Approach to a child with Hematuria

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Be the end of this lecture the student is should be able to evaluate a child with hematuria considering the following:

- Definition
- Causes
- History
- Examination
- Investigations
- Management
Defination

- **Microscopic Hematuria**: five or more red blood cells per high-power field on microscopic evaluation of urinary sediment from two of three properly collected urinalysis specimens
- **Gross Hematuria**: generally recognized with the naked eye
- **Red urine without hematuria occurs in Hemoglobinuria or Myoglobinuria** (Heme-positive urine without RBCs caused by the presence of either hemoglobin or myoglobin) or other causes
Causes of red or high-coloured urine:

- Hematuria (RBC +ve)
- Heme +ve (No RBCs)
  - Hemoglobinuria (Hemolysis)
  - Myoglobinuria (Rhabdomyolysis – Skeletal muscle injury, viral myositis, Hypernatremia, hypophosphatemia, hypotension, DIC, Toxins, Prolonged seizures)
Causes of red or high-coloured urine:

- Heme –ve
  - Drugs: Rifampin, Chloroquine, Deferoxamine, Ibuprofen, Iron sorbitol, Metronidazole, Nitrofurantoin,
  - Dyes: Beetroot, Blackberries, Food colouring agents
  - Metabolites: Homogentisic acid (Alcaptonuria), Melanin, Methemoglobin, Porphyrin, Tyrosinosis, Urates
  - Highly concentrated urine
  - Bile pigments
- different samples of Urine containing blood
Pathophysiology:

- Structural disruption in the integrity of glomerular basement membrane caused by inflammatory or immunologic processes
- Toxic disruptions of the renal tubules
- Mechanical erosion of mucosal surfaces in the genitourinary tract
Causes of Hematuria:

A) Glomerular hematuria

<table>
<thead>
<tr>
<th>Isolated renal disease</th>
<th>Multisystem disease</th>
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</thead>
<tbody>
<tr>
<td>Postinfectious GN (Post streptococcal)</td>
<td>HSP nephritis</td>
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<tr>
<td>IgA nephropathy</td>
<td>SLE nephritis</td>
</tr>
<tr>
<td>Alport syndrome</td>
<td>HUS</td>
</tr>
<tr>
<td>Thin Glomerular Basement membrane disease</td>
<td>Goodpasture syndrome</td>
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<tr>
<td>Membranoproliferative GN</td>
<td>HIV nephropathy</td>
</tr>
<tr>
<td>Membranous nephropathy</td>
<td>Sickle cell glomerulopathy</td>
</tr>
<tr>
<td>Focal segmental glomerulosclerosis</td>
<td>Infective endocarditis</td>
</tr>
</tbody>
</table>
B) Extraglomerular hematuria
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Upper Urinary tract

Vascular:
- Arterial/venous thrombosis
- Malformation (aneurysms, hemangioma)
- Nutcracker syndrome

Crystalluria:
- Calcium, Oxalate, Uric acid

Hemoglobinopathies:
- Sickle cell trait/disease

Medications:
- NSAIDs, anticoagulants

Tubulointerstitial
- Pyelonephritis
- Interstitial nephritis
- Nephrocalcinosis

Anatomic
- Hydronephrosis
- Polycystic kidney disease
- Tumor (Wilms, rare)
- Rhabdomyosarcoma, angiomyolipoma
- Trauma
Lower urinary tract

Inflammation- infectious (Bacterial, viral, Tubercular Schistosomasis)
and non infectious

Cystitis
Urethritis
Urolithiasis, Hypercalciuria, Hyperuricosuria
Trauma, Foreign bodies, Coagulopathy
Heavy exercise
Munchausen syndrome / by proxy
Causes of Gross Hematuria:

- Glomerular
  - IgA nephropathy
  - Alport syndrome
  - Thin glomerular basement membrane disease
  - Post infectious glomerulonephritis
  - HSP nephritis
  - SLE nephritis
- Urinary tract infection
- Meatal stenosis
- Perineal irritation
- Trauma
- Urolithiasis/hypercalciuria
- Coagulopathy
- Tumor
D/D of Symptomatic and Asymptomatic Hematuria

