

PEDIATRIC EMERGENCY MEDICINE PRACTICE

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An Evidence-Based Approach To The Management Of Hematuria In Children In The Emergency Department

Abstract

Hematuria is defined as an abnormal number of red blood cells in urine. Even a tiny amount of blood (1 mL in 1000 mL of urine) is sufficient to make urine appear pink or red. In the pediatric population, the majority of etiologies are benign and often asymptomatic. However, hematuria may also be a sign of renal pathology, local infection, or systemic disease. Hematuria can be differentiated into 2 categories: macroscopic hematuria (visible to the naked eye) and microscopic hematuria (> 5 red blood cells/high-powered field on urinalysis). This review will outline the current literature regarding evaluation and management of pediatric patients who present to the emergency department with hematuria. Obtaining a thorough history and the appropriate diagnostic tests will be discussed in depth.

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CME Objectives

Upon completion of this article, you should be able to:

1. Differentiate between macroscopic and microscopic hematuria.
2. Recognize the most common causes of hematuria in children.
3. Utilize appropriate diagnostic tests for evaluation of hematuria in the emergency department.
4. Identify patients with hematuria who require admission to the hospital.

Prior to beginning this activity, see "Physician CME Information" on the back page.

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Case Presentations

A 12-year-old adolescent boy presents to the emergency department with a chief complaint of urine the color of brown soda. He reports a recent upper respiratory infection. On physical examination, his blood pressure is 145/72 mm Hg, and you note periorbital edema. Urine dipstick is positive for blood and 2+ protein. You consider any emergent laboratory work you need to perform to confirm the diagnosis and wonder if this child requires admission to the hospital...

A 15-year-old adolescent girl is brought in by her parents with a chief complaint of pink urine. Review of systems is significant for muscle soreness, which she attributes to running a half-marathon for her cross-country team the day prior to presentation. Urine dipstick is positive for large occult blood. As you begin initial management, you consider other laboratory work that should be performed...

A previously healthy 5-year-old girl presents to the emergency department with pink urine after visiting her grandmother for the weekend. Review of systems is otherwise negative, and the patient does not take any medications. The physical examination is nonfocal, including the genitourinary examination. Urine dipstick is negative for blood or protein. You wonder what other questions you should ask to confirm the diagnosis. Does she require a repeat urine dipstick and microscopic urinalysis with her pediatrician?

Introduction

Hematuria is an abnormal number of red blood cells (RBCs) in urine and is the chief complaint for 0.1% to 0.15% of pediatric acute care visits.¹ Hematuria is often defined > 5 RBCs per high-powered field (HPF).^{2,3} Even a tiny amount of blood (1 mL in 1000 mL of urine) is sufficient to make urine appear pink or red.⁴ It can be categorized by gross hematuria (visible to the naked eye) or microscopic hematuria (seen on urine dipstick or urinalysis). It is important to distinguish between macroscopic and microscopic hematuria, as the etiologies can be very different. It is also important to determine whether the etiology of the hematuria is glomerular versus nonglomerular and to be aware of the systemic complications associated with the various causes of hematuria. Obtaining a thorough history is key to determining the necessity of testing, the appropriate treatment, and disposition.

The urine dipstick test is the most common initial screening test to determine whether there is blood in the urine. The test utilizes the peroxidase activity of hemoglobin to catalyze a chemical reaction that converts chromogen tetramethylbenzidine to an oxidized chromogen, which has a green-blue color.⁵ This testing has a reported sensitivity as high as 100% and a specificity of 99% to detect 5

to 10 RBC/mcL (which is roughly 2-5 RBC/HPF on microscopic urinalysis).⁶ A urine dipstick that is positive for blood with no RBCs seen on urine microscopy suggests myoglobinuria. A urine dipstick may be positive for proteinuria in the setting of hematuria, but should not exceed 2+ (100 mg/dL) if the only source of protein is from hematuria.⁷

False positives can occur due to alkaline urine (pH > 9), microbial peroxidase associated with urinary tract infections, or oxidizing agents used to clean the perineum (eg, hypochlorite). False negatives may be due to formalin, a large amount of nitrites, a high specific gravity, or a high concentration of ascorbic acid.

In most instances, the etiology of the hematuria is not life-threatening, and clinicians can provide reassurance and recommend outpatient follow-up.

Critical Appraisal Of The Literature

An online search was performed for literature from 1970 to the present using the Pubmed and Ovid MEDLINE[®] databases. The areas of focus were hematuria and pediatrics. Multiple search terms were used, including *pediatric hematuria*, *gross hematuria*, *macroscopic hematuria*, *microscopic hematuria*, *urine dipstick*, *proteinuria*, and *evaluation of hematuria*. More than 100 articles, including case reports and retrospective studies, were analyzed and 80 articles were identified as pertinent to this review. There is a significant amount of literature on pediatric hematuria, but a dearth of literature on the evaluation and acute management of hematuria in the pediatric emergency department (ED).

Epidemiology

Macroscopic (Gross) Hematuria

Macroscopic (gross) hematuria is defined as visibly red, pink, or brown urine. The incidence of gross hematuria in children is roughly 0.13%,^{4,8} and > 56% of cases are due to an identifiable cause.¹ Pink-appearing urine indicates a small amount of blood and is rarely seen in glomerular disease. In contrast, urine in the setting of glomerular disease is typically deep red-brown or dark brown (the color of tea or cola). Patients with vascular bleeding or lower urinary tract bleeding often have bright red or cherry-colored urine. Pink, red, or brown urine can also be caused by pigments from drugs, toxins, foods, or metabolites. (See Table 1, page 3.)

