1. SIGNIFICANCE

Prevalence of urinary tract infections (UTI) varies markedly with sex and age. Symptomatic UTI occur in about 1.4/1,000 newborn infants, with slight male preponderance. In older life manifestation of UTI is more specific and easily controlled with prompt medication. Conversely, infants show generalized response to infection, which cannot be readily differentiated from other infection just on the basis of clinical presentation without careful urine analysis. Moreover, diseased infants may quickly progress to renal scaring and following renal failure, if not timely and adequately treated. For the danger of frequent complications, future physician should know well of pathology of UTI, clinical features, treatment protocol and follow-up measures to reduce probability of unwanted consequences.

2. PREREQUISITES

The skills listed below will not be taught in this lesson but are necessary to perform physical examination of the patient in the intensive care unit during practical training. Therefore, before beginning this lesson, one has to be sure of the ability to:

- Identify abdominal or flank mass suggestive of obstructive uropathy;
- Identify sacral dimple, abnormal gluteal cleft, decreased rectal tone, lipoma suggestive for spinal cord anomalies;
- Observe skin for labial adhesion, trauma, and perineum irritation as risk for UTI;
- Perform gross examination of urine;
- Read urine culture and routine urine analysis.

3. EDUCATIONAL OBJECTIVES

Student should know:

Student should be able:
- to identify the child with urinary tract infections, make correct decisions during physical examination of the patient with listed conditions, take appropriate actions based on those decisions, demonstrate skills to develop treatment plan and follow-up.

4. INTERDISCIPLINARY INTEGRATION

<table>
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<tr>
<th>Discipline</th>
<th>Student should know</th>
<th>Student should be able to</th>
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<tbody>
<tr>
<td>Normal anatomy, Physiology</td>
<td>Anatomic and physiologic features of the urinary system in children of different age groups</td>
<td>Use knowledge of anatomic and physiologic features of urinary system in children for evaluation of clinical findings</td>
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### Normal ranges for the routine biochemical blood analysis

Assess blood biochemistry and comment on deviations from normal in a clinical context.

### Histologic and histochemical presentation of urinary tract illnesses in children

Use knowledge of histologic and histochemical presentation of the urinary tract illnesses in children for evaluation of clinical findings.

### Pathophysiologic mechanisms of the renal failure

Recognize symptom and signs of renal failure.

### Sampling of urine for bacterial cultures

Assess microbiologic findings in clinical context.

### Physical examination of urinary system in children.

Perform physical examination of the urinary system (gross inspection, palpation, percussion), assess the results of urinary tests.

### Indications and methods of imaging studies in urinary tract illnesses

Assess ultrasound examination of kidney.

### Symptoms and signs of renal failure of different stages, its etiology, and principles of intensive care

Recognize renal failure, assess its severity, provide emergency care.

### Differential diagnosis of UTI

It includes urethritis, vaginitis, trauma, hyper-calciuria (dysuria), detrusor/sphincter dysfunction, neurogenic urinary bladder, different anatomical abnormalities.

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<th>TYPE</th>
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<td>Primary</td>
<td>Congenital incompetence of the valvular mechanism of the vesicoureteral junction</td>
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<td>Primary associated with other malformations</td>
<td>Ureteral duplication</td>
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2. Congenital anomalies of urinary tract

Renal agenesis - unilateral renal agenesis incidence of 1 in 450 to 1,000 births. In true agenesis, the ureter and the ipsilateral bladder hemitrigone are absent. The contralateral kidney undergoes compensatory hypertrophy, to some degree prenatally but primarily after birth. Approximately 15% of these children have contralateral vesicoureteral reflux.

Aplasia - nonfunctioning tissue and normal or abnormal ureter. If there is a normal contralateral kidney, renal function should remain normal over time.

Bilateral renal agenesis - incompatible with extrauterine life and is termed Potter syndrome. Death occurs shortly after birth from pulmonary hypoplasia. The newborn has a characteristic facial appearance, termed Potter face.

Familial renal adysplasia describes disease in which renal agenesis, renal dysplasia, multicystic kidney (dysplasia), or a combination, occurs in a single family. This disorder has an autosomal dominant inheritance pattern with a penetrance of 50–90% and variable expression.

Renal dysgenesis refers to maldevelopment of the kidney that affects its size, shape, or structure. The 3 principal types of dysgenesis are:

- Dysplastic
- Hypoplastic
- Cystic.

A multicystic kidney: a congenital condition in which the kidney is replaced by cysts and does not function, and may result from ureteral atresia. Renal size is highly variable. The incidence is approximately 1 in 2,000. An inherited disorder that may be autosomal recessive or autosomal dominant and affects both kidneys. Multicystic kidney usually is unilateral and is not inherited. Bilateral multicystic kidneys are incompatible with life. Multicystic dysplastic kidney is the most common cause of an abdominal mass in the newborn. In most cases it is discovered incidentally during prenatal sonography. Contralateral hydronephrosis is present in 5–10% of patients.

Renal hypoplasia: a small nondysplastic kidney that has fewer than the normal number of calyces and nephrons. If the condition is unilateral, the diagnosis usually is made incidentally. Bilateral hypoplasia usually presents with the manifestations of chronic renal failure and is a leading cause of end-stage renal disease during the first decade of life. A history of polyuria and polydipsia is common. Urinalysis results may be normal.
The Ask-Upmark kidney, also termed segmental hypoplasia. Small kidneys, usually weighing not more than 35 g, with one or more deep grooves on the lateral convexity, underneath which the parenchyma consists of tubules resembling those in the thyroid gland. It is unclear whether the lesion is congenital or acquired. Most patients are 10 yr or older at diagnosis and have severe hypertension. Nephrectomy usually controls the hypertension.

3. Urinary tract infection

Etiology.

*Escherichia coli* is the most common cause of bacterial UTI.

Other organisms: *Klebsiella* spp, *Enterococcus, Staphylococcus saprophyticus, Proteus mirabilis; Pseudomonas, Streptococcus, Candida albicans* (usually associated with complicated UTIs or chronic antibiotic treatment).

Risk factors in all children include:
- Indwelling catheters
- Urologic tract anomalies
- Neurogenic bladders
- Risk factors specific to girls include:
  - Chemical irritants
  - Sexual activity
  - Sexual abuse
  - Constipation
  - Pinworms
- Risk factors specific to boys include:
  - Phymosis

Uncircumcised boys have an incidence of infection 10 times that of circumcised boys.

Epidemiology.

- Bacteriuria is present in 1%–2% of prepubertal children.
- In the first year of life, the risk of infection is equal among boys and girls
- The risk in girls is considerably higher in toddlers and older children.
- The incidence of UTI is 3.0% in febrile infants younger than 12 mo of age without an obvious cause for fever
- Vesicoureteral reflux is present in 18%–50% of children with UTI.

Symptoms.

- In infants, vomiting, poor feeding, and irritability.
- Older children develop dysuria, urgency, frequency, incontinence, hesitancy, and retention; fever, chills, back pain are symptoms that suggest an upper tract infection (pyelonephritis).

Signs.

- Fever
- Jaundice (may be seen in neonates).
- Suprapubic or costovertebral angle tenderness
- Abdominal or flank mass: suggestive of obstructive uropathy.
- Sacral dimple, hairy patch over the sacrum, abnormal gluteal cleft, decreased rectal tone, lipoma: suggest spinal cord anomalies.
- Labial adhesion, trauma, and irritation: may increase the risk of infection.

Investigations.

- Urine culture: considered positive if any organisms are present on a suprapubic collection; > $10^8$ colony forming units (CFU)/mL of a urinary pathogen from a catheterized specimen; > $10^5$ CFU/mL of a urinary pathogen from a clean catch.
- Urinalysis with dipstick: demonstrating positive leukocyte esterase and nitrite test with microscopic examination demonstrating more than five leukocytes per hpf, bacteria is
highly suggestive of a urinary tract infection (UTI); this is not reliable in infants in whom the urine is dilute; 10% may have a negative urinalysis result despite a positive culture.

- Radiographic imaging: indicated in every boy with an infection and girls with pyelonephritis; girls with recurrent lower tract infections or those who are younger than 5 years of age with their first infection should be studied as well.
- Renal and bladder ultrasound: a noninvasive aid to look for hydroureteronephrosis, duplex kidneys, and ureteroceles, which may be a sign of obstruction.
- Voiding cystourethrography: might demonstrate vesicoureteral reflux and is especially important in the male to exclude posterior urethral valves.
- 99m Tc-DMSA scan: controversial; it is an excellent study to identify pyelonephritis as the cause of fever when the source is not known; it is the most sensitive study to determine the presence of scars; however, it may not ultimately change the course of treatment.

Complications.
- Septicemia: more likely to be present in neonates or in children with abnormal urinary tracts.
- Renal scarring: can develop years after infections that occurred in infancy or early childhood; it is associated with hypertension, toxemia, and the risk of chronic renal failure leading to end-stage renal disease.
- Staghorn calculi: can form in the presence of repeated infections.

Treatments

Increased water intake offers several benefits; it dilutes urine, increases voiding frequency, and reduces constipation. Stool softeners should be considered if the latter problem persists. Irritants, particularly soap, should be avoided near the perineum in prepubertal girls. Sexually active women may benefit from postcoital voiding.

Pharmacologic treatment.

Complicated febrile urinary tract infections.

Complicated infections are defined as those seen in infants younger than 6 months of age and any child who is clinically ill, persistently vomiting, moderately dehydrated, or poorly compliant; these cases warrant intravenous antibiotics and hospitalization.

Standard dosage.
- Ampicillin, 50–100 mg/kg/d in four divided doses.
- Gentamicin, 2–2.5 mg/kg/dose every 8 h.
- Ceftriaxone, 75 mg/kg/dose every 12 h (does not cover Enterococcus, which is more frequently encountered in children with recurrent infection and should be avoided in neonates).

Special points. An oral agent can be used after the child improves clinically (>24 h afebrile) pending the results of the culture and sensitivities; total treatment should last 14 d or longer if there is a renal abscess or an abnormal urinary tract.

Uncomplicated febrile urinary tract infections.

