Objectives:

1. Generate a general understanding of the initial approach to the patient with hematuria
2. Discuss the important history questions to ask, physical exam procedures to perform, lab investigations to order, and imaging tests to order.

Introduction:

Gross hematuria is never "normal" and always warrants an evaluation. Sometimes, all that is required is a history and physical exam to make a diagnosis. An example would be gross hematuria in a healthy, young woman that is associated with acute bacterial cystitis which clears completely with treatment of the infection. In this case, further evaluation is not required. In most cases however, imaging of the urinary tract (ultrasound, IVP or CT scan) is mandatory and cystoscopy may be indicated therefore referral to a urologist is appropriate.

Gross, painless hematuria in an adult is strongly suggestive of a malignancy; most commonly a bladder or renal malignancy. Gross hematuria due to benign prostatic hyperplasia (BPH) is not unusual but careful questioning will usually suggest this diagnosis. The hematuria associated with BPH is often described as "initial" hematuria indicating that the blood is most pronounced at the initiation of voiding and that the blood is less noticeable or absent by the end of urination. Also, these patients will typically describe a number of voiding symptoms associated with BPH (nocturia, slow stream, hesitancy, etc…). Hematuria associated with urinary tract infections and/or urolithiasis is usually symptomatic and the diagnosis will be suspected based on the patient's history. Hematuria secondary to trauma requires a thorough radiologic evaluation to document the extent of injuries and plan for surgery, if necessary. Hematuria associated with trivial trauma may indicate an underlying anatomic abnormality or malignancy.

A good framework for students to work with when they first approach a patient with hematuria is:

1. pre-renal:
a. anticoagulants, coagulation defects, sickle cell disease, leukemia, pseudohematuria (e.g. rifampin, beets…)

2. renal:
a. RCC, TCC, pyelonephritis, Tb, glomerulonephritis, trauma, stone, infarct, polycystic kidney disease, AV malformation

3. post-renal (e.g. ureter, bladder, urethra, prostate):
a. stone, tumor, infection, STD,

Hematuria Work-up Reference:

1. History	CC, HPI (constitutional symptoms, timing of blood in stream, frequency, nocturia, dysuria, urgency, hesitancy, straining, decreased force, dribbling), PMH, Soc Hx, Fam Hx, Sexual Hx, Tobacco, Medications
2. Physical	Vitals (including JVP), Abdominal exam (e.g. masses, tenderness), GU exam (e.g. DRE, genitalia), lymph nodes

	(inguinal and supraclavicular)
3. Labs	CBC, electrolytes, BUN, creatinine, urinalysis (casts, crystals, culture and sensitivity, cytology), INR, aPTT
4. Imaging	Ultrasound or IVP or CT
5. Cystoscopy	

1. History:

Important questions to ask:
- onset, duration, alleviating and aggravating factors

1. Is the hematuria gross or microscopic?

- the chance of significant disease increases with increased blood in the urine
* it is uncommon for patients with gross hematuria to have no pathology on investigation, conversely, it is common for patients with microscopic hematuria to have no pathology on investigation
- the most common cause of gross hematuria in an adult over 50 years old is a bladder tumor

2. Timing of the hematuria?

a. Initial: usually arises from the urethra
- most often from the prostatic urethra associated with BPH
- careful questioning will often suggest this diagnosis
- the initial hematuria will usually be accompanied by other symptoms of BPH (slow stream, hesitancy, nocturia…)
- other possible causes of initial hematuria include: anterior urethral lesions (e.g. urethritis, stricture or meatal stenosis in young boys)
b. Total: the source of the blood is above the bladder
- this is the most common type of hematuria
c. Terminal: often secondary to pathology at the bladder neck or trigone or posterior urethra
- occurs at the end of micturition as bladder neck contracts to squeeze out the remaining few milliliters of urine
- possible causes include: posterior urethritis, polyps, tumors of the vesical neck, tuberculosis affecting the prostate or bladder neck, schistosomiasis

