

EAU GUIDELINES ON UROLOGICAL INFECTIONS

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Introduction

The European Association of Urology (EAU) Urological Infections Guidelines Panel has compiled these clinical guidelines to provide medical professionals with evidence-based information and recommendations for the prevention and treatment of urological tract infections (UTIs). These guidelines also aim to address the important public health aspects of infection control and antimicrobial stewardship.

Antimicrobial Stewardship

Stewardship programs have two main sets of actions. The first set mandates use of recommended care at the patient level conforming to guidelines. The second set describes strategies to achieve adherence to the mandated guidance. These include persuasive actions such as education and feedback together with restricting availability linked to local formularies. The important components of antimicrobial stewardship programs are:

- regular training of staff in best use of antimicrobial agents;
- adherence to local, national or international guidelines;
- regular ward visits and consultation with infectious diseases physicians and clinical microbiologists;
- audit of adherence and treatment outcomes;
- regular monitoring and feedback to prescribers of their performance and local pathogen resistance profiles.

Asymptomatic Bacteriuria

Asymptomatic bacteriuria in an individual without urinary tract symptoms is defined by a mid-stream sample of urine showing bacterial growth $\geq 10^5$ cfu/mL in two consecutive samples in women and in one single sample in men.

| Recommendations | Strength rating |
|---|--|
| Do not screen or treat asymptomatic bacteriuria in the following conditions: <ul style="list-style-type: none">• women without risk factors;• patients with well-regulated diabetes mellitus;• post-menopausal women;• elderly institutionalised patients;• patients with dysfunctional and/or reconstructed lower urinary tracts;• patients with renal transplants;• patients prior to arthroplasty surgeries;• patients with recurrent urinary tract infections. | Strong Strong Strong Strong Strong Strong Strong |
| Screen for and treat asymptomatic bacteriuria prior to urological procedures breaching the mucosa. | Strong |
| Screen for and treat asymptomatic bacteriuria in pregnant women with standard short course treatment. | Weak |

Uncomplicated Cystitis

Uncomplicated cystitis is defined as acute, sporadic or recurrent cystitis limited to non-pregnant, pre-menopausal women with no known relevant anatomical and functional abnormalities within the urinary tract or comorbidities.

| Recommendations for the diagnostic evaluation of uncomplicated cystitis | Strength rating |
|---|------------------------|
| <p>Diagnose uncomplicated cystitis in women who have no other risk factors for complicated urinary tract infections based on:</p> <ul style="list-style-type: none"> • a focused history of lower urinary tract symptoms (dysuria, frequency and urgency); • the absence of vaginal discharge or irritation. | Strong |
| Use urine dipstick testing for diagnosis of acute uncomplicated cystitis. | Weak |
| <p>Urine cultures should be done in the following situations:</p> <ul style="list-style-type: none"> • suspected acute pyelonephritis; • symptoms that do not resolve or recur within four weeks after the completion of treatment; • women who present with atypical symptoms; • pregnant women. | Strong |

| Recommendations for antimicrobial therapy for uncomplicated cystitis | Strength rating |
|---|------------------------|
| Prescribe fosfomycin trometamol, pivmecillinam or nitrofurantoin as first-line treatment for uncomplicated cystitis in women. | Strong |
| Do not use aminopenicillins or fluoroquinolones to treat uncomplicated cystitis. | Strong |

| Table 1: Suggested regimens for antimicrobial therapy in uncomplicated cystitis | | | |
|--|----------------------------|----------------------------|---|
| Antimicrobial | Daily dose | Duration of therapy | Comments |
| First-line women | | | |
| Fosfomycin trometamol | 3 g SD | 1 day | Recommended only in women with uncomplicated cystitis. |
| Nitrofurantoin macrocrystal | 50-100 mg four times a day | 5 days | |
| Nitrofurantoin monohydrate/macrocrystals | 100 mg b.i.d | 5 days | |
| Nitrofurantoin macrocrystal prolonged release | 100 mg b.i.d | 5 days | |
| Pivmecillinam | 200 mg t.i.d | 3-5 days | |
| Alternatives | | | |
| Cephalosporins (e.g. cefadroxil) | 500 mg b.i.d | 3 days | Or comparable |
| If the local resistance pattern for <i>E. coli</i> is < 20% | | | |
| Trimethoprim | 200 mg b.i.d | 5 days | Not in the first trimester of pregnancy |
| Trimethoprim-sulphamethoxazole | 160/800 mg b.i.d | 3 days | Not in the last trimester of pregnancy |
| Treatment in men | | | |
| Trimethoprim-sulphamethoxazole | 160/800 mg b.i.d | 7 days | Restricted to men, fluoroquinolones can also be prescribed in accordance with local susceptibility testing. |

SD = single dose; b.i.d = twice daily; t.i.d = three times daily.

Recurrent UTIs

Recurrent UTIs (rUTIs) are recurrences of uncomplicated and/or complicated UTIs, with a frequency of at least three UTIs/year or two UTIs in the last six months.

| Recommendations for the diagnostic evaluation and treatment of rUTIs | Strength rating |
|--|------------------------|
| Diagnose recurrent UTI by urine culture. | Strong |
| Do not perform an extensive routine workup (e.g cystoscopy, full abdominal ultrasound) in women younger than 40 years of age with recurrent UTI and no risk factors. | Weak |
| Advise patients on behavioural modifications which might reduce the risk of recurrent UTI. | Weak |
| Use vaginal oestrogen replacement in post-menopausal women to prevent recurrent UTI. | Weak |
| Use immunoactive prophylaxis to reduce recurrent UTI in all age groups. | Strong |
| Use continuous or post-coital antimicrobial prophylaxis to prevent recurrent UTI when non-antimicrobial interventions have failed. Counsel patients regarding possible side effects. | Strong |
| For patients with good compliance self-administered short term antimicrobial therapy should be considered. | Strong |

Uncomplicated Pyelonephritis

Uncomplicated pyelonephritis is defined as pyelonephritis limited to non-pregnant, pre-menopausal women with no known relevant urological abnormalities or comorbidities.

| Recommendations for the diagnostic evaluation of uncomplicated pyelonephritis | Strength rating |
|--|------------------------|
| Perform urinalysis (e.g. using a dipstick method), including the assessment of white and red blood cells and nitrite, for routine diagnosis. | Strong |
| Perform urine culture and antimicrobial susceptibility testing in patients with pyelonephritis. | Strong |
| Perform imaging of the urinary tract to exclude urgent urological disorders. | Strong |

| Recommendations for the treatment of uncomplicated pyelonephritis | Strength rating |
|--|------------------------|
| Treat patients with uncomplicated pyelonephritis not requiring hospitalisation with short course fluoroquinolones as first-line treatment. | Strong |
| Treat patients with uncomplicated pyelonephritis requiring hospitalisation with an intravenous antimicrobial regimen initially. | Strong |
| Switch patients initially treated with parenteral therapy, who improve clinically and can tolerate oral fluids, to oral antimicrobial therapy. | Strong |
| Do not use nitrofurantoin, fosfomycin, and pivmecillinam to treat uncomplicated pyelonephritis. | Strong |

Table 2: Suggested regimens for empirical oral antimicrobial therapy in uncomplicated pyelonephritis

| Antimicrobial | Daily dose | Duration of therapy | Comments |
|-------------------------------|------------------|---------------------|---|
| Ciprofloxacin | 500-750 mg b.i.d | 7 days | Fluoroquinolone resistance should be less than 10 percent. |
| Levofloxacin | 750 mg q.d | 5 days | |
| Trimethoprim sulphamethoxazol | 160/800 mg b.i.d | 14 days | If such agents are used empirically, an initial intravenous dose of a long-acting parenteral antimicrobial (e.g. ceftriaxone) should be administered. |
| Cefpodoxime | 200 mg b.i.d | 10 days | |
| Ceftibuten | 400 mg q.d | 10 days | |

b.i.d = twice daily; *q.d* = every day.

| Table 3: Suggested regimens for empirical parenteral antimicrobial therapy in uncomplicated pyelonephritis | | |
|---|-------------------|--|
| Antimicrobial | Daily dose | Comments |
| First-line treatment | | |
| Ciprofloxacin | 400 mg b.i.d | |
| Levofloxacin | 750 mg q.d | |
| Cefotaxime | 2 g t.i.d | Not studied as monotherapy in acute uncomplicated pyelonephritis. |
| Ceftriaxone | 1-2 g q.d | Lower dose studied, but higher dose recommended. |
| Second-line treatment | | |
| Cefepime | 1-2 g b.i.d | Lower dose studied, but higher dose recommended. |
| Piperacillin/tazobactam | 2.5-4.5 g t.i.d | |
| Ceftolozane/tazobactam | 1.5 g t.i.d | |
| Ceftazidime/avibactam | 2.5 g t.i.d | |
| Gentamicin | 5 mg/kg q.d | Not studied as monotherapy in acute uncomplicated pyelonephritis. |
| Amikacin | 15 mg/kg q.d | |
| Alternatives | | |
| Imipenem/cilastatin | 0.5 g t.i.d | Consider carbapenems only in patients with early culture results indicating the presence of multi-drug resistance organisms. |
| Meropenem | 1 g t.i.d | |

b.i.d = twice daily; t.i.d = three times daily; q.d = every day.

Complicated UTIs

A complicated UTI (cUTI) occurs in an individual in whom factors related to the host (e.g. underlying diabetes or immunosuppression) or specific anatomical or functional abnormalities related to the urinary tract (e.g. obstruction, incomplete voiding due to detrusor muscle dysfunction) are

believed to result in an infection that will be more difficult to eradicate than an uncomplicated infection.

| Recommendations for the treatment of complicated UTIs | Strength rating |
|--|------------------------|
| Use the combination of: <ul style="list-style-type: none">• amoxicillin plus an aminoglycoside;• a second generation cephalosporin plus an aminoglycoside;• a third generation cephalosporin intravenously as empirical treatment of complicated UTI with systemic symptoms. | Strong |
| Only use ciprofloxacin provided that the local resistance percentages are < 10% when: <ul style="list-style-type: none">• the entire treatment is given orally;• patients do not require hospitalisation;• patient has an anaphylaxis for beta-lactam antimicrobials. | Strong |
| Do not use ciprofloxacin and other fluoroquinolones for the empirical treatment of complicated UTI in patients from the urology department or when patients have used fluoroquinolones in the last six months. | Strong |
| Manage any urological abnormality and/or underlying complicating factors. | Strong |

Catheter-associated UTIs

Catheter-associated UTI refers to UTIs occurring in a person whose urinary tract is currently catheterised or has been catheterised within the past 48 hours.

| Recommendations for diagnostic evaluation of CA-UTI | Strength rating |
|---|------------------------|
| Do not carry out routine urine culture in asymptomatic catheterised patients. | Strong |
| Do not use pyuria as an indicator for catheter-associated UTI. | Strong |
| Do not use the presence or absence of odorous or cloudy urine alone to differentiate catheter-associated asymptomatic bacteriuria from catheter-associated UTI. | Strong |

| Recommendations for disease management and prevention of CA-UTI | Strength rating |
|---|------------------------|
| Treat symptomatic CA-UTI according to the recommendations for complicated UTIs. | Strong |
| Take a urine culture prior to initiating antimicrobial therapy in catheterised patients in whom the catheter has been removed. | Strong |
| Do not treat catheter-associated asymptomatic bacteriuria in general. | Strong |
| Treat catheter-associated asymptomatic bacteriuria prior to traumatic urinary tract interventions (e.g. transurethral resection of the prostate). | Strong |
| Replace or remove the indwelling catheter before starting antimicrobial therapy. | Strong |
| Do not apply topical antiseptics or antimicrobials to the catheter, urethra or meatus. | Strong |
| Do not use prophylactic antimicrobials to prevent catheter-associated UTIs. | Strong |
| The duration of catheterisation should be minimal. | Strong |

| Recommendations for antibiotic prophylaxis following indwelling bladder catheter removal | Strength rating |
|--|------------------------|
| Do not use antibiotic prophylaxis routinely to prevent clinical UTI after urethral catheter removal. | Weak |

Urosepsis

Urosepsis is defined as life threatening organ dysfunction caused by a dysregulated host response to infection originating from the urinary tract and/or male genital organs.

| Recommendations for the diagnosis and treatment of urosepsis | Strength rating |
|--|------------------------|
| Perform the quickSOFA score to identify patients with potential sepsis. | Strong |
| Take a urine culture and two sets of blood cultures before starting antimicrobial treatment. | Strong |
| Administer parenteral high dose broad spectrum antimicrobials within the first hour after clinical assumption of sepsis. | Strong |
| Adapt initial empiric antimicrobial therapy on the basis of culture results. | Strong |
| Remove foreign bodies from and obstruction of the urinary tract. | Strong |
| Provide immediate adequate life-support measures. | Strong |

| Table 4: Suggested regimens for antimicrobial therapy for urosepsis | | |
|--|-------------------|---|
| Antimicrobials | Daily dose | Duration of therapy |
| Cefotaxime | 2 g t.i.d | 7-10 days Longer courses are appropriate in patients who have a slow clinical response |
| Ceftazidime | 1-2 g t.i.d | |
| Ceftriaxone | 1-2 g q.d | |
| Cefepime | 2 g b.i.d | |
| Piperacillin/tazobactam | 4.5 g t.i.d | |
| Ceftolozane/tazobactam | 1.5 g t.i.d | |
| Ceftazidime/avibactam | 2.5 g t.i.d | |
| Gentamicin* | 5 mg/kg q.d | |
| Amikacin* | 15 mg/kg q.d | |
| Ertapenem | 1 g q.d | |
| Imipenem/cilastatin | 0.5 g t.i.d | |
| Meropenem | 1 g t.i.d | |

* Not studied as monotherapy in urosepsis

b.i.d = twice daily; t.i.d = three times daily; q.d = every day.

Urethritis

Inflammation of the urethra usually presents with LUTS and must be distinguished from other infections of the lower urinary tract. The following recommendations are based on a review of several European national guidelines and are aligned with the Center for Disease Control and Prevention's guidelines on sexual transmitted diseases.

| Recommendations for the diagnostic evaluation and antimicrobial treatment of urethritis | Strength rating |
|---|------------------------|
| Perform a gram stain of urethral discharge or a urethral smear to preliminarily diagnose pyogenic urethritis. | Strong |

| | |
|--|--------|
| Perform a validated nucleic acid amplification tests on a mid-stream urine sample or urethral smear to diagnosis chlamydial and gonococcal infections. | Strong |
| Use a pathogen directed treatment based on local resistance data. | Strong |

Table 5: Suggested regimens for antimicrobial therapy for urethritis

| Pathogen | Antimicrobial | Dosage & Duration of therapy | Alternative regimens |
|--|---------------|---|--|
| Gonococcal Infection | Ceftriaxone | 1 g i.m., SD | Cefixime 400 mg p.o., SD Or Azithromycin 1-1.5 g p.o., SD |
| | Azithromycin | 1-1.5 g p.o., SD | |
| | Cefixime | 800 mg p.o., SD | |
| Non-Gonococcal infection (non-identified pathogen) | Doxycycline | 100 mg b.i.d, p.o., 7-10 days | Azithromycin 0.5 g p.o., day 1, 250 mg p.o., day 2-5 |
| <i>Chlamydia trachomatis</i> | Azithromycin | 1.0-1.5 g p.o., SD | Doxycycline 100 mg b.i.d, p.o., for 7 days |
| <i>Mycoplasma genitalium</i> | Azithromycin | 0.5 g p.o., day 1, 250 mg p.o., day 2-5 | Moxifloxacin 400 mg q.d., 5 days however, because of reported failures, some experts recommend 10 -14 days |

| | | | |
|-------------------------------|---------------|----------------------------|---|
| <i>Ureaplasma urealiticum</i> | Doxycycline | 100 mg b.i.d, p.o., 7 days | Azithromycin 1.0-1.5 g p.o., single dose Or clarithromycin 500 mg b.i.d, 7 days (resistance against macrolides is possible) |
| <i>Trichomonas vaginalis</i> | Metronidazole | 2 g p.o., SD | Not in the last trimenon of pregnancy |

SD = single dose; b.i.d = twice daily; q.d = everyday; p.o. = orally, i.m. = intramuscular.

Bacterial Prostatitis

Bacterial prostatitis is a clinical condition caused by bacterial pathogens. It is recommended that urologists use the classification suggested by the National Institute of Diabetes, Digestive and Kidney Diseases of the National Institutes of Health, in which bacterial prostatitis, with confirmed or suspected infection, is distinguished from chronic pelvic pain syndrome.

| Recommendations for the diagnosis of bacterial prostatitis | Strength rating |
|--|-----------------|
| Perform a gentle digital rectal examination to assess the condition of the prostate. | Weak |
| Take a mid-stream urine dipstick to check nitrite and leukocytes in patients with clinical suspicion of acute bacterial prostatitis. | Weak |
| Take a blood culture and a total blood count in case of prostatitis-related symptoms with malaise and fever. | Weak |

| | |
|---|--------|
| Take a mid-stream urine culture in patients with acute prostatitis-related symptoms to guide diagnosis and plan adequate targeted antibiotic treatment. | Weak |
| Perform accurate microbiological evaluation for atypical pathogens such as <i>Chlamydia trachomatis</i> or Mycoplasmata in patients with chronic bacterial prostatitis (CBP). | Weak |
| Perform the Meares and Stamey 2- or 4-glass test in patients with CBP. | Strong |
| Perform transrectal ultrasound in selected cases to rule out the presence of prostatic abscess, calcification in the prostate and dilatation of the seminal vesicles. | Weak |
| Do not routinely perform microbiological analysis of the ejaculate alone to diagnosis CBP. | Weak |

| Recommendations for the disease management of bacterial prostatitis | Strength rating |
|---|------------------------|
| Acute bacterial prostatitis | |
| Treat acute bacterial prostatitis according to the recommendations for complicated UTIs. | Strong |
| Chronic bacterial prostatitis (CBP) | |
| Prescribe a fluoroquinolone (e.g. ciprofloxacin, levofloxacin) as first-line treatment for CBP. | Strong |

| | |
|--|--------|
| Prescribe a macrolide (e.g. azithromycin) or a tetracycline (e.g. doxycycline) if intracellular bacteria have been identified as the causative agent of CBP. | Strong |
| Prescribe metronidazole in patients with <i>Trichomonas vaginalis</i> CBP. | Strong |

Table 6: Suggested regimens for antimicrobial therapy for chronic bacterial prostatitis

| Antimicrobial | Daily dose | Duration of therapy | Comments |
|----------------|-------------------------|---------------------|--|
| Floroquinolone | Optimal oral daily dose | 4-6 weeks | |
| Doxycycline | 100 mg b.i.d | 10 days | Only for <i>C. trachomatis</i> or mycoplasma infections. |
| Azithromycin | 500 mg 3x weekly | 3 weeks | Only for <i>C. trachomatis</i> infections |
| Metronidazole | 500 mg t.i.d. | 14 days | Only for <i>T. vaginalis</i> infections |

b.i.d = twice daily; t.i.d = three times daily; q.d = every day.

Acute Infective Epididymitis

Acute epididymitis is clinically characterised by pain, swelling and increased temperature of the epididymis, which may involve the testis and scrotal skin. It is generally caused by migration of pathogens from the urethra or bladder. Torsion of the spermatic cord (testicular torsion) is the most important differential diagnosis in boys and young men.

| Recommendations for the diagnosis and treatment of acute infective epididymitis | Strength rating |
|--|-----------------|
| Obtain a mid-stream urine and first voided urine for pathogen identification by culture and nucleic acid amplification test. | Strong |
| Initially prescribe a single antibiotic or a combination of two antibiotics active against <i>Chlamydia trachomatis</i> and Enterobacteriaceae in young sexually active men; in older men without sexual risk factors only Enterobacteriaceae have to be considered. | Strong |
| If gonorrhoeal infection is likely give single dose ceftriaxone 500 mg intramuscularly in addition to a course of an antibiotic active against <i>Chlamydia trachomatis</i> . | Strong |
| Adjust antibiotic agent when pathogen has been identified and adjust duration according to clinical response. | Weak |
| Follow national policies on reporting and tracing/treatment of contacts for sexually transmitted infections. | Strong |

Fournier's Gangrene

Fournier's gangrene is an aggressive and frequently fatal polymicrobial soft tissue infection of the perineum, peri-anal region, and external genitalia. It is an anatomical sub-category of necrotising fasciitis with which it shares a common aetiology and management pathway.

| Recommendations for the disease management of Fournier's Gangrene | Strength rating |
|---|-----------------|
| Start treatment for Fournier's gangrene with broad-spectrum antibiotics on presentation, with subsequent refinement according to culture and clinical response. | Strong |
| Commence repeated surgical debridement for Fournier's gangrene within 24 hours of presentation. | Strong |
| Do not use adjunctive treatments for Fournier's gangrene except in the context of clinical trials. | Weak |

Table 7: Suggested regimens for antimicrobial therapy for Fournier's Gangrene of mixed microbiological aetiology

| Antimicrobial | Dosage |
|--|--|
| Piperacillin-tazobactam plus vancomycin | 3.37 g every 6-8 h IV 15 mg/kg every 12 h |
| Imipenem-cilastatin | 1 g every 6-8 h IV |
| Meropenem | 1 g every 8 h IV |
| Ertapenem | 1 g once daily |
| Cefotaxime plus metronidazole or clindamycin | 2 g every 6 h IV 500 mg every 6 h IV 600-900 mg every 8 h IV |

IV = intravenous

Detection of bacteriuria prior to urological procedures

Identifying bacteriuria prior to diagnostic and therapeutic procedures aims to reduce the risk of infectious complications by controlling any pre-operative detected bacteriuria and to optimise antimicrobial coverage in conjunction with the procedure.

| Recommendation for the detection of bacteriuria prior to urological procedures | Strength rating |
|---|------------------------|
| Use laboratory urine culture to detect bacteriuria in patients prior to undergoing urological interventions breaching the mucosa. | Weak |

Peri-Procedural Antibiotic Prophylaxis

The available evidence enabled the panel to make recommendations concerning urodynamics, cystoscopy, stone procedures (extracorporeal shockwave lithotripsy, ureteroscopy and percutaneous nephrolithotomy), and transurethral resection of the prostate and bladder. For nephrectomy and prostatectomy the scientific evidence was too weak to allow the panel to make recommendations either for or against antibiotic prophylaxis.

| Recommendations for peri-procedural antibiotic prophylaxis | Strength rating |
|---|------------------------|
| Do not use antibiotic prophylaxis to reduce the rate of symptomatic urinary infection following: <ul style="list-style-type: none"> • urodynamics; • cystoscopy; • extracorporeal shockwave lithotripsy. | Strong |
| Use antibiotic prophylaxis to reduce the rate of symptomatic urinary infection following ureteroscopy. | Weak |
| Use single dose antibiotic prophylaxis to reduce the rate of clinical urinary infection following percutaneous nephrolithotomy. | Strong |

| | |
|--|--------|
| Use antibiotic prophylaxis to reduce infectious complications in men undergoing transurethral resection of the prostate. | Strong |
| Use antibiotic prophylaxis to reduce infectious complications in high-risk patients undergoing transurethral resection of the bladder. | Weak |

Prostate biopsy

Infection is the most clinically significant harm experienced by men following prostate biopsy. Infection generally occurs by implantation of rectal commensal organisms into the prostate, urethra or bloodstream during needle insertion. Severity of infection will depend on bacterial inoculum, virulence and status of host defence.

| Recommendations for non-antimicrobial intervention and antimicrobial prophylaxis prior to prostate biopsy | Strength rating |
|--|------------------------|
| Use rectal cleansing with povidone-iodine in men prior to transrectal prostate biopsy. | Strong |
| Use antimicrobial prophylaxis in men prior to transrectal prostate biopsy. | Strong |

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-01-1) available to all members of the European Association of Urology at their website, <http://www.uroweb.org/guidelines>.