk of endometrial cancer in women treated with ovary-stimulating drugs for subfertility
EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 3, 2017.
[Systematic Review]
AN: 00075320-100000000-09339
Background
Medical treatment for subfertility principally involves the use of ovary-stimulating agents, including selective oestrogen receptor modulators (SERMs), such as clomiphene citrate, gonadotropins, gonadotropin-releasing hormone (GnRH) agonists and antagonists, as well as human chorionic gonadotropin. Ovary-stimulating drugs may act directly or indirectly upon the endometrium (lining of the womb). Nulliparity and some causes of subfertility are recognized as risk factors for endometrial cancer.
Objectives
To evaluate the association between the use of ovary-stimulating drugs for the treatment of subfertility and the risk of endometrial cancer.

Search methods
A search was performed in CENTRAL, MEDLINE (Ovid) and Embase (Ovid) databases up to July 2016, using a predefined search algorithm. A search in OpenGrey, ProQuest, ClinicalTrials.gov, ZETOC and reports of major conferences was also performed. We did not impose language and publication status restrictions.

Selection criteria
Cohort and case-control studies reporting on the association between endometrial cancer and exposure to ovary-stimulating drugs for subfertility in adult women were deemed eligible.

Data collection and analysis
Study characteristics and findings were extracted by review authors independently working in pairs. Inconsistency between studies was quantified by estimating $I^2$. Random-effects (RE) models were used to calculate pooled effect estimates. Separate analyses were performed, comparing treated subfertile women versus general population and/or unexposed subfertile women, to address the superimposition of subfertility as an independent risk factor for endometrial cancer.

Main results
Nineteen studies were eligible for inclusion (1,937,880 participants). Overall, the quality of evidence was very low, due to serious risk of bias and indirectness (non-randomised studies (NRS), which was reflected on the GRADE assessment.

Authors’ conclusions
The synthesis of the currently available evidence does not allow us to draw robust conclusions, due to the very low quality of evidence. It seems that exposure to clomiphene citrate as an ovary-stimulating drug in subfertile women is associated with increased risk of endometrial cancer, especially at doses greater than 2000 mg and high (more than 7) number of cycles. This may largely be due to underlying risk factors in women who need treatment with clomiphene citrate, such as polycystic ovary syndrome, rather than exposure to the drug itself. The evidence regarding exposure to gonadotropins was inconclusive.

L-carnitine for cognitive enhancement in people without cognitive impairment
Chen, Ning. Yang, Mi. Zhou, Muke. Xiao, Jing. Guo, Jian. He, Li. Institution Li He.

L-carnitine for cognitive enhancement in people without cognitive impairment.

EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 3, 2017.
[Systematic Review]
AN: 00075320-100000000-07822

Background
Safe interventions to enhance cognitive function in cognitively healthy people would be very valuable for several reasons, including a better quality of life and professional success. While L-carnitine has been reported to enhance cognitive function in some conditions, its efficacy is disputed. The evidence of its efficacy for cognitively healthy people has not previously been systematically reviewed.

Objectives
To assess the efficacy and safety of L-carnitine for the enhancement of cognitive function in people without cognitive impairment.

Search methods
We searched ALOIS, the Cochrane Dementia and Cognitive Improvement Group's Specialized Register, on 4 November 2016. We used the search terms 'L-carnitine' or 'acetyl-L-carnitine' or 'propionyl-L-carnitine' or 'ALC' or 'PLC' or 'ALCAR' or 'ALPAR'. We ran additional separate searches in several other sources to ensure that we retrieved the most up-to-date results. We also reviewed the bibliographies of the randomised controlled trials identified and contacted the authors and known experts in the field and pharmaceutical companies to identify additional published or unpublished data.

Selection criteria
Eligible trials were randomised controlled trials (RCTs) or quasi-RCTs, parallel-group or cross-over, that compared L-carnitine or its derivatives, acetyl-L-carnitine or propionyl-L-carnitine, at any dose and for any length of treatment, with placebo or no treatment in cognitively healthy people of any age and either gender.

Data collection and analysis
We used standard methodological procedures expected by Cochrane. Two review authors independently selected trials and evaluated the methodological quality, then extracted and analysed data from the included trials.

Main results
Only two RCTs were eligible. One was a cross-over trial with 18 participants. The other randomised 400 participants to one of four treatments, of which two (L-carnitine and placebo) were relevant to this review, but the exact numbers of participants in these two treatment groups was not reported. All participants were young adults. Methodological details were poorly reported,
and we considered the risk of bias in both studies to be unclear. The trials assessed different cognitive outcomes. We could extract cognitive data on approximately 200 participants from one trial. We found no evidence that L-carnitine has any effect on reaction time, vigilance, immediate memory, or delayed recall after three days of treatment. This trial report stated that there was a small number of adverse effects, none of which were serious. The small cross-over trial also reported no effect of L-carnitine on cognition, but did not provide data; no information was provided on adverse effects. We considered the available evidence to be of very low quality for all reported outcomes.

Authors’ conclusions
Due to the limited number of included trials, short-term treatment, and inadequate reporting, we were unable to draw any conclusions about the efficacy or safety of L-carnitine for cognitive enhancement in healthy adults. Well-designed, randomised, placebo-controlled trials of L-carnitine for cognition enhancement in cognitively healthy people, with large samples and relatively long-term follow-up, are still needed.

784.
Controlled ovarian stimulation protocols for assisted reproduction: a network meta-analysis
EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 3, 2017.
[Protocol]
AN: 00075320-100000000-10992
This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:
We aim to assess the clinical effectiveness and safety profile of currently applied controlled ovarian stimulation (COS) protocols, and to generate a clinically-useful ranking of these protocols.
Clomiphene and other antioestrogens for ovulation induction in polycystic ovarian syndrome


EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 1, 2017.
[Systematic Review]
AN: 00075320-100000000-01646

Background
Subfertility due to anovulation is a common problem in women. First-line oral treatment is with antioestrogens such as clomiphene citrate, but resistance may be apparent with clomiphene. Alternative and adjunctive treatments have been used including tamoxifen, dexamethasone, and bromocriptine. The effectiveness of these is to be determined.

Objectives
To determine the relative effectiveness of antioestrogen agents including clomiphene alone or in combination with other medical therapies in women with subfertility associated with anovulation, possibly caused by polycystic ovarian syndrome.

Search methods
We conducted a search of the Cochrane Gynaecology and Fertility Group Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, PsycINFO, and CINAHL (all from inception to August 2016) to identify relevant randomised controlled trials (RCTs). We searched the United Kingdom National Institute for Clinical Excellence (NICE) guidelines and the references of relevant reviews and RCTs. We also searched the clinical trial registries for ongoing trials (inception until August 2016).

Selection criteria
We considered RCTs comparing oral antioestrogen agents for ovulation induction (alone or in conjunction with medical therapies) in anovulatory subfertility. We excluded insulin-sensitising agents, aromatase inhibitors, and hyperprolactinaemic infertility.

Data collection and analysis
Two review authors independently performed data extraction and quality assessment. The primary outcome was live birth; secondary outcomes were pregnancy, ovulation, miscarriage, multiple pregnancy, ovarian hyperstimulation syndrome, and adverse effects.

Main results
This is a substantive update of a previous review. We identified an additional 13 studies in the 2016 update. The review now includes 28 RCTs (3377 women) and five RCTs awaiting classification. Five of the 28 included trials reported live birth/ongoing pregnancy. Secondary outcomes were poorly reported.
Authors’ conclusions
We found evidence suggesting that clomiphene citrate improves the chance of a clinical pregnancy compared with placebo, but may reduce the chance of live birth or ongoing pregnancy when compared with a gonadotropin. Due to low event rates, we advise caution interpreting these data.

786.
Adjunctive steroid therapy versus antibiotics alone for acute endophthalmitis after intraocular procedure
Background
Endophthalmitis refers to severe infection within the eye that involves the aqueous humor or vitreous humor, or both, and threatens vision. Most cases of endophthalmitis are exogenous (i.e. due to inoculation of organisms from an outside source), and most exogenous endophthalmitis is acute and occurs after an intraocular procedure. The mainstay of treatment is emergent administration of broad-spectrum intravitreous antibiotics. Due to their anti-inflammatory effects, steroids in conjunction with antibiotics have been proposed to be beneficial in endophthalmitis management.
Objectives
To assess the effects of antibiotics combined with steroids versus antibiotics alone for the treatment of acute endophthalmitis following intraocular surgery or intravitreous injection.
Search methods
We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (which contains the Cochrane Eyes and Vision Trials Register) (2016, Issue 11), MEDLINE Ovid (1946 to 8 December 2016), Embase Ovid (1980 to 8 December 2016), LILACS (Latin American and Caribbean Health Sciences Literature Database) (1982 to 8 December 2016), the ISRCTN registry (); searched 8 December 2016, ClinicalTrials.gov (); searched 8 December 2016, and the
WHO International Clinical Trials Registry Platform (ICTRP) (); searched 8 December 2016. We did not use any date or language restrictions in the electronic searches for trials.

