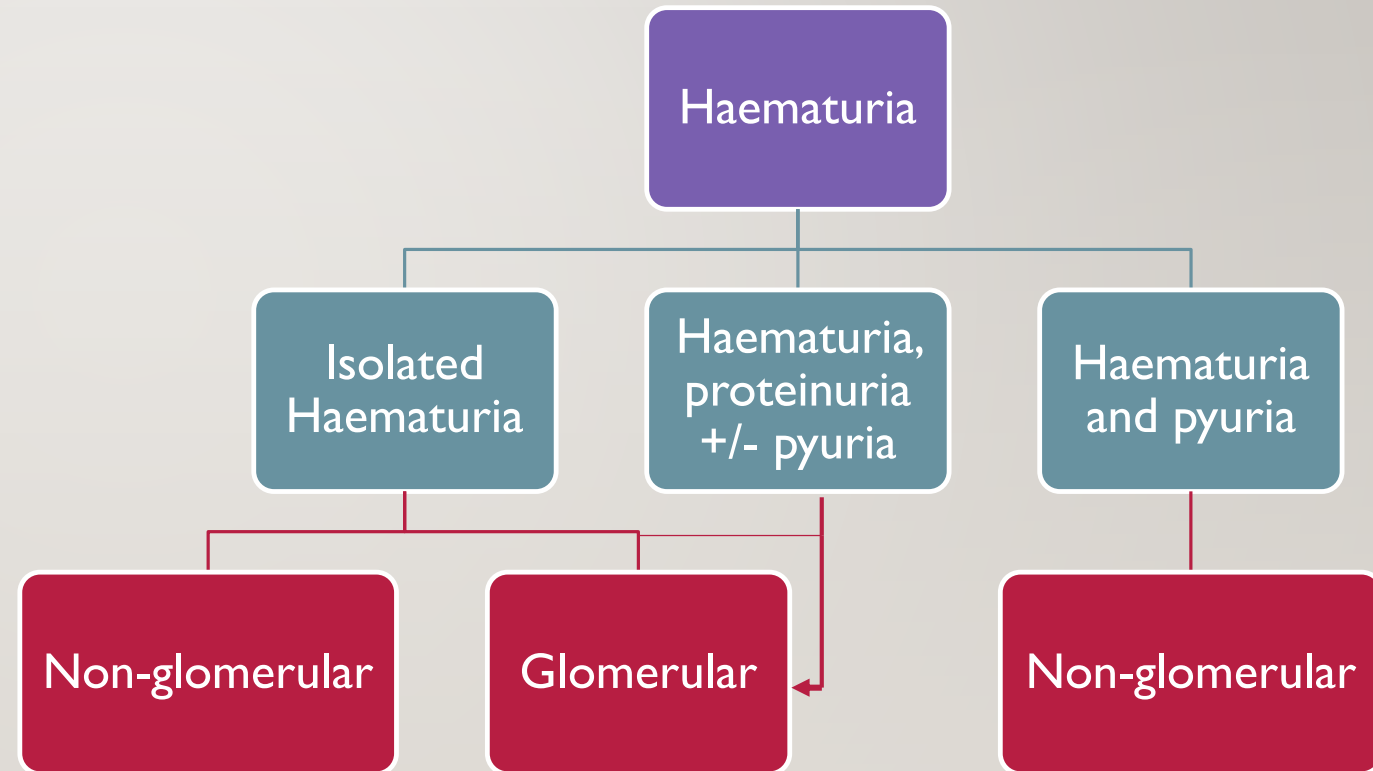
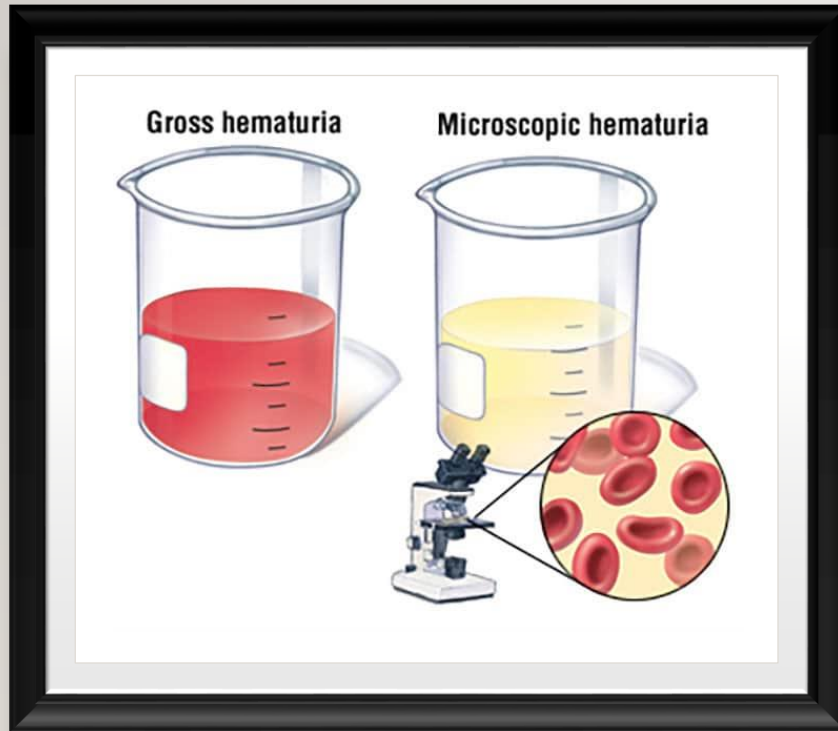


HAEMATURIA

17.6.2020



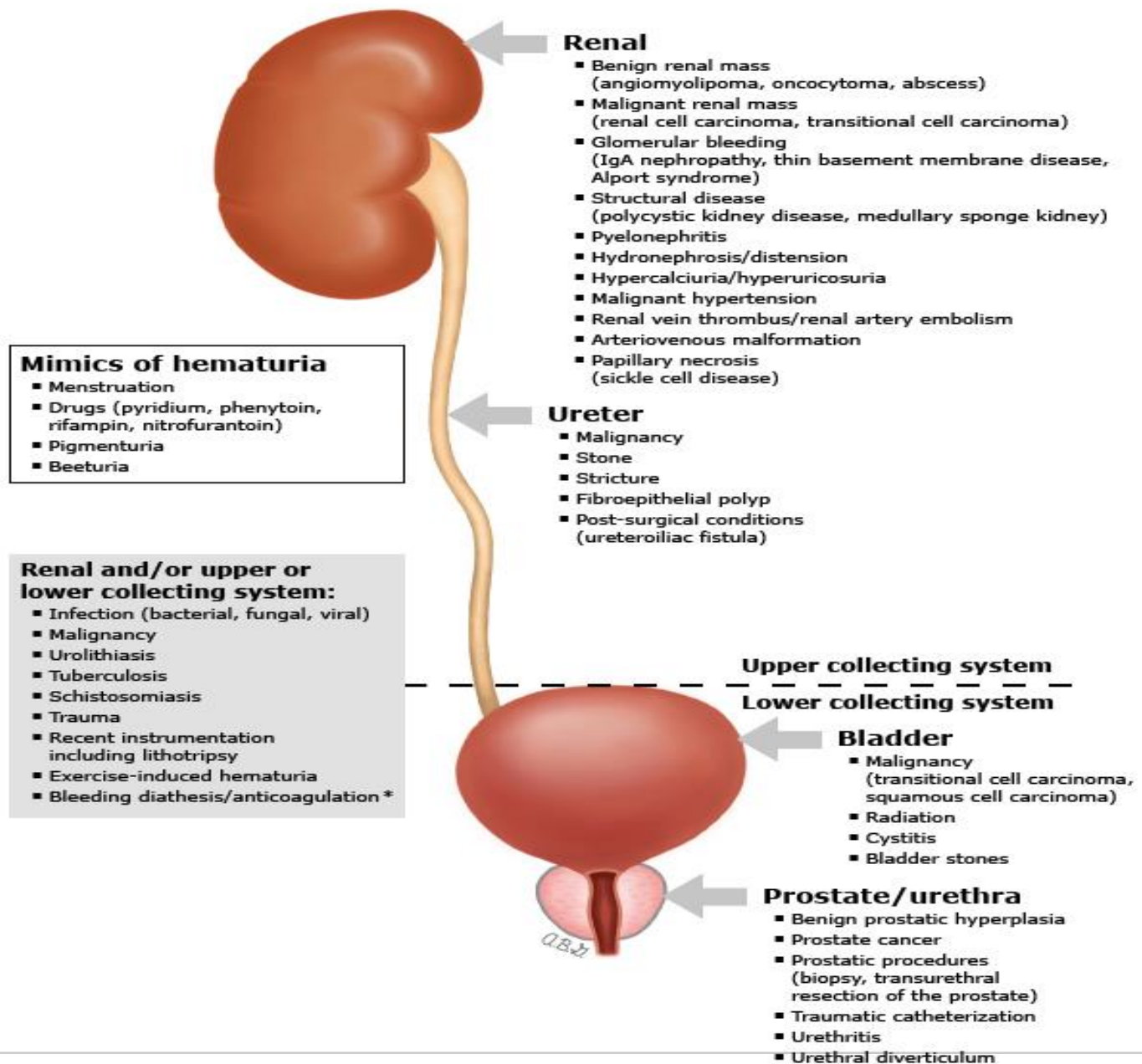


DEFINITION

- **Gross haematuria**
 - suspected when there is the presence of red or brown urine
- **Microscopic haematuria**
 - blood detectable only by microscopy



CAUSES



2020 UpToDate

IgA: immunoglobulin A.

