Recurrent Urinary Tract Infections in Children

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SUMMARY

Urinary tract infections are common in children and present in various ways. Diagnosis is based on findings of pyuria and bacteriuria. Management includes adequate and timely investigation, appropriate antibiotics, treatment of underlying contributing factors, and follow-up advice.

RÉSUMÉ

Les infections urinaires sont courantes chez les enfants et leur présentation revêt plusieurs formes. Le diagnostic repose sur la démonstration d'une pyurie et d'une bactériurie. Le traitement comprend une investigation adéquate et au moment opportun, une antibiothérapie appropriée, le traitement des facteurs contributoires sous-jacents et des conseils visant à assurer le suivi.

Can Fam Physician 1993;39:1623-1631.

URINARY TRACT INFECTIONS (UTIs) are common in children and differ in several ways from such infections in adults.

Diagnosis, investigation, and management are the shared responsibility of general practitioners, pediatricians, urologists, pathologists, and radiologists. Clinically, diagnosis can be altered by age, other disabilities, and coexisting diseases. Crucial to the diagnosis is a reliably collected urine specimen with significant bacteriuria (10^8 colony-forming units/L and 10 white blood cells per high-power field). Imaging and radiologic and urodynamic studies are required more often for children than for adults. Management includes appropriate antibiotics and treatment of the underlying structural abnormalities that are expected in one third of children with UTIs.

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Clinical presentations

Diagnosis of UTIs in infants and young children is frequently missed or delayed because symptoms are not specific and are rarely localized to the urinary tract. Unexplained fever, vomiting, diarrhea, and failure to thrive might be secondary to a UTI, as might unexplained jaundice in a neonate.[1,2]

Children older than 2 years often have symptoms (in addition to fever) that indicate UTI. These include frequency, dysuria, cloudy or foul-smelling urine, abdominal or loin pain, and urinary incontinence in a previously trained child. Gross hematuria (particularly in male patients) occasionally appears as a symptom of an acute UTI.

Early diagnosis and treatment of UTIs is important, particularly for young children, because it helps to prevent or minimize upper tract scarring. Physicians should be aware that UTIs present in various ways in young children and should maintain a high index of suspicion for this possibility, particularly in those younger than 2 years.

Laboratory diagnosis of urinary infections

Collecting uncontaminated urine specimens and evaluating laboratory definitions of significant infection are major challenges in diagnosing recurrent UTIs

in children. Reliable laboratory diagnosis is particularly important in cases where asymptomatic infections can damage patients (eg, prepubertal children, persons with sensory deficits).

Specimen collection. Collection of specimens is especially difficult when children cannot cooperate in providing midstream samples.[3] Incontinence increases the probability of contamination; contamination can lead to problems of interpretation. The importance of careful specimen collection cannot be overemphasized; a few minutes spent on this facet of diagnosis can avoid unnecessary treatment and expensive or hazardous investigations.

Table 1. **Useful antibiotics**

DRUG	DOSE
ORAL	
Trimethoprim-sulfamethoxazole	8 TMP, 40 SUI mg/kg/d, every 12 h
Amoxicillin	20-40 1 mg/kg/d, every 8 h
Cephalexin	25/50 mg/kg/d, every 6 h
Nitrofurantoin	4-6 mg/kg/d, every 6 h
IV	
Ampicillin	25-50 mg/kg/d, every 6 h
Cefazolin*	50 mg/kg/d, every 8 h
Gentamicin*	3 mg/kg/d, every 8 h
Ceftazidime*	30-100 mg/kg/d, every 8 h to a maximum dose of 6 g