Selection criteria
We included randomized controlled trials comparing the effectiveness of adjunctive steroids with antibiotics alone in the management of acute, clinically diagnosed endophthalmitis following intraocular surgery or intravitreous injection. We excluded trials with participants with endogenous endophthalmitis unless outcomes were reported by source of infection. We imposed no restrictions on the method or order of administration, dose, frequency, or duration of antibiotics and steroids.

Data collection and analysis
Two review authors independently screened the search results, assessed risk of bias, and extracted data using methods expected by Cochrane. We contacted study authors to try to obtain missing information or information to clarify risk of bias. We conducted a meta-analysis for any outcomes that were reported by at least two studies. Outcomes reported from single studies were summarized in the text. We assessed the certainty of the evidence using GRADE.

Main results
We included three trials with a total of 95 randomized participants in this review and identified one ongoing trial. The studies were conducted in South Africa, India, and the Netherlands. Out of the 92 analyzed participants, 91 participants were diagnosed with endophthalmitis following cataract surgery. In the remaining participant, endophthalmitis was attributable to penetrating keratoplasty. All studies used intravitreous dexamethasone for adjunctive steroid therapy and a combination of two intravitreous antibiotics that provided gram-positive and gram-negative coverage for the antibiotic therapy. We judged one trial to be at overall low risk of bias and two studies to be at overall unclear risk of bias due to lack of reporting of study methods. None of the three trials had been registered in a clinical trial register.

Authors’ conclusions
Current evidence on the effectiveness of adjunctive steroid therapy versus antibiotics alone in the management of acute endophthalmitis after intraocular surgery is inadequate. We found no studies that had enrolled cases of acute endophthalmitis following intravitreous injection. A combined analysis of two studies suggests adjunctive steroids may provide a higher probability of having a good visual outcome at three months than not using adjunctive steroids. However, considering that most of the confidence intervals crossed the null and that this review was limited in scope and applicability to clinical practice, it is not possible to conclude whether the use of adjunctive steroids is effective at this time. Any future trials should examine whether adjunctive steroids may be useful in certain clinical settings such as type of causative organism or etiology. These studies should include outcomes that take patient's symptoms and clinical examination
into account, report outcomes in a uniform and consistent manner, and follow up at short- and long-term intervals.

Hydroxyurea for reducing blood transfusion in non-transfusion dependent beta thalassaemias
Foong, Cheng Wai. Ho, Jacqueline J. Loh, Khai C. Viprakasit, Vip.Institution Wai Cheng Foong
.TI Hydroxyurea for reducing blood transfusion in non-transfusion dependent beta thalassaemias.
EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 10, 2016.
[Systematic Review]
AN: 00075320-100000000-09969
Background
Non-transfusion dependent beta thalassaemia is a subset of inherited haemoglobin disorders characterised by reduced production of the beta globin chain of the haemoglobin molecule leading to anaemia of varying severity. Although blood transfusion is not a necessity for survival, it is required when episodes of chronic anaemia occur. This chronic anaemia can impair growth and affect quality of life. People with non-transfusion dependent beta thalassaemia suffer from iron overload due to their body's increased capability of absorbing iron from food sources. Iron overload becomes more pronounced in those requiring blood transfusion. People with a higher foetal haemoglobin level have been found to require fewer blood transfusions. Hydroxyurea has been used to increase foetal haemoglobin level; however, its efficacy in reducing transfusion, chronic anaemia complications and its safety need to be established.
Objectives
To assess the effectiveness, safety and appropriate dose regimen of hydroxyurea in people with non-transfusion dependent beta thalassaemia (haemoglobin E combined with beta thalassaemia and beta thalassaemia intermedia).
Search methods
We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group's Haemoglobinopathies Trials Register, compiled from electronic database searches and handsearching of relevant journals. We also searched ongoing trials registries and the reference lists of relevant articles and reviews.
Selection criteria
Randomised or quasi-randomised controlled trials of hydroxyurea in people with non-transfusion dependent beta thalassaemia comparing hydroxyurea with placebo or standard treatment or comparing different doses of hydroxyurea.

Data collection and analysis
Two authors independently applied the inclusion criteria in order to select trials for inclusion. Both authors assessed the risk of bias of trials and extracted the data. A third author verified these assessments.

