

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.

Classification

Urinary tract infections encompass a wide spectrum of clinical and pathologic conditions affecting various parts of the urinary tract. Each condition has its own unique epidemiology, natural history, and diagnostic considerations. A precise distinction is crucial as it significantly impacts treatment and prognosis. Therefore, standardised terminology is essential for effective communication on this subject. The Guidelines Panel has proposed a new classification scheme for UTIs aimed at enhancing consistency in clinical practice and providing a comprehensive framework for understanding various clinical presentations. The proposed classification does not use the terms 'uncomplicated' and 'complicated' anymore; instead, it emphasises the difference between localised and systemic UTIs identified by clinical signs and symptoms.

Figure 1: Classification of UTI

Localised UTI (i.e., cystitis)	Systemic UTI
• Cystitis with typical signs/symptoms (e.g., frequency¹, urgency², suprapubic pain³) • No signs/symptoms of systemic infection • Applies to all sexes⁴ • Risk factors may be present and should be addressed	• UTI with signs/symptoms of systemic infection (e.g., fever⁵, chills⁶) • May also include typical local symptoms (e.g., for pyelonephritis⁷ or prostatitis⁸) • Risk factors may be present and should be addressed
	

Table 1: Localised and systematic signs and symptoms of UTI

Localised UTI¹	Systemic UTI^{1,2}
Dysuria (pain, burning, stinging)	Fever or hypothermia
Urgency	Rigors, shaking chills
Frequency	Delirium
Incontinence	Hypotension
Urethral purulence	Tachycardia
Pressure or cramping in the lower abdomen	Costovertebral angle pain/tenderness

1. Recent onset of these localised and/or systemic signs and symptoms.
2. These signs and symptoms are possibly caused by a systemic UTI, but there may also be alternative explanations.

Risk factors

When managing UTIs, it is essential to consider risk factors that may predispose patients to a severe clinical course or treatment failure. Importantly, in the proposed classification male sex alone is not considered as a risk factor, as it lacks support from contemporary literature. By identifying and addressing these risk factors early in the treatment process, clinicians can optimise patient care and improve treatment outcomes.

Table 2: UTI Risk Factors*

Infants	Immunocompromised state	Male sex • Prostatic involvement
Geriatric or frail patients	Post void residual volume	
Anatomic or functional abnormalities of the urinary tract	Neurourological patients	Female sex • Pregnancy • Pelvic organ prolapse
	Antibiotic use in the past	
Indwelling urinary catheters	Resistant organisms	
Stones	Obstruction	Recent instrumentation

**Both localised and systemic UTIs may be accompanied by risk factors that increase the likelihood of a challenging clinical course and jeopardise treatment success. Clinicians must be aware of these risk factors to adjust treatment if necessary.*

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
Do not screen or treat asymptomatic bacteriuria in the following conditions: • 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
Do not screen or treat asymptomatic bacteriuria in patients prior to cardiovascular surgeries.	Weak
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 or single dose fosfomycin trometamol.	Weak

Cystitis

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 cystitis	Strength rating
Diagnose cystitis in women who have no other risk factors for systemic urinary tract infections based on: • 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 cystitis.	Weak
Urine cultures should be done in the following situations: • 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 the management of cystitis	Strength rating
Non-antibiotic management	
Advise female patients on the possibility of an antibiotic-sparing approach for the treatment and prevention of acute and recurrent cystitis. Patients should be fully informed on the level of evidence for the different approaches.	Strong
Use a combination of xyloglucan, hibiscus, and propolis, or <i>Centaurii herba</i> , <i>Levistici radix</i> , <i>Rosmarini folium</i> to reduce recurrent cystitis episodes and reduce antibiotic use.	Weak
Antimicrobial therapy	
Prescribe fosfomycin trometamol, pivmecillinam or nitrofurantoin as first-line treatment for cystitis in women.	Strong
Use non-antibiotic therapy options as an alternative to antibiotic treatment in non-geriatric patients. Shared decision-making with patients is essential.	Strong
Do not use aminopenicillins or fluoroquinolones to treat cystitis.	Strong

Table 3: Suggested regimens for antimicrobial therapy in cystitis			
Antimicrobial	Daily dose	Duration of therapy	Comments
First-line women			
Fosfomycin trometamol	3 g SD	1 day	Recommended only in women with 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 E. coli 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 cystitis

Recurrent cystitis is defined by at least three episodes of cystitis/year or two episodes of cystitis in the last six months.