**Dosage modification is necessary if renal function is compromised.*

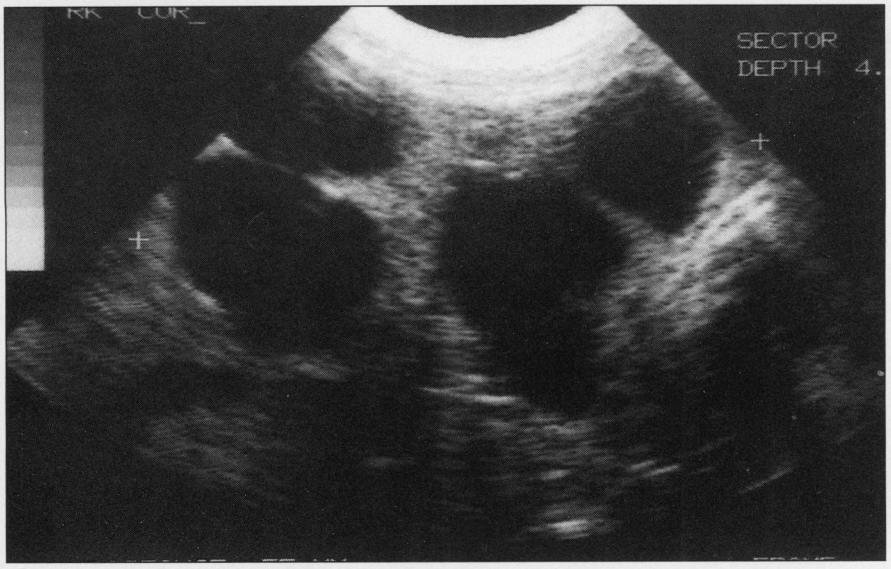
Sterile perineal collection bags, used by children who are unable to provide a midstream urine specimen, are a common cause of contaminated specimens. To minimize contamination, a boy's urinary meatus and perineum should first be cleaned with soapy water then rinsed well with clean water; the foreskin should be retracted throughout the procedure for the uncircumcised. A girl's labia should be held apart and the entire vulvar area washed from front to back with soapy water, then rinsed; the labia should be kept separated after washing and a sterile container inserted into the midstream.[4] Bags should be removed as soon as the child has voided and should not be left in place for more than 30 minutes. General practitioners seldom use catheters for taking specimens, except from meningomyelocele patients for whom a sterile catheter should be used rather than a routine "clean" catheter.[5]

Immediate refrigeration of voided urine and rapid transport to the laboratory are essential for specimens that could become contaminated. Absolute and relative numbers of organisms can change rapidly in warm voided urine: eg, at 35°C populations of *Escherichia coli* will increase 10-fold in little more than 1 hour. *Proteus* grow fairly rapidly and might produce ammonia that lyses leukocytes. By contrast, Gram-positive organisms and *Pseudomonas* grow quite slowly. Such changes can make laboratory reports worthless.

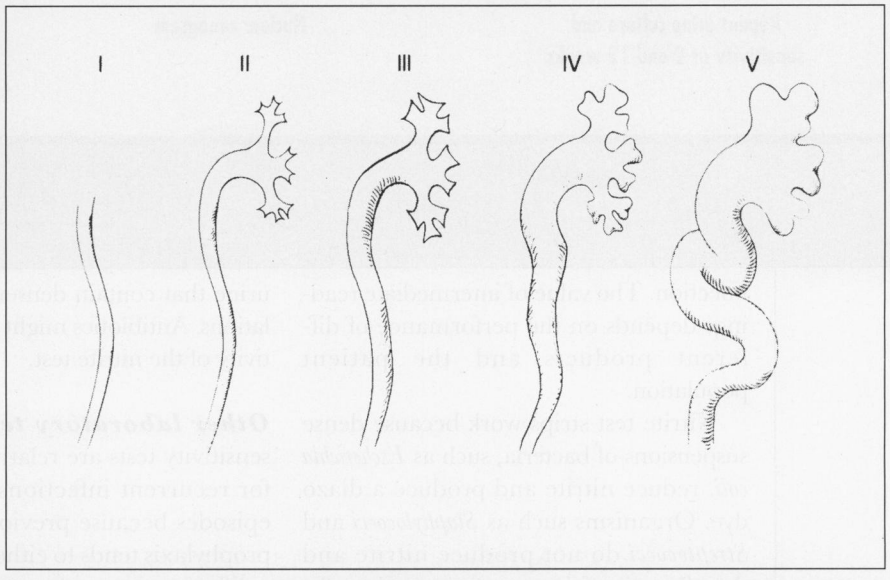
Culture. The 10^8 CFU/L laboratory breakpoint for significant infection was originally intended to detect bladder bacteriuria in adult women by examining consecutive early morning midstream urine specimens.[5] Although this breakpoint is widely used by clinical laboratories, evidence is scant about its relevance for all pediatric populations, especially children with underlying problems, such as functional or anatomic abnormalities of the urinary tract or renal failure. Smaller numbers of bacteria should not override clinical evidence of infection and the need for treatment or referral to a specialist.

