URINARY TRACT INFECTIONS (UTI)

Prevalence
- The prevalence of UTI is 3-5% in girls & 1% in boys.
- In girls, the peak of UTI is during infancy & during toilet training period. 60-80% of girls will develop a 2nd attack of UTI within 18 months of the onset of 1st attack.
- In boys, it is mostly during the 1st year of life. It is much more common in uncircumcised boys.
- The prevalence of UTI varies with age. During the 1st year of life, male:female ratio = 2.8 : 5.4. Beyond 1-2 years of life, male:female ratio = 1 : 10.

Etiology
- UTI is mainly caused by colonic bacteria.
- The most common bacteria in females is E.Coli (75-90%) followed by klebsiella & proteus.
- In males, some reports say that after 1st year of life, proteus = E.coli. Other reports reveals the preponderance of G+ve bacteria.
- Staphylococcus saprophyticus is a pathogen of both sexes.
- 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.

Clinical manifestations & classification
There are 3 basic forms of UTI:
1. Pyelonephritis: It is characterized by any or all of the following symptoms: abdominal or flank pain, fever, rigor, malaise, nausea, vomiting, & occasionally diarrhea. Some newborns & infants may show nonspecific signs & symptoms as jaundice, poor feeding, irritability & weight loss. Acute pyelonephritis may → renal injury which is called "pyelonephritic scarring".
2. Cystitis: It can → dysurea, urgency, frequency, suprapubic pain, incontinence, & malodorous urine. It is usually without fever or renal injury.
3. Asymptomatic bacterurea: 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 & pathology

Nearly all UTIs 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 pyelonephritis. In rare cases, renal infections may occur by hematogenous spread.

- **Risk factors for UTI**: These include:
  - Female sex
  - Uncircumcised male
  - Vesicoureteric reflux
  - Toilet training: In female, UTI often occur at the onset of toilet training due to voiding dysfunction which occurs at that age (incomplete bladder emptying).
  - 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 which may → voiding dysfunction.
  - P fimbriated bacteria: There are 2 types of pilli or fimbriae on the bacterial surface 1 & 2. Type 2 fimbriae which is found on some strains of E.Coli & can be agglutinated by P blood group RBCS, are more likely to cause pyelonephritis.
  - Anatomic abnormalities as labial adhesion.
  - Neuropathic bladder: incomplete bladder emptying & detrusor-sphincter dyssnergia.
  - Sexual activity: in female due to incomplete bladder emptying.
  - Pregnancy: 4-7% have symptomatic bacterura which may → UTI.
  - Breast feeding → ↓ UTI.

Diagnosis

UTI may be suspected depending on clinical findings or GUE findings or both, but the urine culture is necessary for confirmation of the diagnosis & for giving appropriate treatment.

- **Methods of urine sampling for urine culture & sensitivity**:
  1. *Midstream urine sample* (in toilet-trained children, the prepuce must be retracted): If the culture shows > 100,000 colonies of a single pathogen, or ≥ 10,000 + symptomatic patient → UTI.
  2. *Sterile collecting bag* (in infants, requires disinfection of the skin of the genitals, especially useful with -ve culture, however, +ve culture may reflect a contaminant especially in females & uncircumcised males): If GUE is +ve + symptomatic patient + single organism cultured with colny count > 100,000 → there is presumed UTI.
  3. *Catheterized specimen*: It is obtained when greater assurance to the possibility of infection is needed. Proper skin preparation & good technique of catheterization are important (usually No.5 French polyethylene feeding tube in infants & No.8 for older children with proper lubrication, only a few ml by syringe are required). Catheterization shortly after spontaneous voiding measures the residual urine in the bladder & help assessing problems related to the bladder emptying. If the culture shows ≥ 10,000 colonies → +ve culture.
4. **Suprapubic aspiration**: It is the gold standard & unfortunately the most invasive method → not usually done. If the culture shows ≥ 100 colonies → +ve culture.

- 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.
- Pyurea (WBC$^5$ in urine) suggests infections, but infections can occur without pyurea & vice-versa.

