Definition:

- **Haematuria** is the presence of red blood cells in the urine. The presence of 10 or more RBCs per high-power field is abnormal in 3 of 3 consecutive centrifuged specimens obtained at least 1 week apart.

- Urinary dipsticks are very sensitive and can be positive at <5 RBCs per high-power field in 3 of 3 consecutive centrifuged specimens obtained at least 1 week apart.
Types:

According to the amount of RBC in the urine, hematuria can be classified as:

- Gross (ie, overtly bloody, smoky, or tea-colored urine)
- Microscopic > 10 RBC’s /HPF

According to Timing (when it occurs during urination):

- Early (initial) haematuria: Urethral origin, distal to external Sphincter
- Terminal haematuria: Bladder neck or prostate origin
- Diffuse (total) haematuria: Source is in the bladder or upper urinary tract
PATHOPHYSIOLOGY:

- Glomerular
- Non glomerular

**False haematuria**: Discolouration of urine from pigments such as food colouring and myoglobin.

**Silent haematuria** is due to tumours of kidney or bladder unless proved otherwise.
AETIOLOGY

- Diseases of the urinary system - the most common cause
  - Glomerular
  - Interstitial
  - Uroepithelium
  - Vascular
Glomerular
- IgA nephropathy
- Glomerulonephritis

Interstitial
- Allergic interstitial nephritis
- Analgesic nephropathy
- Renal cystic diseases
- Acute pyelonephritis
- Tuberculosis
- Renal allograft rejection
Uroepithelium

- Malignancy
- Trauma
- Papillary Necrosis
- Cystitis/Urethritis/Prostatitis
- Parasitic Diseases (Schistosomiasis)
- Stones

Vascular

- Arterial emboli or thrombosis
- Arteriovenous fistulae
- Renal vein thrombosis
System disorders (less common):

**Haematological disorders**-- aplastic anemia, leukemia hemophilia, ITP (idiopathic thrombocytopenic purpura)

**Infection**-- infective endocarditis, Septicemia, epidemic hemorrhagic fever, scarlet fever, Filariasis

**Connective tissue diseases**-- SLE, polyarteritis nodosa

**Cardiovascular diseases**-- hypertensive nephropathy, chronic heart failure - renal artery sclerosis.

**Endocrine and metabolism diseases**-- gout - diabetes mellitus
Diseases of adjacent organs to urinary tract

Appendicitis
carcinoma of the rectum
carcinoma of the colon
uterocervical cancer

Drug and chemical agents
anticoagulation,Cyclophosphamide, rifampin, sulfonamide, phenytoin,

Miscellaneous
exercise induced hematuria
CAUSES:

Benign:
- Glomerulonephritis
- Infarct
- Renal stone
- Tuberculosis
- Trauma
- Ureteric stone

Malignant:
- Renal tumour
- Papillary carcinoma
- Ureteric tumour

Bleeding disorders:
- Cystitis
- Tuberculosis
- Bladder stone
- Endemic haematuria
- Benign prostatic hyperplasia

Bladder tumours
- Carcinoma prostate

Urethral injury
- Urethral tumours
DIFFERENTIAL DIAGNOSIS

• Polluted urine: menstruation

• Drug and food: Rifampicin, Nitrofurantoin, sulfonamides, adriamycin.

• Porphyria: porphyrin in urine (+)

• Hemoglobinuria (hemolysis)

• Myoglobinuria
Signs and symptoms

The first step in the evaluation of haematuria consists of a detailed history and a thorough **physical examination**.

Efforts should be made to distinguish **glomerular causes** from **extraglomerular** ones:

- Passage of clots in urine suggests an **extraglomerular** cause
- Fever, abdominal pain, dysuria, frequency, and recent enuresis in older children may point to a **urinary tract infection** as the cause
- Recent trauma to the abdomen may be indicative of hydronephrosis
- Early-morning periorbital puffiness, weight gain, oliguria, dark-colored urine, and edema or hypertension suggest a glomerular cause, Hematuria due to glomerular causes is painless
- Recent throat or skin infection may suggest post infectious glomerulonephritis
Joint pains, skin rashes, and prolonged fever in adolescents suggest a collagen vascular disorder (Rheumatoid arthritis, Systemic lupus erythematosus).

Skin rashes and arthritis can occur in Henoch-Schönlein purpura and systemic lupus erythematosus.

Information regarding exercise, menstruation, recent bladder catheterization, intake of certain drugs or toxic substances, or passage of a calculus may also assist in the differential diagnosis.

