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# Urinary Tract Infections (UTI)

## Prevalence

- UTI commonly occurs in children of all ages, though the prevalence varies with age. UTI are most common in children <1 yr. The prevalence of afebrile symptomatic UTI in children >1 yr is about 8% & of febrile UTI is 7%.
- During the 1st year of life, the male:female ratio is 2.8:5.4, while beyond 1-2 yr the ratio is 10:1. In males, most UTI occur during the 1st yr of life. In females, the 1st UTI usually occurs by the age of 5 yr, with peak during infancy, toilet training & onset of sexual activity.

## Etiology

- UTI is primarily caused by colonic bacteria.
- *E.Coli* causes 54-67% of all UTI, followed by *klebsiella* spp., *proteus* spp., *Enterococcus* & *Pseudomonus*. Other bacteria include *Staphylococcus saprophyticus*, GBS, & less commonly *Staphylococcus aureus*, *Candida* spp. & *Salmonella* spp.
- There may be viral causes of UTI ,especially adenoviruses which usually cause cystitis.
- UTI have been considered as an important risk factor for the development of renal insufficiency or end-stage renal disease, but only 2% of current renal insufficiency report a history of UTI which may be due to better recognition of the risk of UTI & prompt diagnosis & treatment. Furthermore, many children receive antibiotics for fever without a focus resulting in partially treated UTI. Some children with end-stage renal disease diagnosed as reflux nephropathy actually have dysplasia associated with reflux rather than scarring caused by infection & reflux.

## Clinical manifestations & classification

- The two basic forms of UTI are pyelonephritis (PN) & cystitis. Focal PN (lobar nephronia) & renal abscesses are less common:

1. PN : It is characterized by any or all of the following: abdominal, back or flank pain, fever, rigor, malaise, nausea, vomiting, & occasionally diarrhea. Fever may be the only manifestation. Particular consideration should occur for a temperature > 39 C without another source lasting >24 hr for males & >48 hr for females.

- Newborns can show nonspecific symptoms as poor feeding, irritability, jaundice & weight loss. PN is the most common serious bacterial infection in infant <24 mo of age who have fever without an obvious focus. Acute PN can result in renal injury which is called " pyelonephritic scarring".
- Acute lobar nephronia (acute lobar nephritis) is a localized renal parenchymal mass caused by acute focal infection without liquefaction. It more commonly occurs in older children. It may be an early stage of renal abscess. Manifestations & causes are similar PN.

- Renal abscess typically occurs following hematogenous spread with *S. aureus* or can occur following a pyelonephritic infection caused by the usual uropathogens. Most abscesses are unilateral & right sided & can affect children at all ages. Both acute lobar nephronia & renal abscess are associated of increased risk of renal scarring.
- Perinephric abscess can occur secondary to contiguous infection in the perirenal area ( as vertebral osteomyelitis, psoas abscess) or PN that dissects to the renal capsule. As with renal abscess, the most common organisms are *S. aureus* & *E. coli*.
- Xanthogranulomatous PN is a rare type of renal infection characterized by granulomatous inflammation & presented as a renal mass or an acute or chronic infection. Renal stones, obstruction & infection with *Proteus* spp. or *E. coli* contribute to this lesion, which usually requires total or partial nephroctomy.

2. Cystitis : Symptoms include dysuria, urgency, frequency, suprapubic pain, incontinence, & possibly malodorous urine (not specific for UTI). Cystitis does not cause high fever or renal injury. Acute hemorrhagic cystitis is often caused by E.coli & may be attributed to adenovirus types 11 & 21. Adenovirus cystitis is more common in boys, self-limiting with hematuria lasting about 4 days & more in patients receiving immunotherapy.
- other rare types of may include eosinophilic cystitis (may present with hematuria) & interstitial cystitis (may present with irritative voiding symptoms with negative urine culture).
- Asymptomatic bacteruria: It is defined as a +ve urine culture without symptoms & occurs almost exclusively in females. This condition is benign & does not cause renal injury except in pregnant women in whom if untreated, it can → symptomatic UTI.

## Pathogenesis

- Nearly all UTI$^S$ are ascending infections. The bacteria arise from the fecal flora, colonize the perineum, & enter the bladder via the urethra. In uncircumcised males, the bacteria arise from the flora beneath the prepuce. In some cases, the bacteria ascend to the kidney to cause PN. In rare cases, renal infections may occur by hematogenous spread as in endocarditis or in some bacteremic neonates.
- Infected urine stimulates an immunologic & inflammatory response, causing renal injury & scarring (the risk is more < 2 yr of age).

Risk factors for UTI:
- Female sex, Uncircumcised male & Vesicouretral reflux
-Toilet training (In female, UTI often occur at the onset of toilet training due to bowel-bladder dysfunction which occurs at that age (incomplete bladder emptying). Bowel-bladder dysfunction can arise in school-age children who refuse to use the school bathroom creating a state of urinary retention.
- Obstructive uropathy → hydronephrosis (urinary stasis).
- Urethral instrumentation (during voiding cystourethrogram or non-sterile catheterization)
- Wipping from back to front, Tight clothing (underwear), Pinworm infestation & Constipation (may→ bladder dysfunction dysfunction).
- Bacterial pilli or fimbria: 2 types of pilli or fimbriae on the bacterial surface 1 & 2. Type 1(most strain of E. coli, mannose sensitive, no role in PN). Type 2 (some strains of E.coli, mannose resistant & can agglutinate by P blood group RBC$^S$ & called P fimbria, are more likely to cause PN).

- Anatomic abnormalities as labial adhesion, Neuropathic bladder (incomplete bladder emptying, detrusor-sphincter dyssynergia & frequent catheterization),
- Sexual activity (in female due to urethral irritation & incomplete bladder emptying) & Pregnancy (4-7% have symptomatic bacteruria which may → UTI)
- Breast feeding → ↓ UTI.

## Diagnosis

- UTI may be suspected based on symptoms or findings on urinalysis, or both. A urine culture is necessary for confirmation and appropriate therapy.
- There are several ways to obtain a urine sample; some are more accurate than others. In toilet-trained children, a midstream urine sample usually is satisfactory; the introitus should be cleaned before obtaining the specimen. In uncircumcised males, the prepuce must be retracted; if the prepuce is not retractable, a voided sample may be unreliable and contaminated with skin flora.
- In children who are not toilet trained, a catheterized urine sample should be obtained. Alternatively, the application of an adhesive, sealed, sterile collection bag after disinfection of the skin of the genitals can be useful only if the urinalysis or culture is negative. However, a positive culture can result from skin contamination, particularly in females and uncircumcised males.
- If treatment is planned immediately after obtaining the urine culture, a bagged specimen should not be the method because of a high rate of contamination often with mixed organisms.
- A suprapubic aspirate generally is unnecessary.
- Prompt examination of the urine sample is important, because if urine remains at room temperature > 60 minutes → overgrowth of a minor contaminant, so, the sample should be stored in the refrigerator. The sample for GUE should be obtained from the same specimen as that cultured.
- Pyuria ($WBC^S$ in urine) suggests infections, but infections can occur without pyuria; this finding is more confirmatory than diagnostic. A WBC count on urinalysis > 3-6/high-power-field is indicative of infection with a likelihood of 10 in symptomatic child. Asymptomatic bacteruria can also have pyuria.
- Nitrates & leukocytes esterase tests are often +ve in infected urine. In febrile infants < 2 mo old, the presence of pyuria, nitrates or leukocyte esterase has a high sensitivity & specifity for UTI.
-Microscopic hematuria is common in acute cystitis, but microhematuria alone does not suggest UTI. WBC casts in the urinary sediments suggest renal involvement (but these are rare).
- Sterile pyuria (positive leukocytes, negative culture) occurs in partially treated bacterial UTIs, viral infections, urolithiasis, renal tuberculosis, renal abscess, UTI + urinary obstruction, urethritis due to a sexually transmitted infection, inflammation near the ureter or bladder (appendicitis, Crohn disease), Kawasaki disease, schistosomiasis, neoplasm, renal transplant rejection and interstitial nephritis.
- If the culture shows >50,000 colony-forming units/mL of a single pathogen & the urinalysis has pyuria or bacteruria in symptomatic child, the child considered to have UTI. In a bag sample, if the urinalysis result is positive & the patient is symptomatic, a catheter sample should be obtained for culture.
- With acute renal infection, leucocytosis, neutrophilia, ↑ESR, ↑proplactonin & ↑CRP are common. Bacteremia in PN is about 3-20% of patients & most common in < 3 mo infants &

with obstructive uropathy. For these high-risk group, blood culture should be done before starting antibiotics.

## Treatment

1. Acute cystitis: The choice of the suitable antibacterial drug should ideally based on the result of urine C & S, however, in acute severe conditions, treatment should begin without waiting for results ( empirical therapy ).

- A 3-5 day course of therapy with Trimethoprim-sulfamethaxasole (6-12 mg trimethoprim /kg/day, in 2 divided doses is effective against most strain of *E. coli*, Nitrofurantoin (5-7 mg/ kg/day, in 3-4 divided doses) also is effective & has the advantage of being active against *Klebsiella & enterobacter* organisms. Amoxicillin (50 mg/kg /day, in 2 divided doses) also may be effective as initial treatment but has a high rate of bacterial resistance.

2. In acute febrile UTI, the possibility of PN should be considered. A course of effective antibiotics for 7-14 days should be used (oral & parenteral routes are equally efficacious). Children who are dehydrated, are vomiting, are unable to drink fluids, have complicated infections, or in whom urosepsis is a possibility should be admitted to the hospital for IV rehydration & IV antibiotics.

- For hospitalized children, parenteral treatment with ceftriaxone (50 mg/kg/day, not > 2 g) or cefipime (100 mg/kg/day q 12 hr) or cefotaxime (100-150 mg/kg/day in 3-4 divided doses) is a reasonable choice until culture results. Oral 3$^{rd}$ generation Cephalosporins as Cefixime (8 mg/kg/day, in 1-2 divided doses) are as effective as parenteral ceftriaxone against a variety of Gram-negative organisms other than *P. aeruginosa*, & may be the drug of choice for oral outpatient therapy. Cephalexin also may be used especially with resistance to amoxicillin.
- Nitrofurantoin should not be used routinely in a febrile UTI, because it does not achieve significant renal tissue level.
- Ciprofloxacin is an alternative drug for resistant microorganism, particularly *P. aeruginosa*, in patients older than 17 yr (occasionally, for short-course therapy in younger child with *P. aeruginosa* UTI). Levofloxacin is an alternative quinolone with good safety profile in children. However, fluroquinolone in children should be used with caution because of potential cartilage damage.
- Some times, with febrile UTI, a loading dose of IM ceftriaxon followed by oral 3$^{rd}$ generation cephalosporins is effective. A repeat urine culture after the termination of treatment of UTI is not routinely needed.

3. Acute lobar nephronia is treated with the same antibiotics as PN but with 2-3 wk duration. Renal or peri-renal abscess or infections with obstructive urinary tract can require surgical or percutaneous drainage, antibiotic therapy & other supportive measures. Kidney loss may occur in 10-20% of cases of renal abscess.

- There is interest in brobiotic therapy (which replaces urogenital flora & inhibit growth of other bacteria) & cranberry juices (may prevent bacterial adhesion) to prevent UTI.
- The main consequence of chronic renal damage caused by PN are arterial hypertension & end-stage renal insufficiency which should be treated appropriately.

## Imaging studies

- The AAP recommends initial U/S of the kidneys, ureters & bladder for children 2-24 mo old with a first episode of UTI.
- Voiding cystourethrogram (VCUG) is indicated only if the U/S study indicates hydronephrosis, scarring, or other findings suggestive of vesicouretral reflux (VUR) or

obstructive uropathy, or if the patient has other atypical complex features (non-*E-coli* infection, positive family history of VUR), as well as, if patient has recurrent febrile UTI.

**Prevention of recurrences**

- In a child with recurrent UTI, identification of predisposing factors is beneficial. Bowel & bladder dysfunction is very important contributor to recurrent UTI & is one of the main reasons for an increase in UTI around the time of toilet training. Some children with UTI may also have constipation. Behavioral modification with treatment of constipation often is effective.
- The AAP does not recommend routine use of antibiotic prophylaxis in children with a first episode of PN in an otherwise anatomically normal urinary tract. Urologic conditions that can cause recurrent UTI which might benefit from long-term prophylaxis include neuropathic bladder, urinary tract stasis & obstruction, severe VUR & urinary calculi.

# ENURESIS

- Enuresis is urinary incontinence in a child who is considered adequately mature to have achieved continence. It is the most common urologic condition in children. Enuresis is classified as nocturnal (nighttime – majority of cases – good prognosis) or diurnal (daytime+ nighttime – more severe – less favorable prognosis). Daytime dryness is expected in the U.S. by age 4 years. Nighttime dryness is expected by age 6 years.
- Another useful classification of enuresis is primary (incontinence in a child who has never achieved dryness – 80% of cases) and secondary (incontinence in a child who has been dry for at least 6 months – 20% of cases).
- The prevalence of enuresis at age 5 yr is 7% in males and 3% in females. At age 10 yr, it is 3% in males and 2% in females, and at age 18 yr, it is 1% in males and extremely rare in females. Evidence suggests different rates of bed-wetting by ethnicity and culture.