Recommendations for the diagnostic evaluation and treatment of recurrent cystitis	Strength rating
Diagnose recurrent cystitis 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 cystitis and no risk factors.	Weak
Advise pre-menopausal women regarding increased fluid intake as it might reduce the risk of recurrent cystitis.	Weak
Use vaginal oestrogen replacement in post-menopausal women to prevent recurrent cystitis.	Strong
Use immunomodulatory prophylaxis to reduce recurrent cystitis in women in the context of well-regulated clinical trials.	Weak
Advise patients on the use of a local or oral probiotic containing strains of proven efficacy for vaginal flora regeneration to prevent cystitis.	Weak
Advise patients on the use of cranberry products, favouring juice, for symptom relief in acute cystitis and to prevent recurrence; however, patients should be informed that the quality of evidence underpinning this is low with contradictory findings.	Strong

Use D-mannose to reduce recurrent cystitis episodes, but patients should be informed of the overall weak and contradictory evidence of its effectiveness.	Weak
Use methenamine hippurate to reduce recurrent cystitis episodes in women without abnormalities of the urinary tract.	Strong
Use endovesical instillations of hyaluronic acid or a combination of hyaluronic acid and chondroitin sulphate to prevent recurrent cystitis in patients where less invasive preventive approaches have been unsuccessful. Patients should be informed that further studies are needed to confirm the results of initial trials.	Weak
Use continuous or post-coital antimicrobial prophylaxis to prevent recurrent cystitis 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

Pyelonephritis

Pyelonephritis is suggested by fever ($> 38^{\circ}\text{C}$), chills, flank pain, nausea, vomiting, or costovertebral angle tenderness, with or without the typical symptoms of cystitis. Pregnant women with acute pyelonephritis need special attention, as this kind of infection may not only have an adverse effect on the mother with anaemia, renal and respiratory insufficiency, but also on the unborn child with more frequent pre-term labour and birth.

Recommendations for the diagnostic evaluation and treatment of pyelonephritis	Strength rating
Diagnostic evaluation	
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
Treatment	
Treat patients with pyelonephritis not requiring hospitalisation with short course fluoroquinolones as first-line treatment.	Strong
Treat patients with 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 pyelonephritis.	Strong

Table 4: Suggested regimens for empirical oral antimicrobial therapy in 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	Standard dosage: 500 mg oral q.d High dosage: 500 mg oral b.i.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 5: Suggested regimens for empirical parenteral antimicrobial therapy in pyelonephritis		
Antimicrobials	Daily dose	Comments
First-line treatment		
Ciprofloxacin	400 mg b.i.d	
Levofloxacin	Standard dosage: 500 mg oral q.d High dosage: 500 mg oral b.i.d	
Cefotaxime	2 g t.i.d	Not studied as monotherapy in acute pyelonephritis.

Ceftriaxone	Standard dosage: 2 g iv q.d High dosage: 2 g iv b.i.d	Lower dose studied, but higher dose recommended.
Second-line treatment		
Cefepime	Standard dosage: 1 g iv t.i.d or 2 g iv b.i.d High dosage: 2 g iv t.i.d	Lower dose studied, but higher dose recommended.
Piperacillin/ tazobactam	Standard dosage: 4.5 g t.i.d High dosage: 4.5 g q.i.d prolonged infusion	
Gentamicin	6-7 mg/kg q.d	Not studied as monotherapy in acute pyelonephritis.
Amikacin	25-30 mg/kg q.d	
Last-line alternatives		
Imipenem/ cilastatin	Standard dosage: 0.5 g iv q.i.d over 30 minutes High dosage: 1 g iv q.i.d over 30 minutes	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	15mg/kg o.d	

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

Systemic urinary tract infections

Systemic UTIs are infections that originate from various organs of the urinary tract. In contrast to localised UTIs (i.e., cystitis), these infections present typically with systemic signs and symptoms of infection. Local signs and symptoms of infection may also be present. Examples of systemic UTI include pyelonephritis, acute prostatitis, and urosepsis. Catheter-associated UTIs might present as localised as well as systemic infections.

Recommendations for the treatment of systemic UTIs	Strength rating
Use the combination of: • amoxicillin plus an aminoglycoside; • a second-generation cephalosporin plus an aminoglycoside; • a third generation cephalosporin.	Strong
Only use ciprofloxacin provided: • the local resistance percentages are < 10%; • the patient has contraindications for third generation cephalosporins or aminoglycosides; • the patient has a hypersensitivity for beta-lactam antimicrobials.	Strong
Do not use ciprofloxacin and other fluoroquinolones for the empirical treatment of systemic 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 (CA-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 UTI (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 disease management and prevention of CA-UTI	Strength rating
Treat symptomatic catheter-associated-UTI (CA-UTI) according to the recommendations for localised and systemic 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 CA-UTI.	Strong
Do not routinely use antibiotic prophylaxis to prevent clinical UTI after urethral catheter removal.	Weak
The duration of catheterisation should be minimal.	Strong
Use hydrophilic coated catheters to reduce CA-UTI.	Strong
Do not routinely use antibiotic prophylaxis to prevent clinical UTI after urethral catheter removal or in patients performing intermittent self-catheterisation.	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 6: 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	Standard dosage: 2 g q.d High dosage: 2 g iv b.i.d	
Cefepime	Standard dosage: 1 g iv t.i.d or 2 g iv bid High dosage: 2 g iv t.i.d	
Piperacillin/tazobactam	Standard dosage: 4 g piperacillin + 0.5 g tazobactam x 4 iv 30-minute infusion or x 3 iv by extended 4-hour infusion High dosage: 4 g piperacillin + 0.5 g tazobactam x 4 iv by extended 3-hour infusion	
Ceftolozane/tazobactam	1.5 g t.i.d	
Ceftazidime/avibactam	2.5 g t.i.d	
Gentamicin*	6-7 mg/kg q.d	
Amikacin*	25 - 30 mg/kg q.d	
Ertapenem	1 g q.d	
Imipenem/cilastatin	0.5 g q.i.d	
Meropenem	Standard dosage: 1 g t.i.d High dosage: 2 g iv t.i.d	

* Not studied as monotherapy in urosepsis

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

iv = intravenously.

Urethritis

Inflammation of the urethra presents usually with subjective symptoms (dysuria, alguria, burning, itching and pain around the distal urethra and external urethral meatus) and clinical signs (urethral discharge, erythema around the external urethral meatus and inguinal lymphadenopathy). These symptoms and signs must be distinguished from other infections of the lower urinary tract.

Recommendations for the diagnostic evaluation and 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
If possible, 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, while maintaining patient confidentiality.	Strong

Table 7: Suggested regimens for antimicrobial therapy for urethritis			
Suspected	Antimicrobial	Dosage & Duration of therapy	Alternative regimens
Gonococcal infection	Ceftriaxone Doxycycline	1-2 g i.m. or i.v.*, SD 100 mg b.i.d, p.o., 7 days	In case of doxycycline allergy, in combination with ceftriaxone: Azithromycin 4-day regimen: Day 1: 1 g; Days 2-4: 500 mg p.o.
Non-Gonococcal infection	Doxycycline	100 mg b.i.d, p.o., 7 days	Azithromycin 4-day regimen: Day 1: 1 g; Days 2-4: 500 mg p.o.

Table 8: Regimens for antimicrobial therapy for urethritis with causing pathogen detected

Pathogen	Antimicrobial	Dosage & Duration of therapy	Alternative regimens
<i>Neisseria gonorrhoeae</i>	Ceftriaxone Doxycycline	1-2 g i.m. or i.v.*, SD 100 mg b.i.d, p.o., 7 days	• Azithromycin 1 g p.o., SD, if <i>M. genitalium</i> has been excluded • Azithromycin 4-day regimen: Day 1 1 g; Days 2-4: 500 mg p.o. if <i>M. genitalium</i> cannot be ruled out • Cefixime 400 mg p.o., SD plus Azithromycin 1 g p.o., SD • Gentamicin 240 mg i.m SD plus Azithromycin 2 g p.o., SD • Gemifloxacin 320 mg p.o. SD plus Azithromycin 2 g p.o. SD • Spectinomycin 2 g i.m. SD • Fosfomycin trometamol 3 g p.o. on days 1, 3 and 5 In case of doxycycline allergy, in combination with ceftriaxone: Azithromycin 4-day regimen: Day 1: 1 g; Days 2-4: 500 mg orally

<i>Chlamydia trachomatis</i>	Doxycycline	100 mg b.i.d, p.o., for 7 days	• Azithromycin 1 g p.o., SD, if <i>M. genitalium</i> has been excluded • Azithromycin 4-day regimen: Day 1 1 g; Days 2–4: 500 mg orally if <i>M. genitalium</i> cannot be ruled out • Levofloxacin 500 mg p.o. q.d. 7 days • Ofloxacin 200 mg p.o. b.i.d., 7 days
<i>Mycoplasma genitalium</i>	Azithromycin	4-day regimen: Day 1 1 g; Days 2–4: 500 mg p.o.	In case of macrolide resistance: • Moxifloxacin 400 mg q.d., p.o., 7 days
<i>Ureaplasma urealyticum</i>	Doxycycline	100 mg b.i.d, p.o., 7 days	Azithromycin 1 g p.o., SD
<i>Trichomonas vaginalis</i>	Metronidazole	1.5-2 g p.o., SD	Tinidazole 2 g p.o., SD

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

* Despite the lack of RCTs there is increasing evidence that intravenous treatment with ceftriaxone is safe and effective for the treatment of gonorrhoeal infections and avoids the discomfort of an intramuscular injection for patients.

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 Mycoplasmas 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
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Recommendations for the management of bacterial prostatitis	Strength rating
Acute bacterial prostatitis	
Treat acute bacterial prostatitis according to the recommendations for systemic 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 9: 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.

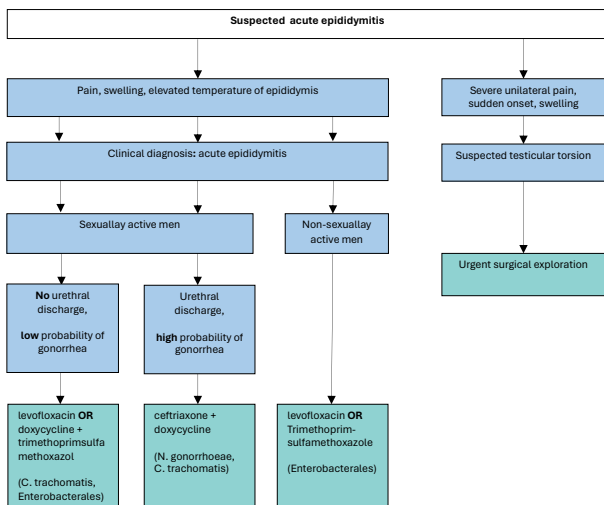
Acute Infective Epididymitis

Acute epididymitis is clinically characterised by unilateral pain, palpable swelling and increased temperature of the epididymis, which worsen over several days. The testis and scrotal skin may be involved. The pain is typically localised to the posterior aspect of the testis affected. Acute epididymitis is generally caused by STIs (sexually transmitted epididymitis) or *Enterobacterales*. Pathogens migrate from the urethra or bladder and can be identified by appropriate diagnostics in up to 90% of patients.

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 <i>Enterobacterales</i> in young sexually active men; in older men without sexual risk factors only <i>Enterobacterales</i> have to be considered.	Strong
If gonorrhoeal infection is likely, give single dose ceftriaxone 500 mg intramuscularly or intravenously* 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

* Despite the lack of RCTs, there is increasing evidence that intravenous treatment with ceftriaxone is safe and effective for the treatment of gonorrhoeal infections and avoids the discomfort of an intramuscular injection for patients.

Figure 2: Diagnostic and treatment algorithm for men with acute epididymitis



Diagnosis
 Treatment
 Follow-up

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

Antimicrobial	Dosage
Piperacillin-tazobactam <u>plus</u> Vancomycin	4.5 g q.i.d or t.i.d iv 15 mg/kg b.i.d
Imipenem-cilastatin	Standard dosage: 0.5 g iv q.i.d over 30 minutes High dosage: 1 g iv q.i.d over 30 minutes
Meropenem	1 g t.i.d iv
Ertapenem	1 g o.d
Gentamicin	6-7 mg/kg iv q.d

Cefotaxime <u>plus</u> metronidazole or clindamycin	2 g q.i.d iv 500 mg q.i.d iv 600-900 mg t.i.d iv
Cefotaxime <u>plus</u> fosfomycine <u>plus</u> metronidazole	2 g q.i.d iv 5 g t.i.d iv 500 mg q.i.d iv

iv = intravenous; b.i.d = twice daily; t.i.d = three times daily; q.i.d = four times daily, q.d = every day; o.d = once daily.

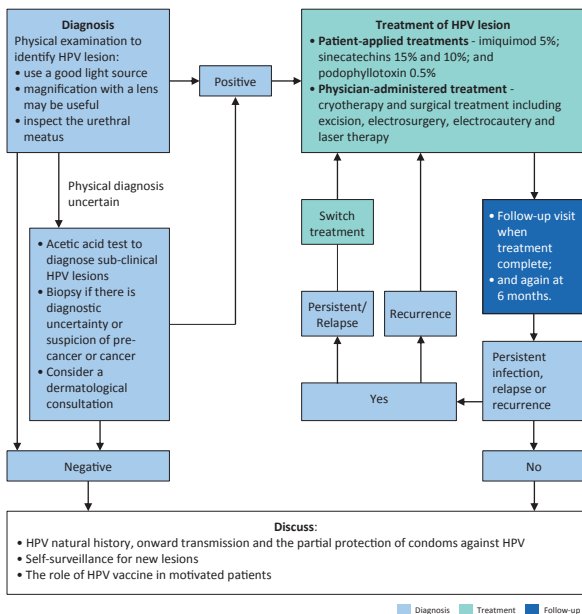
Management of Human papilloma virus in men

Human papilloma virus (HPV) is one of the most frequently sexually transmitted viruses encompassing both oncogenic (low- and high-risk variants) and non-oncogenic viruses.

Recommendations for the treatment of anogenital warts	Strength rating
Use self-administered imiquimod 5% cream applied to all external warts overnight three times each week for sixteen weeks for the treatment of anogenital warts.	Strong
Use self-administered sinecatechins 15% or 10% applied to all external warts three times daily until complete clearance, or for up to sixteen weeks for the treatment of anogenital warts.	Strong
Use self-administered podophyllotoxin 0.5% self-applied to lesions twice daily for three days, followed by four rest days, for up to four or five weeks for the treatment of anogenital warts.	Strong
Use cryotherapy or surgical treatment (excision, electrosurgery, electrocautery and laser therapy) to treat anogenital warts based on an informed discussion with the patient.	Strong

Recommendation male circumcision	
Discuss male circumcision with patients as an additional one-time preventative intervention for HPV-related diseases.	Strong
Recommendation therapeutic HPV vaccination	
Offer HPV vaccine to males after surgical removal of high-grade anal intraepithelial neoplasia.	Weak
Recommendations prophylactic HPV vaccination	
Offer early HPV vaccination to boys with the goal of establishing optimal vaccine-induced protection before the onset of sexual activity.	Strong
Apply diverse communication strategies in order to improve HPV vaccination knowledge in young adult males.	Strong

Figure 3: Management of Human papilloma virus in men



Herpes Simplex Virus

Genital herpes is a highly prevalent lifelong sexually transmitted disease caused by the Herpes Simplex Virus (HSV), which exists in two types: HSV-1 and HSV-2. Both HSV-1 and 2 result in chronic infection, with frequent reactivations and subclinical shedding, leading to a high risk of transmission to sexual partners. Diagnosis can be challenging, as ulcerative lesions may be absent during evaluation. When present, the lesions are typically painful, erythematous, vesicular, and recurrent. Less common presentations include nodular, hypertrophic, verrucous, vegetative or exophytic lesions.

Recommendations	Strength rating
Obtain a comprehensive medical history, including history of previous sexual contacts from all patients presenting with genital ulcers potentially related to HSV.	Strong
Confirm the diagnosis with a clinical swab and type-specific virologic testing, such as PCR or culture, from the lesion.	Strong
Treat the first clinical episode of genital HSV infection.	Strong

Table 11: Treatment regimens for genital HSV infection

Antimicrobials	Dosage
<i>Recommended therapy and dose for first clinical episode HSV</i>	
ACICLOVIR	400 mg orally t.i.d for 10 days OR 200 mg orally five times daily for 10 days.
VALACICLOVIR	500 mg orally b.i.d for 10 days.
<i>Recommended therapy and dose for recurrent genital HSV</i>	
ACICLOVIR	400 mg orally t.i.d for 5 days OR 800 mg b.i.d for 5 days OR 800 mg t.i.d for 2 days.
VALACICLOVIR	500 mg orally b.i.d for 3 days.

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

Genitourinary Tuberculosis (TB)

Genitourinary TB can affect all genitourinary organs and is almost always secondary due to the hematogenous spread of chronic latent TB infection. Diagnosis relies on a high suspicion of infection based on patient history; microbiological, molecular and histological testing; and imaging findings. Patients generally present with non-specific urological complaints for which no obvious cause is identified. Due to lack of high-quality evidence, the Panel is unable to give a recommendation on surgical treatment and imaging diagnostics at this point in time.

Recommendations for diagnosis and treatment of genitourinary tuberculosis	Strength rating
Diagnosis	
Take a full medical history including history of previous tuberculosis infection (pulmonary and extrapulmonary) from all patients presenting with persistent non-specific genitourinary symptoms and no identifiable cause.	Strong
Perform smear microscopy on urine, semen, tissue specimens, discharged or prostatic massage fluid using Ziehl–Neelsen (ZN) or auramine staining in patients with suspected genitourinary tuberculosis (GUTB).	Weak
Perform acid-fast bacilli culture on three midstream first-void urine samples, on three consecutive days for <i>M. tuberculosis</i> isolation in patients with suspected GUTB.	Strong
Use a recommended PCR test system in addition to microbiological reference standard (MRS) in urine specimens as a diagnostic test in patients with signs and symptoms of GUTB.	Weak
Use imaging modalities in combination with culture and/or PCR to aid in the diagnosis of GUTB and to assess the location and extent of damage to the genitourinary system.	Weak
Treatment	
Use medical treatment as first-line treatment for GUTB.	Strong

Use a daily six-month regimen for treatment of newly diagnosed GUTB, this should include an intensive phase of two months with isoniazid, rifampicin, pyrazinamide and ethambutol. Followed by a continuation phase of four-months with isoniazid and rifampicin.	Strong
Treat multi-drug resistant TB with an individualised treatment regime including at least five effective tuberculosis medicines during the intensive phase, including pyrazinamide and four core second-line tuberculosis medicines.	Strong

Table 12: Treatment regimens for newly diagnosed GUTB and MDR-TB

Antimicrobials	Dosage
<i>Six month regimen for treatment of newly diagnosed GUTB</i>	
Intensive two month phase	
Isoniazid	5 mg/kg q.d; max daily dosage 300 mg
Rifampicin	10 mg/kg q.d; max daily dosage 600 mg
Pyrazinamide	25 mg/kg q.d; max daily dosage 2000 mg
Ethambutol	15–20 mg/kg q.d; max daily dosage ranging from 800 mg to 1600 mg depending on body weight
Continuation four month phase	
Isoniazid	5 mg/kg q.d; max daily dosage 300 mg
Rifampicin	10 mg/kg q.d; max daily dosage 600 mg

Treatment regimen for multi-drug resistant TB

Treat multi-drug resistant TB with an individualised treatment regime including at least five effective tuberculosis medicines during the intensive phase, including pyrazinamide and four core second-line tuberculosis medicines*.

Group A Fluoroquinolones	Levofloxacin, Moxifloxacin and Gatifloxacin
Group B Second-line injectables	Amikacin, Capreomycin, Kanamycin and Streptomycin**
Group C Other second-line agents	Ethionamide/ Prothionamide, Cycloserine/ Terizidone, Linezolid and Clofazimine
Group D Add-on agents (not part of the core MDR-TB regime)	D1: Pyrazinamide, Ethambutol, and high-dose isoniazid D2: Bedaquiline and Delamanid D3: p-aminosalicylic acid, Imipenem-cilastatin, Meropenem, Amoxicillin-clavulanate and Thioacetazone***

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

** Drugs should be chosen as follows: 1 from group A, 1 from group B, and at least 2 from group C. If the minimum number of five TB medicines cannot be composed from drugs included in Groups A to C, an agent from group D2 and other agents from group D3 may be added to bring the total to five.*

***Streptomycin can substitute other injectable drugs if none of these agents can be used and if the strain is shown not to be resistant.*

****Thioacetazone should not be used if the patient is HIV seropositive.*

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: • 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
Perform prostate biopsy using the transperineal approach due to the lower risk of infectious complications and better antibiotic stewardship.	Strong
Use rectal cleansing with povidone-iodine in men prior to transrectal prostate biopsy.	Strong
Do not use fluoroquinolones for prostate biopsy in line with the European Commission final decision on EMEA/H/A-31/1452.	Strong

For antibiotic prophylaxis in transrectal biopsy*, and from an antimicrobial stewardship perspective, the following options are recommended**: • First option: Targeted prophylaxis based on rectal swab or stool culture. • Second option: Augmented prophylaxis (using two or more different classes of antibiotics).	Strong
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**Of note the indication of fosfomycin trometamol for prostate biopsy has been withdrawn in Germany as the manufacturers did not submit the necessary pharmacokinetic data in support of this indication. Urologists are advised to check their local guidance in relation to the use of fosfomycin trometamol for prostate biopsy.*

***While most studies have been performed using fluoroquinolones, the applicability of these findings to non-fluoroquinolone antibiotics remains unclear.*

The panel has 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 13: Suggested regimens for antimicrobial prophylaxis prior to urological procedures

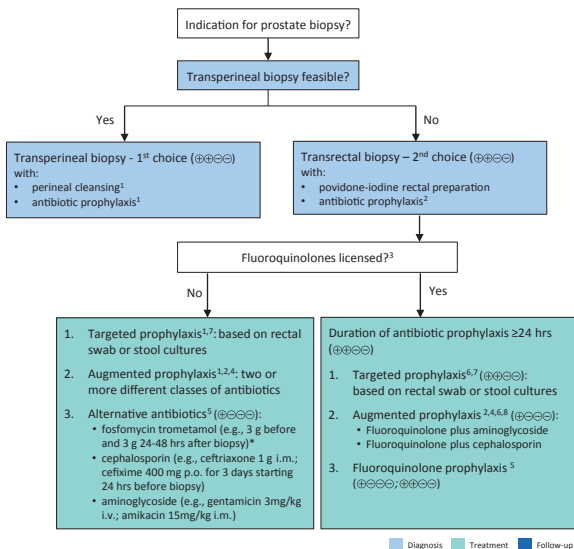
Procedure	Prophylaxis recommended	Antimicrobial
Urodynamics	No	N/A
Cystoscopy	No	
Extracorporeal shockwave lithotripsy	No	

Ureteroscopy	Yes	Trimethoprim Trimethoprim- sulphamethoxazole Cephalosporin group 2 or 3 Aminopenicillin <u>plus</u> 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	1. Targeted prophylaxis - based on rectal swab or stool culture. 2. Augmented prophylaxis - two or more different classes of antibiotics*. 3. Alternative antibiotics • fosfomycin trometamol** (e.g., 3 g before and 3 g 24-48 hrs after biopsy) • cephalosporin (e.g., ceftriaxone 1 g i.m.; cefixime 400 mg p.o. for 3 days starting 24 hrs before biopsy) • aminoglycoside (e.g., gentamicin 6-7 mg/kg iv q.d.; amikacin 25-30 mg/kg iv q.d.)

* Note option 2 is against antibiotic stewardship programmes

** Of note the indication of fosfomycin trometamol for prostate biopsy has been withdrawn in Germany as the manufacturers did not submit the necessary pharmacokinetic data in support of this indication. Urologists are advised to check their local guidance in relation to the use of fosfomycin trometamol for prostate biopsy.

Figure 4: Prostate biopsy workflow to reduce infectious complications



Suggested workflow on how to reduce post biopsy infections.

1. Two systematic reviews including non-RCTs and two RCTs describe comparable rates of post-biopsy infection in patients with and without antibiotic prophylaxis.
2. Be informed about local antimicrobial resistance.
3. Banned by European Commission due to side effects.
4. Contradicts principles of Antimicrobial Stewardship.
5. Fosfomycin trometamol (4 RCTs), cephalosporins (2 RCTs), aminoglycosides (2 RCTs).
6. Only one RCT comparing targeted and augmented prophylaxis.
7. Originally introduced to use alternative antibiotics in case of fluoroquinolone resistance.

8. Various schemes: fluoroquinolone plus aminoglycoside (4 RCTs); and fluoroquinolone plus cephalosporin (1 RCT).
9. Significantly inferior to targeted and augmented prophylaxis.

High certainty: (⊕⊕⊕⊕) very confident that the true effect lies close to that of the estimate of the effect. Moderate certainty: (⊕⊕⊕○) moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Low certainty: (⊕⊕○○) confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect. Very low certainty: (⊕○○○) very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect. Figure reproduced from Pilatz et al., with permission from Elsevier.

* Of note the indication of fosfomycin trometamol for prostate biopsy has been withdrawn in some countries as the manufacturers did not submit the necessary pharmacokinetic data in support of this indication. Urologists are advised to check their local guidance in relation to the use of fosfomycin trometamol for prostate biopsy.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-29-5) available to all members of the European Association of Urology at their website, <http://www.uroweb.org/guidelines>.