Population Covered By The Guidance

This pathway provides guidance on the investigation of adult patients with painless microscopic haematuria.

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Quick User Guide

Move the mouse cursor over the PINK text boxes inside the flow chart to bring up a pop up box with salient points.
Clicking on the PINK text box will bring up the full text.
The relative radiation level (RRL) of each imaging investigation is displayed in the pop up box.

<table>
<thead>
<tr>
<th>SYMBOL</th>
<th>RRL</th>
<th>EFFECTIVE DOSE RANGE</th>
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<td>None</td>
<td>0</td>
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<td><img src="image" alt="Symbol" /></td>
<td>Minimal</td>
<td>&lt; 1 millisieverts</td>
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<td><img src="image" alt="Symbol" /></td>
<td>Low</td>
<td>1-5 mSv</td>
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<td><img src="image" alt="Symbol" /></td>
<td>Medium</td>
<td>5-10 mSv</td>
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<tr>
<td><img src="image" alt="Symbol" /></td>
<td>High</td>
<td>&gt;10 mSv</td>
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Pathway Diagram
**PAINLESS MICROSCOPIC HAEMATURIA**

Exclude transient causes of haematuria

- **Culture urine (MSU)**
  - Positive: Treat and repeat MSU
  - Negative: No further investigation

Three mid-stream urine samples

Renal tests
U&Es, proteinuria, urinary red cell casts, hypertension

Nephrological disease (Glomerular)
- Worsening renal function. Refer patient

Urological disease (Non-glomerular)

- Age < 40 and risk factors absent
  - Ultrasound +/- Cytoscopy
    - Positive: Appropriate management
    - Negative: Follow-up

- Age > 40 or risk factors present
  - US and Cytoscopy +/- MDCT Urography, cytology and IVP
    - Positive: Appropriate management
Image Gallery

*Note: These images open in a new page*

1a

**Transitional Cell Carcinoma (TCC)**

Image 1a and 1b (Computed Tomography): Axial and coronal images of a large transitional cell carcinoma arising from the left lateral wall of the bladder and extending into the rectum and surrounding soft tissues. There is secondary hydronephrosis of the left kidney from ureteric obstruction.

1b

2

**Transitional Cell Carcinoma (TCC)**

Image 2: Cystoprostatectomy and bilateral nephroureterectomy showing severe bilateral hydroureter, hydronephrosis and renal cortical atrophy secondary to an extensive bladder transitional cell carcinoma causing ureteric obstruction.

3

**Transitional Cell Carcinoma (TCC)**

Image 3: Cystectomy showing a polypoid tumour arising from the mucosa of the bladder, confirmed to be a transitional cell carcinoma on histology.

**Teaching Points**

- Glomerular and non-glomerular haematuria should be distinguished in patients with microscopic haematuria
- It is important to risk stratify patients prior to the selection of appropriate diagnostic investigations
- In patients with non-glomerular microscopic haematuria requiring investigation, imaging of the urinary tract may be by ultrasound, intravenous pyelogram (IVP) or CT scan (or a combination of these)
Painless Microscopic Haematuria

- The prevalence of painless microscopic haematuria varies between 0.19-21%, depending on the study population. The yield of serious pathology is approximately 1-2% in a number of large series. This contrasts with macroscopic haematuria, where the yield can be as high as 25%. Due to its high prevalence and low yield of significant pathology, there has been considerable debate as to the appropriate protocol to evaluate patients with microscopic haematuria. These considerations include risk-benefit analysis of extensive diagnostic investigations (with the inherent risk of false positive/false negative results) and cost analysis.
- If the presence of red cells is noted, the urine should be cultured for organisms to ensure an infection of the urinary tract is not the cause of bleeding.
- Dipstick (reagent strip) is moderately useful in the detection of microscopic haematuria. To confirm the diagnosis of microscopic haematuria, it is suggested that three well collected Mid-Stream Urine (MSU) samples be analysed. If at least two of these samples show the presence of red cells in the absence of ‘transient causes’ or infection, evaluation for an underlying cause should be considered.
- In 50-60% of cases despite extensive diagnostic workup, no cause for microscopic haematuria will be found.

MDCT Urography

- Computed tomography has been shown to be superior to trans-abdominal ultrasound in the detection and characterisation of <3cm renal masses. This test has also been shown to improve the diagnostic yield when compared to intravenous pyelogram.
- There is evidence to suggest that MDCT Urography should be employed in the evaluation of patients, when other diagnostic tests fail to elucidate a cause of asymptomatic haematuria. The scan protocol should include; Non contrast scan, arterial/early corticomedullary phase, nephrographic and excretory phase.
- This protocol has been shown to demonstrate a cause of microscopic haematuria in up to 45% of patients, who previously had negative diagnostic investigations. In addition to the improved detection of pathology, sensitivity and specificity (92% and 94% respectively) of CT compared to histopathological specimen and urological surveillance was maintained.
- However the radiation exposure is much higher in MDCT urography and is highly dependant on the exact CT protocol used.

Ultrasound and Flexible Cytoscopy +/- MDCT Urography, Urinary Cytology and IVP

- Patients aged > 40 or with risk factors should have
  - Ultrasound of the upper renal tract and
  - Cystoureteroscopy – The gold standard for lower urinary tract malignancies.
- The following tests should be considered on a case by case basis.
- Multidetector CT-Urography
  - Computed tomography has been shown to be superior to trans-abdominal ultrasound in the detection and characterisation of <3cm renal masses. This test has also been shown to improve the diagnostic yield when compared to intravenous pyelogram.
  - There is evidence to suggest that MDCT Urography should be employed in the evaluation of patients, when other diagnostic tests fail to elucidate a cause of asymptomatic
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- Urinary cytology (sensitivity 25%, specificity 91%). Therefore high positive predictive value but low negative predictive value.\(^1\)
- Intravenous pyelogram – This investigation, in addition to ultrasound is more sensitive than either test in the detection of upper tract urothelial tumours.\(^5\)

Follow-Up

- In 50-60% of cases, despite extensive radiological and urological investigation no cause for painless microscopic haematuria will be found.
- Given the lack of consensus as to the appropriate algorithm to investigate patients with haematuria, it is not surprising that there is disagreement as to how individuals with initial negative diagnostic tests should be followed up.
- The follow-up of patients with painless microscopic haematuria is difficult as evidence does suggest that a cause of bleeding will be identified in a small percentage (up to 5%) of these individuals, including malignancy.\(^6\)
  - MSU and properly collected and analysed urinary cytology every 12 months.
  - Expeditious investigation should be performed in any patient with unexplained microscopic haematuria who develops gross haematuria, recurrent urinary tract infections or changes in voiding characteristics.\(^6\)

Intravenous Pyelogram (IVP)

- Traditionally, has been the initial investigation of choice for the evaluation of the upper renal tract.\(^2,3,4\)
- Allows functional and anatomical assessment of upper and to a lesser extent lower urinary tract.
- Superior to US for detection of stone disease.\(^7\)
- CT is becoming more widely used as the investigation of choice as a normal IVP may not obviate need for CT and if the IVP is abnormal, CT and cystoscopy are still required for staging.

Limitations

- Limited sensitivity in detecting small renal masses (may miss small exophytic anterior and posterior renal masses).\(^8\)
- Inability to distinguish solid from cystic masses. Therefore, when a mass is identified on IVP, further lesion characterisation by US +/- CT is indicated.\(^8,9\)

Advantages

- Widely available
- Relatively inexpensive
- Generally considered better than ultrasound for the detection of renal pelvis and ureteric tumours, although these make up the minority of renal tract malignancies (majority are renal
Disadvantages
- Ionising radiation
- Potential complications due to contrast media

Age And Risk Factor Assessment

- The prevalence of malignancy of the renal tract increases with age. In a large prospective evaluation of patients with microscopic haematuria, in men aged <50 the chance of malignancy was 0.44%. In the case of women <60, the detection rate was 0.75%. This contrasts with macroscopic haematuria where the incidence of malignant disease in comparable age groups was 4.8% in men and 2.1% in women. ²
- Risk factors predisposing to an increased risk of malignancy of the urinary tract include
  - Cigarette smoking
  - Analgesic abuse
  - Occupational exposures to chemicals in certain industries (leather, dye and rubber)
  - Past treatment with high doses of cyclophosphamide
  - Past treatment with pelvic irradiation

Transient Causes Of Asymptomatic Haematuria

- Transient microscopic haematuria may be induced by a variety of activities; vigorous exercise, mild trauma, menstruation and sexual intercourse. ⁴ These causes should be excluded prior to extensive diagnostic work up of microscopic haematuria

Ultrasound +/- Flexible Cystoscopy

- Patients aged <40 and with no risk factors should have an ultrasound of the upper renal tract. This will detect serious upper renal tract pathology with sufficient sensitivity, mitigating the need for additional investigations
- Ultrasound is effective in the detection of upper tract tumours, though more sensitive for renal cell carcinoma than for upper tract transitional cell carcinoma. Compared to the use of US and IVP, US alone provided a sensitivity of 94.5% for the detection of all upper tract malignancies. ²
- A case by case decision should be made as to whether a flexible cystoscopy should be included as part of the diagnostic algorithm

References

References are graded from Level I to V according to the Oxford Centre for Evidence-Based Medicine, Levels of Evidence. Download the document

2. Edwards T, Dickinson A, Natale S. A prospective analysis of the diagnostic yield resulting from the attendance of 4020 patients at a protocol-driven haematuria clinic. BJU Int.

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