3. Is the hematuria associated with pain? (location, quality etc.)

- usually hematuria is not painful unless it is associated with inflammation or obstruction (e.g. cystitis with secondary hematuria, or urolithiasis)
> gross, painless hematuria in an adult should be considered a malignancy (most commonly bladder or renal) until proven otherwise
- it can be intermittent and not recur for months > **must not discount it** because it went away
- usually pain associated with hematuria originates in upper urinary tracts resulting from obstruction of ureters with calculi or blood clots

4. Are there blood clots associated with the hematuria?

- most often indicates more significant hematuria and increased likelihood of real pathology, but rules out glomerulonephritis as the cause
- shape:

o usually amorphous which most often indicates bladder or prostatic origin
o vermiform clots (especially if associated with flank pain) indicates upper urinary tract as origin with formation of clots in the ureter

5. Is the patient bleeding elsewhere? e.g. nosebleeds, rectum, etc…

- an underlying coagulopathy could be present and should be investigated

6. What medications is the patient taking?

- anticoagulants (e.g. warfarin or ASA): if taken in excess can predispose to hematuria
> at normal, therapeutic levels anticoagulants do not predispose to hematuria
- other medications can cause false positive dipsticks and/or urine with a red appearance > pseudohematuria (see later)

7. Are there tissue fragments in the urine?

- likely a bladder tumor

8. Does the patient have any constitutional symptoms?

- likely a malignancy

9. Is the patient a smoker?

- large risk factor for transitional cell carcinoma (TCC)
- small risk factor for renal cell carcinoma

10. What is the patient's occupation?

- exposure to aromatic amines in dyes/cleaners is a risk factor for TCC

11. Does the patient have a history of hematuria, stone disease or malignancy?

12. Are there any associated symptoms?

e.g. renal colic, flank pains, fevers, lower tract symptoms
- this may help to localize the bleeding

13. Trauma?

- hematuria secondary to trivial trauma may indicate an underlying anatomic abnormality or malignancy
- see GU trauma section for more detail on trauma

14. Family history?

- diabetes, sickle cell anemia, polycystic kidney disease, urinary tract calculi

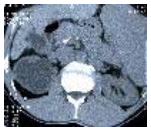
In addition to malignancy other causes of silent or painless hematuria include:

1. staghorn calculus

2. polycystic kidneys

3. sickle cell disease ? due to papillary necrosis

4. hydronephrosis (chronic)



5. acute glomerulonephritis

6. vascular problems (e.g. arteriovenous malformations, arterial or venous thrombosis…)

- joggers or other athletes can present with gross hematuria following excess exercise

o this benign hematuria will be transient and is often associated with proteinuria

- glomerulonephritis (e.g. IgA nephropathy, mesangioproliferative GN…) may appear as gross hematuria but more often causes the urine to appear reddish-brown or tea colored

o microscopy will show shrunken or crenated RBCs and may show RBC casts or granular casts
o the dipstick will also show heavy proteinuria with glomerulonephritis whereas only trace amounts of protein are seen with other 'non-glomerular' causes of hematuria

2. Physical Exam:

- vitals and general appearance:

  o volume status (e.g. JVP), edema, blood pressure – glomerular diseases of the kidney will have symptoms such as these related to protein losses and polyuria
  o temperature – indicates possible infection, tumor or systemic cause (e.g. allergic reaction, autoimmune disease)
  o cachexia – most often suggestive of a tumor
  o pallor – blood loss (e.g. trauma, GI tract, GU tract, coagulopathy), sickle cell disease or hematologic malignancy

- abdominal exam: abdominal masses (including renal or bladder) or tenderness
- GU exam:

  o DRE for prostate – BPH or cancer can be a cause for hematuria
  o external genitalia in males – any indication of STD or other infection, trauma or other gross abnormalities
  o pelvic exam in women – gynecological diseases can be a cause for pseudohematuria or hematuria (e.g. fistulas), it is also occasionally possible to palpate a stone on bimanual exam

- CVA tenderness on fist percussion ---indicates an inflammatory process is present in the region of the kidney (e.g. infection or stone)
> commonly the physical exam will be entirely normal

3. Laboratory:

- hematuria should always be confirmed by **urine microscopy** to rule out causes of pseudohematuria and to gain more information as to the cause of the hematuria

Pseudohematuria:

o the most frequent cause of pseudohematuria is confusion between blood in the urine and blood from the menstrual flow mixing with urine
o hemoglobinuria (from intravascular hemolysis) and myoglobinuria (from rhabdomyolysis or crush injuries to the extremities) will make the urine look red and cause of false positive result on the urine dipstick but will show no RBCs on microscopy
o dyes: beets, rhodamine B in drinks, candy and juices
o laxatives: some contain phenolphthalein
o drugs: rifampin (turns urine orange), phenazopyridine (turns urine red/orange)

- other laboratory tests generally performed on all patients with gross hematuria include WBC, Hb, platelet count, creatinine, urea, INR, PTT and urine culture

o urinary tract infections may not be the cause of the hematuria but may complicate another condition (e.g. stone disease)
> therefore it is an important finding even if it is not the actual cause of the hematuria

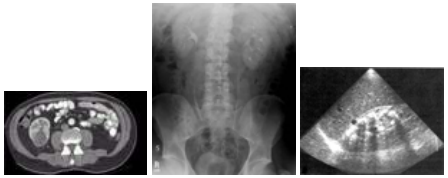
4. Imaging:

Modality	Advangages/Disadvantages
IVP	1. considered by many to be best for initial study for evaluation of urinary tract 2. widely available and most cost-effective in most centers 3. limited sensitivity in detecting small renal masses 4. cannot distinguish solid from cystic masses – therefore must image with another modality if abnormality found 5. better than U/S for detection of TCC in kidney or ureter 6. requires IV contrast that is potentially nephrotoxic, therefore must check kidney function prior to use 7. sensitivity to contrast can lead to anaphylaxis and death
CT	1. preferred modality for detection and characterization of solid renal masses 2. detection rate for renal masses comparable to that of MRI, but more widely available and less expensive 3. best modality for evaluation of urinary stones, renal and perirenal infections and associated complications 4. sensitivity 94-98% for renal stones, compared to 52-59% for IVP and 19% for U/S 5. gross hematuria associated with blunt or penetrating trauma should be evaluated with an abdominal CT scan with IV contrast
U/S	1. excellent for detection and characterization of renal cysts 2. no radiation 3. limitations in detection of small solid lesions 4. pelvic and abdominal U/S is a good first choice for evaluation of painless, gross hematuria ? renal and bladder tumors are seen fairly well but clots can be confused for tumors 5. does not see ureteral lesions or flat bladder tumors well

* partially adapted from Grossfield GD, Wolf JS, Litwin MS, Hricak H, Shuler CL, Agerter DC, Carroll P. Evaluation of asymptomatic microscopic hematuria, in adults: the American Urological Association best practice policy recommendations. Part II: patient evaluation, cytology, voided markers, imaging, cystoscopy, nephrology evaluation, and follow-up. Urology 2001; 57(4).

- in a patient with renal colic and/or flank pain associated with hematuria then an IVP or non-contrast CT scan are indicated first to look for renal or ureteric calc

uli
- trauma to the pelvis or perineum causing hematuria or blood per urethra requires a retrograde urethrogram (in males) and a cystogram
- special imaging techniques (e.g. MRI, angiography…) are used to further evaluate abnormalities seen with the standard imaging techniques



5. Cystoscopy:

- this is indicated in every case of gross hematuria when the bladder, prostate or urethra is the suspected source of the bleeding (except in cases of trauma to the lower urinary tract)

- with cystoscopy the physician can decide whether the source of the blood is urethral, from the bladder or the upper urinary tract

  o the urethra and bladder are visualized directly
  o if the blood originates from the upper urinary tract reddish urine or frank blood can be seen exiting the ureteral orifices

- biopsies of the bladder may be taken at the time of cystoscopy and retrograde pyelogram x-rays may be taken if the ureters and collecting system have not been well visualized with other imaging techniques

- can defer cystoscopy in men and women <40 years old with no risk factors for urological cancer when the upper tract imaging has shown a benign cause for the hematuria