Urinalysis (UA) and the Diagnosis of UTIs

Urinalyses (UAs) are one of the most commonly ordered lab tests in primary care, and urinary tract infections (UTIs) are very common in adults and not uncommon in children. However, the interpretation of UAs is not as straightforward as it may seem, and this has significant implications for diagnoses and treatment. Also treatment recommendations have changed! Enteric bacteria (in particular, Escherichia coli) remain the most frequent cause of UTIs, although the distribution of pathogens that cause UTIs is changing. More important is the increase in resistance to some antimicrobial agents, particularly the resistance to trimethoprim-sulfamethoxazole seen in E. coli.

Urinary tract infections (UTIs) are among the most common bacterial infections. It has been estimated that symptomatic UTIs result in as many as 7 million visits to outpatient clinics annually. The annual cost to the health care system of the United States attributable to community-acquired UTI alone is estimated to be approximately $1.6 billion.

UTIs are challenging, not only because of the large number of infections that occur each year, but also because the diagnosis of UTI is not always straightforward. Physicians must distinguish UTI from other diseases that have a similar clinical presentation. Some UTIs are asymptomatic or present with atypical signs and symptoms. Because of these factors, physicians frequently rely on a small number of imperfect laboratory tests to augment clinical impressions. None of these tests used individually have adequate sensitivity and specificity.

Clinical symptoms of UTIs/cystitis include frequent voiding, burning during and after voiding, suprapubic pain, and/or hematuria +/- cloudy urine with a rapid onset over 24 hours of symptoms. Symptoms of pyelonephritis can include the above and fever, chills, and flank pain.

Interstitial cystitis (IC) is a long-term (chronic) inflammation of the bladder wall. The cause is unknown. It is often misdiagnosed as a urinary tract infection. This condition is most common in ages 30-40, and women are 10 times more likely to have IC than men.
Common symptoms of interstitial cystitis include pain during intercourse, pelvic pain, urinary discomfort, urinary frequency, and urinary urgency.

**Asymptomatic bacteriuria**, a significant number of bacteria in the urine that occurs without usual symptoms such as burning during urination or frequent urination, and with no pyuria/LE, is common and may not need treatment, which makes it different from a bacterial urinary tract infection.

**Preparation for UA**
It is suggested that first-voided specimens (early morning) that have been stored in the bladder for at least 4 hours provide the most accurate results. **At least 2 hours are required to allow the growth of bacteria** – so ask the patient when they previously voided.

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Midstream clean-catch is the method most commonly used in clinical practice

The **UA dipstick** is very helpful. Leukocyte esterase has a sensitivity of 75% and specificity of 98% for the detection of a UTI. [25] A positive nitrite test has a specificity of 90% but a sensitivity as low as 30% for a UTI. [25] Combination of the 2 tests leads to a more accurate detection of a UTI with sensitivity of up to 88%. [25]

**pH** reflects the body’s ability to maintain normal acid-base balance. Infection with urease producing bacteria can result in pH >7-7.5.

**Specific gravity** correlates well with urine osmolality and provides hydration status and concentrating ability of kidneys.

**Nitrites**, a rapid indirect test for asymptomatic bacteriuria. E Coli, Klebsiella and Proteus produce nitrite from nitrate, Pseudomonas, enterococci and S Saprophyticus do not. (43) **4 hours of bladder incubation are required for bacteria to convert nitrate to nitrite**. It is therefore not uncommon to have a nitrite negative urine test result that later shows a positive urine culture result

**Leukocyte esterase (LE)** detects WBCs via esterase, an enzyme released by WBCs after 2 hours, detects the equivalent of 6 or more WBC/hpf. Sensitivity is 94% when a UTI is suspected clinically. However **false-positive results are common** when the urine is contaminated with bacteria present in vaginal fluid, when the specimen contains eosinophils or Trichomonas, and so a UA micro and/or urine culture is necessary if nitrite negative.

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The absence of leukocytes and nitrites in a fresh urine sample confirms its sterility (or inadequate bladder incubation time), while the presence of one of the markers suggests a possible urinary tract infection

**Heme/’Blood’** on dipstick does not necessarily mean there are RBCs present, a UA micro is necessary to evaluate for hematuria (>3 RBC/hpf).

**Proteinuria** is a common finding in UTI. Concern for other causes of proteinuria would require a follow-up test such as UMAC or 24 hour urine for protein.

UA micro is necessary in many cases to accurately diagnose a UTI. A ‘positive’ UA does not necessarily mean a UTI as other conditions may cause that, and a negative UA does not necessarily rule-out a UTI.

**White blood cell count (WBCs)** > 5-10 WBC is considered to be pyuria, which usually indicates a UTI. However white cells from the vagina and cervical infections and
external meatus in men and women may contaminate the urine.

**Red Blood Cell (RBCs)** >3/hpf in the urine is abnormal. Hematuria (blood in urine) associated with cystitis or urethritis will usually resolve after treatment. Persistent hematuria may indicate disease such as malignancy, kidney stones, glomerulonephritis, etc.

