Evaluation of Hematuria for the Non-Urologist

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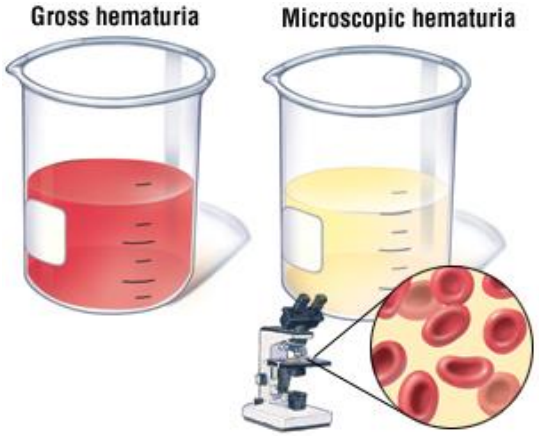
Objectives

- Identify clinically significant malignant and non-malignant etiologies of hematuria.
- Identify risk factors for developing GU malignancy.
- Identify the diagnostic approach to the patient who presents with hematuria.
- Integrate the American Urological Association (AUA) guidelines for diagnosis, evaluation and follow-up of hematuria into clinical practice.
- Recognize findings that should prompt referral to a urologist.

Epidemiology and Incidence of Hematuria

- Gross hematuria has low prevalence but high association with an upper tract malignancy
- Symptomatic hematuria is common and causes are readily identified in most cases, such as infection, stone, benign prostatic hyperplasia (BPH)
- Asymptomatic microscopic hematuria (AMH) is often found during routine health screenings and has a prevalence of 18-31%
- The importance of the finding of hematuria is secondary to the potential underlying risk of clinically significant pathology, including malignancy, urolithiasis and medical renal disease

Definitions



- Hematuria: presence of blood in the urine, either gross or microscopic
- Gross hematuria: blood seen with the naked eye
  - Bright red, tea colored, cola colored, rust colored, pink, brown
- Microscopic hematuria: 3 or more RBCs per HPF in a properly collected urinalysis
  - Mid-stream voided specimen
  - If uncircumcised man, with foreskin fully retracted
  - **Not** the first void of the morning; **not** after vigorous exercise; **not** while a woman is menstruating; **not** after sexual activity
  - Preferably **not** from an indwelling catheter

Dipstick vs Microscopic Analysis

- Dipstick testing positive for blood is NOT confirmatory of hematuria
- A positive dipstick test warrants microscopic analysis of a properly collected specimen
- Patients who have a positive dipstick and a negative microscopic test should have three additional microscopic tests
  - If one positive microscopic test, then work up is indicated
  - If all three microscopic evaluations are negative, then no further work up is indicated

Prevalence of Hematuria

- Rates of hematuria in the general population vary
  - 2-31% (AUA) 21% (Mayo) 20% (Kaiser) 9-18% (Int Med News) 40.9% (JAMA)
- More common in men than women
- More common after age 50 in men, 60 in women
- The presence of dysmorphic red blood cells, proteinuria, cellular casts, and/or renal insufficiency is suggestive of renal parenchymal disease and warrants concurrent nephrologic workup but does not preclude the need for urologic evaluation
- Medical renal disease is more likely in patients younger than 40 years

Etiologies of Hematuria

- Infectious: cystitis, pyelonephritis
- Stone disease
- Stricture disease
- Prostate related: BPH, prostatitis, prostate cancer
- Trauma: penile, vaginal, urethral, foreign body, renal hematoma/laceration,
- Recent instrumentation: ureteral stent or recent catheterization, cystoscopy
- Medical renal disease: glomerulonephritis, acute tubular necrosis
- Hereditary disease: sickle cell, polycystic kidney disease
- Medications: analgesics, anticoagulants, penicillins and other antibiotics, statins, antiretrovirals, anticonvulsants, antihypertensives, and chemotherapy drugs
- Cancer: bladder, ureter, kidney

Gross Hematuria

- Study results vary as to prevalence; up to 30% of patients presenting with gross hematuria will have a GU malignancy, usually upper tract
- All patients with even one episode of gross hematuria **without an identified etiology**, such as infection or stone, need referral to either urologist, nephrologist or both

Symptomatic Hematuria

- *Symptomatic* (or *painful*) hematuria often has a readily identifiable etiology
- Infection, stone, trauma, foreign bodies
- Has there been recent instrumentation or procedure?

If a cause of hematuria is found, treat accordingly, and then repeat microscopic examination to ensure the hematuria has resolved!

Asymptomatic Microscopic Hematuria (AMH)

- AMH (or *painless*) is more elusive, and of concern due to the possibility of an underlying malignancy
- Up to 23% of patients diagnosed with urothelial carcinoma initially present with AMH
- Women: correlation with menstrual cycle?

Any hematuria in patients who are taking anticoagulants requires urologic (and possibly nephrologic) evaluation regardless of the type of anticoagulant therapy!

Evaluation and Management: AUA Guidelines

- Gross hematuria always requires urologic referral
- Identify and treat underlying cause; then repeat microscopic analysis to ensure resolution of hematuria
- If no identifiable cause, the presence of hematuria should prompt a urologic evaluation
- Studies have shown that the recommended diagnostic guidelines are rarely followed

Risk Factors for Malignancy

- Male gender
- Age > 35 years
- Past or current smoking
- Occupational or other exposure to chemicals or dyes (benzenes or aromatic amines)
- Analgesic abuse
- History of pelvic radiation
- History of chronic UTI
- History of chronic indwelling catheter
- History of irritative voiding symptoms

Irritative Voiding Symptoms

- Urgency
- Urge incontinence
- Frequency
- Pain or burning with urination
- Nocturia

- Often attributed to UTI, especially in women
- Often attributed to BPH in men
- How often do you think of GU malignancy?

History

- Have you noticed a change in voiding pattern?
- Irritative voiding symptoms?
- History of radiation therapy, especially pelvic
- Medications
- Family history: stones, medical renal disease, GU malignancy
- Social history: smoking, occupational or other chemical exposure
- Any recent procedures or self-treatment?

Physical Examination

- Age/gender
- Vital signs: blood pressure
- Skin: easy bruising
- Extremities: edema
- External genitalia: trauma
- Pelvic exam for women, especially if menopausal, to assess for vaginal atrophy
- Digital rectal exam for men

Diagnostic Work Up

- CBC, CMP or BMP
  - At the initial evaluation, an estimate of renal function should be obtained (eGRF, creatinine, and BUN) because intrinsic renal disease may have implications for renal related risk during the evaluation and management of patients with AMH.
- Microscopic urinalysis
  - The presence of dysmorphic red blood cells, proteinuria, cellular casts, and/or renal insufficiency, or any other clinical indicator suspicious for renal parenchymal disease warrants concurrent nephrologic workup but does not preclude the need for urologic evaluation
- Urine culture

Diagnostic Imaging

- Presence or absence of symptoms largely guides test selection
- Acute symptoms such as renal colic → Non-contrast CT of abdomen/pelvis
- Major trauma with concern for renal injury → CT abdomen/pelvis with and without contrast
- Gross hematuria or AMH -> CT Urogram (CTU)
- Culture confirmed infection rarely needs imaging studies
- Findings of proteinuria, urinary casts, dysmorphic RBCs → Renal ultrasound

Difference in CT W/WO Contrast & CTU

- With a standard CT abd/pelvis, IV contrast is given in a bolus over 60-70 seconds; serial slices are then taken at various thicknesses
- At 70 seconds, the kidneys have not yet begun to excrete contrast, so the renal pelvis and ureters are seen but not enhanced
- CTU protocols are triphasic examinations that include non-contrast, enhanced, and delayed images
- With a CT Urogram, IV contrast is given in 3 increments over 8 minutes with a small bolus is given just before the scan time to show the renal cortex

Cystoscopy

- Recommended for those at high risk
- Cystoscopy is indicated for complete bladder evaluation
- The ability to biopsy and resect lesions are added benefits of cystoscopy

Overview of Treatment

- Infection: species-sensitive antibiotic therapy
- Stone disease: treatment depends of size, location of stone and other factors
- Prostate related: prostate reduction medications, reduction surgery
- Stricture disease: dilation, ureteroplasty
- Medical renal disease
- Trauma: rarely needs any intervention; monitor hemoglobin. If active bleeding, may need embolization

Hematuria without Identifiable Cause

- In patients with AMH without identifiable cause after thorough work-up, the recommendation is yearly microscopic urinalyses for at least two years following initial evaluation
- If UA is negative for two consecutive years, risk of malignant disease is no greater than that of general population
- If UA remains positive, work-up is negative, and patient remains asymptomatic, recommendation is annual microscopic urinalysis
- For persistent AMH, complete work-up is recommended every 3 to 5 years

Hematuria Risk Index

- Ronald Loo and colleagues at Southern CA Permanente Medical Group
- Prospective cohort of patient in Kaiser Permanente system referred to urologist for hematuria
- Test cohort comprised of 2630 patients who underwent imaging and cystoscopy; 2.1% had a cancer detected
- A validation cohort was subsequently followed through EMR for development of urothelial or renal cancer

Hematuria Risk Index

- Scored as follows:
- Gross hematuria and/or age 50 years or older: 4 points
- History of smoking: 1 point
- Male gender: 1 point
- > 25 RBC/HPF on recent urinalysis: 1 point
- Range from 0 to 11 points, with patients stratified as low risk (0-4 points), moderate risk (5-8 points), or high risk (9-11 points)
- Using this stratification index, cancer was detected in 10.7% of the high-risk group, 2.5% of the moderate-risk group, and 0% of the low-risk group

Summary Statements

- Microscopic hematuria: 3 or more RBCs per HPF in a properly collected urinalysis.
- All patients with even one episode of gross hematuria **without an identified etiology**, such as infection or stone, need referral to either urologist, nephrologist or both.
- If an identifiable cause of hematuria is found, treat accordingly, and **then repeat microscopic examination to ensure the hematuria has resolved**.
- Hematuria in patients who are taking anticoagulants **requires evaluation** regardless of the type of anticoagulant therapy.

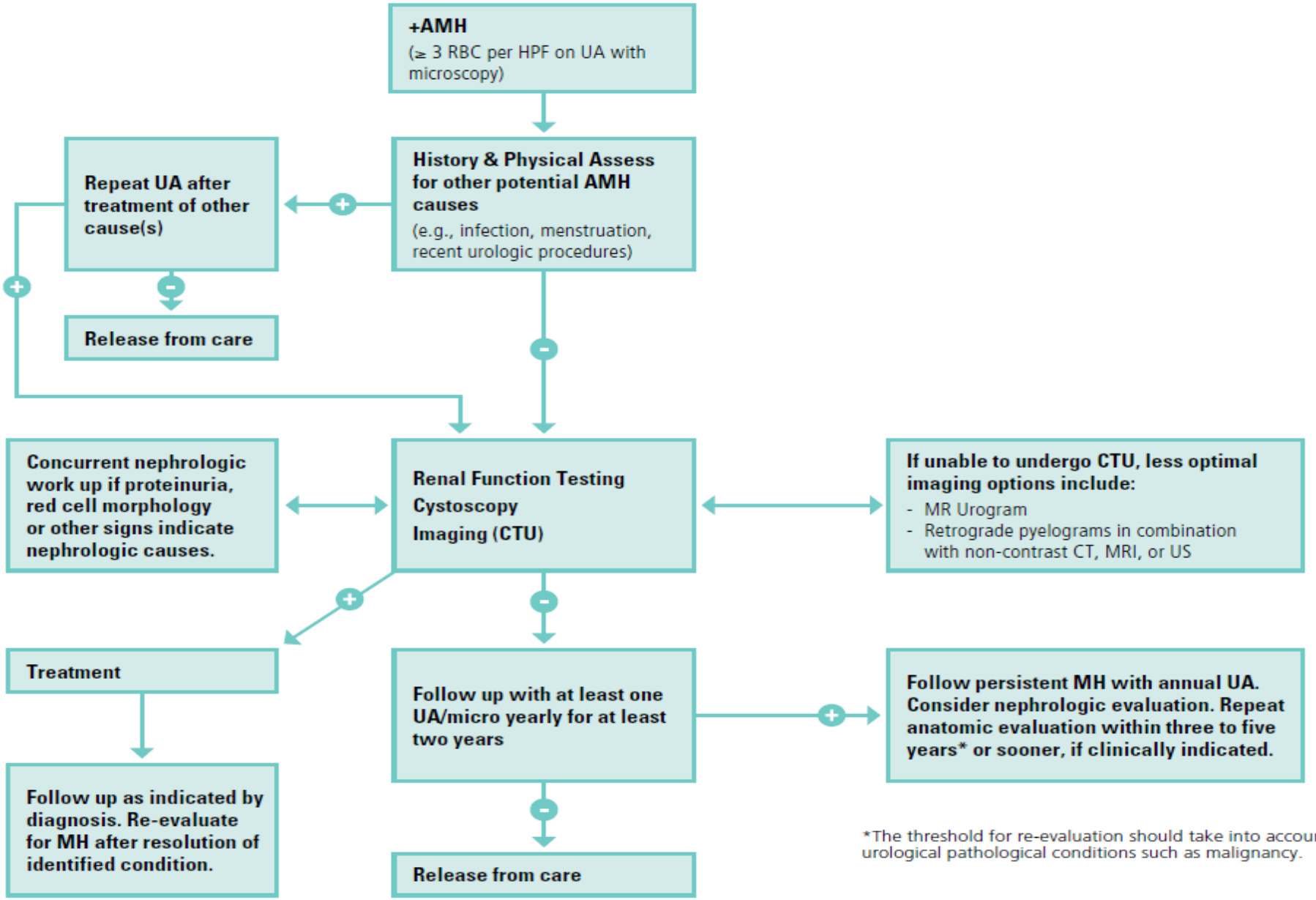
Summary Statements

- High risk factor patients should be referred to urology and have cystoscopy:
  - Male
  - Age 35 or older
  - Past or current smoking
  - Exposure to benzenes or aromatic amines
  - History of pelvic radiation
  - History of chronic UTI
  - History of chronic indwelling catheter

Summary Statements

- If no cause of hematuria is identified by complete work-up, patient should have yearly microscopic analysis.
- If UA is negative for hematuria, then no further evaluation is indicated.
- If UA remains positive for hematuria, repeat complete work-up every 3-5 years.

Diagnosis, Evaluation and Follow-up of AMH



*The threshold for re-evaluation should take into account patient risk factors for urological pathological conditions such as malignancy.

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