

Assessment of Haematuria (presence of red blood cells in urine)

Definitions

Haematuria: presence of red blood cells in urine:

- may be visible, “macroscopic” (VH) or non visible, “microscopic” (NVH) - identified by dipstick urinalysis;
- may be symptomatic (s-VH or s-NVH) haematuria with lower urinary tract symptoms such as dysuria, frequency, hesitancy and urgency; or asymptomatic (a-VH or a-NVH), incidental finding in the absence of symptoms.

Policy¹⁻⁵

It is the responsibility of referring and treating clinicians to ensure compliance with this policy. Referral proforma and surgeon checklists should be attached to the patient notes to aid the clinical audit process and provide evidence of compliance with the policy. For patients not meeting the policy criteria, clinicians can apply for funding to the Exceptional Cases Panel <http://www.cambsphn.nhs.uk/CCPF/ExcptnalandIFR.aspx>.

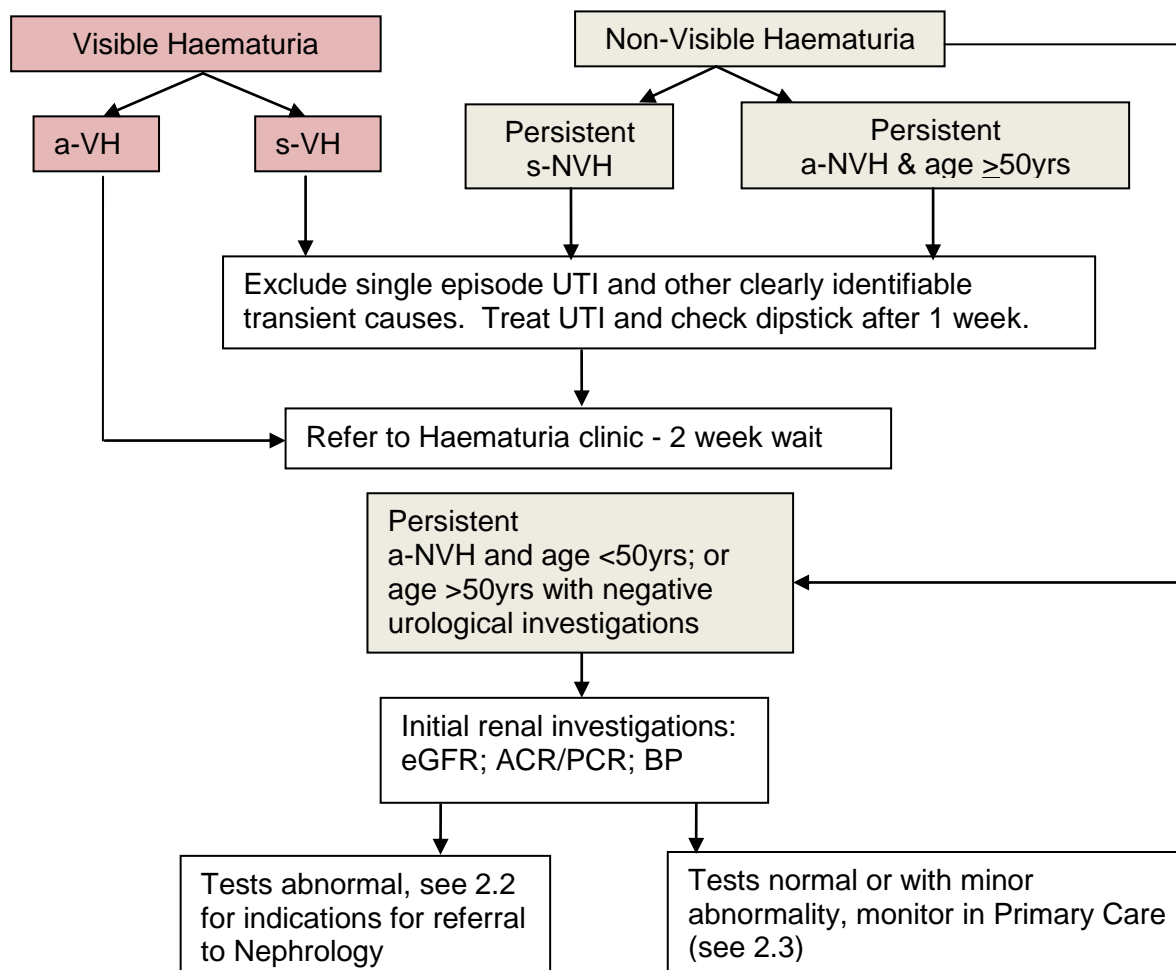
- The CCG does NOT fund direct referral for cystoscopy for haematuriaⁱ.
- The CCG will **ONLY** fund urgent referral to the haematuria clinic for:
 - Visible painless/asymptomatic haematuria (a-VH).
OR for the following symptoms ***after excluding transient causes***ⁱⁱ (such as UTI and drug discolouration).
 - Visible symptomatic haematuria (s-VH).
 - Persistentⁱⁱⁱ symptomatic, non-visible haematuria (s-NVH).
 - Persistent^{iv} asymptomatic non-visible haematuria (a-NVH) older than 50 years (in patients younger than 50 years, consider possible renal disease)^v.

Notes:

- The decision on whether or not cystoscopy is carried out will be a matter for the secondary care physician to whom the patient is referred.
- Exclude (and treat if present) single episode urinary tract infection (UTI) that is clearly associated with the presenting haematuria; and other causes if clearly identifiable: exercise-induced haematuria; myoglobinuria; haemoglobinuria; beeturia; menstruation; or drug discolouration – rifampicin, doxorubicin.
- Persistent means lasting more than would be normally expected. Recurrent and persistent UTI is not transient and needs referral to haematuria clinic, but a single symptomatic urinary infection leading to painful haematuria should be treated in primary care.
- Persistent a-NVH means 2 out of 3 dipsticks, done at weekly intervals within one month, testing positive. (1+ or greater on the dipstick). Urine microscopy should not be used as it has a significant false negative rate, is more labour intensive and adds little to establishing the diagnosis of haematuria.
- If there is no identifiable urological cause, non visible haematuria may be presumed to arise from the kidneys. Consider nephrology referral:
 - if initial investigations for nephrological markers are abnormal in patients younger than 50 years of age – markers being blood pressure to exclude age-related hypertension; reduced estimated Glomerular filtration rate (eGFR) less than 60ml/min; and proteinuria;
 - in isolated haematuria (ie in the absence of significant proteinuria) with hypertension in patients younger than 40 years;
 - evidence of declining GFR: by more than 10ml/min at any stage in the last 5 years or by more than 5ml/min in the last year;
 - stage 4 or 5 CKD (chronic kidney disease): eGFR less than 30ml/min;
 - visible haematuria coinciding with intercurrent (usually upper respiratory) infection.

Assessment Process Prior to Referral to Haematuria Clinic

A patient with haematuria should not be referred directly for a cystoscopy. Patients should be assessed following this pathway.



1. Assessment of Haematuria in Primary Care

1.1 Exclude urinary tract infection (UTI):

UTI with haematuria should be treated appropriately and a dipstick repeated at one week to confirm the post-treatment absence of haematuria and infection. UTI is most readily excluded by a negative dipstick result for both leucocytes and nitrites.

Recurrent and persistent UTI with haematuria could be due to malignancy and needs referral to haematuria clinic, but a single symptomatic urinary infection leading to painful haematuria should be treated in primary care, and the patient subsequently reassessed post treatment to ensure haematuria has resolved.

1.2. Exclude contamination or other transient causes like exercise induced haematuria, myoglobinuria, haemoglobinuria, beeturia, menstruation or drug discolouration – rifampicin, doxorubicin.

1.3. The presence of haematuria (VH or NVH) should not be attributed to anti-coagulant or anti-platelet therapy and patients should be evaluated regardless of these medications. Anticoagulated patients with visible haematuria have a higher risk of harbouring malignancy, as the anticoagulation simply 'unmasks' the pathology.

1.4. The presence of lower urinary tract symptoms (LUTS) such as dysuria, hesitancy, frequency and urgency with haematuria in the absence of UTI could point towards malignancy.

- 1.5. If other symptoms are suggestive, it is important to exclude renal disease as a cause, particularly in younger patients. Initial investigations for nephrological markers are:
- Blood pressure to exclude age related hypertension.
 - Plasma eGFR – reduced eGFR is less than 60ml/min.
 - Urine for Proteinuria – either protein: creatinine ratio (PCR) or albumin: creatinine ratio (ACR) – significant proteinuria is PCR more than 50mg/mmol, or ACR more than 30mg/mmol.
NB: 24-hour urine collections for protein are rarely required. An approximation to the 24-hour urine protein or albumin excretion (in mg) is obtained by multiplying the ratio (in mg/mmol) by 10.

2. **Criteria for Referral to Secondary Care, Following Assessment in Primary Care**

2.1 Referral criteria to the **haematuria clinic under the 2 week wait**

- Asymptomatic visible haematuria (a-VH) at any age.
- Symptomatic visible haematuria (s-VH) at any age, after exclusion of single UTI.
- Persistent Symptomatic NVH (s-NVH) at any age – lower urinary tract symptoms (LUTS): hesitancy, frequency, urgency, dysuria.
- Persistent Asymptomatic NVH (a-NVH) – more than 50 years – which is persistent (2 of 3 dipsticks positive, done at weekly intervals within a month).

2.2 **Nephrology referral** should be considered in the following circumstances for patients (1) age <50 years with a-NVH, and (2) age >50 years with a-NVH and negative urological investigations:

- Stage 3B, 4 or 5 CKD (chronic kidney disease): eGFR less than 45 ml/min.
- Evidence of declining GFR: by more than 10ml/min at any stage within the last 5 years or by more than 5ml/min within the last year.
- Proteinuria: a-NVH with ACR >40 mg/mmol.
- Isolated haematuria (ie in the absence of significant proteinuria) with hypertension in those aged younger than 40 years.
- Visible haematuria coinciding with intercurrent (usually upper respiratory) infection.

2.3. Patients with persistent a-NVH - less than 50 years - and renal investigations not satisfying the requirement for nephrology referral (section 2.2), should be managed in primary care with annual monitoring of BP, urinary protein excretion (by dipstick, with ACR if positive), serum creatinine and referred to nephrology if BP above target with three drugs, or ACR >40 mg/mmol, or eGFR falling by >5ml/min/year (or to <45 ml/min, CKD 3B). Consider urgent referral to urology if high risk of malignancy (eg male, aged over 40 years, smoker, high risk occupation, exposure to carcinogens).

3. **Long term monitoring of patients with Haematuria (Visible or Non-Visible) of undetermined aetiology in Primary Care:**

Patients not meeting the criteria for referral to urology or nephrology, or who have negative urological or nephrological investigations, need long term monitoring due to the uncertainty of the underlying diagnosis.

Patients should be monitored for the development of:

- s-NVH in a patient with a-NVH.
- Lower urinary tract symptoms (LUTS).
- Visible haematuria.
- Significant or increasing proteinuria (see 2.3).
- Progressive renal impairment (falling eGFR) (see 2.3).
- Hypertension (noting that the development of hypertension in older people may have no relation to the haematuria and, therefore, not increase the likelihood of underlying glomerular disease).

All patients with haematuria need to be assessed promptly and considered for further investigation. The '2-week rule' has increased the cancer detection rate in NHS institutions.

Visible haematuria (VH) may be a sign of serious underlying disease, including malignancy, and is a common presentation in patients with cancers of the bladder or kidney which, therefore, warrants a thorough diagnostic evaluation. Around one patient in five who develops visible haematuria is likely to have urological cancer. Clinic based studies (ie of patients who have been referred to secondary care) indicate that 15% to 37% of patients with visible haematuria investigated in that setting have cancer. Higher proportions were found in areas where substantial numbers of people worked in hazardous industries.

Non visible haematuria (NVH) can be an incidental finding that alone is not necessarily abnormal. It is common in young men and rarely associated with any pathology, but is a better predictor of cancer in older men. A large hospital based haematuria clinic study of 1,930 patients in Newcastle, cited by NICE (2002) found that 9.4% of patients with microscopic haematuria (NVH) had cancer.

The major risk factors for urological cancers are male sex, older age, smoking and obesity. Hence a 70yr old, obese, male smoker with s-NVH is more likely to have a urological cancer than a 20 year old, normal weight, female who does not smoke and presents with s-NVH. The relative risks attributable to each of these risk factors are:

Risk Factor		Bladder Cancer		Kidney Cancer	
		Male	Female	Male	Female
Gender	Male vs female	3.4	-	1.9	-
Age	65-74 vs <65	17.3	13.7	7.5	7.0
	>75 vs <65	37.8	31.9	10.6	9.5
Smoking	>35 yr old smoker vs never smoked	3.0	2.4	2.5	1.5
Obesity	Overweight vs normal weight	-	-	1.3	
	Obese vs normal weight	-	-	1.7	

OPCS Codes

M45 Diagnostic endoscopic examination of bladder.
M77 Diagnostic endoscopic examination of urethra.

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Glossary

ACR:	Albumin:Creatinine Ratio, a measure of proteinuria (see below).
Beeturia:	Discolouration of the urine due to the consumption (eating) of beetroot.
Cystoscopy:	Refers to looking inside the bladder for medical reasons using an instrument called a cystoscope.
Dysuria:	Painful urination (weeing).
eGFR:	Refers to estimated Glomerular Filtration Rate, the rate at which the kidneys process blood products and is a measure of the health of the kidneys.
Haematuria:	The presence of red blood cells in the urine (wee). This may be visible, or “macroscopic” (VH for visible haematuria) or non visible, “microscopic” (NVH for non visible haematuria) – identified by dipstick urinalysis of the urine. Haematuria may be symptomatic (s-VH or s-NVH) haematuria with symptoms such as dysuria and urgency; or asymptomatic (a-VH or a-NVH), ie haematuria without symptoms.
Haemoglobinuria:	The presence of blood in the urine caused by the destruction of blood cells in the blood vessels or in the urinary passages. It turns urine a dark red or brown colour. It may be an indication of renal (kidney) disease.
LUTS:	Stands for ‘lower urinary tract symptoms’.
Myoglobinuria:	Is a process of muscle destruction which may, in rare instances, be indicated by haematuria.
Nephrology:	Refers to assessment of renal (kidney) conditions.
PCR:	Protein:Creatinine Ratio, a measure of proteinuria (see below).
Plasma creatinine:	Is a measure of the kidney filtration rate (an indicator of the health of the kidneys).
Prognostic:	An indicator of the course of a disease.
Proteinuria:	The presence of an excess of serum proteins in the urine, often an indication of kidney damage.
Urinary system:	The urinary system is the organ system that produces, stores, and eliminates urine.
UTI:	Urinary tract infection.

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