Leukocyte counts and interpretation of results. Urine white cell counts can be performed several ways. Laboratories and practitioners frequently determine "cells per high-power field." Unfortunately, there is no standard procedure for carrying out this intrinsically inaccurate test, which is unreliable anyway for specimens containing small numbers of leukocytes. Clinical laboratories are slowly switching to disposable quantitative counting chambers. Most healthy children have urine white cell counts of less than 50/μL (approximately 10 per high-power field in urine concentrated 25-fold).

For children with neurogenic bladder due to meningomyelocele or children with suspected contamination, a urine



Renal ultrasound showing gross hydronephrosis in a 10-year-old boy with frequent pain and fever.

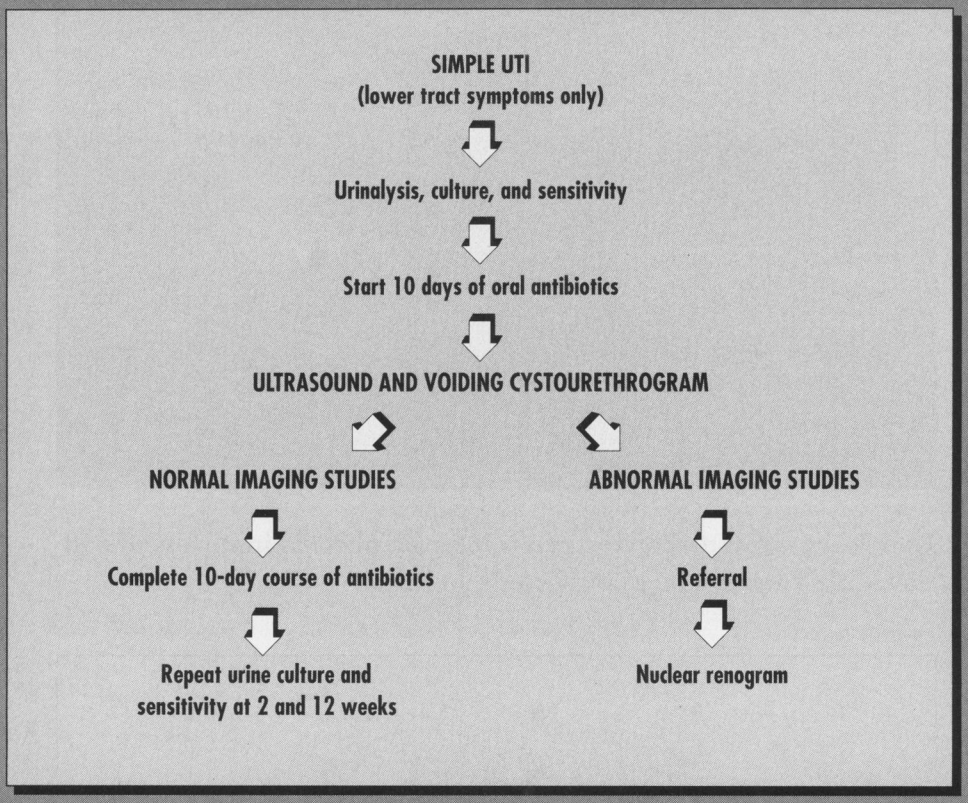


Schematic representation of grades of vesicoureteral reflux.

WBC count will often help differentiate a true disorder from contamination or harmless colonization. We and other centres use a combined breakpoint of more than 10^8 CFU/L and more than 50 leukocytes/μL as a laboratory definition of infection for children with meningomyelocele in whom benign colonization is common. Choosing these values was largely arbitrary, and it is possible that higher values might save unnecessary treatment and prophylaxis without compromising long-term prospects.

