

Hematuria in Children

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Learning Objectives

- Identify the different causes of hematuria in children.
- Evaluate the source of hematuria based on history, physical exam, and diagnostic studies.
- Distinguish between isolated hematuria and hematuria associated with other renal and systemic manifestations that would require nephrology follow-up.

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A 5-year-old Asian boy presents to your office after 2 episodes of cola-colored urine in the past 4 months. Both times he had 2–3 days of rhinorrhea and cough before the onset of his urinary symptoms. He has no associated fevers, sore throat, rash, joint pain, or edema. He denies flank and abdominal pain, dysuria, or changes in his voiding pattern. He has otherwise been healthy.

Based on this history, what is the most likely diagnosis?

What other information do you want to know?

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What is hematuria?

- Blood in the urine, defined as 5 or more RBCs per high-power field in centrifuged urinary sediment on 3 separate occasions
 - Gross hematuria
 - Microscopic hematuria

- What can urine tell us about where the blood comes from?
 - Color/Quality
 - Cola- or tea-colored – glomerular
 - Red or pink, may contain clots – non-glomerular
 - Timing
 - Beginning of urine stream – urethra
 - Throughout urine stream – kidneys (usually)
 - End of urine stream (terminal hematuria) – bladder



How common is hematuria?

- Population studies estimate prevalence of asymptomatic microscopic hematuria in children to be 3%–6% on one-time evaluation. (Dodge, et al. 1976, Vehaskari, et al. 1979).
 - Repeat urine screening lowers the prevalence to 0.5%–1%.
- Diseases associated with hematuria may have predilection for specific gender, race, or ethnicity.
 - IgA nephropathy – Asian, Caucasian
 - Lupus nephritis – African American, Hispanic, female > male
- Predisposition for hematuria is higher in diseases with a known genetic or hereditary basis.
 - Hypercalciuria
 - Thin basement membrane nephropathy/Alport syndrome
 - Autosomal dominant polycystic kidney disease (ADPKD)
 - Atypical hemolytic uremic syndrome (aHUS)



What are common patterns of presentation seen in children?

- Symptomatic hematuria (gross or microscopic)
- Asymptomatic hematuria (gross or microscopic)
- Nephritic syndrome



Symptomatic Hematuria

- Gross or microscopic hematuria associated with abdominal or flank pain, dysuria, urinary frequency or urgency

- Causes
 - Urinary tract infection (pyelonephritis, cystitis, urethritis)
 - Urolithiasis
 - Renal trauma
 - Renal vein thrombosis
 - Tumors of GU origin (Wilms tumor, rhabdomyosarcoma)
 - Nutcracker syndrome – compression of the left renal vein between the superior mesenteric artery and aorta

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Asymptomatic Gross Hematuria

- Exercise-induced hematuria – transient, usually resolves within 48 hours
- Hematologic – hemophilia, thrombocytopenia, coagulopathy, malignancy
- Recurrent episodes of gross hematuria – often in presence of bodily stressor such as illness
 - IgA nephropathy
 - Alport syndrome
 - Thin basement membrane disease
 - Hypercalciuria
- **If proteinuria is present with microscopic hematuria, and is not transient or orthostatic, further evaluation for renal disease by a pediatric nephrologist is warranted.**



Nephritic Syndrome

- Clinical findings related to glomerular injury and inflammation
 - Hematuria, usually with proteinuria
 - Oliguria
 - Azotemia (decreased GFR)
 - Hypertension

- May be acute or chronic, renal-limited, or part of a systemic process
 - Post-infectious or infection-related GN
 - MPGN
 - SLE nephritis
 - IgA nephropathy/Henoch-Schönlein purpura
 - ANCA-associated vasculitis
 - Anti-GBM disease (Goodpasture syndrome)

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Approach To Hematuria

Example Historical Questions	Rationale
Any recent respiratory or skin infections?	<ul style="list-style-type: none"> • Post-infectious GN commonly preceded by pharyngitis or cellulitis • “Synpharyngitic” → concurrent hematuria with infectious symptoms classic for IgA nephropathy
Any recent trauma or significant exercise?	<ul style="list-style-type: none"> • Renal trauma (e.g. from renal biopsy, blunt trauma from fall) can cause gross hematuria • Rule out exercise-induced hematuria, myoglobinuria
Are any new medications or over-the-counter supplements being used?	<ul style="list-style-type: none"> • Certain drugs that may predispose to hematuria with kidney injury (e.g. NSAIDs) • Some drugs can cause pseudohematuria (e.g. phenazopyridine, rifampin)
Is the hematuria associated with other clinical findings or symptoms?	<ul style="list-style-type: none"> • Hypertension, edema → Glomerulonephritis • Fever, back or flank pain → Pyelonephritis • Hearing loss → Alport syndrome • Rash, arthralgias/myalgias → Lupus nephritis, Henoch-Schönlein purpura nephritis, ANCA vasculitis



Approach to Hematuria

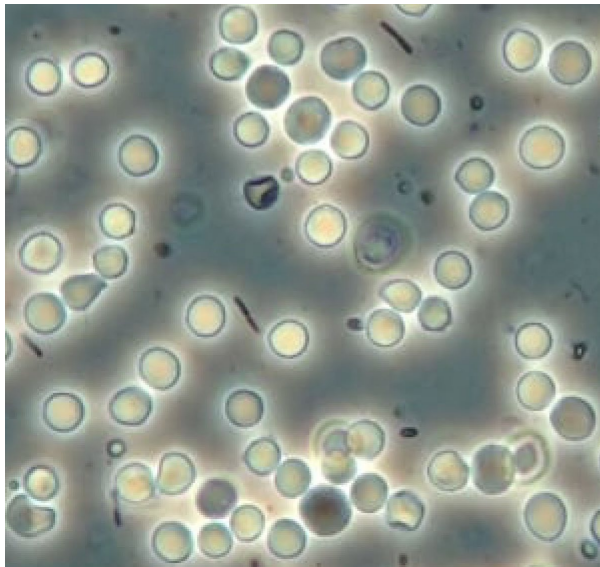
- Must rule out pseudohematuria
 - Positive for heme on urine dipstick but no RBCs on microscopy
 - Myoglobinuria, hemoglobinuria
 - Drugs (e.g. rifampin), dyes in food (e.g. beets)
 - Bleeding from outside the urinary tract
 - Menses

- What does the urine sediment look like?
 - Dysmorphic or fragmented RBCs, RBC casts (glomerular)
 - Round, eumorphic RBCs (extraglomerular)
 - Bacteria (UTI) or crystals (urolithiasis)

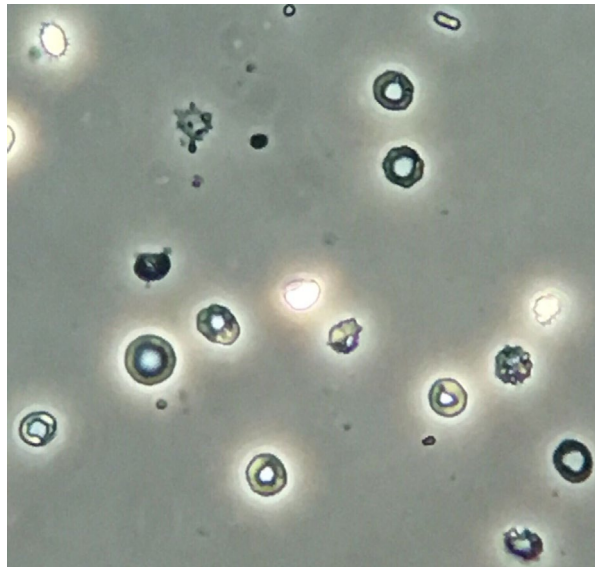


Urine Microscopy

Eumorphic RBCs



Dysmorphic RBCs



RBC Cast



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Initial Evaluation

Physical exam (including external genitalia)

Laboratory studies/imaging to consider based on history/exam:

- Urine protein-to-creatinine ratio → assess for concurrent proteinuria

“Glomerular” Studies	“Non-Glomerular” Studies
CBC, electrolytes, BUN, Cr	Urine culture → if evidence of UTI
Complement (C3, C4)	Urine calcium-to-creatinine
ASO and ANA titers	Renal and bladder ultrasound
ANCA, anti-GBM, infectious serologies where clinically indicated	Coagulation studies → if concerned for bleeding diathesis
Family urines → Assess for familial hematuria	Helical CT, MRA, or MRU



Laboratory Patterns of Select Glomerular Diseases

	C3	C4	ANA	ASO	ANCA
Post-streptococcal glomerulonephritis	↓	↔	neg	pos	neg
MPGN	↓	↔	neg	neg	neg
Lupus nephritis	↓	↓	pos	neg	neg
IgA nephropathy	↔	↔	neg	neg	neg
ANCA-associated vasculitis	↔	↔	neg	neg	pos

Note: Serum IgA is elevated in only about 8%–16% of children with IgA nephropathy.

Suspect MPGN in a patient who presents with apparent post-streptococcal glomerulonephritis, but C3 remains low after 6–8 weeks!



Indications for Renal Biopsy

- Microscopic or gross hematuria associated with proteinuria
- Suspected involvement with systemic disease, such as lupus nephritis and ANCA-associated vasculitis
- Unexplained reduced kidney function
- Persistently low C3 after an episode of suspected post-infectious glomerulonephritis
- Family history of Alport syndrome in a child with hematuria, with/without extrarenal symptoms

Consider urologic evaluation for persistent or recurrent gross hematuria if renal disease is not suspected.



Back to our case...

A 5-year-old Asian boy presents to your office after 2 episodes of cola-colored urine in the past 4 months. Both times he had 2–3 days of rhinorrhea and cough before the onset of his urinary symptoms. He has no associated fevers, sore throat, rash, joint pain, or edema. He denies flank and abdominal pain, dysuria, or changes in his voiding pattern. He has otherwise been healthy.

Based on this history, what is the most likely diagnosis?

What other information do you want to know?

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Based on this history, what is the most likely diagnosis?

IgA nephropathy

- Recurrent episodes of gross hematuria
- “Synpharyngitic” – no latency between infectious symptoms and onset of hematuria
- Common cause of primary glomerulonephritis, especially in Asians

What other information do you want to know?

- Physical exam → especially presence of hypertension, volume excess (edema)
- Urinalysis/microscopy, urine protein-to-creatinine ratio
 - Assess concurrent proteinuria, morphology of RBCs
- Laboratory/imaging studies
 - CBC, serum chemistries, BUN, Cr → assess renal function
 - C3, C4 → rule out hypocomplementemic diseases
 - ASO or anti-DNase B → if concern for post-streptococcal GN
 - Renal ultrasound → if hematuria is possibly lower urinary tract, assess kidney structure and presence of stones or masses

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Further Reading

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