In several studies of pediatric patients presenting with gross hematuria in both the inpatient and outpatient setting, 14% to 50% of patients were diagnosed with a urinary tract infection; 11% to 18% with perineal/urethral irritation; 13% with underlying congenital anomalies; 7% due to trauma; 4% with acute nephritis; 3% with coagulopathy; and 2% to

5% with nephrolithiasis.^{1,13,14} In a study by Bergstein et al of 274 patients who presented in the outpatient setting, the most common cause of gross hematuria was hypercalciuria.¹⁴ A study by Feld et al found hypercalciuria in 9% of patients.¹⁵

Microscopic Hematuria

Microscopic urinalysis is the gold standard for the detection of microscopic hematuria.^{2,3} Asymptomatic isolated microscopic hematuria occurs in 0.41% to 4% of school-aged children.^{8,9,16} The most common cause is hypercalciuria, which accounts for roughly 11% to 30% of asymptomatic isolated microscopic hematuria.^{14,15,17} Other common causes include benign familial hematuria, immunoglobulin A (IgA) nephropathy, sickle cell trait or sickle cell anemia, Alport syndrome nephritis, postinfectious glomerulonephritis, trauma, exercise, nephrolithiasis, and Henoch-Schönlein purpura.¹⁰ In 30% to 80% of cases, no diagnosis is made after evaluation.^{12,14,18,19}

Asymptomatic microscopic hematuria with proteinuria (> 1+ on dipstick or > 100 mg/dL on urinalysis) has a prevalence of 0.06% to 0.7% in school-aged children and is associated with a higher risk of significant renal disease.^{3,8-10,12,18-20} However, due to its low yield, the American Academy of Pediatrics (AAP) currently does not recommend routine urine dipstick screenings by primary care physicians for asymptomatic children and adolescents.²¹

Pathophysiology

RBCs can originate from any point along the urinary tract; however, in children, the most common source of bleeding is from the glomeruli. RBCs cross the endothelial-epithelial barrier of the glomeruli and enter the capillary lumen through discontinuities in

the capillary wall.²¹ In most cases of glomerulopathies, proteinuria, dysmorphic RBCs, and RBC casts are seen in addition to hematuria.²²

Glomerular bleeding is usually brown, cola-colored, or tea-colored due to hematin formation from hemoglobin in an acidic environment. RBC casts develop when RBCs are entangled in the glomerular protein matrix. Trauma can cause contusions, hematomas, or lacerations at any point along the urinary tract. Grossly bloody urine (bright red or pink) most likely originates from the lower urinary tract.

Etiology And Differential Diagnosis

The etiology of hematuria can be divided into glomerular causes, nonglomerular renal causes, extrarenal causes, and systemic diseases.

Glomerular Causes

Primary Glomerular Causes

Postinfectious or poststreptococcal glomerulonephritis (PSGN) is the most common glomerular cause of hematuria with an incidence of 9.5 to 28.5 per 100,000 individuals per year.^{24,25} It often presents with tea- or cola-colored urine (macroscopic hematuria), but can present with only microscopic hematuria.²⁶ Most patients have had an upper respiratory infection or skin infection in the preceding 2 to 4 weeks. Patients may also complain of malaise, fatigue, headache, nausea, vomiting, abdominal pain, and oliguria. The physical examination may be significant for edema and elevated blood pressure. The most common cause of PSGN is a recent infection with Group A beta-hemolytic streptococci. Urinalysis will reveal RBC casts and proteinuria. Laboratory markers may be significant for elevated blood urea nitrogen (BUN) or creatinine levels; however, they can be normal as well. Most patients have a normal serum C4 level with a decreased level of C3, which will normalize within 6 to 8 weeks. Antistreptolysin O (ASO) titers and streptozyme may be positive within 10 days of the onset of symptoms.²⁷ In most patients, hematuria and proteinuria resolve within a few weeks to months.

IgA nephropathy (also known as Berger disease) is due to mesangial proliferation and glomerular deposition of IgA. It is one of the most common pathologic causes of hematuria in children and often presents with a history of gross hematuria preceded by an upper respiratory or gastrointestinal illness.²⁸ Although there is no specific treatment, clinicians often try angiotensin-converting enzyme inhibitors, angiotensin-II receptor blockers, lipid-lowering agents, and immunosuppressive therapy. The rate of progression of renal disease is typically slow, although 15% to 30% of patients with this disease will eventually develop end-stage renal disease. Predictors of poorer outcome include older age at onset,

Table 1. Causes Of Red Urine Without Hematuria⁹⁻¹²

Drugs	Food
Benzene	Beets
Chloroquine	Blackberries
Phenazopyridine	Red food coloring
Deferoxamine	Mushrooms
Phenolphthalein	Metabolites
Naphthalene	Free hemoglobin
Sulfonamides	Porphyrins
Tin compounds	Urates
Lead	Bile pigment
Methicillin	Homogentisic acid
Phenol	Melanin
Sulfonamides	Methemoglobin
Turpentine	Tyrosine
Ticlopidine	Other
Ibuprofen	Myoglobin
Iron	Carbon monoxide

hypertension, and significant proteinuria.^{29,30}

Alport syndrome is an X-linked recessive disorder that is characterized by episodes of recurrent or persistent microscopic (and occasionally macroscopic) hematuria as well as proteinuria. It can lead to progressive renal insufficiency and high-frequency hearing loss.³¹⁻³³ This syndrome is due to a defect in the alpha-5 chain of type-IV collagen. There is usually a strong family history with only 15% of mutations occurring de novo.³⁴ Patients present with persistent glomerular hematuria, and initial treatment involves angiotensin-converting enzyme inhibitors, angiotensin-II receptor blockers, and aldosterone inhibitors to reduce proteinuria.³⁵

Thin basement membrane nephropathy (also known as benign familial hematuria) is an autosomal dominant disease that causes persistent microscopic glomerular hematuria. Glomerular hematuria that persists > 1 year is typically due to thin basement membrane nephropathy.³⁵⁻³⁸ This condition affects 1% of the population and typically has a benign course; however, there is a risk of hypertension, proteinuria, and renal failure.³⁸

Membranous proliferative glomerulonephritis, focal segmental glomerulosclerosis, membranous nephropathy, and rapidly progressive glomerulonephritis are other causes of glomerulonephritis that present with signs and symptoms similar to postinfectious glomerulonephritis. However, the courses and prognoses of these diseases are much less benign. They cause significant renal disease and are diagnosed by renal biopsy.

Acute interstitial nephritis is associated with microscopic or macroscopic hematuria, pyuria, and acute renal failure. Patients often present with signs of acute renal failure (including oliguria, nausea, vomiting, or malaise). The typical offending agents include ibuprofen, diuretics, and antibiotics (such as penicillins, cephalosporins, rifampin [Rifadin[®], Rifater[®], Rimactane[®]], and sulfonamides).³⁹ Management includes withdrawal of the offending agent and supportive therapy.

Systemic Glomerular Causes

Systemic causes of hematuria include serum sickness, hemolytic-uremic syndrome, systemic lupus erythematosus, Henoch-Schönlein purpura, polyarteritis nodosa, hepatitis, Goodpasture disease, polyarteritis granulomatosa (also known as Wegener granulomatosis), thrombotic thrombocytopenic purpura, and systemic infections (such as malaria, leptospirosis, infective endocarditis, and tuberculosis). In particular, hemolytic-uremic syndrome is a small-vessel disease that may present with acute renal failure, hypertension, and neurologic signs. A urinalysis typically shows hematuria and proteinuria. Henoch-Schönlein purpura is a systemic vasculitis that can present with abdominal pain, joint pain,

lower extremity palpable purpura, and glomerulonephritis. Approximately 50% of children with Henoch-Schönlein purpura have renal involvement (including transient hematuria and proteinuria).⁴⁰ Relapses and remissions can manifest as episodes of gross hematuria; however, only 2% develop long-term renal insufficiency.^{41,42}

Rhabdomyolysis can cause dark-colored urine and myoglobinuria that may be mistaken for hematuria. It is characterized by skeletal muscle breakdown and is most commonly caused by infections, trauma, exertion, drugs, metabolic disorders, and electrolyte disorders in children. Patients typically present with muscle pain, weakness, and red or brown urine. In cases of rhabdomyolysis, the urine dipstick will be positive for occult blood, but urine microscopy will show no RBCs. Once the diagnosis is confirmed with laboratory testing showing an elevated creatine phosphokinase level, patients are treated with supportive measures (including intravenous and oral hydration) and rest.⁴³

Nonglomerular Renal Causes

Urinary tract infections or acute pyelonephritis commonly present with fever in infants, and dysuria or cloudy urine in older children. These conditions are more common in boys in the first year of life, but have a higher incidence, overall, in girls.^{44,45} Hemorrhagic cystitis (bacterial, viral, or drug-induced) is most commonly caused by adenovirus and cyclophosphamide exposure.

Hypercalciuria is determined by a urine calcium/creatinine ratio > 0.2 in children aged > 6 years or a 24-hour urine calcium > 4 mg/kg/day. There are many conditions that can result in hypercalciuria (including hyperparathyroidism, immobilization, and vitamin D intoxication) with the most common cause being idiopathic.^{15,46,47} It has been proposed that hypercalciuria leads to hematuria due to irritation of the uroepithelium by microcalculi. There is often a family history of renal stones. In idiopathic hypercalciuria without urolithiasis, patients are often asymptomatic; however, symptoms can include dysuria, suprapubic pain, or renal colic.⁴⁸

Similarly, nephrocalcinosis and urolithiasis can cause microscopic hematuria, and they are associated with prematurity, furosemide treatment, cystinuria, hyperoxaluria, hyperuricosuria, renal tubular acidosis, hypercalciuria, cystic fibrosis, spina bifida, inflammatory bowel disease, and other metabolic disorders.^{49,52} Urolithiasis is less common in the pediatric population compared to adults, with only 1 in 1000 adult hospital admissions and 1 in 75,000 pediatric hospital admissions.^{53,54} Patients typically present with abdominal pain, dysuria, incontinence, hematuria, renal colic, or a urinary tract infection. Diagnosis is made by renal ultrasound or spiral computed tomography (CT).

Vascular abnormalities (such as hemangiomas, renal vein or artery thrombosis, hereditary hemorrhagic telangiectasias, and arteriovenous malformations) can cause significant hematuria. Hemangiomas are rare and often impossible to locate, but can be seen in Klippel-Trenaunay syndrome or Proteus syndrome.⁵⁵⁻⁵⁸

Anatomic abnormalities (including ureteropelvic junction obstruction, posterior urethral valves, urethral prolapse, urethral diverticula, autosomal dominant polycystic kidney disease, tumors, or multicystic dysplastic kidney) can also cause hematuria. Wilms tumor (nephroblastoma) typically presents with a flank mass and macroscopic hematuria and is the most common urological malignancy in children. Other tumors include renal cell carcinoma (rare in children), uroepithelial tumors, rhabdoid tumors, and angiomyolipomas. Renal cysts are often discovered incidentally or after minor trauma, and hematuria can be the result of cyst hemorrhage, a urinary tract infection, or malignancy.⁵⁹ Urinary tract anomalies presenting as hematuria are extremely rare due to routine detection by prenatal ultrasonography. Methods to differentiate glomerular from nonglomerular causes of hematuria are presented in **Table 2**.

Extrarenal Causes

Hemoglobinopathies or hematologic causes of hematuria include sickle cell disease and sickle cell trait (due to renal papillary necrosis), coagulopathies, Von Willebrand disease, renal vein thrombosis, and thrombocytopenia. Hematuria (both microscopic and macroscopic) is the most frequent complication of sickle cell trait.⁶⁵⁻⁶⁸

Nutcracker syndrome is left renal vein compression between the proximal superior mesenteric artery and aorta, and may be associated with left flank pain and hematuria. Occasionally, a varicocele is seen on physical examination in male patients. The diagnosis may be confirmed by renal Doppler ultrasound.⁶⁹⁻⁷¹

Strenuous exercise alone can cause hematuria; however, the pathophysiology is unknown. Several hypotheses have been proposed, including bladder or kidney trauma, dehydration, hemolysis, renal ischemia, and peroxidation of red cells.⁷²

In addition, false-positive extrarenal causes of hematuria include poor collection technique in the setting of menses, vaginitis with skin breakdown, and urethral prolapse.

Trauma

Hematuria can occur due to renal contusions or trauma, and any degree of hematuria may be associated with a significant intra-abdominal injury. Urine dipsticks are often poor screening tests for urinary tract injury in the setting of trauma, due to false positives and false negatives.⁶⁰ In general, children with > 50 RBC/HPF should undergo imaging with an abdominal CT scan.^{61,62} However, recent studies have shown that urologic injuries can occur with or without hematuria.^{63,64} Furthermore, hematuria associated with minor trauma may unmask an underlying congenital anomaly. More common causes of lower urinary tract trauma include bicycle riding or tree climbing leading to direct trauma to the groin and perineal area. The emergency clinician should always consider nonac-

Table 2. Differentiating Glomerular From Nonglomerular Causes Of Hematuria^{4,22,23}

	Glomerular Causes	Nonglomerular Causes
History	<ul style="list-style-type: none"> • Oliguria or polyuria • Recent respiratory, skin, or gastrointestinal infection • Deafness • Medication exposure • Family history of hearing loss or renal failure • Rash • Joint pain/swelling • Hemoptysis • Medication exposure 	<ul style="list-style-type: none"> • Dysuria or polyuria • Renal colic/abdominal pain • Fever • Medication exposure • Trauma history • Family history of sickle cell disease, hemophilia, or Von Willebrand disease • Strenuous exercise
Physical examination	<ul style="list-style-type: none"> • Hypertension • Edema • Rash • Arthritis • Pallor 	<ul style="list-style-type: none"> • Normotension • Costovertebral angle tenderness • Suprapubic pain • Signs of trauma
Urinalysis	<ul style="list-style-type: none"> • Brown-, tea-, or cola-colored urine • Proteinuria often present • Red blood cell casts • > 20% dysmorphic red blood cells 	<ul style="list-style-type: none"> • Bright red urine • +/- proteinuria • No red blood cell casts • Positive nitrites or leukocyte esterase
Laboratory testing	<ul style="list-style-type: none"> • Elevated blood urea nitrogen/creatinine • Anemia • Abnormal complement levels (C3, C4) 	<ul style="list-style-type: none"> • Normal blood urea nitrogen/creatinine

cidental trauma as a cause of hematuria.

A summary of the various causes of hematuria is provided in **Table 3**.

Prehospital Care

Prehospital care often includes stabilization and efficient transport of patients. In particular, patients with trauma should be stabilized according to Pediatric Advanced Life Support (PALS) guidelines. Blood pressure should be monitored in patients with possible glomerular causes of hematuria.

Emergency Department Evaluation

History

A thorough history should be obtained with evaluation of the chief complaint, including onset, duration, and worsening and alleviating factors. In particular, pertinent history should include the presence of prior episodes of hematuria, recent trauma, dysuria, polyuria, fever, flank pain, edema, oliguria, urine color, recent infection (including pharyngitis, impetigo, or a gastrointestinal illness), history of frequent bleeding (eg, heavy menses, prolonged nosebleeds, hemarthrosis, and bleeding associated with surgical procedures), abdominal pain, joint pain, rashes, pallor, and exposure to medications. Family

history should address sickle cell disease (particularly in patients of African descent), hemophilia, hearing loss, hematuria, cystic disease, and urolithiasis. Neonatal history should include previous umbilical vessel catheters and birth asphyxia (corticomedullary necrosis). Lastly, infection by *Schistosoma haematobium* should be considered in patients who have recently traveled to foreign countries.⁷³

Physical Examination

The initial physical examination should include vital signs, with close attention to blood pressure and temperature. Hypertension can occur in glomerulonephritis, Wilms tumor, polycystic kidney disease, vasculitis, and anatomic obstruction. The abdominal examination should assess for masses, costovertebral tenderness, and signs of trauma. A genitourinary examination should include signs of trauma (contusions, hematomas, or lacerations). An extremity examination is important to address systemic causes of hematuria. Pallor, fever, skin rashes, or musculoskeletal findings may indicate systemic diseases.

Diagnostic Studies

Laboratory Evaluation

Initial laboratory testing should include a urine dipstick; if positive for blood, a complete urinalysis

Table 3. Etiology Of Hematuria^{4,19,22,23}

Glomerular Causes

Primary

- Poststreptococcal glomerulonephritis
- Immunoglobulin A nephropathy
- Alport syndrome
- Thin basement membrane disease/benign familial hematuria
- Membranoproliferative glomerulonephritis
- Focal segmental glomerulosclerosis
- Membranous nephropathy
- Rapidly progressive glomerulonephritis
- Acute interstitial nephritis

Systemic

- Serum sickness
- Hemolytic-uremic syndrome
- Systemic lupus erythematosus
- Henoch-Schönlein purpura
- Polyarteritis nodosa
- Hepatitis B or C
- Goodpasture disease
- Polyarteritis granulomatosis
- Thrombotic thrombocytopenic purpura
- Systemic infections (eg, malaria, leptospirosis, infective endocarditis, tuberculosis)

Nonglomerular Causes

- Urinary tract infection
- Pyelonephritis
- Hemorrhagic cystitis (bacteria, viral, parasitic, drug-induced)
- Hypercalciuria
- Nephrolithiasis/urolithiasis/nephrocalcinosis
- Vascular abnormalities
 - Hemangiomas
 - Renal vein or artery thrombosis
 - Hereditary hemorrhagic telangiectasias
 - Arteriovenous malformations
- Anatomic abnormalities
 - Ureteropelvic junction obstruction
 - Posterior urethral valves
 - Urethral prolapse
 - Urethral diverticula
 - Autosomal dominant polycystic kidney disease
 - Multicystic dysplastic kidney
 - Tumors (Wilms tumor, renal cell carcinoma, uroepithelial tumor, rhabdoid tumor, angiomyolipomas)
 - Renal contusion or trauma

Extrarenal Causes

- Hemoglobinopathies (sickle cell disease or sickle cell trait)
- Other hematologic causes (coagulopathies, hemophilia, Von Willebrand disease, thrombocytopenia)
- Nutcracker syndrome
- Strenuous exercise

with microscopy can then determine the number of RBCs present and distinguish between hemoglobin and myoglobin. Of note, if the urine dipstick suggests a diagnosis (such as urinary tract infection), a complete urinalysis may not be necessary. The presence of RBC casts and dysmorphic cells are consistent with glomerular bleeding.^{22,74,75} A value > 20% dysmorphic RBCs is suggestive of glomerular hematuria.^{74,76,77} As previously noted, proteins are excreted with hematuria; however, gross hematuria should cause $\leq 2+$ proteinuria on urine dipstick. Any value > 2+ protein should raise concern for glomerular disease.^{7,23} Urinary catheterization usually induces little to no hematuria, so urinary tract disease or injury should be considered in patients who are status post catheterization and show significant hematuria on urinalysis.⁷⁸ **Figure 1** shows samples of macroscopic and microscopic hematuria.

A complete blood count (CBC) to assess for anemia and a basic metabolic panel (BMP) (including BUN, creatinine, and electrolytes) should be considered in patients with abnormal urine dipsticks or urinalyses to evaluate for signs of renal insufficiency. A urine culture should be obtained in patients with fever, polyuria, or dysuria, or in patients with a urine dipstick suggestive of urinary tract infection. In patients with a strong family history of sickle cell disease, a hemoglobin electrophoresis should be sent if the patient is not already known to have sickle cell disease. Lastly, patients with both proteinuria and hematuria should have complement studies to evaluate for immune complex diseases, acute glomerulonephritis, and systemic lupus erythema-

Figure 1. Samples Of Macroscopic And Microscopic Hematuria



This photo illustrates 2 samples of gross hematuria (the 2 center specimens) and 2 samples of microscopic hematuria (the 2 outer specimens that appear normal in color).

To view a full-color version of this photo, scan the QR code with a smartphone or tablet or go to: www.ebmedicine.net/HematurialImage.



tosus. In patients with suspected poststreptococcal glomerulonephritis, consider obtaining ASO titers, antihyaluronidase titers, an anti-deoxyribonucleic acidase B, and a throat culture.

Imaging

In an asymptomatic child with normal creatinine and blood pressure and without proteinuria or RBC casts, it is reasonable to defer further emergent workup. If the patient has gross hematuria, an urgent renal ultrasound should be completed to exclude malignancy or cystic renal disease.²³ Renal ultrasound can also evaluate for urolithiasis, tumors, renal parenchymal disease, hydronephrosis, structural anomalies, Nutcracker syndrome, renal parenchymal dysplasia, inflammation of the bladder, posterior urethral valves, and bladder polyps. Due to ionizing radiation exposure, some clinicians advocate obtaining an ultrasound to diagnose urolithiasis, even though a noncontrast spiral CT is more sensitive. However, ultrasound is known to miss some small stones (< 3 mm) and stones in certain areas of the renal tract (eg, the ureter and the corticomedullary junction). Therefore, patients with nondiagnostic ultrasounds should undergo a CT scan if there is concern for urolithiasis.

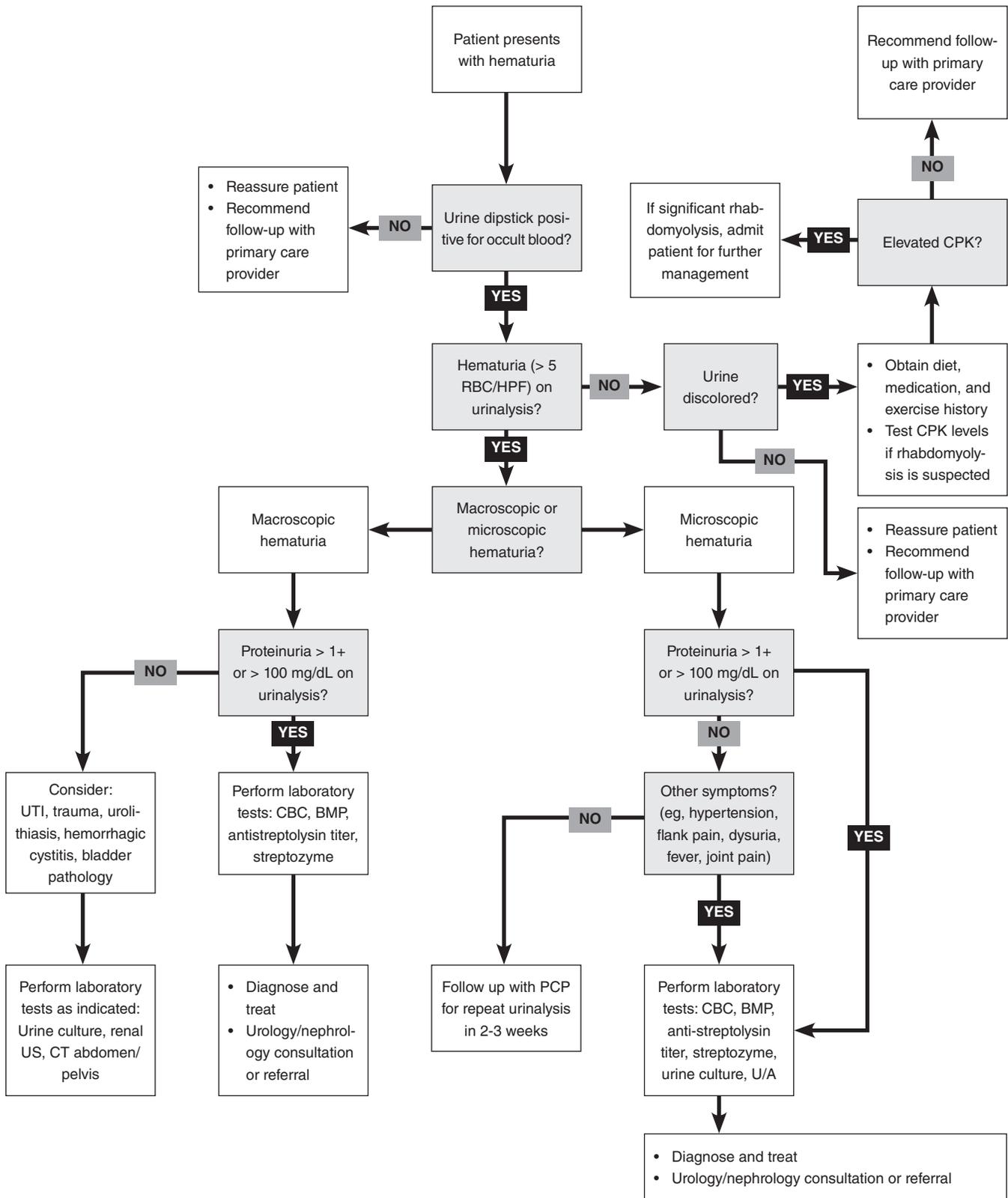
Treatment

Treatment of hematuria in the ED varies based on the diagnosis. If the clinical signs and symptoms (eg, dysuria, fever, or urgency) and urine dipstick and/or urinalysis are consistent with a urinary tract infection (eg, positive nitrites, positive leukocyte esterase, > 5 WBC/HPF, or significant bacteria), antibiotics should be given to treat empirically for a urinary tract infection. Patients with abdominal pain, incontinence, hematuria, or renal colic found to have urolithiasis on CT scan or renal ultrasound should be treated with medications to control pain and intravenous hydration. If hypertension (systolic or diastolic blood pressure > 95th percentile for gender, age, and height)⁷⁹ is present in patients with glomerular disease, blood pressure should be managed acutely to avoid end-organ damage or other complications. If blood pressure is normal and the patient has normal urine output, it is unlikely that microscopic hematuria requires immediate treatment. As isolated hematuria is often a benign finding, reassurance and follow-up are often most important.

Disposition

Disposition of the patient is based on appearance, etiology (life-threatening vs non-life-threatening), treatment options (inpatient vs outpatient, social concerns, ability to follow up), and the family's com-

Clinical Pathway For Management Of Hematuria In Children



Abbreviations: BMP, basic metabolic panel; CBC, complete blood count; CPK, creatine phosphokinase; CT, computed tomography; HPF, high-powered field; RBC, red blood cells; U/A, urinalysis; US, ultrasound; UTI, urinary tract infection.

fort level. (See Table 4.) Patients who may require admission include those with acute intra-abdominal injury, hypertension, edema, oliguria, significant proteinuria or RBC casts on urinalysis, renal failure (as indicated by electrolyte, BUN, and creatinine levels), inability to orally hydrate, or the need for intravenous hydration. In addition, patients with signs of systemic diseases should be admitted for further management. Patients with asymptomatic isolated microscopic hematuria and a normal physical examination can follow up with a primary care provider. A urine dipstick and microscopic urinalysis should be repeated 2 times within 2 weeks by a primary care provider to confirm hematuria.²⁶

Patients with oliguria, uncontrollable bleeding, urolithiasis with urosepsis, rhabdomyolysis, and those in severe pain often require immediate consultation and admission. Stable patients with signs of glomerular disease (microscopic hematuria) should have an outpatient referral to nephrology. (See Table 5.) Patients with recurrent nonglomerular macroscopic hematuria or a kidney stone > 10 mm in size with failure to pass should be referred to urology for further management. (See Table 6). In addition, pediatric patients with urolithiasis should be referred to pediatric nephrology or urology for a metabolic workup.

Special Circumstances/Populations

Patients with known sickle cell disease, rheumatologic disorders, Henoch-Schönlein purpura, hepatitis, Goodpasture disease, or polyarteritis granulomatosa should be managed with a higher concern for significant renal disease. In particular, blood pressure and renal function should be monitored closely, and appropriate services should be consulted (eg, nephrology, hematology, rheumatology).

Table 4. Criteria For Hospitalization^{22,80}

- Uncontrollable hypertension
- Uncontrollable bleeding
- Urolithiasis causing significant pain
- Edema
- Significant proteinuria
- Acute intra-abdominal injury
- Inability to orally hydrate or need for intravenous hydration
- Oliguria
- Red blood cell casts
- Signs of systemic disease
- Renal insufficiency
- Patients with social concerns
- Lack of ability to follow up
- Family's comfort level

Controversies And Cutting Edge

Although many general pediatricians are still performing routine urine dipstick screenings, the AAP currently does not recommend routine urine dipstick tests for asymptomatic children and adolescents.²¹

Imaging in the setting of traumatic hematuria remains controversial. Some clinicians advocate obtaining a CT scan for patients with urine microscopy of at least 20 to 50 RBC/HPF, some for > 50 RBC/HPF, and others only for gross hematuria. At the opposite end of the spectrum, some clinicians recommend obtaining a CT scan of the abdomen and pelvis on every trauma patient with any degree of hematuria on urinalysis, as urine dipsticks are often poor screening tests for urinary tract injury in the setting of trauma due to false negatives and false positives.⁶⁰ Though still controversial, more recent studies have shown that urologic injuries may occur with or without hematuria.^{63,64}

Cystoscopy rarely reveals the etiology for hematuria in pediatric patients; however, this should be considered when bladder pathology is suspected.²²

Table 5. Criteria To Consult Or Refer To A Nephrologist²²

- Microscopic hematuria with glomerular disease
 - Poststreptococcal glomerulonephritis
 - Immunoglobulin A nephropathy
 - Alport syndrome
 - Thin basement membrane nephropathy
 - Membranoproliferative glomerulonephritis
 - Membrane nephropathy
 - Acute interstitial nephritis
- Hypercalciuria, urolithiasis, or family history of hypercalciuria (for metabolic workup)
- Hemoglobinopathies with hematuria
- Hematuria due to systemic causes (eg, systemic lupus erythematosus, thrombotic thrombocytopenic purpura, Goodpasture disease)
- Family history of renal failure or hearing loss
- Persistent hematuria of unknown etiology

Table 6. Criteria To Consult Or Refer To A Urologist²²

- Urolithiasis or nephrocalcinosis
- Gross hematuria without signs of glomerular involvement
- Vascular abnormalities
- Anatomic abnormalities
- Tumor
- Nutcracker syndrome
- Hematuria due to recurrent urinary tract infections

Risk Management Pitfalls In The Evaluation And Management Of Hematuria

- 1. "Hematuria can account for 3+ protein in the urine."**

Proteins are excreted with hematuria; however, gross hematuria does not account for > 2+ proteinuria on dipstick. Any level > 2+ protein should raise concern for glomerular disease.^{7,23}
- 2. "A lack of RBCs on urinalysis in a trauma patient rules out intra-abdominal injury."**

Recent studies have shown that urologic injuries can occur with and without hematuria on urinalysis.^{61,62} Urine dipsticks are often poor screening tests for urinary tract injury due to false positives and false negatives.⁶⁰ Emergency clinicians should consider the mechanism of action, abdominal examination findings, and urinalysis results when considering further imaging in trauma patients.
- 3. "Every patient with microscopic hematuria needs a nephrology referral."**

Patients with asymptomatic isolated microscopic hematuria and a normal physical examination can follow up with a primary care provider. A urine dipstick and microscopic urinalysis should be repeated 2 times within 2 weeks by a primary care provider.²⁶ Patients with hematuria and proteinuria or symptomatic hematuria require further evaluation, which may include a referral to a nephrologist.
- 4. "Every pediatric patient with microscopic hematuria needs emergent imaging."**

For most cases of isolated microscopic hematuria, no imaging is necessary. For cases associated with trauma or if urolithiasis is suspected, consider emergent imaging. A renal ultrasound is necessary for gross hematuria.
- 5. "Every pediatric patient with urolithiasis requires hospital admission."**

If the stone is < 4 mm in size, there is a high likelihood of passing. As long as pain control can be achieved with oral pain medications and the patient can maintain hydration, the patient does not require admission to the hospital.
- 6. "Gross hematuria is most commonly due to trauma and requires a trauma or urology consultation."**

In several studies of patients presenting with gross hematuria, the most common cause was urinary tract infection (14%-50%) followed by perineal/urethral irritation (11%-18%), and underlying congenital anomalies (13%). Trauma only accounted for 7% of patients with gross hematuria.^{1,13,14} Additionally, in a study by Bergstein et al, the most common cause of gross hematuria was hypercalciuria.^{14,15} A careful review of the patient's history and physical examination should be taken into account prior to referral.
- 7. "A full workup should be pursued until an etiology is found for microscopic hematuria."**

In many cases of microscopic hematuria, no diagnosis is made after evaluation (30%-80%).^{12,14,18,22}
- 8. "Normotensive patients with postinfectious or poststreptococcal glomerulonephritis should be admitted or observed for blood pressure monitoring."**

Patients without significant edema or hypertension can be discharged and followed closely by a primary care provider. Hematuria and proteinuria should resolve within a few weeks to months.²⁷
- 9. "Urolithiasis is typically seen on renal ultrasound."**

Although renal ultrasound avoids radiation, it can often miss small stones (< 3 mm) and stones in certain areas of the renal tract. Patients with nondiagnostic ultrasounds should have a spiral CT scan if there is concern for urolithiasis.
- 10. "Patients with Henoch-Schönlein purpura often present with hematuria as the chief complaint."**

Fifty percent of children with Henoch-Schönlein purpura have renal involvement (including transient hematuria and proteinuria); however, they rarely present with hematuria as the chief complaint.⁴⁰ Relapses and remissions can manifest as episodes of gross hematuria, though only 2% develop long-term renal insufficiency.^{41,42}

Summary

It is important to distinguish between macroscopic and microscopic hematuria, as the etiologies can be very different. It is also important to determine whether the etiology of the hematuria is glomerular versus nonglomerular and to be aware of the systemic complications associated with the various causes of hematuria. This will guide management, treatment, and disposition. In most instances, the etiology is not life-threatening, and clinicians can provide reassurance and recommend outpatient follow-up.

Case Conclusions

You diagnosed the 12-year-old adolescent boy with post-streptococcal glomerulonephritis after you performed laboratory studies that showed a normal BUN and creatinine, a low C3, and an elevated ASO titer. He was admitted to the hospital for hypertension management and discharged home to follow up with nephrology in 6 to 8 weeks.

After completion of laboratory studies, the 15-year-old adolescent girl was found to have rhabdomyolysis due to strenuous exercise. The urine dipstick was positive for a large amount of blood, but there were no RBCs on microscopic examination, which was consistent with myoglobinuria. Her creatine kinase level was elevated to 35,000 IU/L. You started her on intravenous hydration and admitted her for further management.

The previously healthy 5-year-old girl was discharged home after further history revealed that she had eaten a significant number of blackberries with her grandmother the day prior. Although not necessary, you recommended that a repeat urine dipstick should be completed at her pediatrician's office.

Time- And Cost-Effective Strategies

1. Patients with isolated asymptomatic microscopic hematuria who are normotensive can be safely discharged from the ED with close follow-up by a primary care provider.
2. Patients with Henoch-Schönlein purpura do not require admission unless they have significant renal insufficiency or abdominal pain or bleeding, causing concern for intussusception.
3. The most common cause of hematuria in children is urinary tract infection. Therefore, even without other signs or symptoms, urine microscopy and urine culture should be obtained.
4. Imaging is not necessary for isolated asymptomatic hematuria.
5. Patients with hematuria and signs of glomerular disease who are normotensive with normal urine output may follow up with pediatric nephrology as an outpatient.

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study will be included in bold type following the reference, where available. The most informative references cited in this paper, as determined by the author, will be noted by an asterisk (*) next to the number of the reference.