Main results
No trials comparing hydroxyurea with placebo or standard care were found. However, we included one randomised controlled trial (n = 61) comparing 20 mg/kg/day with 10 mg/kg/day of hydroxyurea for 24 weeks.

Authors’ conclusions
There is no evidence from randomised controlled trials to show whether hydroxyurea has any effect compared with controls on the need for blood transfusion. Administration of 10 mg/kg/day compared to 20 mg/kg/day of hydroxyurea resulted in higher haemoglobin levels and seems safer with fewer adverse effects. It has not been reported whether hydroxyurea is capable of reducing the need for blood transfusion. Large well-designed randomised controlled trials with sufficient duration of follow up are recommended.

788.
Antibiotic treatment for the sexual partners of women with bacterial vaginosis
Antibiotic treatment for the sexual partners of women with bacterial vaginosis.
EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 10, 2016.
[Systematic Review]
AN: 00075320-100000000-10068

Background
Bacterial vaginosis (BV) is an infection that has a prevalence between 10% to 50% worldwide. BV results in an imbalance of the normal vaginal flora. Microorganisms associated with BV have been isolated from the normal flora of the male genital tract, and their presence could be related
to the recurrence of BV after antibiotic treatment. Therefore, the treatment of sexual partners could decrease the recurrence of infection and possibly the burden of the disease.

Objectives
To assess the effectiveness in women and the safety in men of concurrent antibiotic treatment for the sexual partners of women treated for BV.

Search methods
We searched the Cochrane Sexually Transmitted Infections Group Specialized Register (23 July 2016), CENTRAL (1991 to 23 July 2016), MEDLINE (1946 to 23 July 2016), Embase (1974 to 23 July 2016), LILACS (1982 to 23 July 2016), the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (23 July 2016), ClinicalTrials.gov (23 July 2016) and the Web of Science[TM] (2001 to 23 July 2016). We also handsearched conference proceedings, contacted trial authors and reviewed the reference lists of retrieved studies.

Selection criteria
Randomized controlled trials (RCTs) that compared the concurrent use of any antibiotic treatment with placebo, no intervention or any other intervention by the sexual partners of women treated for BV.

Data collection and analysis
Three review authors independently assessed trials for inclusion, extracted data and assessed the risk of bias in the included studies. We resolved any disagreements through consensus. We assessed the quality of the evidence using the GRADE approach.

Main results
Seven RCTs (1026 participants) met our inclusion criteria, and pharmaceutical industry funded four of these trials. Five trials (854 patients) compared any antibiotic treatment of sexual partners with placebo. Based on high quality evidence, antibiotic treatment does not increase the rate of clinical or symptomatic improvement in women during the first week (risk ratio (RR) 0.99, 95% confidence interval (CI) 0.96 to 1.03; 712 participants, four studies; RR 1.06, 95% CI 1.00 to 1.12; 577 patients, three studies, respectively), between the first and fourth week (RR 1.02, 95% CI 0.94 to 1.11; 590 participants, three studies; RR 0.93, 95% CI 0.84 to 1.03; 444 participants, two studies; respectively) or after the fourth week of treatment (RR 0.98, 95% CI 0.90 to 1.07; 572 participants, four studies; RR 1.03, 95% CI 0.90 to 1.17; 296 participants, two studies; respectively). Antibiotic treatment does not lead to a lower recurrence during the first and fourth week (RR 1.28, 95% CI 0.68 to 2.43; 218 participants, one study; low quality evidence) or after the fourth week of treatment (RR 1.00, 95% CI 0.67 to 1.52; 372 participants, three studies; low quality evidence) in women, but increases the frequency of adverse events (most frequently gastrointestinal symptoms) reported by sexual partners (RR 2.55, 95% CI 1.55 to 4.18; 477 participants, three studies; low quality evidence).
Two trials (172 participants) compared any antibiotic treatment for sexual partners with no intervention. When we compared it with no intervention, the effects of antibiotic treatment on recurrence rate after the fourth week (RR 1.71, 95% CI 0.65 to 4.55; 51 participants, one study), clinical improvement between the first and fourth week (RR 0.93, 95% CI 0.70 to 1.25; 152 participants, two studies) and symptomatic improvement after the fourth week (RR 0.66, 95% CI 0.39 to 1.11; 70 participants, one study) were imprecise and there were no differences between groups. We downgraded the quality of the evidence to low or very low.