A family history that is suggestive of Alport syndrome, collagen vascular diseases, urolithiasis, or polycystic kidney disease is important.

Alport syndrome is a genetic condition characterized by kidney disease, hearing loss, and eye abnormalities. People with Alport syndrome experience progressive loss of kidney function. Almost all affected individuals have blood in their urine (haematuria), which indicates abnormal functioning of the kidneys.
Physical examination

- Measurement of the blood pressure and volume status is especially important when glomerulonephritis is a consideration.

- Evaluation for the presence of periorbital puffiness or peripheral edema

- Detailed skin examination to look for purpura.

- Abdominal examination to look for palpable mass reveals a renal tumor or hydrenephrosis may exist,

- A palpable bladder after voiding indicates obstruction or retention
A bruit over the kidney suggests a vascular cause.

Always check for extrarenal manifestations and co morbid conditions.

Check for other sites of bleeding. PR examination should not be missed. to diagnose prostatitis, prostate cancer, epididymitis, meatal stenosis, and other structural causes of hematuria.

Inspect external genitalia in male for trauma.

Atrial fibrillation raises the possibility of renal embolic infarction, especially if the patient has flank pain.

Costovertebral angle tenderness is also suggestive of pyelonephritis, nephrolithiasis, or ureteropelvic junction obstruction.

Detailed ophthalmologic evaluation (in familial hematuria)
Diagnosis

- The laboratory tests ordered for the evaluation of hematuria must be based on the clinical history and the physical examination. Tests that may be helpful include the following:
  - Urinalysis with careful microscopic review of the urine sample
  - **Urine dip strip analysis it is the most** commonly used method of testing the urine for blood is the urine test strip or dipstick, which utilizes the peroxidase-like activity of hemoglobin to generate a color change.
  - False-positive tests may occur in the setting of myoglobinuria or hemoglobinuria, confirmed by the absence of RBCs on microscopic examination.
- Phase-contrast microscopy to help determine the source of the bleeding

- Hematologic and coagulation studies (eg, full blood count [FBC] and, sometimes, platelet counts)

- Blood urea nitrogen (BUN) for paraneoplastic syndrome and serum creatinine levels for kidney failure.

- Serologic testing (eg, complement, antistreptolysin [ASO], anti-DNase B, antinuclear antibody [ANA], and double-stranded DNA [dsDNA])

- Urine culture for suspected urinary tract infection (UTI)
Research from Pacific Edge\(^1\) shows that messenger RNA (mRNA) levels of specific biomarkers are present at higher levels of concentration in patient urine samples that are positive for bladder cancer than in patients who are negative for the disease.

Cxbladder Biomarker Gene Descriptions

- **MDK: Blood vessel growth and cell migration**  
  Principally involved in cell proliferation, migration and angiogenesis in cancer cells.

- **HOXA13: Cell differentiation**  
  Principally involved in cell differentiation and the morphogenesis and differentiation of the genitourinary tracts.

- **CDC2 (CDK1): Cell division**  
  Cyclin dependent kinase. Essential to mitotic cell cycle: cell proliferation.

- **IGFBP5: Programmed cell death**  
  Acts as an anti-apoptotic gene.

- **CXCR2: Inflammation**  
  Mediates neutrophil migration to sites of inflammation. Moderates non-malignant inflammation (False Positives).
A small sample (5 mL) of mid stream urine is required for the test. The sample undergoes a precise set of processes to extract and purify the mRNA present in the patient urine sample.
The purified RNA is then quantified by a technique called Reverse Transcription quantitative Polymerase Chain Reaction or RT-qPCR. RT-qPCR first involves the conversion of RNA to DNA and then the amplification of that DNA by millions of fold, regulated by a repetitive cycle of temperature adjustment. The resulting millions of copies of DNA are detected by a probe whose fluorescence is directly proportional to the number of copies of DNA present.
In the Cxbladder test, each of the five biomarkers of interest to us is quantified by a different probe and the relationship between the individual biomarkers is determined by a mathematical equation. The calculated outcome provides a measure of the probability of the presence of urothelial carcinoma (UC).
**Cx Bladder Cancer Test**

- **How Cxbladder can be used in your practice:**
  - Replace the need for other urine-based tests in primary workup.
  - Complement cystoscopy for bladder cancer detection.
  - Detect urothelial tumors not visible by cystoscopy.
  - Replace the need for CT / IVP in primary workup in some instances.
  - Improve patient compliance with accurate, non-invasive testing.
Pacific Edge Named in TIN100 Top 10 List

- We are delighted to be named in the top 10 Hot Emerging Companies in the TIN100 2016 report, alongside amazing people from Vend, PushPay, ARANZ Medical and FlintFox, to name a few. TIN Managing Director, Greg Shanahan, said: "These ten companies almost doubled the record performance of the companies on last year's list with a continued revenue growth of over $61 million (or 138%). "All ten companies are exciting examples of how technology is disrupting the way we do business, from the development of wireless power systems to new remote methods for diagnosing cancer," Mr. Shanahan added. http://bit.ly/2emSWLc
Imaging studies

The following may be helpful:
- Renal and bladder ultrasonography
- Voiding cystourethrography
- CT urography: now replaces IVU.
- MRI.
- Retrograde pyelography.
- Renal biopsy: in nephrological cases
- Cystoscopy
Kidney biopsy is rarely indicated:

- Significant proteinuria
- Abnormal renal function
- Recurrent persistent hematuria
- Serologic abnormalities (abnormal complement, ANA, or dsDNA levels)
- Recurrent gross hematuria
- A family history of end-stage renal disease
- **Glomerular haematuria:**
  Brown-colored urine, RBC casts, and dysmorphic (small, deformed, misshapen, sometimes fragmented) RBCs and proteinuria

- **Nonglomerular hematuria:**
  Reddish or pink urine, passage of blood clots, and eumorphic (normal-sized, biconcavely shaped) Erythrocytes.
Management:

- Haematuria is a **sign** and **not itself a disease**; thus, therapy should be directed at the process causing it.

- Asymptomatic (isolated) haematuria generally does not require treatment.

- In conditions associated with abnormal clinical, laboratory, or imaging studies, treatment may be necessary, as appropriate, with the primary diagnosis.
Surgical intervention may be necessary with certain anatomic abnormalities (e.g., ureteropelvic junction obstruction, tumor, or significant urolithiasis).

Dietary modification is usually not indicated, except for children who may tend to develop hypertension or edema as a result of the primary disease process (e.g., nephritis).

Patients with persistent microscopic haematuria should be monitored every 6-12 months for the appearance of signs or symptoms indicative of progressive renal disease.
MORTALITY/MORBIDITY

• IN GENERAL, CHILDREN WITH ISOLATED ASYMPTOMATIC MICROSCOPIC HAEMATURIA TEND TO DO WELL,

• WHEREAS THOSE WITH ASSOCIATED FINDINGS (EG, HYPERTENSION, PROTEINURIA, ABNORMAL SERUM CREATININE LEVELS) ARE MORE LIKELY TO HAVE SERIOUS PROBLEMS.

• SINCE HAEMATURIA IS THE END RESULT OF VARIOUS PROCESSES, THE MORBIDITY AND MORTALITY RATES OF THE CONDITION DEPEND ON THE PRIMARY PROCESS THAT INITIATED IT.

Uh... when you say “MICROScopic Hematuria”...does that mean it is just a Little problem?
RACE:

• THE INCIDENCE OF HAEMATURIA IN SPECIFIC RACIAL GROUPS IS DETERMINED BY THE PRIMARY CAUSE.

• FOR EXAMPLE, IDIOPATHIC HYPERCALCIURIA IS INFREQUENT IN BLACK AND ASIAN CHILDREN,

• BUT RELATIVELY COMMON IN WHITES. CONVERSELY, HAEMATURIA CAUSED BY SICKLE CELL DISEASE IS MORE COMMON IN BLACKS THAN IN WHITES.
SEX:

• SEX MAY PREDISPOSE A CHILD TO SPECIFIC DISEASES THAT MANIFEST AS HAEMATURIA.

• FOR EXAMPLE, THE SEX-LINKED FORM OF ALPORT SYNDROME HAS A MALE PREPONDERANCE,

• WHEREAS LUPUS NEPHRITIS IS MORE COMMON IN ADOLESCENT GIRLS
AGE:

• PREVALENCE OF CERTAIN CONDITIONS VARIES WITH AGE.

• FOR INSTANCE, WILMS TUMORS ARE MORE FREQUENT IN CHILDREN OF PRESCHOOL AGE,

• WHEREAS ACUTE POSTINFECTIONOUS GLOMERULONEPHRITIS IS MORE FREQUENT IN THE SCHOOL-AGED POPULATION.

• IN ADULTS, HEMATURIA IS OFTEN A SIGN OF MALIGNANCY OF THE GENITOURINARY TRACT (EG, RENAL CELL CARCINOMA, BLADDER TUMORS, PROSTATIC TUMORS). THESE CONDITIONS ARE RARE IN CHILDREN.
THANK YOU