

GUIDELINES ON UROLOGICAL INFECTIONS

(Text update April 2014)

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Introduction

Urinary tract infections (UTIs) pose a serious health problem for patients with high cost to society. UTIs are also the most frequent healthcare associated infections.

E. coli is the predominate pathogen in uncomplicated UTIs whilst *Enterobacteriaceae* and *Enterococcus spp* are predominate in patients with urological diseases. Microbial resistance is developing at an alarming rate with country-specific resistance rates related to the amount of antibiotics used. Particularly of concern is the increasing resistance to broad spectrum antibiotics. It is thus essential to limit the use of antibiotics in general and fluoroquinolones and cephalosporins in particular, especially in uncomplicated infections and asymptomatic bacteriuria.

Classification and definitions

For practical clinical reasons, UTIs and male genital tract infections are classified into entities defined by the predominant clinical symptoms (Table 1).

Table 1: Traditional classification of urinary tract and male genital infections
Uncomplicated lower UTI (cystitis)
Uncomplicated pyelonephritis
Complicated UTI with or without pyelonephritis
Urosepsis
Urethritis
Prostatitis, epididymitis, orchitis

The definitions of bacteriuria are listed in Table 2.

Table 2: Relevant bacterial growth in adults
1. $\geq 10^3$ uropathogens/mL in midstream urine in acute uncomplicated cystitis in women.
2. $\geq 10^4$ uropathogens/mL in midstream urine in acute uncomplicated pyelonephritis in women.
3. $\geq 10^5$ uropathogens/mL in midstream urine in women or 10^4 uropathogens/mL in midstream urine in men (or in straight catheter urine in women) with complicated UTI.
4. In a suprapubic bladder puncture specimen, any count of bacteria is relevant.

Pyuria

The diagnostic requirement for pyuria is 10 white blood cells per high-power field (HPF) ($\times 400$) in the re-suspended sediment of a centrifuged aliquot of urine or per mm^3 in unspun urine. For routine investigation, a dipstick method can also be used, including a leukocyte esterase test and assessment of haemoglobin and nitrites.

Asymptomatic bacteriuria

Asymptomatic bacteriuria is defined as two positive urine cultures taken more than 24 hours apart containing $\geq 10^5$

uropathogens/mL of the same bacterial strain (in a patient without any clinical symptoms).

Urethritis

Symptomatic urethritis is characterised by alguria and purulent discharge.

Classification of prostatitis/chronic pelvic pain syndrome (CPPS)

It is recommended to use the classification according to NIDDK/NIH (Table 3).

I	Acute bacterial prostatitis (ABP)
II	Chronic bacterial prostatitis (CBP)
III	Chronic pelvic pain syndrome (CPPS)
IIIA	Inflammatory CPPS: WBC in EPS/voided bladder urine-3 (VB3)/semen
IIIB	Non-inflammatory CPPS: no WBC/EPS/VB3/semen
IV	Asymptomatic inflammatory prostatitis (histological prostatitis)

Epididymitis, orchitis

Most cases of epididymitis, with or without orchitis, are caused by common urinary pathogens. Bladder outlet obstruction and urogenital malformations are risk factors. Consider *Chlamydia trachomatis* infection in the younger male population.

Diagnosis

UTI (general)

A disease history, physical examination and dipstick urine analysis, including white and red blood cells and nitrite reac-

Table 4: Recommendations for antimicrobial therapy in urology

Diagnosis	Most frequent pathogen/species
Cystitis acute, sporadic and uncomplicated	<ul style="list-style-type: none">• <i>E. coli</i>• <i>Klebsiella</i>• <i>Proteus</i>• Staphylococci
Pyelonephritis acute, uncomplicated (usually febrile)	<ul style="list-style-type: none">• <i>E. coli</i>• <i>Proteus</i>• <i>Klebsiella</i>• Other enterobacteria• Staphylococci
UTI with complicating factors (febrile)	<ul style="list-style-type: none">• <i>E. coli</i>• Enterococci• <i>Pseudomonas</i>• Staphylococci
Nosocomial UTI	<ul style="list-style-type: none">• <i>Klebsiella</i>• <i>Proteus</i>
Pyelonephritis severe acute, complicated	<ul style="list-style-type: none">• <i>Enterobacter</i>• Other enterobacteria• (<i>Candida</i>)

Initial, empirical antimicrobial therapy	Therapy duration
<ul style="list-style-type: none"> • Nitrofurantoin • Fosfomycin trometamol • Pivmecillinam Alternative: <ul style="list-style-type: none"> • TMP-SMX¹ • Fluoroquinolone^{2,3} 	(5-)7 days 1 dose (3-)5 days 3 days (1-)3 days
<ul style="list-style-type: none"> • Fluoroquinolone² • Cephalosporin (group 3a) Alternatives: <ul style="list-style-type: none"> • Aminopenicillin/BLI • Aminoglycoside 	7-10 days
<ul style="list-style-type: none"> • Fluoroquinolone² • Aminopenicillin/BLI • Cephalosporin (group 2) • Cephalosporin (group 3a) • Aminoglycoside 	3-5 days after defervescence or control/elimination of complicating factor
In case of failure of initial therapy within 1-3 days or in clinically cases: Anti- <i>Pseudomonas</i> active: <ul style="list-style-type: none"> • Fluoroquinolone, if not used initially • Acylaminopenicillin/BLI • Cephalosporin (group 3b) • Carbapenem • ± Aminoglycoside In case of <i>Candida</i> : <ul style="list-style-type: none"> • Fluconazole • Amphotericin B 	

Prostatitis acute, chronic	<ul style="list-style-type: none"> • <i>E. coli</i> • Other enterobacteria
Epididymitis Ureaplasma: Acute	<ul style="list-style-type: none"> • <i>Pseudomonas</i> • Enterococci Chronic: <ul style="list-style-type: none"> • Staphylococci
Urosepsis	<ul style="list-style-type: none"> • <i>Chlamydia</i> • <i>Ureaplasma</i> • <i>E. coli</i> • Other enterobacteria After urological interventions - multi-resistant pathogens: <ul style="list-style-type: none"> • <i>Pseudomonas</i> • <i>Proteus</i> • <i>Serratia</i> • <i>Enterobacter</i>

¹Only in areas with resistance rate < 20% (for *E. coli*).

²Fluoroquinolone with mainly renal excretion (see text).

³Avoid Fluoroquinolones in uncomplicated cystitis whenever possible.

BLI = beta-lactamase inhibitor; UTI = urinary tract infection.

tion, is recommended for routine diagnosis. A urine culture is recommended in all types of UTI before treatment, except for sporadic episodes of uncomplicated UTI (cystitis) in premenopausal women, in order to adjust antimicrobial therapy if necessary.

Pyelonephritis

In cases of suspected pyelonephritis, it may be necessary to evaluate the upper urinary tract to rule out upper urinary tract obstruction or stone disease.

<ul style="list-style-type: none"> • Fluoroquinolone² <p>Alternative in acute bacterial prostatitis:</p> <ul style="list-style-type: none"> • Cephalosporin (group 3a/b) <p>In case of <i>Chlamydia</i> or <i>Ureaplasma</i>:</p> <ul style="list-style-type: none"> • Doxycycline • Macrolide <ul style="list-style-type: none"> • Cephalosporin (group 3a/b) • Fluoroquinolone² • Anti-<i>Pseudomonas</i> active acylaminopenicillin/BLI • Carbapenem • ± Aminoglycoside 	<p>Acute: 2-4 weeks</p> <p>Chronic: 4-6 weeks or longer</p> <p>3-5 days after defervescence or control/elimination of complicating factor</p>
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Urethritis

Pyogenic urethritis is indicated by a Gram stain of secretion or urethral smear that shows more than five leukocytes per HPF (x1,000) and in case of gonorrhoea, gonococci are located intracellularly as Gram-negative diplococci. A positive leukocyte esterase test or more than 10 leukocytes per HPF (x400) in the first voiding urine specimen is diagnostic.

Prostatitis/CPPS

In patients with prostatitis-like symptoms, an attempt should be made to differentiate between bacterial prostatitis and CPPS. This is best done by the four glass test according to Meares & Stamey, if acute UTI and STD can be ruled out.

Treatment and Prophylaxis

Treatment of UTI depends on a variety of factors. Table 4 provides an overview of the most common pathogens, antimicrobial agents and duration of treatment for different conditions. Prophylactic treatment may only be recommended for patients with recurrent UTI, after counselling and other prevention methods have failed. The regimens shown in Table 5 have a documented effect in preventing recurrent UTI in women.

Special situations

UTI in pregnancy

A urine culture is recommended. Asymptomatic bacteriuria and cystitis are treated with a 3-5 day course based on sensitivity testing. For recurrent infections (symptomatic or asymptomatic), either cephalexin, 125-250 mg/day, or nitrofurantoin, 50 mg/day, may be used for prophylaxis.

UTI in postmenopausal women

In women with recurrent infection, intravaginal oestriol is recommended. If this is not effective, antibiotic prophylaxis could be considered.

UTI in children

Treatment periods should be extended to 7-10 days. Tetracyclines and fluoroquinolones should not be used because of adverse effects on teeth and cartilage.

Acute uncomplicated UTI in young men

Treatment should last at least 7 days.

Complicated UTI due to urological disorders

The underlying disorder must be managed if a permanent cure is to be achieved. Whenever possible, treatment should be guided by urine culture to avoid inducing resistant strains.

Sepsis in urology (urosepsis)

Patients with UTI may develop sepsis. Early signs of systemic inflammatory response (fever or hypothermia, tachycardia, tachypnoea, hypotension, oliguria, leukopenia) should be recognised as the first signs of possible multi-organ failure. As well as appropriate antibiotic therapy, life-support therapy in collaboration with an intensive care specialist may be necessary. Any obstruction in the urinary tract must be drained.

Table 5: Recommendations for antimicrobial prophylaxis of recurrent uncomplicated UTI

Agent ¹	Dose
Standard regimen	
Nitrofurantoin	50 mg/day
Nitrofurantoin macrocrystals	100 mg/day
TMP-SMX	40/200 mg/day or three times weekly
TMP	100 mg/day
Fosfomycin trometamol	3 g/10 day
'Breakthrough' infections	
Ciprofloxacin	125 mg/day
Norfloxacin	200-400 mg/day
Pefloxacin	800 mg/week
During pregnancy	
Cephalexin	125 mg/day
Cefaclor	250 mg/day
¹ Taken at bedtime.	

TMP = trimethoprim-sulphamethoxazole; UTI = urinary tract infection.

Follow-up of patients with UTI

- For routine follow-up after uncomplicated UTI and pyelonephritis in women, dipstick urine analysis is sufficient.
- In women with a recurrence of UTI within 2 weeks, repeated urinary culture with antimicrobial testing and urinary tract evaluation is recommended.
- In the elderly, newly developed recurrent UTI may warrant a full evaluation of the urinary tract.
- In men with UTI, a urological evaluation should be performed in adolescent patients, cases of recurrent infection and all cases of pyelonephritis. This recommendation should also be followed in patients with prostatitis, epididymitis and orchitis.
- In children, investigations are recommended after two episodes of UTI in girls and one episode in boys. Recommended investigations are ultrasound of the urinary tract supplemented by voiding cystourethrography.

Urethritis

The following guidelines for therapy comply with the recommendations of the Center for Disease Control and Prevention (2010). For the treatment of gonorrhoea, the following antimicrobials can be recommended:

First choice

Ceftriaxone 1 g im
as a single dose
(im with local anaesthetic)
Azithromycin 1g orally as
a single dose

Second choice

Ciprofloxacin 500 mg orally or
Ofloxacin 400 mg orally or
Levofloxacin 250 mg orally
as a single dose

As gonorrhoea is often accompanied by chlamydial infection, an antichlamydial active therapy should be added.

The following treatment has been successfully applied in *Chlamydia trachomatis* infections:

First choice

Azithromycin
1 g (= 4 caps @ 250 mg)
orally as single dose
Doxycycline
2 times daily 100 mg orally
for 7 days

Second choice

Erythromycin
4 times daily 500 mg
orally for 7 days
Ofloxacin 2 times daily
300 mg orally or
Levofloxacin once daily
500 mg orally
for 7 days

If therapy fails, infections with *Trichomonas vaginalis* and/or *Mycoplasma* spp. should be considered. These can be treated with a combination of metronidazole (2 g orally as a single dose) and erythromycin (500 mg orally, 4 times daily, for 7 days).

Prostatitis

Acute bacterial prostatitis can be a serious infection. The parenteral administration of high doses of bactericidal antibiotics, such as an aminoglycoside and a penicillin derivative or a third-generation cephalosporin, is required until defervescence occurs and infection parameters return to normal. In less severe cases, a fluoroquinolone may be given orally for at least 10 days.

In chronic bacterial prostatitis and inflammatory CPPS, a fluoroquinolone or trimethoprim should be given orally for 2 weeks after the initial diagnosis. The patient should then be reassessed and antibiotics only continued if the pretreatment cultures were positive or if the patient has reported positive effects from the treatment. A total treatment period of 4-6 weeks is recommended.

Combination therapy with antibiotics and α -blockers:

Urodynamic studies have shown increased urethral closing pressure in patients with chronic prostatitis. Combination

Table 6: Recommendations for peri-operative antibacterial

Procedure	Pathogens (expected)	Prophylaxis (standard)
<i>Diagnostic procedures</i>		
Transrectal biopsy of the prostate ¹	Enterobacteriaceae (Anaerobes)	All patients
Cystoscopy Urodynamic study	Enterobacteriaceae Enterococci Staphylococci	No
Ureteroscopy	Enterobacteriaceae Enterococci Staphylococci	No
<i>Endourological surgery and SWL</i>		
SWL	Enterobacteriaceae Enterococci	No
Ureteroscopy for uncomplicated distal stone	Enterobacteriaceae Enterococci Staphylococci	No
Ureteroscopy of proximal or impacted stone and percutaneous stone extraction	Enterobacteriaceae Enterococci Staphylococci	All patients
TUR of the prostate	Enterobacteriaceae Enterococci	All patients

prophylaxis in urology

Antibiotics

Remarks

Fluoroquinolones
TMP ± SMX
Metronidazole²

Single dose effective in low risk. Consider prolonged course in risk patients

TMP ± SMX
Cephalosporin 2nd generation

Consider in risk patients

TMP ± SMX
Cephalosporin 2nd generation

No studies

TMP ± SMX
Cephalosporin 2nd or 3rd generation
Aminopenicillin/BLI³

In patients with stent or nephrostomy tube or other risk factor

TMP ± SMX
Cephalosporin 2nd or 3rd generation
Aminopenicillin/BLI

Consider in risk patients

TMP ± SMX
Cephalosporin 2nd or 3rd generation
Aminopenicillin/BLI
(Fluoroquinolones)

Short course,
Length to be determined
Intravenous suggested at operation

TMP ± SMX
Cephalosporin 2nd or 3rd generation
Aminopenicillin/BLI

Low-risk patients and small-size prostate require no prophylaxis

TUR of bladder tumour	Enterobacteriaceae Enterococci	No
Open or laparoscopic urological surgery⁴		
Clean operations	Skin-related pathogens, e.g. staphylococci Catheter-associated uropathogens	No
Clean-contaminated (opening of urinary tract)	Enterobacteriaceae Enterococci Staphylococci	Recommended
Clean-contaminated/ contaminated (use of bowel segments):	Enterobacteriaceae Enterococci Anaerobes Skin-related bacteria	All patients
Implant of prosthetic devices	Skin-related bacteria, e.g. staphylococci	All patients

BLI = beta-lactamase inhibitor; TMP ± SMX = trimethoprim with or resection.

¹Increased resistance of faecal flora recorded (see text).

²No evidence for the use of metronidazole in prostate core biopsies.

³Gram-negative bacteria excluding *Pseudomonas aeruginosa*.

⁴Classifications of surgical field contamination (CDC).

TMP ± SMX Cephalosporin 2 nd or 3 rd generation Aminopenicillin/BLI	Consider in risk patients and large tumours
	Consider in high-risk patients. Short post-operative catheter requires no treatment
TMP ± SMX Cephalosporin 2 nd or 3 rd generation Aminopenicillin/BLI	Single peri-operative course
Cephalosporin 2 nd or 3 rd generation Metronidazole	As for colonic surgery
Cephalosporin 2 nd or 3 rd generation Penicillin (penicillinase stable)	

without sulphamethoxazole (co-trimoxazole); TUR = transurethral

treatment with α -blockers and antibiotics has been reported to have a higher cure rate than antibiotics alone in inflammatory CPPS. This treatment option is favoured by many urologists.

Surgery

Generally, surgery should be avoided in the treatment of prostatitis, except for the drainage of prostatic abscesses.

Epididymitis, orchitis

Prior to antimicrobial therapy, a urethral swab and midstream urine sample should be obtained for microbiological investigation. The first choice of drug therapy should be fluoroquinolones, preferably those agents that react well against *C. trachomatis* (e.g. ofloxacin, levofloxacin), because of their broad antibacterial spectra and favourable penetration into urogenital tract tissues.

In cases caused by *C. trachomatis*, treatment may also be continued with doxycycline, 200 mg/day, for a total treatment period of at least 2 weeks. Macrolides are alternative agents. In cases of *C. trachomatis* infection, the sexual partner should also be treated.

Perioperative antibacterial prophylaxis in urological surgery

The aim of antimicrobial prophylaxis in urological surgery is to reduce the load of bacteria at the site of surgery and thus to prevent symptomatic or febrile urogenital infections, such as acute pyelonephritis, prostatitis, epididymitis and urosepsis, as well as serious wound infections in conjunction with surgery. In recent years increased resistance of the faecal flora, especially against fluoroquinolones, has been recorded which may impact on prophylaxis mode. It is recommended to assess the risk, i.e. prior to prostate biopsy. The basic recommendations for short-term peri-operative antibacterial prophylaxis in standard urological interventions are listed in table 6.

This short booklet text is based on the more comprehensive EAU guidelines (ISBN 978-90-79754-70-0), available to all members of the European Association of Urology at their website, <http://www.uroweb.org>.