



NCC Pediatrics Continuity Clinic Curriculum: Urinary Tract Infections *Faculty Guide*



Goals & Objectives:

- Identify signs and symptoms of urinary tract infections
- Discuss how to properly diagnose urinary tract infections
- List indications for admitting a patient with a UTI
- Compare and contrast UTI management in infants, toddlers, school-age children, and adolescents
- Apply the new AAP clinical practice guideline to the case of an infant with their first UTI

Pre-Meeting Preparation:

- “Urinary Tract Infections in Children” (*PIR, 2018*)
- “The New AAP Urinary Tract Infection Guideline” (*Pediatrics, 2011—commentary on 2011 AAP CPG—please note that the CPG contains the most up to date recommendations regarding VCUG and prophylaxis for VUR*).
- Parent Handout for UTIs

Conference Agenda:

- Review UTI Quiz
- Complete UTI Cases
- **“Hands-on” Activity:** Review urine dipstick use in the clinic. Residents and staff may provide their own “mystery samples” for practice dipping.

Post-Conference: Board Review Q&A

Extra-Credit:

- **“Urinary Tract Infection: Clinical Practice Guideline for the Diagnosis and Management of the Initial UTI in Febrile Infants and Children 2 to 24 Months”** (*Pediatrics, 2011*)
- • **Background Commentary of RIVUR Investigators** (*Pediatrics, 2008*)
- **RIVUR Study Website** (*includes Study Description, Toolkits for Parents & Physicians*)
- **Update of the EAU/ESPU guidelines on urinary tract infections in children** (*Journal of Pediatric Urology, 2021*)

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Urinary Tract Infections in Children

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Educational Gaps

Consideration of risk factors for urinary tract infections (UTIs) in young children with fever is critical for accurate diagnosis, as well as prevention of overtesting. The use of perineal bags to collect urine from young children should be limited to specific indications in the diagnosis of UTIs. Screening for and managing bowel and bladder dysfunction reduces the risk of UTIs in older children.

Objectives After completing this article, readers should be able to:

1. Recognize the risk factors for urinary tract infections (UTIs) in children.
2. Review the interpretation of urinalysis and urine cultures.
3. Review antibiotic therapy choices for UTIs.
4. Describe which children need imaging after febrile UTIs.
5. Discuss prevention strategies to discuss with families.

CASE STUDY

Charlotte is a 13-month-old girl with a history of 2 febrile urinary tract infections (UTIs) 4 and 6 months ago. She had normal renal and bladder ultrasonographic findings 6 months ago. She presents with a fever that began yesterday. She has no other new symptoms. Her 4-year-old brother had a self-limited febrile illness 1 week ago, which resolved. At examination, she is fussy but consolable and alert. She is non-toxic appearing. Her physical examination findings show tachycardia with a heart rate of 130 beats/min, without murmur. Her respiratory rate is 28 breaths/min, without distress or retractions. Her lungs are clear bilaterally. Her tympanic membranes appear normal. Her abdomen is soft and nontender. Her genital examination findings appear normal, without erythema or labial adhesions. Her temperature is 102.5°F (39.2°C). A bag is placed to collect a urine sample. The urinalysis from the bag sample has 5 to 10 white blood cells (WBCs) per high-power field, a 1+ leukocyte esterase result, and a 1+ ketone result. Should a bag have been placed to collect urine? Does Charlotte have a UTI? How should she be treated at this point?

EPIDEMIOLOGY

UTIs are one of the most common bacterial infections in childhood, accounting for 5% to 14% of pediatric emergency department visits. (1) The prevalence of

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ABBREVIATIONS

AAP	American Academy of Pediatrics
CFU	colony-forming unit
DMSA	dimercaptosuccinic acid
IV	intravenous
UTI	urinary tract infection
VCUG	voiding cystourethrogram
WBC	white blood cell

UTIs and their effect on the health of children are substantial throughout childhood, from the neonatal period to late adolescence (2). Infants and toddlers cannot localize UTI symptoms, cannot submit spontaneous urine samples, and have other distinct characteristics when compared to children over 24 months of age; therefore, we will simplify this review of UTIs into 2 age groups: children less than 24 months of age (whom we will define as *infants and toddlers* in this review) and children 2 years of age and older.

Infants and Toddlers under 24 Months of Age

Roughly 7% of infants and toddlers who present with fever have a UTI. (1) Race, age, sex, circumcision status in male infants and toddlers, and other factors alter the prevalence. Knowledge of how these risk factors affect the likelihood of a UTI in a particular child is critical when assessing whether the child should ultimately undergo urine testing. When considering race, 10% of white febrile infants and toddlers without focal findings to suggest another source of infection will have a UTI, while 2% of black febrile infants and toddlers will have a UTI. (3) When considering sex and age, female febrile infants 12 months of age or less have a 6% to 8% prevalence of UTI, while febrile girls older than 12 months have a prevalence of 2%. The prevalence of UTI in febrile male infants is markedly affected by the circumcision status of the infant. Uncircumcised febrile male infants less than 3 months of age have a 20% risk of UTI, compared with a 2.4% risk in similar but circumcised male infants. In both circumcised and uncircumcised male patients, the prevalence of UTIs decreases with age. For example, circumcised febrile boys older than 12 months have a less than 1% risk of UTI. Additional factors, such as duration of fever, previous history of UTIs, and congenital anomalies of the urinary tract, alter the likelihood of UTI.

Children 2 Years of Age and Older

Children 2 years of age and older who present with urinary symptoms (dysuria, urinary hesitancy) have an overall 8% risk of UTI. (1) However, as in infants, important factors should be considered that modify risk. After 2 years of age, children are more able to report and localize specific symptoms, such as dysuria. The prevalence of UTI in boys 2 years of age and older is low, especially in circumcised boys. Important factors that affect prevalence in this age group include bladder- or bowel-withholding behaviors, congenital anomalies of the urinary tract, and previous history of UTI.

PATHOGENESIS

UTIs are usually caused when bacteria invade and ascend up the urinary tract from the urethra and into the bladder.

Cystitis, a lower UTI, occurs when the infection and inflammatory response are localized to the bladder. Pyelonephritis is an upper UTI in which the bacteria and subsequent inflammatory response further ascend to the ureters and kidneys. Colonic bacteria are typically the culprits. *Escherichia coli* is the most common bacteria that causes UTIs in all ages, accounting for 54% to 67% of UTIs in children. *Klebsiella* (6%–7%), *Proteus* (5%–12%), *Enterococcus* (3%–9%), and *Pseudomonas* (2%–6%) are other common causative organisms. (4)

Hematogenous spread to the urinary system is a rare cause of UTI that can occur in neonates and children with immunodeficiency. Group B *Streptococcus*, *Staphylococcus aureus*, *Candida*, and *Salmonella* can cause pyelonephritis through the hematogenous route.

Mouse models have demonstrated that *E coli* attach to the superficial cells of the bladder lining, then invade the cells and multiply. These cells are shed in defense, which exposes lower layers of cells for bacterial invasion. These lower-layer cells that have bacteria could be the source of recurrent UTIs. Toll-like receptors are an important component of the host defense of UTIs. These toll-like receptors are on the surface of the bladder and activate the host inflammatory response by attracting WBCs to the surface of the bladder. (5)

CLINICAL PRESENTATION AND ESTIMATING RISK OF UTI

The clinical presentation of UTI varies with age. Infants generally present late in the course of infection because of initial nonspecific signs, such as fever, and the inability to express symptoms or localize pain. Older children can usually localize early symptoms of UTI, such as dysuria or abdominal pain, and therefore present earlier in the clinical course.

Infants and Toddlers under 24 Months of Age

Infants and toddlers under 24 months of age who have a UTI most often present with fever. Fever is a common and nonspecific symptom for which clinicians should consider UTI as an etiologic origin, especially when there are no other obvious signs or symptoms to suggest another diagnosis. Obvious signs such as a new rash may suggest a viral syndrome. Recent new respiratory symptoms, such as cough and congestion, suggest a respiratory infection. In the absence of other obvious symptoms, clinicians should be vigilant when assessing risk factors because about 7% of febrile infants and toddlers without an obvious source have a UTI. Clinicians should use the American Academy of

Pediatrics (AAP) Clinical Practice Guideline for the Diagnosis and Management of the Initial UTI in Febrile Infants and Children 2 to 24 months of age when assessing risk of UTI in this age group. (6) The risk factors in Table 1 from the 2011 AAP Clinical Practice Guideline allow the clinician to evaluate the likelihood that a febrile infant has a UTI.

The guidelines use both a probability of UTI of up to 1% and up to 2% to allow clinicians to use their judgment in what is considered low risk and therefore to determine which children need to be further tested for UTIs. The probability of a UTI increases as the number of risk factors increases. The guidelines allow clinicians to calculate a pretest probability of UTI to make an informed decision

about which children require further evaluation for UTI. Clinicians should also take into account other factors, such as ability to follow up and previous history of UTI, and include the family in the decision-making. If the decision is made to forego testing for UTI, follow-up is crucial, as risk factors such as severity and duration of fever may change.

