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Urinary Tract Infection

By 11 years of age, approximately 1% of boys and 3% of girls will have had a UTI according to a classic Swedish study from the early '70s. More recent data however suggest that the incidence of symptomatic UTI may be higher – almost 2% in boys and 8% in girls by 7 years of age.

The infectious process is multifactorial, encompassing host factors and bacterial virulence factors. The vagina and periurethral region are colonized by native flora. In females the short urethra permits ready access to the bladder, whereas the lengthy male urethra provides a barrier to bacterial ascent.

Once in the bladder, the offending bacteria's virulence factors come into play. Bacteria must adhere to the bladder urothelium or be washed away when the bladder is emptied. The receptors for uropathogenic bacteria are carbohydrate residues located on the surface glycolipids and glycoproteins of urothelial cells. Several bacterial adhesions which adhere to these urothelial cell surface antigens have been identified. Endotoxin decreases ureteral peristalsis which facilitates ascent up the ureter to the kidney. Capsular antigens may provide resistance to phagocytosis by host immune cells. Furthermore, some bacteria produce hemolysins which are toxic to renal tubular cells.

Bacterial access to the kidneys is achieved as a result of these numerous factors or as a consequence of urinary

tract pathology. Ureteral obstruction is present in 2-10% of children with acute pyelonephritis. Vesicoureteral reflux is present in 20-50% of children with UTIs. Obstruction precludes efficient clearance of upper tract bacteria, while reflux provides bacteria with unimpeded access to the kidneys. Non-obstructive upper tract dilations may predispose to infection as well because of urinary stasis.

Extra-urinary factors increase the risk for infection and must be considered in any child with recurrent UTIs. Infrequent voiders commonly do not void upon awakening in the morning, and they may void only 2 or 3 times a day. They secondarily develop unusually large bladders and emptying is often incomplete. Constipation predisposes to voiding dysfunction with incomplete bladder emptying. A history of constipation must therefore be sought in any child with recurrent UTIs.

Diagnosis

It must be emphasized that infants and young children are often afebrile and commonly present with nonspecific symptoms. A UTI should be considered in any infant or child with fever, failure to thrive, irritability, or vomiting and diarrhea. One must first determine whether the urine is truly infected and if so, why? Doing so requires a thorough history and physical examination, including an inquiry into the child's voiding and bowel habits.

Urinalysis should be performed on a fresh specimen collected whether by midstream clean catch or urethral catheterization. Bagged specimens in infants are conveniently obtained, however these specimens are easily contaminated and only negative results are meaningful. The urine should be dipsticked for nitrite and leukocyte esterase and a microscopic examination is advisable as well to quantify the degree of pyuria. A positive specimen should be sent for organism identification and antibiotic sensitivities.

Diagnosis of UTI requires pyuria and bacteriuria. A positive culture in the absence of pyuria implies colonization or improper handling of the specimen after collection. The gold standard for documentation of a UTI has long been a colony count > 100,000, however symptomatic UTIs can exist with counts as low as 10² organisms. **Antibiotics should be started immediately** and then adjusted as necessary according to culture results.

Evaluation

Radiologic evaluation is indicated after the very first UTI in all boys of any age and in all pre-adolescent girls. Furthermore, any girl with a febrile infection or recurrent UTIs should be studied regardless of her age. Unfortunately, making the diagnosis of acute pyelonephritis in children with febrile infections is quite unreliable when based solely upon clinical and laboratory observations. Prompt investigation after



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a single documented UTI is convincingly argued because of the seriousness of acute bacterial pyelonephritis and the risk for permanent renal injury, hypertension and renal failure.

The imaging modalities chosen to study a particular child should be tailored to the individual situation. Radiation exposure and discomfort for the child should be minimized; however, information gathering should be maximized and not compromised. The preferred initial study is renal and bladder ultrasonography (US), followed by a voiding cystourethrography (VCUG)

Ultrasound provides data concerning (1) the kidneys – location, size, contour, parenchymal thickness, hydronephrosis or cystic changes and (2) the bladder – contour, wall thickness and post void residual volumes. Intravenous pyelography (IVP) is generally reserved for further anatomic detail in cases of renal duplication or megaureters.

The VCUG permits evaluation of the lumbosacral spine, bladder contour and morphology, and the presence of vesicoureteral reflux, ureteroceles and posterior urethral valves. Reflux can also be graded, and primary and secondary causes of reflux can be distinguished.

Nuclear cystography does not permit evaluation of the bladder, nor does it permit grading of reflux. The nuclear VCUG however does have utility in the evaluation of children with a normal contrast VCUG and a history of recurrent pyelonephritis because of its greater sensitivity for reflux. It is also excellent for follow up in children with known reflux.

A history of febrile UTIs warrants further investigations for the presence of renal scarring. It should be noted however, that scarring may take 6 to 24 months to be clinically detectable after a bout of

pyelonephritis. Unfortunately, **4.5% of children will have confirmed scars after presentation for their first UTI, while 17% will have renal scars after having had 2 infections prior to radiologic evaluation.** Scarring is best assessed via renal scintigraphy using dimercaptosuccinic acid (DMSA) or glucoheptonate.

Interestingly, approximately 17% of children with asymptomatic bacteriuria will have renal scarring as well. Since the severity of symptoms does not correlate with the risk of significant infection or renal injury, one cannot overstate the importance for a **thorough urologic evaluation after the first UTI.**

Management

Prevention of scarring demands (1) early recognition and treatment of infection, and (2) antibiotic suppression to prevent recurrences until reflux has resolved spontaneously or has been surgically corrected. Close follow up is mandatory in any child with a history of recurrent UTIs, reflux or known renal scarring. Long-term outcome is generally good; however significant renal scarring in one or both kidneys, and/or the presence of hypertension or renal insufficiency will portend a guarded outcome regarding long-term kidney function.

Siblings and offspring of reflux patients should be studied as well because they have a 25 – 46% risk of reflux. Therefore, screening with US and VCUG is recommended for first degree relatives < 5 years old, while US alone is probably sufficient beyond 5 years old. Furthermore, all newborns with antenatally detected hydronephrosis should undergo postnatal investigation by US and VCUG because of the 25% risk of reflux in these children.

The seriousness of reflux cannot be overemphasized when one considers the

potential sequelae of untreated infection, namely renal failure and hypertension. Reflux nephropathy (chronic pyelonephritis) accounts for 20% of children with end-stage renal disease. Long-term prospective follow up of patients with documented UTIs and reflux as children revealed an 8% incidence of hypertension, while 3% had borderline or labile hypertension not yet requiring medication, and another 4% had an elevated serum creatinine.

Antibiotic suppression is low dose and is given once daily, generally at bedtime. The most commonly used medications include trimethoprim-sulfamethoxazole, nitrofurantion or trimethoprim alone. Infections in the setting of suppressive antibiotics must be carefully examined to determine patient compliance with the medication. The type of organism and its antibiotic sensitivity also provide clues to the source of the problem. The presence of resistant bacteria may imply too high an antibiotic dose the resultant eradication of the susceptible bowel flora and their replacement by resistant flora. Resistant organisms may also herald previously unsuspected voiding dysfunction which would need further investigation.

Surgical correction of reflux is recommended for children with breakthrough UTIs, noncompliance with antibiotic suppression, poor follow up, or persistence of reflux despite several years of regular follow up. A 6-12 month course of suppressive antibiotics is also advisable for children with frequent symptomatic UTIs (>3 UTIs in 6 months or 5 in a year) or cystitis cystica. This prolonged course should provide an infection free period during which any deep-seated inflammation can subside.

Extra-urinary problems must also be addressed and corrected. Constipation should be controlled if present. Proper perineal hygiene is emphasized with front



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to back wiping. Vaginal reflux can be prevented by voiding with the legs apart or by straddling the toilet seat. Maintaining a well hydrated state is also important because increased urine output will enhance the simple but effective mechanical elimination of any bacteria that gain access to the bladder.

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