**Symptomatic**
- Renal symptoms
  - Urinary tract infections
  - Nephrolithiasis
  - Urethrorrhagia
- Systemic symptoms
  - Henoch-Schönlein purpura

**Asymptomatic**
- Hypercalciuria
- Cystic disease
- Obstruction
- Vascular
- Arteriovenous malformation

- Thrombosis
- Trauma
- Tumor
- Hemoglobinopathies
- Coagulopathies
- Exercise-induced hematuria
- Benign familial hematuria (thin basement membrane)
- Glomerulonephritis (resolving)
- Acute postinfectious nephritis
- IgA nephropathy
Causes of Hematuria in the Newborn:

- Renal vein thrombosis (Asphyxia, dehydration, shock)
- Renal artery thrombosis
- Autosomal recessive polycystic kidney disease
- Obstructive uropathy
- Urinary tract infection
- Bleeding and clotting disorders
- Trauma, bladder catheterization
- Cortical necrosis (Hypoxic/ischemic perinatal insult)
- Nephrocalcinosis (Frusemide in premature)
## Colour of urine:

<table>
<thead>
<tr>
<th>Colour</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dark yellow</td>
<td>Normal concentrated urine</td>
</tr>
<tr>
<td>Dark brown or black</td>
<td><strong>Bile pigments</strong></td>
</tr>
<tr>
<td></td>
<td>Homogentisic acid, melanin, tyrosinosis, methemoglobinuria</td>
</tr>
<tr>
<td>Cola coloured</td>
<td><strong>Glomerular hematuria</strong></td>
</tr>
<tr>
<td>Red or pink urine</td>
<td>Extraglomerular hematuria, Hemoglobin, Myoglobin, Porphyrins, drugs, Beets, blackberries, Rifampin, Red dyes in food, Urates</td>
</tr>
</tbody>
</table>
D/D of high coloured urine:

All that glitters (yellow) is not gold.

Red is not blood
History:

Characteristics of urine  Red Urine

- Amount of urine: Reduced in AGN, ARF
- Clots in urine: Extraglomerular
- ↑ Frequency, Dysuria, recent enuresis: UTI
- Frothy urine: Suggests Proteinuria seen in Glomerular diseases
- Timing: Initial stream – from urethra (Urethrorrhagia – spotting in underwear); Terminal (with suprapubic pain, disturbance of micturition) – from bladder shistosomaasis
History:

Associated Symptoms:
- Fever: Infections, SLE, AGN
- Facial puffiness, Oedema of legs, weight gain, Shortness of breath: **Acute Glomerulonephritis**
- Hypertension (Headache, visual changes, epistaxis, seizures): AGN, ARF
- Abdominal pain: Urolithiasis (Loin to groin), UTI, clots,
- Painless: Glomerular
- Abdominal mass: Hydronephrosis, PKD, Wilm’s tumour
- Joint pain (HSP, SLE)
- Rashes (HSP, SLE,
- Neurologic – SLE, HUS (seizures, irritability)
- Jaundice: Hemolysis,
History:

- H/o exercise, menstruation, recent bladder catheterization or passage of a calculus
- Recent upper respiratory (1-2wks back), skin infection (3-6 wks): PSGN or GI infection: HUS, HSP nephritis Gross hematuria precipitated by URI: Alport syndrome,
- H/o bleeding from other sites: Bleeding disorders,
- H/o Trauma, abdominal surgery, Child abuse (Social factors - Munchausen), crush injury
- H/o ingestion of drugs (Rifampicin, Ibuprofen, Chloroquine, Metronidazole, Iron), i.v. contrast agents (Toxic nephropathy, RVT)
History:

- Family h/o: Hereditary glomerular diseases (Alport syndrome, Thin glomerular Basement Membrane Disease, IgA Nephropathy), Urolithiasis, Hypercalciuria, Sickle cell disease/trait; H/o consanguinity or affected siblings in ARPKD,
Examination:

- **Vitals:**
  - BP: ↑ in AGN, PKD
  - Temperature
- **Oedema:** in AGN
- **Pallor:** Bleeding disorders, HUS, SLE, CRF
- **Anthropometry**
- **Skin lesions** (HSP, SLE, ), Bruises (Trauma)
- **Per abdomen:** Mass: Hydronephrosis (Urinary tract obstruction), Wilms tumour; ARPKD, RV thrombosis in neonate, hydronephrosis
Examination:

- Kidneys
- Bladder palpable: Distal obstruction
- Tenderness: HSP

hypospadias, Genital trauma, Foreign bodies
Examination:

- Signs of Congestive cardiac failure, HTNsive encephalopathy: AGN
- Joint swelling, tenderness: HSP, SLE
- Hearing assessment: Alport (B/L SNHL)
Investigations:

- Detail history and comprehensive examination → Aids in diagnosis and directs the course of investigations

Steps:

I. Cause of the colour change: Urinalysis for RBC, hemoglobin/myoglobin or other causes
II. Localization of bleeding site: Glomerular or Extraglomerular (Upper or lower urinary tract)
III. R/o infection
IV. R/o Structural anomalies
V. Renal function
VI. R/o Systemic diseases
Investigations:

- **Urine dipstick test** Based on the peroxidase-like activity of hemoglobin (a reagent strip impregnated)
  - It can detect trace amounts (0.02 to 0.03 mg/dL) of hemoglobin and myoglobin.
  - Can detect 5-10 intact RBC per mm$^3$ of unspun urine
  - False +ve: Urine pH >9, H$_2$O$_2$
  - False –ve: High ascorbic acid, formalin
- Also for urine albumin
Investigations:

Urine microscopy: Presence of RBCs and casts (> 5 RBCs per HPF) in centrifuged urine

**Glomerular**
1. Brown, cola coloured or smoky
2. RBC casts
3. Proteinuria 2+ or more
4. Deformed urinary RBCs

**Non-glomerular**
1. Bright red, pink
2. Terminal hematuria/
   Passage of clots
3. Proteinuria of < 2+
4. Normal morphology of RBCs
Investigations:

Urine microscopy:
- Albumin: Glomerular cause
- Pus cells, WBC casts: Urinary tract infection, AGN, Eosinophils in Interstitial nephritis
- Crystals (Oxalates), bacteria, protozoa (*Schistosoma hematobium* ova)

Confirmation by dipstick and sediment examination is necessary to differentiate between true hematunia, pigmenturia, and interfering compounds such as beets or aniline dyes.
APPROACH TO HEMATURIA

History & PE

URINALYSIS

Hb/RBC absent

RBC +/- Hb

Check RBC morphology

Hb only, No RBC

myoglobinuria or hemoglobinuria

Search other cause of red urine

GLOMERULAR

NON-GLOMERULAR
Microscopic hematuria with proteinuria

Oedema, Hypertension

Yes

CBC, RFT, Alb, Chol, ASO, dsDNA titre, Renal USG, C3, C4

Yes

AGN Abn

No

+ve

Rpt. Urine in 1 wk

-ve

F/U as indicated
Investigations:

- **Urine C/S**
- **RFT**: Blood urea nitrogen/serum creatinine, Na/K (↓Na in AGN, ↑K in ARF)
- **Complete blood counts (CBC)**: Hb - ↓ in bleeding, HUS, SLE, CRF; Abnormal TC, DC in infections, HUS, ↓ in SLE;
- **Platelet counts and Coagulation studies**: (history suggestive of bleeding disorder, HUS), Sickle cell (Hemoglobin electrophoresis)
- **PBS**: Microangiopathic hemolytic anemia
- **ESR, CRP**: Infections
- **24 hr urinary protein, Spot urinary protein**: Creatinine ratio, Serum al and cholesterol if associated proteinuria (Nephrotic syndrome)
- **Urine calcium**: Hypercalciuria is a relatively common finding in children.
  - 24-hour urinary calcium (>4 mg/kg/d), or
  - Spot urine calcium-creatinine ratio >0.21
Investigations:

**SeroLogic testing:**
- ASO titer, Anti-DNase B
- Low serum C₃ are seen in postinfectious glomerulonephritis, SLE nephritis, Bacterial endocarditis and membranoproliferative glomerulonephritis.
- ANA, anti dsDNA (SLE)
- ANCA, Anti-GBM Ab

Throat swab C/S
Investigations:

- **Imaging Studies**
  - Renal and bladder **sonography**: Urinary tract anomalies, such as hydronephrosis, hydroureter, nephrocalcinosis, tumor, and urolithiasis, Renal parenchymal disease
  - **X-Ray KUB**: calculi
  - **Doppler study of renal vessels and IVC**: Renal vein thrombosis
  - Intravenous urography
  - **Spiral CT scan**: Urolithiasis, Wilms tumor and polycystic kidney disease, Renal trauma
  - **Micturating cystourethrogram**: Urethral and bladder abnormalities (eg, cystitis), in recurrent UTI to r/o VUR, anomalies
  - **Radionuclide studies**: Renal function and perfusion
  - Angiogram
  - **Chest X-Ray**: (Pulmonary oedema, CHF)
Investigations:

Investigations for recurrent/multiple Urolithiasis:

- Serum Calcium, Phosphorus, Uric acid, electrolytes, Alkaline phosphatase, Creatinine
- Urine: C/S, Ca:Cr ratio; 24 hr Urinary Calcium, Creatinine, Phosphorus, oxalate, uric acid; Spot test for cystine
Investigations:

Renal biopsy:

**Relative indications** -

- Significant proteinuria (3+ or more) or nephrotic syndrome +
- Recurrent persistent hematuria (Microscopic \( \geq 2 \text{ yrs} \))
- Abnormal renal function, Persistent HTN
- Hematuria, Proteinuria, diminished renal function, low C3 level persist beyond 2 mo of onset of AGN
- Absence of evidence of streptococcal infection
- Serologic abnormalities (abnormal ANA or dsDNA levels)
- A family history of end stage renal disease or evidence of Chronic renal disease in patient
Investigations:

- Cystourethroscopy: Terminal hematuria, disturbances of micturition, suprapubic pain (Only if strong suspicion of bladder ulceration, tumours)
- Screening of first degree relatives in persistent hematuria
- Investigations for other causes of red urine: Methemoglobin level, Plasma Tyrosine, Urine homogentisic acid, Uroporphyrins
Management:

According to cause:

- Reassurance and F/U
- Treat cystitis, pyelonephritis, AGN: Antibiotics
- Supportive treatment: Fluid and salt restriction, Antihypertensives
- Monitoring – BP, I/O, weight, Urine R/M
- Treat Hyperkalemia, ARF, CHF, acidosis, fluid overload, HTN and its complications
- ACE inhibitors useful in proteinuria
- Immunosuppressive therapy: Depending on cause (Steroids, cyclophosphamide) SLE
Is it related to our talk
Cola/brown urine? 
Proteinuria > 30mg/dL? 
RBC cast? 
acute nephritic syndrome?

**YES**

Glomerular hematuria
- CBC with differential
- Electrolytes, ca
- BUN/creatinine
- Serum protein/albumin
- Cholesterol
- C3/C4
- ASO/Anti DNase B
- ANA
- Antineutrophil antibody
- throat/skin culture if indicated
- 24 hour urine total protein creatinine clearance

**Extraglomerular hematuria**

Step 1
- Urine culture

Step 2
- Urine calcium/creatinine
- Sickle prep
- Renal/bladder USG

Step 3
- Urine analysis, siblings, parents
- Serum electrolytes, Cr,Ca
- 24hr urine Ca, creatinine, uric acid, oxalate( if crystauria, nephrolithiasis
- Cystogram, +/- renal scan if hydronephrosis/pyelocallictasis

**NO**
THANK YOU