Risk factors for UTIs in female infants of this age group include white race, age less than 12 months, temperature greater than or equal to 102.2°F (39°C), and absence of another source of infection. The probability of UTI for male patients is most influenced by circumcision status. In febrile, uncircumcised male infants and toddlers under 24 months of age, the risk of UTI exceeds 1% without any additional risk factors.

Ill-appearing children who present with nonspecific symptoms such as fever have important additional diagnostic considerations that include bacteremia and sepsis. Ill-appearing children who warrant antibiotics because of the concern for a serious infection, such as sepsis, should be tested for a UTI. Urine specimens should be collected for urinalysis and culture because the antibiotics may treat an otherwise unknown UTI, masking the diagnosis from the clinician. Even though antibiotics for sepsis or bacteremia may adequately treat UTI, it is important to establish the diagnosis to determine antibiotic duration and choice, future risk of UTI, and possible preventative measures, as discussed in the management section.

Differentiating a lower UTI from an upper tract infection in infants on the basis of signs and symptoms is difficult, but if fever is present, most consider the infant to have upper tract involvement and therefore pyelonephritis. Laboratory values such as procalcitonin and C-reactive protein, when increased, have been shown to be helpful in assessing infants for renal involvement during an infection. (7) If further clarification is necessary, a dimercaptosuccinic acid (DMSA) scan can be performed. In a DMSA scan, DMSA is combined with a radionuclide to image the kidneys by using gamma cameras. A DMSA scan provides the best means of definitively identifying upper UTI but should not be routinely performed because typically, the management will not be altered on the basis of the results and because of radiation exposure related to DMSA. (8)

Infants less than 2 months of age are not included in the AAP guidelines. UTI should be considered for every febrile infant less than 2 months of age. Clinicians should be vigilant in assessing febrile infants less than 2 months of age for UTIs, even those with obvious respiratory symptoms. Infants in this age group with respiratory symptoms have an appreciable risk of UTI, with 1 study showing

TABLE 1. Probability of Urinary Tract Infection Among Febrile Infant Girls and Boys According to Number of Findings Present

PARAMETER	VALUE
Girls	
Individual risk factors	White race Age <12 mo Temperature ≥102.2°F (39°C) Fever ≥2 d Absence of another source of infection
Probability of urinary tract infection	
≤1%	No. of risk factors present: No more than 1
≤2%	No. of risk factors present: No more than 2
Boys	
Individual risk factors	Nonblack race Temperature ≥102.2°F (39°C) Fever ≥24 h Absence of another source of infection
Probability of urinary tract infection	
≤1%	No. of risk factors present: For circumcised boys, no more than 2.*
≤2%	No. of risk factors present: For circumcised boys, no more than 3. For uncircumcised boys: No additional risk factors.

*For uncircumcised febrile boys, probability of UTI exceeds 1% even with no risk factors other than being uncircumcised

respiratory syncytial virus–positive febrile infants having a UTI risk of 7%. (9) In infants who present with symptoms of bronchiolitis or respiratory syncytial virus–positive bronchiolitis, 1 systematic review showed that the risk of UTI was 3.3%. (10)

Children 2 Years of Age and Older

In older children, symptoms such as dysuria, urinary frequency, and/or suprapubic discomfort are common with cystitis. These symptoms should prompt testing for UTI. However, when evaluating children for UTI, other diagnoses should be considered. Patients should be evaluated for non-UTI causes of dysuria, such as obstruction, *Candida* infection, and vulvovaginitis in female patients, by compiling a history and performing a physical examination. (11)

Dysuria and urinary symptoms, along with more systemic symptoms, such as flank pain, costovertebral pain, abdominal pain, and/or fever, are suggestive of upper urinary tract involvement and thus pyelonephritis. However, older children with UTI may present with systemic symptoms without dysuria or urinary symptoms. The differential diagnosis for symptoms of pyelonephritis includes appendicitis, viral gastroenteritis, bacterial enteritis, renal stones, and, in the female adolescent, pelvic infections.

DIAGNOSIS

Accurately diagnosing UTIs is critical. Establishing the diagnosis is important to be able to treat and resolve the infection with appropriate antibiotics, prevent further ascension of the infection to the kidneys, determine future risk of UTI, and avoid long-term renal disease. However, overtesting and overtreating expose children to painful procedures, unnecessary antibiotics, and worry. Therefore, careful assessment of the diagnostic test results is important.

The diagnosis of UTI in children is based on the results of urinalysis and urine culture. (6) Demonstration of both inflammation in the urine (WBCs, leukocyte esterase) and bacteria growing in the culture is critical. There are diseases that cause urinary inflammation without bacteria (sterile pyuria) in the urine. Examples include Kawasaki disease and infections outside the urinary system, such as viral infections or pneumonia. Also, bacteria may be present in the urinary tract without causing inflammation and infection (asymptomatic bacteriuria).

Compiling a history and performing a physical examination are important in establishing the diagnosis in all ages. Clinicians should screen for conditions that predispose the patient to or mimic UTIs, such as labial adhesions, *Candida* infection, and vulvovaginitis in female patients. In male patients, an obstructed urinary stream (such as dribbling of urine from the urethra) may suggest posterior urethral valves or phimosis.

Infants and Toddlers under 24 Months of Age

Urine Collection. Infants are generally not able to submit a clean-caught, voided specimen; therefore, catheterization is often performed to collect a urine sample for urinalysis and culture. Urine collection with a bag is also an option with special considerations, but the urine collected should only be analyzed for urinalysis and not culture. Bacteria growing on the skin in the genital area and not in the urinary tract could contaminate the bag specimen. When evaluating infants for UTIs, the clinician can review with the family the advantages and disadvantages of urine collection through catheterization or by using a bag, as reviewed in Table 2.

In 1 study, a pediatric emergency department was able to reduce the use of urinary catheterizations by one-half in infants and toddlers 6 months to 24 months of age, without missing UTIs by obtaining urine from bag specimens that were placed by the nurse early in the visit. (12) Patients with

TABLE 2. Advantages and Disadvantages of Urine Collection via Bag versus Catheterization

	ADVANTAGES	DISADVANTAGES
Catheterization	Quick Urine culture can be sent initially	Pain and discomfort
Bag specimen	May prevent the pain and discomfort from catheterization if urinalysis findings are normal	If urinalysis findings are abnormal (increased white blood cell count or leukocyte esterase) then would proceed to catheterization to confirm May take a substantial amount of time for an infant to void in the bag

bag urine specimens with evidence of inflammation (moderate or large leukocyte esterase or nitrites) underwent catheterization for culture and had antibiotics started while culture results were pending.

Suprapubic needle aspiration of urine from the bladder is also an option for obtaining urine specimens but is less commonly used because the procedure is more painful than catheterization and the success rate is low, being 53% in 1 study. (13)(14) A newer approach for urine collection in neonates and infants is the bladder stimulation technique first described in 2013. (15) The technique requires 3 trained providers and involves holding the infant upright while alternating between tapping the bladder and massaging the lower back. During this process, the third clinician waits, ready to collect the urine specimen midstream into a sterile container. Further studies are required to validate this technique before widespread use.

Interpretation of the Urinalysis Results. Once a urinalysis is obtained, the clinician must interpret the results carefully. Urine dipsticks can be used to analyze the presence of leukocyte esterase (a marker of WBCs) and nitrites (a marker of some gram-negative bacteria) among other things; however, urine dipsticks cannot be used to detect the concentration of WBCs. Microscopy of the urine allows WBC concentration data to be collected, which, together with leukocyte esterase and nitrite data, improve the sensitivity for UTIs, as shown in Table 3.

The nitrite test has poor sensitivity in infants because infants empty their bladders frequently, often before the 4 hours required for gram-negative bacteria to form nitrites. As such, absence of urinary nitrites does not rule out a UTI. However, with specificity of 98%, presence of nitrites is highly suggestive of UTI. Generally, 5 or more WBCs per

high-power field or 25 WBCs per microliter is considered pyuria and increases the likelihood of UTI. (6)

Interpretation of the Urine Culture Results. Urine culture results also need to be carefully interpreted. The number of colony-forming units (CFUs) per milliliter, the number and types of species of bacteria identified, and the time elapsed in processing of the urine sample should all be considered. Generally, 50,000 CFU/mL and higher represents considerable urine bacterial growth and is clinically significant. (6) However, 10,000 to 50,000 CFU/mL may represent UTI, especially in neonates, children with immunodeficiency, children with urinary tract abnormalities, or children already taking antimicrobial therapy.

Even if a clinically significant amount of bacteria grows in the urine culture, this does not always represent UTI. Bacterial species, such as coagulase-negative staphylococci and *Corynebacterium*, are generally noninvasive in healthy children and could be contaminants or bacterial colonizers not causing infection.