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CME Questions



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- A urine dipstick that is strongly positive for blood with no RBCs seen on urine microscopy suggests:**
 - The urine dipstick has been left exposed to air for too long
 - The presence of myoglobinuria or hemoglobinuria
 - The patient has a *Pseudomonas* urinary tract infection
 - Glomerular disease
- Beets and mushrooms can cause factitious hematuria.**
 - True
 - False
- Which of the following is NOT a common cause of pediatric gross hematuria?**
 - Urinary tract infection
 - Hypercalciuria
 - Poststreptococcal glomerulonephritis
 - All of the above are all common causes of pediatric gross hematuria.
- IgA nephropathy is characterized by:**
 - Ocular anomalies
 - Deafness
 - Glomerular hematuria
 - All of the above
- A 14-year-old adolescent boy presents with dark red-brown urine and myalgias. His urine microscopy shows 0 to 3 RBC/HPF. You suspect:**
 - Rhabdomyosarcoma of the bladder
 - Alport syndrome
 - Rhabdomyolysis
 - Wilms tumor
- The most common urologic malignancy in children is:**
 - Wilms tumor (nephroblastoma)
 - Rhabdomyosarcoma of the bladder
 - Mesonephric blastoma
 - Renal cell carcinoma
- Factors to consider when weighing imaging modality options for urolithiasis include:**
 - CT scan exposes the patient to radiation, but is more sensitive than ultrasound.
 - Ultrasound may miss small stones or calculi in certain areas of the urinary tract.
 - Some stones are radiolucent (such as uric acid calculi) and will be missed on plain films.
 - All of the above
- An 8-year-old boy presents to the ED, and you suspect he has poststreptococcal glomerulonephritis. Which of the following symptoms would likely necessitate admission?**
 - Positive ASO titers
 - Tea-colored urine
 - 2+ proteinuria
 - Blood pressure of 146/96 mm Hg
- Which of the following is NOT an admission criterion for a patient with hematuria?**
 - Anuria
 - Uncontrolled hypertension
 - Diagnosis of Henoch-Schönlein purpura
 - Urolithiasis causing significant pain
- All of the following are criteria to refer a patient with hematuria to a nephrologist EXCEPT:**
 - Urolithiasis
 - Asymptomatic microscopic hematuria
 - Family history of renal failure
 - Hemoglobinopathy

Coming Soon In *Pediatric Emergency Medicine Practice*

Emergency Department Management Of Blunt Abdominal Trauma In The Pediatric Patient

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Blunt abdominal trauma is the third most common cause of pediatric trauma deaths, but it is the most common unrecognized fatal injury. This issue will discuss common mechanisms and injuries of blunt abdominal trauma seen in children and take a closer look at current evaluation and management. The mainstay of diagnostic evaluation includes laboratory, sonography, and computed tomography studies. However, the routine use of these studies may not be necessary, and controversy exists as to which are beneficial and which are less valuable. The concern for radiation-induced malignancy has led to increased efforts to limit radiation exposure by decreasing the use of unnecessary CT scans. The history and physical examination, combined with the mechanism of action, should be used to develop a thoughtful and directed diagnostic workup.

Time- And Cost- Effective Strategies

- Do not perform a “trauma panel” or head-to-toe CT scan on every patient. Use the history and physical examination to guide workup. Ordering laboratory tests and imaging studies that are not needed will lead to increased costs and unnecessary radiation exposure for the patient.
- If a patient has worsening abdominal pain, he should be taken to the operating room, not for repeat imaging studies. A repeat CT scan is unlikely to confidently exclude a bowel injury. Patients with increasing abdominal pain should be taken to the operating room to exclude other injuries.
- As per Advanced Trauma and Life Support guidelines, to avoid duplication of imaging, the referring hospital should not obtain a CT scan unless it would somehow alter management of the patient. Obtaining imaging prior to transfer ultimately delays transfer to the trauma facility. Additionally, images can be lost in transport or the referring and receiving imaging systems could be incompatible and images would not be able to be viewed. Consequently, imaging studies would need to be unnecessarily repeated, exposing the patient to additional radiation and adding to the cost of treatment.

An Evidence-Based Approach To Neonatal Vomiting In The Emergency Department

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Vomiting can account for up to 36% of neonatal visits to the emergency department. The causes of vomiting can range from benign to life-threatening. This issue reviews the approach that the emergency clinician should take in evaluating an infant with vomiting. Evidence to guide diagnosis and management in the emergency department is limited. The history and physical examination are extremely important in these cases, especially in identifying red flags, such as bilious or projectile emesis. There is a multitude of imaging modalities available for the evaluation of vomiting, and choosing the most appropriate one can be intimidating. A thorough review is presented discussing plain abdominal radiography, upper gastrointestinal studies, ultrasonography, and contrast enema. A systematic approach in the emergency department, as outlined in this review, is required to identify the serious causes of vomiting in the neonate.

Time- And Cost-Effective Strategies

- Do not perform unnecessary tests on neonates with vomiting while in the emergency department. Well-appearing infants with symptoms consistent with gastroesophageal reflux disease should be managed conservatively.
Risk Management Caveat: Ensure that the family can follow up closely with the infant’s pediatrician. The infant may not have lost weight, but it could be early in the course of GERD, and without proper follow-up, there is concern for failure to thrive. Secondly, if suspicion for pyloric stenosis is not high enough to obtain an ultrasound, educate the parents about the signs and symptoms that would warrant a return visit to the emergency department.
- Do not perform screening electrolytes on all neonates with vomiting, as even those with surgical causes will most likely have normal electrolytes.
Risk Management Caveat: It is recognized that clinical signs of dehydration do not always align with laboratory values. A significant electrolyte abnormality may be missed in a neonate who does not appear dehydrated.



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Target Audience: This enduring material is designed for emergency medicine physicians, physician assistants, nurse practitioners, and residents.

Goals: Upon completion of this activity, you should be able to: (1) demonstrate medical decision-making based on the strongest clinical evidence; (2) cost-effectively diagnose and treat the most critical ED presentations; and (3) describe the most common medicolegal pitfalls for each topic covered.

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