- *Presence of RBC's in urine*
- > 2-3 RBC/HPF(x400) of centrifugal, freshly voided urine
- DD from urine discoloration by pigments
  - Proteinaceous materials;
    - Hemoglobin: in acute hemolytic attack
    - myoglobin : in rhabdomyolysis
  - Other substances;
    - food dyes,
    - drugs (Rifampicin)

## Initial approach to patient with hematuria

1. genuine erythrocyturia
   a. Dip stick test to confirm genuine erythrocyturia (and exclude rare hemoglobinuria/myoglobinuria)
   b. followed by microscopy to confirm erythrocyte presence
2. Microscopic or macroscopic?
   a. By Change in urine colour
3. Intermittent or sustained: gives indication to site of bleeding within the UT
   a. Start of voiding then urine becomes clear: urethra.
   b. Throughout stream: bladder or above.
   c. End of micturition: prostate or base of bladder
4. Is it accompanied with proteinuria?
   a. proteinuria if protein > 1000 mg/24hr
5. Associated with menstruation or catheterization?
6. Associated with infection if:
   a. Microscopy (clean sample of midstream urine):
      i. Pyuria; 10 or more WBCs/cm3
      ii. Positive bacterial culture. Culture before antibiotic therapy for sensitivity.
   b. Dipstick test for nitrates

## Types of Hematuria

| Glomerular | Non-Glomerular | Intermediate |
|---|---|---|
| Presence of dysmorphic RBC | erythrocytes have normal morphology | some dysmorphic erythrocytes |
| Proteinuria>1000 mg/24 hr | Proteinuria absent or <500 mg/24 hr | Proteinuria present but <1000 mg/24 hr |
| Presence of erythrocytes casts | Absence of erythrocyte casts | Absence of erythrocyte casts |
| Absence of symptoms, signs or other evidence of nonglomerular hematuria | Symptoms, signs, or other evidence of nonglomerular urinary tract pathology | |
| Microscopic and macroscopic | Microscopic and macroscopic | Microscopic and macroscopic |

## Why do we see casts in Glomerular aetiologies and not non-Glomerular?

Answer: because casts appear when there is abnormal cells that adhere to Tamm-Horsfall protein, this protein is found in the tubules and that is why casts don't appear in Non-Glomerular disease

## Causes of hematuria:

1. Glomerular hematuria

| Primary glomerulonephritis | Multi-system Autoimmune Disease | Other |
|---|---|---|
| 1. **Mesangial proliferative glomerulonephritis (IgA Nephropathy) – most common** | 1. Systemic Lupus Erythematosus | Hereditary (e.g., Alport's disease, thin membrane disease, nail-patella syndrome, Fabry's disease) |
| 2. **Membranoproliferative glomerulonephritis** | 2. Vasculitis (e.g., Wegener's granulomatosis, microscopic polyangiitis, Churg- Strauss angiitis, Henoch-Schönlein purpura) | Infection-associated glomerulonephritis (e.g., 1. HIV nephropathy, 2. poststreptococcal glomerulonephritis, 3. Infective endocarditis, 4. shunt nephritis |
| 3. **Crescentic glomerulonephritis** | 3. Scleroderma glomerulopathy | |
| 4. **Anti–glomerular basement membrane disease ( goodpasture syndrome)** | 4. Thrombotic microangiopathy (e.g., anti-phospholipid syndrome, hemolytic uremic syndrome) | |
| 5. **Focal, segmental glomerulosclerosis** | | |
| 6. **Membranous glomerulonephritis (<30%)** | | |
| 7. **Minimal change glomerulonephritis (<20%)** | | |
| 8. **Fibrillary glomerulopathy** | | |

2. **Nonglomerular hematuria**
    a. **Renal in origin:**
        i. Interstitial disease
            1. Tubulointerstitial disorder
            2. Hypersensitivity tubulointerstitial nephritis
            3. Tubulointerstitial nephritis with uveitis
            4. Sjögren's syndrome
        ii. Vascular:
            1. Vascular disorder
            2. Malignant hypertension
            3. Scleroderma renal crisis
            4. Polyarteritis nodosa
            5. Renal embolism or arterial or venous thrombosis

6. Arteriovenous malformation

iii. Neoplasia (e.g., renal cell carcinoma, Wilms' tumor, leukemia, lymphoma, metastatic disease)
iv. Papillary necrosis (causes include diabetes mellitus, sickle cell anemia, analgesic abuse, and obstructive uropathy) MCQ!
v. Infection
    1. pyelonephritis,
    2. tuberculosis,
    3. hantavirus,
    4. BK virus in transplants
vi. Hereditary
    1. polycystic kidney disease
    2. medullary sponge kidney
vii. Trauma
viii. Idiopathic renal hematuria

b. Urinary tract origin:
    i. Neoplasia
        1. Transitional cell carcinoma
        2. Carcinoma of bladder, prostate, or urethra
    ii. Mechanical injury
        1. Calculi (e.g., calcium oxalate/phosphate, uric acid, xanthine, cysteine, struvite, drugs)
        2. Trauma or foreign body
    iii. Infection (e.g., periureteritis, cystitis, prostatitis, urethritis, tuberculosis, Schistosoma haematobium)
    iv. Inflammatory
        1. Retroperitoneal fibrosis/aortitis
        2. Endometriosis
        3. Diverticulitis, appendicitis, Crohn's disease
        4. Hypersensitivity cystitis or urethritis
        5. Vasculitis (polyarteritis nodosa and Churg-Strauss angiitis)
    v. Malformations
        1. Nevi
        2. Vascular malformations
        3. Hereditary hemorrhagic telangiectasia
    vi. Drug and radiation-induced hematuria (e.g., by cyclophosphamide, nitrogen mustard)
    vii. Urinary obstruction or relief of obstruction
c. Other:
    i. Loin-pain hematuria syndrome
    ii. Acquired cystic disease of renal failure
    iii. Coagulation disorder (e.g., thrombocytopenia, hemophilia, anticoagulant therapy)
    iv. Factitious (malingering)

## Approach to patient with hematuria:

- History:
    - Recent symptoms:
        - Fever
        - Rash
        - Weight loss
    - Previous disease
        - DM
        - Malignancy
    - Family history

    - Drug history
        - Aspirin
        - Herbal medicine
- Examination:
    - Purpura in vasculitis
    - Deafness in Alport Syndrome
    - Flank mass in polycystic disease
- Lab Findings:

| Relevant Abnormal Findings | Diagnosis |
|---|---|
| • **C3/C4, C3 nephritic factor**<br>• **Cryoglobulins**<br>• **Hepatitis B/C** | Membranoproliferative Glomerulonephritis (MPGN) |
| • **Anti-GBM antibodies**<br>• **Chest radiograph** | Anti-GBM Disease |
| • **ANA**<br>• **Anti-dsDNA**<br>• **ENAs**<br>• **C3/C4**<br>• **Anticardiolipin** | SLE (Systemic Lupus Erythmatosus) |
| • **ANCA (C-ANCA/PR3-ANCA or P-ANCA/ MPO-ANCA)** | Vasculitis:<br>• Wegener's granulomatosis<br>• Microscopic polyangiitis<br>• Churg-Strauss angiitis |
| • **Anti-cardiolipin**<br>• **Lupus anticoagulant** | Thrombotic microangiopathy |
| **Hereditary** | |
| • **Abnormal audiometry** | Alport syndrome |
| • **Plasma alpha-galactosidase A activity** | Fabry's disease |
| **Infection-Associated Glomerulonephritis** | |
| • **HIV positive** | HIV nephropathy |
| • **ASO (Antistreptolysin O Titer)**<br>• **Anti-DNAase**<br>• **C3/C4**<br>• **Rheumatoid factor** | Poststreptococcal Glomerulonephritis |
| • **Echocardiography**<br>• **C3/C4**<br>• **Rheumatoid factor** | Infective Endocarditis |