

Current Management of Urinary Tract Infections



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Urinary Tract Infections (UTIs) are among the most common infections in both the out and inpatient settings. Increasing antimicrobial resistance of urinary pathogens has highlighted the need for reevaluation of the treatment options.¹⁻³ Since management of UTIs widely varies, these guidelines may help physicians choose cost-effective options.⁴⁻¹⁰

Diagnosing a UTIs often requires examination of a urine sample in addition to clinical signs or symptoms (Table 1). However, many guidelines indicate that a urine culture is not needed in most cases of uncomplicated lower UTI or cystitis.^{11, 12} *Escherichia coli* remains the most common etiologic agent of community-acquired, uncomplicated UTIs, particularly in women under 50 years of age, with *Staphylococcus saprophyticus* the second commonest. For this reason, in treating uncomplicated cystitis, the first-line empiric antibiotic recommendations are those which are narrow-spectrum and used predominantly only for this indication.

Risk factors in UTIs

Factors of functional and anatomical alterations play the important role in the pathogenesis of UTIs. In women, the shortness of urethra, with its close proximity to the anus, makes it easy for bacteria to ascend the genito-urinary tract. Therefore, fecal-perineal-urethral contamination is the most common cause of UTIs.

Altered vaginal flora (AVF) also plays a similar role in the pathogenesis of UTI in women. *Lactobacilli* is the dominant bacteria found in the vagina, possessing antimicrobial properties that regulate the local vaginal host defenses, by maintaining an acidic pH and producing hydrogen peroxide. The use of *Lactobacillus*-containing probiotics has been studied as a potential prophylactic for recurrent UTIs. However, the efficacy of this result of UTI prophylaxis remains as yet inconclusive. Alteration in vaginal flora can also be observed in UTIs occurring in postmenopausal women, because estrogen stimulates the proliferation of *Lactobacilli* and reduces local pH.¹³⁻¹⁴

Pregnancy and UTIs.

Bacteriuria is the most common finding in pregnant women. Many studies have shown that upper UTI or acute pyelonephritis is more common in the second or third trimester of pregnant women with asymptomatic bacteriuria. For this reason asymptomatic bacteriuria in pregnant women has to be treated.^{15, 16}

Table 1: Definition of terms²⁰

Term	Standard definition	Application to management of urinary tract infection (UTI) in elderly patients
Significant bacteriuria	Presence of a specified number (usually > 10 ⁵ CFU/mL) of a single species of bacteria in freshly voided, midstream specimen of urine.	This level of bacteriuria is significant because it is unlikely that it can be explained by contamination of the urine sample with perineal flora. It DOES NOT indicate clinically significant bacteriuria. "Significant" bacteriuria is often asymptomatic and does not necessarily require treatment. Lower levels may sometimes be significant.
Uncomplicated urinary tract infection	Lower urinary tract infection in an adult woman who is not pregnant and has no underlying abnormality of the urinary tract or indwelling urinary device.	The evidence about effectiveness of short (3 day) courses of treatment for UTI only applies to uncomplicated UTIs. All UTIs in males, all UTIs associated with urinary catheters, and all UTIs with systemic symptoms are complicated UTIs.
Lower urinary tract infection	Infection confined to the tissue of the bladder or urethra. The presence of symptoms or signs of systemic infection indicates upper urinary tract infection.	Both nitrofurantoin and fosfomycin only achieve effective concentrations in the lower urinary tract infection. These antibiotics should not be used to treat patients with systemic symptoms or signs.

Diabetes and UTIs

The risk of developing symptomatic UTI is increased in diabetes.¹⁷ Asymptomatic bacteriuria is also increased in patients with diabetes over a longer duration. However studies showed only a weak correlation between increased risk of symptomatic UTIs and poor control of diabetes and microalbuminuria or macrovascular complications, also, antibiotic treatment did not decrease incidence of symptomatic UTI.^{18,19}

Antibiotic treatment of UTIs^{4, 21-23}

An appropriate antibiotic varies according to the following information or criteria:

1. Patient's individual risk
2. Patient's previous antibiotic treatment
3. Pathogen spectrum and susceptibility
4. Pathogen resistance prevalence
5. Drug effects including adverse reactions

Antibiotic of choice for acute uncomplicated cystitis

1. Trimethoprim-Sulfamethoxazole for 3 days is an appropriate choice of therapy in USA, if local resistance rate of uropathogens causing cystitis do not exceed 20% (A-I)
2. Fluoroquinolones : Ofloxacin, Ciprofloxacin and Levofloxacin are highly effective in 3 days regimens (A-I)

In many countries, where the uropathogen resistance to Trimetoprim-Sulfamethoxazole and Fluoroquinolone

is high, those agents may no longer be recommended for empiric treatment of UTI.

3. Fosfomycin trometamal, 3 gm sachet, in a single dose is an alternative for those with drug-resistant UTIs, but it appears to be less efficacious when compared with the standard 3-5 days regimen of other antibiotics according to data published.^{23,24}

4. β -lactam antibiotics, including Cephalosporin (2nd or 3rd generation), and betalactam-betalactamase inhibitors, such as amoxicillin-clavulanate/ampicillin-sulbactam, in 3-7 days regimens are appropriate choices when other agents cannot be used. (B-III)

Antibiotic treatment for acute pyelonephritis

From a clinical point of view, acute pyelonephritis should be considered as tissue infection of the whole urinary tract; whereas an exact anatomical distinction on clinical grounds can often not be made. Blood and urine cultures should always be performed, and initial empirical intravenous antibiotic should be started as fast as possible, due to the somewhat higher incidence of bacteria in adult pyelonephritis. (A-III)

Most patients with acute pyelonephritis require hospitalization and initially intravenously administered empiric antibiotics, such as cephalosporin, fluoroquinolone, aminoglycoside or carbapenem; the choice between these agents should be based on local resistance data. Later, the antibiotic regimen should be tailored on the basis of susceptibility results.

Table 2: Strength of recommendations and Quality of Evidence

Category/grade	Definition
Strength of recommendation	
A	Good evidence to support a recommendation for or against use
B	Moderate evidence to support a recommendation for or against use
C	Poor evidence to support a recommendation
Quality of evidence	
I	Evidence from ≥ 1 properly randomized, controlled trial
II	Evidence from ≥ 1 Well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from > 1 center); from multiple time-series; or from dramatic results from uncontrolled experiments
III	Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

NOTE. Data is from periodic health examination. Canadian Task Force on the Periodic Health Examination. Health Canada, 1979. Adapted and Reproduced with the permission of the Minister of Public Works and Government Services Canada, 2009

The appropriacy of the initial or empirical antibiotic for acute pyelonephritis also depends on the severity of illness at presentation as well as local resistance and comorbidity of patients, and host factors.

For some areas of the world, including Thailand, the prevalence of Fluoroquinolone resistance exceeds 10%; therefore the generally recommended initial antibiotic is a parenteral 3rd generation long-acting cephalosporin, normally ceftriaxone.

Duration of antibiotic therapy for lower UTI

A 3-day course of highly effective antibiotics or tissue-directed antibiotic such as Trimethoprim-Sulfamethoxazole and Fluoroquinolone, is recommended for women and a 7-day course for men.²⁵ If β -lactam is used, the duration recommended is 5 days for women, of all ages.

Duration of antibiotic therapy for upper UTI- (acute pyelonephritis)

Most published guidelines recommend a 14 days regimen (A-I),^{4, 26-30} however a 7-10 days regimen is also recommended if a highly active agent, such as Fluoroquinolone, is used.

Recently, the Infectious Diseases Society of America in collaboration with the European Society for Microbiology and Infectious Diseases (ESCMID) have systematically updated ISDA clinical practice guidelines for treating acute uncomplicated cystitis and pyelonephritis in women. (Table 2)^{4, 32}

Management of asymptomatic bacteriuria

Definition of asymptomatic bacteriuria^{33, 34}

1. Asymptomatic women, defined as 2 consecutive voided urine culture with isolation of the same bacteria, counts $\geq 10^5$ CFU/ml (B-II)
2. A single, clean-catch voided urine of $\geq 10^5$ CFU/ml (B-II)
3. A single catheterized urine of $\geq 10^5$ CFU/ml in women or men (A-II)

Asymptomatic bacteriuria is common in many groups of patients with indwelling catheters, where there is a very high prevalence of asymptomatic bacteriuria; such as in patients with spinal cord injury, where the prevalence ranges between 23-89%.³⁵

Studies have shown that it is worth treating asymptomatic bacteriuria only in pregnant women and patients in whom a urinary tract intervention is intended that may be expected to damage the mucosa.

Conclusion

Urinary tract infections are responsible for a large proportion of antibiotic administrations; bacterial resistance is increasing. For this reason, in treating UTIs, treatment recommendation should take into account to the efficacy of the antibiotics and also, especially factors relating to their sustainability. Asymptomatic bacteriuria should only be treated in a few exceptional cases, such as during pregnancy or before genitourinary tract interventions.

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Questions of Urinary Tract Infections

- Q1.** Which of the following duration of antibiotics for treatment of uncomplicated cystitis is not correct?
- a. 3 days of Fluoroquinolone is adequate
 - b. 5 days of oral Cephalosporin is adequate
 - c. Single dose of Fosfomycin trometamol is effective
 - d. Single dose of Parenteral Ceftriaxone is effective
 - e. 5 days of Amoxicillin-Clavulanate is effective
- Q2.** What is the most appropriate and cost-effective parenteral antibiotic for acute pyelonephritis?
- a. Cefuroxime
 - b. Ceftazidime
 - c. Cefotaxime
 - d. Ceftriaxone
 - e. Ampicillin-Sulbactam
- Q3.** In which of the following patients does asymptomatic bacteriuria need to be treated with antibiotic?
- a. Diabetes Mellitus
 - b. The elderly
 - c. Pregnant women
 - d. Hypertension
 - e. Spinal cord injury
- Q4.** Regarding duration of antibiotic in acute pyelonephritis, which of the following is not correct?
- a. Based on current evidence, 14 days is recommended for most antibiotics
 - b. If Fluoroquinolone is used, 7-10 days is probably adequate
 - c. If 3rd generation Cephalosporin is used, 7-10 days is adequate
 - d. If Amoxicillin-Clavulanic is used, 14 days is recommended
 - e. In bacteremic patient, duration should be more than 14 days.
- Q5.** Duration of antibiotic therapy for UTI could be shorter if using tissue-directed antibiotic(s) such as...?
- a. Ciprofloxacin
 - b. Cefdinir
 - c. Cefditoren
 - d. Levofloxacin
 - e. Amoxicillin-clavulanate

Answers of Urinary Tract Infections

Answer 1: d. Duration of treatment of uncomplicated cystitis with any β -lactam recommended by most authors is 3-5 days.

Answer 2: d. Ceftriaxone is the most cost-effective parenteral antibiotic, due to good PK-PD against uropathogens.

Answer 3: c. From many published studies, antibiotic treatment is only beneficial in pregnant women with asymptomatic bacteriuria.

Answer 4: e. From many published studies, duration of antibiotic in bacteremic adult pyelonephritis did not differ from non bacteremic patients.

Answer 5: a and d. Fluoroquinolones are tissue-directed antibiotics with high tissue and urine concentration, so called good PK/PD, bactericidal: for this reason duration could be shorter than β -lactam.