* Hematuria may not be attributed solely to alterations in coagulation or platelet function until competing causes have been ruled out.

PREVALENCE

Macroscopic haematuria

More concerning and requires thorough investigations

Urological malignancy - typically 3 - 6%, but can be up to 19%^{1,2}

Lag time between onset of symptom and diagnosis³ – a diagnosis found in 18% of a studied population at 90 days, and 37 - 42% at 3 years

Microscopic haematuria

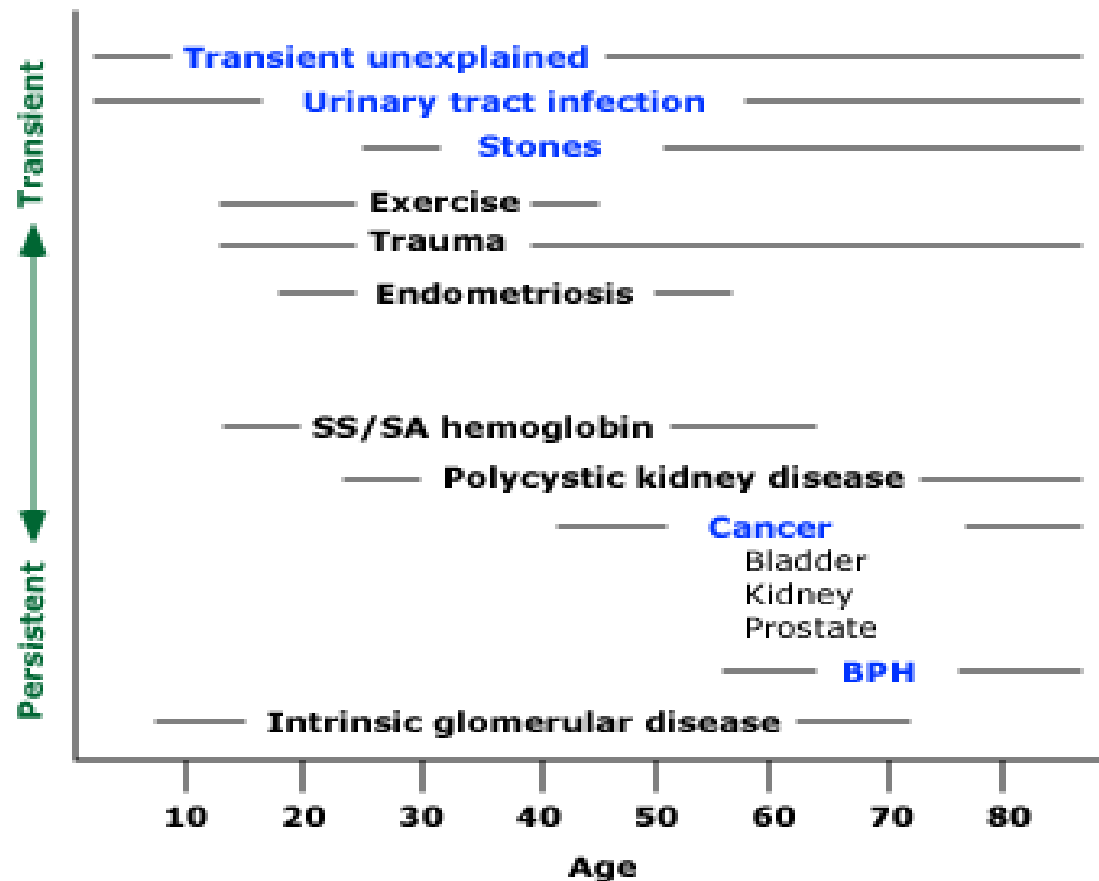
Common, up to 39% of population. Often transient and benign

Persistent haematuria occurs in 2.5 – 4.3% of adults seen in Primary Care⁴

A urological cause is often not identified, up to 61% in a study⁵

A symptom of malignancy in patients > age 35

Major causes of hematuria by age and duration



Schematic representation of the major causes of hematuria in relation to the age at which they usually occur (horizontal axis), transience or persistence (vertical axis), and frequency (blue implies more frequent).

BPH: benign prostatic hyperplasia.

HISTORICAL CLUES

- Dysuria and pyuria (UTI, renal tract tumour)
- Recent URTI (post infectious GN, IgA nephropathy)
- Unilateral flank pain (stones, pyelonephritis, tumours)
- Cyclic haematuria (menstruation, endometriosis)
- Hesitancy and dribbling (BPH, prostate cancer, bladder neck tumour)
- Recent vigorous exercise or trauma
- Frothy urine (proteinuria due to glomerular disease)

HISTORICAL CLUES

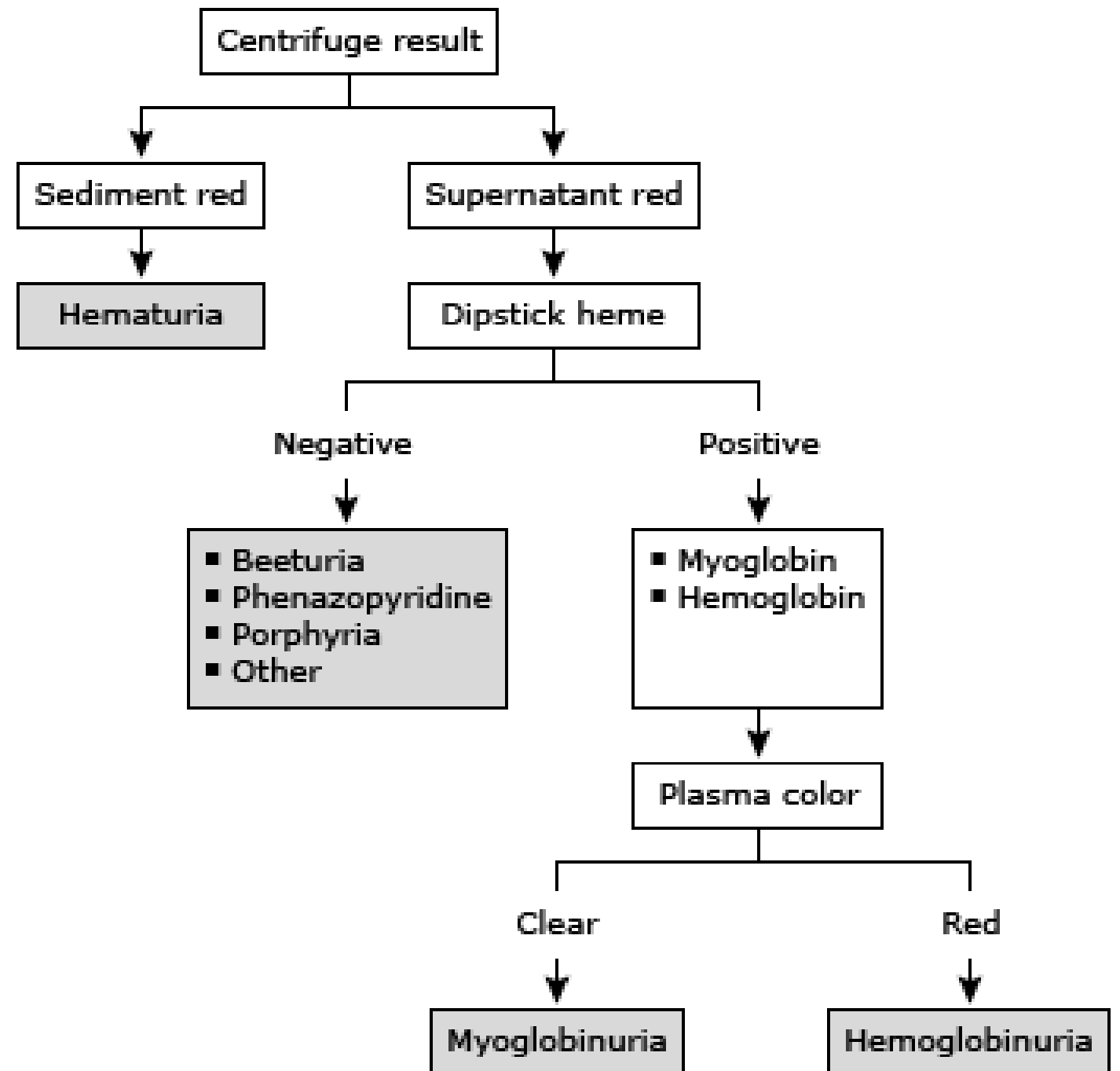
- History of a bleeding disorder or bleeding from multiple sites (anticoagulant)
- Medications (NSAIDs, colchicine, statin)
- Travel or residence in areas endemic for *Schistosoma haematobium* or TB
- Occupational history (exposure to chemicals and dyes such as benzenes and aromatic amines)
- Smoking history (increases risk of renal tract malignancy)
- Family history (polycystic kidney disease, Alport syndrome with hearing impairment)
- Ethnicity (African immigrants) - sickle cell disease

Glomerular	Non-Glomerular				Hematuria Mimics
	Non-Glomerular Kidney	Ureter / Bladder / Urethra	Prostate	Unknown	
<u>Immune-complex mediated</u> <ul style="list-style-type: none"> • IgA nephropathy • IgA vasculitis • Lupus nephritis • Infection-related glomerulonephritis 	Pyelonephritis Renal cell carcinoma Polycystic kidney disease Medullary sponge kidney	UTI** Urothelial cancer* (e.g. bladder cancer) Ureteral stones** (nephrolithiasis) Ureteral stricture <u>Hemorrhagic cystitis</u> <ul style="list-style-type: none"> • Chemotherapy • Pelvic irradiation Traumatic Foley catheter placement or removal Recent urologic procedure	BPH*? Prostate cancer	Exercise-induced hematuria* Idiopathic*	Contamination from menstrual blood Rhabdomyolysis (Myoglobinuria) Hemolytic anemia (Hemoglobinuria) Porphyria Beet ingestion (a.k.a. beeturia) Fictitious hematuria
<u>Anti-GBM disease</u> (a.k.a. Goodpasture's syndrome)					
<u>ANCA-associated vasculitis</u> <ul style="list-style-type: none"> • Polyangiitis with granulomatosis • Microscopic polyangiitis • Churg-Strauss syndrome 					
<u>Genetic disorders</u> <ul style="list-style-type: none"> • Thin basement membrane nephropathy 					

* Most common causes of gross hematuria

* Most common causes of microscopic hematuria

CONFIRMATION OF MACROSCOPIC HAEMATURIA



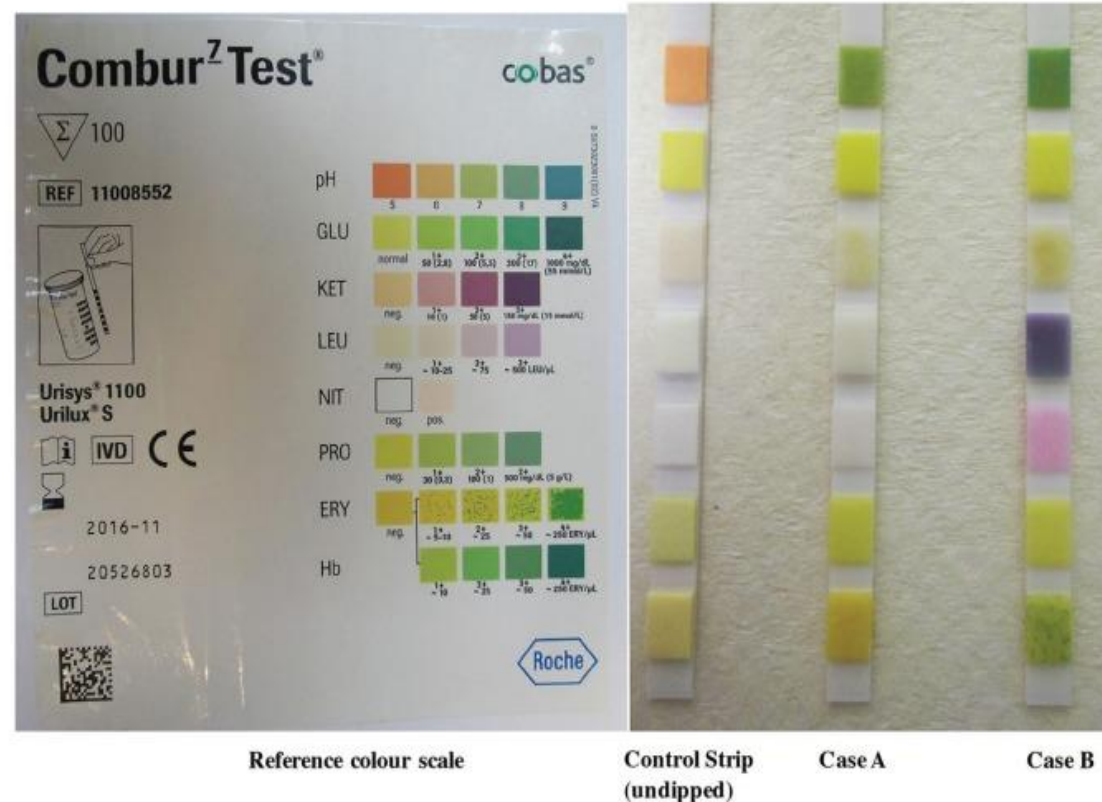
CONFIRMATION OF MICROSCOPIC HAEMATURIA

Urine dipstick

- Detect ≥ 2 RBCs per high-power field
- False positive tests due to
 - Semen
 - Alkaline urine with a pH > 9
 - Contamination with oxidizing agents used to clean the perineum
- False negative tests due to ingestion of large amounts of vitamin C

Urine microscopy

- Gold standard
- ≥ 10 RBCs per high-power field in NZ and Australia
- $\geq 3 - 10$ RBCs in USA and Europeans countries



NON-GLOMERULAR VS. GLOMERULAR HAEMATURIA

	Non-Glomerular	Glomerular
Colour if macroscopic	Red or Pink	Red, smoky brown, or “Coca-Cola”
Clots	May be present	Absent
Proteinuria**	< 0.5g / day	> 0.5g / day
RBC morphology**	Normal	Some are dysmorphic or <i>Acanthocytes</i>
RBC casts	Absent	May be present

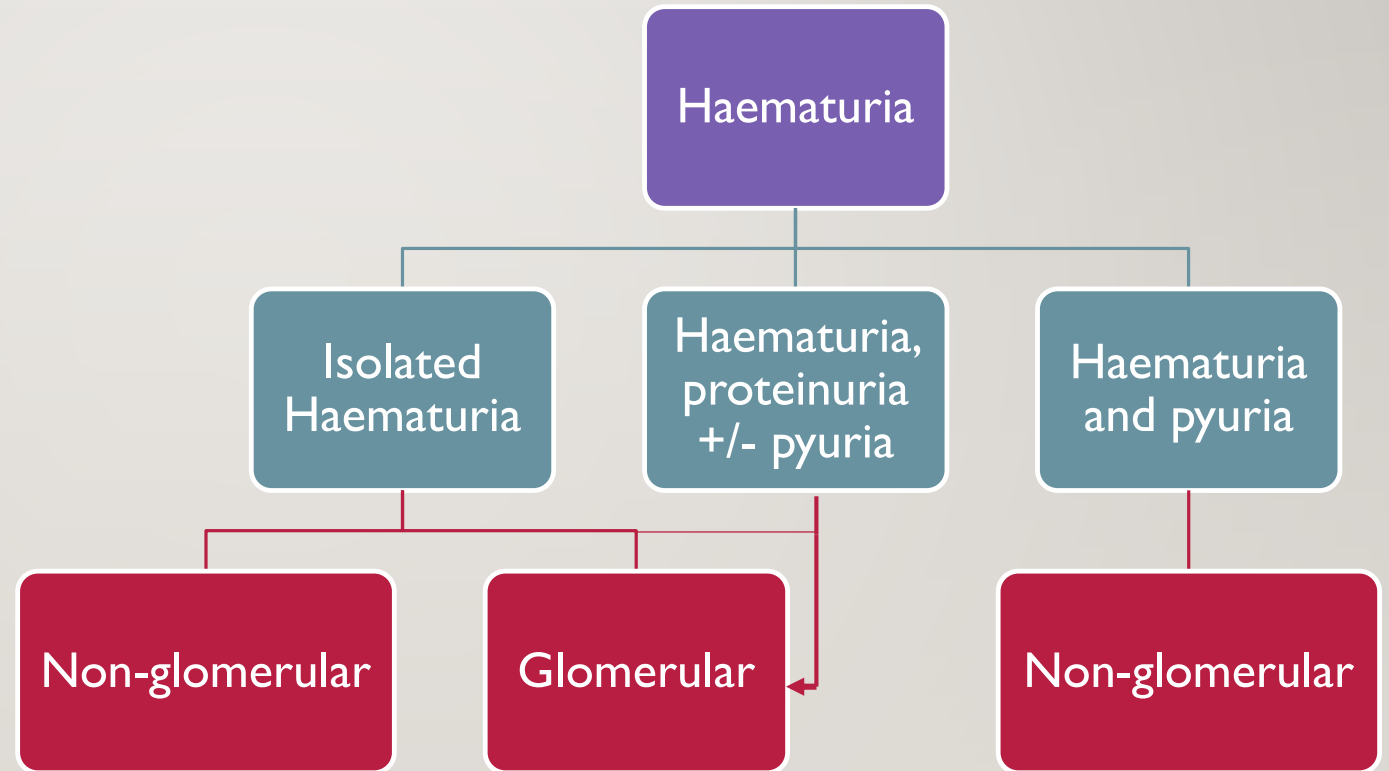
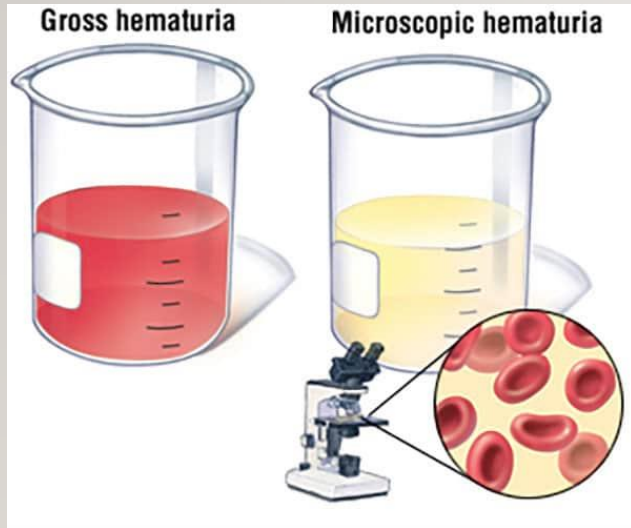
OTHER URINE INVESTIGATIONS

Urine Culture

- if findings suggestive of a urinary tract infection

Urine Cytology

- Poor sensitivity 40 – 76% in detecting a urological cancer, not a “rule-out” test
- Sensitivity 11% for low-grade cancer, and 60% of urothelial tumors present as low-grade and early stage
- Operator dependent



TRANSIENT ASYMPTOMATIC HAEMATURIA

- Common in adults
- No obvious aetiology found in most patients with transient haematuria
- Fever, infection, trauma and exercise are potential causes, and can occur with UTI
- Ideally repeat urine test in 6 weeks after an identified cause has resolved to see if there is persistent haematuria requiring further investigations
- Urological malignancy risk increases in patients over age 40 years

RISK FACTORS FOR RENAL TRACT MALIGNANCY

- Male gender
- Age > 35 years (> 40 years in NZ)
- Past or current smoking history
- Occupational exposure to chemicals or dyes (benzenes or aromatic amines), such as textile dye and rubber tyre industries, painters, leather works, shoemakers, and those working with aluminum, iron and steel
- Gross haematuria
- Chronic UTI
- Pelvic Irradiation
- Exposure to Cyclophosphamide
- Chronic indwelling foreign body
- Exposure to aristolochic acid
- History of analgesic abuse

RENAL TRACT MALIGNANCY

- A study of 1930 patients (mean age of 58 years, 62% male) who were referred to a haematuria clinic
- 12% had bladder cancer, 0.7% had kidney and upper renal tract tumours
- 61% had no cause identified

50 – 59 years			60 – 69 years		
Gender	Gross Haematuria	Microscopic Haematuria	Gender	Gross Haematuria	Microscopic Haematuria
Male	20.4%	1.9%	Male	28.9%	7.9%
Female	8.9%	1.9%	Female	21.5%	4.5%

IMAGING TO INVESTIGATE HAEMATURIA

CT Urography

- Low-dose radiation due to newer imaging techniques
- Preferred imaging modality and has replaced IVP and USS
- A pooled sensitivity 96% and pooled specificity 99% for detecting urothelial malignancy

Ultrasound

- Less sensitive in detecting renal tract malignancy, small renal masses and calculi.
- Preferred for pregnant women

MRI Urography

- Less sensitive for renal tract tumours
- Stones are nearly invisible
- Useful in detecting small renal masses and identifying tumours causing hydronephrosis

IMAGING TO INVESTIGATE HAEMATURIA

Cystoscopy

- A direct visualization of bladder, prostate and urethra
- May identify source of bleeding

Retrograde Pyelography

- Comparable with CTU in diagnosis of upper renal tract tumours
- Combined with cystoscopy to evaluate the urothelium if iodinated contrast is contradicted

UNEXPLAINED PERSISTENT AND ISOLATED HAEMATURIA

- No cause found from history, urinalysis, imaging studies or cystoscopy
- Mild glomerulopathy & predisposition to stone disease, in young and middle-aged patient
- Glomerular disease
 - IgA nephropathy +/- family history
 - Thin glomerular basement membrane nephropathy with +ve family history
 - Mesangioproliferative GN without IgA deposits
 - Alport syndrome (hereditary nephritis) +ve family and hearing impairment
- Non-glomerular
 - Hypercalciuria and hyperuricosuria

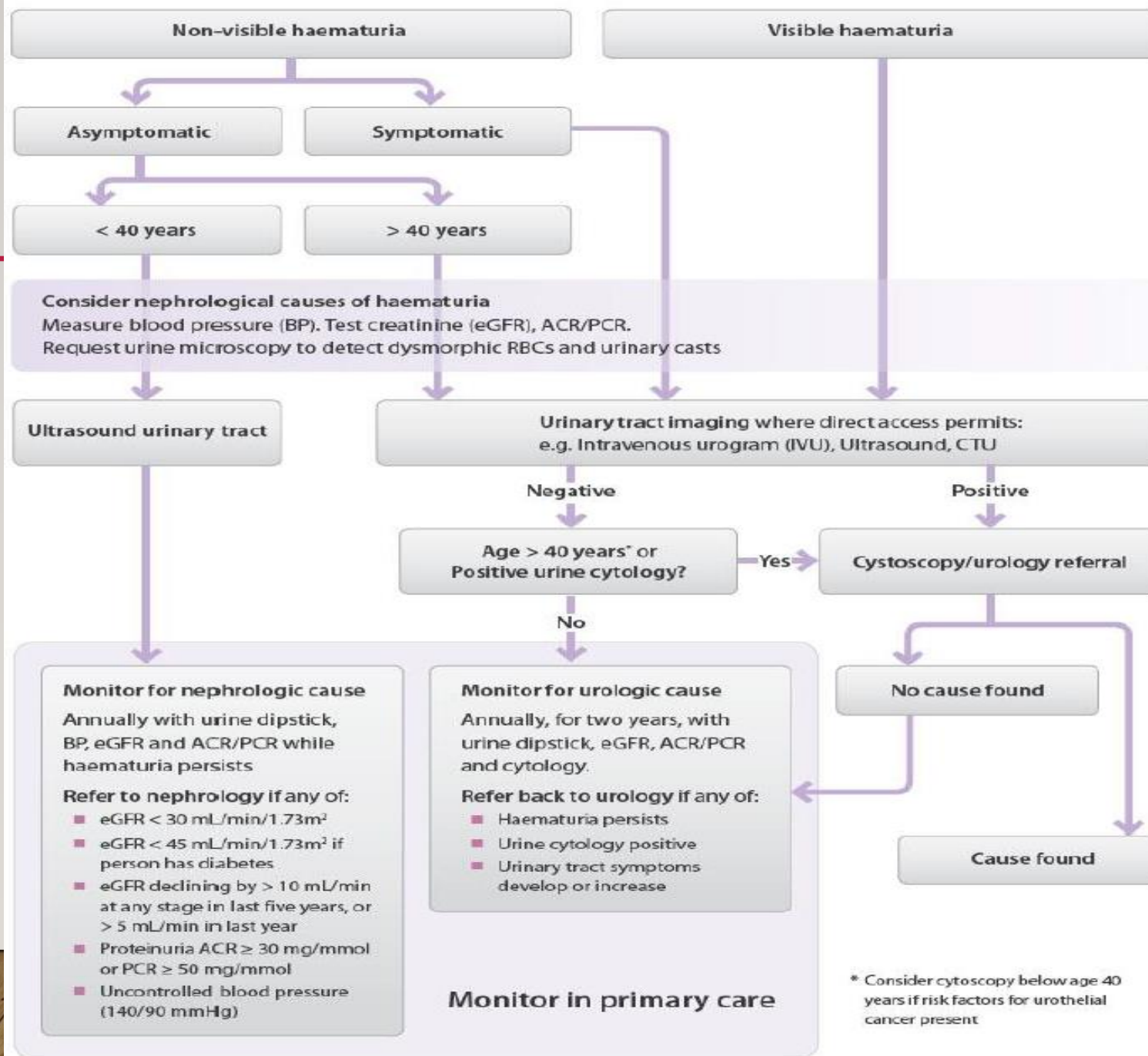
UNEXPLAINED TRANSIENT HAEMATURIA

- Heavy exercise
- Post-infectious glomerulonephritis

OTHER RARE CONDITIONS

- Hereditary haemorrhagic telangiectasis
- Radiation cystitis
- Schistosomiasis
- AV malformation and fistulas
- Nutcracker syndrome
- Loin pain-haematuria syndrome

Figure 2: Clinical assessment pathway



MONITORING IF RENAL BIOPSY NOT PERFORMED FOR ISOLATED GLOMERULAR BLEED

- Yearly lab tests for at least 5 years
- Serum creatinine, urinalysis, urine protein:creatinine ratio
- 560000 adults in a study -> 11% developed proteinuria at a mean follow up of 5.8 years
- 1.2million population study – 0.7% vs. 0.045% developed ESRD over 21.88 years of follow-up
- Progressive disease is more common if haematuria is due to IgA nephropathy

TAKE HOME MESSAGE

- Transient microscopic haematuria is common in healthy young adults
- Thorough investigation if risk factors for renal tract malignancy are present
- Monitor renal function and urinalysis at least yearly even if no cause is identified, and refer to either urologist or nephrologist