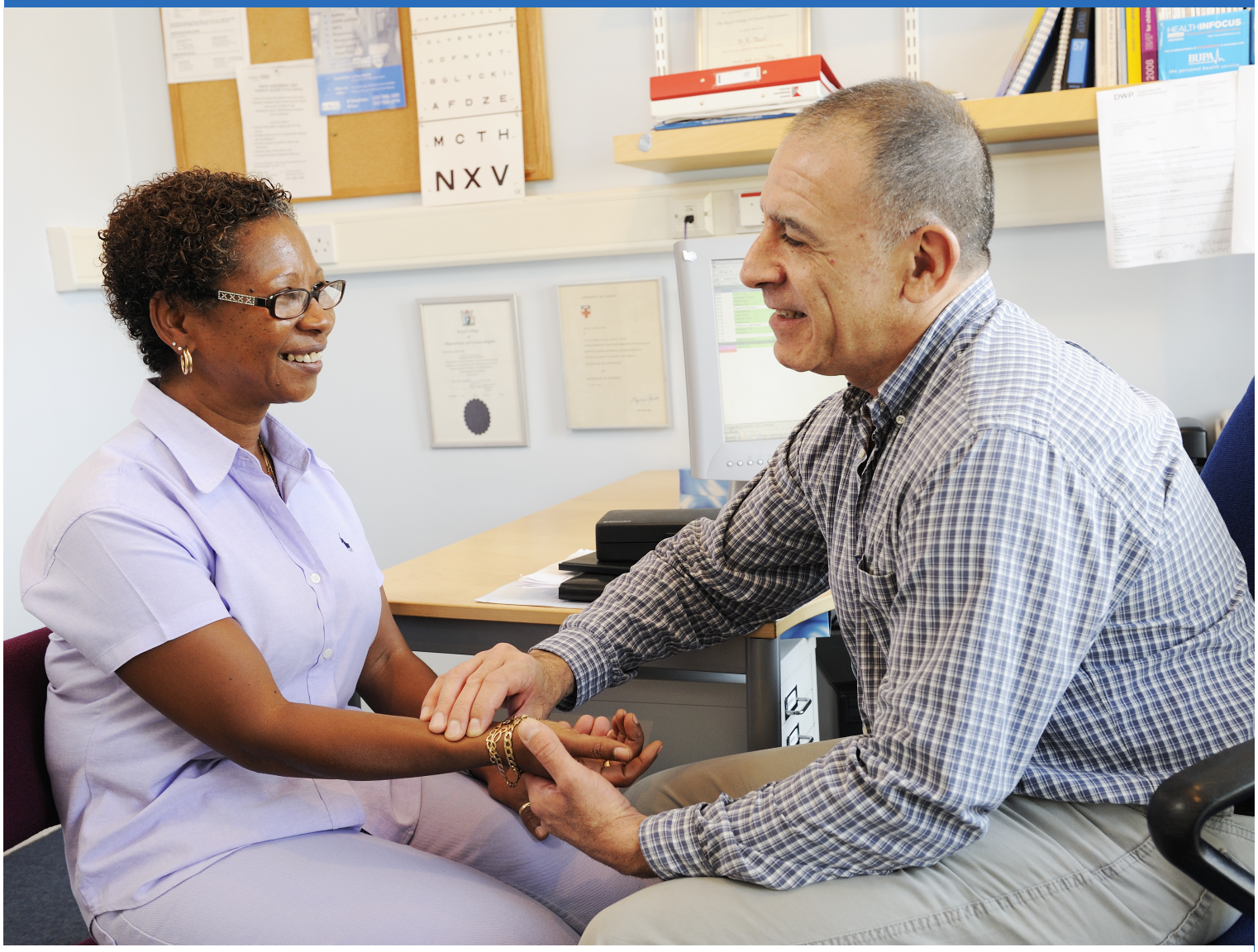
BMJ Best Practice

Assessment of microscopic haematuria

The right clinical information, right where it's needed



Last updated: Oct 03, 2016

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Summary

◊ **Definition :**
Urine sediment after centrifuge normally contains 2 to 3 RBCs per high power field (RBC/HPF) on microscopic examination.[1] [2] [3] There is consensus that ≥3 RBC/HPF in 2 of 3 urine specimens signals microscopic haematuria (MH). However, fewer RBCs from just 1 specimen should not exclude patients with risk for malignancy from a complete evaluation, because intermittent bleeding may occur.[1] [3]

◊ **Significance :**
Although less commonly associated with malignancy than gross haematuria, MH may signal cancer. However, about half of cases of MH are idiopathic.[2] [3] [4] [5] [6] [7] [AUA: diagnosis, evaluation and follow-up of asymptomatic microhematuria (AMH) in adults]

◊ **History :**
The most important initial diagnostic step is a detailed history, with the aim of identifying risk factors for malignancy. History may also indicate less serious causes (e.g., recent exercise or sexual activity, UTI, and menstruation).

◊ **Cancer risk factors :**
The risk of urinary tract malignancy increases with age >40 years, tobacco use, previous radiation exposure, and certain occupational exposures (dyes, benzenes, aromatic amines) and medications such as phenacetin (available only in Japan), cyclophosphamide, and aristolochic acid in some herbal weight loss preparations).[6] If malignancy is suspected, based on a high-risk profile, then evaluation of the entire urinary tract, including upper tract imaging and cystoscopy for the lower tract, is required.[1] [6] [8] [9] [10] [11] [12] By contrast, the work-up of low-risk patients can be more focused towards the suspected cause without a complete urinary tract survey.

