

Infectious Disease Update: March 2011

Appropriate Management of Urinary Tract Infection and Asymptomatic Bacteriuria

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Overview

Symptomatic urinary tract infection (UTI) is one of the most common infections encountered in practice requiring antimicrobial treatment.¹ Asymptomatic bacteriuria is also a common problem, variable in prevalence according to certain characteristics like age, sex and presence of genitourinary abnormalities, but is more nuanced in its specific requirement for antimicrobial treatment.² The VIHA Antimicrobial Review Subcommittee (VIHA-ARS) has developed treatment algorithms (see insert) to provide direction for the empiric treatment of suspected urinary tract infection and asymptomatic bacteriuria. Because many published guidelines/recommendations recommend empiric antimicrobial agents that are associated with significant resistance^{1, 3-5}, we have endeavored to incorporate local susceptibility data to ensure the best chance of clinical success and to preserve key agents in our antimicrobial armamentarium. These algorithms address the treatment of cystitis, pyelonephritis, and asymptomatic bacteriuria, with a focus on the management of patients seen in or admitted to the hospital.

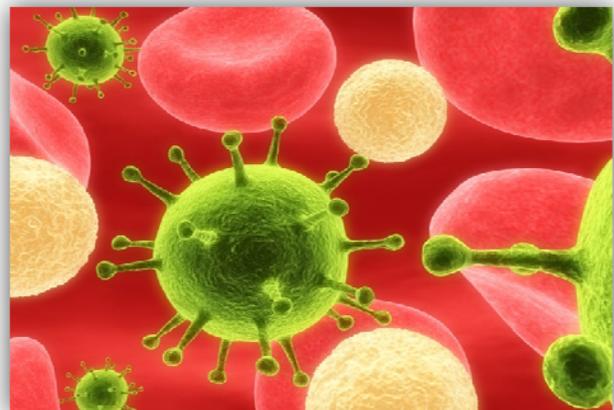
Uncomplicated Cystitis

Uncomplicated cystitis occurs in young healthy women (average age 16-35 years), and is classically associated with symptoms of dysuria, urinary frequency with or without urgency, and hematuria.³ *Escherichia coli* continues to be the most common pathogen, contributing to approximately 80-85% of infections. Other pathogens are *Staphylococcus saprophyticus* (~5-15%), *Proteus mirabilis*, *Klebsiella* species and occasionally *Enterococcus spp.*^{3, 5} When cystitis is suspected, a midstream urine specimen should be collected for routine and microscopic urinalysis, as well as culture and sensitivity.

Empiric antimicrobial therapy targeting the most likely urinary tract pathogens should be initiated when urinalysis results and symptomatology support the diagnosis of cystitis, even when urine culture and sensitivity results are pending. Urine culture and sensitivity results serve both to establish definitive antimicrobial therapy as well as to provide surveillance data on antimicrobial resistance.

Trimethoprim/sulfamethoxazole (TMP/SMX) and ciprofloxacin have historically been recommended as empiric agents for the treatment of uncomplicated UTI.¹ According to the 2005 VIHA antibiogram, *E. coli* susceptibilities to TMP/SMX and ciprofloxacin were 79% and 71%, respectively.⁶ Current interim data for 2008 indicate susceptibilities of 81% and 77%. By convention, an antimicrobial agent's efficacy is considered adequate when a target organism's *in vitro* susceptibility is greater than 80%. Accordingly, the empiric use of ciprofloxacin as a first-line agent for UTI can no longer be recommended. Resistance to TMP/SMX is also a concern although it remains an alternative in cases of contraindications to other effective therapies.

Uncomplicated cystitis can almost always be treated with orally administered antimicrobials. Based on local susceptibility data, nitrofurantoin, TMP/SMX and cefixime are all reasonable options for empiric treatment. The advantage of TMP/SMX and cefixime is that either can be used effectively for durations as short as 3 days.^{7, 8} Nitrofurantoin, given as the macrocrystal formulation for 5 days, has recently been shown to be as effective as 3 days of TMP/SMX.⁹ Despite being a relatively old agent, nitrofurantoin has been associated with little bacterial resistance.⁴ Selection should take into account previous antimicrobial use, presence of relative/absolute contraindications (e.g. beta-lactam or sulfa allergy, renal impairment), and cost.



Complicated Cystitis

Complicated urinary tract infection occurs in both women and men and in any age group, and is usually characterized by presence of a structural or functional abnormality of the genitourinary tract.¹⁰ In broad terms, complicated cystitis usually occurs in those patients other than young, healthy, non-pregnant women. Complicated infections may include the following features¹¹:

- symptoms lasting greater than seven days
- male gender
- females greater than 55 years of age
- diabetes mellitus
- abnormality of the urinary tract, spinal cord injury or multiple sclerosis
- pregnancy
- chronic catheterization
- recurrent UTI

The commonly implicated pathogens include not only those seen in uncomplicated UTI, but also other *Enterobacteriaceae*, *Enterococcus* spp, Group B *Streptococcus*, *Pseudomonas aeruginosa* and *Candida* spp.¹⁰ An increasing problem with complicated infections is the emergence of extended spectrum beta-lactamase (ESBL) producing bacteria.¹² Patients who have chronic infections, or who have been recently/recurrently hospitalized are at risk for developing antibiotic resistant organisms, and may require agents beyond the scope of this algorithm.

Generally, treatment for complicated cystitis is indicated for 7 days.¹¹ In the case of abnormality of the urinary tract (anatomic, functional, or metabolic), treatment is indicated for 10-14 days and often is due to a broader range of possible pathogens, including *Enterococcus* spp.¹¹ It is important to note that amoxicillin-clavulanic acid is one of few oral alternatives that provides enterococcal coverage with the exception of *E. faecium*.

Catheterized Patients

In the chronically catheterized patient with a symptomatic UTI, the catheter should be changed prior to obtaining a urine specimen (through the clean catheter), as indwelling catheters are often colonized with bacteria. In some situations, catheter change alone will improve symptoms, and antibiotics may not be required. Although symptomatic UTI is often accompanied by pyuria identified by routine and/or microscopic urinalysis, pyuria is also present in most patients with

indwelling catheters and asymptomatic bacteriuria and thus is not diagnostic of UTI.¹⁰

Cystitis in Males

First-episode cystitis is usually treated for 7 days. Recurrent cystitis is treated for 6 weeks in conjunction with urologic work-up to rule out chronic bacterial prostatitis.¹¹

Diabetes Mellitus

Patients with diabetes are predisposed to infection with group B *Streptococci*, therefore a beta lactam antibiotic may be preferred.¹¹

Recurrent or Relapsing Cystitis

More than 90% of cases of recurrent cystitis 2-4 weeks following treatment are due to reinfection, usually with a different organism or strain.¹¹ Relapse (with the same organism and strain) is usually within 2 weeks following treatment.¹¹ However, the urine should be re-cultured in either scenario as there may be a new organism or the sensitivities could have changed from the previous microbiology report.

Pyelonephritis

Pyelonephritis involves the upper urinary tract and is generally associated with systemic symptoms such as fever, chills, nausea, malaise, ipsilateral costovertebral angle tenderness and abdominal or flank pain.³ Complicating factors for pyelonephritis are similar to those seen with cystitis, and the key differences in approach are reflected in the level of diagnostics and aggressiveness of treatment.

Blood cultures (2 sets), in addition to urine cultures, should be collected to assist in establishing a diagnosis. In the patient who is hemodynamically stable and is able to take medication by mouth, outpatient oral antibiotic treatment may be appropriate. Otherwise, intravenous antibiotics are usually indicated and can be administered through an outpatient antibiotic therapy program (if available) or will require hospital admission. As the patient improves and microbiological susceptibilities become known, antibiotic therapy should be narrowed and/or administered orally to complete a usual treatment course of 10-14 days.

Specific IV to PO switch criteria include:

- temperature less than 38°C for 24 hours
- WBC less than 11 or decreasing trend
- clinical improvement while on IV treatment

Table 1. VIHA susceptibilities of common organisms in UTI (2008)

	ampicillin	cephalexin	amoxicillin/clavulanate	cefixime	ceftriaxone	ciprofloxacin	gentamicin	nitrofurantoin	trimethoprim/sulfamethoxazole
Escherichia coli	62%	61%	84%	91%	92	77%	94%	96%	81%
Staphylococcus saprophyticus	Susceptibility testing is not routinely performed as antibiogram is predictable. Antibiotics of choice are nitrofurantoin, trimethoprim-sulfamethoxazole or ciprofloxacin.								
Enterococcus spp.	95%	N/A	95%	N/A	N/A	62%	N/A	92%	N/A
Klebsiella pneumoniae/oxytoca	0%	88%	92%	94%	94%	97%	98%	45%	94%
Proteus mirabilis	83%	90%	92%	95%	95%	91%	93%	0%	90%

N/A = not appropriate for this organisms

Table 2. Daily costs* of common oral antibiotic regimens for treating UTI

Regimen	Average Daily Cost
amoxicillin 500 mg TID	\$1.10
amoxicillin/clavulanic Acid 500 mg TID	\$3.00
cefixime 400 mg once daily	\$3.70
cephalexin 500 mg QID	\$1.80
ciprofloxacin 500 mg BID	\$3.40
nitrofurantoin (Macrobid®) 100 mg BID	\$1.48
trimethoprim/sulfamethoxazole 1 DS tablet BID	\$0.26

* Figures listed represent drug acquisition cost only and do not include dispensing fee.

- absence of gastrointestinal abnormalities that may reduce absorption

Like uncomplicated cystitis, uncomplicated pyelonephritis is usually caused by *E. coli*, although the disease-causing strains have unique virulence characteristics.⁵ In complicated pyelonephritis, pathogens include other *Enterobacteriaceae* (e.g. *Enterobacter*, *Serratia*, *Proteus*, *Klebsiella*) in addition to *E. coli*, *Pseudomonas*, *Enterococcus* and group B *Streptococci*.¹¹ As for complicated cystitis, patients with complicated pyelonephritis who have been recently/recurrently hospitalized are at risk for developing antibiotic resistant organisms, and may require agents beyond the scope of this algorithm. The increased risk of enterococcal involvement in the setting of complicated pyelonephritis generally warrants specific empiric enterococcal treatment with either intravenous ampicillin (in combination with gentamicin or ceftriaxone) or oral amoxicillin/clavulanate.

Gentamicin is a good empiric option for pyelonephritis as it concentrates well in the urine and is highly effective against *E. coli*.⁶ Its pharmacodynamic activity allows it to be given as a once-daily dose for patients with adequate renal function (GFR greater than 60mL/min). Due to the risk of nephrotoxicity and irreversible vestibular and oto toxicity, it is important that gentamicin be switched to an appropriate oral agent as soon as possible.

Asymptomatic Bacteriuria

With the exception of patients who are pregnant or who will be undergoing a urologic procedures where mucosal bleeding is anticipated (e.g. transurethral resection of the prostate), antimicrobial treatment for asymptomatic bacteriuria is generally not indicated.² Asymptomatic bacteriuria, while infrequent in adults, may be present in up to 50% of elderly patients, especially females. This increase in bacteriuria is partially attributable to urinary incontinence and catheterization.² In this population, routine screening measures are not indicated, as treatment is unwarranted.² There is no evidence that asymptomatic bacteriuria in the

elderly is associated with incontinence, decreased renal function, or hypertension.¹¹ Unnecessary treatment leads to increased local resistance to antibiotics and has not been shown to alter overall cognition, morbidity or mortality.¹³

Pregnancy

In pregnancy, asymptomatic patients should be treated as there is an increased risk for pyelonephritis, preterm labor, fetal mortality, and gestational hypertension.¹⁴ Screening for bacteria is recommended at 12-16 weeks. If bacteria are present, pre and post treatment urine cultures are recommended along with monthly urine cultures for the remainder of the pregnancy.¹¹ Antibiotic treatment is directed toward the specific pathogen cultured in pregnant women with asymptomatic bacteriuria and should be decided on according to urine culture and sensitivity reports. Nitrofurantoin should be avoided near term (36-42 weeks) and during labour, due to the risk of hemolytic anemia in the newborn.¹¹ Trimethoprim and TMP/SMX should be avoided during the first trimester because of concerns that that trimethoprim may act as a folate acid antagonist and lead to fetal abnormalities. TMP/SMX should also be avoided during the last 6 weeks of pregnancy due to the risk of hemolytic anemia, jaundice and kernicterus in the newborn.¹¹ Amoxicillin, cephalexin, and cefixime represent safe options that can be given for the full duration of pregnancy.¹¹

Transurethral Resection of Prostate (TURP) or other Urologic Surgery

Empiric antibiotic prophylaxis is often indicated prior to urologic procedures, depending on risk of resultant bacteremia. Urine cultures are collected before high-risk procedure and when positive, antibiotic prophylaxis should be directed toward the specific pathogens cultured.

References

Available upon request.

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