Hematuria Evaluation and Work-up

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What is hematuria?

- Either presence of red blood CELLS or visible blood in urine.
  - Microscopic Hematuria- presence of cells
  - Gross Hematuria- visible blood in urine
## Urine Evaluation

<table>
<thead>
<tr>
<th>Dipstick +</th>
<th>Microscopic</th>
<th>Gross</th>
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<tbody>
<tr>
<td>- Urine dipstick sensitivity is 95% and specificity is 75%</td>
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<tr>
<td>- False positives d/t menses, medications, heavy exercise, dehydration, and some antiseptic solutions (Povodone-iodine)</td>
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<tr>
<td>- Confirm with MH screening.</td>
<td>- 3 red blood cells per high powered field (rbc/hpf)- single specimen.</td>
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<td>- 2+ proteinuria-nephrologic</td>
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<td>- + significant epithelial cells – skin or vaginal contamination (repeat)</td>
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</table>
Why does my patient have hematuria?

- Small number of patients no cause identified.
- Could me benign
- Could be malignant.

Risk factors for malignancy:

<table>
<thead>
<tr>
<th>Older Age</th>
<th>Male gender</th>
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<tbody>
<tr>
<td>Hx of smoking (education)</td>
<td>Hx of occupational exposure to dyes, rubber, and petrochemicals.</td>
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<td>Hx of cyclophosphamide/ifosfamide chemo</td>
<td>Hx of pelvic radiation</td>
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<tr>
<td>History of chronic indwelling catheters</td>
<td>Family history of urothelial cancers</td>
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<tr>
<td>Lynch Syndrome (Urothelial)</td>
<td>Schistosomiasis (Consider for Middle East and Egypt) (Squamous Cell Bladder)</td>
</tr>
</tbody>
</table>
Table 2. Common Risk Factors for Urinary Tract Malignancy in Patients with Microscopic Hematuria

- Age older than 35 years
- **Analgesic abuse**
- Exposure to chemicals or dyes (benzenes or aromatic amines)
- Male sex
- Past or current smoking
- History of any of the following:
  - Chronic indwelling foreign body
  - Chronic urinary tract infection
  - Exposure to known carcinogenic agents or alkylation chemotherapeutic agents
  - Gross hematuria
  - Irritative voiding symptoms
  - Pelvic irradiation
  - Urologic disorder or disease

Sources of Bleed:
<table>
<thead>
<tr>
<th>Glomerular (Kidney)</th>
<th>Non-Glomerular</th>
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</thead>
<tbody>
<tr>
<td>Berger’s disease (IgA nephropathy)</td>
<td>Upper tract (kidney or ureter): <strong>Kidney stones</strong></td>
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<tr>
<td></td>
<td>Kidney infection</td>
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<tr>
<td>Thin glomerular basement membrane dz.</td>
<td>RCC or other malignant or benign tumors</td>
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<tr>
<td></td>
<td>Upper tract urothelial carcinoma</td>
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<td></td>
<td>Obstruction (above bladder)</td>
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<tr>
<td></td>
<td>Trauma</td>
</tr>
<tr>
<td>Alport’s Sydrome (hereditary nephritis)</td>
<td>Lower Tract (bladder or urethra):</td>
</tr>
<tr>
<td></td>
<td>Cystitis (bacterial, interstitial or radiation)</td>
</tr>
<tr>
<td></td>
<td>Prostatitis</td>
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<td></td>
<td><strong>BPH</strong></td>
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<td></td>
<td><strong>UTI</strong></td>
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<td></td>
<td>Strenuous exercise</td>
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<tr>
<td></td>
<td>Urothelial carcinoma of bladder/urethra</td>
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<td></td>
<td>Prostate Cancer</td>
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<tr>
<td></td>
<td>Instrumentation</td>
</tr>
</tbody>
</table>

Concurrent Urology and Nephrology workup indicated when protein, red cell casts, dysmorphic red cells, and/or renal insufficiency.
Evaluation/Work-up

- Ensure thorough physical and history
  - Onset, duration, and symptoms
* Flank pain, fever, dysuria, straining, nocturnal enuresis?
* Hx of cigarette smoking and occupational exposure?
* Chronic catheters, stone, and recurrent UTI?
* Edema and cardiac arrhythmia?
* CVA tenderness?
  - Fever with flank pain/CVA tenderness?
  - Any recent or excessive NSAID use?
  - Trauma/Falls/Sporting injuries

If infection is suspected- Obtain urine culture BEFORE starting antibiotics and follow up for treatment of cure. Especially if the treatment is prolonged or resistance to first line treatment. Still RBC present?

ALL patients with hematuria should be evaluated by a Urologist.

What can a PCP or inpatient provider check prior to Urology referral?
- Renal function (BMP)
- CBC
- Coags
- PSA (depending on risk factors, age, and desire for screening)
  Can be falsely elevated with recent catheterization or DRE

If GROSS hematuria-
workup by urology will also include:
- Cystoscopy
- CTU or MRI
If you patient has the following symptom combination, you should be concerned for metastatic renal cancer.

