Paediatric Nephro-Urology: guideline for management of the child with persistent haematuria

Summary
This guideline is for the use of any colleague looking after a child with persistent haematuria .i.e. the Evelina paediatric renal team and can be shared with network hospitals, in the investigation and management of children who have haematuria

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INTRODUCTION:
The majority of children will have isolated asymptomatic microscopic haematuria and do not need immediate investigation, but require follow up with repeat urinalysis to identify if it is persistent. Haematuria associated with pain, oedema, hypertension or proteinuria needs urgent investigation.

MANAGEMENT AFTER DETECTION OF HAEMATURIA

History:

- Previous history of haematuria
- Symptoms of urinary infection: dysuria, frequency, abdo pain, fever
- Systemic symptoms e.g. fatigue, oedema, rash, arthralgia
- Recent surgery/trauma including non-accidental injury
- Family history of haematuria,
- FH of renal disease/ stones, visual or hearing loss
- History of underlying bleeding disorder or immunodeficiency
- Medication history (e.g. NSAIDs, rifampicin, metronidazole, nitrofurantoin, cyclophosphamide)
- Food intake (beetroot and berries can colour urine to pink or red)
- Exercise

Examination:

Urinalysis
Weight and height
Blood pressure (manual) assessed according to age, gender & height centiles
Physical exam including eyes, skin, genitalia, joint tenderness/swelling, and signs of oedema or organomegaly

RED FLAGS:
Haematuria AND any of:
Proteinuria
Hypertension
Fluid overload: oedema, ascites
Flank/abdominal pain
Immuno-compromise
Deranged renal function

Warrant urgent referral to paediatric nephrology

Investigations and Management:
In children with incidentally detected **isolated asymptomatic microscopic haematuria** (>10 RBC/µl) and no other abnormal findings:

Request GP to perform urinalysis on 2 further occasions, at least 1 week apart from each other (no intercurrent illness, not during menstruation and no exercise on day of testing).
No other investigations are necessary in the interim.
Commonly resolves spontaneously. If microscopic haematuria has not resolved following three consecutive tests warrants paediatric assessment and further **initial investigations** as below:

In children with **isolated but persistent microscopic haematuria** (i.e. 3 positive separate samples that occur ≥1 week apart, without prior exercise nor during menstruation):

Although most cases are idiopathic, the most common identifiable causes are

- hypercalciuria (with or without kidney stones),
- urinary tract infections and
- urinary tract malformations,
- disorders of the GBM (including Alport syndrome), and
- IgA Nephropathy.

Thus, the initial approach can be managed by a general paediatrician with a focus on evaluating for those diagnoses by getting a thorough personal and family history and physical examination as above plus the following **initial investigations:**

<u>Initial investigations</u> for persistent microscopic haematuria:

- Urine microscopy to confirm RBC>10/ µl and cytology to look for casts/dysmorphic red cells (if present suggests upper urinary tract cause).
- Urine protein:creatinine and calcium:creatinine ratios
- Basic renal paed profile(aka U&Es), FBC, albumin, coagulation profile
- Urinary tract ultrasound
- Haemoglobinopathy screen should also be considered in high-risk populations.
- Urinalysis of immediate family to assess for incidental microscopic haematuria as well as proteinuria

In children with macroscopic haematuria:
Macroscopic haematuria (blood visible in urine without microscopy) is more likely to come from the bladder or urethra rather than the kidney. Haematuria 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).

Blood in the urine may also come from sources other than the urinary tract (e.g. vaginal bleeding, rectal fissure).

Additional investigations if macroscopic haematuria:
Same initial investigations as above In addition to the above, if painless haematuria +/- systemic symptoms, consider glomerulonephritis screen (ESR, ANA, dsDNA, ANCA, c3/c4, ASOT, Hepatitis B serology, immunoglobulins).

Further investigations to consider:
If nephrocalcinosis-extended screen for this (urinary urate, cystine, citrate, oxalate creatinine ratio). If medullary nephrocalcinosis and suggestive ethnicity, consider haemoglobinopathy screen.
If recurrent UTIs, nuclear medicine imaging to look for reflux and scarring
Genetic testing:
COL4A genetic screen (R194 in National Genomic Test Directory for rare inherited diseases) if family history of deafness, visual problems (not myopia related) or haematuria in 1st degree relatives.
If nephrocalcinosis and family history of stones consider **Nephrocalcinosis or nephrolithiasis genetic screen** (R256).
(1) Test Order Form (2) Record of Discussion (3) Genetic Specimen Form-Viapath) found at https://southeastgenomics.nhs.uk/glh/core-rd/
Send completed forms to: gst-tr.viapathgeneticsadmin@nhs.net; gst-tr.londonsouthglh@nhs.net

If recurrent episodes of macroscopic haematuria with or without red flags without identifiable cause, consider if renal biopsy required.

REFERRALS TO PAEDIATRIC NEPHROLOGY OR UROLOGY ELCH:

- **Non-urgent referral to Paediatric Nephrology team** if isolated microscopic haematuria present >6 months. Earlier referral if any red flags.
  - Ensure family members have been checked with urine dip and BP at GP.
  - Please provide families with Infokid leaflet on haematuria: https://www.infokid.org.uk/haematuria
  - Please include results of the above investigations in referral letter (i.e. not "investigations requested")

  In addition, ensure there has been a discussion with the Paediatric Nephrology team if:
  - Macroscopic haematuria ± symptoms or associated with proteinuria, impaired renal function or hypertension
  - Other evidence supporting a nephritis (change in urine output/oedema/systemic features such as rash/arthralgia/ fatigue etc
  - Stones or nephrocalcinosis
  - Family history of significant renal disease or persistent haematuria of unknown cause
- **Urgent paediatric nephrology team referral** if
  - Child is systemically unwell
  - Haematuria is present with any red flag
  - The paediatric renal registrar is available to take calls and referrals (Monday-Friday, 9am-5pm) on 07990 800 587 or 020 7188 7188, bleep 1141. Out of hours, a paediatric nephrologist is on call and can be contacted via the hospital switchboard on 020 7188 7188.
- **Refer to Paediatric Urology, ELCH** If dysuria associated with episodes of macroscopic haematuria (with no red flags) in first instance. If no urological cause found and haematuria persistent, urology team to refer to paediatric nephrology, ensuring initial investigations as above performed.

- If stones- consider referral to Paediatric Stones clinic at ELCH). If abdominal mass, consider consultation with paediatric surgical or urology team based on ultrasound findings. If concerns about neoplasm, refer to oncology centre.

NB. It is important to make the family aware that referral to the paediatric urology and nephrology team is to ensure concerning pathological conditions have been excluded. The child may be referred back to local services once this happens as they will need ongoing annual follow-up, to ensure no concerning features subsequently develop in the child with isolated haematuria (hypertension, proteinuria etc), given that some conditions evolve and become apparent over time. This may occur at the local hospital or with GP, with advice to re-refer at that point.