Other Studies. Additional studies, such as blood culture and serum chemistry levels in infants suspected of having a UTI, are sometimes obtained in the initial workup of the fever. Assessing which infants with a UTI also have bacteremia is difficult and, in infants older than 2 months, is often not necessary, especially if the infant is well appearing. (16) The prevalence of bacteremia in infants less than 12 months of age with a UTI is about 4% and as high as 17% in infants less than 2 months of age. (16)(17)

Children 2 Years of Age and Older

Older children are more able to voluntarily submit a clean-caught voided urine specimen for analysis, making the need for catheterization or bag collection usually

TABLE 3. **Sensitivity and Specificity of Components on the Urinalysis, Alone and in Combination**

PARAMETER	SENSITIVITY (RANGE), %	SPECIFICITY (RANGE), %
Leukocyte esterase test	83 (67–94)	78 (64–92)
Nitrite test	53 (15–82)	98 (90–100)
Leukocyte esterase or nitrite test, positive findings	93 (90–100)	72 (58–91)
Microscopy, white blood cells	73 (32–100)	81 (45–98)
Microscopy, bacteria	81 (16–99)	83 (11–100)
Leukocyte esterase test, nitrite test, or microscopy, positive findings	99.8 (99–100)	70 (60–92)

From the AAP urinary tract infection guidelines. (6)

unnecessary. A clean-catch midstream void technique is recommended. (18)

Urinalysis and culture results should be interpreted similarly and carefully, as in infants. When interpreting the urinalysis results with clean-caught voided samples, clinicians should consider the number of squamous epithelial cells at microscopy. Squamous epithelial cells are predictive of a poor urine sample, and thus a poor performance of the urinalysis, because these cells suggest local genital skin contamination. (19) One should consider repeating the sample collection if there is a clinically significant concentration of squamous epithelial cells (5 cells per high-power field or higher). Sterile pyuria in older children may be caused by Kawasaki disease, non-UTIs, sexually transmitted infections, pelvic inflammatory disease, and appendicitis (if the inflamed appendix is close to the bladder).

Children with Neurogenic Bladder Dysfunction. Children with neurogenic bladder dysfunction deserve special consideration because these children are not able to empty the bladder normally and require clean, intermittent catheterization to prevent chronic renal disease, from both high urinary pressures and chronic UTIs. Examples include children with spina bifida and spinal cord injury. Children with neurogenic bladder dysfunction have a high prevalence of asymptomatic bacteriuria; therefore, the presence of bacteria at culture alone should not suggest a UTI. The definition of a UTI in this population has not been widely established, but most agree that all of the following should be established to assign a diagnosis: presence of symptoms (fever, pain, incontinence, or cloudy urine), inflammation at urinalysis, and clinically significant growth of a single bacterial species in the urine culture. (20)

MANAGEMENT

The care of children with UTIs requires consideration of the child's age, medical history, risk factors, degree of current illness, and other unique circumstances. Besides resolving the acute infection, management is important to prevent renal injury and subsequent long-term renal insufficiency.

Antibiotics

Many antibiotics, both oral and intravenous (IV), treat the bacteria responsible for UTIs. Oral antibiotics alone are as effective as IV antibiotics for UTIs, including pyelonephritis. (21)(22) However, IV antibiotics should be administered when a child is clinically toxic appearing and may also have bacteremia and/or sepsis or when the child cannot tolerate oral antibiotics. If IV antibiotics are warranted, the child

should be transitioned to oral antibiotics when the clinical condition improves and when the patient can tolerate medications by mouth.

Culture results typically take 12 to 24 hours before bacterial growth is detected, 1 to 2 days before the specific bacterium is identified, and 2 to 3 days before susceptibilities are available. In infants and often in older children, antibiotics should be empirically initiated in suspected UTI after urinalysis but before culture results are interpreted to resolve the infection in a timely manner. However, in older children with mild symptoms, waiting for culture results can minimize unnecessary use or ineffective use of antibiotics.

The choice of the empirical antibiotic should be tailored to local bacterial susceptibility data, patient compliance, medication cost, and, if the patient has a history of prior UTI, the individual susceptibility pattern in prior infections. Antibiograms from local hospitals provide local susceptibility patterns of infectious organisms and are crucial because of varying geographic patterns. (6) See Table 4 for specific oral antibiotic choices. Table 5 depicts parental treatment options for UTIs.

A first-generation cephalosporin, like cephalexin, typically provides good coverage of uropathogens and is well tolerated, widely available, and cheap but must be taken at least 3 times per day. Trimethoprim-sulfamethoxazole is also tolerated well, is inexpensive, and requires twice-per-day dosing but has had increased resistance in past years

TABLE 4. **Some Empirical Antimicrobial Agents for Oral Treatment of UTI**

ANTIMICROBIAL AGENT	DOSAGE
Amoxicillin clavulanate	20–40 mg/kg per d in 3 doses
Sulfonamides	
Trimethoprim-sulfamethoxazole (should not be used in infants less than 2 mo of age)	6–12 mg/kg trimethoprim and 30–60 mg/kg sulfamethoxazole per d in 2 doses
Sulfisoxazole	120–150 mg/kg per d in 4 doses
Cephalosporins	
Cefixime	8 mg/kg per d in 1 dose
Cefpodoxime	10 mg/kg per d in 2 doses
Cefprozil	30 mg/kg per d in 2 doses
Cefuroxime axetil	20–30 mg/kg per d in 2 doses
Cephalexin	50–100 mg/kg per d in 4 doses

From the AAP urinary tract infection guidelines. (6)

TABLE 5. Some Empirical Antimicrobial Agents for Parenteral Treatment of UTI

ANTIMICROBIAL AGENT	DOSAGE
Ceftriaxone	50 mg/kg, every 24 h
Cefotaxime	150 mg/kg per d, divided every 6–8 h
Ceftazidime	100–150 mg/kg per d, divided every 8 h
Gentamicin	7.5 mg/kg per d, divided every 8 h
Tobramycin	5 mg/kg per d, divided every 8 h
Piperacillin	300 mg/kg per d, divided every 6–8 h

in some localities. Nitrofurantoin has good coverage of uropathogens but should not be used in pyelonephritis (and therefore younger children) because this drug does not penetrate renal tissue or blood well.

The duration of antibiotic therapy should depend on the age of the child and the degree of illness, such as lower versus upper tract involvement. For infants and toddlers less than 24 months of age or for older children with pyelonephritis, 7 to 14 days of antibiotics is recommended. (6) For older children with cystitis, a 3- to 7-day course may be adequate. Asymptomatic bacteriuria should not be treated except in pregnancy. Asymptomatic bacteriuria in pregnancy should be treated for 3 to 7 days. (23)

Imaging

Renal and bladder ultrasonography is recommended for infants and toddlers less than 24 months of age after a febrile UTI to detect anatomic abnormalities, such as an obstructive process. (6) The timing of the ultrasonographic examination depends on the clinical situation. Children who are very ill or who do not improve as expected (generally within 12–36 hours) should undergo ultrasonography within the first couple of days to assess them for an obstructive anatomic abnormality or renal abscess. Children with nonsevere infection can undergo ultrasonography after the acute phase of the infection has passed to reduce false-positive findings from renal inflammation 1 to 2 weeks later.

A voiding cystourethrogram (VCUG) should not be routinely performed in children after a first UTI. (6) A VCUG is used to evaluate the patient for vesicoureteral reflux (abnormal reflux of urine from the bladder into the ureters). Vesicoureteral reflux is graded from grade I (reflux into only the ureter) to grade V (clinically significant reflux to the kidney, with dilated ureters and calyces). Vesicoureteral reflux may predispose the child to upper urinary tract involvement

and thus possible renal damage and, ultimately, long-term renal insufficiency. However, the cost, discomfort, and radiation from routine VCUGs after a first febrile UTI offset the potential benefit of identifying clinically relevant vesicoureteral reflux in every child with UTI. VCUG is, however, recommended in children less than 24 months of age who have had a febrile UTI and who had an abnormal renal and bladder ultrasonographic finding because these children are at higher risk of grade V vesicoureteral reflux.

Prophylaxis

Antibiotic prophylaxis with trimethoprim-sulfamethoxole for children with vesicoureteral reflux reduces the risk of UTI occurrence by one-half. (24) However, more than 5,500 doses of antibiotic are needed to prevent 1 UTI. (25) Antibiotic prophylaxis has not been shown to reduce renal scarring. (24) Twice-daily administration of an antibiotic may also lead to antibiotic resistance. The decision to routinely start antibiotic prophylaxis in children with vesicoureteral reflux remains controversial. When considering this option, the clinician should take into account each child's unique characteristics and involve the family in the decision. Children with grade V reflux have been excluded from most studies of this subject. These children should receive special attention and referral to a specialist, as most treat these children with antibiotic prophylaxis and sometimes surgical correction.