Authors’ conclusions
High quality evidence shows that antibiotic treatment for sexual partners of women with BV, compared with placebo, does not increase the rate of clinical or symptomatic improvement during the first, between the first and fourth or after the fourth week into the women. Low quality evidence suggests that antibiotic treatment does not led to a lower recurrence rate during the first and fourth or after the fourth week of treatment into the women, but increases the frequency of adverse events reported by sexual partners. Finally, compared with no intervention, antibiotic treatment does not decrease the recurrence rate after the fourth week and does not increase the frequency of clinical or symptomatic improvement between the first and fourth or after the fourth week into the women, respectively.

789.
Adjunctive Peony-Glycyrrhiza Decoction for antipsychotic-induced hyperprolactinemia
EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 11, 2016.
[Protocol]
AN: 00075320-100000000-10836
This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:
To assess the effectiveness and safety of adjunctive Peony-Glycyrrhiza Decoction for treating antipsychotic-induced hyperprolactinemia.
Progestin-only contraceptives: effects on weight


EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 8, 2016.[Systematic Review]
AN: 00075320-100000000-07259

Background
Progestin-only contraceptives (POCs) are appropriate for many women who cannot or should not take estrogen. POCs include injectables, intrauterine contraception, implants, and oral contraceptives. Many POCs are long-acting, cost-effective methods of preventing pregnancy. However, concern about weight gain can deter the initiation of contraceptives and cause early discontinuation among users.

Objectives
The primary objective was to evaluate the association between progestin-only contraceptive use and changes in body weight.

Search methods
Until 4 August 2016, we searched MEDLINE, CENTRAL, POPLINE, LILACS, ClinicalTrials.gov, and ICTRP. For the initial review, we contacted investigators to identify other trials.

Selection criteria
We considered comparative studies that examined a POC versus another contraceptive method or no contraceptive. The primary outcome was mean change in body weight or mean change in body composition. We also considered the dichotomous outcome of loss or gain of a specified amount of weight.

Data collection and analysis
Two authors extracted the data. Non-randomized studies (NRS) need to control for confounding factors. We used adjusted measures for the primary effects in NRS or the results of matched analysis from paired samples. If the report did not provide adjusted measures for the primary analysis, we used unadjusted outcomes. For RCTs and NRS without adjusted measures, we computed the mean difference (MD) with 95% confidence interval (CI) for continuous variables. For dichotomous outcomes, we calculated the Mantel-Haenszel odds ratio (OR) with 95% CI.

Main results
We found 22 eligible studies that included a total of 11,450 women. With 6 NRS added to this update, the review includes 17 NRS and 5 RCTs. By contraceptive method, the review has 16
studies of depot medroxyprogesterone acetate (DMPA), 4 of levonorgestrel-releasing intrauterine
contraception (LNG-IUC), 5 for implants, and 2 for progestin-only pills.

Authors’ conclusions
We considered the overall quality of evidence to be low; more than half of the studies had low
quality evidence. The main reasons for downgrading were lack of randomizations (NRS) and high
loss to follow-up or early discontinuation.

791.
Interventions for men and women with their first episode of genital herpes
Interventions for men and women with their first episode of genital herpes.
EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 8, 2016.
[Systematic Review]
AN: 00075320-10000000-09006

Background
Genital herpes is incurable, and is caused by the herpes simplex virus (HSV). First-episode
genital herpes is the first clinical presentation of herpes that a person experiences. Current
treatment is based around viral suppression in order to decrease the length and severity of the
episode.

Objectives
To determine the effectiveness and safety of the different existing treatments for first-episode
genital herpes on the duration of symptoms and time to recurrence.

Search methods
We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (from inception to
April 2016), MEDLINE (from inception to April 2016), the Specialised Register of the Cochrane
Sexually Transmitted Infections Review Group (from inception to April 2016), EMBASE (from
inception to April 2016), PsycINFO (from inception to April 2016), CINAHL (from inception to April
2016), LILACS (from inception to April 2016), AMED (from inception to April 2016), and the
Alternative Medicines Specialised Register (from inception to April 2016). We handsearched a
number of relevant journals, searched reference lists of all included studies, databases of
ongoing trials, and other Internet databases.

Selection criteria
We included randomised controlled trials (RCTs) on participants with first-episode genital herpes. We excluded vaccination trials, and trials in which the primary objective assessed a complication of HSV infection.

Data collection and analysis
All studies written in English were independently assessed by at least two review authors for inclusion, risk of bias for each trial, and to extract data. Studies requiring translation were assessed for inclusion, trial quality, and data extraction by external translators.