These children do not appear clinically ill, can take oral antibiotics, and are only mildly dehydrated (if at all) and compliant. Treatment can start with one dose of a parenteral agent (ceftriaxone, 75 mg/kg i.v. or i.m.; gentamicin, 2.5 mg/kg i.v. or i.m.) followed by oral therapy or with oral therapy alone. Good follow-up is essential to ensure the child has responded appropriately, with treatment lasting 10–14 d.

Standard dosage.
- Cotrimoxazole, 6–12 mg/kg/d trimethoprim divided twice daily.
- Amoxicillin, 20–40 mg/kg/d divided 3 times daily (many strains of E. coli are resistant to amoxicillin).
- Cephalexin, 25–50 mg/kg/d divided 4 times daily.
- Cefprozil, 15–30 mg/kg/d divided 2 times daily.
- Afebrile urinary tract infections (acute cystitis).
Oral therapy with the agents listed above for a total of 5–7 d assuming clinical improvement is seen; in addition, nitrofurantoin 5–7 mg/kg/d divided 4 times daily can be considered; the liquid form of nitrofurantoin is not well tolerated.

Covert (asymptomatic) bacteriuria.
The treatment of this subgroup is controversial even in the presence of reflux; treatment may lead to the emergence of resistant organisms.

Prophylaxis.
Standard dosage.
Cotrimoxazole: 1–2 mg/kg trimethoprim daily.
Nitrofurantoin, 1–2 mg/kg/d.
Both of the above medications should be avoided in infants younger than 6 months of age.
Amoxicillin (10 mg/kg/d) or cephalexin (10 mg/kg/d) can be used instead.

Other treatments.
Infection in the presence of obstruction requires effective drainage of the urinary tract (e.g., nephrostomy, bladder catheterization) in addition to antibiotic therapy.
Surgical correction of vesicoureteral reflux in indicated when the reflux is massive, when breakthrough infections develop, or when poor compliance is suspected.

Prognosis.
Risk for renal damage includes infant and young children with febrile infections in whom treatment is delayed.
Children with massive vesicoureteral reflux, and those with anatomic or neuropathic urinary tract obstruction.
Follow-up and management
Follow-up cultures should be obtained in children with febrile UTIs to assure an appropriate response.
Infants and young children with documented vesicoureteral reflux should remain on antibiotic prophylaxis until the reflux resolves.
Some children with recurrent infections benefit from a short course of prophylactic therapy even when reflux is not present.

6. MATERIALS FOR METHODOLOGICAL BACKGROUND OF THE WORKSHOP

6.1. Quiz
1. Describe pathology associated with renal agenesis.
2. Describe pathology associated with renal aplasia.
3. Describe pathology associated with renal dysgenesis.
4. Describe pathology associated with a multicystic kidney.
5. Renal hypoplasia: a small nondysplastic kidney that has fewer than the normal.
6. Describe pathology associated with the Ask-Upmark kidney.
7. What is etiology of UTI?
8. What is epidemiology of UTI?
9. What is most common pathogen isolated from the urine in UTI?
10. Which pathogens will be isolated if patient received chronic antibiotic therapy?
11. What is predisposing factor for the development of UTI in boys?
12. Grade vesicoureteral reflux by degree of urine reflux?
13. What are symptoms in UTI?
14. What is urgency?
15. What is dysuria?
16. What is hesitancy?
17. When urine culture is considered positive?
18. What is urine analysis with dipstick?
19. When is radiographic imaging needed?
20. What renal and bladder ultrasound reveal in UTI?
21. What is the best method to document of vesicoureteral reflux?
22. What is the meaning of 99m Tc-DMSA in UTI?
23. What are complications of UTI?
24. What treatment aims in UTI do you know?
25. What are diet and lifestyle requirements in patients with UTI?
26. Define complicated UTI.
27. What is the treatment of complicated UTI?
28. What is uncomplicated febrile UTI?
29. What are approaches to covert bacteriuria?
30. What is prophylaxis plan for recurrent UTI?

6.2. Multi-choice questions
A 17-years old boy came to hospital with the following complaints: headache, burning pain during urination, frequent urination, supra-pubic pain, mild fever 37°C, and weakness. He also said that his urine was cloudy and smelled bad. In the anamnesis, boy admitted having sexual contacts without using condoms. The urine analysis for *E. coli* showed more than 10⁵ CFU/ml. Ultrasound did not show any abnormalities in kidneys. Tests for gonorrhea and genital herpes were negative. What likely diagnosis?
A. Acute cystitis/urethritis
B. Acute pyelonephritis
C. Acute renal failure with hyper-calciuria
D. Vesico-ureteral reflux
E. Neurogenic urinary bladder

6.3. Sample case report
A 12 years old girl is complaining on pain in suprapubic area, frequent painful urination by small portions, temperature is 37,80°C. Pasternatsky symptom is negative. Urine analysis: protein - 0,033 g/L, WBC - 20-25 in f/vis, RBC - 1-2 in f/vis.
1. What is the diagnosis?
2. What is the differential diagnosis?
3. What is the follow-up?

Suggested reading

Additional reading