Prevention by Recognizing Bowel and Bladder Dysfunction

Preventing UTIs by screening for, identifying, and treating bowel and bladder dysfunction is not controversial and is underrecognized, effective, and safe. Inquiring about constipation symptoms, daytime wetting, and withholding behaviors will help identify children with bowel or bladder dysfunction. Bowel and bladder dysfunction occurs in 20% of all children and 50% of children with a history of UTI. (26) Constipation should be treated and managed. Among children with chronic constipation, 33% of girls and 3% of boys have UTIs. (27) One study showed that in children who had relief from their chronic constipation, UTIs were eliminated in those without anatomic abnormalities. (27) Bladder dysfunction can be treated by recommending scheduled voiding, such as every 3 to 4 hours, thereby preventing the child from voluntarily withholding urine until the last minute.

Children with a history of UTIs are at higher risk of developing subsequent UTIs than are healthy children. Families of these children should be educated to seek medical evaluation early for symptoms of a UTI—especially fever. (6)

CASE STUDY CONTINUED

Thirteen-month-old Charlotte's risk factors for UTI include a febrile illness without a clear source, a history of prior UTIs, a temperature over or equal to 102.2°F (39°C), and fever duration of 2 days. She is definitely not considered low risk ($\leq 2\%$) per the AAP UTI guidelines for infants and toddlers less than 24 months of age. A urine specimen should be collected to evaluate Charlotte for a UTI. She had urine collected from a bag that showed an increased WBC count and the presence of leukocyte esterase. The urine collected from a bag should not be sent for culture because of a substantial contamination rate; therefore, a catheterization should be performed to obtain a urine specimen for culture. Catheterization-obtained urine for culture and repeat urinalysis still demonstrated 5 to 10 WBCs per high-power field. The patient was started on cephalexin because local susceptibility patterns show that more than 90% of *E coli* are susceptible to this antibiotic. Charlotte's fever resolves in 2 days, and her culture result shows 50,000 CFU/mL of pan-sensitive *E coli*. After discussion with the family, it is decided to perform a VCUG to evaluate Charlotte for vesicoureteral reflux and, if present, administer possible antibiotic prophylaxis.

Summary

1. On the basis of strong research evidence, clinicians treating young children with fever without an apparent source should include UTI as part of the differential diagnosis. Clinicians should evaluate risk factors for UTI, including age, race, temperature, fever duration, and, in male patients, circumcision status.
2. On the basis of strong research evidence, young children with symptoms who are not low risk for UTI should undergo urinalysis. The urine specimen for urinalysis can be obtained via either bag or catheterization. Urine specimens obtained from bags can be helpful to rule out UTI if the results of the urinalysis are normal. However, if the urinalysis from the bag specimen has evidence of inflammation, catheterization is necessary for culture and repeat urinalysis. A culture should not be performed on a bag specimen.

3. On the basis of some research evidence, as well as consensus, the diagnosis of a UTI should include clinical symptoms, urinalysis with evidence of inflammation (leukocyte esterase and/or at least 5 WBCs per high-power field), and culture results of at least 50,000 CFU/mL of a typical uropathogen.
4. On the basis of strong research evidence, the choice of antibiotic therapy should take into account local susceptibility data, cost of the antibiotic, and patient compliance issues. Typical good choices, depending on local susceptibility, include cephalexin and trimethoprim-sulfamethoxazole. Trimethoprim-sulfamethoxazole should not be used in infants less than 2 months of age.
5. On the basis of some research evidence, as well as consensus, young children with a febrile UTI should undergo renal and bladder ultrasonography to rule out anatomic abnormalities or signs of obstruction. VCUG should not be performed routinely after the first febrile UTI.
6. On the basis of some research evidence, as well as consensus, clinicians should screen for and manage bowel and bladder dysfunction in older children. Appropriately managing bowel and bladder dysfunction reduces the development of UTIs.

To view teaching slides that accompany this article, visit <http://pedsinreview.aappublications.org/content/39/1/3.supplemental>.

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 Pediatrics in Review

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References for this article are at <http://pedsinreview.aappublications.org/content/39/1/3>.

Additional Resources for Pediatricians

AAP Textbook of Pediatric Care, 2nd Edition

- Chapter 344: Urinary Tract Infections - <https://pediatriccare.solutions.aap.org/chapter.aspx?sectionId=125490707&bookId=1626>

Point-of-Care Quick Reference

- Urinary Tract Infections - <https://pediatriccare.solutions.aap.org/content.aspx?gbsid=165581>

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The New American Academy of Pediatrics Urinary Tract Infection Guideline

This issue of *Pediatrics* includes a long-awaited update¹ of the American Academy of Pediatrics (AAP) 1999 urinary tract infection (UTI) practice parameter.² The new guideline is accompanied by a technical report³ that provides a comprehensive literature review and also a new meta-analysis, for which the authors obtained individual-level data from investigators. The result is an exceptionally evidence-based guideline that differs in important ways from the 1999 guideline and sets a high standard for transparency and scholarship.

The guideline and technical report address a logical sequence of questions that arise clinically, including (1) Which children should have their urine tested? (2) How should the sample be obtained? (3) How should UTIs be treated? (4) What imaging and follow-up are recommended after a diagnosis of UTI? and (5) How should children be followed after a UTI has been diagnosed? I will follow that same sequence in this commentary. I will mention some important areas of agreement and make other suggestions when I believe alternative recommendations are supported by available evidence.

WHICH CHILDREN SHOULD HAVE THEIR URINE TESTED?

Unlike the 1999 practice parameter, which recommended urine testing for all children aged 2 months to 2 years with unexplained fever,² the new guideline recommends selective urine testing based on the prior probability of UTI, which is an important improvement. The guideline and technical report do an admirable job summarizing the main factors that determine that prior probability (summarized in Table 1 in the clinical report). This table will help clinicians estimate whether the probability of UTI is $\geq 1\%$ or $\geq 2\%$, values that the authors suggest are reasonable thresholds for urine testing.

The guideline appropriately states that the threshold probability for urine testing is not known and that “clinicians will choose a threshold depending on factors such as their confidence that contact will be maintained through the illness. . . and comfort with diagnostic uncertainty.” However, the authors assert that this threshold is below 3%, which indicates that it is worth performing urine tests on more than 33 febrile children to identify a single UTI. This is puzzling, because the only study cited to support a specific testing threshold found that 33% of academicians and 54% of practitioners had a urine culture threshold higher than 3%.⁴

An evidence-based urine-testing threshold probability would be based on the risks and costs of urine testing compared with the benefits of diagnosing a UTI. These benefits are not known and probably are not uniform; the younger and sicker an infant is and the longer he or she has been febrile, the greater the likely benefit of diagnosing and treating a UTI. Because acute symptoms of most UTIs seem to resolve un-

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ABBREVIATIONS

AAP—American Academy of Pediatrics

UTI—urinary tract infection

VCUG—voiding cystourethrogram

VUR—vesicoureteral reflux

Opinions expressed in these commentaries are those of the author and not necessarily those of the American Academy of Pediatrics or its Committees.

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FREE

eventfully, even without treatment,^{5,6} some of the impetus for diagnosing UTIs rests on the belief that doing so will reduce the risk of renal scarring and associated sequelae.⁷ This belief needs to be proven, and the benefit quantified, if a urine-testing threshold is to be evidence-based. Until then, rather than automatically testing urine on the basis of the risk factors and the 1% or 2% threshold suggested in Table 1, clinicians should continue to individualize. It seems reasonable, for example, to defer urine tests on the large number of febrile infants for whom, if their parents had called for advice, we would have estimated their probability of UTI or other serious illness to be low enough that they could be safely initially watched at home.

A potential source of confusion is that Table 1 lists “absence of another source of infection” as a risk factor, and the technical report indicates that this factor has a likelihood ratio of ~1.4 for UTI. However, the inclusion of this risk factor in the table is inconsistent with the text of the guideline, which directs clinicians to assess the likelihood of UTI in febrile infants with no apparent source for the fever. If children with an apparent source for their fever are included, the use of Table 1 could lead to excessive urine testing (eg, among infants with colds). For example, even using the 2% testing threshold, according to Table 1 all non-black uncircumcised boys younger than 24 months with any fever of any duration, even with an apparent source, would need their urine tested. I doubt that this level of urine testing is necessary or was intended by the authors of the guideline.

HOW SHOULD THE SAMPLE BE OBTAINED?

I am glad the new guideline continues to offer the option of obtaining urine for urinalyses noninvasively, but I am

not convinced that the bag urine can never be used for culture. If the urinalysis is used to select urine for culture, the prior probability may sometimes be in a range where the bag culture will be useful. For example, the technical report calculates that “with a prevalence of 5% and specificity of 70%, the positive predictive value of a positive culture obtained by bag would be 15%.” However, with the same 5% pretest probability, a positive nitrite test would raise the probability of UTI to ~75% (using the median sensitivity [58%] and specificity [99%] in the technical report). This is high enough to make the positive culture on bag urine convincing (and perhaps unnecessary).