Main results
We included 26 trials with 2084 participants analysed. Most of the studies were conducted in the United Kingdom (UK) and United States (US), and involved men and women experiencing their first episode of genital herpes, with the exception of three studies which included only women. We rated the majority of these studies as having an unclear risk of bias; largely due to lack of information supplied in the publications, and due to the age of the trials. This review found low quality evidence from two studies of oral acyclovir, when compared to placebo, reduced the duration of symptoms in individuals undergoing their first episode of genital herpes (mean difference (MD) -3.22, 95% confidence interval (CI) -5.91 to -0.54; I\(^2\) = 52%). In two studies (112 participants), intravenous acyclovir decreased the median number of days that patients with first-episode herpes suffered symptoms. Oral valaciclovir (converted to acyclovir) also showed a similar length of symptom duration when compared to acyclovir in two studies. There is currently no evidence that topical acyclovir reduces symptoms (MD -0.61 days, 95% CI -2.16 to 0.95; 3 RCTs, 195 participants, I\(^2\) statistic = 56%). There is also no current evidence that the topical treatments of cicloxolone cream, carbenoxolone sodium cream, adenosine arabinoside, idoxuridine in dimethyl sulfoxide, when compared to placebo reduced the duration of symptoms in people undergoing their first episode of herpes.

Authors’ conclusions
There is low quality evidence from this review that oral acyclovir reduced the duration of symptoms for genital herpes. However, there is low quality evidence which did not show that topical antivirals reduced symptom duration for patients undergoing their first episode of genital herpes. This review was limited by the inclusion of skewed data, resulting in few trials that we were able to meta-analyse.
Quality improvement interventions for improving the detection and management of curable sexually transmitted infections in primary care
EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 10, 2016.
[Protocol]
AN: 00075320-100000000-10778
This is the protocol for a review and there is no abstract. The objectives are as follows:
To assess the effectiveness and safety of quality improvement interventions for the detection and management of curable sexually transmitted infections in primary care.

793.
Inositol for subfertile women with polycystic ovary syndrome
EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 9, 2016.
[Protocol]
AN: 00075320-100000000-10775
This is the protocol for a review and there is no abstract. The objectives are as follows:
To evaluate the effectiveness and safety of oral supplementation with inositol on reproductive outcomes for subfertile women with polycystic ovary syndrome (PCOS).

794.
Screening for genital chlamydia infection
Background

Genital infections caused by Chlamydia trachomatis are the most prevalent bacterial sexually transmitted infection worldwide. Screening of sexually active young adults to detect and treat asymptomatic infections might reduce chlamydia transmission and prevent reproductive tract morbidity, particularly pelvic inflammatory disease (PID) in women, which can cause tubal infertility and ectopic pregnancy.

Objectives

To assess the effects and safety of chlamydia screening versus standard care on chlamydia transmission and infection complications in pregnant and non-pregnant women and in men.

Search methods

We searched the Cochrane Sexually Transmitted Infections Group Specialised Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, LILACS, CINAHL, DARE, PsycINFO and Web of Science electronic databases up to 14 February 2016, together with World Health Organization International Clinical Trials Registry (ICTRP) and ClinicalTrials.gov. We also handsearched conference proceedings, contacted trial authors and reviewed the reference lists of retrieved studies.

Selection criteria

Randomised controlled trials (RCTs) in adult women (non-pregnant and pregnant) and men comparing a chlamydia screening intervention with usual care and reporting on a primary outcome (C. trachomatis prevalence, PID in women, epididymitis in men or incidence of preterm delivery). We included non-randomised controlled clinical trials if there were no RCTs for a primary outcome.

Data collection and analysis

Two review authors independently assessed trials for inclusion, extracted data and assessed the risk of bias. We resolved disagreements by consensus or adjudication by a third reviewer. We described results in forest plots and conducted meta-analysis where appropriate using a fixed-effect model to estimate risk ratios (RR with 95% confidence intervals, CI) in intervention vs control groups. We conducted a pre-specified sensitivity analysis of the primary outcome, PID incidence, according to the risks of selection and detection bias.