- Gross hematuria
- Flank pain
- AND palpable mass
Risk Stratification: Micro-hematuria

<table>
<thead>
<tr>
<th>Table 4. AUA Microhematuria Risk Stratification</th>
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</thead>
<tbody>
<tr>
<td><strong>Low Risk</strong></td>
</tr>
<tr>
<td>• Age: Women &lt; 50 years old; Men &lt; 40 years old</td>
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<tr>
<td>• Smoking history: Never or &lt; 10 pack year history</td>
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<tr>
<td>• Urinalysis: 3-10 RBC/HPF</td>
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<tr>
<td><strong>Intermediate Risk</strong></td>
</tr>
<tr>
<td>• Age: Women 50-59 years old; Men 40-59 years old</td>
</tr>
<tr>
<td>• Smoking history: 10-30 pack year history</td>
</tr>
<tr>
<td>• Urinalysis: 11-25 RBC/HPF</td>
</tr>
<tr>
<td><strong>High Risk</strong></td>
</tr>
<tr>
<td>• Age: 60+ years old</td>
</tr>
<tr>
<td>• Smoking history: &gt; 30 pack year history</td>
</tr>
<tr>
<td>• Urinalysis: &gt; 25 RBC/HPF</td>
</tr>
<tr>
<td>• Gross hematuria</td>
</tr>
</tbody>
</table>

Shared decision making

Thorough testing
Patient with microhematuria
≥3 RBC/HPF on UA with microscopy

History and physical exam
Focus on risk factors for urothelial cancer and non-malignant causes of blood in urine

Non-malignant or gynecologic source

Evaluation directed by signs/symptoms
Include urine culture if infection is suspected

Non-malignant or gynecologic source ruled out

Non-malignant or gynecologic source identified

Treat non-malignant or gynecologic source

Repeat urinalysis positive

Low Risk
All of the following:
- Women age < 50; Men age < 40 yrs
- Never smoker or < 10 pack-years
- 3-10 RBC/HPF on one UA
- No additional risk factors for urothelial cancer
- No prior episodes of MHP

Intermediate Risk
Any of the following:
- Women age 50-59; Men age 40-59 yrs
- 10-30 Pack-years smoking
- 11-25 RBC/HPF on one UA
- One or more additional risk factors for urothelial cancer
- Previously low-risk, no prior evaluation and > 3 RBC/HPF on repeat UA

High Risk
Any of the following:
- Women and men age > 60 yrs
- >30 Pack-years smoking
- >25 RBC/HPF on one UA
- History of gross hematuria
- Previously low-risk, no prior evaluation, and > 25 RBC/HPF on repeat UA

Repeat urinalysis negative

Cystoscopy and Renal Ultrasound

Cystoscopy and CT Urogram

Cytoscopy and Renal Ultrasound

Cystoscopy and CT Urogram

Repeat urinalysis within 6 months OR Cystoscopy and Renal Ultrasound

Repeat urinalysis performed

Consider Repeat Urinalysis within 12 months

Re-evaluate

If patient develops gross hematuria, increase in degree of microhematuria or new urologic symptoms

1. Main risk factors for urothelial cancer are those in the AUA risk stratification system (age, male sex, smoking, degree of microhematuria and history of gross hematuria). Additional risk factors for urothelial carcinoma include but are not limited to: irritative lower urinary tract voiding symptoms, history of cyclophosphamide or ifosfamide chemotherapy, family history of urothelial carcinoma or Lynch Syndrome, occupational exposures to benzene chemicals or aromatic amines, history of chronic indwelling foreign body in the urinary tract.

2. If medical renal disease is suspected, consider nephrologic evaluation but pursue concurrent risk-based urological evaluation.

3. Patients may be low-risk at first presentation with microhematuria, but may only be considered intermediate- or high-risk if found to have persistent microhematuria.

4. There are non-malignant and gynecologic sources of hematuria that do not require treatment and/or may confound the diagnosis of MHP. Clinicians can consider catheterized urine specimen in women with vaginal atrophy or pelvic organ prolapse. Clinicians must use careful judgment and patient engagement to decide whether to pursue MHP evaluation in the setting of chronic conditions that do not require treatment, such as the aforementioned gynecologic conditions, non-obstructing stones or BPH.

5. Clinician may perform cross-sectional imaging with urography or retrograde pyelogram if hematuria persists after negative renal ultrasound.

6. MRI Urogram or Non-contrast imaging plus retrograde pyelogram if contraindications to CT Urogram.
Statistics:

- Identified cause of hematuria – 57% asymptomatic and 92% gross hematuria
- Malignancy identified – 3-5% asymptomatic and 23% gross hematuria

* What if no cause is identified despite appropriate work-up?
  - Repeat UA in a year
  - Refer to Nephrology as appropriate (red cell casts, renal dysfunction, etc)
  - If persistent gross hematuria consider cysto and URS every 2 years if no identified nephrological source.
Diagnostic Testing

• If gross hematuria, and in most persistent microscopic hematuria, cases patient will need cystoscopy AND CTU OR MRI Abd/Pelvis.