Although bag urine cultures can lead to errors, catheterized urine cultures are not perfect¹ and urethral catheterization is painful,⁸ frightening,⁹ and risks introducing infection.¹⁰ Fortunately, if other recommendations in the guideline are followed (including the elimination of routine voiding cystourethrograms [VCUGs] and outpatient rather than inpatient antimicrobial therapy; see below), the adverse consequences of falsely positive bag cultures will be markedly attenuated.

HOW SHOULD UTIs BE TREATED?

The guideline recognizes regional variation in antimicrobial susceptibility patterns and appropriately suggests that they dictate the choice of initial treatment. However, I would adjust the choice on the basis of the clinical course rather than on sensitivity testing of the isolated uropathogen, as recommended in the guideline. At the University of California at San Francisco we have the option of a “screening” urine culture, which provides only the colony count and Gram-stain results for positive cultures (eg, “10⁵ Gram-negative rods”). We can later add identification and sensitivities of the organism in the rare instances in which

obtaining them is clinically indicated. Use of screening cultures can lead to considerable savings, because identification of organisms and antimicrobial susceptibility testing are expensive and unnecessary in the majority of cases in which patients are better within 24 hours of starting treatment.

The guideline and technical report cite good evidence that oral antimicrobial treatment is as effective as parenteral treatment and state that the choice of route of administration should be based on “practical considerations.” However, the examples they cite for when parenteral antibiotics are reasonable (eg, toxic appearance and inability to retain oral medications) seem more like clinical than practical considerations. Given equivalent estimates of efficacy and the dramatic differences in cost, the guideline could have more forcefully recommended oral treatment in the absence of clinical contraindications.

WHAT IMAGING IS INDICATED AFTER UTI?

As in the 1999 AAP guideline, the current guideline recommends a renal/bladder ultrasound examination after a first febrile UTI to rule out anatomic abnormalities (particularly obstruction) that warrant further evaluation. Although the yield of this test is low, particularly if there has been a normal third-trimester prenatal ultrasound scan, the estimated 1% to 2% yield of actionable abnormalities was believed to be sufficient to justify this noninvasive test. This may be so, but it is important to note that it is not just the yield of abnormalities but also the evidence of an advantage of early detection and cost-effectiveness that must be considered when deciding whether an ultrasound scan is indicated after the first febrile UTI, and this evidence was not reviewed.

The recommendation most dramatically different from the 1999 guideline

is that a VCUG not be routinely performed after a first febrile UTI. The main reason for this change is the accumulation of evidence casting doubt on the benefit of making a diagnosis of vesicoureteral reflux (VUR). To put these data in historical perspective, operative ureteral reimplantation was standard treatment for VUR until randomized trials found it to be no better than prophylactic antibiotics at preventing renal scarring.^{11–13} Although, as one commentator put it, “It is psychologically difficult to accept results that suggest that time-honored methods that are generally recommended and applied are of no or doubtful value,”¹⁴ ureteral reimplantation was gradually replaced with prophylactic antibiotics as standard treatment for VUR. This was not because of evidence of benefit of antibiotics but because their use was easier and less invasive than ureteral reimplantation. Finally, in the last few years, several randomized trials have investigated the efficacy of prophylactic antibiotics for children with reflux and have found little, if any, benefit.^{1,3} Thus, the risks, costs, and discomfort of the VCUG are hard to justify, because there is no evidence that patients benefit from having their VUR diagnosed.^{15–18}

The recommendation not to perform a VCUG after the first UTI is consistent with a guideline published by the

United Kingdom’s National Institute for Health and Clinical Excellence (NICE).¹⁹ However, unlike the AAP, the NICE does not recommend that VCUGs be performed routinely for recurrent UTIs in infants older than 6 months, which makes sense; the arguments against VCUGs after a first UTI still hold after a second UTI. The AAP recommendation to perform a VCUG after the second UTI is based on the increasing likelihood of detecting higher grades of reflux in children with recurrent UTIs and the belief that detecting grade V reflux is beneficial. However, the guideline appropriately recognizes that grade V reflux is rare and that the benefits of diagnosing it are still in some doubt. Therefore, the guideline suggests that parent preferences be considered in making these imaging decisions.

HOW SHOULD CHILDREN BE FOLLOWED AFTER A UTI HAS BEEN DIAGNOSED?

The guideline recommends that parents or guardians of children with confirmed UTI “seek prompt (ideally within 48 hours) medical evaluation for future febrile illnesses to ensure that recurrent infections can be detected and treated promptly.” As pointed out in the guideline, parents will ultimately make the judgment to seek medical care, and there is room for judgment here. After-hours or weekend visits would not generally be required for in-

fants who appear well, and the necessity and urgency of the visit would be expected to increase with the discomfort of the child, the height and duration of the fever, the absence of an alternative source, and the number of previous UTIs.

It should be noted that the guideline does not recommend prophylactic antibiotics to prevent UTI recurrences. This was a good decision; meta-analyses^{3,20} have revealed no significant reduction in symptomatic UTI from such prophylaxis regardless of whether VUR was present. Even in the study that showed a benefit,²¹ the absolute risk reduction for symptomatic UTI over the 1-year follow-up period was only ~6%, and there was no reduction in hospitalizations for UTI or in renal scarring. Thus, as one colleague put it, if UTI prophylaxis worked, it would offer the opportunity to “treat 16 children with antibiotics for a year to prevent treating one child with antibiotics for a week.” (A. R. Schroeder, MD, written communication, June 24, 2011).

CONCLUSIONS

I salute the authors of the new AAP UTI guideline and the accompanying technical report. Both publications represent a significant advance that should be helpful to clinicians and families dealing with this common problem.

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Urinary Tract Infections in Young Children



Urinary tract infections (UTIs) are common in young children. UTIs may go untreated because the symptoms may not be obvious to the child or to parents. These infections can lead to serious health problems. From this brochure, parents can learn more about urinary tract infections—what they are, how children get them, and how they are treated.

The Urinary Tract

The urinary tract makes and stores urine. It is made up of the kidneys, ureters, bladder, and the urethra (see illustration). The kidneys produce urine. Urine travels from the kidneys down two narrow tubes called the ureters to the bladder. The bladder is a thin muscular bag that stores urine until it is time to empty urine out of the body. When it is time to empty the bladder, a muscle at the bottom of the bladder relaxes. Urine then flows out of the body through a tube, called the urethra. The opening of the urethra is at the end of the penis in boys and above the vaginal opening in girls.

Urinary Tract Infections

Normal urine has no germs (bacteria). However, bacteria can get into the urinary tract from two sources: the skin around the rectum and genitals and the bloodstream from other parts of the body. Bacteria may cause infections in any or all parts of the urinary tract, including the following:

- the urethra (called "urethritis")
- the bladder (called "cystitis")
- the kidneys (called "pyelonephritis")

UTIs are common in infants and young children. About 3 percent of girls and 1 percent of boys will have a UTI by 11 years of age. A young child with a high fever and no other symptoms, has a 1 in 20 chance of having a UTI. The frequency of UTIs in girls is much greater than in boys. Uncircumcised boys have slightly more UTIs than those who have been circumcised.

Symptoms

Symptoms of UTIs may include the following:

- fever
- pain or burning during urination
- need to urinate more often, or difficulty getting urine out
- urgent need to urinate, or wetting of underwear or bedding by a child who knows how to use the toilet
- vomiting, refusal to eat
- abdominal pain
- side or back pain
- foul-smelling urine
- cloudy or bloody urine
- unexplained and persistent irritability in an infant
- poor growth in an infant

Diagnosis

If your child has symptoms of a UTI, your pediatrician will do the following:

- ask about your child's symptoms
- ask about any family history of urinary tract problems
- ask about what your child has been eating and drinking (certain foods can irritate the urinary tract and cause similar symptoms)
- examine your child
- get a urine sample from your child

Your pediatrician will need to test your child's urine to see if there are bacteria or other abnormalities. There are several ways to collect urine from a child.

- The preferred method to diagnose a UTI is to place a small tube, called a catheter, through the urethra into the bladder. Urine flows through the tube into a special urine container.
- Another method is to insert a needle through the skin of the lower abdomen to draw urine from the bladder. This is called needle aspiration.
- If your child is very young or not yet toilet trained, the pediatrician may place a plastic bag over the genitals to collect the urine. Since bacteria can contaminate the urine and give a false test result, this method is used only to screen for infection.
- An older child may be asked to urinate into a container.

Your pediatrician will discuss with you the best way to collect your child's urine.

Treatment

UTIs are treated with antibiotics. The way your child receives the antibiotic depends on the severity and type of infection. If your child has a fever or is vomiting and unable to keep fluids down, the antibiotics may be put directly into the bloodstream or muscle using a needle. This is usually done in the hospital. Otherwise, the antibiotics can be given by mouth, as liquid or pills.

