

Hematuria

II. Hematuria

- A. **Definition.** Hematuria is defined as the presence of red blood cells (RBCs) in the urine. Hematuria may be seen on voiding (**gross hematuria**) or only on urinalysis (**microscopic hematuria**). **Microscopic** hematuria is defined as ≥ 5 –6 RBCs per high-power field (HPF) detected on two or more consecutive samples.
- B. **Epidemiology.** Approximately 5% of school children have microscopic hematuria detected on a single voided urine sample, but only 0.5–2% have persistent microscopic hematuria.
- C. **Clinical significance.** Microscopic hematuria may be an indicator of a serious medical condition such as a tumor or chronic glomerulonephritis or may be of no serious medical consequence. Discolored urine may not be from blood in the urine. See [Figure 11-1](#) for clues regarding the causes of discolored urine. The **differential diagnosis of hematuria** is outlined in [Figure 11-2](#).
- D. **Evaluation ([Figure 11-1](#)).** Detection of hematuria may be by urinary dipstick or by microscopy. **Urinary dipstick** detects the presence of hemoglobin or myoglobin in the urine. **False-negative results** may occur with **ascorbic acid** (vitamin C) ingestion. **Microscopic urinalysis may also provide helpful clues.** When RBCs are present on microscopic examination, **careful examination of RBC morphology and identification of other urine elements, such as casts or bacteria, may be extremely helpful** in determining the cause of the hematuria.
 - 1. **RBC morphology**
 - a. RBCs originating in the glomerulus are dysmorphic in character, often with blebs in the RBC membrane.
 - b. RBCs that appear to be normal biconcave disks usually originate in the lower urinary tract.
 - 2. **RBC casts** are diagnostic of glomerular bleeding, which usually occurs in acute or chronic glomerulonephritis.
 - a. **Crystals** may be indicative of renal stone disease.
 - b. Large numbers of RBCs (especially in the presence of dysuria) may indicate **acute hemorrhagic cystitis**, which may result from bacterial infections, viral infections (e.g., adenovirus), or chemotherapeutic agents (e.g., cyclophosphamide).

