GUIDELINES ON THE MANAGEMENT OF URINARY AND MALE GENITAL TRACT INFECTIONS

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Introduction

Infections of the urinary tract pose a serious health problem, partly because of their frequent occurrence. Clinical and experimental evidence support the ascent of micro-organisms within the urethra as the most common pathway leading to urinary tract infections, especially for organisms of enteric origin (i.e. *Escherichia coli* and other Enterobacteriaceae). This also provides a logical explanation for the greater frequency of UTIs in women than in men and for the increased risk of infection following bladder catheterization or instrumentation.

Classification and Definitions

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

Table 1: Classification of urinary and male genital tract infections

- Uncomplicated lower UTI (cystitis)
- Uncomplicated pyelonephritis
- Complicated UTI with or without pyelonephritis

- Urosepsis
- Urethritis
- Prostatitis, epididymitis, orchitis

The definitions of bacteriuria and pyuria are listed in Table 2.

Table 2: Significant bacteriuria in adults

1. ≥ 10^3 uropathogens/mL of midstream urine in acute uncomplicated cystitis in female
2. ≥ 10^4 uropathogens/mL of midstream urine in acute uncomplicated pyelonephritis in female
3. ≥ 10^5 uropathogens/mL in midstream urine of women or 10^4 uropathogens/mL of 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.

Asymptomatic bacteriuria

Asymptomatic bacteriuria is defined as two positive urine cultures taken more than 24 hours apart containing 10^5 uropathogens/mL of the same bacterial strain (usually only the species can be detected).

Pyuria

The diagnostic requirement for pyuria is 10 white blood cells per high-power field (HPF) (x400) in the resuspended 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 the assessment of haemoglobin and of nitrites.

Urethritis

Symptomatic urethritis is characterized by alguria and purulent discharge.

Classification of prostatitis/chronic pelvic pain syndrome (CPPS)

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

Table 3: Classification of prostatitis according to NIDDK/NIH

I Acute bacterial prostatitis (ABP)
II Chronic bacterial prostatitis (CBP)
III Chronic pelvic pain syndrome (CPPS)
  A. Inflammatory CPPS: WBC in EPS/voided bladder urine-3 (VB3)/semen
  B. 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 for this type of infection.

Diagnosis

UTI (general)

A disease history, physical examination and dipstick urinalysis, including white and red blood cells and nitrite reaction, is recommended for routine diagnosis. Except in isolated episodes of uncomplicated lower UTI (cystitis) in premenopausal,

healthy women, a urine culture is recommended in all other types of UTI before treatment, so allowing antimicrobial therapy to be adjusted 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.

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 Mearse & 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 be recommended for patients with recurrent UTI. The regimens shown in Table 5 have a documented effect in preventing recurrent UTI in women.

Table 4: Recommendations for antimicrobial therapy in urology

Diagnosis	Most frequent pathogen/species
Cystitis	• *E. coli*
acute,	• *Klebsiella*
uncomplicated	• *Proteus*
	• Staphylococci
Pyelonephritis	• *E. coli*
acute,	• *Proteus*
uncomplicated	• *Klebsiella*
	• Other enterobacteria
	• Staphylococci
UTI with	• *E. coli*
complicating	• Enterococci
factors	• *Pseudomonas*
	• Staphylococci
Nosocomial UTI	• *Klebsiella*
	• *Proteus*
Pyelonephritis	• *Enterobacter*
acute,	• Other enterobacteria
complicated	• *(Candida)*

Initial, empirical antimicrobial therapy	Therapy duration
• TMP-SMX°	3 days
• Fluoroquinolone*	(1-)3 days
• Fosfomycin trometamol	1 day
• Pivmecillinam	(3-)7 days
• Nitrofurantoin	(5-)7 days
• Fluoroquinolone*	7-10 days
• Cephalosporin (group 3a)	
Alternatives:	
• Aminopenicillin/BLI	
• Aminoglycoside	
• Fluoroquinolone*	3-5 days after
• Aminopenicillin/BLI	defeverescence or
• Cephalosporin (group 2)	control/elimination
• Cephalosporin (group 3a)	of complicating
• Aminoglycoside	factor
In case of failure of initial therapy	
within 1-3 days or in clinically severe	
cases:	
Anti-*Pseudomonas* active:	
• Fluoroquinolone, if not used initially	
• Acylaminopenicillin/BLI	
• Cephalosporin (group 3b)	
• Carbapenem	
• ± Aminoglycoside	
In case of Candida:	
• Fluconazole	
• Amphotericin B	

Prostatitis	• *E. coli*
acute, chronic	• Other enterobacteria
	• *Pseudomonas*
Epididymitis	• Enterococci
acute	• Staphylococci
	• *Chlamydia*
	• *Ureaplasma*
Urosepsis	• *E. coli*
	• Other enterobacteria
	After urological
	interventions - multi-
	resistant pathogens:
	• *Pseudomonas*
	• *Proteus*
	• *Serratia*
	• *Enterobacter*

BLI = beta-lactamase inhibitor; UTI = urinary tract infection.
**Fluoroquinolone with mainly renal excretion (see text).*
° only in areas with resistance rate < 20% (for E. coli).

Special situations

UTI in pregnancy.
Asymptomatic bacteriuria is treated with a 7-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 rec-

• Fluoroquinolone*	Acute:
Alternative in acute bacterial prostatitis:	2-4 weeks
• Cephalosporin (group 3a/b)	
In case of *Chlamydia or Ureaplasma:*	Chronic:
• Doxycycline	4-6 weeks or longer
• Macrolide	
• Cephalosporin (group 3a/b)	3-5 days after
• Fluoroquinolone*	defeverescence or
• Anti-*Pseudomonas* active	control/elimination
acylaminopenicillin/BLI	of complicating
• Carbapenem	factor
• ± Aminoglycoside	

ommended. If this is not effective, antibiotic prophylaxis should be added.

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 recognized 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

TMP = trimethoprim-sulphamethoxazole.

[1]*Taken at bedtime.*

Follow-up of patients with UTI

- For routine follow-up after uncomplicated UTI and pyelonephritis in women, dipstick urinanalysis 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, an 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 indicated after two episodes of UTI in girls and one episode in boys. Recommended investigations are ultrasonography 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 (2002). For the treatment of gonorrhoea, the following antimicrobials can be recommended:

First choice	Second choice
Cefixime 400 mg orally as a single dose	Ciprofloxacin 500 mg orally or Ofloxacin 400 mg orally or Levofloxacin 250 mg orally as a single dose
Ceftriaxone 125 mg im as a single dose (im with local anaesthetic)	

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	Second choice
Azithromycin 1 g (= 4 caps @ 250 mg) orally as single dose	Erythromycin 4 times daily 500 mg orally for 7 day
Doxycycline 2 times daily 100 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 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.

Table 6: Recommendations for peri-operative antibacterial

Procedure	Pathogens (expected)	Prophylaxis
Diagnostic procedures		
Transrectal biopsy of the prostate	Enterobacteriaceae Anaerobes?	All patients
Cystoscopy Urodynamic examination	Enterobacteriaceae Enterococci Staphylococci	No
Ureteroscopy	Enterobacteriaceae Enterococci Staphylococci	No
Endourological surgery and ESWL		
ESWL	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

prophylaxis in urology

Antibiotics	Remarks
Fluoroquinolones TMP ± SMX Metronidazole?	Short course (≤ 72h)
Cephalosporin 2nd generation TMP ± SMX	Consider in risk patients
Cephalosporin 2nd generation TMP ± SMX	
Cephalosporin 2nd or 3rd generation TMP ± SMX Aminopenicillin/BLI[a]	In patients with stent or nephrostomy tube Consider in risk patients
Cephalosporin 2nd or 3rd generation TMP ± SMX Aminopenicillin/BLI Fluoroquinolones	In patients with stent or nephrostomy tube Consider in risk patients
Cephalosporin 2nd or 3rd generation TMP ± SMX Aminopenicillin/BLI Fluoroquinolones	Short course, Length to be determined Intravenous suggested

TUR of the prostate	Enterobacteriaceae Enterococci	All patients
TUR of bladder tumour	Enterobacteriaceae Enterococci	No
Open urological surgery		
Clean operations	Skin-related pathogens, e.g. staphylococci Catheter-associated uropathogens	No
Clean-contaminated (opening of urinary tract)	Enterobacteriaceae Enterococci Staphylococci	Recommended
Clean-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
Laparoscopic procedures		

BLI = beta-lactamase inhibitor; TMP ± SMX = trimethoprim with or without su

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

out sulphamethoxale (co-trimoxazole); TUR = transurethral resection.

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 main aim of antimicrobial prophylaxis in urology is to prevent symptomatic or febrile genitourinary infections, such as acute pyelonephritis, prostatitis, epididymitis and urosepsis, as well as serious wound infections. The recommendations for short-term peri-operative antibacterial prophylaxis in standard urological interventions are listed in table 6.

This short booklet is based on the more comprehensive EAU guidelines (ISBN 90-70244-37-3), available to all members of the European Association of Urology at their website: http://www.uroweb.org.