EAU GUIDELINES ON UROLOGICAL INFECTIONS

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Introduction

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

Antimicrobial Stewardship

Antimicrobial stewardship programmes aim to optimise the outcome of prevention and treatment of infection whilst curbing overuse and misuse of antimicrobial agents. The most 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, with audit;
- treatment outcome evaluation;
- monitoring and regular feedback to prescribers of their antimicrobial prescribing 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 ≥ 10^5 cfu/ml, in two consecutive samples in women and in a single sample in men

Recommendations for the management of asymptomatic bacteriuria	LE	GR
Do not screen or treat asymptomatic bacteriuria in the following conditions:		
• women without risk factors;	2a	A*
• patients with well-regulated diabetes mellitus;	1b	A
• post-menopausal women;	1a	A
• elderly institutionalised patients;	1a	A
• patients with dysfunctional and/or reconstructed lower urinary tracts;	2b	B
• patients with catheters in the urinary tract;	4	C
• patients with renal transplants;	1b	A
• patients prior to arthoplasty surgeries;	1b	A
• patients with recurrent urinary tract infections.	1b	A
Screen for and treat asymptomatic bacteriuria prior to urological procedures breaching the mucosa.	1a	A
Screen for and treat asymptomatic bacteriuria in pregnant women with standard short course treatment.	1a	A
Take a urine culture following treatment of asymptomatic bacteriuria to secure treatment effect.	4	C

** Upgraded based on panel consensus.*

Uncomplicated cystitis

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

Recommendations for the diagnostic evaluation of uncomplicated cystitis	LE	GR
Diagnose uncomplicated cystitis based on: • a focused history of lower urinary tract symptoms (dysuria, frequency and urgency); • the absence of vaginal discharge or irritation, in women who have no other risk factors for complicated urinary tract infections.	2a	B
Use urine dipstick testing, as an alternative to culture for diagnosis of acute uncomplicated cystitis.	2a	B
Urine cultures should be done in the following situations: • suspected acute pyelonephritis; • symptoms that do not resolve or recur within two-four weeks after the completion of treatment; • women who present with atypical symptoms; • pregnant women.	4	B*

** Upgraded based on panel consensus.*

Recommendations for treatment of uncomplicated cystitis					
Antimicrobial	**Daily dose**	**Duration of therapy**	**Comments**	**LE**	**GR**
First choice					
Fosfomycin trometamol	3 g SD	1 day	Recommended in women not men.	1	A
Nitrofurantoin macrocrystal	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	1b	B
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.	1b	B
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, fluoro-quinolones can also be prescribed in accordance with local susceptibility testing.	4	C

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 recurrent UTIs	LE	GR
Do not perform an extensive routine workup in women with recurrent UTI without risk factors.	1b	B
Advise patients on behavioural modifications which might reduce the risk of recurrent UTI.	3	C
Use vaginal oestrogen replacement in post-menopausal women to prevent recurrent UTI.	1b	A
Use immunoactive prophylaxis to reduce recurrent UTI in all age groups.	1a	A
When non-antimicrobial interventions have failed continuous or post-coital antimicrobial prophylaxis should be used to prevent recurrent UTI, but patients should be counselled regarding possible side effects.	2b	B
For patients with good compliance self-administrated short term antimicrobial therapy should be considered.	2b	A*

** Upgraded based on panel consensus.*

Uncomplicated pyelonephritis

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

Recommendations for the diagnostic evaluation of uncomplicated pyelonephritis	LE	GR
Perform urinalysis (e.g. using a dipstick method), including the assessment of white and red blood cells and nitrite.	4	A*
Perform urine culture and antimicrobial susceptibility testing in patients with pyelonephritis.	4	A*
Perform ultrasound of the upper urinary tract to exclude obstructive pyelonephritis.	4	A*
Additional imaging investigations, such as an unenhanced helical computed tomography should be done if the patient remains febrile after 72 hours of treatment or in patients with suspected complications e.g. sepsis.	4	A*