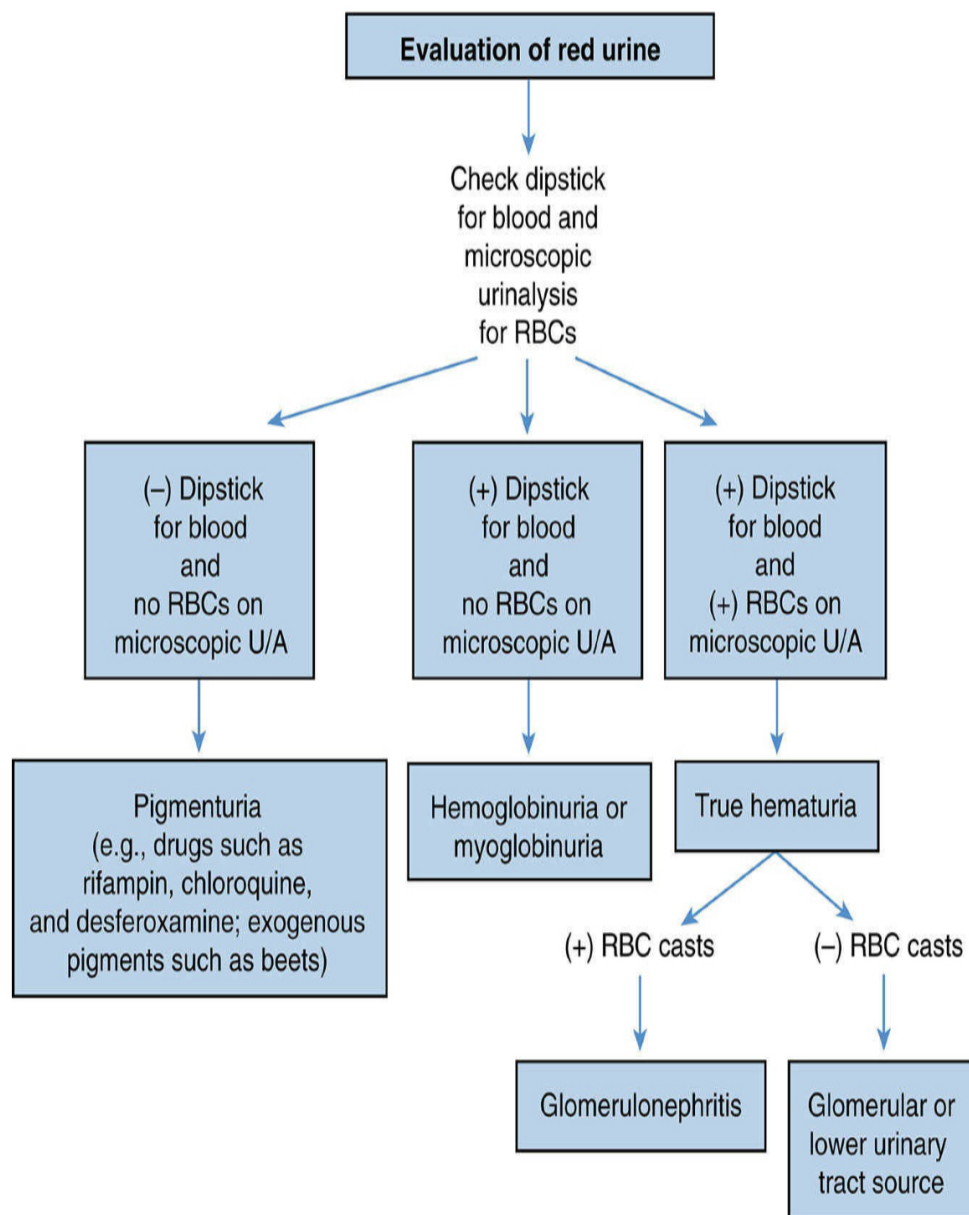
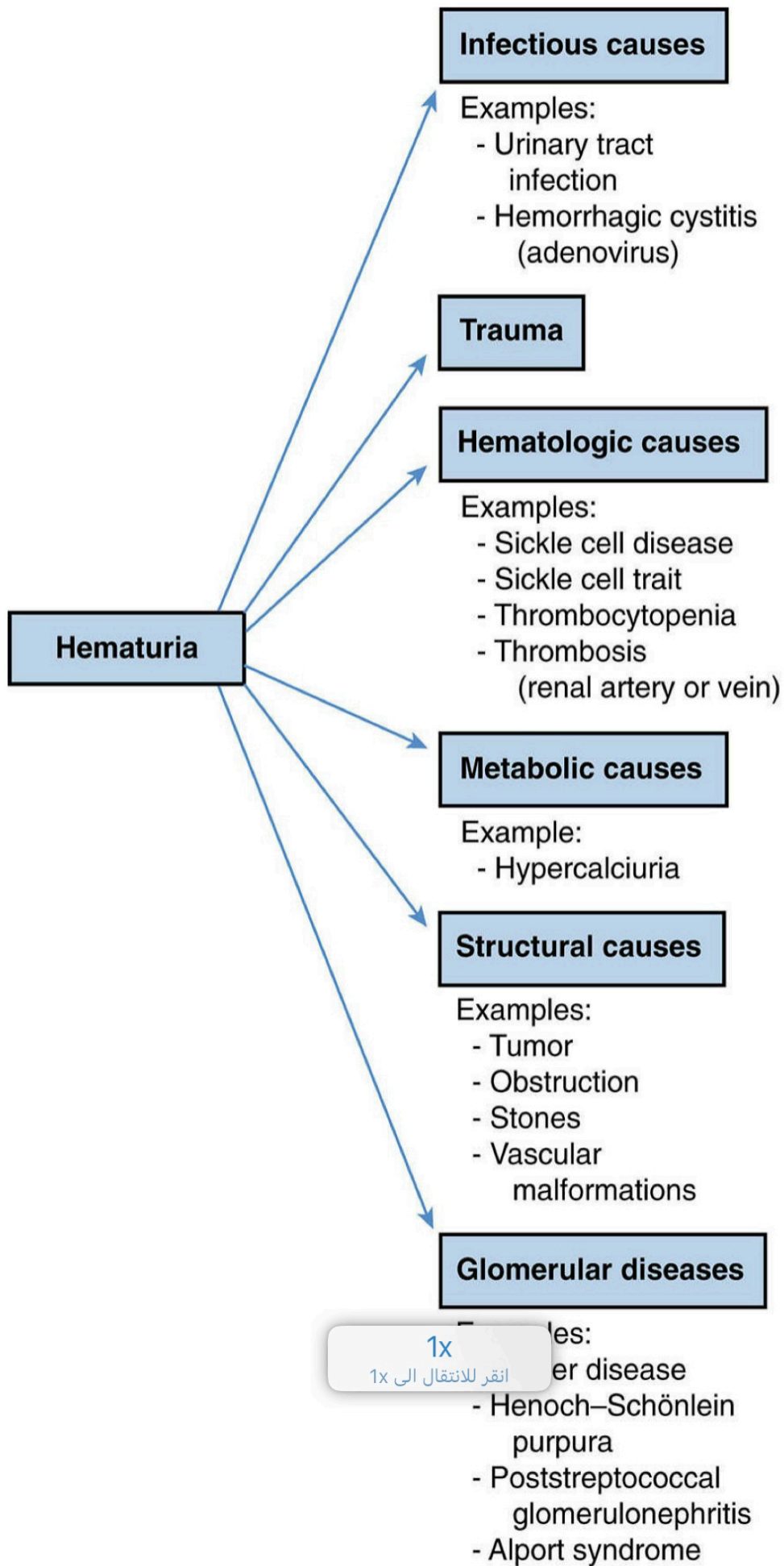


FIGURE 11-1 An approach to red urine. RBC = red blood cell; U/A = urinalysis.



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Clinical Evaluation of the Child with Hematuria

- ? Hematuria defined as the presence of at least 5 red blood cells (RBCs) per microliter of urine
- ? occurs with prevalence of 0.5-2.0% among school-age children.
- ? normal children can excrete more than 500,000 RBCs per 12 hr period >> this increases with fever or exercise.
- ? qualitative estimates by urinary dipstick uses very sensitive peroxidase chemical reaction between hemoglobin (or myoglobin) and colorimetric chemical indicator impregnated on the dipstick.
- ? Chemstrip >> common commercially available dipstick for detecting 3-5 RBCs/ μ L of Unspun urine.
- ? The presence of 10-50 RBCs/ μ L suggest underlying pathology
- ? significant hematuria considered as >50 RBCs/ μ L.
- ? False negative results occur in
 - ? the presence of formalin (used as a urine preservative)
 - ? high urinary concentrations of ascorbic acid as in with vitamin C intake >2000 mg/day).
- ? False-positive results
 - ? seen in child with alkaline urine (pH > 8)
 - ? following contamination with oxidizing agents such as hydrogen peroxide used to clean the perineum before obtaining specimen.
- ? Microscopic analysis of 10-15 mL of freshly voided and centrifuged urine for confirming the presence of RBCs suggested by >10 RBCs/ μ L, or 1+ positive urinary dipstick reading.
- ? heme-positive urine without RBCs caused by the presence of hemoglobin or myoglobin.
- ? Hemoglobinuria without hematuria occur in the presence of acute or chronic hemolysis.
- ? Myoglobinuria without hematuria occurs in the presence of rhabdomyolysis resulting from skeletal muscle injury associated with 5-fold increase in the plasma concentration of creatinine kinase.
- ? Rhabdomyolysis lead to acute renal injury >> It occur due to
 - ? viral myositis
 - ? crush injury
 - ? severe electrolyte abnormalities as hypernatremia, hypophosphatemia
 - ? hypotension
 - ? disseminated intravascular coagulation
 - ? toxins as drugs or venom
 - ? metabolic disorders of muscles
 - ? prolonged seizures
- ? innocuous غير ضار heme-negative urine appear red, cola colored, or burgundy اللون عذابي due to
 - ? ingestion of various drugs, foods (blackberries, beets)
 - ? dyes used in food and candy
- ? dark brown (or black) urine due to various urinary metabolites.
- ? Evaluation of the child with hematuria with history , physical examination and urinalysis.
 - ? used to determine the level of hematuria (upper vs lower urinary tract)
 - ? determine the urgency of the evaluation based on symptom
- ? Special consideration needs for family history.
 - ? identification of anatomic abnormalities and malformation syndromes.
 - ? presence of gross hematuria
 - ? manifestations of hypertension, edema, or heart failure.
- ? Upper urinary tract sources of hematuria
 - ? originate within the nephron as glomerulus

- associated with brown, cola- or tea-colored, or burgundy urine
- proteinuria >100 mg/dL via dipstick
- urinary microscopic findings of RBC casts, and deformed urinary RBCs (particularly acanthocytes).
- ? tubular system associated with the presence of leukocytes or renal tubular casts
- ? Lower urinary tract sources of hematuria originate from the pelvocaliceal system, ureter, bladder, or urethra.
- ? associated with gross hematuria that bright red or pink
- ? terminal hematuria >> gross hematuria occurring at the end of the urine stream
- ? blood clots, normal urinary RBC morphology
- ? minimal proteinuria on dipstick (<100 mg/dL).
- ? Patients with hematuria present with symptoms suggesting specific disorders.
- ? Tea- or cola-colored urine, facial or body edema, hypertension, and oliguria >> glomerulonephritis.
- ? history of recent upper respiratory, skin, or gastrointestinal infection :
 - postinfectious glomerulonephritis,
 - hemolytic-uremic syndrome
 - HSP nephritis.
- ? Rash and joint complaints
 - ? HSP nephritis
 - ? SLE nephritis.
- ? Hematuria associated with glomerulonephritis >> painless but can associated with flank pain when acute or severe.
- ? Frequency, dysuria, and unexplained fevers >> urinary tract infection
- ? renal colic suggests nephrolithiasis.
- ? flank mass
 - ? hydronephrosis,
 - ? renal cystic diseases,
 - ? renal vein thrombosis
 - ? tumor.
- ? Hematuria associated with headache, mental status changes, visual changes (diplopia), epistaxis, Heart failure >> hypertension.
- ? Patients with hematuria and history of trauma require immediate evaluation
- ? Child abuse must suspected in the child presenting with unexplained perineal bruising and hematuria.
- ? careful family history critical in the initial assessment of the child with hematuria for genetic causes of renal disorders.
- ? Hereditary glomerular diseases include
 - ? hereditary nephritis (Alport syndrome)
 - ? thin glomerular basement membrane disease
 - ? SLE nephritis
 - ? IgA nephropathy (Berger disease).
- ? Other hematuria renal disorders with hereditary component include
 - ? autosomal recessive and autosomal dominant polycystic kidney diseases
 - ? atypical hemolytic-uremic syndrome
 - ? urolithiasis
 - ? sickle cell disease/trait.
- ? complete physical examination to assess the cause of hematuria.
- ? Hypertension, edema, or signs of heart failure >> acute glomerulonephritis.
- ? Several malformation syndromes associated with renal disease including:
 - ? VATER

- vertebral body anomalies
- anal atresia
- tracheoesophageal fistula
- renal dysplasia
- ? Abdominal masses caused by
 - bladder distention in posterior urethral valves
 - hydronephrosis in ureteropelvic junction obstruction
 - polycystic kidney disease
 - Wilms tumor.
- ? Hematuria seen in patients with neurologic or cutaneous abnormalities due to syndromic renal disorders including
 - ? tuberous sclerosis
 - ? von Hippel-Lindau syndrome
 - ? Zellweger (cerebrohepato renal) syndrome.
- ? Anatomic abnormalities of the external genitalia associated with hematuria or renal disease.
- ? The most common cause of gross hematuria >> bacterial urinary tract infection.
- ? Urethrorrhagia >> urethral bleeding in the absence of urine
 - ? associated with dysuria and blood spots on underwear after voiding.
 - ? This condition occurs in prepubertal boys at intervals several months apart
 - ? has benign self-limited course.
 - ? Less than 10% of patients have evidence of glomerulonephritis.
- ? Recurrent episodes of gross hematuria
 - ? IgA nephropathy
 - ? Alport syndrome
 - ? thin glomerular basement membrane disease.
- ? Dysuria and abdominal or flank pain
 - ? idiopathic hypercalciuria
 - ? urolithiasis.
- ? Asymptomatic patients with isolated microscopic hematuria should not undergo extensive diagnostic Evaluation >> because such hematuria often transient and benign.
- ? The child with asymptomatic isolated microscopic hematuria that persists on at least 3 urinalyses observed over minimum of a 2 wk period poses dilemma in regard to the degree of further diagnostic testing that should be performed.
 - ? The initial evaluation of these children include
 - urine culture
 - spot urine for hypercalciuria with calcium : creatinine ratio in culture-negative patients.
 - ? In African-American patients >> sickle cell screen should be included.
 - ? If these studies normal >> urinalysis of all first-degree relatives indicated.
 - ? Renal and bladder ultrasonography considered to rule out structural lesions such as tumor, cystic disease, hydronephrosis, or urolithiasis.
 - most informative in patients presenting with gross hematuria, abdominal pain, flank pain or trauma.
 - ? if these initial studies normal >> assessment of serum creatinine and electrolytes recommended.
- ? The finding of hematologic abnormalities narrow the differential diagnosis.
 - ? Anemia in this setting caused by
 - hypervolemia with dilution associated with acute renal failure
 - decreased RBC production in chronic renal failure
 - hemolysis from hemolytic uremic syndrome, chronic hemolytic anemia, or SLE
 - blood loss from pulmonary hemorrhage, as in Goodpasture syndrome and melena in patients with HSP or hemolytic-uremic syndrome.

- ? Inspection of the peripheral blood smear reveal microangiopathic process>> hemolytic-uremic syndrome
- ? The presence of autoantibodies in SLE result in positive Coombs test and the presence of antinuclear antibody
- ? Leukopenia
- ? multisystem disease.
- ? Thrombocytopenia
 - ? decreased platelet production (malignancies)
 - ? increased platelet consumption as SLE , idiopathic thrombocytopenic purpura, hemolytic-uremic syndrome , renal vein thrombosis , congenital hepatic fibrosis with portal hypertension due to autosomal recessive polycystic Kidney disease).
- ? urinary RBC morphology normal with lower tract bleeding
 - ? dysmorphic from glomerular bleeding
 - ? it is not sensitive enough to delineate the site of hematuria.
- ? bleeding diathesis is unusual cause of hematuria >> Coagulation studies not routinely obtained unless personal or family history suggests bleeding Tendency.
- ? voiding cystourethrogram required in patients with
 - ? urinary tract infection
 - ? renal scarring,
 - ? hydroureter
 - ? pyelocaliectasis.
- ? Cystoscopy unnecessary and costly procedure in most pediatric patients with hematuria and carries the associated risks of anesthesia.
 - ? The diagnosis of urethral stenosis as indication for cystoscopy should viewed with high degree of Suspicion >> because true urethral stenosis is quite rare.
 - ? This procedure should reserved for evaluating
 - bladder mass noted on ultrasound
 - urethral abnormalities caused by trauma, posterior urethral valves, or tumor.
 - ? The finding of unilateral gross hematuria localized by cystoscopy rare but it indicate vascular malformation or another anatomic abnormality.
- ? Children with persistent asymptomatic isolated hematuria and normal evaluation should have their blood pressure and urine checked every 3 mo until the hematuria resolves
- ? Referral to pediatric nephrologist should considered for patients with persistent asymptomatic hematuria greater than 1 yr duration
 - ? with nephritis (glomerulonephritis, tubulointerstitial nephritis)
 - ? hypertension
 - ? renal insufficiency
 - ? urolithiasis or nephrocalcinosis
 - ? family history of renal disease such as polycystic kidney disease or hereditary nephritis.
- ? Renal biopsy indicated for
 - ? children with persistent microscopic hematuria.
 - ? children with recurrent gross hematuria associated with decreased renal function, proteinuria, Or hypertension.

HUS: Hemolytic Uremic Syndrome

Summary

Hemolytic uremic syndrome (HUS) is a **thrombotic microangiopathy** in which microthrombi, consisting primarily of platelets, form and occlude the arterioles and capillaries. These occlusions result in the simultaneous occurrence of microangiopathic hemolytic anemia, thrombocytopenia, and acute kidney injury (AKI). HUS predominantly affects children and is caused by bacterial toxins, most commonly the Shiga-like toxin of enterohemorrhagic *Escherichia coli* (*E. coli*) O157:H7. If there is a strong suspicion of HUS based on clinical presentation and initial laboratory tests, treatment should begin immediately, as the condition may result in renal failure. Patients receive symptomatic treatment for renal symptoms, anemia, and complications affecting other organs, such as the brain and GI tract.

Etiology

- **Bacterial exotoxins** [2]
 - **Shiga-like toxin** (verotoxin)
 - From enterohemorrhagic *E. coli* (EHEC) strain **O157:H7**
 - Usually transmitted via contaminated foods (e.g., undercooked beef or raw leafy vegetables)
 - **Shiga toxin** produced by ***Shigella dysenteriae***
- ***Streptococcus pneumoniae* infection**
- **Atypical hemolytic uremic syndrome:** Complement dysregulation (hereditary or acquired) accounts for approx. 5% of HUS cases with noninfectious etiologies, referred to as atypical HUS (aHUS).



Approx. 15% of children infected with *E. coli* O157:H7 will go on to develop HUS.

Epidemiology

Mainly children < 5 years of age [1]

Epidemiological data refers to the US, unless otherwise specified.

Pathophysiology

HUS is a **thrombotic microangiopathy**, a condition characterized by the formation of microthrombi occluding the microvasculature. The other main thrombotic microangiopathy is thrombotic thrombocytopenic purpura (TTP). The two conditions have some pathophysiology and clinical findings in common, but different etiologies. HUS is caused by bacterial toxins. [4]

1. Infection with **enterohemorrhagic *E. coli* (EHEC)** or another causative organism
2. Mucosal inflammation facilitates bacterial toxins entering systemic circulation.
3. Toxins cause **endothelial cell damage** (especially in the glomerulus).
4. Damaged endothelial cells secrete cytokines that promote vasoconstriction and platelet microthrombus formation at the site of damage (**intravascular coagulopathy**) → thrombocytopenia (consumption of platelets)
5. RBCs are mechanically destroyed as they pass through the platelet microthrombi occluding small blood vessels (i.e., arterioles, capillaries) → hemolysis (schistocytes), and end-organ ischemia and damage, especially in the kidneys → decreased glomerular filtration rate (GFR)



E. coli O157:H7 infection → Shiga-like toxin in systemic circulation → **toxin-mediated endothelial injury** → microthrombus formation → blockage of small vessels → RBC fragmentation (hemolysis) and end-organ damage

Clinical features

A **diarrheal** illness (usually **bloody**) for the past 5–10 days precedes the onset of HUS symptoms in many children. The triad of clinical findings occurring in HUS consists of: 🗨️

- **Thrombocytopenia**
 - Petechiae, purpura
 - Mucosal bleeding
 - Prolonged bleeding after minor cuts
- **Microangiopathic hemolytic anemia**
 - Fatigue, dyspnea, and pallor
 - Jaundice
- **Impaired renal function**
 - Hematuria, proteinuria
 - Oliguria, anuria



The typical HUS patient is a preschooler who has had a diarrheal illness for the past 5–10 days and presents with petechiae, jaundice, and oliguria.

Diagnostics

- **Hematology**
 - Hemolytic markers
 - ↓ Hemoglobin 🗨️
 - ↓ Haptoglobin
 - ↑ Indirect bilirubin
 - ↑ Reticulocytes
 - ↑ LDH
 - ↑ **Schistocytes** on blood smear (up to 10% of RBCs) 🗨️
 - Coagulation profile
 - ↓ **Platelets** 🗨️
 - Normal/slightly elevated prothrombin time (PT) and activated partial thromboplastin time (aPTT) in contrast to DIC (see “Differential diagnoses” below)
 - Normal/slightly elevated fibrin degradation products and D-dimer levels
 - ↑ WBC count 🗨️
 - Negative Coombs test
- **Serum chemistry**: ↑ **BUN** and ↑ **creatinine** (impaired renal function)
- **Urinalysis**: hematuria, proteinuria

Treatment

- **Supportive care** ^[2]
 - Avoid antibiotics and antimotility agents (may increase the likelihood of HUS in suspected infection with EHEC).
 - Monitor and correct:
 - Fluid status abnormalities (for more information, see “Clinical assessment of volume status”)
 - Electrolyte disturbances (for more information, see “Electrolyte metabolism”)
 - Acid-base disorders
 - Blood pressure (due to hypertension or septic shock)
 - RBC transfusions 🗨️
 - Antiepileptic drugs (e.g., diazepam, phenytoin) in patients with seizures
- **Dialysis** (as indicated for AKI): Up to 50% of HUS patients require dialysis.
- **Plasma exchange therapy**: only in refractory cases 🗨️
- **Eculizumab**
 - Effective for the treatment of aHUS ^[5]
 - May be beneficial in HUS with neurological symptoms ^[6]



Post-diarrheal HUS is a nationally notifiable condition. ^[7]



Platelet transfusions should be administered with caution unless patients are bleeding or require an invasive procedure. Some studies suggest that they can exacerbate microangiopathy.

Pneumococcal HUS

1. Pneumococcal HUS is triggered by infection with pneumococcus and accounts for about 5% of the cases of HUS.
2. It is mediated by neuraminidase, which functions as a toxin in the presence of a *S. pneumoniae* infection. Plasma infusions may worsen the symptoms in this type of HUS, and if plasma exchange is considered, albumin should be used instead of plasma.
3. It often carries a worse prognosis than STEC-HUS because of necrotizing pneumonia.

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Atypical HUS (aHUS)

1. **Epidemiology.** aHUS is much less common than STEC-HUS.
2. **Etiology**
 - a. **Drugs** (e.g., oral contraceptives, cyclosporine, tacrolimus) or pregnancy may cause aHUS.
 - b. **Inherited** aHUS occurs with both autosomal dominant and autosomal recessive inheritance patterns, although not all patients have identifiable mutations. These genetic mutations cause chronic, excessive activation of complement, which also leads to platelet activation, endothelial cell damage, and systemic thrombotic microangiopathy.
3. **Clinical features.** Clinical findings are similar to those of STEC-HUS. Diarrhea may also be present, and severe proteinuria and hypertension are more consistently found. The clinical course is generally more severe with multiorgan damage.
4. **Management. Treatment is supportive.** Inciting medications, if any, must be stopped immediately.
5. **Prognosis.** Some patients have a chronic relapsing course (recurrent HUS). All patients with aHUS have a higher risk of progression to ESRD than patients with STEC-HUS.

Urolithiasis:

- A. **Epidemiology.** Renal stones are uncommon in children, and predisposing metabolic disorders should be sought in any child presenting with urinary calculi. There is a higher incidence in overweight and obese children.
- B. **Etiology.** The most common stones seen in childhood include stones of calcium salts, uric acid, cysteine, or magnesium ammonium phosphate (struvite). Conditions associated with urolithiasis that should be considered include the following:
1. **Hypercalciuria**, which predisposes to calcium-containing stones. Hypercalciuria may be idiopathic or caused by hypercalcemia, familial hypercalciuria, or furosemide use (especially in premature infants).
 2. **Hypocitraturia**, which predisposes to calcium-containing stones and is an inherited condition.
 3. **Hyperoxaluria**, which may be inherited or secondary to malabsorption from the GI tract (e.g., inflammatory bowel disease)
 4. **Distal RTA**
 5. **Hyperuricosuria**, which may occur during the treatment of leukemia or lymphoma, with Lesch-Nyhan syndrome or with primary gout
 6. **Cystinuria**, which is an autosomal recessive disorder that may lead to radiopaque renal stones
 7. **UTI**, especially with *Proteus mirabilis*
 8. **Hyperparathyroidism**
- C. **Clinical features.** Clinical findings include flank or abdominal pain, gross or microscopic hematuria, or symptoms of cystitis or pyelonephritis.
- D. **Diagnosis and evaluation.** Because of the possibility of an underlying metabolic disorder, children with urolithiasis should have a careful evaluation, including the following:
1. **Laboratory testing** should include electrolytes, BUN, creatinine, calcium, phosphorus, parathyroid hormone (PTH) level, uric acid level, and venous blood gas to rule out RTA.
 2. **Urine testing** should include urinalysis with microscopy, urinary oxalate-to-creatinine ratio to identify hyperoxaluria, random first morning urine for calcium-to-creatinine ratio to identify hypercalciuria and uric acid-to-creatinine ratio to identify hyperuricosuria, urine culture, and testing for cystinuria. Twenty-four-hour urine collections are important to measure 24-hour urinary excretion of creatinine, oxalate, uric acid, citrate (low urinary citrate predisposes to stone formation), calcium, phosphorus, magnesium, and cysteine.
 3. **Imaging studies**, including a plain radiograph of the abdomen and renal ultrasound, are necessary to confirm and identify the stone(s). Sometimes a high-resolution abdominal CT scan can identify the stone.
 4. **Stone fragment analysis**, if a fragment is collected.
- E. **Management.** Management is aimed first at hydration and the relief of any obstruction, treating any associated UTI, and then specific therapy on the basis of the underlying predisposing cause of the urolithiasis. On an on-going basis, patients should have increased water intake at least to the maintenance fluid range, as well as reduced sodium intake. Patients with hypocitraturia can be treated with increased fluids that contain citrate.

Wilms tumor

Summary

Nephroblastoma (Wilms tumor) is the most common renal malignancy in children, typically affecting children between 2 and 5 years of age. A minority of cases are associated with specific syndromes (e.g., WAGR, Beckwith-Wiedemann) and gene mutations (e.g., WT1). Nephroblastoma is typically an incidental finding that manifests as a large abdominal mass. Other signs and symptoms may occur, such as hematuria and abdominal pain, especially in tumors that are large, ruptured, or metastasized. Treatment consists of tumor resection and chemotherapy for all stages (except for very low-risk tumors), while radiation is predominantly used in advanced disease.

Clinical features

Abdominal symptoms

- Palpable abdominal mass (often found incidentally)
 - Non-tender
 - Unilateral and large but not crossing midline
 - Smooth and firm
- Abdominal pain (~ 40% of cases)

Other signs and symptoms

- Hematuria (~ 25% of cases)
- Hypertension (~ 25% of cases)
- In cases of subcapsular hemorrhage:
 - Anemia
 - Possibly fever
- Symptoms caused by metastatic spread (e.g., pulmonary symptoms)

! Nephroblastoma should be suspected in a toddler with a non-tender abdominal mass, especially if it is firm, smooth, and associated with hematuria and/or hypertension.

! Careless palpation of a nephroblastoma can result in rupture of the renal capsule and tumor spillage!

- Nephroblastoma (Wilm's tumor)
- Second most common malignant abdominal tumor
 - Usual age 2–5 years
 - One or both kidneys (bilateral in 7%)
- Associations:
 - Hemihypertrophy
 - Aniridia
 - Genitourinary anomalies
 - WAGR
- Clinical presentation—most are asymptomatic abdominal mass (unless invasive, at diagnosis some with ↑ BP it renal ischemia)
- Diagnosis
 - Best initial test—ultrasound
 - Abdominal CT scan confirmatory test
- Treatment
 - Surgery
 - Then chemotherapy and radiation
 - Bilateral renal—unilateral nephrectomy and partial contralateral nephrectomy
- Prognosis—54 to 97% have 4-year survival

Wilms tumor (nephroblastoma)

Epidemiology	- Most common renal malignancy in children - Peak age 2-5 - Usually sporadic but may be associated with: - WAGR (Wilms tumor, Aniridia, Genitourinary abnormalities, mental Retardation) - Beckwith-Wiedemann syndrome - Denys-Drash syndrome
Clinical features	- Usually asymptomatic - Unilateral abdominal mass ± Abdominal pain, hypertension, hematuria
Treatment	- Surgical excision - Chemotherapy ± Radiation therapy
Prognosis	90% survival rate with treatment

Polycystic kidney disease:

Summary

Polycystic kidney disease (PKD) is an inherited disorder characterized by the development of multiple cysts in the kidneys. It is classified into two distinct disorders: autosomal recessive PKD (ARPKD) and autosomal dominant PKD (ADPKD). ARPKD manifests with severe pulmonary insufficiency and progressive renal failure with onset during infancy or early childhood. If left untreated, ARPKD is typically lethal before adolescence. ADPKD manifests with flank pain, arterial hypertension, and progressive kidney disease with onset in adulthood. Early diagnosis and treatment may prevent or delay end-stage renal disease in both conditions, but kidney transplantation is the only curative treatment option.

D. Autosomal recessive polycystic kidney disease (ARPKD) or infantile polycystic kidney disease

1. **Epidemiology.** ARPKD is uncommon, occurring in approximately 1 in 10,000–40,000 live births.
2. **Clinical features**
 - a. The most severely affected infants have a maternal history of oligohydramnios secondary to nonfunctioning or poorly functioning kidneys in utero. This leads to pulmonary hypoplasia, which may be incompatible with life.
 - b. Greatly enlarged cystic kidneys
 - c. Severe hypertension is common.
 - d. Liver involvement of variable clinical severity is a constant finding, including cirrhosis with portal hypertension.
3. **Prognosis.** Although the degree of renal insufficiency in infancy may range from mild to severe, ARPKD is progressive and ultimately all patients require renal transplantation.

E. Autosomal dominant polycystic kidney disease (ADPKD) or adult polycystic kidney disease

1. **Epidemiology.** ADPKD is a common genetic disorder (affecting about 1 in 500 individuals) that usually presents in adulthood (20–40 years of age). There are two gene mutations that cause ADPKD; ADPKD1 mutations are more common and cause an earlier onset of disease than ADPKD2 mutations.
2. **Clinical features.** Clinical findings are variable and include abdominal pain, flank masses, urinary tract infection (UTI), gross or microscopic hematuria, hypertension, or

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renal insufficiency. Associated cerebral aneurysms may occur, with early death.

3. **Prognosis.** Most patients develop severe hypertension and renal insufficiency, eventually requiring transplantation.

F. **Medullary sponge kidney.** This condition occurs sporadically or may have autosomal dominant inheritance. Patients may be asymptomatic or have hematuria, UTI, or nephrolithiasis.

G. **Nephronophthisis.** This is a ciliopathy that occurs in several forms. The infantile, juvenile, and adolescent forms are autosomal recessive and lead to ESRD in childhood or young adulthood, and there are often significant associated extrarenal manifestations in 10–15% of patients, including retinal degeneration, cerebellar vermis hypoplasia, occipital encephalocele, hepatic fibrosis, situs inversus, bronchiectasis, and skeletal defects. More than 13 mutated genes have been described that lead to nephronophthisis.

ARPKD

- **Symptom onset:** Symptoms most commonly manifest in infancy or childhood.
- **Renal manifestations**
 - Protruding abdomen (nontender abdominal mass) due to bilateral renal enlargement and/or hepatomegaly
 - **Chronic renal failure:** frequently hematuria, proteinuria, and oliguria
 - Severe in-utero renal impairment → oliguria in utero → maternal oligohydramnios → **Potter sequence**
 - Craniofacial abnormalities (retrognathia, low-set ears, flat nose) and clubbed feet
 - Pulmonary hypoplasia → respiratory insufficiency in neonates
- **Extrarenal manifestation**
 - **Hypertension**
 - Early manifestation
 - Often not responsive to monotherapy
 - Can result in complications if inadequately controlled (e.g., cardiac hypertrophy, heart failure, cerebrovascular diseases, progressive renal impairment)
 - Liver involvement: congenital hepatic and portal fibrosis → progressive liver failure and **portal hypertension**

Potter syndrome

A collection of fetal abnormalities caused by oligohydramnios. The classical triad of Potter sequence is craniofacial abnormalities, clubbed feet, and pulmonary hypoplasia. The prognosis of patients born with Potter sequence depends on the root cause of oligohydramnios but the condition is often deadly due to pulmonary hypoplasia.

FEEDBACK

Pathophysiology

Clinical features

ADPKD

- **Symptom onset**
 - Symptoms usually occur after 30 years of age, but the disease may also manifest during childhood.
 - Symptoms are less severe and tend to manifest later in individuals with the PKD2 mutation compared to those with the PKD1 mutation.
- **Renal manifestations**
 - Gross hematuria
 - Flank or abdominal pain
 - Recurrent urinary tract infections
 - Nephrolithiasis
 - Kidneys might be palpable and enlarged on abdominal exam (they are usually normal at birth)
 - Signs of chronic kidney disease (e.g., hypertension, fluid overload, uremia)
- **Extrarenal manifestations**
 - Multiple benign hepatic cysts (prevalence increases with age)
 - Cysts may also occur in the pancreas, spleen, ovary, and testicles.
 - Cerebral berry aneurysm (~8%)
 - The risk is higher in patients with a family history positive of ADPKD.
 - May rupture and cause subarachnoid hemorrhage (the risk for growth and rupture is the same in patients with ADPKD as in the general population)
 - **Cardiovascular**
 - Signs of arterial hypertension (e.g., morning headaches) through increased renin production
 - Heart valve defects (particularly mitral valve prolapse)

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