23 HEMATURIA, MICROSCOPIC

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Microscopic hematuria is much more common than gross hematuria in children, with a prevalence of 3% to 4% in a single urine sample and 1% to 2% in two or more urine samples. There is no consensus on the definition of microscopic hematuria, although more than 5 to 10 red blood cells (RBCs) per high-power field is considered significant. It is generally recommended that at least two of three uninalyses show microscopic hematuria over 2 to 3 weeks before further evaluation is performed. No consensus exists on a stepwise evaluation, but this chapter provides an approach to the evaluation of the child with microscopic hematuria.

Hematuria may originate from the glomeruli, renal tubules and interstitium, or urinary tract, which includes the collecting systems, ureters, bladder, and urethra. In children, the source of bleeding is most often from the glomeruli. In most cases, proteinuria, RBC casts, and dysmorphic RBCs in the urine accompany hematuria caused by glomerulonephritis. The most common causes of persistent microscopic hematuria in children include glomerulopathies (e.g., IgA nephropathy, thin basement membrane disease), Alport syndrome, hypercalciuria, and urinary tract infection (UTI).

The presence of hematuria must be confirmed by microscopic examination of the spun sediment of urine because other substances besides blood can give a false-positive dipstick test for blood. The dipstick and microscopic urinalysis should be repeated twice within 2 weeks after the initial specimen. If the hematuria resolves, no further tests are needed. If persistent microscopic hematuria is confirmed, a thorough history (with particular attention to the family history) and physical examination should be performed.

Two diagnostic tests should be performed: a test for proteinuria and a microscopic examination of the urine for RBCs and RBC casts. Proteinuria usually does not exceed 2+ (100 mg/dL) if the only source of protein is from the blood. Patients with 1+ to 2+ proteinuria should be evaluated for orthostatic proteinuria. A patient with more than 2+ proteinuria should be evaluated for glomerulonephritis and nephrotic syndrome. The presence of RBC casts is a highly specific marker for glomerulonephritis. In addition to these tests, many authorities also recommend urine culture, urine calcium-to-creatinine ratio, and renal ultrasound examination for confirmed cases of microscopic hematuria.

Microscopic hematuria that persists falls into one of three categories: asymptomatic isolated microscopic hematuria, asymptomatic microscopic hematuria with proteinuria, and symptomatic isolated microscopic hematuria.

Asymptomatic isolated microscopic hematuria is common in children. Many experts recommend observation of these children if the examination is normal, with further evaluation only if proteinuria, hypertension, or gross hematuria is present. In the child with asymptomatic isolated microscopic

hematuria, the early morning urinalysis should be repeated weekly for 2 weeks with no exercise before the collection of the urine sample. If the hematuria persists, urine culture should be obtained and, if positive, the patient should be treated with antibiotics. If the urine culture is negative, the patient should be followed up every 3 months with a history, physical examination, blood pressure measurement, and urinalysis. If the hematuria persists for 1 year, measurement of the urine calcium-creatinine ratio should be obtained, and the parents and siblings should be tested for hematuria. Hemoglobin electrophoresis should be performed if sickle cell trait is a consideration. Figure 23-1 provides an algorithm for the evaluation of a child with asymptomatic microscopic hematuria.

Asymptomatic microscopic hematuria with proteinuria is associated with a higher risk for significant renal disease. In this case, urinary protein excretion should be quantified. If protein excretion is greater than 4 mg/m^2 per hour or the urine protein-to-creatinine ratio is greater than 0.2 mg protein per milligram of creatinine in children older than 2 years or greater than 0.5 mg of protein per milligram of creatinine in younger children, the patient should be referred to a pediatric nephrologist. If urinary protein excretion is less than these values, the patient should be reevaluated in a few weeks. If the hematuria and proteinuria have resolved, no further evaluation is indicated. If there is only asymptomatic microscopic hematuria, the patient may be monitored as for asymptomatic isolated microscopic hematuria. If the hematuria and proteinuria persist, the patient should be referred to a pediatric nephrologist. Additional testing is outlined below. Figure 23-2 provides an algorithm for the evaluation of a child with microscopic hematuria associated with proteinuria, symptoms, or abnormalities in the history or physical examination.