UTIs need to be treated right away for the following reasons:

- to get rid of the infection
- to prevent the spread of the infection
- to reduce the chances of kidney damage

Infants and young children with UTIs usually need to take antibiotics for 7 to 14 days, sometimes longer. Make sure your child takes all the medicine your pediatrician prescribes. Do not stop giving your child the medicine until the pediatrician says the treatment is finished, even if your child feels better. UTIs can return if not fully treated.

Follow-up

After your child finishes the antibiotics, your pediatrician may want to test another urine sample to make sure the bacteria are gone. In addition, your pediatrician will want to make sure the urinary tract is normal and that the infection did not cause any damage. Several tests are available to do this, including the following:

Kidney and bladder ultrasound: Uses sound waves to examine the bladder and kidneys.

Voiding cystourethrogram (VCUG): A catheter is placed into the urethra and the bladder is filled with a liquid that can be seen on X-rays.

Intravenous pyelogram: A liquid that can be seen on X-rays is injected into a vein and then travels into the kidneys and bladder.

Nuclear scans: Radioactive materials are injected into a vein to see if the kidneys are normal. There are many kinds of nuclear scans, each giving different information about the kidneys and bladder. The radioactive materials give no more radiation than other kinds of X-rays.

Keep in mind, UTIs are common and most are easy to treat. Early diagnosis and prompt treatment are important because untreated or repeated infections can cause long-term medical problems. Talk to your pediatrician if you suspect that your child might have a UTI.

The information contained in this publication should not be used as a substitute for the medical care and advice of your pediatrician. There may be variations in treatment that your pediatrician may recommend based on individual facts and circumstances.

From your doctor

UTI Quiz

1. The prevalence of UTI in febrile infants and toddlers with no source of infection is 7%.
The incidence for uncircumcised boys < 3 months is 20%.
The incidence for circumcised boys < 3 months is 2.4%.
2. AAP guidelines use a probability of UTI up to 1% and 2% to determine need for further testing.
3. The gold standard test for diagnosing a UTI is a urine culture obtained by sterile technique. In general, how many colony-forming units/mL of growth from a specimen are required to diagnose a UTI? >50,000 CFU/mL (but only 10-50 CFU/mL in certain high risk groups including neonates, immunodeficient children, children with UT anomalies, children already on antibiotics)
4. What common condition in children leads to voiding dysfunction and is strongly correlated to recurrent UTIs? **Constipation**
5. List 4 host risk factors that predispose to urinary tract infections:
No circumcision; no breastfeeding in 1st 6mo of life, constipation, recent antibiotic use, recent sexual intercourse.
6. Which imaging study is the gold standard for diagnosing VUR? VCUG.
Renal scarring? DMSA.
7. Based on the AAP Clinical Practice Guideline, what are the indications for performing a VCUG? **If a renal/bladder ultrasound shows hydronephrosis, scarring, or if a child has recurrent febrile UTIs.**

UTI Cases

Case 1:

A 3 week old term female presents to the ED with a fever to 102.2F and fussiness that started 12 hours prior. Mother of child was GBS negative and had no history of HSV. The child is still breastfeeding well without emesis and has no focal findings of infection on exam.

Discuss which diagnostic studies you would obtain and your treatment plan including antibiotic choice.

This child warrants a **full sepsis work-up**, to include CBC, Blood Culture, Urinalysis, Urine Culture, CSF studies, and CSF Culture. Would empirically start Ampicillin and Gentamicin.

CSF studies are reassuring, but her WBC is 19,000 and the U/A is positive for Leukocyte Esterase, negative for nitrites and urine microscopy shows 20 WBC/hpf. A day into her admission, the urine culture (cath specimen) grows >10,000 cfu of E. Coli, which is resistant to ampicillin.

What imaging study if any would you order?

- Based on the AAP Clinical Practice Guidelines, Action Statement 5, febrile infants with UTI should undergo **renal and bladder ultrasonography** to look for hydronephrosis, scarring, or other findings suggesting obstructive uropathy. (*See: "What Imaging is Indicated After UTI"*).
- Based on the AAP CPG, Action Statement 6, **VCUG should not be performed routinely after the first febrile UTI**. VCUG is indicated if U/S reveals hydronephrosis, scarring, or other findings that would suggest either high-grade VUR or obstructive uropathy, as well as in other atypical or complex clinical circumstances. Further evaluation (i.e. with a VCUG) should be conducted if there is recurrence of febrile UTI.

Discuss discharge criteria, length of treatment (IV vs oral) and whether you would start prophylactic antibiotics.

- Before discharge, the child should be afebrile and well-appearing and transitioned to oral antibiotics—options in this 1mo infant include Cephalexin (Keflex), Cefdinir (Omnicef), and Nitrofurantoin.
- **Antibiotic prophylaxis for VUR is controversial**, as several studies over the past decade have demonstrated that prophylaxis *does not* prevent recurrent febrile UTIs and only leads to the development of *resistant organisms*. However, in this patient, some might argue for prophylaxis *if the U/S shows hydronephrosis, or until the VCUG can be performed (if the decision is made to obtain one based on U/S findings)*.

Case 2:

A 15 month old Caucasian girl is brought to the ED with the complaint of fever to 103 for two days and “acting fussy”. She has had no other symptoms, and has a non-focal exam.

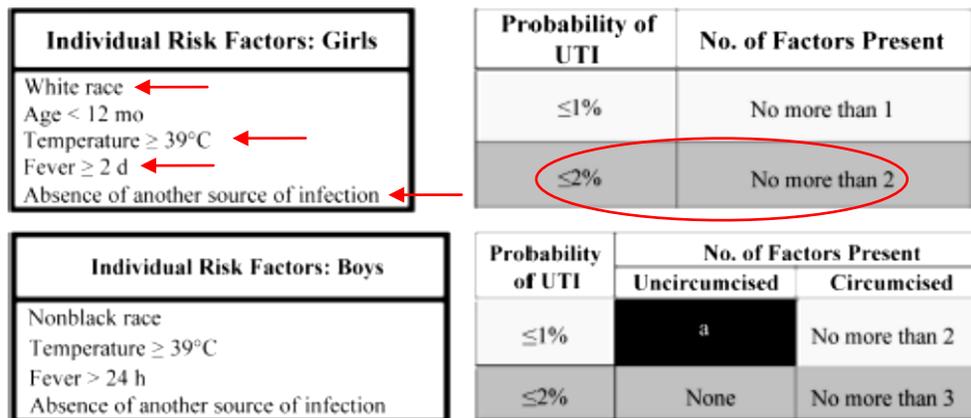
What conditions are in your differential diagnosis?

UTI, URI, AOM, Viremia, Occult Bacteremia, Peritonsillar Abscess

What are some of the symptoms that may accompany UTI in an infant or toddler?

- 0-3mo: May be nonspecific— fever, hypothermia, vomiting, diarrhea, jaundice, difficulty feeding, malodorous urine, irritability, hematuria, FTT.
- 3-24mo: More specific—cloudy or malodorous urine, increased frequency, hematuria. Some children may still present with fever without a source.
- 2-6yr: abdominal pain, suprapubic pain, CVA pain, dysuria, urgency, secondary enuresis.

Using Figure 2 from the [AAP UTI Clinical Practice Guideline](#), estimate this patient’s risk of having a UTI: >2%, based on more than 2 risk factors for UTI.



The bag U/A performed in the ED is negative for nitrites, but has trace leukocyte esterase.

How does this influence your thinking?

Nitrite test is only 53% sensitive for UTI (N.B. 2010 PIR article says 37% sensitive); therefore, not very good for ruling out UTI, especially in infants who void frequently. Also, not all urinary pathogens reduce nitrates to nitrites (e.g. enterococcus, Staph). Leukocyte esterase, in contrast, is 83% sensitive for UTI (N.B. 2010 PIR article says 73%).

Test	Sensitivity (Range), %	Specificity (Range), %
Leukocyte esterase test	83 (67–94)	78 (64–92)
Nitrite test	53 (15–82)	98 (90–100)
Leukocyte esterase or nitrite test positive	93 (90–100)	72 (58–91)

The parents adamantly refuse a urethral catheterization to obtain a urine culture. The child throws up a dose of tylenol she received 10 minutes prior.

Do you insist on performing a cath U/A? If so, how do you convince the parents? Yes (*See CPG Action Statement 3*). Discuss how a urine culture confirms the diagnosis and helps target antibiotic therapy. Pyuria is not adequate to diagnose a UTI and is not a substitute for a urine culture. A catheterized specimen avoids contamination from skin flora inherent in a bagged specimen. (*See Table 2 in PIR or Harriet Lane for minimum CFUs by method of collection*).

Discuss treatment options (which antibiotic? IV vs Oral? Duration?), as well as indications for admission and imaging. See Figure 2 for practice algorithm.

