혈뇨의 진단과 치료적 접근

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Urine collection and Urinalysis

- Avoid strenuous physical exercise before 72 hours
  - To avoid exercise induced proteinuria, hematuria, or cylindruria
- Avoid during menstruation
  - To avoid blood contamination
- Second morning urine specimen
- Midstream, clean catch
  - Washing hands and external genitalia
  - Women: spread the labia
  - Men: withdraw the foreskin of the glans
  - Suprapubic bladder puncture
  - Through permanent catheters
  - possibly associated with bacteriuria, hematuria, leukocyturia

Detection of hematuria

Urine dipstick

- The simplest way to detect AMH
  - Indirect examination of urine with dipstick
  - Detect heme moiety of Hb (Pseudoperoxidase activity)

- Very useful to detect MH
  - Sensitivity: 91-100%
  - Specificity: 65-99%

- False-positive results
  - Hemoglobinuria
  - Myoglobinuria
  - High concentration of bacteria with pseudoperoxidase activity
    (enterobacteriaceae, staphylococci, streptococci)
  - Semen

Urine microscopy

- Positive dipstick test
  - Always be confirmed with microscopic examination

- Recommendation
  - Freshly voided, clean-catch, midstream urine
  - Evaluation within 1 hr or refrigerating specimen

- RBC (Erythrocyte)
  - Diameter: 4-10μm
  - Isohpicic vs Dysmorphic
  - Glomerular hematuria: DRBC >80%
  - Non-glomerular hematuria: Isomeric RBC>80%
  - Mixed hematuria
Urine microscopy (Dysmorphic RBC)

Urine microscopy (RBC cast)

Definition of Hematuria

- **Originiate from any site of urinary tract**
- **Gross hematuria (Red urine)**

Definition of Hematuria

- **Microscopic hematuria**
  - No safe lower limit below which significant disease can be excluded
  - Lowering the cut-off value: false positive test results
  - Higher cut-off values: miss the presence of significant abnormalities
  - Commonly defined as the presence of ≥ 3 RBCs/hpf in two of three properly collected urine samples

Definition of Hematuria

- **Pseudohematuria**
  - Drugs
    - Analgesics: acetaminophen, aspirin, ibuprofen, indomethacin
    - Anticoagulants: warfarin, heparin
    - Anticonvulsants: phenytoin, carbamazepine
    - Antifungicides: azole antifungicides
    - Antineoplastics: vincristine, methotrexate, cisplatin
    - Antiparkinson: levodopa
  - Vegetable dyes and foods
    - Urinary pigment: bile, melanin, porphyrins, urochrome, Serrata marcesens
  - Metabolic disease
    - Alcaptonuria, urates, phosphates

Epidemiology of Hematuria

- **Prevalence of dipstick RBC (+)**
  - KNHANES (2008-2010, n=20,791)
    - Spot urine blood ≥ 1+: 16.4%
    - Spot urine blood ≥ 1+: 17.2%

- **Prevalence of microscopic examination (+)**
  - 5–6% of the general population
  - Age: Older > younger
  - First 3–4 decades: <1%, Older age: 13%
  - Sex: female > male
**Evaluation of Hematuria**

- **Primary renal disease**
- **Urologic malignancy**

<table>
<thead>
<tr>
<th>Nephronal</th>
<th>Non-nephronal</th>
</tr>
</thead>
<tbody>
<tr>
<td>color</td>
<td>dark</td>
</tr>
<tr>
<td>clcr</td>
<td>-</td>
</tr>
<tr>
<td>RBC cast</td>
<td>+</td>
</tr>
<tr>
<td>proteinuria</td>
<td>+</td>
</tr>
<tr>
<td>Dystrophic-RBC</td>
<td>&gt;75%</td>
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**Evaluation of Hematuria: Hx taking**

- **Evaluation for hematuria should begin with a detailed medical history**
- **Recreational, occupational, radiation exposures, all medications**
  - Cigarette smoking: risk of bladder cancer x3-5
  - Aromatic amines and amides
    (leather and rubber manufacturing, aniline dye factory)
  - Medications: cyclophosphamide, mitotane, phenacetin, penicillins and cephalosporins
  - Oral anticoagulant: warfarin
    (significant urologic condition in 13-45% of this cohort)

**Evaluation of Hematuria: PEx**

- **Flank mass, bruit, pulsatile aortic aneurysm**
- **Costovertebral angle tenderness**
  - nephrolithiasis, UPJ obstruction, pyelonephritis...
- **Genital and rectal examination (male)**
  - prostatitis, prostate cancer, epididymitis...
- **Urethral and vaginal examination (female)**
  - exclude local cause of MIH
- **Peripheral edema (NS), cardiac abnormalities such as Atrial fibrillation (RA embolism)**
Evaluation of Hematuria: repeated UA

- Menstruation
- Vigorous exercise
- Sexual activity
- Viral illness
- Obtaining in 48 hrs
- Hematuria with UTI: 6 wks after antibiotics

Evaluation of Hematuria: Urine cytology

- Voided urine cytology
  - Relatively low sensitivity: 40.76%
  - Improved by obtaining early morning voided specimens
  - Depend on the number of urine specimen, stage and grade of bladder tumor, expertise of the pathologist
- Bladder wash cytology
  - More sensitive than voided urine cytology
  - Invasive procedure

Evaluation of Hematuria: Imaging studies

- Intravenous urography (IVU)
  - Considered by many the best initial study
  - Widely available and most cost-efficient in most centers
  - Limited sensitivity in detecting small renal masses
  - Cannot distinguish solid from cystic masses
  - Better than USG for detection of TCC in kidney and ureter

Evaluation of Hematuria: Urine cytology

- Positive urine cytology
  - Presence of urothelial cancer
- “Atypical and/or suspicious”
  - 15% of cases: underlying urinary tract malignancy
  - Should undergo complete evaluation including cystoscopy
- Negative urine cytology
  - High incidence of false-negative results
  - May exclude the presence of high grade tumor

Evaluation of Hematuria: Imaging studies

- Ultrasonography (USG)
  - Absence of radiation and lack of IV contrast
  - Excellent for detection and characterization of solid renal masses
  - Limitations in detection of small solid lesions (<3cm)
Evaluation of Hematuria: Imaging studies

- Nearly replacing IVU and US as primary imaging study for hematuria due to helical imaging and 3D reconstruction (MDCT)
- Accurate detection and characterization of renal cysts and masses
- Renal and perirenal infection
- Urinary structures (eg, renal vein) and abnormalities in nonurologic organs (liver, aorta etc.)
- Sensitivity for detection of stones: 94-98% (52-59% for IVU, 19% for US)
- Upper tr. evaluation for CT vs. IVU for AMH (Gray-Sears, 2002)
  Sensitivity 100% vs. 93.5% and Specificity 97.4 vs. 90.5%

Evaluation of Hematuria: Cystoscopy

- Flexible versus Rigid cystoscopy

<table>
<thead>
<tr>
<th>Flexible</th>
<th>Rigid</th>
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<tbody>
<tr>
<td>Pain during the procedure</td>
<td>less</td>
</tr>
<tr>
<td>Postprocedure symptoms</td>
<td>less</td>
</tr>
<tr>
<td>Procedure time</td>
<td>more simple</td>
</tr>
<tr>
<td>Positioning and preparation</td>
<td>same or superior</td>
</tr>
<tr>
<td>Diagnostic accuracy</td>
<td>-</td>
</tr>
</tbody>
</table>
- Low risk patient with AMH
  - Low yield (less than 1%)
  - Urine cytology ± (cystoscopy)

Evaluation of Hematuria: Follow-up study

- 8-10% of patients with AMH
  - No cause for hematuria at initial evaluation
  - 1-3% of patients
    - Subsequently diagnosed urologic malignancy
    - Within 3 years of initial evaluation
  - Significant issues
    - Who should undergo follow-up
    - What should the follow-up entail
    - Should the follow-up be different for individuals
    - How long should the follow-up continue
- Repeating urinalysis, voided urine cytology, blood pressure at 6, 12, 24, and 36 mo

Evaluation of Hematuria

Risk assessment and Urologic Evaluation

Initial Evaluation of Asymptomatic Microscopic Hematuria

Exclude benign causes, including menstruation, vigorous exercise, sexual activity, viral illness, trauma and infection.

If one or more of the following are present:
- Microscopic hematuria accompanied by significant proteinuria
- Dysmorphic red blood cells or red cell casts
- Elevated serum creatinine level (based on normal reference ranges for men and women)

Evaluation for primary renal disease

High risk patients:
- Gross hematuria
- Smoking history
- Occupational exposure to chemicals or dyes (benzenes or aromatic amines)
- History of gross hematuria
- Age > 40 years
- Previous urologic disorder or disease
- History of relative voiding symptoms
- History of recurrent urinary tract infection despite appropriate use of antibiotics
- Cyclophosphamide

Complete WU (Upper tract imaging, Cytology, Cystoscopy)
UA, BP, Cytology at 6, 12, 24, 36 months

Referral based on lesion

- Negative for 3 yrs
  - Persistent hematuria, proteinuria, and hypertension
  - Gross hematuria, irritative urinary 5x, abnormal cytology
  - No further WU
  - Nephrology WU

Repeat Complete urologic WU (Upper tract imaging, Cytology, Cystoscopy)