

Approach to Hematuria
Medplex Conference – 5/08
J. Lewis, M.D.

Fact Sheet About Hematuria

Review prior to case.

1. There are few general population-based studies and no systematic reviews that define the correct work-up for asymptomatic microhematuria. It is **not** recommended that screening for hematuria be performed on the general asymptomatic population. Case-control studies suggest patients with microhematuria have no increased risk for urinary cancers. However, the AUA and medico-legal considerations make failure to perform a work-up risky.
2. Hematuria is defined as $\geq 2-3$ RBCs/HPF from 2 of 3 properly collected specimens. High-risk patients can be evaluated on the basis of a single UA. Menstruation, vigorous exercise, sexual activity, or trauma may cause hematuria and can be excluded by repeat testing. Anticoagulation therapy should not be assumed to be the cause of hematuria. Sickle cell trait can occasionally cause hematuria. Clots occur only with non-glomerular causes.
3. Risk factors for underlying disease in microscopic hematuria are smoking history, occupational exposure to benzenes or aromatic amines, history of gross hematuria, age >40 , history of urologic disorder or disease, history of irritative voiding symptoms, history of UTI, analgesic abuse, history of pelvic irradiation, chronic cyclophosphamide use, use of the herbal weight-loss preparation aristolochic acid, and schistosomiasis infection.
4. Proteinuria of 1+ (then confirmed by a 24-hour urine of 300-500+ mg or a spot urine protein to urine creatinine ratio of >0.3), predominance of dysmorphic RBCs, RCS casts, or an elevated creatinine should cause evaluation for renal parenchymal disease or referral to a nephrologist. The three most common glomerular causes are IgA nephropathy, hereditary nephritis, and thin basement membrane disease. A renal biopsy is usually obtained for rising creatinine, rising protein excretion, or unexplained rise in blood pressure.
5. A complete urologic evaluation should be performed for non-nephrologic hematuria to include helical CT scan with and without contrast (to detect stones and cancer), urine cytology x 3 for patients > 40 , and cystoscopy for abnormal cytology or risk factors for bladder cancer.
6. Patients with a UTI (pyuria also) should be treated appropriately and UA repeated 6 weeks after therapy.
7. Persistent microscopic hematuria in patients \geq age 50 should prompt cystoscopy as should gross hematuria.

Causes of Hematuria

Extraglomerular

- Cancer – bladder, prostate, ureteral, renal
- Nephrolithiasis
- Cystitis
- Hypercalcuria
- Hyperuricosuria
- BPH
- Tuberculosis
- Endometriosis
- SS trait or SS disease
- Exercise
- Menstruation
- Sexual activity
- Trauma
- Papillary necrosis
- AV fistula, AV malformations
- Polycystic kidney disease
- Loin-hematuria syndrome
- Polyps – bladder, urethral
- Anticoagulation therapy – but search for underlying etiology
- Schistosomiasis

Glomerular

- IgA nephropathy
- Thin basement membrane disease
- Alport syndrome
- Other glomerulopathies

Case

A 55 y.o. male is referred to you for evaluation of microscopic hematuria noted on routine UA performed during a company physical. The patient has a 60-pack year smoking history and is employed as a chemist. He denies any history of gross hematuria and also denies any family history of renal disease. He also denies vigorous exercise, sexual activity, or trauma just prior to his first UA. He has mild urinary hesitancy and nocturia - once per night. His physical examination is normal except for mild prostatic enlargement. A basic metabolic profile and CBC are normal, but UA reveals 3-5 RBCs/HPF, trace proteinuria, and an otherwise benign sediment. Please answer the following T-F questions about this patient:

1. The presence of trace proteinuria mandates a 24-hour urine for creatinine clearance and total protein to see if a glomerulonephritis is present.
2. The patient has at least 3 risk factors for bladder cancer.
3. The presence of only 3-5 RBCs/HPF does not mandate further work-up for urologic cancer.
4. The correct work-up for this patient consists of a helical CT with and without contrast, urine cytology, and cystoscopy.

References:

1. Grossfield G et al. Asymptomatic microscopic hematuria in adults: summary of the AUA best practice policy recommendations. *Am Fam Physician* 2001;63:1145-54.
2. Cohen R and Brown R. Microscopic hematuria. *N. Engl J Med* 2003;348:2330-2338.
3. Malmstrom P. Time to abandon testing for microscopic hematuria in adults? *BMJ* 2003;326:813-815.
4. Rose B, Fletcher R. Evaluation of hematuria in adults. *UpToDate* Vol. 16.1. 2008.
5. Yun E et al. Evaluation of the patient with hematuria. *MCNA* 2004;88:329-343.

Answer Sheet

Case

A 55 y.o. male is referred to you for evaluation of microscopic hematuria noted on routine UA performed during a company physical. The patient has a 60-pack year smoking history and is employed as a chemist. He denies any history of gross hematuria and also denies any family history of renal disease. He also denies vigorous exercise, sexual activity, or trauma just prior to his first UA. He has mild urinary hesitancy and nocturia - once per night. His physical examination is normal except for mild prostatic enlargement. A basic metabolic profile and CBC are normal, but UA reveals 3-5 RBCs/HPF, trace proteinuria, and an otherwise benign sediment. Please answer the following T-F questions about this patient:

1. The presence of trace proteinuria mandates a 24-hour urine for creatinine clearance and total protein to see if a glomerulonephritis is present. **False**

Comment: The trace amount of protein could be caused by hematuria. Proteinuria $\geq 1^+$ mandates a 24-hour urine or a urinary protein to creatinine ratio. $\geq 300 - 500$ mg protein per 24 hours or a ration of ≥ 0.3 requires the evaluation for GN as do dysmorphic RBCs or RBC casts.

2. The patient has at least 3 risk factors for bladder cancer. **True**

Comment: Age >40 , smoking history, and occupational exposure (e.g., chemist) to benzenes or aromatic amines confer \uparrow risk. Other risk factors for bladder cancer are heavy phenacetin use and/or long-term cytoxan use.

3. The presence of only 3-5 RBCs/HPF does not mandate further work-up for urologic cancer. **False**

Comment: $\geq 2-3$ RBCs/HPF does mandate further investigation. By definition microhematuria is 2-3 RBCs/HPF from two to three properly collected urinalysis specimens. A high-risk patient such as this one should be evaluated even with a single abnormal UA.

4. The correct work-up for this patient consists of a helical CT, urine cytology, and cystoscopy. **True**

Comment: If there were no risk factors for cancer and the patient was $<$ age 40-50, then no further work-up is indicated. However, in patients at higher risk, both must be done. US could also be selected as an upper tract screening modality. IVP is less sensitive for renal masses. If work-up is negative, consider periodic cytology and UA-perhaps at 6, 12, 24, and 36 months.