- Recent studies show that oral abx may be just as effective as IV abx in treating pyelonephritis and for shorter courses (3-7 days); however, traditionally, **10-14 day abx courses** were recommended depending on severity of infection.
- Indications for admission include age <3mo, dehydration, **inability to take PO fluids, ill-appearing child**, patients with chronic illnesses that complicate infection (e.g. sickle cell disease, DM, immunocompromise, CF, urinary tract/renal abnormalities).
- This patient may be admitted due to inability to take PO. *See Tables 4 and 5 of PIR article for antibiotic choices, stratified by location of UTI and inpatient vs. outpatient.* Ceftriaxone 50 mg/kg/day is one option for inpatient treatment in this age-group.
- Consider **renal U/S** or **DMSA scan** if uncertain of diagnosis of acute pyelonephritis, or concern for complication such as renal abscess. If this is her first febrile UTI, by the new guidelines, she will need a renal U/S but *not* a VCUG.

Case 3:

A 16-year-old girl presents with 3 days of dysuria, urgency and 1 day of fever to 103F, chills, nausea, emesis, and abdominal pain. **Use the chart below to develop a differential diagnosis and discuss how you would rule in/out that diagnosis:**

Differential Diagnosis	Pertinent (+) and (-) History and Exam Findings	Helpful lab/imaging studies to rule in/out
Pyelonephritis	Fever, emesis Dysuria, hematuria, increased frequency, hesitancy. Back pain, CVA tenderness	- U/A, UCx - Renal U/S vs. DMSA
Ectopic pregnancy	Adnexal pain, RLQ/LLQ pain, amenorrhea	- β -HCG - Transvaginal or abdominal U/S
Appendicitis	McBurney's; psoas/obturator signs Guarding Rectal exam Peritoneal findings, absent BS	- CT or U/S of abdomen - CBC
Tubo-ovarian abscess	+ GC/Chlamydia Adnexal pain on bimanual exam	- CT vs. U/S pelvis
Pancreatitis	Epigastric pain radiating to back	- Amylase/Lipase - CT vs. U/S abdomen

Based on the presence of pyuria and a positive urine culture for E.coli you diagnose this patient with pyelonephritis. Two days into her admission and course of IV ceftriaxone she remains febrile to 102 and with rigors. **Are you concerned by these findings? What is the expected clinical course for this patient?**

It is common for patients with acute pyelonephritis to continue to have high fevers, chills, nausea/emesis for 3-5 days after initiation of antibiotics. No clinical improvement *after* this time should prompt consideration of lobar nephronia/renal abscess.

UTI Board Review

1. Voiding cystourethrography in a 9-month-old boy who has new-onset febrile urinary tract infection reveals grade II vesicoureteral reflux (VUR). The parents ask you about their son's prognosis.

Of the following, you are MOST likely to explain that

- A. approximately 80% of children who have newly diagnosed febrile urinary tract infections have VUR when tested
- B. once VUR is established, no follow-up radiologic testing is indicated
- C. males have a worse prognosis than females
- D. referral to urology for ureteral reimplantation is warranted

E. unilateral grade II reflux has a high likelihood of resolution within 5 years of the diagnosis

2008PREPQ: A child who has a febrile urinary tract infection (UTI) has a 30% to 50% likelihood of having underlying vesicoureteral reflux (VUR). VUR is the reflux of urine from the bladder into the ureter and possibly kidney across the ureterovesical junction (UVJ). It may be caused by anatomic abnormalities of the UVJ or bladder (eg neurogenic bladder) or bladder outlet dysfunction (eg posterior urethral valves). VUR is estimated to occur 10 times more frequently in Caucasians than in African-Americans. Males and females are nearly equally affected, and their prognosis is similar.

There appears to be a strong familial association for VUR, with approximately 30% of siblings of an index case also having VUR when studied by voiding cystourethrography (VCUG). Despite this association, screening of asymptomatic siblings of affected children is controversial because VCUG is an invasive procedure and the benefit of identifying and treating (with prophylactic antibiotics) a child who is well and lacks symptoms is uncertain. At present, there is no consensus of opinion, although the trend is not to study asymptomatic older siblings who are toilet trained; some recommend that asymptomatic siblings younger than 1 year of age undergo VCUG.

The American Academy of Pediatrics recommends performing ultrasonography and VCUG in all children after their first febrile UTI. The present standard of care for patients who have VUR is to receive prophylactic antibiotics until the reflux has resolved. Patients typically undergo a follow-up VCUG every 12 to 18 months; the time between VCUG studies is somewhat dependent on the age of the patient and the severity of reflux.

An international classification system for VUR has grades ranging from mild (grade I) to severe (grade V). A nonsurgical approach is recommended for children who have grades I to III reflux; spontaneous resolution occurred in 80% of cases within 5 years of the diagnosis in one study. Grade IV reflux also often is managed nonsurgically. Grade V reflux traditionally has been managed surgically. A newer technique that involves endoscopic subureteral injection of dextranomer/hyaluronic acid may offer an alternative to conventional ureteral reimplantation surgery. Long-term data for this technique are not yet available.

2. A mother brings in her 3-year-old daughter because of daytime urinary incontinence and abdominal pain. The mother explained that the girl was toilet trained at 2 years of age. On physical examination, growth parameters and vital signs are normal, although the girl has mild suprapubic tenderness without associated costovertebral angle tenderness or sacral dimples. Urinalysis shows a urine specific gravity of 1.025, pH of 6.5, 2+ blood, 1+ protein, 3+ leukocyte esterase, and positive nitrite. Urine microscopy demonstrates 5 to 10 red blood cells/high-power field, 20 to 50 white blood cells/high-power field, and 3+ bacteria.

Of the following, the MOST likely etiologic agent is

- A. *Enterococcus faecalis*
- B. *Escherichia coli***
- C. *Klebsiella pneumoniae*
- D. *Proteus mirabilis*
- E. *Staphylococcus saprophyticus*

Escherichia coli is the causative organism in 80% to 90% of first-time urinary tract infections (UTIs) in children. Other pathogens include *Klebsiella pneumoniae*, *Proteus* sp, *Enterococcus* sp, and *Staphylococcus saprophyticus*. *Pseudomonas* also can be a pathogen in immunocompromised patients or those who have received repeated courses of antibiotics for recurrent infections. The clinician must assess the patient for a UTI based on signs, symptoms, and urinalysis findings.

Organisms such as *E coli*, *K pneumoniae*, and *Proteus* sp can reduce dietary nitrate to nitrite, so a positive urine dipstick test for nitrite, as reported for the girl in the vignette, is virtually diagnostic of gram-negative bacteruria. If the test result is negative in an older child in whom a UTI is suspected, the infection may be caused by a gram-positive organism such as *Enterococcus* sp or *S saprophyticus*. Of note, the nitrite test is much less helpful in infants.

Conversion of nitrate to nitrite may take up to 4 hours. Because infants and young children have small bladder volumes and urinate frequently, there may be insufficient time for nitrites to be formed and, therefore, the nitrite test may be negative even in the presence of a UTI caused by a gram-negative organism. Urine pH also may be useful in diagnosing UTIs. Urease-producing organisms (eg, *Proteus mirabilis*, some strains of *S saprophyticus*) degrade urea into ammonia, resulting in an elevated urine pH (8.0 to 8.5).

The girl described in the vignette has symptoms of a lower UTI. Options for therapy include trimethoprim-sulfamethoxazole (if local resistance patterns indicate low levels of *E coli* resistance) or a third-generation cephalosporin (eg, cefixime, cefdinir). These antibiotics also may be used for outpatient management of acute pyelonephritis. For hospitalized patients, a third-generation cephalosporin such as ceftriaxone or cefotaxime provides adequate coverage. An alternative regimen is ampicillin plus gentamicin.

3. You employ voiding cystourethrography (VCUG) to evaluate a 4-year-old girl who had a febrile urinary tract infection 1 month ago. The study reveals a smooth-walled bladder, absence of vesicoureteral reflux, and a mildly narrowed urethra.

Of the following, the MOST appropriate management in this situation is

- A. administration of prophylactic antibiotics until 6 years of age
- B. no treatment**
- C. placement of the child on a clean intermittent catheterization program
- D. repeat VCUG in 6 months
- E. urologic consultation for cystoscopic evaluation

2009 PREPQ: The patient described in the vignette has had a febrile urinary tract infection (UTI), but voiding cystourethrography (VCUG) failed to demonstrate vesicoureteral reflux. It did, however, demonstrate a narrow urethra with an otherwise normal bladder. The question that arises is whether the "narrow urethra" is associated with potential voiding dysfunction and development of the UTI.

The recognition of a distal urethral ring in some females who had UTIs in the 1960s led to the hypothesis that a narrowed urethra or "urethral stenosis" was responsible for UTIs. However, it is now recognized

that the previously termed "narrow urethra" in females is a normal variant. Indeed, dilatations led to more invasive surgeries of the internal urethra to prevent "restenosis." A recent survey of Fellows in the Section of Urology of the American Academy of Pediatrics found that 61% of respondents never use dilatation under any circumstance, and only 2% perform this procedure regularly. Therefore, no treatment is needed for the child in the vignette.

Children who have recurrent UTIs may have vesicoureteral reflux or dysfunctional voiding with incomplete bladder emptying. More recently, greater emphasis has been placed on the effects of pelvic floor muscle dysfunction in the child who has dysfunctional voiding and symptoms of enuresis, UTI, and constipation. It is theorized that the pelvic floor muscles responsible for continence in such children are hyperactive, resulting in abnormal bladder emptying and high post-void residual volumes. Biofeedback is being used to teach children how to improve relaxation of pelvic floor muscles and reduce urinary retention and UTI risk.

There is no indication for prophylactic antibiotics for a child who has a single UTI and no vesicoureteral reflux. Only children who have significant urinary retention, such as seen with neurogenic bladder (myelomeningocele) or detrusor sphincter dyssynergia (Hinman syndrome), warrant intermittent catheterization. Follow-up VCUG is not needed for the patient in the vignette. Cystoscopy is not indicated in a child who has a smooth wall bladder and no urinary symptoms.

4. You are evaluating a 5-year-old girl who has a urinary tract infection. She has had four lower urinary tract infections in the last 2 years, all of which resolved completely with oral antibiotics. She denies symptoms of urgency and frequency. The only significant finding on her medical history is constipation. Results of renal ultrasonography and voiding cystourethrography are normal. Her growth parameters and physical examination findings are normal. You prescribe oral trimethoprim-sulfamethoxazole.

Of the following, the MOST appropriate additional step to help reduce the incidence of further urinary tract infection is to

- A. begin an evaluation for immunodeficiency
- B. perform renal scintigraphy
- C. prescribe a stool softener and regular bowel routine**
- D. prescribe oral oxybutynin
- E. refer her to a pediatric nephrologist

Constipation is defined by infrequent or difficult passage of large or hard fecal material. It occurs commonly in the pediatric population, and its association with urinary tract dysfunction has been well described. Constipation can cause detrusor instability, which can lead to urinary incontinence, large bladder capacity, and dyscoordinated voiding. Urinary retention is common, either from dyscoordinated voiding or from outflow tract obstruction caused by large rectal fecal masses. All of these types of urinary dysfunction can lead to recurrent urinary tract infections.

One study of children who had urinary retention found that 13% had functional constipation as the cause of their retention. Another found that approximately 30% of chronically constipated children complained of urinary incontinence, and 11% had urinary tract infection. Treatment of the underlying constipation improved urinary incontinence and prevented recurrent urinary tract infections.

The girl described in the vignette is otherwise healthy and growing well, and she has no anatomic urinary tract abnormalities. Accordingly, treatment of her underlying constipation is the next best step in the prevention of recurrent infections. Fecal disimpaction, stool softeners, and regular bowel evacuation using timed toilet sitting are the mainstays of treatment.

An evaluation for immunodeficiency is not warranted at this time, but could be considered if her growth parameters were abnormal or if she had additional infections outside of the urinary tract. Renal scintigraphy is used to assess renal anatomy and function and may be warranted in a child who has recurrent urinary tract infections, but it is not helpful in preventing future infections. Anticholinergic therapy, such as oxybutynin, can be helpful if overactive or unstable bladder is suspected, but the girl in the vignette has no symptoms of these conditions. Referral to a pediatric nephrologist may be indicated if evidence of renal dysfunction is present, but treatment of underlying risk factors, such as constipation, should be initiated first.

5. A 6-year-old girl is experiencing daytime and nighttime enuresis of 1 month's duration. She achieved daytime continence at age 3 and has been dry at night since age 4. She has no history of fever, but does have some dysuria. The physical examination is remarkable only for suprapubic tenderness. Urinalysis demonstrates a specific gravity of 1.015, pH of 6.5, 1+ blood, trace protein, 3+ leukocyte esterase, and positive for nitrite. Microscopy reveals 2 to 5 red blood cells/high-power field (HPF), 20 to 50 white blood cells/HPF, and 3+ bacteria. Results of a urine culture are pending.

Of the following, the MOST appropriate empiric treatment for this patient is

- A. amoxicillin
- B. cefixime
- C. cephalexin
- D. ciprofloxacin

E. trimethoprim-sulfamethoxazole

2009PREPQ: The child described in the vignette has dysuria, incontinence, and suprapubic tenderness, but she is otherwise well and has no fever or systemic symptoms. Based on the urinary findings of positive leukocyte esterase and nitrite with pyuria on microscopy, she most likely has a lower urinary tract infection (UTI) or cystitis.

Cystitis is treated with empiric outpatient oral antibiotic therapy directed at the most likely urinary pathogens until the urine culture and antibiotic susceptibilities are available. Approximately 90% of UTIs are caused by *Escherichia coli*. Because *E coli* are usually sensitive to trimethoprim-sulfamethoxazole (TMP-SMX), it is an excellent agent for initial treatment of cystitis. In some regions of the country, bacterial resistance to this agent may be increasing, but it still is considered the best first-line agent because it may be more effective than beta-lactam antibiotics (eg, amoxicillin) in treating UTI, is inexpensive and readily available, and allows the clinician to reserve more broad-spectrum antibiotics for treatment failures. Due to high resistance rates, amoxicillin should not be used as first-line empiric treatment for cystitis.

Broader-spectrum antibiotics such as first-generation (cephalexin) and third-generation (cefixime) cephalosporins or fluoroquinolones (ciprofloxacin) should be reserved for second-line treatment unless the child has recurrent UTI and a history of resistance or allergy to TMP-SMX.

The standard duration of treatment is 7 to 14 days. A recent meta-analysis supported the use of a short course (2 to 4 days) of antibiotics, which compared favorably with a standard course (7 to 14 days) in terms of treatment failures and recurrence of lower UTI. Single-dose antibiotic regimens have been used in adults, but pediatric studies demonstrate an increased number of treatment failures and UTI recurrences compared with standard 7- to 14-day treatment regimens.

6. A 16-year-old girl presents with symptoms of burning with micturition and back pain. Her temperature is 101.3°F (38.5°C), heart rate is 88 beats/min, respiratory rate is 14 breaths/min, and blood pressure is 108/64 mm Hg. You can elicit costovertebral angle tenderness on the left side and suprapubic tenderness. Her urinalysis demonstrates a urine specific gravity of 1.025, pH of 6.5, 2+ blood, 1+ protein, 3+ leukocyte esterase, and positive for nitrite. Microscopy reveals 5 to 10 red blood cells/high-power field (HPF), 50 to 100 white blood cells/HPF, 4+ bacteria, and occasional squamous epithelial cells.

Of the following, the MOST likely diagnosis is

- A. acute bacterial cystitis
- B. acute glomerulonephritis
- C. acute pyelonephritis**
- D. bacterial urethritis
- E. nephrolithiasis

The adolescent described in the vignette presents with classic symptoms of acute pyelonephritis (upper urinary tract infection [UTI]): fever, back pain, and dysuria associated with physical findings of costovertebral angle and suprapubic tenderness.

UTIs typically are classified as lower urinary tract (involving the bladder and urethra) and upper urinary tract (involving the ureters, renal pelvis, and kidneys). In an adolescent, a bladder infection (cystitis) is not accompanied by flank pain or fever. Urethritis, which may be caused by a sexually transmitted infection, is accompanied by symptoms of dysuria, but not symptoms of flank pain or fever.

Distinguishing between upper and lower UTI may be more difficult in younger children. In neonates and infants, the presence of fever in the setting of a UTI characterizes an upper tract infection (pyelonephritis). In contrast, the absence of fever suggests lower tract infection. The diagnosis often is made during the evaluation of an infant for fever and irritability. A study from Taiwan revealed that a UTI was present in 13.6% of infants younger than 8 weeks of age who presented with fever. Urine white blood cell counts greater than 10/high-power field (pyuria) were the best indicators of UTI in this setting. Bacteremia accompanies UTI in 31% of pediatric patients younger than 1 month of age and 21% of those 1 to 2 months of age. Febrile infants who have no apparent source of fever had UTI in 7.5% of cases in another study. Older infants present with fever and vomiting, and the diagnosis is based on a positive urine culture collected by transurethral or suprapubic catheterization. The incidence of bacteremia falls to 3% in children 2 to 36 months of age. As children develop verbal skills, it becomes easier to distinguish between upper and lower tract infection because they can express their symptoms of dysuria and frequency.

Acute glomerulonephritis does not present with dysuria and flank pain. Nephrolithiasis can present with flank pain and possibly dysuria (if accompanied by crystalluria), but the presence of suprapubic pain, fever, and disproportionate pyuria to hematuria in the setting of a positive nitrite result make this diagnosis unlikely.