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

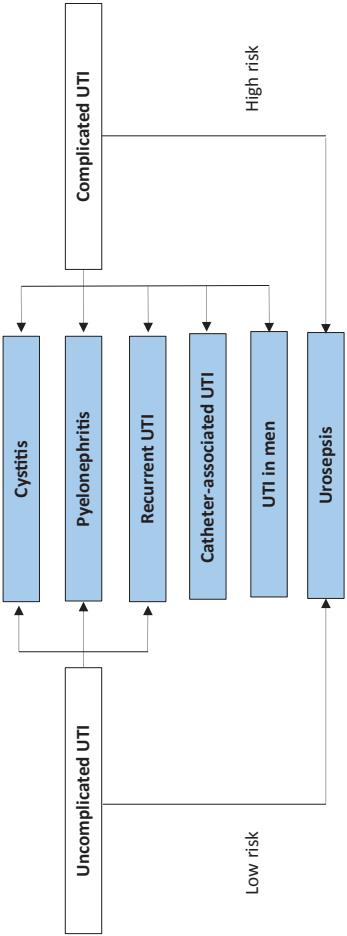
Stewardship programs have two main sets of actions. The first set mandates use of recommended care at the patient level conforming to guidelines. The second set describes strategies to achieve adherence to the mandated guidance. These include persuasive actions such as education and feedback together 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 ≥ 105 cfu/mL in two consecutive samples in women and in one single sample in men.

Figure 1: Concept of uncomplicated and complicated UTI



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 arthoplasty 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

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: • a focused history of lower urinary tract symptoms (dysuria, frequency and urgency); • the absence of vaginal discharge.	Strong
Use urine dipstick testing for diagnosis of acute uncomplicated 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

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
First-line women			
Fosfomycin trometamol	3 g SD	1 day	First-line women 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 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 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 pre-menopausal women regarding increased fluid intake as it might reduce the risk of recurrent UTI.	Weak
Use vaginal oestrogen replacement in post-menopausal women to prevent recurrent UTI.	Strong
Use immunoactive prophylaxis to reduce recurrent UTI in all age groups.	Strong
Advise patients on the use of a local or oral probiotic containing strains of proven efficacy for vaginal flora regeneration to prevent UTIs.	Weak

Advise patients on the use of cranberry products to reduce recurrent UTI episodes; however, patients should be informed that the quality of evidence underpinning this is low with contradictory findings.	Weak
Use D-mannose to reduce recurrent UTI episodes, but patients should be informed of the overall weak and contradictory evidence of its effectiveness.	Weak
Use methenamine hippurate to reduce recurrent UTI 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 UTIs 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 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: 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	2g t.i.d	
Meropenem-vaborbactam	2g 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.

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: • 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; • 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 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 disease management and prevention of CA-UTI	Strength rating
Treat symptomatic catheter-associated-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
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 catheter-associated UTIs.	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 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 CDC'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: 1-1 g p.o., SD	• Cefixime 400 mg p.o., SD plus Azithromycin 1 g p.o., SD In case of cephalosporin allergy: • 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 azithromycin allergy, in combination with ceftriaxone or cefixime: • 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 days	Azithromycin 500 mg p.o., day 1, 250 mg p.o., 4 days

Chlamydia trachomatis	Azithromycin: 1.0-1.5 g p.o., SD OR Doxycycline: 100 mg b.i.d, p.o., for 7 days	• Levofloxacin 500 mg p.o., q.d., 7 days • Ofloxacin 200 mg p.o., b.i.d., 7 days
Mycoplasma genitalium	Azithromycin: 500 mg p.o., day 1, 250 mg p.o., 4 days	In case of macrolide resistance: • Moxifloxacin 400 mg q.d., 7-14 days
Ureaplasma urealyticum	Doxycycline: 100 mg b.i.d, p.o., 7 days	Azithromycin 1.0-1.5 g p.o., SD
Trichomonas vaginalis	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 plus Metronidazole: 400 mg b.i.d. p.o., 5 days	If macrolide resistant *M. genitalium* is detected moxifloxacin should be substituted for azithromycin
After first-line azithromycin	Moxifloxacin: 400 mg p.o. q.d., 7–14 days plus 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; i.v. = intravenous.

** 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 *Chlamydia trachomatis* 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 *T. vaginalis* 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 *C. trachomatis* or mycoplasma infections
Azithromycin	500 mg once daily	3 weeks	Only for *C. trachomatis* infections
Metronidazole	500 mg t.i.d.	14 days	Only for *T. vaginalis* infections

b.i.d = twice daily; t.i.d = three times daily.

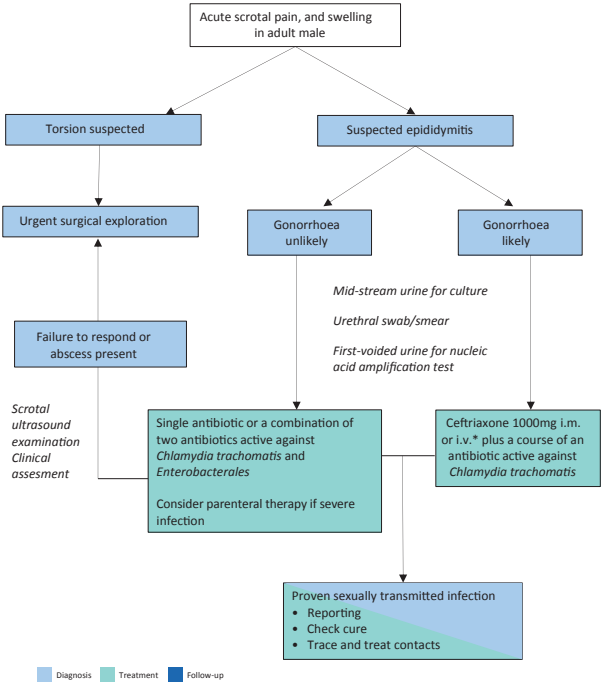
Acute Infective Epididymitis

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 *Chlamydia trachomatis* 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 1000 mg intramuscularly or intravenously* in addition to a course of an antibiotic active against *Chlamydia trachomatis*.	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



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	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 plus metronidazole or clindamycin	2 g every 6 h IV 500 mg every 6 h IV 600-900 mg every 8 h IV

Cefotaxime plus fosfomycine plus metronidazole	2 g every 6 h IV 5 g every 8 h IV 500 mg every 6 h IV

IV = intravenous.

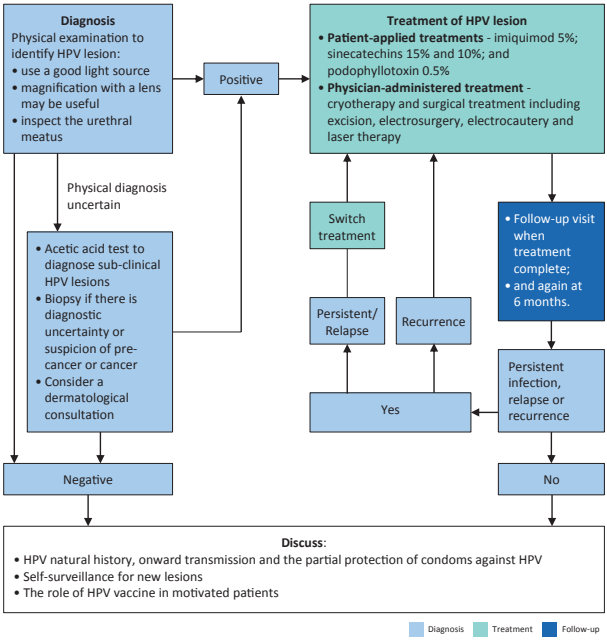
Management of Human papilloma virus in men

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 imiquimd 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



Genitourinary Tuberculosis

Genitourinary TB can affect all genitourinary organs and is almost always secondary due to the haematogenous 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 are 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-fact bacilli culture on three midstream first-void urine samples, on three consecutive days for *M. tuberculosis* 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 8: Treatment regimens for newly diagnosed GUTB and MDR-TB

Antimicrobials	Dosage
Six month regimen for treatment of newly diagnosed GUTB	
Intensive two month phase	
Isoniazid	5 mg/kg every 24 h; max daily dosage 300 mg
Rifampicin	10 mg/kg every 24 h; max daily dosage 600 mg
Pyrazinamide	25 mg/kg every 24 h; max daily dosage 2000 mg
Ethambutol	15–20 mg/kg every 24 h; max daily dosage ranging from 800 mg to 1600 mg depending on body weight
Continuation four month phase	
Isoniazid	5 mg/kg every 24 h; max daily dosage 300 mg
Rifampicin	10 mg/kg every 24 h; max daily dosage 600 mg

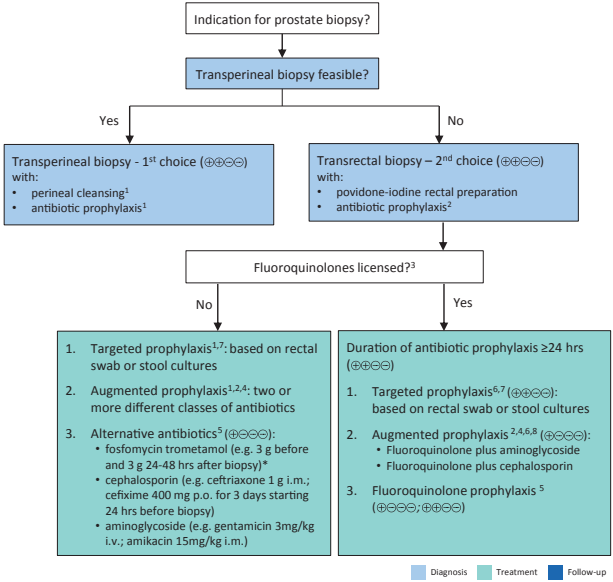
Treatment regimen for multi-drug resistant TB	
Treat multi-drug resistant TB with an individualised treatment regime including at least five effective tuberculosis medicines during the intensive phase, including pyrazinamide and four core second-line tuberculosis medicines*.	
Group A Fluoroquinolones	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 Delamamid D3: p-aminosalicylic acid, Imipenem-cilastatin, Meropenem, Amoxicillin-clavulanate and Thioacetazone***

** 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 neprolithotomy), 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.

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.*

GRADE Working Group grades of evidence. 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 adapted from Pilatz et al., with permission from Elsevier.

** 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.*

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.	Strong
Use routine surgical disinfection of the perineal skin for transperineal biopsy.	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
Use either target prophylaxis based on rectal swab or stool culture; augmented prophylaxis (two or more different classes of antibiotics); or alternative antibiotics (e.g. fosfomycin trometamol*, cephalosporin, aminoglycoside) for antibiotic prophylaxis for transrectal biopsy.	Weak

**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.*

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 9: 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 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	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 3mg/kg i.v.; amikacin 15mg/kg i.m.)

** 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.*

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-23-3) available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines.