Hematuria

GLMS

23 Feb 2019

Case 1

- 23 years old man otherwise healthy
- No family history of kidney disease
- Found to have microscopic hematuria on medical check up for joining army (2 occasions)
- Has been undergoing running for his fitness for army selection
- Fit looking and muscular
- BP 130/75 mmHg, Pulse 64 per min, Height 1.8 m, Weight 80 kilo
- Normal physical examination

Case 1

- Urine microscopy shows rbc >100, wbc <10, nil epithelial cell
- Spot urine Albumin/Creatinine ratio 4 (<2.3)
- eGFR >90 ml/min/1.73 m2

What investigations next?

Case 2

- 28 years old man, fit and healthy, regular gym goer
- Presented to emergency department after sustaining groin injury while playing indoor soccer
- Father has hypertension nil else
- Nil regular medications
- Non-smoker, social alcohol
- A year ago, eGFR >90ml/min, Urine Albumin/ Creatinine ratio 4.6 (2.3), no urine microscopy available

Case 2

- X ray – no bony injury, discharged on pain relief with GP follow up
- BP 145/90 mmHg, P 102 per min, anxious
- Was given Brufen and Paracetamol
- Urine microscopy rbc >100, wbc 15, Albumin/ Creatinine ratio 110
- eGFR 84 ml/min/1.73m2 at time of presentation to ED
- Review 1 week later with repeat labs at regular GP

Case 2

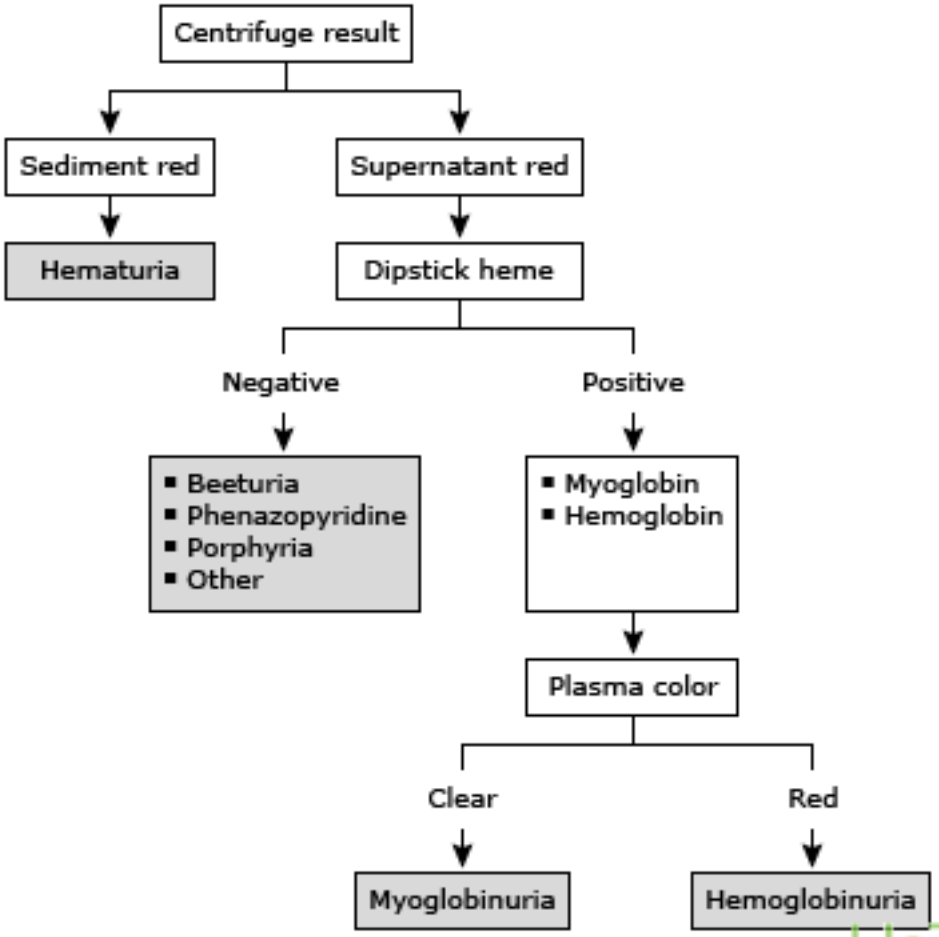
- Anxious with his situation
- BP 146/87 mmHg, Pulse 88 per min
- Normal physical examination apart from minor painful hip
- eGFR 76 ml/min/1.73m2, Urine microscopy rbc >100, 2++ protein, ACR 146

➢ What next?

Definitions

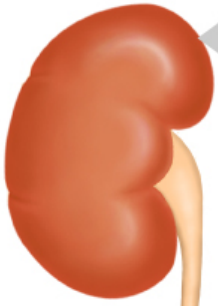
- Gross hematuria — Gross hematuria is suspected because of the presence of red or brown urine
- Microscopic hematuria — Microscopic hematuria refers to blood detectable only on examination of the urine sediment by microscopy
- Hematuria is common and frequently benign in young patients, and a cause is often not identified
- By contrast, even transient hematuria may be a symptom of an underlying serious condition, particularly in patients over age 35 years

Approach to the patient with red or brown urine



UpToDate®

Causes of hematuria



Renal
- Benign renal mass (angiomyolipoma, oncocytoma, abscess)
- Malignant renal mass (renal cell carcinoma, transitional cell carcinoma)
- Glomerular bleeding (IgA nephropathy, thin basement membrane disease, Alport syndrome)
- Structural disease (polycystic kidney disease, medullary sponge kidney)
- Pyelonephritis
- Hydronephrosis/distension
- Hypercalciuria/hyperuricosuria
- Malignant hypertension
- Renal vein thrombus/renal artery embolism
- Arteriovenous malformation
- Papillary necrosis (sickle cell disease)

Mimics of hematuria
- Menstruation
- Drugs (pyridium, phenytoin, rifampin, nitrofurantoin)
- Pigmenturia
- Beeturia

Ureter
- Malignancy
- Stone
- Stricture
- Fibroepithelial polyp
- Post-surgical conditions (ureteroiliac fistula)

Renal and/or upper or lower collecting system:
- Infection (bacterial, fungal, viral)
- Malignancy
- Urolithiasis
- Tuberculosis
- Schistosomiasis
- Trauma
- Recent instrumentation including lithotripsy
- Exercise-induced hematuria
- Bleeding diathesis/anticoagulation*

Upper collecting system

Lower collecting system

Bladder
- Malignancy (transitional cell carcinoma, squamous cell carcinoma)
- Radiation
- Cystitis
- Bladder stones

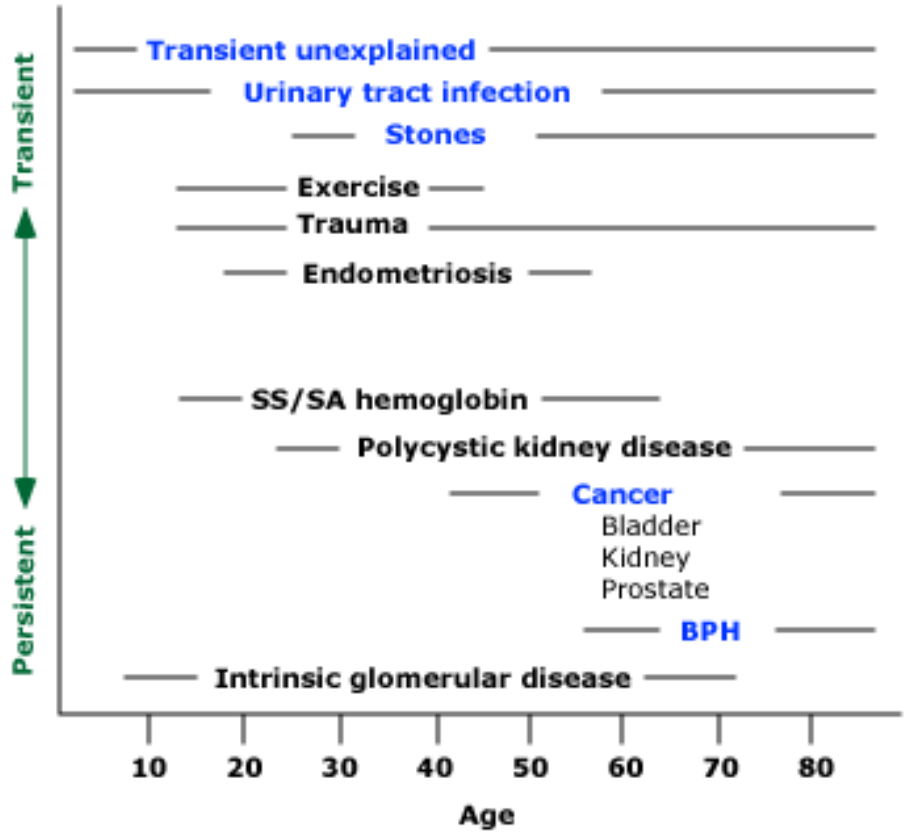
Prostate/urethra
- Benign prostatic hyperplasia
- Prostate cancer
- Prostatic procedures (biopsy, transurethral resection of the prostate)
- Traumatic catheterization
- Urethritis
- Urethral diverticulum

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

Courtesy of Michael Kurtz, MD.

UpToDate®

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.

History

- Concurrent pyuria and dysuria, which are usually indicative of a urinary tract infection but may also occur with bladder malignancy.
- A recent upper respiratory infection or symptoms of upper respiratory disease raise the possibility of postinfectious or infection-related glomerulonephritis, immunoglobulin A (IgA) nephropathy,
- Vasculitis, anti-glomerular basement membrane (GBM) disease, or sometimes hereditary nephritis.
- A positive family history of renal disease, as in hereditary nephritis, polycystic kidney disease, or sickle cell disease.
- Unilateral flank pain, which may radiate to the groin, usually suggests ureteral obstruction due to a calculus or blood clot but can occasionally be seen with malignancy or IgA nephropathy.

History

- Symptoms of prostatic obstruction in older men such as hesitancy and dribbling.
- Recent vigorous exercise or trauma in the absence of another possible cause.
- History of a bleeding disorder or bleeding from multiple sites due to excessive anticoagulant therapy. These observations indicate that hematuria in an anticoagulated patient should be evaluated in the same fashion as in other patients.
- Cyclic hematuria in women that is most prominent during and shortly after menstruation, suggesting endometriosis of the urinary tract .
- Contamination with menstrual blood is always a possibility and should be ruled out by repeating the urinalysis when menstruation has ceased

Distinguishing extraglomerular from glomerular hematuria

	Extraglomerular	Glomerular
Color (if macroscopic)	Red or pink	Red, smoky brown, or "Coca-Cola"
Clots	May be present	Absent
Proteinuria	<500 mg/day	May be >500 mg/day
RBC morphology	Normal	Some RBCs are dysmorphic
RBC casts	Absent	May be present

RBC: red blood cell.

UpToDate®

Glomerular versus nonglomerular bleeding

- Red cell casts - virtually diagnostic of glomerulonephritis or vasculitis
- Red cell morphology -dysmorphic appearance with renal lesions
- Acanthocytes - appear to be most predictive of glomerular disease
- Red to brown urine -typically red to pink with nonglomerular bleeding, smoky brown or cola color
- Blood clots - almost always due to **nonglomerular** bleeding
- Proteinuria - proteinuria that is temporally related to the hematuria is suggestive of glomerular disease

Role of renal biopsy

- Presence of risk factors for progressive disease such as proteinuria and/or an elevation in the serum creatinine concentration
- Kidney biopsy is **not** usually performed for isolated glomerular hematuria
- Most common findings are a normal biopsy, IgA nephropathy, thin basement membrane disease, mild nonspecific glomerular abnormalities, and hereditary nephritis (Alport syndrome)

Transient or Persistent Hematuria

- Common problem in adults

Prospective cohort study including 2,421,585 members (of all ages)

- 967,297 (40 percent) had asymptomatic microscopic hematuria
- Second urinalysis was positive for microscopic hematuria in 643,304 (66 percent)
- Approximately one-third of individuals with an initially positive urinalysis had transient hematuria

Transient or Persistent Hematuria

Study evaluated 1000 young men who had yearly urinalyses between the ages of 18 and 33 years

- Hematuria was seen in 39 percent on at least one occasion
- 16 percent on two or more occasions
- No obvious etiology can be identified in most patients with transient hematuria
- Fever, infection, trauma, and exercise are potential causes
- Can occur with UTI (pyuria)

Risk Factors For renal tract malignancy

American Urological Association:

- Age >35
- Smoking
- Occupational exposure
- Chronic cystitis or irritative voiding
- Pelvis irradiation
- Exposure to cyclophosphamide
- Chronic indwelling foreign body
- Analgesic abuse (paracetamol RR 1.28, NSAIDs RR 1.25)
  - meta-analysis of 20 observational studies (Choueiri et al, Int J Cancer 2014)
- Gross haematuria

Urinary Tract Malignancy

- Prospective cohort study of 4414 members of a managed care organization with unexplained, asymptomatic microscopic hematuria
  - 111 cancers were identified (2.5 percent); 100 were bladder cancers, and 11 were renal cancers
  - Prevalence of malignancy was 11.2% among patients 50 years or older who also had a history of gross hematuria plus at least one additional risk factor (smoking, male, rbc > 25)
  - <50 years without gross hematuria, cancer prevalence rate was 0.2%

Urinary Tract Malignancy

- Study of 1930 patients (mean age of 58 years, 62 percent male) who were referred to a hematuria clinic

➢ 12 percent had bladder cancer, 0.7 percent had kidney and upper tract tumors

➢ 61 percent had no cause identified

50 – 59 years

Sex	Gross	Microscopic
Male	20.4%	1.9%
Female	8.9%	1.9%

60 – 69 years

Sex	Gross	Microscopic
Male	28.9%	7.9%
Female	21.5%	4.5%

Urinary Tract Malignancy

- 1034 patients with microscopic hematuria
- Evaluated by ultrasound, IVP, urinary cytology, and cystoscopy.
- ➢ Incidence of malignancy (bladder, kidney, or prostate) was 2.4 percent
- ➢ Kidney stones or glomerular or other intrinsic renal disease -20%
- ➢ 78 percent had either no identifiable cause
- ➢ Neither cytology nor IVP reliably detected all of the tumors

Imaging

- Unexplained hematuria (glomerular bleeding is excluded)
- Imaging of kidney, ureter, bladder combined with cystoscopy (bladder and urethral lesion)
- CTU with or without contrast (preferred initial)
- IVP or US replaced by CTU
- US preferred for pregnant women
- MRU less data
- Cystoscopy – entire bladder can be visualised + prostate and urethra

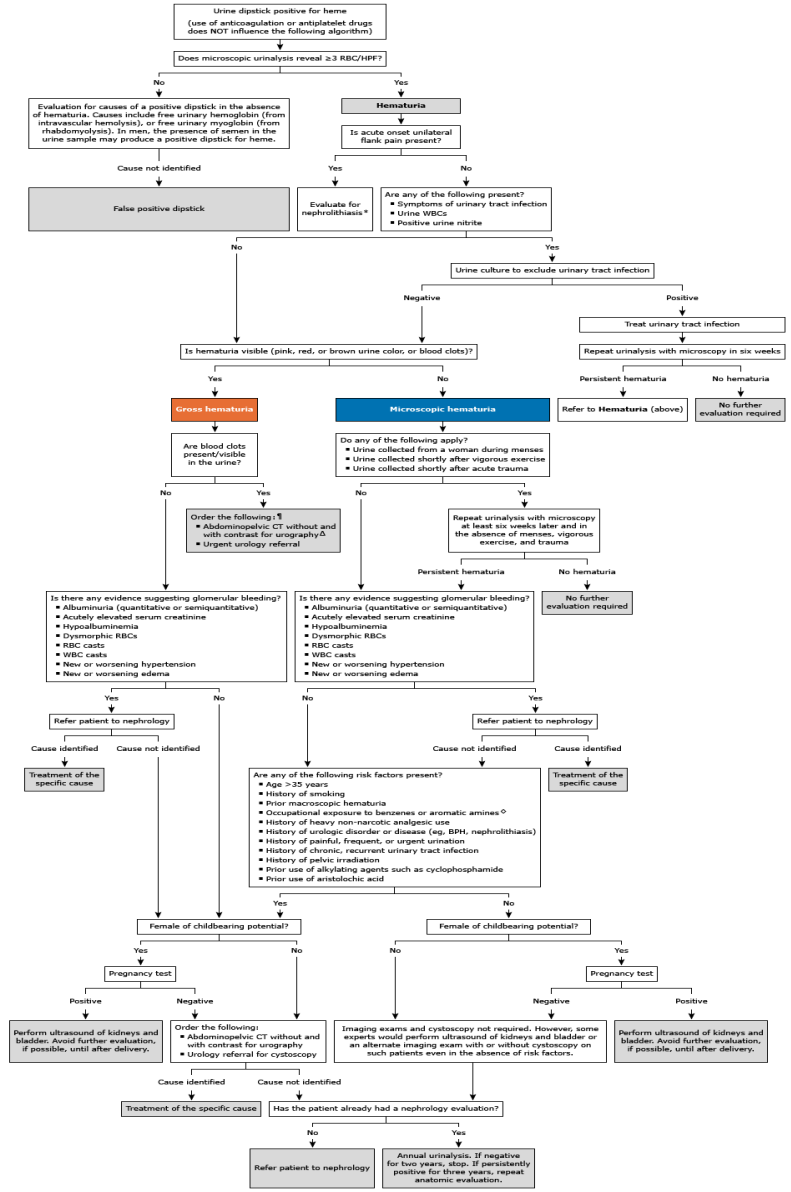
Unexplained Hematuria

- No Dx from history, urinalysis, imagings or cystoscopy
- Mild glomerulopathy and predisposition to stone disease
- Glomerular disease – asso with proteinuria, rbc casts, renal insufficiency
- Persistent glomerular hematuria (isolated) – IgA, Thin basement membrane, mesangioprooliferative, Alport syndrome
- Postinfectious GN and exercise are other cause but typically transient

Rare conditions

- Hereditary hemorrhagic telangiectasis
- Radiation cystitis
- schistosomiasis
- AVM
- Nutcracker syndrome
- Loin pain-hematuria syndrome

Evaluation of the adult with asymptomatic hematuria



RBC: red blood cell; HPF: high-power field; WBC: white blood cell; CT: computed tomography; BPH: benign prostatic hyperplasia.

* Abdominopelvic CT without contrast using a low radiation dose is recommended in most patients. For additional recommendations, refer to UpToDate topics on diagnosis of nephrolithiasis.

¶ Some patients with gross hematuria cannot empty their bladder due to severe clots and therefore develop urinary retention. Such patients should undergo prompt imaging and urology evaluation.

Δ Patients age <35 with noncontrast CT positive for nephrolithiasis may not need postcontrast imaging. For patients with contraindications to iodinated contrast, refer to UpToDate content for imaging options.

◇ For a list of potential environmental/workplace exposures that increase risk for bladder cancer, see http://www.cancer.org/cancer/bladdercancer/detailedguide/bladder-cancer-risk-factors.

UpToDate

Take Home Message

- Transient microscopic hematuria in healthy young adults are common
- Identify risk factors are important for gross or microscopic hematuria in patients above 35 years for urinary tract malignancy
- Decreased eGFR and proteinuria are important risk factor for progressive renal disease