- Nitrates & leukocytes esterase tests are usually +ve in infected urine.
- Microscopic hematurea is common in acute cystitis.
- WBC casts in the urinary sediments suggest renal involvement (but these are rare).
- With acute renal infection → leucocytosis, neutrophilia, ↑ESR & CRP.
- With renal abscess → WBC > 20,000 - 25,000/mm$^3$.
- Blood culture is indicated with suspicion of sepsis which is common in pyelonephritis especially in infants & in any child with obstructive uropathy.
- If the child is asymptomatic & GUE is normal → UTI is unlikely.
- If the child is symptomatic & GUE is normal → UTI is likely.
- Acute hemorrhagic cystitis is frequently caused by E.Coli & attributed also to adenovirus type 11 & 21. Adenovirus cystitis is most frequent in males, with self-limiting hematurea which lasts about 4 days.

**Treatment**

- **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). The course is that of 3-5 days or, some times, 7-10 days of (one) the following oral antibiotics:
  - Trimethoprim-sulfamethaxasole, 4-6 mg trimethoprim / kg / day, divided into 2 doses,
  - Nitrofurantoin, 5-7 mg / kg / day, in 3-4 divided doses. It should not be used with the febrile UTI because it does not achieve significant renal tissue level.
  - Amoxicillin, 50 mg / kg / day, in 2-3 divided doses.

- **Acute pyelonephritis**: The course is that of 14 days of one of the following parenteral antibiotics:
  - Ceftriaxon, 50-75 mg / kg / day (not more than 2 gm / day).
  - Ampicillin, 100 mg / kg / day + Gentamicin, 3-5 mg / kg /day, in 1-3 divided doses. (S/E of gentamicin include: ototoxicity & nephrotoxicity. Serum creatinine & gentamicin level must be obtained before treatment then daily assessment.
Aminoglycosides are particularly effective against pseudomonas & alkallinization of urine with NaHCO3 → ↑ their effectiveness in the urinary tract.

Other oral antibiotics include one of the following:

- Oral 3rd generation Cephalosporin as Cefixime, 8 mg / kg / day, in 1-2 divided doses. This drug may be the drug of choice of oral treatment. It is not effective against pseudomonas.
- Oral Ciprofloxacin, 15-30 mg / kg / day, in 2 divided doses, is an alternative drug for resistant organisms especially pseudomonas in patients > 17 years & in patients < 17 years with cystic fibrosis, pulmonary infections secondary to pseudomonas, & occasionally for children with pseudomonas UTI (S/E of ciprofloxacin → potential cartilage damage in children → restricted use).
- Some times, with febrile UTI, a loading dose of IM Ceftriaxon followed by oral 3rd generation Cephalosporins is effective.

■ Renal or peri-renal abscess or infections with obstructive uropathy → surgical or percutaneous drainage + antibiotics + other supportive treatment.

Notes → 1. Urine C&S should be performed 1 week after the termination of treatment of any UTI 2. Follow-up urine culture should be performed periodically for 1-2 years even with asymptomatic child.

■ Supportive therapy:

- ↑ fluid intake.
- Antipyretics as Paracetamol, 10 mg/kg/dose, 4-6 times per day or Iboprunfen 10-15 mg/kg/dose, 3-4 times per day.
- Bladder analgesics may be used in older children to relief pain associated with severe dysurea as Phenazopyridine (Urisept, tab.=100 mg), 10mg/kg/day, in 3 divided doses.
- Alkalinizing agents as NaHCO3 or Na-citrate are especially useful with aminoglycosides. The dose is one teaspoon of granules+some water, 2 times per day.

■ Long term antibiotics prophylaxis:

It is the prophylaxis against re-infection using either Trimethoprim-Sulfamethoxasole or Nitrofurantoin at 1/3 of the therapeutic dose once a day which is often effective. Prophylaxis with Amoxicillin or Cephalexin may be inappropriate because of the rapid development of bacterial resistance. A 6-12 months course is indicated. If infection recurs after stopping prophylaxis, antibiotics should be resumed. Indication for antibiotics prophylaxis are:
1. Infants or children with their 1\textsuperscript{st} UTI, who have finished their course of treatment & waiting for completion of other studies as voiding cystourethrography (VCUG) or renal ultrasound

2. Patients with known urologic abnormalities which place them at high risk of recurrent UTI as neurogenic bladder, urinary tract stasis & obstruction, vesico-uretral reflux (VUR), calculi & posterior urethral valve (PUV).