*NT

**Epithelial cells** in urine usually indicate contamination of the specimen from the distal urethra in men and the opening of the vagina in women. *NT

**Bacteriuria** is defined as the presence of bacteria in the urine; however, because the specimen can be contaminated with periurethra flora during collection, infection is confirmed by counting the number of bacteria.

**Urine Cultures** (UC) determine colony count and identify bacteria, and antimicrobial susceptibility. The time the urine resides in the bladder (bladder incubation time) is an important determinant of the magnitude of the colony count. The concept that more than 100,000 CFUs/ml indicates a UTI was based on morning collections of urine from adult women. Sometimes even 1-10,000 CFUs/ml (or fewer) is significant (per the Infectious Diseases Society of America definition of cystitis). 1/3 of young women with symptomatic UTI have < 10,000 CFU/ml. In infants and children 50,000 CFU per ml of a single urinary pathogen is considered significant, when pyuria is present.

UC may not be necessary as part of the evaluation of outpatients with uncomplicated UTIs [55, 56]. However, urine cultures are necessary for all children, and adults with recurrent UTIs, treatment failures, or complicated UTIs.

**Treatment of UTIs in Children (per Up-To-Date)**
Recommendations for treatment of UTIs in children has changed over the past 10 years. Diagnosis is made on the basis of the presence of both pyuria and at least 50,000 colonies per ml of a single uropathogenic organism in an appropriately collected specimen of urine. Sensitivities should be done so antibiotic choice can be adjusted if necessary. Amoxicillin and ampicillin are not routinely recommended for empiric therapy because of the high rate of resistance of *E. coli*. Similarly, amoxicillin-clavulanate, first-generation cephalosporins (eg, cephalexin), and TMP-SMX should be used with caution because of the increasing rates of resistance to these drugs in some communities. **Third-generation cephalosporins** (eg, cefotaxime, ceftriaxone, cefepime) are appropriate first-line agents for empiric treatment of UTI in children.

Fluoroquinolones (eg, ciprofloxacin) are effective for *E. coli*, and resistance is rare. However, the safety of quinolones in children is still under study [28] Ciprofloxacin should not be used as a first-line agent. The American Academy of Pediatrics (AAP) Committee on Infectious Diseases recommends that the use of ciprofloxacin for UTI in children be limited to UTI caused by *Pseudomonas aeruginosa* or other multidrug-resistant, gram-negative bacteria [28].

After 7 to 14 days of antimicrobial treatment, close clinical follow-up monitoring should be maintained to permit prompt diagnosis and treatment of recurrent infections. Ultrasonography of the kidneys and bladder should be performed to detect anatomic abnormalities. Pediatrics 2011;128: 595–610
http://pediatrics.aappublications.org/content/early/2011/08/24/peds.2011-1330
Treatment of UTIs in Adults per Up-To-Date

Nitrofurantoin 100 mg bid for 5-7 days shows clinical efficacy 90 to 95% based on randomized trials [39-42]. Nitrofurantoin should be avoided if there is suspicion for early pyelonephritis, and is contraindicated when creatinine clearance is <60 mL/minute. Trimethoprim-sulfamethoxazole TMP-SMX DS [160/800 mg] bid for 3-7 days shows clinical efficacy rate 86 to 100% [39,40,43,44]. Empiric TMP-SMX should be avoided if the prevalence of resistance is known to exceed 20 percent [22,23] or if the patient has taken TMP-SMX for cystitis in the preceding 3 months [18,19]. In some regions trimethoprim (100 mg twice daily for three days) is used in place of TMP-SMX and is considered equivalent [35]. If factors preclude use of the above antibiotics, fluoroquinolones (ciprofloxacin, levofloxacin, ofloxacin in 3-day regimens) are reasonable, though, when possible, fluoroquinolones should be reserved for important uses other than acute cystitis. Nitrofurantoin and beta-lactams should usually not be used in men with cystitis, since they do not achieve reliable tissue concentrations and would be less effective for occult prostatitis.

Conclusion

Most patients with uncomplicated acute cystitis have cases that are clinically straightforward, and they may not require any laboratory testing beyond urinalysis. For a significant number of patients, however, the clinical history and physical findings alone may be insufficient to make a definitive diagnosis of UTI. For those patients and for patients with complicated UTIs, laboratory tests are necessary to make the diagnosis and to provide specific information regarding the identity and the antimicrobial susceptibility pattern of pathogens. Both the laboratory diagnosis and the clinical diagnosis of laboratory test results must be made in light of the method of collection used. Of the available laboratory tests, urinalysis is helpful primarily as a means of excluding bacteriuria, but it is not a surrogate for culture. Although cultures identify pathogens, the accurate interpretation of culture results requires clinical information that is usually available only to the clinician. We hope that primary care providers will understand both the strengths and the limitations of the laboratory-based diagnostic studies for UTIs that have been reviewed, and that they will incorporate this understanding with current treatment guidelines [65] to optimize patient care.

References:


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