Symptomatic microscopic hematuria may manifest with fever, weight loss, malaise, rash, arthritis, edema, hypertension, dysuria, or oliguria. The presence of these symptoms suggests a systemic process or significant disease affecting the urinary tract. History and physical examination may provide important clues to the diagnosis. The laboratory evaluation includes serum creatinine, blood urea nitrogen (BUN), electrolytes, complete blood count (CBC), C3, C4, and albumin. Additional testing to consider is outlined below. Important causes of symptomatic microscopic hematuria include acute postinfectious glomerulonephritis, hemolytic-uremic syndrome, Henoch-Schönlein purpura, menbranoproliferative glomerulonephritis, IgA nephropathy, and focal segmental glomerulosclerosis.

Medications Associated with Hematuria

- Amitriptyline
- Antibiotics
- Anticoagulants
- Anticonvulsants

- Chlorpromazine
- Cyclophosphamide
- Indinavir
- Nonsteroidal anti-inflammatory drugs (NSAIDs)
- Ritonavir
- Toluene

Causes of Hematuria

Bleeding Disorders

- Coagulopathy (congenital or acquired)
- Hemophilia A or B
- Platelet disorder
- Thrombocytopenia
- von Willebrand disease

Glomerular Causes

- Acute poststreptococcal glomerulonephritis
- Alport syndrome
- Bacterial endocarditis
- Goodpasture's disease
- Hemolytic uremic syndrome
- Henoch-Schönlein purpura
- Idiopathic hypercalciuria without urolithiasis
- IgA nephropathy
- Membranoproliferative glomerulonephritis
- Mesangial proliferative glomerulonephritis
- Microangiopathic polyarteritis nodosa
- Polycystic kidney disease
- Rapidly progressive glomerulonephritis
- Systemic lupus erythematosus
- Thin basement membrane disease (benign familial hematuria)
- Thrombotic thrombocytopenic purpura
- Wegener granulomatosis

Interstitial Disease

- Acute interstitial nephritis
- Pyelonephritis
- Tubulointerstitial nephritis with uveitis

Neoplastic

- Angiomyolipoma
- Congential mesoblastic tumor
- Renal cell carcinoma
- Rhabdoid tumors
- Uroepithelial tumors
- Wilms' tumor

Urinary Tract

- Bacterial
- Cyclophosphamide cystitis
- Cystitis
- Foreign body
- Idiopathic hypercalciuria
- Schistosomiasis
- Severe hydronephrosis
- Trauma
- Tuberculosis
- Urethritis
- Urolithiasis
- Viral (adenovirus)

Vascular

- Arteriovenous thrombosis
- Hemangioma/hamartoma
- Malignant hypertension
- Nutcracker syndrome
- Renal artery or vein thrombosis
- Sickle cell disease and trait
- Exercise-related hematuria
- Trauma

Key Historical Features

✓ Dysuria
✓ Frequency
✓ Urgency
✓ Fever
✓ Flank pain

- ✓ Abdominal pain
- ✓ Trauma
- ✓ Recent febrile illness
- ✓ Recent pharyngitis
- ✓ Recent streptococcal skin infection
- ✓ Recent trauma, menstruation, or strenuous exercise
- ✓ Medical history
  - History of heavy or frequent bleeding
  - Exposure to tuberculosis
  - Recent bladder catheterization
- ✓ Surgical history
- ✓ Family history of renal disease, hematuria, hearing loss, coagulopathy, hemoglobinopathy, calculi, dialysis, or renal transplantation
- ✓ Review of systems
  - Shortness of breath
  - Edema
  - Weight gain
  - Chest pain
  - Fatigue
  - Diarrhea
  - Joint pains
  - Rash
  - Cough or hemoptysis
  - Hematochezia
  - Hair loss
  - Mouth ulcers