- Treatment of consequences of chronic renal damage caused by pyelonephritis as hypertension & renal insufficiency.

**Imaging studies**

The goal of imaging studies in children with UTI is to identify the anatomic abnormalities which predispose to infection:

1. **Renal ultrasound:** It should be obtained to rule out:
   - Hydronephrosis
   - Renal or perirenal abscess
   - Acute pyelonephritis in 30-60% of cases by demonstrating enlarged which may require prompt drainage of the collecting system by percutaneous nephrostomy.

   Normally, the difference in renal lengths of 2 kidneys is <1 cm & large disparity may → impaired renal growth. Renal ultrasound can be done with other studies or at time of hospital admission if the patient appears toxic, or hypertensive, or if there is evidence of ↓ renal function.

2. **Voiding cystourethrogram (VCUG):** It is indicated in the following conditions:
   - All children < 5 years of age.
   - Any child with febrile UTI.
   - School aged girls with ≥ attacks of UTI.
   - Any male with UTI.

   - The most common finding is vesico-ureteric reflux (VUR) which is identified in about 40% of cases.

   - Timing of VCUG is controversial. In some centers, the study is delayed for 2-6 weeks to allow the inflammation in the bladder to resolve, however, the incidence of VUR is identical, irrespective of whether the VCUG obtained during treatment or after 6 weeks, so obtaining VCUG before discharging from the hospital is recommended.

   - If available, a radionuclide VSUG instead of contrast VSUG can be used in females due to less radiation exposure of gonads, however, it does not provide the anatomic definition of the bladder, allow precise grading of VUR, demonstrate a paraureteric diverticulum, or show whether reflux is occurring into a duplicated collecting system or an ectopic ureter. In males, the radiographic definition of the urethra is important, so
contrast VCUG is recommended for initial workup.

- Because of the concern that the VCUG is traumatic to the child, some parents question the need for VCUG with normal ultrasound, however, the ultrasound is insensitive in detecting VUR (only 40% of children of VUR have any abnormality on ultrasound).
- The VCUG should not be performed by using general anesthesia because of side effects & cost of anesthesia & because the study is incomplete without voiding phase. In selected cases, oral or nasal midazolam may be used (up to 0.5 mg / kg oral, or 0.2 mg / kg nasal) with monitoring of vital signs.

3. Technitium-labeled DMSA (dimercaptosuccinic acid) or glucoheptonate: It is useful when the diagnosis of acute pyelonephritis is uncertain.
   - The presence of photopenia support the diagnosis of pyelonephritis & the experienced radiologists can differentiate an acute from chronic process.
   - Acute pyelonephritis is present in about 50% in children with febrile UTI & in about 80-90% in children with febrile UTI + 3 or 4 or 5 VUR.
   - If DMSA scan shows acute pyelonephritis → about 50% of patients will develop renal scar over the following 5 months, however, if DMSA scan is normal during febrile UTI, no scarring will develop from this particular infection. Computed tomography can diagnose acute pyelonephritis (less clinical experience).
   - If VUR is present, the DMSA scan often is performed to assess whether renal scarring is present. The DMSA scan is the most sensitive & accurate study for demonstrating scarring.

4. Excretory urography: It is not as sensitive as the DMSA scan in demonstrating renal scarring, in addition, the visualization of the collecting system in infants & young children often is suboptimal, there is high risk of contrast allergy, & it can take 1-2 years for renal scar to appear in urogram.

5. Computed tomography: It may demonstrate renal scarring.

Notes: Frequently performed cystoscopies & measurement of the urethral caliber in females add nothing to the therapeutic decision in children with UTI & are contraindicated. The narrowing of female urethra has no relation to recurrent UTI.