"Dip and read" test strips. Dip and read test strips are an inexpensive alternative to conventional laboratory tests. In general, for a breakpoint of 50 leukocytes/μL, negative leukocyte test strip results have good negative predictive value; high test strip values (eg, 500/μL) have good positive predictive value for

Figure 1. **Managing simple UTIs**



infection. The value of intermediate readings depends on the performance of different products and the patient population.

Nitrite test strips work because dense suspensions of bacteria, such as *Escherichia coli*, reduce nitrite and produce a diazo dye. Organisms such as *Staphylococci* and *Streptococci* do not produce nitrite and therefore give false-negative reactions for bacteria. The low sensitivity of the nitrite test precludes its application to patient populations, such as prepubertal girls, for whom accurate diagnosis is critical.

Because *Staphylococcus saprophyticus* rarely causes pediatric infections and coliforms (usually present in greater numbers) provoke a more vigorous leukocyte response than Gram-positive organisms, nitrite test strips can be used as a negative screen for certain patient populations, such as those with meningomyeloceles. The apparent sensitivity of nitrite strips is enhanced for "overnight" specimens of urine that contain denser bacterial populations. Antibiotics might reduce the sensitivity of the nitrite test.

Other laboratory tests. Antibiotic sensitivity tests are relatively more useful for recurrent infections than for acute episodes because previous treatment or prophylaxis tends to either select resistant coliforms, or to a lesser extent, intrinsically resistant bacteria, such as *Pseudomonas*. General practitioners seldom localize infection in the "upper" or "lower" tract. The antibody-coated bacteria test is unreliable for children. In summary, collecting good urine specimens from children is difficult, but is absolutely necessary for diagnosis and will help avoid unnecessary treatment and investigation. Specimens should be refrigerated and transported to the laboratory as quickly as possible. For many children, a bacterial count of $\geq 10^8$ CFU/L indicates a significant infection,

especially if it is combined with a leukocyte count of >50/μL (about 10 per high-power field). Lower values might be significant for children with clinical evidence of disease.

Evaluation and investigation

One in three children with a documented UTI will demonstrate an anatomic abnormality on radiologic investigation. All children presenting with their first well documented UTI should have a workup. Investigations will help identify risk factors that predispose children to recurrent infection or renal damage caused by obstruction, reflux, or stasis. The basic radiologic evaluation of a child with infected urine comprises an ultrasound examination, a voiding cystourethrogram (VCU), and a nuclear renal scan.