**Etiology**

Enuresis is a symptom with multiple possible etiologic factors, including developmental difference, organic illness, or psychological distress.

A. Primary enuresis:

1. Maturational delay: Primary nocturnal enuresis due to maturational delay is by far the most common type of enuresis. It is 3 times commoner in boys than in girls & it is also commoner in the first born child & in low socioeconomic classes. A strong family history is present. The severity of enuresis is variable from one child to another but daily wetting is common in most cases & the condition may be exaggerated by parental punishment. On the other hand, understanding, encouragement & simple reward may be helpful. The prognosis for ultimate recovery is excellent.
2. Organic causes: They account for only small number of cases but they should be routinely excluded. Mental retardation, sacral anomalies (spina bifida, meningocele) & urological anomalies (bladder neck or urethral anomalies) are the main causes. In these cases, enuresis is commonly severe & diurnal.

B. Secondary enuresis: mostly nocturnal & caused by either emotional stress or organic causes :

1. Emotional stresses : Death of a parent, birth of a new sibling, move to a new house or marital conflicts are commonly responsible for secondary enuresis. Detailed environmental history is important in every case of secondary enuresis.
2. Organic causes: polyuria & urinary tract infection should be routinely excluded in every case of secondary nocturnal enuresis. History of dysuria or weight loss are particularly important. Urine examination should be a routine step.

**Treatment**

- The best approach to treatment is to reassure the child & his parents that this condition is self-limited & to avoid punitive measures that can affect the child psychological development adversely. Fluid intake should be restricted to 2 oz after 6 or 7 PM & avoiding extraneous sugar & caffeine after 5 PM. The parents should be certain that the child voids at bedtime. If the child snores & the adenoids are enlarged, referral to otolaryngologist should be considered, because adenoidectomy can cure enuresis in some case.
- Treatment of underlying organic causes of enuresis, including UTIs, diabetes mellitus, sleep disorders, and urologic abnormalities, is essential. Elimination of underlying chronic constipation is often curative.
- Active treatment should be avoided in children < 6 yr of age, because enuresis is extremely common in younger children. Treatment is more successful with increasing age & with motivated children to stay dray & less successful with overweight.
- The simplest initial measure is motivational therapy & include a star charts for dry nights. Waking children a few hrs after they go to sleep to void often help them to awaken dry, although this measure is not curative.
- Conditioning therapy by using a loud auditory or vibratory alarm attached to a moisture sensor in the underwear. The success rate is 30-60% with significant relapse rate. It should be used for several months & is most effective in older children.
- self-hypnosis is effective in some children & the primary role of psychological therapy is to help the child deal with enuresis psychologically & motivate him to void at night when awakes with a full bladder.
- Pharmacologic therapy is regarded as second line & not curative with more relapse rate than conditioning therapy, although the initial response rates are equivalent.
- Desmopressin acetate, a synthetic analog of ADH, reduces urine production at night. It is FDA approved & available as tablet (0.2-0.6 mg at night) with few S/E with long term use. Nasal spray is no longer used because it may cause hyponatremia & convulsion in some children. Fluid restriction at night is important & the drug should not be used with vomiting & diarrhea or polydipsia. The success rate is up to 40% & most effective in those approaching puberty. If effective, the drug should be used for 3-6 mo & then tapering the dose (if tapering causes relapse, return with higher dose). Some families use desmopressin intermittently with success (school trips, sleepovers, vacations).
- Anticholinergic therapy is used for therapy-resistant enuresis & with symptoms of overactive bladder. Oxybutynin 5 mg or tolterodine 2 mg at bedtime often is indicated (the dose may be doubled if there is no response) & constipation is a potential S/E.
- Imipramine is a tricyclic antidepressant & regarded as a third-line treatment with mild anticholinergic & α-adrenergic effects, reduces the urine output slightly & may alter the sleep pattern. The dose is 25 mg (in 6-8 yr), 50 mg (in 9-12 yr) & 75 mg (in teenagers) with 30-60% success rate & S/E (as anxiety, insomnia, dry mouth & heart rhythm may be affected). Long QT

syndrome should be excluded if there is history of palpitation or syncope in the child, or sudden cardiac death or unstable arrhythmia in the family. Imipramine is one of the most common causes of poisoning in younger children.

- Combining therapy often is effective in unsuccessful monotherapy cases (as alarm therapy plus desmopressin & Oxybutynin chloride plus desmopressin or Desmopressin plus imipramine).