**Upgraded based on panel consensus.*

Recommendations for empirical oral antimicrobial therapy in uncomplicated pyelonephritis					
Antimicrobial	**Daily dose**	**Duration of therapy**	**LE**	**GR**	**Comments**
Ciprofloxacin	500-750 mg b.i.d	7-10 days	1b	B	Fluoroquinolone resistance should be < 10%.
Levofloxacin	750 mg q.d	5 days	1b	B	
Trimethoprim sulphamethoxazol	160/800 mg b.i.d	7-14 days	1b	B	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	4	B*	
Ceftibuten	400 mg q.d	10 days	4	B*	

**Upgraded based on panel consensus.*
b.i.d = twice daily; q.d = every day.

Recommendations for empirical parenteral antimicrobial therapy in uncomplicated pyelonephritis				
Anti-microbials	**Daily dose**	**LE**	**GR**	**Comments**
Ciprofloxacin	400 mg b.i.d	1b	B	
Levofloxacin	750 mg q.d	1b	B	
Cefotaxime	2 g t.i.d	2	A*	Not studied as monotherapy in acute uncomplicated pyelonephritis.
Ceftazidime	1-2 g t.i.d	2	A*	
Co-amoxiclav	1.5 g t.i.d	2	C	Not studied as monotherapy in acute uncomplicated pyelonephritis. Mainly for Gram-positive pathogens.
Ceftriaxone	1-2 g q.d	1b	A*	Lower dose studied, but higher dose recommended. Same protocol for acute uncomplicated pyelonephritis and complicated UTI (stratification not always possible).
Cefepime	1-2 g b.i.d	1b	B	
Piperacillin/ tazobactam	2.5-4.5 g t.i.d	1b	A*	
Ceftolozane/ tazobactam	1.5 g t.i.d	1b	B	
Ceftazidime/ avibactam	2.5 g t.i.d	1b	B	
Gentamicin	5 mg/ kg q.d	1b	B	Not studied as monotherapy in acute uncomplicated pyelonephritis.
Amikacin	15 mg/ kg q.d	1b	B	
Ertapenem	1 g q.d	1b	B	Same protocol for acute uncomplicated pyelonephritis and complicated UTI (stratification not always possible).
Imipenem/ cilastatin	0.5/0.5 g t.i.d	1b	B	
Meropenem	1 g t.i.d	2	B	
Doripenem	0.5 g t.i.d	1b	B	

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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	LE	GR
Do not use amoxicillin, co-amoxiclav, trimethoprim and trimethoprim-sulphamethoxazole for empirical treatment of complicated UTI.	2	A
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.	2	A
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.	2	A
Do not use ciprofloxacin and other fluoroquinolones for the empirical treatment of complicated UTI in patients from the urology department or when patients have used fluoroquinolones in the last six months.	2	A

Use an initial one-time intravenous dose of a long-acting antimicrobial, such as a third generation cephalosporin or an aminoglycoside if the prevalence of fluoroquinolone resistance is thought to be > 10% and resistance data are pending.	2	A
If the prevalence of fluoroquinolone resistance is thought to be > 10% and the patient has contra indications for third generation cephalosporins or an aminoglycoside, ciprofloxacin can be prescribed as an empirical treatment in women with uncomplicated pyelonephritis.	2	A
In the event of hypersensitivity to penicillin, a third generation cephalosporin can still be prescribed, with the exception of systemic anaphylaxis in the past.	2	A
In patients with a UTI with systemic symptoms empirical treatment should cover ESBL in the initial treatment only in patients who are colonised with ESBL-producing micro-organisms. The resistance pattern of the ESBL strain should guide empirical therapy.	2	A

ESBL = Extended-spectrum beta-lactamase.

Catheter-associated UTIs

Catheter-associated urinary tract infection 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 catheter-associated UTIs	LE	GR
Do not carry out routine urine culture in asymptomatic catheterised patients.	1a	A
Do not use pyuria as an indicator for catheter-associated UTI.	2	A
Do not use the presence, absence, or degree of pyuria to differentiate catheter-associated asymptomatic bacteriuria from catheter-associated UTI.	2	A
Do not use the presence or absence of odorous or cloudy urine alone to differentiate catheter-associated asymptomatic bacteriuria from catheter-associated UTI.	3	C

Recommendations for disease management and prevention of catheter-associated UTIs	LE	GR
Take a urine culture prior to initiating antimicrobial therapy in catheterised patients in whom the catheter has been removed.	3	A*
Do not treat catheter-associated asymptomatic bacteriuria in general.	1a	A
Treat catheter-associated asymptomatic bacteriuria prior to traumatic urinary tract interventions (e.g. transurethral resection of the prostate).	1a	A
Replace or remove the indwelling catheter before starting antimicrobial therapy.	4	B*
Do not apply topical antiseptics or antimicrobials to the catheter, urethra or meatus.	1a	A
Do not use prophylactic antimicrobials to prevent catheter-associated UTIs.	1a	A

The duration of catheterisation should be minimal.	2a	B
Remove an indwelling catheter after non-urological operation within the same day.	1b	B
Change long-term indwelling catheters at intervals adapted to the individual patient.	3	C

** Upgraded based on panel consensus.*

Urosepsis

Urosepsis is a systemic, deleterious host response to infection originating from the urinary tract and/or male genital organs. Urosepsis is accompanied by signs of systemic inflammation, presence of symptoms of organ dysfunction and persistent hypotension associated with tissue anoxia.

Recommendations for parenteral antimicrobial therapy of urosepsis				
Anti-microbials	**Daily dose**	**LE**	**GR**	**Comments**
Cefotaxime	2 g t.i.d	2	A*	Not studied as monotherapy in acute uncomplicated pyelonephritis.
Ceftazidime	1-2 g t.i.d	2	A*	
Ceftriaxone	1-2 g q.d	1b	A*	Lower dose studied, but higher dose recommended. Same protocol for acute uncomplicated pyelonephritis and complicated UTI (stratification not always possible).
Cefepime	1-2 g b.i.d	1b	B	
Piperacillin/ tazobactam	2.5-4.5 g t.i.d	1b	A*	
Ceftolozane/ tazobactam	1.5 g t.i.d	1b	B	
Ceftazidime/ avibactam	2.5 g t.i.d	1b	B	
Gentamicin	5 mg/kg q.d	1b	B	Not studied as monotherapy in acute uncomplicated pyelonephritis.
Amikacin	15 mg/kg q.d	1b	B	
Ertapenem	1 g q.d	1b	B	Same protocol for acute uncomplicated pyelonephritis and complicated UTI (stratification not always possible).
Imipenem/ cilastatin	0.5/0.5 g t.i.d	1b	B	
Meropenem	1 g t.i.d	2	B	
Doripenem	0.5 g t.i.d	1b	B	

** Upgraded based on panel consensus.*
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Urethritis

Inflammation of the urethra presents usually with symptoms of the lower urinary tract (LUT) and must be distinguished from other infections of the LUT. From a therapeutic and clinical point of view, gonorrhoeal urethritis must be differentiated from non-gonococcal urethritis.

Recommendations for the diagnostic evaluation of urethritis	LE	GR
Use a gram stain of urethral discharge or a urethral smear to preliminarily diagnosis pyogenic urethritis.	3	B
Use a validated nucleic acid amplification test to diagnosis chlamydial and gonococcal infections.	3	B

Recommendations for antimicrobial therapy of urethritis					
Pathogen	**Antimicrobial**	**Dosage & Duration of therapy**	**LE**	**GR**	**Alternative regimens**
Gonococcal Infection	Ceftriaxone	1 g i.m., SD	1a	A	Cefixime 400 mg p.o., SD **Or** Azithromycin 1-1.5 g p.o., SD
	Azithromycin	1-1.5 g p.o., SD			
	Cefixime	800 mg p.o., SD			
Non-Gonococcal infection (non-identified pathogen)	Doxycycline	100 mg b.i.d, p.o., 7-10 days	1b	A	Azithromycin 0.5 g p.o., day 1, 250 mg p.o., day 2-5
Chlamydia trachomatis	Azithromycin	1.0-1.5 g p.o., SD	1b	A	Doxycycline 100 mg b.i.d, p.o., for 7 days