Main results
We included six trials involving 359,078 adult women and men. One trial was at low risk of bias in all six specific domains assessed. Two trials examined the effect of multiple rounds of chlamydia screening on C. trachomatis transmission. A cluster-controlled trial in women and men in the general population in the Netherlands found no change in chlamydia test positivity after three yearly invitations (intervention 4.1% vs control 4.3%, RR 0.96, 95% CI 0.84 to 1.09, 1 trial, 317,304 participants at first screening invitation, low quality evidence). Uptake of the intervention was low (maximum 16%). A cluster-randomised trial in female sex workers in Peru found a reduction in chlamydia prevalence after four years (adjusted RR 0.72, 95% CI 0.54 to 0.98, 1 trial, 4465 participants, low quality evidence).

Authors’ conclusions
Evidence about the effects of screening on C. trachomatis transmission is of low quality because of directness and risk of bias. There is moderate quality evidence that detection and treatment of chlamydia infection can reduce the risk of PID in women at individual level. There is an absence of RCT evidence about the effects of chlamydia screening in pregnancy.

795.
Treatment for osteoporosis in people with [latin sharp s]-thalassaemia
Bhardwaj, Amit. Swe, Mon Kye. Sinha, Nirmal K. Osunkwo, Ifeyinwa.Institution Kye Mon Min
Swe .TI Treatment for osteoporosis in people with [latin sharp s]-thalassaemia.
EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 3, 2016.
[Systematic Review]
AN: 00075320-100000000-08822
Background
Osteoporosis is a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture. Osteoporosis represents an important cause of morbidity in people with beta-thalassaemia and its pathogenesis is multifactorial. Factors include bone marrow expansion due to ineffective erythropoiesis, resulting in reduced trabecular bone tissue with cortical thinning; endocrine dysfunction secondary to excessive iron loading, leading to increased bone turnover; and lastly, a predisposition to physical inactivity due to disease complications with a subsequent reduction in optimal bone mineralization.
Objectives
To review the evidence on the efficacy and safety of treatment for osteoporosis in people with beta-thalassaemia.

Search methods
We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group's Haemoglobinopathies Trials Register comprising references identified from comprehensive electronic database searches and handsearches of relevant journals and abstract books of conference proceedings.

Selection criteria
Randomised, placebo-controlled trials in people with thalassaemia with a bone mineral density z score of less than -2 standard deviations for: children less than 15 years old; adult males (15 to 50 years old); and all pre-menopausal females above 15 years and a bone mineral density t score of less than -2.5 standard deviations for post-menopausal females and males above 50 years old.

Data collection and analysis
Two review authors assessed the eligibility and risk of bias of the included trials, extracted and analysed data and completed the review. We summarised results using risk ratios or rate ratios for dichotomous data and mean differences for continuous data. We combined trial results where appropriate.

Main results
Four trials (with 211 participants) were included; three trials investigated the effect of bisphosphonate therapies and one trial investigated the effect of zinc supplementation. Only one trial was judged to be of good quality (low risk of bias); the remaining trials had a high or unclear risk of bias in at least one key domain.

Authors’ conclusions
There is evidence to indicate an increase in bone mineral density at the femoral neck, lumbar spine and forearm after administration of bisphosphonates and at the lumbar spine and hip after zinc sulphate supplementation. The authors recommend that further long-term randomised control trials on different bisphosphonates and zinc supplementation therapies in people with beta-thalassaemia and osteoporosis are undertaken.

796.

Growth hormone therapy for people with thalassaemia

EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 7, 2016.

[Protocol]
AN: 00075320-100000000-10689
This is the protocol for a review and there is no abstract. The objectives are as follows:
To assess the risks and benefits of GH therapy in people with thalassaemia.

797.
Cleavage stage versus blastocyst stage embryo transfer in assisted reproductive technology

EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 6, 2016.

[Systematic Review]
AN: 00075320-100000000-01578
Background

Advances in cell culture media have led to a shift in in vitro fertilisation (IVF) practice from cleavage stage embryo transfer to blastocyst stage transfer. The rationale for blastocyst transfer is to improve both uterine and embryonic synchronicity and enable self selection of viable embryos, thus resulting in better live birth rates.

Objectives

To determine whether blastocyst stage (day 5 to 6) embryo transfers improve the live birth rate, and other associated outcomes, compared with cleavage stage (day 2 to 3) embryo transfers.

Search methods

We searched the Cochrane Gynaecology and Fertility Group Specialised Register of controlled trials, Cochrane Central Register of Controlled Trials (CENTRAL; the Cochrane Library; 2016, Issue 4), MEDLINE, EMBASE, PsycINFO, CINAHL, and Bio extracts from inception to 4th April 2016. We also searched registers of ongoing trials and the reference lists of studies retrieved.