◊ **Classification scheme :**
Considering the source of bleeding by anatomical site offers an organised approach. The upper urinary tract includes the kidneys (glomerular or non-glomerular) and ureters, with remaining structures in the lower urinary tract. These dividing lines are useful to apply during the history and physical examination, as well as when ordering diagnostic tests, because no one diagnostic test evaluates the urinary tract completely.

◊ **Diagnostic testing :**
Diagnostic testing must first confirm the presence of MH. Secondly, testing may distinguish an upper tract glomerular source from other causes, allowing a more refined work-up, but upper and lower tract diagnostic tests (imaging and cystoscopy) remain necessary in all patients with risk factors for urinary tract malignancy. Using urinary tumour markers for diagnosing urinary tract cancer has not demonstrated adequate specificity for reliable diagnosis in research trials. However, the markers may play a role in assessing treatment efficacy and in identifying recurrences after treatment.[13] [14]

◊ **Screening :**
The most often identified cancer in patients with MH is bladder transitional cell carcinoma.[5] [8] [15] [16] [17] The US Preventive Services Task Force estimates a positive predictive value of 5% to 8% for MH indicating bladder cancer and recommends against routine screening.[7] [18] 1[B]Evidence One case-control study including people with renal neoplasms found that patients with ≥4 RBC/HPF or ≥5 RBC/HPF in a single urine sample were twice as likely to have concomitant MH (odds ratio of 2.2 for ≥4 RBC/HPF and 2.0 for ≥5 RBC/HPF) as patients without malignancy.[19]

Aetiology

Upper urinary tract (non-glomerular)

Upper urinary tract non-glomerular causes of MH include infection (pyelonephritis); stone formation (nephrolithiasis); and 3 broader groups: mass lesions, and abnormalities of vascular inflow and urine outflow. Mass lesions range from benign simple renal cysts to malignancy (renal cell carcinoma and calyceal or ureteral transitional cell carcinoma). Renal artery infarction, renal vein thrombosis, arteriovenous malformations, and papillary necrosis (or sickle cell disease) are vascular inflow examples. Hydronephrosis, vesicoureteral reflux, calyceal diverticula, and ureteropelvic junction obstruction relate to urine outflow. Other renal pathologies, such as polycystic kidney disease, atrophic kidney, and medullary sponge kidney, can present with MH.

Upper urinary tract (glomerular)

Kidney disorders involving the glomerulus (acute glomerulonephritis, lupus nephritis, thin glomerular basement membrane disease, and IgA nephropathy) and producing MH can be identified early in the diagnostic evaluation by RBC morphology and the presence of proteinuria.[3] [6] [20] [21] [22] Early recognition of these allows for a more focused work-up and prompts nephrology consultation.

Lower urinary tract

The lower urinary tract includes the bladder and urethra, as well as the prostate and penis. As with the upper urinary tract, infection (cystitis, urethritis, prostatitis), stone formation, tumours (e.g., bladder papilloma), and diverticula also contribute to MH originating from the lower urinary tract. Most often a malignant lesion causing MH occurs within the lower urinary tract, specifically a transitional cell carcinoma of the bladder.[5] [8] [15] [16] [17] Non-infectious causes of cystitis (radiation-induced, interstitial, and eosinophilic cystitis) and disorders occurring only in men (BPH, prostate cancer, phimosis, penis cancer) also need to be considered as possible causes of MH. Other lower urinary tract causes include bladder neck contracture and urethral stricture.

Non-urinary tract origin

Several causes do not fit within the other categories. Some readily identifiable causes belong in this group and should be inquired about early in the history. Examples include menstruation and trauma (sexual activity, contusion, exercise). Other miscellaneous causes include HIV, lymphoma, multiple myeloma, and urinary tract tuberculosis.[23]

Urgent considerations

(See **Differential diagnosis** for more details)

Malignancy

The diagnostic evaluation recommended for MH may take several weeks to complete and therefore should begin promptly, but the possibility of a malignant cause does not require immediate evaluation or admission to hospital.

Infection

When identified, a UTI needs appropriate treatment to prevent complications that may warrant urgent treatment, such as pyelonephritis and bacteraemia.

Vascular

If renal infarction, renal vein thrombosis, or papillary necrosis is suspected as the aetiology for MH, urgent treatment is important to attempt to preserve renal function.

Red flags

- Pyelonephritis
- Renal cell carcinoma
- Transitional cell carcinoma (kidney or ureter)
- Renal infarction
- Renal vein thrombosis
- IgA nephropathy
- Acute glomerulonephritis
- Lupus nephritis
- Hereditary nephritis (Alport's syndrome)
- Transitional cell carcinoma (bladder)
- Prostate cancer
- Penile cancer
- HIV
- Lymphoma
- Multiple myeloma

Step-by-step diagnostic approach

History

A complete history assists in determining the work-up for MH. The circumstances surrounding the patient's haematuria should be explored. The presence of dysuria, urgency, urinary frequency, and fever may indicate UTI. Identifying a concomitant history of infection, menses, recent sexual activity, or exercise will avoid an extensive work-up. Typically, haematuria due to intense exercise will clear within a few hours.[24] Consideration should be given to repeating a urinalysis 6 weeks after treatment of UTI.[25] Additional history regarding risk factors for urinary tract cancer may identify the need for a detailed evaluation including imaging and cystoscopy.[1] [5] [25] Other important findings include family history of upper tract glomerular and non-glomerular disorders, or personal or family history of bleeding disorders or sickle cell anaemia. Finally, occupational exposures other than those known to relate to cancer risk (e.g., pesticide plant workers) may induce MH.[26]

Risk factors for urinary tract cancer include:

- Age: unusual before 40 years of age;[9] [10] [11] [12] risk increases with advancing age beyond 40 years[1] [8] [10] The incidence below the age of 40 years was found to be 1% to 2.4%.[27]
- Tobacco use
- Medications: phenacetin (available only in Japan); cyclophosphamide; aristolochic acid in some herbal weight loss preparations[6]
- Past medical history: radiation exposure
- Occupational exposures: dyes, benzenes, aromatic amines.

