Guidelines for the management of a child with haematuria

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DISCLAIMER: These guidelines were produced in good faith by the author(s) in conjunction with the paediatric nephrology team at the University Hospital of Wales, Cardiff reviewing available evidence/opinion. They were designed for use by paediatric nephrologists at the University Hospital of Wales, Cardiff for children under their care. They are neither policies nor protocols but are intended to serve only as guidelines. They are not intended to replace clinical judgment or dictate care of individual patients. Responsibility and decision-making (including checking drug doses) for a specific patient lie with the physician and staff caring for that particular patient.

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February 2020

Summary
These guidelines are aimed at providing the doctors presented with a child with haematuria with information to help identify the underlying problem and to guide management.

Introduction

Haematuria is an important sign of urinary tract and renal disease. Healthy children can have occasional red cells in the urine but persistent microscopic haematuria is considered significant if there are > 10 red cells/high power field in at least 3 fresh samples collected a minimum of 1 week apart.
Haematuria can be gross (i.e. the urine is overtly bloody, smoky, or tea coloured) or microscopic, symptomatic or asymptomatic, transient or persistent, and either isolated or associated with other urinary abnormalities such as proteinuria.
Gross or macroscopic haematuria deserves prompt investigation to determine its cause. The degree of haematuria bears no relationship to the seriousness of the underlying cause. It may be initial (suggesting a urethral cause); total/complete (due to kidney or diffuse bladder pathology) or terminal (in prostatic, trigonal or posterior urethral disorders). Substances other than red blood cells (RBCs) can cause the urine to become red in colour (see table 1).

Table 1. Confounding factors in dipstick analysis for blood.

False positive tests (no RBCs on microscopy)	**False negative tests**
Haeme positive (dipstick positive) - Haemoglobinuria, Myoglobinuria **Haeme negative (dipstick negative) -** Red urine without haematuria • Drugs e.g. Rifampicin, Chloroquin, Metronidazole, Nitrofurantion • Foods e.g. beetroot, food colourings, blackberries • Inborn error of metabolism e.g. alkaptonuria, porphyria	Formalin (preservative) Ascorbic acid in high concentration Specific gravity <1.010
Other - fever, post-exercise, factitious	

Microscopic haematuria, seen more often than gross haematuria, may be an incidental finding. Urine dipsticks are used routinely for detection of haematuria because of their relatively high sensitivity. This can lead to over-investigation.

Causes of haematuria

Although most causes of isolated haematuria are benign (1,2), it is important to identify those patients with significant underlying renal or urological disease.

Table 2. Common causes of haematuria

Glomerular causes		Non-glomerular causes
Renal	**Multisystem**	
Post infectious glomerulonephritis* IgA nephropathy* Membranoproliferative and membranous glomerulonephritis* Alport's syndrome* Focal segmental glomerulosclerosis Thin basement membrane nephropathy	Systemic lupus erythematosis* Henoch-Schönlein purpura* Wegener granulomatosis Goodpasture's syndrome* Polyarteritis nodosa Haemolytic uremic syndrome, Sickle cell nephropathy*	**Upper urinary tract** Cystic/ polycystic kidney disease Nephrocalcinosis/hypercalciuria* Pyelonephritis, interstitial nephritis Arterial/venous thrombosis* tumours* Trauma*, stones* **Lower urinary tract** Infections*/inflammation*, stones*, Trauma*, coagulopathy*, drugs Tumours*

* might cause macroscopic haematuria

A distinction has conventionally been drawn between glomerular and extraglomerular bleeding, separating nephrologic and urologic disease (Table 3). Glomerular haematuria indicates blood originating from the nephron. The RBCs exhibit typical morphological changes as a consequence of being distorted when passing through the glomerular structures and are dysmorphic (deformed or acanthocytic). Bleeding from the upper or lower collecting system (extraglomerular haematuria) results in normal appearing (eumorphic- uniform size and shape) RBCs in the urine.

Table 3. Differentiating glomerular from non-glomerular haematuria

Feature	Glomerular	Non-glomerular
History and examination	Suggestive of glomerular causes	Suggestive of non-glomerular cause
Urine analysis		
Colour (if macroscopic)	Smoky brown, tea or cola	Bright red or pink
Clots	Absent	May be present
Proteinuria	Usually > 2+ (0.5-1 gm/day)	< 2+ (<0.5 gm/day) if present
RBC morphology[#]	Dysmorphic (>80% RBCs) Vary in size and shape	Normal Uniform in size and shape
RBC casts	May be present	Absent

[#] by phase contrast microscopy

Approach to a child with haematuria

1. Establish the presence of true haematuria

The presence of haematuria is easily established in patients with macroscopic bleeding but beware of other causes of red urine (see table 1). On centrifugation of the urine specimen the sediment is red in haematuria whereas the supernatant is red in other causes of red urine (see figure 1).
In patients with microscopic haematuria confirm the presence of RBCs by microscopy of a fresh urine sample and make sure it is confirmed on at least 3 samples, to exclude transient associated with intercurrent febrile illnesses.

2. Clinical evaluation

A detailed history and examination together with urinalysis provide vital information to determine the cause, source of haematuria (upper versus lower urinary tract) and urgency of evaluation (3). Enquire about symptoms of specific conditions causing haematuria (see table 1). Ask about recent upper respiratory tract or gastrointestinal

infections (bloody diarrhoea), nephritic/nephrotic syndrome, skin rashes, joint pain/ swelling, loin pain, renal colic, urinary symptoms and flank mass. Various genetic renal diseases should be kept in mind and relevant family history (of haematuria, renal failure, arthritis and deafness) is essential.
Physical examination should look for evidence of underlying illnesses. Hypertension, oedema, hepatomegaly, and other signs of cardiac decompensation might suggest nephritis. Dysmorphic features (suggesting syndromic conditions), abdominal masses and abnormalities of spine, external genitalia, skin and nervous system should be part of the evaluation.

3. Investigation, treatment and identification of patients needing referral
Table 4 lists the investigations performed in selected group of patients with haematuria. Morphologic study of urinary RBCs (dysmorphic or eumorphic) with a phase-contrast microscope might be helpful in distinguishing glomerular from non-glomerular bleeding.

Table 4. Investigations in selected patients with haematuria

Blood	Urine	Radiology
U&E, creatinine, bicarbonate, bone profile, LFT C3 & C4, ASOT FBC	Dipstick, microscopy, Calcium : creatinine ratio Protein : creatinine ratio	Renal ultrasound[#]

[#] Urgently in macroscopic haematuria or if anatomical, obstructive lesions/ malignancy suspected

In patients with features of an underlying nephritis (hypertension, proteinuria or raised creatinine) or positive family history additional investigations may be indicated: Anti-dsDNA, ANA, ANCA, IgA, anti-GBM antibody.

A stepwise approach to children with macroscopic haematuria and microscopic haematuria has been suggested in Fig 1 and 2.

If common causes (e.g. UTI) are found they should be treated and followed up locally. Haematuria if macroscopic ± symptoms or associated with proteinuria, impaired renal function or hypertension requires referral to paediatric nephrology. Referral is also recommended for children with nephritis, stones, nephrocalcinosis, and a family history of significant renal disease or persistent haematuria of unknown cause.

4. Genetic testing
There are criteria for identifying which cases should have genetic testing in the National Genomic Test Directory:

Proband with haematuria and ONE of:
1. A first degree relative with haematuria or unexplained chronic renal failure, OR
2. Histological evidence following electron microscopy on renal biopsy of EITHER Alport syndrome (thickening and splitting of glomerular basement membrane +/- electron lucent areas) OR thin basement membrane disease (TBMD), OR

3. Clinical features of Alport syndrome (high tone sensorineural hearing loss or characteristic ophthalmic signs such as perimacular flecks or anterior lenticonus)

Haematuria panels are available and the optimum test request should be discussed with genetics.

References

1. Feld, LG, Waz, WR, Perez, LM, Joseph, DB. Haematuria. An integrated medical and surgical approach. Pediatr Clin North Am 1997; 44:1191.
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3. ID Davis and ED Avner. Clinical evaluation of the child with haematuria, in Kliegman RM, Behrman RE, Jensen HB and Stanton BF (eds) Nelson's textbook of paediatrics, 18th edn. vol 2 Philadelphia, Saunders 2007; 2168-2170.

Figure 1. Approach to a child with microscopic haematuria

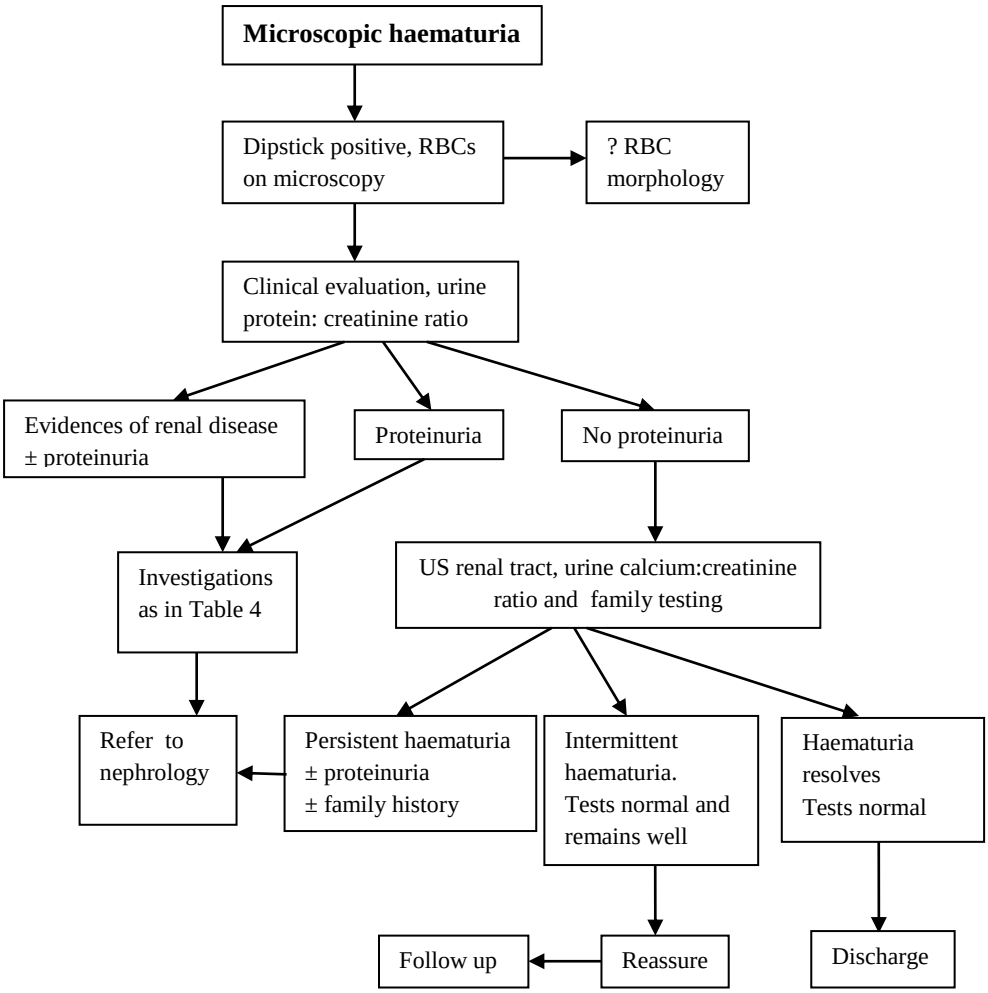
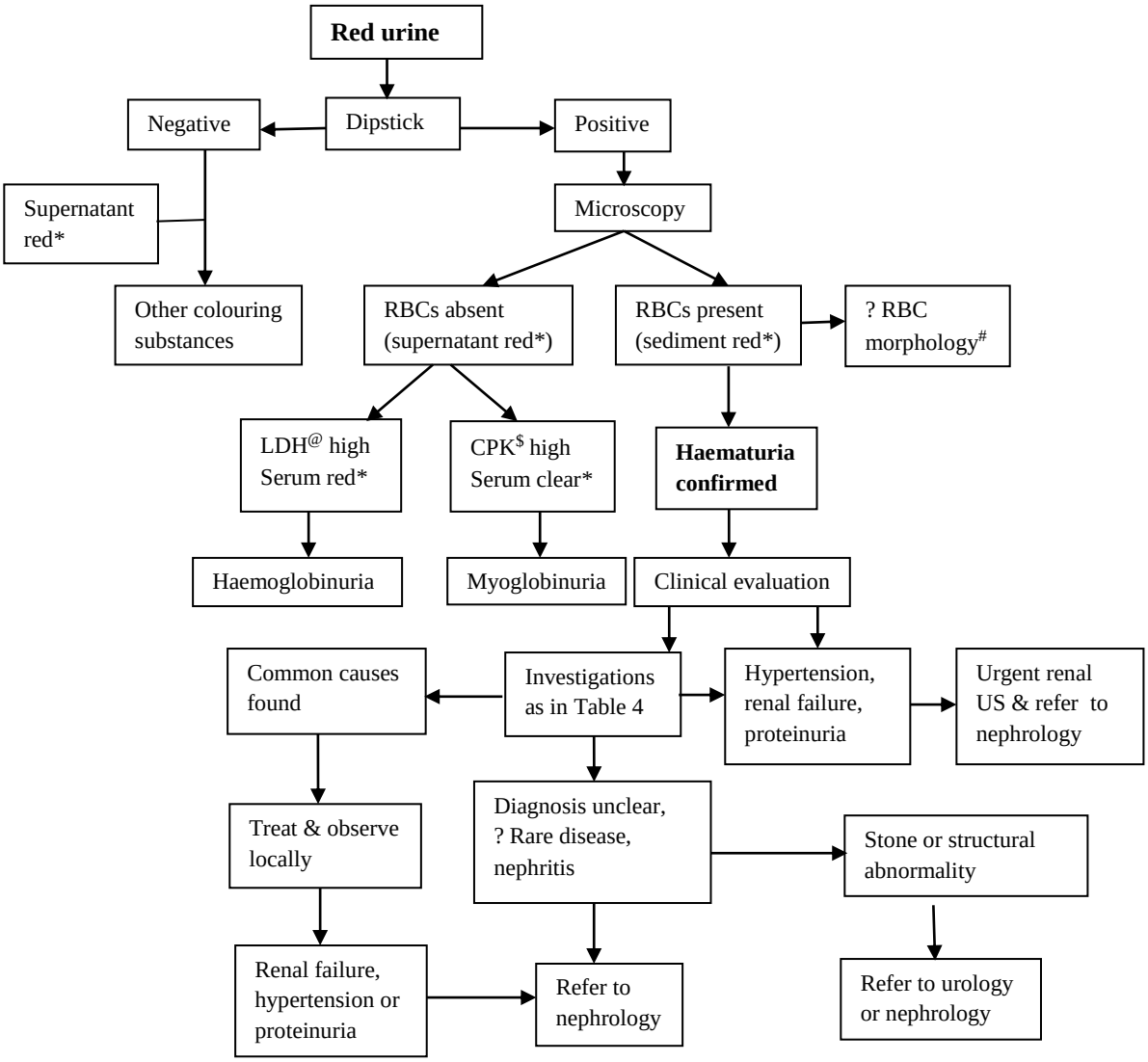


Figure 2. Approach to a child with macroscopic haematuria



* On centrifugation
# by phase contrast microscopy
@ Lactate dehydrogenase with other signs of haemolysis
$ Creatine phosphokinase