Key Physical Findings

- ✓ Vital signs, especially blood pressure and temperature
- ✓ Assessment of growth
- ✓ General appearance, especially for pallor
- ✓ Abdominal examination for abdominal or flank masses
- ✓ Back examination for costovertebral angle tenderness
- ✓ Skin examination for rashes
- ✓ Extremity examination for musculoskeletal findings such as arthritis

Suggested General Work-Up of Microscopic Hematuria

Test for proteinuria	To determine whether significant proteinuria is present
Microscopic examination of the urine for RBCs and RBC casts	To confirm the presence of hematuria and evaluate for underlying glomerulonephritis
Urine culture	To evaluate for UTI
Urine calcium-to-creatinine ratio	To evaluate for hypercalciuria if hematuria persists for 1 year (urine calcium-creatinine ratio less than 0.2 is normal)
Renal ultrasound	Should be considered to evaluate for stones, tumors, hydronephrosis, structural anomalies, renal parenchymal dysplasia, medical renal disease, inflammation of the bladder, bladder polyps, and posterior urethral valves
Hearing test	If there is any reason to suspect familial renal disease

Suggested Work-Up of Isolated Asymptomatic Microscopic Hematuria

Urine culture	To evaluate for UTI
Serum creatinine	To evaluate for renal insufficiency
Renal ultrasound	Should be considered to evaluate for stones, tumors, hydronephrosis, structural anomalies, renal parenchymal dysplasia, medical renal disease, inflammation of the bladder, bladder polyps, and posterior urethral valves
Urine calcium-to-creatinine ratio	To evaluate for hypercalciuria if hematuria persists for 1 year (urine calcium/creatinine ratio less than 0.2 is normal)

Additional Work-Up of Isolated Asymptomatic Microscopic Hematuria

24-hour urine calcium excretion, serum electrolytes, calcium, phosphorus, magnesium	If hypercalciuria is identified
Coagulation studies	If an underlying coagulopathy is considered

Suggested Work-Up of Asymptomatic Microscopic Hematuria with Proteinuria

Quantification of urinary protein excretion with 24-hour collection or spot urine protein/creatinine ratio	To quantify urinary protein excretion
Serum creatinine and BUN, CBC, serum albumin, antistreptolysin O (ASO) titers streptozyme test, serum albumin, serum complement C3 and C4	To evaluate for glomerulonephritis
Antinuclear antibodies (ANA)	If lupus is suspected

Suggested Work-Up of Symptomatic Microscopic Hematuria

Serum creatinine and BUN, CBC, serum albumin, ASO titers, streptozyme test, serum albumin, serum complement C3 and C4	To evaluate for glomerulonephritis
ANA	To evaluate for lupus
Renal ultrasound or computed tomography (CT) scan	To evaluate for stones, tumors, hydronephrosis, structural anomalies, renal parenchymal dysplasia, medical renal disease, inflammation of the bladder, bladder polyps, and posterior urethral valves

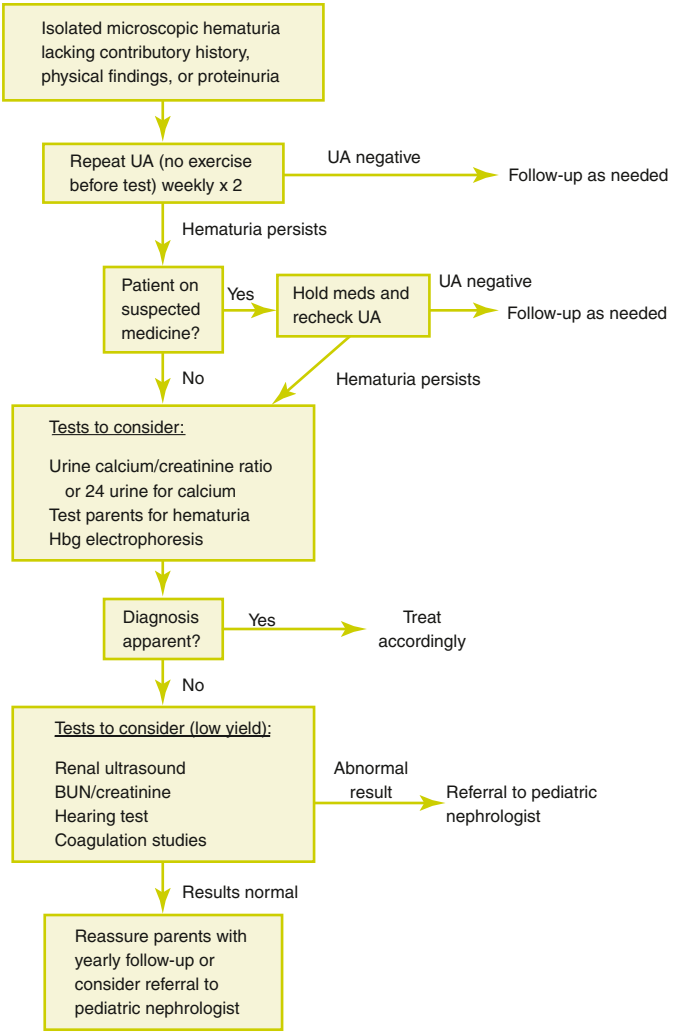

Figure 23-1. Evaluation of a child with asymptomatic microscopic hematuria. (From Patel HP, Bissler JJ. Hematuria in children. *Pediatr Clin North Am* 2001;48:1519–1537, with permission.)

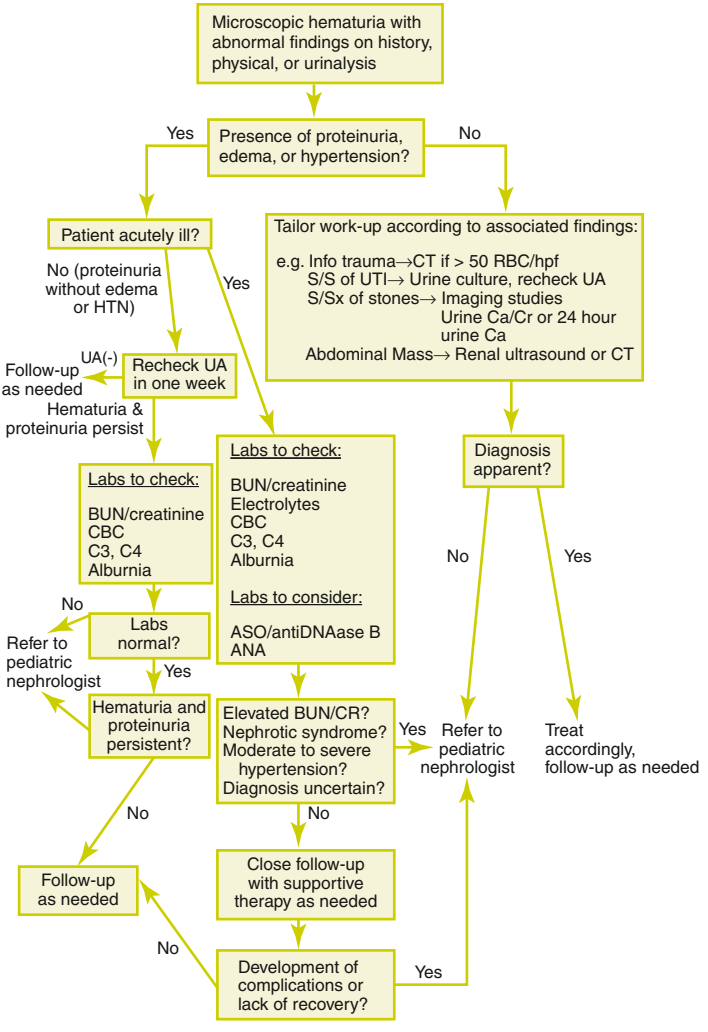

Figure 23-2. Evaluation of a child with microscopic hematuria associated with proteinuria, symptoms, or abnormalities in the history or physical examination. (From Patel HP, Bissler JJ. Hematuria in children. *Pediatr Clin North Am* 2001;48:1519–1537, with permission.)

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