

A Practical Guide to Diagnosis and Treatment of Infection in the Outpatient Setting

Diagnosis and Treatment of Urinary Tract Infections

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Urinary tract infections (UTI) encompass a wide range of infections each involving a portion of the urinary tract. Subtypes of UTIs include urethritis, prostatitis, epididymitis, vaginitis, cystitis, pyelonephritis, emphysematous pyelonephritis, and perinephric abscesses. Since the focus of this article is on outpatient treatment of urinary tract infections, the more serious forms of UTI that require inpatient treatment will not be discussed. In fact, we will concentrate on diagnosis and treatment of simple cystitis.

The exact incidence of cystitis in adults is not known, although surveys of adult women suggest that up to 50% have had at least one symptomatic episode during their lifetime. Men have a much lower incidence of cystitis with approximately 5 to 8 UTIs occurring per year per 10,000 young to middle-aged men.

Although cystitis may occur in otherwise healthy individuals, certain predisposing factors increase the likelihood of infection. These include anything that adversely alters any of the natural body defenses against UTI which are: 1) urine pH, 2) urine flow, 3) bactericidal activity of cytokines released by normal bladder mucosa, 4) urinary inhibitors of bacterial adherence (Tamm-Horsfall protein, bladder mucopolysaccharide, sIgA, etc), 5) inflammatory response (PMNs, cytokines), 6) intact immune system, and 7) prostatic secretions.

Microbiology. The most common cause of urinary tract infections is *E.coli* which causes 80 to 85% of all cases. Over the years, *E. coli* has exhibited an ever increasing degree of resistance to the antibiotics usually employed as first line drugs for the treatment of simple cystitis. Resistance to ampicillin and trimethoprim/sulfamethoxazole has now become so prevalent among community strains of *E. coli* that these drugs can no longer be trusted as empiric therapy.

Other gram-negative organisms that cause community acquired cystitis are *Proteus* and *Klebsiella* species. Among gram positive organisms, *enterococcus* species, *Staphylococcus saprophyticus* and group B *streptococcus* are the most clinically significant, the latter being most important in pregnant women.

Diagnosis of cystitis. By definition, cystitis is a superficial infection involving the bladder mucosa. It is not an invasive disease, although if left untreated sometimes may advance to pyelonephritis which is an invasive infection.

Symptoms can, but don't always, include dysuria, urinary frequency, and pelvic or low back pain. Dysuria can also be seen in patients with urethritis and vaginitis, so a careful vaginal exam should be done, looking for vaginal discharge and inflamed vaginal mucosa, and swabs should be sent for detection of GC and Chlamydia in appropriate cases. Dysuria and urinary frequency will not be discernable in a catheterized patient, but

other symptoms such as pelvic pain, malaise or bladder spasms might tip one off to the diagnosis. Fever, nausea/vomiting and flank pain is rare in simple cystitis and should prompt the physician to consider a diagnosis of pyelonephritis.

Urine culture combined with urinalysis is the gold standard for *confirming* the clinical diagnosis of cystitis. Urine samples are best obtained as a midstream, clean catch specimen to avoid contamination with surface colonizing bacteria and epithelial cells.

Urinalysis needs to accompany every urine culture. A common error that many primary care physicians make is that they order a urine culture without a urinalysis. A diagnosis cannot be made by urine culture alone. A positive urine culture in the absence of significant pyuria may represent a contaminated specimen, or asymptomatic bacteriuria (addressed below). If no urinalysis is ordered, it is extremely difficult to distinguish between a contaminated culture and one that represents true infection.

A review of each component of a urinalysis will be given here:

Urinary WBCs – Greater than 10 WBC per high power field (hpf) in unspun urine represents true pyuria. Urinary WBC less than this virtually rules out UTI, except in the case of neutropenic patients who do not have the ability to generate a pyogenic response. On the flip side, the presence of pyuria does not always equate with infection. Although this is a quantified value, functionally it is only a qualitative result. Degree of pyuria does not correlate well with severity of infection since changes in the volume of urine output can either dilute or concentrate the urine, thus changing the number of WBC per hpf. For this same reason, serial urine WBCs are not useful for monitoring response to therapy.

Urinary RBCs – Presence of microhematuria is common in simple cystitis. Its presence, however, virtually rules out urethritis or vaginitis in patients with dysuria.

Urine nitrite – This test detects the presence of bacteria in urine. Bacteria reduce nitrates, naturally present in urine, to nitrites. This test is not very sensitive and may be falsely negative when bacteria are present in lower concentrations. It has fairly high specificity. In other words, if it is positive it usually indicates the presence of bacteria. Bacteriuria may be present in the absence of infection, so a positive nitrite does not always indicate UTI.

Leukocyte esterase – This dip-stick test detects the presence of pyuria. It is up to 96% sensitive and 98% specific for detecting urinary WBCs when present greater than 10 per hpf of urine.

Microscopic examination of urine for bacteria or yeast – This is a controversial test. Some authors feel it is very sensitive, others doubt its reliability in diagnosing UTIs. The presence of one bacterial cell per oil-immersion field of clean catch, gram stained, uncentrifuged urine correlates with at least 100,000 bacteria per ml of urine. Results, however, can vary because of urinary dilution or the level of ability and skill of the lab technician. Presence of large number of monomorphic bacteria or yeast in the presence of pyuria should be enough information to guide a physician on choosing an effective empiric antimicrobial regimen.

Epithelial cells - More than 5 – 10 epithelial cells per hpf usually indicates that a specimen has come in contact with surface epithelium (meatal skin or vaginal mucosa) and is therefore contaminated. If the urine culture is positive and there are numerous epithelial cells in the urinalysis, then the culture may represent a surface colonizer rather than a pathogen.

Urine culture – Due to the difficulty in sterilizing the urethral meatus urine cultures can become easily contaminated. In addition to a urinalysis, the colony count of bacteria in the urine culture aids in determining whether true infection is present. As a general rule, colony counts greater than 100,000 bacteria per ml of a *clean catch, midstream* urine specimen represent a UTI, whereas colony counts of less than 10,000 represent contaminants. This rule is, however, not perfect. There are many instances when someone with a frank UTI has low colony counts in the urine and other instances when high colony counts occur in the absence of infection. The Infectious Disease Society of America (IDSA) indicates that a colony count of greater than 100,000 is 80% sensitive and 90% specific in making a diagnosis of cystitis.

The bottom line of making a diagnosis of cystitis is that there must first be a clinical suspicion that a UTI is present (suggestive symptoms and signs), *then* urinalysis and urine culture are performed to *confirm* the diagnosis. Correct diagnosis prevents inappropriate use of antibiotics.

Empiric antibiotics for treatment of cystitis. The results of the urine culture aid in choosing a proper antibiotic. However, urine cultures are frequently not finalized for two to three days during which time the patient should be on some sort of antibiotic. A sound knowledge of the sensitivity patterns in one's community is central to picking a proper empiric regimen. Below is a sample of percent sensitivities from the Las Vegas area for the most common bacteria involved in UTIs.

	Ampicillin	TMP/SMX	Cephalexin	Levaquin
E. coli	55	78	92	90
P. mirabilis	74	75	92	76
K. pneumoniae	0	76	76	78
E. faecium	14	NA	NA	0
E. faecalis	100	NA	NA	36

Based on the above information, it is apparent that ampicillin and trimethoprim/sulfamethoxazole (TMP/SMX), which for many years were the drugs of choice for treatment of UTI, are no longer reliable empiric antibiotics. Now, cephalexin (Keflex) or a quinolone like Levaquin are the drugs of first choice for cystitis before the results of urine cultures are known.

Obviously, if one has the luxury of knowing the results of the urine culture before treatment has begun, the antibiotic should be chosen according to antibiotic sensitivities reported by the lab. One must realize that not all antibiotics to which the organism is listed as being sensitive will be effective. For example, tetracycline is not excreted into the urine, so even if the lab indicates that an organism is sensitive to tetracycline, using it would surely lead to treatment failure.

Treatment of uncomplicated cystitis is for 3 days. The presence of any complicating variables, such as an anatomical abnormality in the bladder, the presence of kidney stones, the presence of a urinary catheter, or recurrent UTIs require a longer course of 7 to 10 days.

Asymptomatic bacteriuria is defined by the IDSA as:

- For asymptomatic women, bacteriuria is defined as 2 consecutive voided urine specimens with isolation of the same bacterial strain in quantitative counts 100,000 cfu/mL
- A single, clean-catch voided urine specimen with 1 bacterial species isolated in a quantitative count 100,000 cfu/mL identifies bacteriuria in men
- A single catheterized urine specimen with 1 bacterial species isolated in a quantitative count 100 cfu/mL identifies bacteriuria in women or men

Asymptomatic bacteriuria does not require antibiotic treatment. If left untreated, most patients experience no adverse consequences. On the flip side, studies show that they derive no benefit from antibiotics. Don't be fooled by pyuria either. If it occurs in an asymptomatic patient, no treatment is required.

The incidence of asymptomatic bacteriuria increases with age. School age girls have an incidence of 1%, while healthy women over the age of 80 have an incidence of over 20%. Married, premenopausal women have a rate of 4.6% while nuns of comparable age have a rate of 0.7%, which suggests that sexual activity increases the risk of developing bacteriuria. In men, it is less common. In young men, bacteriuria is so rare that if identified, it requires a thorough work-up for urologic abnormalities. In men over 75, the incidence increases to 10 to 15%, probably due to prostatism.

Overuse of antibiotics in the treatment of UTIs comes from urinalyses and urine cultures obtained from asymptomatic patients by well-meaning physicians who believe that they should routinely screen patients for UTI. Urine studies are *confirmatory* tests. In other words, one first has the clinical suspicion that a patient has a urinary tract infection, then one orders the urine studies to confirm his suspicion. It is the rare case that someone without signs or symptoms will have a UTI. Therefore, the practice of urinary screening is to be discouraged.

The IDSA has released clinical guidelines for asymptomatic bacteriuria. In it, they advise *against* routine screening of urine for the following patients:

- Premenopausal, nonpregnant women
- Diabetic women
- Older persons living in the community; elderly, institutionalized subjects
- Persons with spinal cord injury

- Catheterized patients while the catheter remains in situ

The only cases where routine urine screening is recommended are:

- Pregnant women, who have a greater propensity to progress to pyelonephritis (40%), have an increased risk of preterm birth and low birth weight babies and have a higher rate of perinatal mortality when asymptomatic bacteriuria is present.
- Before transurethral resection of the prostate
- Before urologic procedures for which mucosal bleeding is anticipated

In these cases, asymptomatic bacteriuria can be adequately treated with three to seven days of antibiotics. Pregnant women should have follow up urinalysis and urine culture to assure clearance of the subclinical infection.

Summary. The diagnosis of simple cystitis requires clinical suspicion based on symptoms of dysuria, urinary frequency, pelvic and/or lower back pain. The clinical suspicion is then confirmed using a urinalysis and urine culture. A urine culture sent without a urinalysis is difficult to interpret. If significant pyuria, a positive nitrite and/or positive leukocyte esterase is reported on the urinalysis with a low number of epithelial cells, then the diagnosis of UTI is confirmed and the patient can be started on antibiotics. Cephalexin or Levaquin is preferred if treating empirically, or other effective antibiotics based on urine culture sensitivity data if such a report is available.

One must resist the urge of obtaining a urinalysis or urine culture from a patient without signs or symptoms of UTI, except in pregnant women or in patients about to have a urologic procedure. Remember, treating asymptomatic bacteriuria does no good and withholding treatment does no harm.

Check out the IDSA website at www.idsociety.org and click on “practice guidelines” on blue control bar at the top of the page to view all of the IDSA recommendations. Currently, guidelines for diagnosis and treatment of asymptomatic bacteriuria is listed under “guidelines published in the last six months”

Look for the next article in the series on outpatient treatment of cellulitis.