Differential Diagnoses of Hematuria: What Is Manageable and When to Refer
Learning Objectives

By participating in this educational program, health care providers can expect to:

▪ Define hematuria

▪ Describe the differential diagnoses of hematuria

▪ Review the appropriate investigation and management of hematuria

▪ Determine when to refer a patient with hematuria to a urologist
Hematuria Classification

- Macroscopic (gross) vs. microscopic
- Symptomatic vs. asymptomatic
- Transient vs. persistent
- Definition: > 2 RBC/hpf on two microscopic urinalysis without recent exercise, menses, sexual activity, or instrumentation


RBC/hpf = Red blood cells on high-power field
Evaluation of Hematuria

- Dipstick vs. microscopy
- Dipsticks cannot differentiate among:
  - Myoglobinuria
  - Hemoglobinuria
  - Red blood cells
- Positive dipsticks should be further evaluated by microscopy
  - False-positive rate as high as 35%

## Glomerular vs. Extraglomerular Bleeding

<table>
<thead>
<tr>
<th>Urinary finding</th>
<th>Glomerular</th>
<th>Extraglomerular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red cell casts</td>
<td>May be present</td>
<td>Absent</td>
</tr>
<tr>
<td>Red cell morphology</td>
<td>Dysmorphic</td>
<td>Uniform</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>May be present</td>
<td>Absent</td>
</tr>
<tr>
<td>Clots</td>
<td>Absent</td>
<td>May be present</td>
</tr>
<tr>
<td>Colour</td>
<td>May be red or brown</td>
<td>May be red</td>
</tr>
</tbody>
</table>

Evaluation of Asymptomatic Hematuria

History of vigorous exercise (within the past week), trauma to urethra, menses

- Yes
  - Recollect/retest once contributing factors cease

- No

Findings of glomerular disease (proteinuria, increased creatinine, red cell casts, dysmorphic RBCs)

- Yes
  - Proceed to Renal ultrasound & urinary cytology
  - Age > 40 yrs

- No
  - No further evaluation

Any risk factors for urinary disease

- Yes
  - Proceed to cystoscopy

- No

Exercise-Induced Hematuria

- Diagnosis of exclusion
- Must be temporally related to exercise
- Must remit within days to one week (max.)
- Must be differentiated from:
  - March hemoglobinuria: destruction of RBCs caused by repeated pounding of the feet
  - Myoglobinuria: presence of myoglobin in the urine, usually associated with rhabdomyolysis (muscle destruction)
- Benign condition if transient

Renal Causes of Hematuria: Glomerular

- Acute postinfectious glomerulonephritis (APIGN)
- Benign recurrent or persistent hematuria (thin membrane disease)
  1. Sporadic
  2. Familial
- Lupus nephritis
- Henoch-Shönlein purpura nephritis
Renal Causes of Hematuria: Nonglomerular

- Infection (pyelonephritis)
  - Interstitial nephritis
  - Metabolic (uric acid, nephrocalcinosis)
  - Renal malformation (cystic kidney)
  - Tumours (Wilm’s, acute leukemia)
  - Idiopathic hypercalciuria
  - Trauma
Causes of Urinary Tract-related Hematuria

- Infection
- Urolithiasis — stones
- Trauma
- Drugs (cyclophosphamide, anticoagulants) — hemorrhagic cystitis
- Tumours
- TCC, RCC, PCa
- Prostatic diseases
Routine Hematuria Screening Not Recommended for Asymptomatic Patients

- Routine screening of all adults for microscopic hematuria with dipstick testing is not currently recommended because of the intermittent occurrence of this finding and the low incidence of significant associated urologic disease

- Discouraged by United States Preventive Task Force

- Not recommended by the Canadian Task Force on the Periodic Health Examination and the American Urological Association (AUA)

2. Canadian Task Force on the Periodic Health Examination, 1994: 826-36
Patients with Findings Suggesting a Glomerular Cause Should be Referred

- Findings consistent with glomerular pathology:
  - Proteinuria
  - Red cell casts
  - Dysmorphic red blood cells on microscopic exam
  - Elevated creatinine

- Patients with these features should be referred promptly to a nephrologist

Role of Radiographic Assessment in Microscopic Hematuria

- Patients with microscopic hematuria should have radiographic assessment of the upper urinary tract followed by urine cytology studies
  - Micro: renal US
  - Macro (gross): CT-IVP, IVP-US

- Note: recent AUA guidelines no longer recommend cytology as part of the routine evaluation of asymptomatic hematuria

CT = Computed tomography; IVP = Intravenous pyelogram

KUB: Left Ureteral Stone
Role of Cystoscopy in Microscopic Hematuria

The following patients should undergo cystoscopy in addition to radiographic assessment of the upper tracts:

- Older than 40 years of age
- Younger but with risk factors for bladder cancer
- Those with abnormal urine cytology results

Cystoscopy
Hematuria Follow-up

- Repeat urinalysis and urine cytology at 6, 12, 24, and 36 months

- No need for further re-evaluation with cystoscopy unless there is a change in the clinical picture

- Re-evaluate immediately if:
  - Abnormal urine cytology
  - Gross hematuria
  - Increased irritative voiding symptoms in the absence of UTI (concerns about carcinoma in situ of the bladder)

- Refer to nephrology if hypertension or proteinuria is present

Key Messages

- Microscopic hematuria
  - Requires urology consultation
  - If persistent (in setting of negative urine culture): requires ultrasound + urine cytology + cystoscopy (if risk factors or symptomatic)

- Gross hematuria (with negative urine culture): CT-IVP (IVP) + urine cytology + cystoscopy
  - Requires urology consultation

- Hematuria in presence of infection: no further investigations
Clinical Vignette #1

- 62-y.o. man
- Healthy
- PSA = 1.2 ng/mL
- DRE: normal-feeling, small (not enlarged) prostate
- Mild LUTS
- 1 episode of gross hematuria that spontaneously resolved

How would you approach this patient?

1. No action: reassess in 6 months
2. Initiate an alpha-blocker and 5ARI
3. Rx ciprofloxacin for 10 days for presumed UTI
4. Refer to urology
Clinical Vignette #2

- 72-y.o. woman
- Healthy
- U/A: 5 rbc/hpf on two occasions
- Asymptomatic

How would you approach this patient?

1. No action: reassess in 6 months
2. Initiate ditropan for OAB
3. Rx oxybutynin for 10 days for presumed UTI
4. Refer to urology
Clinical Vignette #3

- 40-y.o. woman
- Non-smoker
- Healthy
- On oral contraceptive
- No history of chemotherapy/radiation
- U/A: + nitrates
- Severe dysuria, frequency, urgency + gross hematuria (isolated case – not recurrent)

How would you work up this patient?
1. Cystoscopy, cytology, CT-IVP
2. Cystoscopy, cytology, CT-IVP + antibiotics
3. Cystoscopy, cytology, ultrasound
4. Antibiotics only
Clinical Vignette #4

- 60-y.o. man
- 40 pack-year smoker
- Hypertensive
- Diabetic
- Urine C&S negative
- Painless gross hematuria

How would you work up this patient?
1. Cystoscopy, cytology, CT-IVP
2. Cystoscopy, cytology, CT-IVP + antibiotics
3. Cystoscopy, cytology, ultrasound
4. Antibiotics only
Clinical Vignette #5

- 45-y.o. man
- Non-smoker
- Healthy
- Urine C&S negative
- Labs show persistent microscopic hematuria

How would you work up this patient?

1. Cystoscopy, cytology, CT-IVP
2. Cystoscopy, cytology, CT-IVP + antibiotics
3. Cystoscopy, cytology, ultrasound
4. Antibiotics only