

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.

Important notice:

On March 11, 2019 the European Commission implemented stringent regulatory conditions regarding the use of fluoroquinolones due to their disabling and potentially long-lasting side effects. This legally binding decision is applicable in all EU countries. National authorities have been urged to enforce this ruling and to take all appropriate measures to promote the correct use of this class of antibiotics.

Antimicrobial Stewardship

Stewardship programmes 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 programmes 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
<p>Do not screen or treat asymptomatic bacteriuria in the following conditions:</p> <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

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 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
Diagnose uncomplicated cystitis in women who have no other risk factors for complicated urinary tract infections based on: <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
Urine cultures should be done in the following situations: <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

In uncomplicated cystitis a fluoroquinolone should only be used when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.

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
<i>First-line women</i>			
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	400 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 trimenon of pregnancy
Trimethoprim- sulphamethoxazole	160/800 mg b.i.d	3 days	Not in the last trimenon 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 work-up (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, oral 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%.
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

Antimicrobials	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	
Gentamicin	5 mg/kg q.d	Not studied as monotherapy in acute uncomplicated pyelonephritis.
Amikacin	15 mg/kg q.d	

Last-line alternatives		
Imipenem/ cilastatin	0.5 g t.i.d	Consider only in patients with early culture results indicating the presence of multi-drug resistant organisms.
Meropenem	1 g t.i.d	
Ceftolozane/ tazobactam	1.5 g t.i.d	
Ceftazidime/ avibactam	2.5 g t.i.d	
Cefiderocol	2 g t.i.d	
Meropenem- vaborbactam	2 g t.i.d	
Plazomicin	15 mg/kg o.d	

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

Complicated UTIs

A complicated UTI 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 urology departments 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 sole indicator for catheter-associated (CA-UTI).	Strong
Do not use the presence or absence of odorous or cloudy urine alone to differentiate catheter-associated asymptomatic bacteriuria from CA-UTI.	Strong

Recommendations for disease management and prevention of CA-UTI	Strength rating
Treat symptomatic CA-UTI according to the recommendations for complicated UTI.	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 routinely use antibiotic prophylaxis 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
Initiate source control including removal of foreign bodies, decompression of obstruction and drainage of abscesses in 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 presents usually with lower urinary tract symptoms 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'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 gonococcal urethritis.	Strong
Perform a validated nucleic acid amplification test (NAAT) on a first-void urine sample or urethral smear prior to empirical treatment to diagnose chlamydial and gonococcal infections.	Strong
Delay treatment until the results of the NAATs are available to guide treatment choice in patients with mild symptoms.	Strong
Perform a urethral swab culture, prior to initiation of treatment, in patients with a positive NAAT for gonorrhoea to assess the antimicrobial resistance profile of the infective strain.	Strong
Use a pathogen directed treatment based on local resistance data.	Strong
Sexual partners should be treated maintaining patient confidentiality.	Strong

Table 5: Suggested regimens for antimicrobial therapy for urethritis

Pathogen	Antimicrobial	Alternative regimens
Gonococcal Infection:	Ceftriaxone: 1 g i.m. or i.v., SD Azithromycin: 1 g p.o., SD	<ul style="list-style-type: none">• Cefixime 400 mg p.o., SD plus Azithromycin 1 g p.o., SD <p>In case of cephalosporin allergy:</p> <ul style="list-style-type: none">• Gentamicin 240 mg i.m SD <u>plus</u> Azithromycin 2 g p.o., SD• Gemifloxacin 320 mg p.o., SD <u>plus</u> Azithromycin 2 g p.o., SD• Spectinomycin 2 g i.m., SD• Fosfomycin trometamol 3 g p.o., on days 1, 3 and 5 <p>In case of azithromycin allergy, in combination with ceftriaxone or cefixime:</p> <ul style="list-style-type: none">• Doxycycline 100 mg b.i.d, p.o., 7 days
Non-Gonococcal infection (non-identified pathogen)	Doxycycline: 100 mg b.i.d, p.o., 7-10 days	Azithromycin 500 mg p.o., day 1, 250 mg p.o., 4 days

<i>Chlamydia trachomatis</i>	Azithromycin: 1.0-1.5 g p.o., SD <u>OR</u> Doxycycline: 100 mg b.i.d, p.o., for 7 days	<ul style="list-style-type: none"> Levofloxacin 500 mg p.o., q.d., 7 days Ofloxacin 200 mg p.o., b.i.d., 7 days
<i>Mycoplasma genitalium</i>	Azithromycin: 500 mg p.o., day 1, 250 mg p.o., 4 days	In case of macrolide resistance: <ul style="list-style-type: none"> Moxifloxacin 400 mg q.d., 7-14 days
<i>Ureaplasma urealyticum</i>	Doxycycline: 100 mg b.i.d, p.o., 7 days	Azithromycin 1.0-1.5 g p.o., SD
<i>Trichomonas vaginalis</i>	Metronidazole: 2 g p.o., SD Tinidazole: 2 g p.o., SD	Metronidazole 500 mg p.o., b.i.d., 7 days

Persistent non-gonococcal urethritis

After first-line doxycycline	Azithromycin: 500 mg p.o., day 1, 250 mg p.o., 4 days <u>plus</u> Metronidazole: 400 mg b.i.d. p.o., 5 days	If macrolide resistant <i>M. genitalium</i> is detected moxifloxacin should be substituted for azithromycin
After first-line azithromycin	Moxifloxacin: 400 mg p.o. q.d., 7-14 days <u>plus</u> Metronidazole: 400 mg b.i.d. p.o., 5 days	

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
Do not perform prostatic massage in acute bacterial prostatitis (ABP).	Strong
Take a mid-stream urine dipstick to check nitrite and leukocytes in patients with clinical suspicion of ABP.	Weak
Take a mid-stream urine culture in patients with ABP symptoms to guide diagnosis and tailor antibiotic treatment.	Weak
Take a blood culture and a total blood count in patients presenting with ABP.	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.	Weak
Do not routinely perform microbiological analysis of the ejaculate alone to diagnose 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 UTI.	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 once daily	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.

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 a 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>C. 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 <u>plus</u> Vancomycin	4.5 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
Gentamicin	5 mg/kg daily
Cefotaxime <u>plus</u> metronidazole or clindamycin	2 g every 6 h IV 500 mg every 6 h IV 600-900 mg every 8 h IV
Cefotaxime <u>plus</u> fosfomycine <u>plus</u> metronidazole	2 g every 6 h IV 5 g every 8 h IV 500 mg every 6 h IV

IV = intravenous.

Peri-Procedural Antibiotic Prophylaxis

The available evidence enabled the panel to make recommendations concerning urodynamics, cystoscopy, stone procedures (extracorporeal shockwave lithotripsy, ureteroscopy and per-cutaneous nephrolithotomy), transurethral resection of the prostate, transurethral resection of the bladder and prostate biopsy. 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
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

Note: As stated in section 3.14.1.4 of the full text guideline the panel have decided not to make recommendations for specific

agents for particular procedures, those listed below represent possible choices only. Urologists should choose a specific antimicrobial based on their knowledge of local pathogen prevalence for each type of procedure, their antibiotic susceptibility profiles and virulence.

Table 8: Suggested regimens for antimicrobial prophylaxis prior to urological procedures

Procedure	Prophylaxis recommended	Antimicrobial
Urodynamics	No	
Cystoscopy	No	
Extracorporeal shockwave lithotripsy	No	
Ureteroscopy	Yes	Trimethoprim Trimethoprim-sulphamethoxazole Cephalosporin group 2 or 3 Aminopenicillin plus a beta-lactamase inhibitor
Percutaneous nephrolithotomy	Yes (single dose)	
Transurethral resection of the prostate	Yes	
Transurethral resection of the bladder	Yes in patients who have a high risk of suffering post-operative sepsis.	
Transrectal prostate biopsy	Yes	Fluoroquinolones if permitted Cephalosporins, fosfomycin, aminoglycosides, if fluoroquinolones are not permitted

This short booklet text is based on the more comprehensive AU Guidelines (ISBN 978-94-92671-07-3) available to all members of the European Association of Urology at their website, <http://www.uroweb.org/guidelines>.