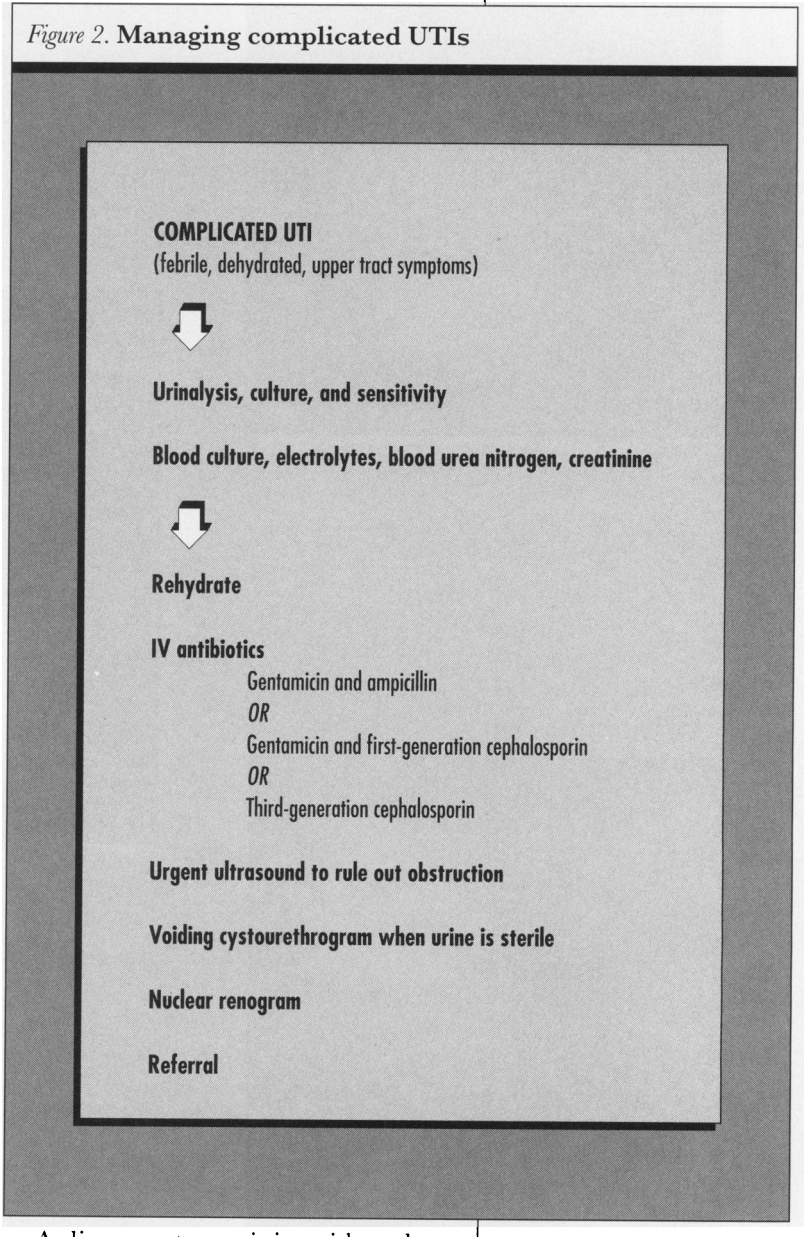
Ultrasonography. A renal and bladder ultrasound, ordered at the time of diagnosis,[6] can demonstrate abnormalities of number, position, duplication, hydronephrosis, gross parenchymal scarring, dysplasia, cysts, or stones. Ureteral dilation can be identified, as can bladder lesions, such as ureteroceles, diverticula, or a thickened detrusor muscle that suggests outlet obstruction or dyssynergic voiding.

Voiding cystourethrogram. Because a VCU requires catheterization, it should be performed only after the urine has been sterilized with antibiotics and any fever is resolved (preferably after 3 to 4 weeks). The VCU can demonstrate obstruction, residual urine, neuropathic bladder changes, or reflux. The cystogram from an intravenous pyelogram shows insufficient detail to rule out subtle but significant degrees of reflux.

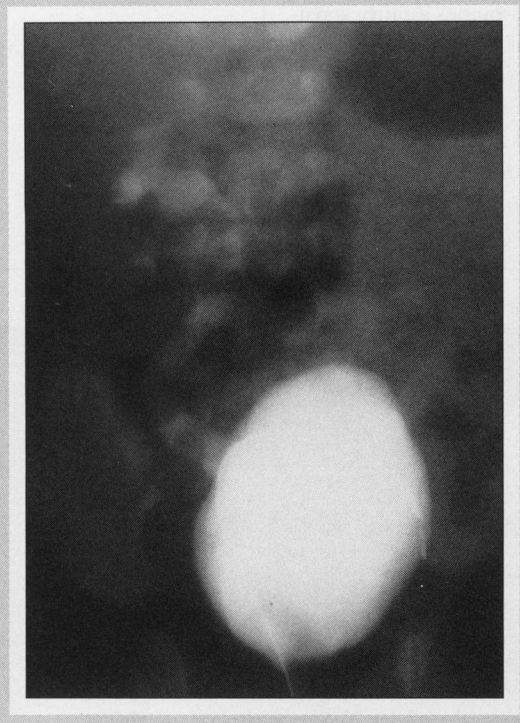
A nuclear cystogram is the most sensitive indicator of reflux. While it does not provide adequate anatomic information to determine the grade of reflux, it will make the diagnosis when a VCU is false negative (20%) or provide a useful follow-up study for asymptomatic children with known reflux.