Examination

The physical examination needs to include a search for disorders directly related to the urinary tract, as well as other systemic diseases. For example, blood pressure can be elevated with upper tract glomerular diseases, and petechiae, bruising, or lymphadenopathy may signal bleeding disorders or blood cell cancers. Examination of the abdomen and of the external genitalia may also reveal a source for MH. In men, a digital rectal examination will identify BPH and potentially discover prostate cancer. The physical examination can, like a detailed history, preclude an extensive evaluation if an obvious source is identified.

Basic laboratory tests

Initial laboratory testing should evaluate for systemic disorders in the appropriate clinical settings and include coagulation studies, ESR, creatinine, and C-reactive protein. A urine culture will confirm UTI if suspected. Prostate-specific antigen testing aids in identifying the prostate as a source for MH.

Urine microscopy

Before pursuing any work-up, the presence of haematuria should be confirmed by urine microscopy.[1] [6] [20] Urine dipstick testing is highly sensitive for blood but lacks specificity.[1] [6] [28] False-positives occur due to povidone-iodine, myoglobin, free haemoglobin, hypochlorite solutions, oxidising agents, and high levels of ascorbic acid.[3] There is consensus that ≥3 RBC/HPF in 2 of 3 centrifuged urine specimens signals microscopic haematuria (MH).[18] However, fewer RBCs from just 1 specimen should not exclude patients with risk for malignancy from a complete evaluation, because intermittent bleeding may occur.[1] Microscopy should examine freshly voided midstream urine, immediately after dipstick testing if dipstick testing is performed.[1] [28] Microscopy confirms MH, but it also directs the further work-up by identifying dysmorphic RBCs and RBC casts, which suggest an upper tract glomerular source of bleeding.[3] [20] [25] [28] 2[B]Evidence

Urine protein

The presence of proteinuria and MH together is highly suggestive of an upper tract glomerular source.[3] [22] [25] [29] [30] 3[B]Evidence A urine protein to creatinine ratio of ≥0.3 or a urine albumin to total urine protein ratio of ≥0.59 suggests renal parenchymal disease.[6] [21] The latter ratio has a sensitivity of 97% for distinguishing glomerular from non-glomerular bleeding. Nephrology consult is warranted and renal biopsy decisions should be directed by the nephrologist, because most often renal biopsy in patients with MH does not alter management decisions.[3] [31] Additionally, renal biopsy is unnecessary if proteinuria does not co-exist with haematuria.[6]

Imaging

If the history and physical examination do not identify a source of bleeding and microscopy confirms the presence of MH, then imaging of the urinary tract is indicated unless an upper tract glomerular source is suspected.[3] Any patient, however, with risk factors for urinary tract cancer also requires imaging.[1] [5] [25] Three separate modalities are primarily used for evaluation: IV urogram (IVU), ultrasound, or CT. Whereas the upper tract is predominantly evaluated using these 3 modalities of imaging, advances in imaging technology mean that bladder pathologies can be identified through helical CT urography[32] [33] and/or virtual CT cystoscopy,[34] and 3-dimensional ultrasound.[35]

Helical CT with IV contrast provides the single best test, if available.[36] [32] [33] [37] 4[B]Evidence One trial demonstrated an overall 91% sensitivity with helical CT urography; this included a 94% sensitivity for bladder tumours but <90% sensitivity for other bladder pathology.[32] Virtual CT cystoscopy has shown up to 93% sensitivity in a recent meta-analysis.[34] If stones are suspected the initial helical CT should not include contrast. IVU or ultrasound may be considered instead of CT, with IVU as the first choice.[25] IVU and ultrasound compare favourably with each other, but both have limitations.[38] Each may miss small renal masses.[25] Also, IVU provides better identification of transitional cell carcinomas of the upper tract,[39] while ultrasound better recognises cystic lesions.[38]

Cystoscopy

Cystoscopy is recommended as standard in evaluating those patients without an identifiable cause by history and physical examination, those without a suspected upper tract glomerular source, and all patients with risk factors for malignancy.[25] Furthermore, a source for bleeding may be identified in only 30% of patients with imaging alone, and cystoscopy performs better than urine cytology.[6] 5[A]Evidence Evidence has demonstrated that even after a negative initial work-up (including IVU and urine cytology), cystoscopy identified lesions in approximately a further 25% of patients, with up to 56% of lesions labelled as "significant".[40]

Urine tumour markers

Using urinary tumour markers for diagnosing urinary tract cancer has not demonstrated adequate specificity for reliable diagnosis in research trials. However, the markers may play a role in assessing treatment efficacy and in identifying recurrences after treatment.[14] [13]

Differential diagnosis overview

Common
Menstruation
Cystitis (UTI)
Pyelonephritis
Nephrolithiasis
Acute prostatitis
Benign prostatic hyperplasia (BPH)
Trauma (sexual activity, exercise, contusion)
Uncommon
Bladder stone
Renal cell carcinoma
Transitional cell carcinoma (kidney or ureter)
Simple renal cyst
Polycystic kidney disease
Medullary sponge kidney
Atrophic kidney
Calyceal diverticulum
Renal infarction
Renal vein thrombosis
Arteriovenous malformations
Papillary necrosis
Sickle cell disease

