Investigating the child with haematuria

Each month we present authoritative advice on the investigation of a common clinical problem, specially written for family doctors by the Board of Continuing Medical Education of the Royal Australasian College of Physicians.

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When is haematuria significant?

Macroscopic haematuria is always significant and requires prompt evaluation. Haematuria associated with abnormalities such as proteinuria, abnormal renal function and hypertension is almost always significant, whereas isolated microscopic haematuria is usually a benign and transient phenomenon.

Some causes of haematuria in children are listed in Table 1.

Presentations

Haematuria in children is most commonly detected incidentally by dipstick testing to exclude infection or investigate abdominal pain or fever. Dipsticks are very sensitive and can detect as few as 5 red blood cells per µL (the normal range is less than 10 cells/µL). Occasionally, children will present with macroscopic haematuria.

Postinfectious glomerulonephritis develops seven to 21 days after a group A beta-haemolytic streptococcal throat or skin infection (Figure 1). The typical presentation is brown urine, oliguria, oedema, hypertension and (often) renal insufficiency; in mild cases, however, microscopic haematuria may be the only feature.

Conditions causing glomerular bleeding do not usually cause pain. Occasionally, however, pain may occur with IgA nephropathy, which presents with recurrent episodes of macroscopic haematuria in association with pharyngitis or other respiratory infections.

A child with gross haematuria associated with loin pain or dysuria may have a urine infection, renal calculi, hypercalciuria or IgA nephropathy. Not all urine infections are bacterial – for example, haemorrhagic cystitis with macroscopic haematuria may be caused by adenoviral infection. Hypercalciuria is a common cause of isolated nonglomerular haematuria. Usually no reason for hypercalciuria is found, but a child with this condition may be at risk for later stone formation.

IN SUMMARY

- **Dipsticks can detect as few as 5 red blood cells per µL of urine. The normal range is less than 10 cells/µL.**
- **Children with haematuria should be assessed differently to adults.**
- **The temporal relationship of recent infections with the haematuria should be established carefully.**
- **All children with haematuria require a urine microscopic examination and culture.**
- **The nature of haematuria is variable, and therefore several urine samples should be tested, at intervals of one to two weeks, to confirm initial findings. If haematuria is confirmed, further evaluation is required.**
- **Macroscopic haematuria requires prompt evaluation, and a diagnosis is usually determined. Microscopic haematuria is usually transient and benign, and arriving at a firm diagnosis is often difficult.**

Figure 1. Urine from a child with poststreptococcal glomerulonephritis.

Skin rashes, joint pain and abdominal pain are seen with Henoch–Schönlein purpura; a malar rash may be present in systemic lupus erythematosus (SLE). Bladder or bowel dysfunction may suggest a tumour.

Table 1. Causes of haematuria in children

Glomerular causes

- Postinfectious glomerulonephritis
- Henoch–Schönlein purpura
- IgA nephropathy (Berger's disease)
- Haemolytic uraemic syndrome
- Hereditary nephritis (Alport's disease)
- Benign familial haematuria (thin basement membrane disease)
- Lupus nephritis
- Chronic glomerulonephritis

Nonglomerular causes

- UTIs
- Urolithiasis
- Hypercalciuria
- Fever
- Exercise
- Cystic kidney disease
- Hydronephrosis
- Trauma
- Coagulation disturbance
- Tumours
- Drugs

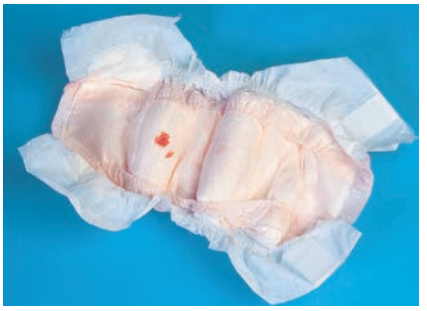

Figure 2. Amorphous urates in the urine of newborn babies can give the appearance of haematuria.

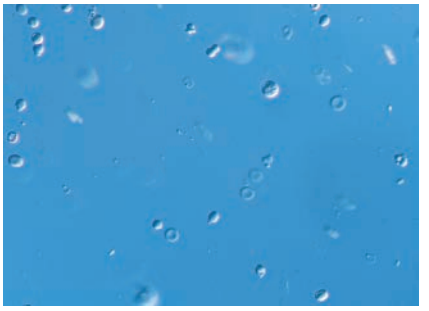

Figure 3. Phase contrast microscopy showing dysmorphic red blood cells seen in haematuria of glomerular origin.

Benign familial haematuria (thin basement membrane disease) can be diagnosed only by renal biopsy, but may be suspected when members of a family have isolated microscopic haematuria. Benign familial haematuria may be a variant of hereditary nephritis, and some individuals can develop progressive renal disease.

Occasionally, discoloured urine from other causes can be misinterpreted as haematuria – beetroot ingestion is a well known example. Neonates and young infants can pass amorphous urates that will leave a characteristic pink stain on the nappy (see Figure 2).

Evaluation

Investigation should be conducted in a stepwise fashion determined by the nature of the haematuria, association with other abnormalities, and presence of abnormal physical signs (see Table 2). For example, painless macroscopic haematuria may be caused by postinfectious glomerulonephritis and, if the history is suggestive, investigation should proceed accordingly.

Children with haematuria should be assessed differently to adults. In adults, haematuria is a common presenting feature of urological malignancy, and cystoscopy is often a first line investigation. This is not the case in children, in whom urological malignancy is uncommon. It is important to remember that haematuria in a child may be found in association with a Wilm's tumour, but there will almost always be a palpable abdominal mass at presentation. Cystoscopy is an invasive and expensive procedure, only rarely providing helpful information in the work up of the child with haematuria.

Microscopic haematuria can be more difficult to address than macroscopic haematuria because a cause is less likely to be found. Parental anxiety occasionally necessitates a more aggressive approach than would otherwise be taken.

Initial work up

For each child with haematuria, a freshly voided urine sample should be sent for microscopic examination and culture to evaluate numbers of red blood cells and detect leucocytes, bacteria, casts (indicating glomerular disease), and crystals. The presence of large amounts of blood in the urine often results in a positive dipstick test for proteinuria; thus, the urine should be clear of gross haematuria before testing for proteinuria can be performed reliably.

Clues to the origin of haematuria may be obtained by the morphology of the red blood cells – those cells that traverse the glomerular basement membrane become distorted and exhibit a wide range of morphological variations ('dysmorphic', see Figure 3), whereas those from lower urinary tract bleeding appear like normal peripheral red blood cells ('eumorphic'). However, the direction of investigations that is taken should not

be determined by blood cell morphology alone because such laboratory reports can be misleading.

A patient's urine calcium excretion should be estimated on a spot urine sample, requesting the laboratory to perform a calcium/creatinine ratio. Hypercalciuria, if documented, needs to be confirmed, preferably on a first morning urine sample. Urine from both of the child's parents should be examined to exclude benign familial haematuria.

Further investigations

If microscopic haematuria is persistent or associated with proteinuria, further investigation to look for evidence of glomerulonephritis is important. This includes a full blood count, urea, creatinine, electrolytes, serum complement components (C3 and C4), and streptococcal serology. A test for antinuclear factor and antibodies against double-stranded DNA may be ordered to exclude SLE.

A renal tract ultrasound may detect renal stones, and a plain abdominal x-ray is important when stones are suspected. Cystic kidney disease or hydronephrosis secondary to an obstruction of the pelviureteric junction may be detected on ultrasound.

If the preceding investigations are normal, follow up should be arranged with repeated urinalyses until the child's haematuria resolves or the cause is clear.

Follow up

In many children with haematuria, laboratory work up fails to identify a cause for the problem. In such cases, the child should be reviewed and the urine examined every two to three months. Often the haematuria will disappear over several months to years. If other abnormalities develop or the haematuria increases, specialist review would be appropriate.

The finding of haematuria in a child can cause considerable anxiety to parents. Some families request that a renal biopsy be performed to obtain a diagnosis, even with the knowledge that the chance of detecting a treatable renal disease is small.

If the degree of a child's haematuria is unchanged after a period of follow up and there are no associated abnormalities, periodic review every six to 12 months is all that is required. Reassurance can be given that the problem is likely to be benign, but a very small percentage of children with persistent haematuria will develop progressive renal disease. MT

Table 2. Finding the cause of haematuria in children

Investigations	Reasons
Initial work up	
Urinalysis, microscopy and culture	Proteinuria (may indicate glomerular disease) Red blood cell casts (glomerular disease) Crystals (hypercalciuria, cystinuria, etc) Infection
Morphology analysis on urine red blood cells	Site of bleeding (dysmorphic red cells suggest glomerular bleeding; eumorphic red cells suggest lower tract bleeding)
Spot urine calcium/creatinine	Hypercalciuria (calcium/creatinine ratio >0.74 mmol/mmol on first morning urine after overnight fast is abnormal
Parents' urine tests	Familial haematuria (urinalysis and microscopy of urine from both parents)
Further investigations	
Streptococcal serology, urea, creatinine, electrolytes*	Postinfectious glomerulonephritis – elevated titres of antistreptolysin-O titre (pharyngitis) or anti-DNAse B (impetigo)
Complement components C3 and C4*	Postinfectious glomerulonephritis: C3 is decreased and returns to normal in eight weeks; persistently low C3 is seen in SLE and membranoproliferative glomerulonephritis
Renal ultrasound (with or without abdominal x-ray)	Anatomical abnormalities Cystic disease Hydronephrosis Urolithiasis Tumours
Audiogram	Hereditary nephritis (high tone hearing loss, often with a family history)
Sickle screen	Sickle cell trait and disease suspected in a child at risk (i.e. a family history or African descent)
Blood count, coagulation profile	Bleeding disorders (haematuria is not usually a presenting feature
Renal biopsy	Glomerulonephritis or hereditary nephritis Thin basement membrane disease
Micturating cystourethrogram	Bladder or urethral pathology Vesicoureteric reflux
Cystoscopy†	Bladder or urethral pathology (only if suspected)

* Part of the initial work up if postinfectious glomerulonephritis is suspected.
† Almost never helpful in assessing children with haematuria.