Selection criteria
We included randomised controlled trials (RCTs) which compared the effectiveness of blastocyst versus cleavage stage transfers.

Data collection and analysis
We used standard methodological procedures recommended by Cochrane. Our primary outcomes were live birth and cumulative clinical pregnancy rates. Secondary outcomes were clinical pregnancy, multiple pregnancy, high order pregnancy, miscarriage, failure to transfer embryos, and embryo freezing. We assessed the overall quality of the evidence for the main comparisons using GRADE methods.

Main results
We included 27 RCTs (4031 couples or women).

Authors’ conclusions
There is low quality evidence for live birth and moderate quality evidence for clinical pregnancy that fresh blastocyst stage transfer is associated with higher rates than fresh cleavage stage transfer. There was no evidence of a difference between the groups in cumulative pregnancy rates derived from fresh and frozen-thawed cycles following a single oocyte retrieval, but the evidence for this outcome was very low quality. Thus, although there is a benefit favouring blastocyst transfer in fresh cycles, it remains unclear whether the day of transfer impacts on cumulative live birth and pregnancy rates. Future RCTs should report rates of live birth, cumulative live birth, and miscarriage to enable couples or women undergoing assisted reproductive technology (ART) and service providers to make well informed decisions on the best treatment option available.

798.
Hematopoietic stem cell transplantation for people with sickle cell disease
Oringanje, Chioma. Nemecek, Eneida. Oniyangi, Oluseyi. Institution Chioma Oringanje .TI
Hematopoietic stem cell transplantation for people with sickle cell disease.
EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 5, 2016.
[Systematic Review]
AN: 00075320-100000000-05591
Background
Sickle cell disease is a genetic disorder involving a defect in the red blood cells due to its sickled hemoglobin. The main therapeutic interventions include preventive and supportive measures.
Hematopoietic stem cell transplantations are carried out with the aim of replacing the defective cells and their progenitors (hematopoietic, i.e. blood forming) stem cells in order to correct the disorder. This is an update of a previously published review.

Objectives
To determine whether stem cell transplantation can improve survival and prevent symptoms and complications associated with sickle cell disease. To examine the risks of stem cell transplantation against the potential long-term gain for people with sickle cell disease.

Search methods
We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group Group's Haemoglobinopathies Trials Register compiled from electronic searches of the Cochrane Central Register of Controlled Trials (CENTRAL) (updated each new issue of The Cochrane Library) and quarterly searches of MEDLINE.

Selection criteria
Randomized controlled and quasi-randomized studies that compared any method of stem cell transplantation with either each other or with any of the preventive or supportive interventions (e.g. periodic blood transfusion, use of hydroxyurea, antibiotics, pain relievers, supplemental oxygen) in people with sickle cell disease irrespective of the type of sickle cell disease, gender and setting.

Data collection and analysis
No relevant trials were identified.

Main results
Ten trials were identified by the initial search and none for the update. None of these trials were suitable for inclusion in this review.

Authors' conclusions
Reports on the use of hematopoietic stem cell transplantation improving survival and preventing symptoms and complications associated with sickle cell disease are currently limited to observational and other less robust studies. No randomized controlled trial assessing the benefit or risk of hematopoietic stem cell transplantations was found. Thus, this systematic review identifies the need for a multicentre randomized controlled trial assessing the benefits and possible risks of hematopoietic stem cell transplantations comparing sickle status and severity of disease in people with sickle cell disease.
Psychological interventions for adults who are overweight or obese
Brennan, Leah. Murphy, Kylie D. de la Piedad Garcia, Xochitl. Ellis, Miriam E. Metzendorf, Marialnti. McKenzie, Joanne E.Institution Leah Brennan .TI Psychological interventions for adults who are overweight or obese.
EBM Reviews - Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews. 3, 2016.
[Protocol]
AN: 00075320-100000000-10529
This is the protocol for a review and there is no abstract. The objectives are as follows:
To assess the effects of psychological interventions for the treatment of overweight and obese adults. Specific objectives are to examine the efficacy of:
All psychological therapies versus minimal or no intervention;
All psychological therapies versus an active diet and/or exercise intervention;
Behavioural psychological therapies (first, second or third wave) versus other psychological interventions.
Secondary objectives are to examine if the magnitude of intervention effects (objectives 1, 2, and 3) for the primary outcome of BMI are modified by particular intervention characteristics (length of follow-up), or participant characteristics (degree of excess weight). We also plan to investigate whether the effects of behavioural therapy are modified by the type of behaviour intervention (first, second or third wave).