# Approach to hematuria

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Goals for the primary care physician in the management of a child with hematuria are:

- To recognize and confirm the finding of hematuria
- To identify common etiologies
- To identify patients with significant urinary system disease that might require further expertise in either diagnosis or management.

Haematuria - abnormal number of red blood cells in urine

May be a normal transient finding in children,

Accompanying a non specific viral infection or

Indicator of renal-urinary tract pathology, local infection or systemic disease

Haematuria categorised as :

- Macroscopic – gross haematuria, visible to naked eye
- Microscopic – seen on microscopic analysis / on urine dipstick

On basis of aetiology as :

- Glomerular
- Non glomerular

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

Children with hematuria may come to the attention of the practitioner with one of the following:

(i) gross hematuria

(ii) urinary or other symptoms with the incidental finding of microscopic hematuria

(iii) inadvertent discovery of microscopic hematuria during a routine urinalysis.

| GLOMERULAR | NON GLOMERULAR |
|---|---|
| Glomerulonephritis (GN): | Urinary tract infection |
| Primary GN | Hypercalciuria |
| Post-infectious acute GN | Renal calculi |
| Membranoproliferative GN | Trauma |
| Membranous nephropathy | Exercise-induced |
| Rapidly progressive GN | Chemical cystitis such as cyclophosphamide |
| IgA nephropathy | Coagulopathy |
| Secondary GN | Vascular malformations |
| Systemic lupus erythematosus | Nutcracker syndrome |
| Henoch Schönlein purpura | Urinary schistosomiasis |
| Polyarteritis nodosa | Malignancy |
| ANCA positive systemic vasculitis | Renal: nephroblastoma |
| Hemolytic uremic syndrome | Bladder: rhabdomyosarcoma |
| Renal vein thrombosis | Menarche |
| Interstitial nephritis | Factitious |
| Cystic renal disease | |

Causes of Hematuria in the Newborn

- Renal vein thrombosis
- Renal artery thrombosis
- Autosomal recessive polycystic kidney disease
- Obstructive uropathy
- Urinary tract infection
- Bleeding and clotting disorders
- Trauma, bladder catheterization

| Example Historical Questions | Rationale |
| --- | --- |
| Any recent respiratory or skin infections? | • Post-infectious GN commonly preceded by pharyngitis or cellulitis<br>• "Synpharyngitic" → concurrent hematuria with infectious symptoms classic for IgA nephropathy |
| Any recent trauma or significant exercise? | • Renal trauma (e.g. from renal biopsy, blunt trauma from fall) can cause gross hematuria<br>• Rule out exercise-induced hematuria, myoglobinuria |
| Are any new medications or over-the-counter supplements being used? | • Certain drugs that may predispose to hematuria with kidney injury (e.g. NSAIDs)<br>• Some drugs can cause pseudohematuria (e.g. phenazopyridine, rifampin) |
| Is the hematuria associated with other clinical findings or symptoms? | • Hypertension, edema → Glomerulonephritis<br>• Fever, back or flank pain → Pyelonephritis<br>• Hearing loss → Alport syndrome<br>• Rash, arthralgias/myalgias → Lupus nephritis, Henoch-Schönlein purpura nephritis, ANCA vasculitis |

# Differentiating Glomerular from Non glomerular Haematuria

| | **GLOMERULAR** | **NON GLOMERULAR** |
|---|---|---|
| HISTORY | ○ Oliguria or polyuria<br>○ Recent respiratory, skin, or gastrointestinal infection<br>○ Deafness<br>○ Medication exposure<br>○ Family history of hearing loss or renal failure<br>○ Rash<br>○ Joint pain/swelling<br>○ Hemoptysis<br>○ Medication exposure | ○ Dysuria or polyuria<br>○ Renal colic/abdominal pain<br>○ Fever<br>○ Medication exposure<br>○ Trauma history<br>○ Family history of sickle cell disease, hemophilia, or Von Wil-<br>○ lebrand disease<br>○ Strenuous exercise |

| | GLOMERULAR CAUSE | NON GLOMERULAR CAUSE |
|---|---|---|
| PHYSICAL EXAMINATION | ○ Hypertension<br>○ Edema<br>○ Rash<br>○ Arthritis<br>○ Pallor | ○ Normotension<br>○ Costovertebral angle tenderness<br>○ Suprapubic pain<br>○ Signs of trauma |
| URINALYSIS | ○ Brown-, tea-, or cola-colored urine<br>○ Proteinuria often present<br>○ Red blood cell casts<br>○ > 20% dysmorphic red blood cells | ○ Bright red urine<br>○ +/- proteinuria<br>○ No red blood cell casts<br>○ Positive nitrites or leukocyte esterase |
| LABORATORY TESTS | ○ Elevated blood urea nitrogen/creatinine<br>○ Anemia<br>○ Abnormal complement levels (C3, C4) | ○ Normal blood urea nitrogen/creatinine |

**CONFIRMATION OF HEMATURIA:**

1) microscopic examination of the urine :

More than 5 RBCs/ hpf.

Centrifuging 10 mL of a fresh urine sample at 2000 rpm for 5 min, decanting the supernatant and re-suspending the sediment in the remaining 0.5 mL.

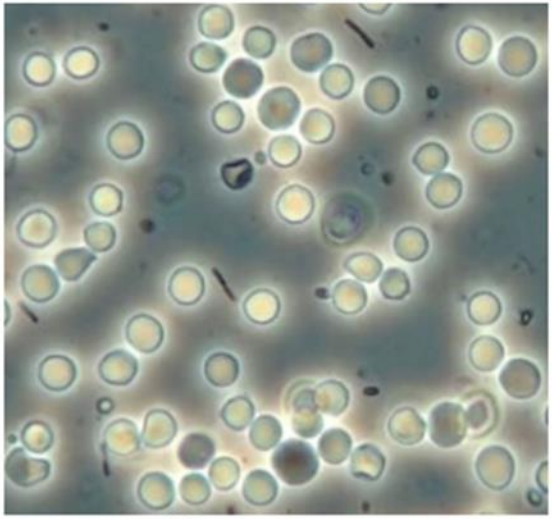
The sediment is examined by microscopy at high power, counting RBCs in twenty fields and the average is reported.

In the absence of gross hematuria, the *persistent finding of microscopic hematuria in at least two of three urinalyses, performed over 2-3 weeks, warrants further evaluation*

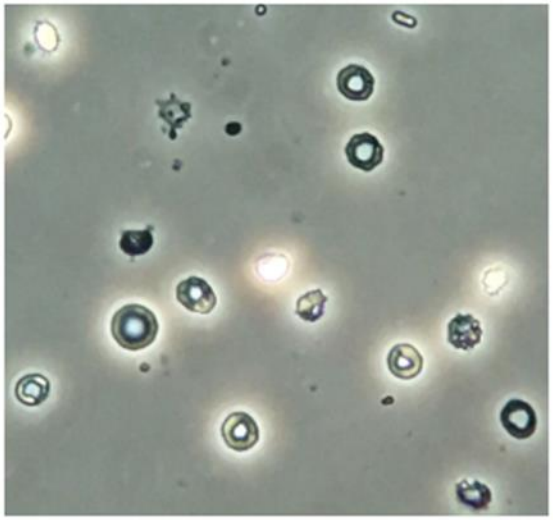
What does the urine sediment look like?

1. Dysmorphic or fragmented RBCs, RBC casts (glomerular)
2. Round, eumorphic RBCs (extraglomerular)
3. Bacteria (UTI) or crystals (urolithiasis)

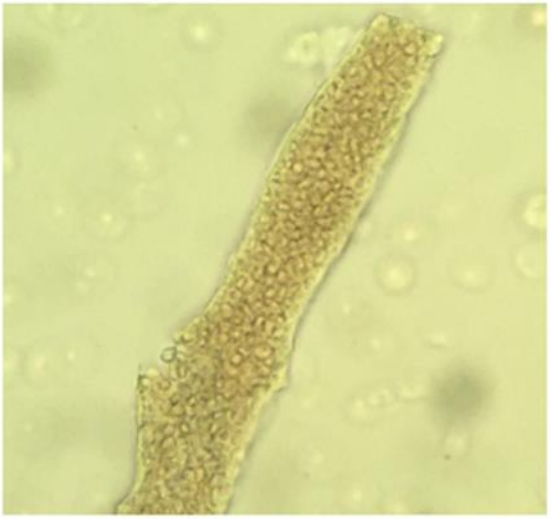
Eumorphic RBCs



Dysmorphic RBCs



RBC Cast



2)The reagent strip reaction:

Pseudoperoxidase activity of hemoglobin (or myoglobin) in presence of chromogen tetramethyl benzidine -- oxidized chromogen,  green-blue color.

Briefly dip the strip in the urine, tap off excess urine, and read the strip at the recommended time (usually one minute)

Positive dipstick for blood in the absence of RBCs by microscopy is indicative of myoglobinuria or hemoglobinuria, not true hematuria.

False positive -Dehydration, exercise, hemoglobinuria, myoglobinuria, highly alkaline urine, oxidizing agents uses to clean perineum

False negative – Elevated specific gravity, pH <5.1, proteinuria,

vitamin C, dipstick exposed to air

Agents that colour urine:

Red or pink

- Red cells, free hemoglobin, myoglobin,
- Urates
- Drugs: chloroquine, phenazopyridine
- Beets, red dyes in food
- Porphyrins

Dark yellow or orange

- Normal concentrated urine
- Rifampicin, pyridium

Dark brown or black

- Bile pigments
- Methemoglobinemia
- Homogentesic acid

| "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 |

Children with isolated microscopic hematuria - dipstick and microscopic urinalysis should be repeated twice within 2 weeks.

Renal ultrasonography - screening test because it is noninvasive and provides important information.

In a small number of children with isolated microscopic hematuria, without proteinuria - cause not be found - keep under surveillance

An early consultation should be obtained with a pediatric nephrologist, since most will require additional expertise in investigation and management

# Renal biopsy when hematuria is associated with:

- Significant proteinuria, except in postinfectious glomerulonephritis
- Persistent low serum complement C3
- Unexplained azotemia
- Systemic diseases such as systemic lupus erythematosus or ANCA-positive vasculitis
- Family history of significant renal disease - familial hematuria syndromes
- Recurrent gross hematuria of unknown etiology where investigations are suggestive of a glomerular pathology
- Persistent glomerular hematuria where the parents are anxious about the diagnosis and prognosis

Thank you