**Microscopic Hematuria (Persistent)**

**Effective Date:** April 22, 2009

**Scope**

This guideline deals with investigation of blood on dipstick urine testing and persistent microscopic hematuria in adults (age 19 and over).

Microscopic hematuria is defined as the presence of more than 3 red blood cells (> 3 RBC) per high power field (HPF) in the centrifuged urinary sediment. It becomes clinically significant, or persistent, when the result is visible in two of three properly collected urine samples (taken over a 10-day or longer time period).

**Diagnostic Code:** 599.7

**Risk Factors**

Hematuria is the most common sign of bladder cancer. However, the incidence of bladder cancer in patients with microscopic hematuria is low.

- Overuse of analgesic drugs
- Age >40 years; risk increases with age and is twice as high in men
- Exposure to certain drugs (phenacetin, cyclophosphamide, HIV therapies)
- Exposure to pelvic radiation
- History of gross hematuria
- History of urinary tract infection (UTI) or irritative voiding symptoms
- Occupational exposure to chemicals or dyes (e.g. benzenes or aromatic amines)
- Smoking, past or present including exposure to second hand smoke
- Previous urologic disease (e.g. renal calculi, urologic tumours)

**Diagnosis/Investigation** (see Algorithm)

Screening the general population for microscopic hematuria is not recommended due to the low incidence of significant urological disease.

If blood is detected on urine dipstick testing incidentally, confirm the finding after controlling for benign causes such as menstruation, exercise, sexual activity, urological instrumentation or prostate exam. If the repeat dipstick remains positive for blood, confirm with laboratory macroscopic and microscopic urinalysis. It should be noted that there is not necessarily a correlation between the degree of hematuria and the severity of the underlying disease.

The most typical clinical scenario for finding microscopic hematuria is during the evaluation of patients with suspected urinary tract infection. **Rule out infection prior to referral.** Treat for urinary tract infection if pyuria, bacteria or nitrites are present. It cannot be assumed that isolated hematuria represents a urinary tract infection. Anticoagulants including aspirin predispose patients to hematuria only in the presence of urinary tract disease. **It is recommended that patients on anticoagulants with hematuria be investigated.**
Algorithm: Investigation of Persistent Microscopic Hematuria in Adults

Microscopic evaluation to confirm presence of RBCs (>3 RBC/HPF) in 2 of 3 samples

Signs or symptoms of infection (e.g. dysuria, frequency, flank pain, leukocyte esterase, nitrites, white blood cells, bacteria)

Treat infection; confirm resolution of microscopic hematuria with follow up urinalysis 6 weeks after completion of therapy

Findings in support of glomerular cause (e.g. proteinuria, elevated creatinine level, red cell casts, dysmorphic RBCs abnormal sediment ≥ 5-10 white blood cells (WBC)/HPF or reduced renal function). Cytology is a poor screening test and is not recommended in the initial workup.

Refer to nephrologist

Other etiology probable (e.g. vigorous exercise, trauma to urethra, menstruation, offending medication)

Retest urine after possible contributing factor is stopped

Proceed with radiographic evaluation of the urinary tract.

1. Renal Ultrasonography
   Strengths: inexpensive and safest detection of solid masses >3 cm in diameter and hydronephrosis, no ionizing radiation
   Limitations: detection of solid tumours < 3cm in diameter.
   Renal ultrasound is preferred over IVP and CT as it has comparable sensitivity and specificity and lower morbidity and costs.¹

2. Computed Tomography (CT)
   Strengths: detection of renal calculi, small renal and pararenal abscesses,
   Limitations: high cost and limited availability in some areas, = 2-3 years background radiation exposure*¹

3. Intravenous Pyelogram (IVP)
   Strengths: detecting transitional cell carcinoma of kidney or ureter in renal masses > 3cm in diameter
   Limitations: detecting renal masses < 3cm or lesions of the bladder or urethra, = 1 year background radiation exposure*¹

If negative, proceed with urine cytology

If positive, refer to urology subspecialist

Negative findings, low risk (patient- <40 and no risk factors)

Positive findings, or all patients >40, or younger patients with risk factors for urothelial tumours

Follow-up: perform urinalysis and measure blood pressure. If hematuria persists > 3 mo, consider referral to a specialist

Referral to urology subspecialist for cytoscopy

* Please note that CT and IVP do not assess lower urinary tract

¹ Microscopic Hematuria (Persistent)
Tests

a) Urinalysis (dipstick):
Microscopic urinalysis can distinguish between dysmorphic red cells (renal parenchyma) and isomorphic red cells (urinary collecting system) providing initial direction for appropriate referral and investigation. Persistent unexplained microscopic hematuria (two or more samples out of three) requires investigation prior to referral. Urine dipstick may be misleading as it lacks the ability to distinguish red blood cells from myoglobin or hemoglobin. Thus, a positive dipstick test requires follow up examination by microscopic technique to confirm the presence of red blood cells.

i) Lab sample: For routine urinalysis, a midstream specimen collected in a clean container without prior cleansing of the genitalia provides a satisfactory sample. If the specimen is likely to be contaminated by vaginal discharge or menstrual blood, repeat the sample later.

Ideally, the specimen for routine analysis should be examined while fresh. If this is not possible, refrigeration until examination is recommended. Because it is concentrated, the first specimen voided upon rising is the preferred specimen for routine urinalysis. Red cells and casts are more likely to deteriorate if the urine specific gravity is low (<1.015) or the pH high (≥7.0). However, a randomly collected specimen is more convenient for the patient and is usually acceptable for most purposes.

b) Imaging:
Most adult patients with persistent microscopic hematuria usually require imaging evaluation. However, young women presenting with a clinical picture of simple cystitis and whose hematuria resolves after successful therapy may not require imaging. Patients who have clear-cut evidence of glomerulopathy may be appropriately investigated with renal ultrasound and chest radiography. Renal ultrasonography computed tomography (CT) and intravenous pyelogram (IVP) are often used to evaluate the upper urinary tract of patients with microscopic hematuria. Renal ultrasound is preferred over IVP and CT as it has comparable sensitivity and specificity, as well as lower morbidity and costs.

Following imaging of the upper urinary tract:

- Urine cytology studies are recommended for all patients with persistent microscopic hematuria.
- Cystoscopy is recommended for all patients >40 with persistent microscopic hematuria and patients of any age with persistent microscopic hematuria and risk factors for bladder cancer.

Follow Up

No cause will be found for microscopic hematuria in many cases. If initial ultrasound and other investigations reveal no disease, cystoscopy for persistent asymptomatic microscopic hematuria is not warranted in patients under 40 without risk factors for bladder cancer unless gross hematuria, a significant increase in the number of red blood cells, or urinary tract symptoms develop. When no specific cause for persistent microscopic hematuria is found, perform urinalysis and measure blood pressure. If the hematuria persists beyond three months, consider referral to a specialist.

Rationale

Microscopic hematuria is often an incidental finding but may be associated with urologic malignancy in up to 10 percent of adults. The incidence of underlying renal or bladder malignancy in those over 40 with microscopic hematuria increases with age (average age 60) and bladder cancer is twice as common in men as in women. There is considerable variation between recommendations from population-based studies versus referral based studies as to the prevalence of significant disease in patients with microscopic hematuria.
References


This guideline is based on scientific evidence current as of the Effective Date.

This guideline was developed by the Guidelines and Protocols Advisory Committee, approved by the British Columbia Medical Association and adopted by the Medical Services Commission.

The principles of the Guidelines and Protocols Advisory Committee are to:
- encourage appropriate responses to common medical situations
- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

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