Uncommon
Hydronephrosis
Ureteropelvic junction obstruction
Vesicoureteral reflux
IgA nephropathy
Thin glomerular basement membrane disease
Acute glomerulonephritis
Lupus nephritis
Hereditary nephritis (Alport's syndrome)
Transitional cell carcinoma (bladder)
Cystitis (interstitial)
Cystitis (radiation-induced)
Cystitis (eosinophilic)
Bladder diverticulum
Bladder papilloma
Prostate cancer
Prostate stone
Bladder neck contracture
Urethritis
Urethral stricture
Phimosis
Penile cancer
HIV

Uncommon
Lymphoma
Multiple myeloma
Urinary tract tuberculosis

Differential diagnosis

Common

◊ Menstruation

History	Exam	1st Test	Other tests
identified by obtaining a menstrual history	typically no examination findings	»**none:** diagnosis is based on typical history	

◊ Cystitis (UTI)

History	Exam	1st Test	Other tests
typically presents with dysuria, frequency, or urgency	suprapubic tenderness may be present; otherwise examination is often normal	»**urine culture:** ≥10^2 colony-forming units	

◊ Pyelonephritis

History	Exam	1st Test	Other tests
fever, chills, flank pain	costovertebral angle tenderness	»**urinalysis:** pyuria with WBC casts and bacteriuria	»**urine culture:** ≥10^2 colony-forming units »**ultrasound:** may suggest inflammation or obstruction »**helical CT of urinary tract with IV contrast:** may suggest inflammation or obstruction

◊ Nephrolithiasis

History	Exam	1st Test	Other tests
flank or groin pain	non-specific or may find flank tenderness	»**helical CT of urinary tract without contrast:** visible stone present	»**IV urography:** filling defect Should be used if helical CT is not available.

Common

◊ Acute prostatitis

History	Exam	1st Test	Other tests
fever, dysuria, and frequency occur and are often associated with suprapubic, perineal, or sacral pain; obstructive symptoms may occur in severe cases	fever may be present and digital rectal examination demonstrates a tender "boggy" prostate; examination often diagnostic	»**none:** clinical examination often diagnostic	»**culture of prostate secretions:** positive growth of bacteria Prostate secretions may be obtained by prostate massage during digital rectal examination, but caution should be taken, as this may induce bacteraemia.

◊ Benign prostatic hyperplasia (BPH)

History	Exam	1st Test	Other tests
urine outflow obstruction symptoms (difficulty voiding, changes in urine volume, lower abdominal discomfort or bladder fullness, and nocturia) occur	enlarged firm prostate on digital rectal examination; suprapubic tenderness may be present due to bladder fullness if severe obstruction; examination is often diagnostic	»**post void residual volume:** high post void residual volume suggests bladder outlet obstruction	»**transrectal ultrasound:** enlarged prostate Ultrasound is not routinely required because the examination and history are often diagnostic.

◊ Trauma (sexual activity, exercise, contusion)

History	Exam	1st Test	Other tests
recent sexual activity, strenuous exercise, or injury to the back (costovertebral angle area) or genitalia	may reveal signs of trauma (mucosal tears, ecchymoses) of the external genitalia; typically no examination findings	»**none:** diagnosis is based on typical history and examination	

Uncommon

◊ Bladder stone

History	Exam	1st Test	Other tests
dysuria or frequency may occur	no specific examination findings	»**ultrasound:** presence of shadowing that moves with patient repositioning	»**helical CT of urinary tract with IV contrast:** visible stone that moves with patient repositioning »**IV urography:** filling defect within bladder

Uncommon

◊ Bladder stone

History	Exam	1st Test	Other tests
			»**virtual cystoscopy:** visible stone

◊ Renal cell carcinoma

History	Exam	1st Test	Other tests
more common in men and associated with risk factors for urinary tract cancer including age >40 years; tobacco use; occupational exposure to dyes, benzenes, aromatic amines; use of medication containing phenacetin (available only in Japan), cyclophosphamide, and aristolochic acid (in some herbal weight loss preparations); family history of renal cell carcinoma; flank pain	examination normal or a renal mass may be palpable; evidence of anaemia can occur as well as paraneoplastic syndromes	»**helical CT of urinary tract with IV contrast:** solid renal mass with contrast enhancement	»**IV urography (IVU):** enhancing solid renal mass IVU may miss small renal lesions, making helical CT a better upper tract diagnostic study, with a 96% sensitivity for renal neoplasms and 91% sensitivity for ureteral lesions.[25] [32] »**renal ultrasound:** solid renal mass Renal ultrasound may miss small renal lesions, making helical CT a better upper tract diagnostic study, with a 96% sensitivity for renal neoplasms and 91% sensitivity for ureteral lesions.[25] [32]

◊ Transitional cell carcinoma (kidney or ureter)

History	Exam	1st Test	Other tests
microscopic or gross haematuria (in 70% to 95%), pain (in 8% to 40%), bladder irritation (in 5% to 10%), or constitutional symptoms (in <5%)[17] [15]	generally normal, rarely a flank mass is palpable	»**helical CT of urinary tract with IV contrast :** filling defect or visualised non-cystic mass with contrast enhancement	»**IV urography (IVU):** filling defect IVU may miss small renal lesions, making helical CT a better upper tract diagnostic study, with a 96% sensitivity for renal neoplasms and 91% sensitivity for ureteral lesions.[25] [32] »**urine cytology:** positive for malignant cells

Uncommon

◊ Transitional cell carcinoma (kidney or ureter)

History	Exam	1st Test	Other tests
			Lower yield with upper tract tumours; better yield with bladder tumours, but sensitivity ranges between 66% and 79% for the lower urinary tract.[6] »**ureteroscopy with biopsy:** biopsy positive for malignant cells

◊ Simple renal cyst

History	Exam	1st Test	Other tests
usually found incidentally; flank pain may be the presenting symptom	generally normal; rarely a flank mass is palpable	»**renal ultrasound:** fluid-filled (cystic) mass	»**helical CT of urinary tract with IV contrast:** fluid-filled (cystic) mass »**CT-guided aspiration:** aspiration of fluid Aspiration of fluid differentiates a cyst from a solid tumour but is rarely necessary; cytology studies negative for malignancy confirm a benign cyst.

◊ Polycystic kidney disease

History	Exam	1st Test	Other tests
most common presenting symptoms abdominal pain and haematuria; positive family history may be present	hypertension, palpable kidney or liver, and/or a cardiac murmur may be present	»**renal ultrasound:** 2 cysts (if <30 years); 2 cysts each kidney (if 30-59 years); 4 cysts each kidney (if ≥60 years)	»**helical CT of urinary tract with IV contrast:** multiple cystic lesions bilateral kidneys Adequate for diagnosis and can replace ultrasound first-line as part of work-up for haematuria.

Uncommon

◊ Medullary sponge kidney

History	Exam	1st Test	Other tests
most patients are asymptomatic and go undiagnosed; risk is increased for calculus and infection renal colic; dysuria or haematuria may be presenting symptoms	generally negative	»**IV urography (IVU):** dilated collecting tubules; stones may be present within the collecting tubules	»**helical CT of urinary tract with IV contrast:** dilated collecting tubules; stones may be present within the collecting tubules Adequate for diagnosis and can replace IVU first-line as part of work-up for haematuria.

◊ Atrophic kidney

History	Exam	1st Test	Other tests
often no specific history suggests atrophic kidney, although occurs with some congenital abnormalities; history of chronic pyelonephritis, renal artery stenosis, or obstructive uropathy	typically normal but there may be findings of congenital abnormality; in older people hypertension or an abdominal bruit may exist suggesting renal artery stenosis	»**IV urography:** atrophic kidney Adequate renal function should be established before giving contrast.	»**helical CT of urinary tract with or without IV contrast:** atrophic kidney Adequate renal function should be established before giving contrast.

◊ Calyceal diverticulum

History	Exam	1st Test	Other tests
no presenting symptoms, generally an incidental finding	non-specific	»**IV urography:** visible diverticulum	

◊ Renal infarction

History	Exam	1st Test	Other tests
patient may have no symptoms; if occlusion is acute, then aching flank or abdominal pain, nausea, vomiting, fever, haematuria, and rarely new-onset hypertension may occur; may be history of acute myocardial infarction, atrial fibrillation,	examination is non-diagnostic	»**CT angiography :** renal artery occlusion Adequate renal function should be established before giving contrast; non-ionic contrast material, if available, is preferred.	»**magnetic resonance angiography (MRA):** renal artery occlusion Useful when abnormal renal function precludes use of potentially nephrotoxic contrast material with CT angiography.

Uncommon

◊ Renal infarction

History	Exam	1st Test	Other tests
endocarditis, trauma, surgery, or angiography as a precipitating event			»**renal artery Doppler:** renal artery occlusion Reasonable alternative when MRA not available or cost prohibitive; test is operator-dependent and patient obesity can interfere.

◊ Renal vein thrombosis

History	Exam	1st Test	Other tests
symptoms of renal failure, nausea/vomiting, haematuria, and decreased urine output; flank or abdominal pain may be present; history of systemic hypercoagulability	examination is non-diagnostic	»**CT with IV contrast :** renal vein occlusion Adequate renal function should be established before giving contrast; non-ionic contrast material, if available, is preferred.	»**renal venography:** renal vein occlusion Adequate renal function should be established before giving contrast. »**magnetic resonance venography:** renal vein occlusion Preferred test if impaired renal function does not allow use of contrast material.

◊ Arteriovenous malformations

History	Exam	1st Test	Other tests
most commonly associated with previous trauma (e.g., needle biopsy, surgery) or may be congenital	auscultation for abdominal bruits may help support the diagnosis	»**renal angiography :** visible arteriovenous malformation	

◊ Papillary necrosis

History	Exam	1st Test	Other tests
occurs with prolonged and excessive use of analgesics, especially non-steroidal	generally non-specific	»**CT without contrast:** decreased renal volume, bumpy renal contours, and papillary calcifications	

Uncommon

◊ Papillary necrosis

History	Exam	1st Test	Other tests
anti-inflammatory drugs (NSAIDs) (e.g., patients with a history of chronic pain or headaches); patients may present with complaint of pain resembling ureteric colic			

◊ Sickle cell disease

History	Exam	1st Test	Other tests
presenting symptoms of renal colic or flank pain and haematuria may occur; history of sickle disease with prior episodes of a pain crisis; more common among black people	examination is non-specific with possible costovertebral angle tenderness	»**CBC with peripheral smear:** sickle-shaped RBCs	»**haemoglobin electrophoresis:** presence of haemoglobin S »**CT angiography:** papillary necrosis Haematuria is believed to be caused by ischaemia within the renal papillae producing episodes of papillary necrosis.

◊ Hydronephrosis

History	Exam	1st Test	Other tests
flank pain especially if acute and concurrent to nephrolithiasis; history of urinary obstructive disease with voiding difficulties (lower urinary tract obstruction); bladder pain may occur if lower tract obstruction	generally non-specific; rarely a flank mass is palpable; costovertebral angle tenderness may occur, and abdominal examination may identify palpable tender bladder with lower tract obstruction	»**IV urography:** dilated kidney with dilated collecting system (calyces, ureter)	»**renal ultrasound:** may suggest obstruction »**helical CT of urinary tract with IV contrast:** dilated kidney with dilated collecting system (calyces, ureter)

◊ Ureteropelvic junction obstruction

History	Exam	1st Test	Other tests
abrupt onset of flank pain particularly after consuming large quantities of fluids	generally non-specific but with possible costovertebral tenderness	»**nuclear renal scan :** obstruction with hydronephrosis	»**IV urography:** obstruction with hydronephrosis

Uncommon

◊ Vesicoureteral reflux

History	Exam	1st Test	Other tests
usually presents with history of recurrent UTI or pyelonephritis and more commonly in children; rarely renal pain with voiding occurs; voiding difficulties (e.g., adult men with BPH)	non-specific	»**voiding cysto-urethrogram :** urine reflux from the bladder into the upper urinary tract Reflux is graded based on the height of the reflux within the ureter and the anatomical distortion of the ureter and kidney.	

◊ IgA nephropathy

History	Exam	1st Test	Other tests
often recurrent painless macroscopic haematuria; Henoch-Schonlein purpura; more common in people from the Mediterranean and Pacific Rim, less common in North Americans; more common in men	ranges from normal (asymptomatic haematuria) to hypertension or oedema in patients with nephrotic syndrome and progressed disease, but no specific examination finding confirms the diagnosis	»**urinalysis:** proteinuria Proteinuria occurs in 30% to 40% of cases and, although not diagnostic when present, it is highly suggestive of a glomerular disorder.[3] [22] [25] [29] [30] 3[B]Evidence	»**renal biopsy:** IgA deposition in the mesangium with mesangial proliferation as the disease progresses

◊ Thin glomerular basement membrane disease

History	Exam	1st Test	Other tests
often positive family history without family history of renal failure	a lack of examination findings helps to distinguish this from other glomerular disorders	»**urine microscopy :** RBC casts; no proteinuria RBC casts suggest an upper tract glomerular source of bleeding; proteinuria is absent in this disorder, differentiating it from other glomerular disorders.[3] [20] [25] [28] 2[B]Evidence	»**renal biopsy:** extremely thin glomerular basement membrane A presumptive diagnosis is made without renal biopsy in most cases based on family history of haematuria without progression to renal insufficiency.

Uncommon

◊ Acute glomerulonephritis

History	Exam	1st Test	Other tests
often associated with fever from recent infection (e.g., streptococcal infection); there may be nausea and vomiting, oedema, sore throat, rash, arthralgia, and complaints of dark urine or oliguria; a history of hepatitis, endocarditis, or systemic autoimmune disease may suggest a cause	examination could demonstrate hypertension, skin changes (jaundice, rash, purpura), pericardial rub with uraemia, ascites (liver failure), oedema, arthritis, or neurological abnormalities with renal failure	»**urinalysis:** proteinuria The presence of haematuria with proteinuria is highly suggestive of a glomerular source of bleeding.[3] [22] [25] [29] [30] 3[B]Evidence »**microscopic examination of urine:** RBC casts RBC casts suggest upper tract glomerular bleeding.[3] [20] [25] [28] 2[B]Evidence	»**renal biopsy:** proliferative glomerular changes and/or immunoglobulin deposits (varies with specific disease state) Renal biopsy unnecessary when specific source for acute glomerulonephritis is identified (e.g., poststreptococcal).

◊ Lupus nephritis

History	Exam	1st Test	Other tests
multi-system disease that may include CNS, heart, or lung complaints; more often presents with arthralgia, rash, or Raynaud's phenomenon	American College of Rheumatology criteria establish the diagnosis; examination findings included among the criteria are malar rash, discoid rash, oral ulcers, arthritis, and serositis;[41] examination may identify abnormalities associated with CNS, heart, or lung involvement	»**urinalysis:** proteinuria The presence of haematuria with proteinuria is highly suggestive of a glomerular source of bleeding.[3] [22] [25] [29] [30] 3[B]Evidence »**microscopic examination of urine:** RBC casts RBC casts suggest upper tract glomerular bleeding.[3] [20] [25] [28] 2[B]Evidence	»**ANA:** positive with higher titres being more suggestive (1:160 highly suggestive) ANA is one of the American College of Rheumatology diagnostic criteria; at least 4 of the 11 criteria are required for the diagnosis. »**renal biopsy:** glomerular or tubular deposits of immunoglobulin and complement in a granular pattern

◊ Hereditary nephritis (Alport's syndrome)

History	Exam	1st Test	Other tests
more common in males, and family history may suggest the diagnosis; ocular changes and sensorineural hearing loss also occur	hearing loss and eye examination findings such as perimacular pigment changes and lenticonus (congenital lens abnormalities) may be	»**urinalysis:** proteinuria The presence of haematuria with proteinuria is highly suggestive of a glomerular source of bleeding. Ultimately, findings of	»**renal biopsy:** reticulation and thickening of the glomerular basement membrane

Uncommon

◊ Hereditary nephritis (Alport's syndrome)

History	Exam	1st Test	Other tests
	identified along with hypertension	renal failure may present.[3] [22] [25] [29] [30] 3[B]Evidence	

◊ Transitional cell carcinoma (bladder)

History	Exam	1st Test	Other tests
more common in men and associated with risk factors for urinary tract cancer including age >40 years; tobacco use; occupational exposure to dyes, benzenes, and aromatic amines; use of medication containing phenacetin (available only in Japan), cyclophosphamide, and aristolochic acid (in some herbal weight loss preparations)	non-specific	»**cystoscopy with biopsy:** biopsy demonstrating transitional cell carcinoma	

◊ Cystitis (interstitial)

History	Exam	1st Test	Other tests
more common in women; symptoms may increase with stress, menses, or sexual intercourse and include urgency, frequency, or pressure and pain in the pelvic and perineal area; pain in men may involve the penis or scrotum	suprapubic tenderness may be present	»**cystoscopy :** visible bladder wall inflammation	»**urinary bladder biopsy:** variable Not routinely needed unless excluding other conditions.

◊ Cystitis (radiation-induced)

History	Exam	1st Test	Other tests
symptoms of urgency or frequency, or pressure or pain in the pelvic and perineal area in a patient	suprapubic tenderness may be present	»**cystoscopy :** pale mucosa and telangiectasia	

Uncommon

◊ Cystitis (radiation-induced)

History	Exam	1st Test	Other tests
with a history of irradiation cancer therapy			

◊ Cystitis (eosinophilic)

History	Exam	1st Test	Other tests
symptoms of urgency or frequency, or pressure or pain in the pelvic and perineal area	suprapubic tenderness may be present	»**cystoscopy:** biopsy demonstrates eosinophilia	

◊ Bladder diverticulum

History	Exam	1st Test	Other tests
may be associated with obstructive symptoms and recurrent UTI	suprapubic tenderness may be present if obstruction occurs	»**cystoscopy :** visible diverticulum	»**helical CT of urinary tract with IV contrast :** visible diverticulum »**virtual cystoscopy:** visible diverticulum

◊ Bladder papilloma

History	Exam	1st Test	Other tests
obstructed urine flow	suprapubic tenderness if urine flow is obstructed	»**cystoscopy :** visible papilloma and pathology from biopsy demonstrating absence of cancer cells	»**IV urography:** filling defect within bladder »**helical CT of urinary tract with IV contrast :** filling defect within bladder »**virtual cystoscopy:** filling defect within bladder

◊ Prostate cancer

History	Exam	1st Test	Other tests
often no symptoms; may be associated with urine outflow obstruction symptoms (difficulty voiding, changes in urine volume, lower abdominal	palpable nodule or asymmetry may be present on digital rectal examination	»**serum PSA:** typically >4 micrograms/L (4 nanograms/mL) Prostate cancer occurs at PSA <4 micrograms/L (4 nanograms/mL); should be	»**transrectal ultrasound-guided biopsy:** positive for cancer cells

Uncommon

◊ Prostate cancer

History	Exam	1st Test	Other tests
discomfort or bladder fullness, and nocturia)		suspected with progressively increasing PSA at any level.	

◊ Prostate stone

History	Exam	1st Test	Other tests
rarely symptomatic or may be associated with chronic prostatitis	usually an incidental radiographic finding but if large could be palpable on digital rectal examination	»**transrectal ultrasound:** visible stone within the prostate	»**helical CT of urinary tract :** visible stone within the prostate

◊ Bladder neck contracture

History	Exam	1st Test	Other tests
difficulty voiding, changes in urine volume, lower abdominal discomfort (bladder fullness) with or without history of recurrent UTI	palpable bladder fullness and suprapubic tenderness may be present	»**post void residual volume:** high post void residual volume suggests bladder outlet obstruction »**cystoscopy :** visible obstruction at bladder neck	»**voiding cysto-urethrogram:** visible obstruction at bladder neck

◊ Urethritis

History	Exam	1st Test	Other tests
recent sex partner change may suggest STD; presents similar to typical UTI with dysuria, or frequency	may not be associated with abnormal examination findings; if caused by STD, men may have demonstrable penile discharge and women may have mucopurulent cervicitis	»**urine culture:** negative culture (≥10^2 colony-forming units confirms UTI) Urine culture is most often negative in urethritis but is warranted to exclude UTI.	»**gonorrhoea/chlamydia DNA probe:** positive for gonorrhoea or chlamydia Indicated when STD suspected.

Uncommon

◊ Urethral stricture

History	Exam	1st Test	Other tests
difficulty voiding, changes in urine volume, lower abdominal discomfort (bladder fullness) with or without history of recurrent UTI	palpable bladder fullness and suprapubic tenderness may be present	»**post void residual volume:** high post void residual volume suggests bladder outlet obstruction »**cystoscopy :** visible obstruction within the urethra	»**voiding cysto-urethrogram:** visible obstruction within the urethra

◊ Phimosis

History	Exam	1st Test	Other tests
inability to retract the foreskin with possible foreskin irritation or pain; may be history of UTI	inability to retract the foreskin	»**none:** diagnosis is clinical based on inability to retract the foreskin	

◊ Penile cancer

History	Exam	1st Test	Other tests
a non-healing or fungating painless lesion of the penis; most often in uncircumcised men	examination may demonstrate an erythematous lesion early in the course of disease; later the lesion becomes a non-healing ulcer or an exophytic fungating growth	»**penis biopsy :** squamous cell carcinoma	

◊ HIV

History	Exam	1st Test	Other tests
symptoms from none to those of full-blown immunodeficiency; history of risk factors such as sexual activity and exposure to blood products	no specific examination findings confirm HIV; findings may be consistent with opportunistic infections suggestive of HIV	»**serum HIV test (ELISA and Western blot):** positive antibodies on both ELISA and Western blot	

Uncommon

◊ Lymphoma

History	Exam	1st Test	Other tests
often presents with a complaint of lymphadenopathy; may also have fever, night sweats, and weight loss; symptoms of a mass effect may occur and vary by location of the mass (chest, abdomen, CNS, genitourinary)	the examination often demonstrates lymphadenopathy especially in the neck region; other findings vary based on the organ involved (e.g., pleural effusion in the chest)	»**lymph node biopsy:** positive for cancer cells	»**helical CT of urinary tract with IV contrast:** mass lesions with or without findings of urinary tract obstruction CT as a part of the work-up of MH may suggest lymphoma.

◊ Multiple myeloma

History	Exam	1st Test	Other tests
bone pain with persistent generalised weakness and fatigue suggests the diagnosis	no specific examination finding confirms multiple myeloma but pallor is common and hepatosplenomegaly may occur	»**serum protein electrophoresis:** M-spike >2g for IgA but needs to be >3.5g for IgG Multiple myeloma is classically recognised by a triad of bone marrow plasmacytosis, lytic bone lesions, and a monoclonal gammopathy.	»**bone marrow aspirate/biopsy:** plasmacytosis >10% »**bone radiographs (classically the skull):** "punched out" lytic lesions

◊ Urinary tract tuberculosis

History	Exam	1st Test	Other tests
symptoms like those of UTI occur: dysuria, frequency, or costovertebral angle pain with kidney involvement; history of previous episodes with sterile pyuria may indicate tuberculosis	no specific examination findings	»**acid-fast bacillus urine culture:** positive growth of mycobacterium	»**CT urography (IV contrast):** calcifications, cavitations, or signs of obstruction suggest tuberculosis

Diagnostic guidelines

North America

SOGC clinical practice guideline: recurrent urinary tract infection

Published by: Society of Obstetricians and Gynaecologists of Canada
Last published: 2010

Online resources

1. AUA: diagnosis, evaluation and follow-up of asymptomatic microhematuria (AMH) in adults *(external link)*

Evidence scores

1. Identification of urinary tract cancer: there is medium-quality evidence that screening for haematuria to identify urinary tract cancer is not beneficial.[4] [8] [11] [19] [29]
Evidence level B: Randomized controlled trials (RCTs) of <200 participants, methodologically flawed RCTs of >200 participants, methodologically flawed systematic reviews (SRs) or good quality observational (cohort) studies.

2. Identification of renal source of haematuria: there is medium-quality evidence that the presence of dysmorphic RBC and RBC casts in the urine suggests renal parenchymal disease.[20] A cut-off value for dysmorphic cells of 80% accurately predicts a renal source.[28]
Evidence level B: Randomized controlled trials (RCTs) of <200 participants, methodologically flawed RCTs of >200 participants, methodologically flawed systematic reviews (SRs) or good quality observational (cohort) studies.

3. Identification of significant underlying renal disease: there is medium-quality evidence that haematuria concomitantly occurring with proteinuria suggests significant underlying renal disease.[22] [29] [30]
Evidence level B: Randomized controlled trials (RCTs) of <200 participants, methodologically flawed RCTs of >200 participants, methodologically flawed systematic reviews (SRs) or good quality observational (cohort) studies.

4. Identification of a source of haematuria: there is medium-quality evidence that in patients with a previously negative urological work-up including IV urography (IVU) or ultrasound, CT urography identified a source of recurrent haematuria with a sensitivity of 91% and specificity of 94%.[32] Comparison of CT urography and IVU findings demonstrated an upper urinary tract sensitivity of 94% and 50%, respectively.[37]
Evidence level B: Randomized controlled trials (RCTs) of <200 participants, methodologically flawed RCTs of >200 participants, methodologically flawed systematic reviews (SRs) or good quality observational (cohort) studies.

5. Excluding malignancy: there is good-quality evidence that urine cytology is not a useful test in ruling out malignancy or excluding patients from other diagnostic testing.[28]
Evidence level A: Systematic reviews (SRs) or randomized controlled trials (RCTs) of >200 participants.

Key articles

- Grossfeld GD, Litwin MS, Wolf JS, et al. Evaluation of asymptomatic microscopic hematuria in adults: the American Urological Association best practice policy - part I: definition, detection, prevalence and etiology. Urology. 2001;57:599-603. Abstract
- Chou R, Dana T. Screening adults for bladder cancer: a review of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med. 2010;5:153:461-468. Abstract
- Nielsen M, Qaseem A; High Value Care Task Force of the American College of Physicians. Hematuria as a marker of occult urinary tract cancer: advice for high-value care from the American College of Physicians. Ann Intern Med. 2016;164:488-497. Full text Abstract
- Feldstein MS, Hentz JG, Gillett MD, et al. Should the upper tracts be imaged for microscopic haematuria? BJU Int. 2005;96:612-617. Abstract
- Grossfeld GD, Litwin MS, Wolf JS, et al. Evaluation of asymptomatic microscopic hematuria in adults: the American Urological Association best practice policy - part II: patient evaluation, cytology, voided markers, imaging, cystoscopy, nephrology evaluation, and follow-up. Urology. 2001;57:604-610. Abstract
- Rodgers M, Nixon J, Hempel S, et al. Diagnostic tests and algorithms used in the investigation of haematuria: systematic reviews and economic evaluation. Health Technol Assess. 2006;10:1-259. Abstract

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Contributors:

// Authors:

Timothy J. Benton, MD

Regional Chairman
Associate Professor, Department of Family and Community Medicine, Texas Tech University Health Sciences Center at the Permian Basin, Odessa, TX
DISCLOSURES: TJB declares that he has no competing interests.

Beverly Axe-Lewis, DO

Associate Professor
Regional Chief Medical Informatics Officer, Medical Director Haven Health Clinics, Department of Family Medicine, Texas Tech University Health Sciences Center, Amarillo, TX
DISCLOSURES: BAL declares that she has no competing interests.

// Peer Reviewers:

Robert Tompkins, MD

Associate Professor
Department of Family Medicine, University of Texas Health Science Center, Tyler, TX
DISCLOSURES: RT declares that he has no competing interests.

Junaid Masood, MBBS, FRCS (Eng), MSc (Urol), FRCS (Urol)

Consultant Urological Surgeon
Bart's and The London NHS Trust, London, UK
DISCLOSURES: JM declares that he has no competing interests.