Renography. Renography using the radiopharmaceutical diethylenetriamine pentaacetic acid (DTPA) supplemented by furosemide diuresis provides a fairly sensitive measurement of renal function and differentiates obstruction from simple dilation when hydronephrosis is present. Like other functional studies, its usefulness is limited in the first month of life or during renal failure when the glomerular filtration rate is low.[7]

Figure 2. **Managing complicated UTIs**



A dimercaptosuccinic acid nuclear renal scan provides more detailed information about scarring than ultrasound or DTPA scans, and if results are normal, will effectively rule out pyelonephritis when the diagnosis is suspected clinically but cannot be confirmed by culture. This could prevent unnecessary use of antibiotics and hospitalization.



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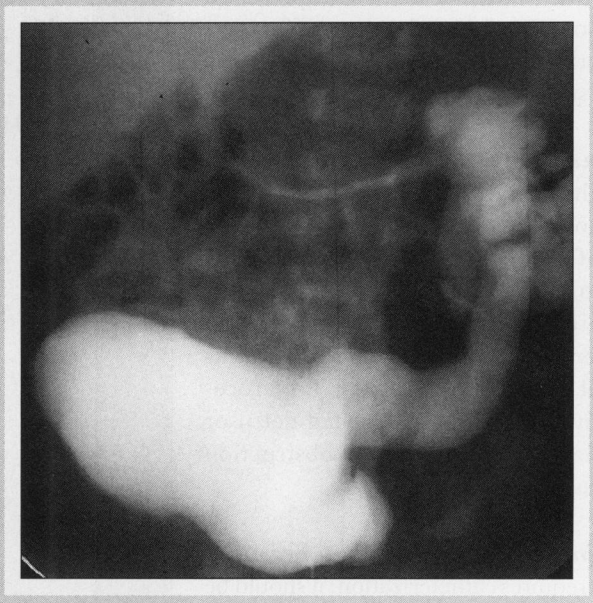

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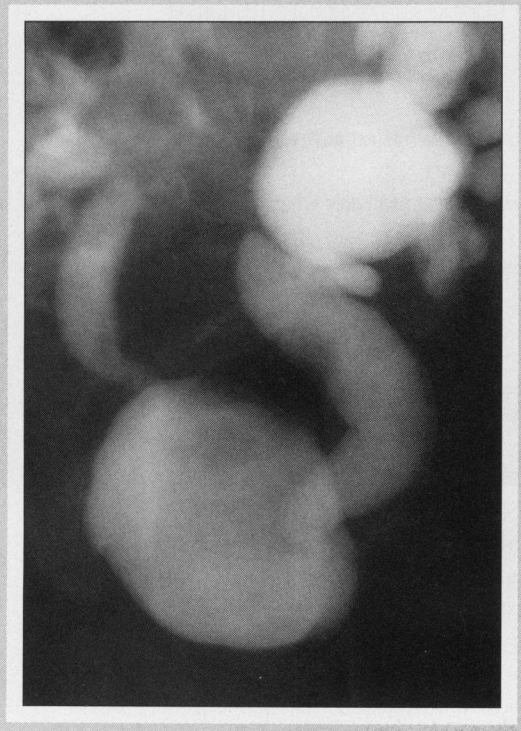

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Cystogram (VCU) showing degrees of reflux: *A) Minor unilateral reflux (grade II), B) High grade (grade IV) of unilateral reflux, C) High grade (grade V) of bilateral reflux.*

Intravenous pyelography. Other important ancillary studies are sometimes necessary. Intravenous pyelography has been supplanted by newer technology. It is used only when ultrasonography and nuclear renography are unavailable.

Plain films. An abdominal plain film can show fecal overload. Physicians should use lumbosacral plain films if spina bifida is suspected.

Magnetic resonance imaging. If tethering or other neurologic cord lesions are suspected, MRI scans are valuable.

Urodynamics. Urodynamics prove useful for children with infections related to neurogenic bladders, dyssynergic voiding, and uninhibited bladders, especially if associated with trabeculation, hydronephrosis, or reflux.

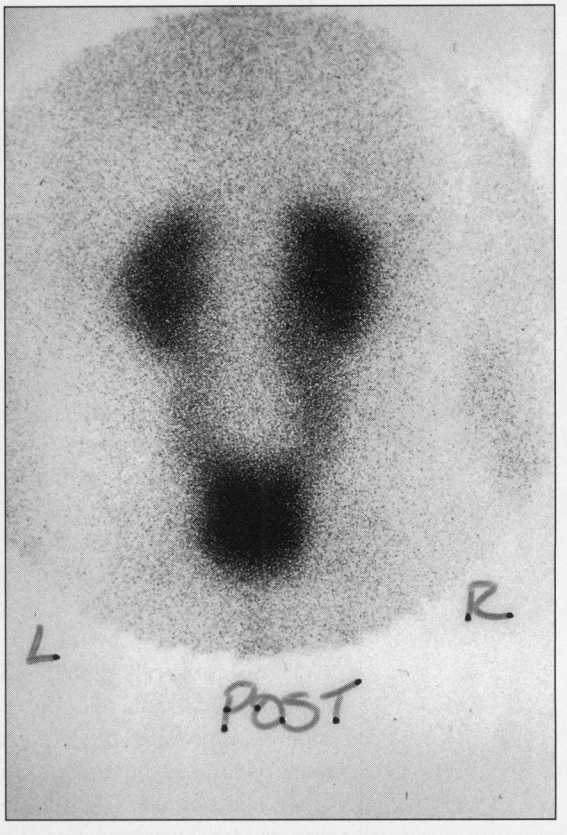
Endoscopy. Cystoscopy is rarely indicated during the acute stages of infection, but can help relieve obstruction in certain cases of posterior urethral valves, ureteroceles, stones, or strictures. Documentation of chronic metaplastic mucosal changes, ectopic ureteral orifices, or endoscopic antireflux procedures also requires cystoscopy.

Management

Infections are managed with antibiotics (*Table 1*) and by correcting risk factors for recurrence. Reinfection is the most common cause of treatment failure, but antibiotic resistance or a focus of bacterial persistence, such as stasis, reflux, or obstruction, must be ruled out.

Important nonspecific measures include maintaining regular bowel habits and good urinary hygiene. Children cannot effectively empty their bladders when the anal sphincter is constantly struggling for fecal continence against a rectum full of stool. Constipation absolutely must be cleared with enemas and stool softeners (pediatric phosphate enemas are available). Modification of behaviour and diet are also important. Docusate sodium and bran are excellent dietary supplements, but do not substitute for the time, effort, understanding, patience, and commitment of medical personnel and the child's parents. Fecal flora usually provide the infective pathogen: direction of wiping should be discussed. Bubble baths should be avoided.

Simple UTIs. A child with a clinical afebrile UTI should provide an appropriately collected urine specimen for routine and microscopic examinations, culture, and sensitivity. Physicians should prescribe a course of antibiotics for 10 days, to be altered pending sensitivity results. During the course of antibiotics, ultrasonography and a VCU should be completed. If an anatomic abnormality is detected, antibiotics should be continued until the child can be referred to a specialist (*Figure 1*). If special treatment is not recommended, general practitioners should complete the



Diethylenetriamine pentaacetic acid nuclear renogram complete with furosemide at 6 hours shows hydroureteronephrosis and obstruction at ureterovesical level.

course of antibiotics and do follow-up urine cultures at 2 and 12 weeks.

The most useful antibiotics include trimethoprim-sulfamethoxazole, amoxicillin, nitrofurantoin, and cephalexin (*Table 1*). Fluoroquinolones that might injure growing cartilage and tetracyclines that stain developing dental enamel are contraindicated for children. Use trimethoprim-sulfamethoxazole cautiously during the first month of life because of the theoretic risk of jaundice.

Complicated infections. When a UTI presents with fever and dehydration (*Figure 2*), physicians should admit the child to hospital for rehydration and treatment. Blood and urine cultures, complete blood cell count, electrolytes, blood urea nitrogen, and creatinine should be drawn and intravenous antibiotics started. An aminoglycoside in combination with either ampicillin or a first-generation cephalosporin treats nearly all suspected pathogens. For neonates and other patients with impaired renal function, a third-generation cephalosporin alone is a safer choice. Intravenous antibiotics should be continued until fever and sepsis have cleared; then oral antibiotics (as dictated by sensitivities) should be taken for 3 weeks.

Ultrasonography should be immediately performed to rule out obstruction. If the situation is pressing, the VCU can be done safely as soon as the urine is sterile and the fever has abated. Ideally, it should be deferred for 3 weeks to allow for resolution of changes caused by the infection itself. Prophylactic antibiotics should continue until the VCU has been performed.

A nuclear renogram will complement the ultrasound study. All cases of unexplained pyelonephritis in prepubescent children should be discussed with a urologist, nephrologist, or pediatrician with expertise in genitourinary infection.

Special considerations

Reflux. Vesicoureteral reflux is a risk factor for upper and lower UTIs and renal scarring. Reflux could be secondary to a neurogenic bladder, voiding dysfunction, or outlet obstruction, or could be a primary idiopathic phenomenon. Reflux causes dilation, stasis, and in some cases, obstruction, in upper tracts. It causes the most harm to young children. Mild reflux usually improves with age.

Most urologists in North America agree that the severest grades of reflux should be repaired surgically when diagnosed. Mild or moderate reflux can be monitored by serial imaging and managed with antibiotics.

The decision to operate on less severe primary reflux is influenced by the patient's age, sex, presence or progression of renal scarring, compliance, the number and severity of breakthrough infections, and parental satisfaction with daily medications. Secondary reflux often improves when its antecedent cause has been treated.

Recurrent infections and asymptomatic bacteriuria. Recurrent symptomatic infections, despite normal results from radiologic monitoring, can be vexing. Review of voiding and bowel habits might reveal previously unidentified problems with hygiene, constipation, uninhibited detrusor contractions, or tethered cord. Urodynamics might be helpful. A large residual volume of urine might require intermittent catheterization. A 3-month course of prophylactic antibiotics, such as trimethoprim-sulfamethoxazole nightly or nitrofurantoin twice daily, can be tried with careful monitoring for side effects. Reinfection from preputial colonization, especially if associated with balanitis, might require circumcision to resolve infection.[8]

Whether asymptomatic bacteriuria in children should be treated with antibiotics is currently hotly debated. However, most agree that a full urologic workup will help rule out correctable factors.

Physicians should be especially careful about epididymitis. Extremely rare in children, it should never be diagnosed in a prepubertal boy without seeking an immediate opinion from a urologist. If torsion of testis is missed, orchidectomy will be needed. ■

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References

1. Shortliffe LMD. Urinary tract infections in infants and children. In: Walsh P, editor. *Campbell's urology*. Vol 2, 6th ed. Philadelphia: WB Saunders Co, 1992:1669-81.

2. Rushton HG. Urinary tract infections. In: Kelalis P, King L, Belman B, editors. *Clinical pediatric urology*. Vol 1, 3rd ed. Philadelphia: WB Saunders Co, 1992:286-364.
3. Lohr JA. Use of routine urinalysis in making a presumptive diagnosis of urinary tract infection in children. *Pediatr Infect Dis J* 1991;10:646-50.
4. Stansfield JM, Webb JKG. Observations on pyuria in children. *Arch Dis Child* 1953;28:386-91.
5. Montplaisir S, Courteau C, Martineau B, Pelletier M. Limitations of the direct immunofluorescence test for antibody-coated bacteria in determining the site of urinary tract infections in children. *Can Med Assoc J* 1981; 125:993-6,1002.
6. Alon U. Ultrasonography in the radiologic evaluation of children with urinary tract infections. *Pediatrics* 1986;78(1):58-64.
7. Johnson HW, Gleave M, Nadel H, Raffel J, Weckworth P. Neonatal renomegaly. *J Urol* 1987;138:1023-7.
8. Lohr JA. The foreskin and urinary tract infections. *J Pediatr* 1989;114(3):502-4.

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