Mycoplasma genitalium	Azithromycin	0.5 g p.o., day 1, 250 mg p.o., day 2-5	2a	B	Moxifloxacin 400 mg q.d., 5 days; however, because of reported failures, some experts recommend 10 -14 days
Ureaplasma urealiticum	Doxycycline	100 mg b.i.d, p.o., 7 days	1b	A	Azithromycin 1.0-1.5 g p.o., single dose **Or** clarithromycin 500 mg b.i.d, 7 days (resistance against macrolides is possible)
Trichomonas vaginalis	Metronidazole	2 g p.o., SD	1a	A	In case of persistence 4 g daily for 3-5 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 infection of the prostate gland. It is recommended that urologists use the classification suggested by the National Institute of Diabetes, Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health (NIH), in which bacterial prostatitis, with confirmed or suspected infection, is distinguished from chronic pelvic pain syndrome.

Recommendations for the diagnostic evaluation of bacterial prostatitis	LE	GR
Perform digital rectal examination to assess the condition of the prostate.	4	A*
Take a mid-stream urine culture in patients with acute prostatitis-related symptoms for diagnosis and targeted treatment planning.	3	A*
Perform the Meares and Stamey four-glass test in patients with chronic bacterial prostatitis.	2b	B
Accurate microbiological evaluation for atypical pathogens such as *Chlamydia trachomatis* or *Mycoplasmata* is recommended in patients with chronic bacterial prostatitis.	2b	B
Perform transrectal ultrasound only in selected cases to rule out the presence of prostatic abscess, calcification in the prostate and dilatation of the seminal vesicles.	3	B
Ejaculate analysis and prostate specific antigen measurement should not be performed as routine, due to the high number of false positive results.	3	B

**Upgraded based on panel consensus.*

Recommendations for the disease management of bacterial prostatitis					
Antimicrobial	**Daily dose**	**Duration of therapy**	**LE**	**GR**	**Comments**
Acute febrile bacterial prostatitis with symptoms and fever					
Levofloxacin	500 mg q.d	All parental treatment should be given until deferves-cence	2	B	All of these anti-microbials can be administered in conjunction with amino-glycosides e.g. Gentamicin 5 mg/kg q.d or Amikiacin 15 mg/kg q.d.
Ciprofloxacin	500 mg b.i.d				
Ceftriaxone	2 g q.d				
Piperacillin/ tazobactam	4.5 g t.i.d				
Cefepime	2 g b.i.d				
Acute afebrile bacterial prostatitis with symptoms or after defervescence					
Levofloxacin	500 mg q.d	2-4 weeks	2	B	
Ciprofloxacin	500 mg b.i.d or 1000 mg p.d	2-4 weeks			
Trimethoprim	200 mg b.i.d	2-4 weeks			
Co-trimoxazole	960 mg b.id	2-4 weeks			
Doxycycline	100 mg b.i.d	10 days	2	B	Only for *Chlamydia trachomatis* or mycoplasma infections.

Chronic bacterial prostatitis					
Levofloxacin	500 mg q.d	4-6 weeks	3	B	
Ciprofloxacin	500 mg b.i.d or 1000 mg q.d	4-6 weeks			
Trimethoprim	200 mg b.i.d	4-6 weeks			
Co-trimoxazole	960 mg b.i.d	4-6 weeks			
Doxycycline	100 mg b.i.d	10 days	2	B	Only for *Chlamydia trachomatis* or mycoplasma infections.

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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. The predominant pathogens isolated are *Chlamydia trachomatis*, Enterobacteriaceae (typically *Escherichia coli*) and *Neisseria gonorrhoeae*.

Recommendations for the treatment of acute infective epididymitis	LE	GR
Obtain a mid-stream urine and a first voided urine for pathogen identification.	3	A*
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.	3	A*
If gonorrhoeal infection is likely give single dose ceftriaxone 500 mg intramuscularly in addition to a course of an antibiotic active against *Chlamydia trachomatis*.	3	A*
Adjust antibiotic agent when pathogen has been identified and adjust duration according to clinical response.	3	A*
Follow national policies on reporting and tracing/treatment of contacts for sexually transmitted infections.	3	A*

** Upgraded based on Panel consensus.*

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. Evidence regarding investigation and treatment is predominantly from case series.