You will want to make sure CTU includes usage of contrast (if pt without renal insufficiency) And has 15 minute delayed imaging.
### Non-Glomerular

#### Upper tract (kidney or ureter):
- **Kidney stones**
- Kidney infection
- RCC or other malignant or benign tumors
- Upper tract urothelial carcinoma
- Obstruction (above bladder)
- Trauma

#### Lower Tract (bladder or urethra):
- Cystitis (bacterial, interstitial or radiation)
- Prostatitis
- **BPH**
- **UTI**
- Strenuous exercise
- Urothelial carcinoma of bladder/urethra
- Prostate Cancer
- Instrumentation
Normal Urogram
RCC on imaging
Ureteral lesion
Prostate Tumor
Bladder Stone
Cystoscopy
Normal Cystoscopy

(A) Internal bladder neck
(B) Bladder wall
(C) Proximal urethra
(D) Bladder neck cystoscopy
Bladder Stones
Prostate Tumor
Bladder Tumor
UTUC
Case Study #1
• 34 year old AAM presents to clinic for annual exam. Has been feeling well since last visit with no complaints today.

- Med Hx: reflux, HTN, vitamin D deficiency.
- Surg Hx: None
- Fam Hx: No family history of cancer. + DM, HTN, HLD, ESRD.
- Social Hx: Never smoker, rare ETOH socially

PE all normal

Labs ordered: CBC, CMP, UA, Vitamin D level
UA Shows:

- SG 1.026
- pH 6.0
- Color yellow, clear
- Negative glucose
- Negative bilirubin
- Negative ketones
- 1+ Blood
- Negative protein
- Negative nitrites
- No WBC
- 0-2 RBC/HPF
- Bacteria None

What would you do next with this patient?

A. Obtain urine culture
B. Obtain repeat microscopic sample
C. Refer to Urology for evaluation
D. Do nothing

Go to slido.com using code #738576 to participate.
• What would you do next with this patient?

A. Obtain urine culture
B. Obtain repeat microscopic sample
C. Refer to Urology for evaluation
D. Do nothing
Case Study #2

• 40 year old white female presents for episodic visit related “blood in urine one and off”. Blood has been coming and going for about 6 months, never clots present, sometimes has low pelvic pain but not always.

• Med Hx: Paraplegia after MVC 2 years ago, neurogenic bladder, depression, anxiety, HTN, HLD.

• Surg Hx: Broken bones were repaired at time of MVC, lap cholecystectomy 4 years prior.

• Fam Hx: Mom with DM, breast cancer. Dad healthy.

• Social Hx: 2 PPD smoker x15 years, social ETOH,

• PE with no unexpected findings. BLE Flaccid with passive ROM only.
UA Results

- SG normal
- pH normal
- Color red, clear
- Negative glucose
- Negative bilirubin
- Negative ketones
- 3+ Blood
- Negative protein
- Positive nitrites
- No WBC
- 3 RBC/HPF
- Bacteria present

What would you do next with this patient?

A. Obtain urine culture
B. Obtain microscopic sample
C. Refer to Urology for evaluation
D. Both A and B
E. None of the above

Go to slido.com using code # to participate.
What would you do next with this patient?

A. Obtain urine culture  
B. Obtain microscopic sample  
C. Refer to Urology for evaluation  
D. Both A and B  
E. None of the above

What can a PCP or inpatient provider check prior to Urology referral?
- Renal function (BMP)  
- CBC  
- Coags  
- PSA (depending on risk factors, age, and desire for screening)  
Can be falsely elevated with recent catheterization or DRE
Case Study#3
• 72 year old white male, presents for routine annual exam. Only thing he has noticed over past 2 weeks he has a “hard time peeing and sometimes it has blood in it”. He has seen a few “chunks like clots”.

• Med Hx: HTN, HLD, DM, CAD with 2 stents 15 years ago, Hard of Hearing,
• Surg Hx: None
• Fam Hx: Mom and dad both had DM and HTN
• Social Hx: 2 PPD smoker x45 years (for about 1 year got up to 3PPD), denies ETOH

• PE with no unexpected findings or changes from last visit.
• Pt provided urine sample that was red with small clots noted in container.
What is your next step with this patient?

A. Repeat a urine sample in 2 weeks to see if it is clear yellow.
B. Urine culture
C. Refer to Urology
D. Both B and C

What can a PCP or inpatient provider check prior to Urology referral?
- Renal function (BMP)
- CBC
- Coags
- PSA (depending on risk factors, age, and desire for screening) Can be falsely elevated with recent catheterization or DRE

[Diagram of patient care process]
References: