

# 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, also because of their frequent occurrence.

Clinical and experimental evidence support that the ascent of micro-organisms within the urethra is the most common pathway leading to urinary tract infections, especially for organisms of enteric origin (i.e. *Escherichia coli* and other Enterobacteriaceae). This is a logical explanation for the greater frequency of UTIs in women than in men and the increased risk of infection following bladder catheterisation or instrumentation.

## Classification of Urinary and Male Genital Tract Infections

For practical clinical reasons, urinary tract infections (UTIs) and male genital tract infections are classified according to entities with predominating clinical symptoms: (1) uncomplicated lower UTI (cystitis); (2) uncomplicated pyelonephritis; (3) complicated UTI with or without pyelonephritis; (4) urosepsis; (5) urethritis, and (6) prostatitis, epididymitis, orchitis.

## Definitions

The definitions of bacteriuria and pyuria are as follows:

Significant bacteriuria in adults:

1.  $\geq 10^3$  uropathogens/ml of midstream urine in acute uncomplicated cystitis in the female;
2.  $\geq 10^4$  uropathogens/ml of midstream urine in acute uncomplicated pyelonephritis in the female;
3.  $\geq 10^5$  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.

In a suprapubic bladder puncture specimen any count of bacteria is relevant.

*Asymptomatic bacteriuria (ABU).*

ABU is defined as two positive urine cultures taken more than 24h apart with  $10^5$  uropathogens/ml of the same bacterial strain (mostly only the species is available).

*Pyuria.*

The requirement for pyuria is 10 white blood cells per high-power field (400) in the resuspended sediment of a centrifuged aliquot of urine or per  $\text{mm}^3$  in unspun urine. For the routine a dipstick method can also be used, including leukocyte esterase test, haemoglobin and probably nitrite reaction.

### Table 1: 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. Noninflammatory CPPS: no WBC/EPS/VB3/ semen
- IV. Asymptomatic inflammatory prostatitis (histological prostatitis)

## Diagnosis

Disease history, physical examination and urine analysis by dipstick including white and red blood cells as well as nitrite reaction is recommended for routine diagnosis.

**Table 2: Recommendations for antimicrobial therapy in urology**

<i>Diagnosis</i>	<i>Most frequent pathogen</i>
<i>Cystitis, acute, uncomplicated</i>	<i>E. coli</i> <i>Klebsiella</i> <i>Proteus</i> <i>Staphylococcus</i>
<i>Pyelonephritis, acute, uncomplicated</i>	<i>E. coli</i> <i>Proteus</i> <i>Klebsiella</i> <i>Other Enterobacteria</i> <i>Staphylococcus</i>
<i>UTI with complicating factors</i> <i>Nosocomial UTI</i> <i>Pyelonephritis, acute, complicated</i>	<i>E. coli</i> <i>Enterococcus</i> <i>Staphylococcus</i> <i>Klebsiella</i> <i>Proteus</i> <i>Enterobacter</i> <i>Other Enterobacteria</i> <i>Pseudomonas</i> <i>(Candida)</i>

In case of suspicion of pyelonephritis, evaluation of the upper urinary tract may be necessary to rule out upper urinary tract obstruction or stone disease.

<b>Initial, empiric antimicrobial therapy</b>	<b>Therapy duration</b>
Trimethoprim/sulfamethoxazole	3 days
Fluoroquinolone <sup>a</sup>	3 days
Alternatives:	
Fosfomycin trometamol	1 day
Pivmecillinam	7 days
Nitrofurantoin	7 days
Fluoroquinolone <sup>a</sup>	7–10 days
Cephalosporin Gr. 2 <sup>b</sup> /3a	
Alternatives:	
Aminopenicillin/BLI	
Aminoglycoside	
Fluoroquinolone <sup>a</sup>	3–5 days after defervescence or control/elimination of complicating factor
Aminopenicillin/BLI	
Cephalosporin Gr. 2 <sup>b</sup>	
Cephalosporin Gr. 3a	
Aminoglycoside	
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 Gr. 3b	
Carbapenem	
±Aminoglycoside	
In cases of Candida	
Fluconazole	
Amphotericin B	

<b>Diagnosis</b>	<b>Most frequent pathogen</b>
Prostatitis, acute, chronic	<i>E. coli</i>
Epididymitis, acute	Other Enterobacteria <i>Pseudomonas</i> <i>Enterococcus</i> <i>Staphylococcus</i> <i>Chlamydia</i> <i>Ureaplasma</i>
Urosepsis	<i>E. coli</i> Other Enterobacteria  After urological interventions- multiresistant pathogens: <i>Proteus</i> <i>Serratia</i> <i>Enterobacter</i> <i>Pseudomonas</i>

<sup>a</sup> Fluroquinolone with mainly renal excretion; BLI =  $\beta$ -lactamase inhibitor.  
<sup>b</sup> 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> generation respectively (3a- without; 3b- with anti-*Pseudomonas* activity)

## Treatment

Treatment of UTI is dependent on a variety of factors. An overview of most frequent pathogens, antimicrobial agents and duration of treatment in various conditions is given in table 2. Patients with recurrent UTI may be recommended prophylactic treatment. The following regimens have a documented effect in preventing recurrent UTI in women (table 3).

<b>Initial, empiric antimicrobial therapy</b>	<b>Therapy duration</b>
Fluoroquinolone <sup>a</sup>	Acute: 2 weeks
Alternative in acute bacterial prostatitis:	
Cephalosporin Gr. 2	Chronic: 4–6 weeks or longer
Cephalosporin Gr. 3a/b	
In case of Chlamydia or Ureaplasma:	
Doxycycline	
Macrolide	
Cephalosporin Gr. 3a/b	3–5 days after defervescence or control/elimination of complicating factor
Fluoroquinolone <sup>a</sup>	
Anti-Pseudomonas active	
Acylaminopenicillin/BLI	
Carbapenem	
Aminoglycoside	

**Table 3: Antimicrobial regimens for prevention of acute uncomplicated urinary infection in women**

<b>Agent</b>	<b>Dose</b>
<i>Standard regimens (taken at bedtime)</i>	
Trimethoprim/sulfamethoxazole	40/200 mg/day or 3 times weekly
Trimethoprim	100 mg/day
Nitrofurantoin	50 mg/day
Nitrofurantoin macrocrystals	100 mg/day
<i>Others</i>	
Cephalexin	125 or 250 mg/day
Norfloxacin	200 mg/day
Ciprofloxacin	125 mg/day

## 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.
- *UTI in postmenopausal women.* In women with recurrent infection intravaginal estriol is recommended. If this does not work, in addition antibiotic prophylaxis is indicated.
- *UTI in children.* Treatment periods should be extended to 7-10 days. Tetracyclines and fluoroquinolones should not be used due to effects on teeth and cartilage.
- *Acute uncomplicated UTI in young men.* The treatment should last at least 7 days.
- *UTI in diabetes mellitus and renal insufficiency.* After treatment, a prophylactic regimen may be recommended.
- *Complicated UTI due to urological disorders.* The underlying disorder must be managed if permanent cure is to be expected. In order to avoid inducing resistant strains, treatment should be guided by urine culture whenever possible.
- *Sepsis syndrome in Urology (urosepsis).*  
Patients with UTI may develop into sepsis. Early signs of systemic inflammatory response (fever or hypothermia, tachycardia, tachypnea, hypotension, oliguria, leukopenia) should be recognized as the first signs of possible multi-organ failure. In conjunction with appropriate antibiotic therapy, life supporting therapy in collaboration with an intensive care specialist may be necessary. Any obstruction in the urinary tract needs to be drained.

## Follow-up of patients with UTI

- For follow-up after uncomplicated UTI and pyelonephritis in women, a urinalysis by dipstick is enough for routine use.
- In women who will have recurrence within 2 weeks, repeated urinary culture with antimicrobial testing and evaluation of the urinary tract is recommended.
- In the elderly, newly developed recurrent UTI may warrant a full evaluation of the urinary tract.
- In men with UTI, a urologic evaluation should be done when the patient is in adolescence, in cases with recurrent infection and in all causes with pyelonephritis. Also patients with prostatitis, epididymitis and orchitis should follow these recommendations.
- 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

Symptomatic urethritis is characterized by alguria and purulent discharge.

### *Diagnosis*

The Gram stain of secretion or urethral smear showing more than 5 leukocytes per high-power field (HPF) (1,000) and eventually gonococci located intracellularly as Gram-negative diplococci indicate a pyogenic urethritis. A positive leukocyte esterase test or more than 10 leukocytes per high-power field (400) in the first voiding urine specimen are diagnostic.

## Therapy

The following guidelines for therapy comply with the recommendations of the Center for Disease Control and Prevention (1998).

For the treatment of gonorrhoea the following antimicrobials can be recommended:

Cefixime 400 mg orally as a single dose	Ciprofloxacin 500 mg orally as single dose
Ceftriaxone 250 mg i.m. as a single dose (i.m. with local anaesthetic)	Ofloxacin 400 mg orally as single dose

As gonorrhoea is frequently accompanied by chlamydial infection, an antichlamydial active therapy should be added. The following treatment has been successfully applied in *C. trachomatis* infections:

<u>First choice</u>	<u>Second choice</u>
Azithromycin 1 g (= 4 caps.@ 250 mg) orally as single dose	Erythromycin 4 times daily 500 mg orally for 7 days
Doxycycline 2 times daily 100 mg orally for 7 days	Ofloxacin 2 times daily 200 mg orally for 7 days

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

## Prostatitis, Epididymitis and Orchitis

### *Prostatitis*

#### *Treatment*

- Acute bacterial prostatitis can be a serious infection and parenteral administration of high doses of bactericidal antibiotic such as aminoglycosides and a penicillin derivative or a 3rd generation cephalosporin are required until defervescence and normalization of infection parameters. In less severe cases a fluoroquinolone may be given orally for at least 10 days.
- In chronic bacterial prostatitis and chronic inflammatory pelvic pain syndrome a fluoroquinolone or trimethoprim should be given orally for 2 weeks after the initial diagnosis. Then the patient should be reassessed and antibiotics only continued if pretreatment cultures were positive or if the patient reports positive effect of the treatment. A total treatment period of 4-6 weeks is recommended.

### *Epididymitis, Orchitis*

The majority of cases of epididymitis are due to common urinary pathogens. Bladder outlet obstruction and urogenital malformations are risk factors for this type of infection.

#### *Treatment*

Prior to antimicrobial therapy a urethral swab and midstream urine should be obtained for microbiological investigation. Fluoroquinolones, preferably those which react well against *C. trachomatis*, e.g. ofloxacin, levofloxacin, should be first-choice drugs because of their broad antibacterial spectra and their favourable penetration into the tissues of the urogenital tract. In case *C. trachomatis* has been detected as etiologic agent, treatment could also be continued with doxycycline

**Table 4: Recommendations for perioperative antibacterial prophylaxis**

<b>Procedure</b>	<b>Most common pathogen(s)</b>
<b>1. Open operations</b>	
Urinary tract including bowel segments	Enterobacteria Enterococci Anaerobes Wound infection: Staphylococci
Urinary tract without bowel segments	Enterobacteria Enterococci Wound infection: staphylococci
Implant/prosthesis: penis, sphincter Reconstructive genital operation	Staphylococci Staphylococci
Other interventions outside of the urinary tract	Staphylococci
<b>2. Endoscopic-instrumental operations</b>	
Urethra, prostate, bladder, ureter; kidney, incl. percutaneous litholapaxy and ESWL	Enterobacteria Staphylococci Enterococci
<b>3. Diagnostic intervention</b>	
Transrectal biopsy of the prostate (with thick needle)	Enterobacteria Enterococci Anaerobes Streptococci
Perineal biopsy of the prostate, urethrocystoscopy, ureterorenoscopy, percutaneous pyeloscopy, laparoscopic procedures	Enterobacteriaceae Enterococci Staphylococci

BLI =  $\beta$ -Lactamase inhibitor; ESWL = extracorporeal shock-wave lithotripsy.  
 1°, 2°, 3° = 1<sup>st</sup>, 2<sup>nd</sup>, and 3<sup>rd</sup> generation, respectively.

<sup>a</sup> Fluroquinolone with sufficient renal excretion.

## hylaxis in urology

<b>Antibiotic(s) of choice</b>	<b>Alternative antibiotic(s)</b>	<b>Remarks</b>
Aminopenicillin + BLI Cephalosporin 2°+ Metronidazole	In high-risk patients: Cephalosporin 3° Acylaminopenicillin + BLI	In all patients
Fluoroquinolone <sup>a</sup> Cephalosporin 2° Aminopenicillin + BLI	In high-risk patients: Cephalosporin 3° Acylaminopenicillin + BLI	In patients with increased risk of infection
Cephalosporin 1°/2° Cephalosporin 1°/2°		In all patients In secondary operations and in patients with increased risk of infection
Cephalosporin 1°/2°		In patients with increased risk of infection
Fluoroquinolone <sup>a</sup> Aminopenicillin + BLI, Cephalosporin 2° Fosfomicin Trometamol	Cotrimoxazole Aminoglycoside	In patients with increased risk of infection
Fluoroquinolone <sup>a</sup> Aminopenicillin + BLI Cephalosporin 2° + Metronidazole	Aminoglycoside Cotrimoxazole	In all patients
Fluoroquinolone <sup>a</sup> Aminopenicillin + BLI Cephalosporin 2°	Cotrimoxazole	In patients with increased risk of infection

200 mg/day for a total treatment period of at least 2 weeks. Macrolides may be alternative agents. In case of *C. trachomatis* infection, the sexual partner should be treated as well.

#### *Antibiotics and $\alpha$ -Blockers in Combination.*

Urodynamic studies have shown increased urethral closing pressure in patients with chronic prostatitis. A combination treatment of  $\alpha$ -blockers and antibiotics is reported to have a higher cure rate than antibiotics alone in inflammatory CPPS. This is a treatment option favoured by many urologists.

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

### **Perioperative Antibacterial Prophylaxis in Urological Surgery**

Table 4 (on the two previous pages)

The main aim of antimicrobial prophylaxis in urology is to prevent symptomatic/febrile genitourinary infections, such as acute pyelonephritis, prostatitis, epididymitis and urosepsis as well as serious wound infections.

*This short booklet text is based on the more comprehensive EAU guidelines (ISBN 90-806179-3-8), available to all members of the European Association of Urology at their website - <http://uroweb.org>.*