Recommendations for the disease management of Fournier's Gangrene	LE	GR
Commence full, repeated surgical debridement within 24 hours of presentation.	3	B
Start treatment with broad-spectrum antibiotics on presentation, with subsequent refinement according to culture and clinical response.	3	A*
Do not use adjunctive treatments such as pooled immunoglobulin and hyperbaric oxygen, except in the context of clinical trials.	3	A*

** Upgraded based on panel consensus.*

Detection of bacteriuria prior to urological procedures

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

Recommendation	LE	GR
Laboratory urine culture is the recommended method to determine the presence or absence of clinically significant bacteriuria in patients prior to undergoing urological interventions.	3	B

Perioperative antibacterial prophylaxis in urology

The aim of antimicrobial prophylaxis in urology is to prevent infectious complications resulting from diagnostic and therapeutic procedures. However, evidence for the best choice of antimicrobials and regimens is limited.

Recommendations for peri-operative antibacterial prophylaxis in urology				
Procedure	**Comments**	**Antimicrobial prophylaxis**	**LE**	**GR**
Diagnostic procedures				
Cystoscopy	Low frequency of infection. Consider individual risk factors for UTI (i.e. asympto-matic bacteriuria, history of febrile UTI).	No	1b	A
Urodynamic study	Low frequency of infections. Consider individual risk factors for UTI (i.e. asympto-matic bacteriuria, history of febrile UTI).	No	1a	A
Transrectal core biopsy of prostate	High risk of infection.	Fluoroquinolones Trimethoprim ± sulphamethoxazole. Targeted alterna-tive.	1b	A
Diagnostic ureteroscopy	No available studies.	Optional	4	C

Common endourological/endoscopic therapeutic procedures (examples)				
Fulguration of small bladder tumours	Low frequency of infections.	Optional	2b	C
Transurethral resection of the bladder	Poor data. No concern given to burden of tumour, i.e. size, multiplicity, necrosis.	Trimethoprim ± sulphamethoxazole. Aminopenicillin/ Beta-lactamase inhibitor. Cephalosporin group 2 or 3.	2b	C
Transurethral resection of the prostate	High risk of infection.		1a	A
Shock-wave lithotripsy	Low frequency of infections.		1a	A
Ureteroscopy for stone management	Distal stone removal.		2b	B
Percutaneous and retrograde intra-renal stone management	High risk of infection.		1b	A
Common open and/or laparoscopic surgery				

Nephrectomy ± ureterectomy Adrenalectomy Radical prostatectomy	Surgical site infection/wound infection poorly documented. Secondary post-operative catheter-related asymptomatic bacteriuria/UTI.	Optional	3	C
Planned scrotal surgery, vasectomy, surgery for varicocele	Conflicting data.	No	3	C
Prosthetic implants, artificial sphincter	Limited documentation.	Aminopenicillin/ Beta-lactamase inhibitor Piperacillin/ Tazobactam	3	B
Uretero-pelvic junction repair		Optional	4	C
Partial bladder resection		Optional	3	C
Cystectomy with urine deviation	High risk of infection.	Cefuroxim or Aminopenicillin/ Beta-lactamase inhibitor + Metronidazole	2a	B

Prostate biopsy infection

Histological examination of needle biopsies of the prostate is the principle method for prostate cancer diagnosis. Infection is the most clinically significant harm experienced by men following prostate biopsy and includes urinary tract infection, prostatitis, and urosepsis.

Recommendations for the prevention of infection resulting from prostate biopsy	LE	GR
Use rectal cleansing with povidone-iodine in men prior to transrectal prostate biopsy.	1a	B*
Use antimicrobial prophylaxis in men prior to transrectal prostate biopsy.	1a	A

**Downgraded as highest quality trial in meta-analysis showed no difference.*

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-90-79754-91-5), available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines.