Ashford and St. Peter's Hospitals
NHS Foundation Trust

Approach to Paediatric Haematuria

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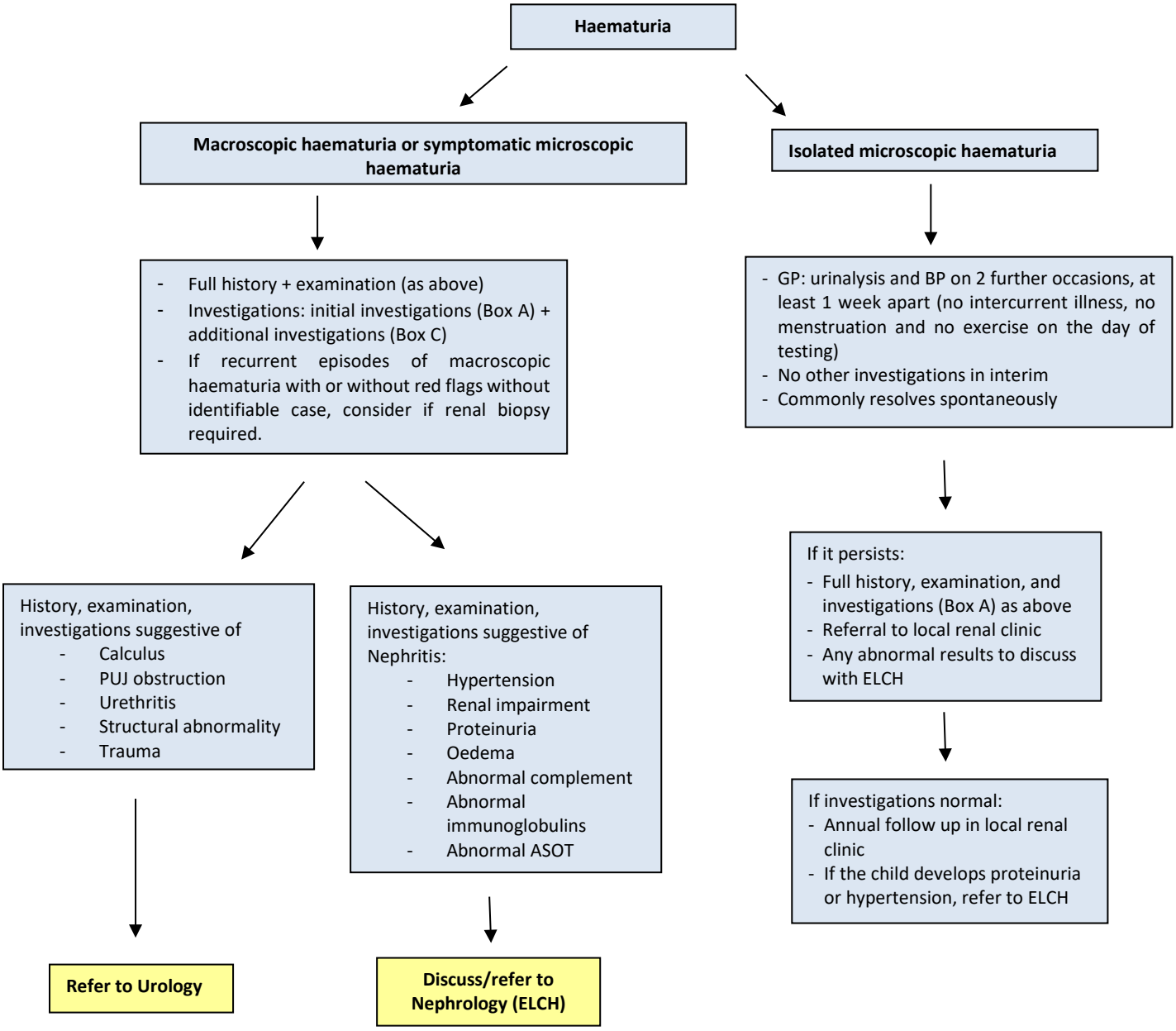
Guideline History		
Date	**Comments**	**Approved By**
September 2010	- New guideline	Paediatric guidelines group
July 2013	- Whole Document review	Paediatric guidelines group
December 2014	- Whole Document review	Paediatric guidelines group
March 2018	- Whole document review, no changes	Paediatric guidelines group
May 2024	- Whole document review - New approach - Referrals section added - Children's stones investigations added to the appendix	Paediatric guidelines group

Patients first • Personal responsibility • Passion for excellence • Pride in our team

Haematuria Flowchart



- **If the child develops proteinuria (+1 or more) at any point, please manage according to proteinuria guidelines.**

Contents

1. Guideline 4

a. Introduction 4

b. Definitions 4

c. Causes 4

d. Approach 6

e. Management 9

f. Referrals 12

g. Appendix 13

2. Supporting References 15

3. Supporting Trust Guidelines 15

4. Guideline Governance 16

a. Scope

b. Purpose

c. Duties and Responsibilities

d. Approval and Ratification

e. Dissemination and Implementation

f. Review and Revision Arrangements

g. Equality Impact Assessment

h. Document Checklist

1. Approach to Paediatric Haematuria

a. Introduction

- Most children have isolated asymptomatic microscopic haematuria
- Most of the cases of isolated microscopic haematuria are benign but careful history and thorough examination are important to rule out significant causes
- **Haematuria associated with pain, oedema, hypertension or proteinuria needs investigation**
- Haematuria is a very common finding in paediatrics and healthy children can have occasional red cells in the urine
- 1+ or greater on repeated urine dip samples is regarded as significant.
- RBCs lyse rapidly in dilute or acidic urine and so negative microscopy for red blood cells is only valid if performed promptly on a freshly voided specimen.

b. Definitions

- **Haematuria** = the presence of an increased number of **red blood cells (RBCs)** in the urine. However, it is important to be aware that urine dipstick actually detects **haem molecules** in urine. (Table 2)
- **Microscopic haematuria =** detection of 1+ or greater of bloods by urine dipstick
- **Persistent microscopic haematuria =** 3 positive separate samples that occur ≥1 week apart, without prior exercise nor during menstruation.
- **Isolated asymptomatic microscopic haematuria =** the presence of microscopic haematuria without clinical symptoms or any other abnormalities in the urine e.g. proteinuria.
- **Macroscopic haematuria =** the urine is visibly discoloured with blood

c. Causes

- Common causes of haematuria in paediatrics include:
    - Isolated asymptomatic microscopic haematuria
    - Glomerulonephritis
    - Viral infections
    - UTI
    - Trauma
    - HSP
    - Hypercalciuria
    - Inherited abnormalities of the glomerular basement membrane
- Haematuria can be a sign of glomerular, extraglomerular or extrarenal diseases. It can also be due to vaginal bleeding or rectal fissures.
- Urate crystals (orangish colour) in babies' nappies can be misinterpreted as blood.
- A wider range of causes are presented below (Table 1)
- It is important to confirm that the child has 'true' haematuria as there are other causes of red urine that can be misinterpreted as blood in urine (Table 2)
- Urine microscopy can be very useful in differentiating between glomerular versus non-glomerular causes of haematuria (Table 3)

Table 1: Causes of haematuria

Glomerular causes		**Non-glomerular causes**
Renal	**Multisystem**	
Post infectious glomerulonephritis * IgA nephropathy * Membranoproliferative & membranous glomerulonephritis * Alport's syndrome Focal segmental glomerulosclerosis Thin basement nephropathy	Systemic lupus erythematosus * Henoch-Schonlein purpura * Wegener granulomatosis Goodpasture's syndrome * Polyarteritis nodosa Haemolytic uraemic 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*

Reference: Welsh Clinical Network for Paediatric Nephrology Guidelines
* Might cause macroscopic haematuria

Table 2: Confounding factors in dipstick analysis for blood

False positive tests (no RBC on microscopy)	**False negative tests**
Haem positive (dipstick positive) - Haemoglobinuria - Myoglobinuria **Haem negative (dipstick negative) – red urine without haematuria** - Drugs (e.g. rifampicin, chloroquine, metronidazole, nitrofurantoin) - Foods (e.g. beetroot, food colourings, blackberries) - Inborn errors of metabolism (e.g. alkaptonuria, porphyria)	- Formalin (preservative) - Ascorbic acid in high concentration - Specific gravity <1.010

Reference: Welsh Clinical Network for Paediatric Nephrology Guidelines

Table 3: Differentiating between extraglomerular and glomerular causes of haematuria under microscopy

	Extraglomerular	**Glomerular**
Colour (if macroscopic)	Red or pink	Red, smoky brown or "Coca-Cola" coloured
clots	May be present	Absent
Proteinuria	Usually absent	May be present
RBCs morphology	Normal	Dysmorphic
RBCs casts	Absent	May be present

Reference: UpToDate

d. Approach

Is it true haematuria?

- Urine microscopy to confirm (>10 RBCs/microlitre)

History

- Previous history of haematuria.
- Sore throat
- Cola/tea coloured urine (glomerular) vs red (extraglomerular or lower urinary tract causes)
- Vulvovaginitis
- Symptoms of urinary infection: dysuria, frequency, abdominal pain, fever.
- Flank pain with fever and rigors suggests acute pyelonephritis
- Unilateral flank pain radiating to the groin suggests obstruction by a calculus
- Timing of the haematuria:
  - Initial: urethral cause
  - Total/complete: kidney or diffuse bladder pathology
  - Terminal: prostatic, trigonal or posterior urethral disorders
- Systemic symptoms e.g. fatigue, oedema, rash, arthralgia.
- Recent history of pharyngitis or URTI
  - two to three weeks ago suggests poststreptococcal GN
  - one or two days ago suggests IgA nephropathy
- Recent surgery/trauma including non-accidental injury
- History of sickle cell disease/trait (as appropriate)
- Family history of haematuria
- Family history 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-related.

Examinations:

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

RED FLAGS (may need urgent referral to paediatric nephrology):

Haematuria AND any of:

- Proteinuria (check proteinuria guidelines)
- Hypertension
- Fluid overload: oedema, ascites
- Flank/abdominal pain
- Immuno-compromise
- Deranged renal function

Investigations

Box A: Initial Investigations for persistent microscopic haematuria:

Initial Investigations:

- Urine microscopy to confirm RBCs >10
- Urine culture
- Urine cytology to look for casts/dysmorphic red cells (if present suggests upper urinary tract cause)
- Urine protein:creatinine ratio
- Urine calcium:creatinine ratio
- U&Es, FBC, albumin, coagulation profile, LFT
- Renal tract ultrasound
- Haemoglobinopathy screen (in high risk populations)
- Urinalysis of immediate family members (assess for incidental microscopic haematuria & proteinuria)

Box B: Further investigations:

Further Investigations

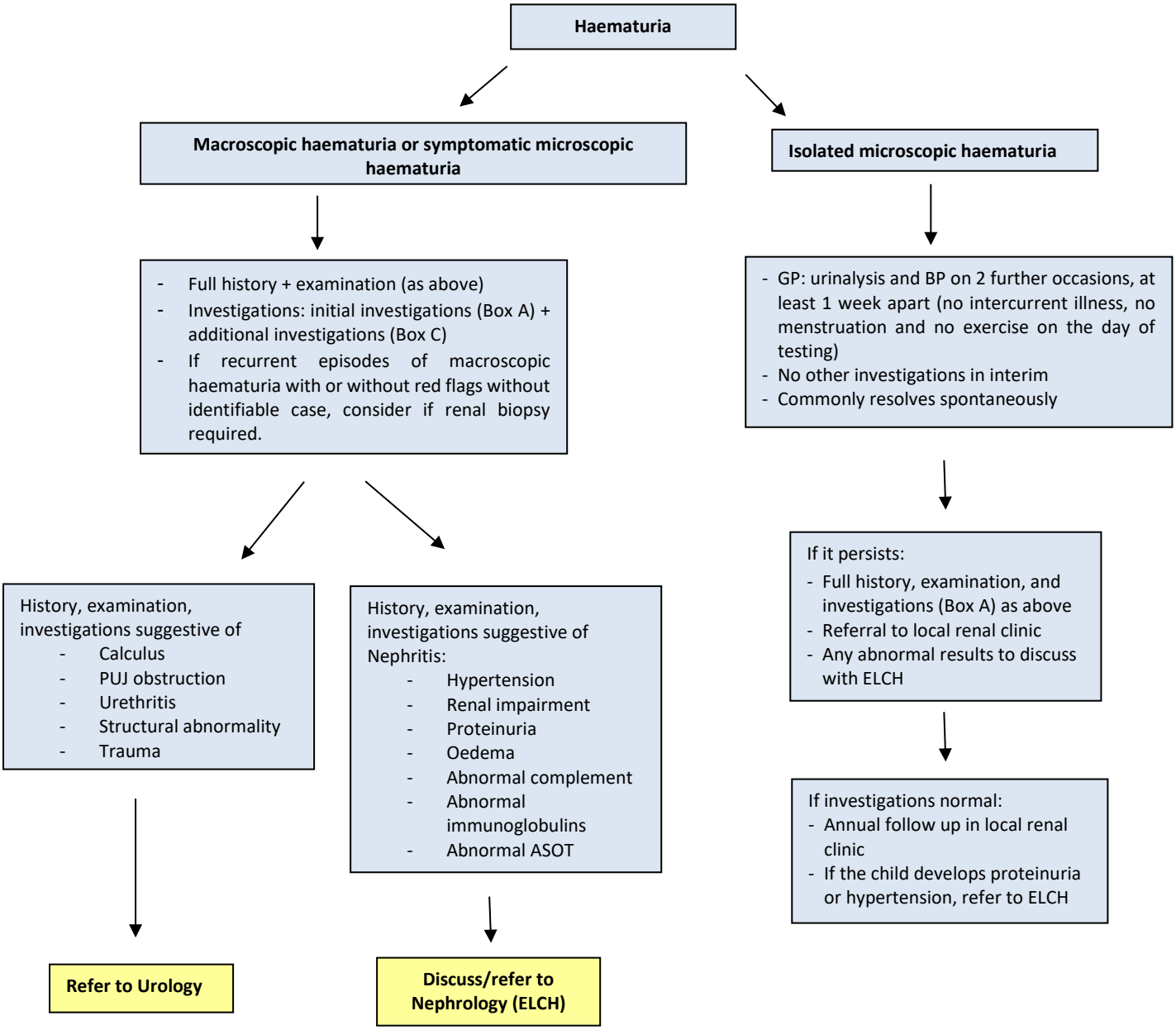
1. Nephrocalcinosis (**see stone screen in the appendix**):
    - Urine urate
    - Urine cystine
    - Urine citrate
    - Urine oxalate:creatinine ratio
    - Consider haemoglobinopathy screen
2. Recurrent UTI:
    - MCUG/MAG3 to look for reflux
    - DMSA to look for scarring
3. Genetic testing:
    - Family history of deafness / visual problems / haematuria in 1st degree relatives: **COL4A genetic screen (R194 panel)**
    - Nephrocalcinosis + family history stones: **nephrocalcinosis or nephrolithiasis (R256 panel)**
    - Need 1) Test order form 2) Record of Discussion 3) Genetic Specimen Form (https://southeatgenomics.nhs.uk/glh/core-rd/)
    - Send completed forms to gst-tr.viapathgeneticsadmin@nhs.net; gst-tr.londonsouthglh@nhs.net
4. Recurrent episodes of macroscopic haematuria with or without red flags without identifiable cause:
    - Consider if renal biopsy required

Box C: Additional investigations for macroscopic haematuria:

Additional Investigations

- Initial investigations (Box A) +
- ESR
- ANA
- dsDNA
- ANCA
- C3/C4
- ASOT
- Hepatitis B serology
- Immunoglobulins
- Imaging if suspected nephrolithiasis (CT) or trauma – Has to be discussed with urology

e. Management (check next pages for more details)



- **If the child develops proteinuria (+1 or more) at any point, please manage according to proteinuria guidelines.**

For the purpose of this guideline, our approach to haematuria will be divided into these sections:

1. Isolated asymptomatic microscopic haematuria
2. Isolated but persistent microscopic haematuria
3. Asymptomatic microscopic haematuria with proteinuria
4. Symptomatic microscopic haematuria or gross Haematuria

1. <u>Isolated asymptomatic microscopic haematuria</u>
   - Definition: Presence of microscopic haematuria (>10 RBC/microlitre) without clinical symptoms or any other abnormalities in the urine e.g. proteinuria
   - It is usually transient and is generally not associated with significant clinical disease.
   - Extensive diagnostic evaluation including laboratory testing is reserved only in children with proteinuria, hypertension, or gross haematuria

   - Most common identifiable causes are:
     - Idiopathic (most of the cases)
     - Hypercalciuria (with or without kidney stones)
     - Urinary tract malformations
     - Disorders of the GBM (including Alport syndrome)

   - Management:
     - Follow the approach as above (Is it true haematuria?, take full history and perform relevant examinations) → confirm it is isolated asymptomatic microscopic haematuria
     - Then refer to the GP to perform urinalysis and BP on 2 further occasions, at least 1 week apart from each other (no intercurrent illness, no menstruation and no exercise on the day of testing)
     - No other investigations in interim
     - Commonly resolves spontaneously
     - If microscopic haematuria has not resolved following 3 consecutive tests, then needs a paediatric referral (local renal clinic) and further investigation (initial investigations, Box A) and managed as isolated persistent microscopic haematuria (2).
     - Any abnormal results to discuss with Evelina renal team (see referral section below).
     - If all -ve/normal:
       - Annual follow up in local renal clinic
       - If the child develops proteinuria or hypertension, refer to ELCH

2. Isolated but persistent microscopic haematuria

- Definition: 3 positive separate samples that occur >1 week apart, without prior exercise nor during menstruation and with no other abnormalities in the urine microscopy/dip.

- Most common identifiable causes are as above.

- Management:
    - Refer to local renal clinic
    - **Initial investigations (Box A)** with personal and family history and examination
    - Any abnormal results to discuss with Evelina renal team (see referral section below).
    - If all -ve/normal:
        - Annual follow up in local renal clinic
        - If the child develops proteinuria or hypertension, refer to ELCH

3. Asymptomatic microscopic haematuria and proteinuria

- Refer to paediatric proteinuria guidelines.

4. Symptomatic microscopic haematuria or macroscopic (gross) haematuria

- **Definitions:**
    - **Macroscopic (gross) haematuria:** blood visible in the urine without microscopy
    - **Symptoms associated with microscopic haematuria** can include: flank pain, fever, dysuria, etc.

- Macroscopic haematuria:
    - is more likely to come from bladder or urethra rather than kidney
    - causes according to where in stream haematuria is:
        - Initial – urethral
        - Total/complete – kidney or diffuse bladder problem
        - Terminal – prostatic, trigonal, posterior urethral disorders
    - may also come from sources other than urinary tract (e.g. vaginal bleeding, rectal fissure)

- Management:
    - Follow the approach as above (Is it true haematuria?, take full history and perform relevant examinations)
    - **Initial investigations (Box A) + additional investigations (Box C)**
    - If recurrent episodes of macroscopic haematuria with or without red flags without identifiable case, consider if renal biopsy required
    - If history, examinations and investigations are suggestive of nephritis (hypertension, renal impairment, proteinuria, oedema, abnormal complement, abnormal immunoglobulins, abnormal ASOT, etc): discuss/refer to nephrology (ELCH)
    - If history, examinations and investigations are suggestive of calculus, PUJ obstruction, urethritis, structural abnormalities or trauma, refer to urology

f. Referrals

ELCH Nephrology Referrals

Monday-Friday, 9am-5pm:

- Renal SpR on 07990800587 or on 02071887188 (bleep 1141)

For out of hours referrals:

- Paediatric Specialities SpR on 07514719077 or on 02071887188 (bleep 1139)
- A paediatric nephrologist is on call and can be contacted via the hospital switchboard on 02071887188.

1. **Non-urgent referral to paediatric nephrology team ELCH** if:
   - Isolated microscopic haematuria present >6 months or 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

2. **Discussion with the paediatric nephrology team ELCH** 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

3. **Urgent paediatric nephrology team ELCH referral** if:
   - Child is systemically unwell
   - Haematuria is present with any red flags

4. **Refer to Paediatric Urology (SGH)** if:
   - Calculus, PUJ obstruction, urethritis, structural abnormalities or trauma present
   - Dysuria is associated with episodes of macroscopic haematuria (with no red flags) in first instance.
   - If no urological causes were found and haematuria persists, the case should be discussed with paediatric nephrology (ELCH), while ensuring initial investigations are performed.

5. **Refer to Paediatric Stone Clinic ELCH** if:
   - A stone is detected (see stone screen in the appendix)

6. **Refer to surgeons / urology SGH** if:
   - Abdominal mass present

7. **Refer to Oncology (RMH)** if
   - Concerns about a neoplasm

g. Appendix: Evelina London Children's Hospital: Children's Stone Unit - Investigation of Children with Kidney Stones

- All children with renal calculi and nephrocalcinosis should have a basic metabolic screen regardless of the clinical history or stone composition.
- Submit stone for biochemical analysis whenever possible.
- Metabolic screen should preferably be performed once the patient is stone free.

<table>
<tr><th>Investigations</th><th>Normal range</th></tr>
<tr><td>Urea & Electrolytes, liver function tests

Venous blood gas- if abnormal bicarbonate on initial laboratory results

Full blood count</td><td>22-26mmol/l</td></tr>
<tr><td>Plasma magnesium

Plasma chloride</td><td>0.65-1.05 mmol/l

98-107mmol/l</td></tr>
<tr><td>Plasma calcium, phosphate, alkaline phosphatase

Parathyroid hormone level</td><td>Calcium: 2.19- 2.69 mmol/l; Phosphate: 0.8- 1.9 mmol/l

Alkaline Phosphotase: 163- 375 IU/L

PTH: 10- 65 ng/L</td></tr>
<tr><td>Plasma urate</td><td></td></tr>
<tr><td>MSU for micro and C/S

Urine pH on dipstick testing

Urine osmolarity</td><td><u>Urine volumes < 1litre/day and urine osmolarity >600mOsm/kg</u>
If above observed this may be a predisposing factor and needs addressing. Proportionately lesser volumes for younger children</td></tr>
<tr><td>Urine Calcium/creatinine ratio</td><td><u>Hypercalciuria</u>
a. Random non-fasting urinary calcium/creatinine ratio

<table><tr><td>Age</td><td>Random Ca:Cr ratio,
95th centile (mmol/mmol)[1]</td></tr><tr><td><7 months</td><td>1.96</td></tr><tr><td>8–18 months</td><td>1.4</td></tr><tr><td>19 months–6 years</td><td>0.78</td></tr><tr><td>6–16 years</td><td>0.56</td></tr></table>
b. 24-hour urine collection abnormal if >4 mg/kg/day (0.1 mmol/kg/day)</td></tr>
<tr><td>Urine Oxalate/ Creatinine ratio</td><td><u>Hyperoxaluria</u>
a. Random non-fasting urinary oxalate/creatinine ratio

<table><tr><td>Age</td><td>Random Oxalate:Cr ratio (micromol/mmol)</td></tr><tr><td><12 months</td><td>4-98</td></tr><tr><td>1-4 years</td><td>4-72</td></tr><tr><td>4-11 years</td><td>3-71</td></tr><tr><td>>11 years</td><td>1-38</td></tr></table>
Repeat random abnormalities should be confirmed where possible 24- hour urine collection into an acidified container along with urine for determination of urinary glycolate and urine glycerate concentrations.

a. 24-hour urine collection abnormal if >0.7 mmol/1.73m^2/24 hours
> 1.5x upper normal for age</td></tr>
</table>

<table>
<tr><td></td><td>If patient has renal insufficiency or renal failure Urine oxalate >0.5 mmol/1.73m^2/24 hours and/or Plasma oxalate >20 micromol/l is abnormal.</td></tr>
<tr><td>Urine amino acids</td><td><u>Urine amino acid analysis for Cystinuria</u>
Random urine specimen in micromol/mmol

<table>
<tr><th>Age</th><th>CYSTINE</th><th>ORNITHINE</th><th>LYSINE</th><th>ARGININE</th></tr>
<tr><td><6 months</td><td>13-37</td><td>0-40</td><td>15-137</td><td>0-10</td></tr>
<tr><td>6 months - 4 years</td><td>11-12</td><td>0-19</td><td>10-48</td><td>0-36</td></tr>
<tr><td>4 -21 years</td><td>4-15</td><td>2-8</td><td>10-68</td><td>3-11</td></tr>
</table></td></tr>
<tr><td>Urine urate/creatinine ratio</td><td><u>Hyperuricosuria</u>
a. Random urine specimen in mmol/mmol

<table>
<tr><th>Age</th><th>Random urate/creat ratio (mmol/mmol)</th></tr>
<tr><td><6 months</td><td>0.3 – 2.50</td></tr>
<tr><td>>6 months</td><td>0.1 – 1.50</td></tr>
</table>

b. 24-hour urine collection abnormal if >470 mg/m^2
>600 mg/24-hour</td></tr>
<tr><td>Urine citrate/creatinine ratio</td><td><u>Hypocitraturia</u>
a. Random non fasting urinary citrate/ creatinine ratio below 0.11- 0.55 mmol/mmol
Other definitions include urine citrate/ creatinine ratio less than 408 mg/gm of creatinine

b. Urine citrate concentration <1.7 mmol/l/24-hour</td></tr>
<tr><td>Stone for caluculus biochemistry</td><td></td></tr>
<tr><td>Renal USS</td><td></td></tr>
<tr><td>Baseline DMSA if undergoing surgery</td><td></td></tr>
</table>

Additional notes

1. Patients with persistent hyperoxaluria may need mutation analysis for AGXT gene: Primary hyperoxaluria type 1 and GR/HPR gene: Primary hyperoxaluria type 2. Some cases may need a liver biopsy to measure enzyme activity.
2. Recurrent stone formers or some other specific patient groups may require Dietary assessment for salt, protein and oxalate.
3. Some patients may additionally need Urine for tubular proteinuria and DNA for mutation analysis e.g. Dents disease

2. Supporting References

- Uptodate.com
  - Evaluation of microscopic haematuria in children
  - Evaluation of gross haematuria in children
- Welsh Clinical Network for Paediatric Nephrology: https://cavuhb.nhs.wales/our-services/welsh-clinical-network-for-paediatric-nephrology/guidelines/
- Evelina London Children's Hospital clinical guidelines (guideline for management of the child with persistent haematuria
- PIER Network guidelines: https://www.piernetwork.org/haematuria.html
- The Royal Children's Hospital Melbourne: Clinical Practice Guidelines : Haematuria (rch.org.au)
- Hospitals Bristol and Weston NHS Foundation Trust: https://www.uhbristol.nhs.uk/for-clinicians/clinical-guidelines/renalnephrology/

3. Supporting relevant trust guidelines

- Approach to Primary Nephrotic Syndrome in Paediatrics
- Approach to Paediatric Proteinuria

4. Guideline Governance

a. Scope

This guideline is relevant to all staff caring for all children from 0-18 years old across the emergency department, inpatient ward and outpatient department.

b. Purpose

i. This guidelines aims to facilitate a common approach to the management of children. At times deviation from the guideline may be necessary, this should be documented and is the responsibility of the attending consultant.

ii. This guideline is subject to regular review to ensure ongoing evidence based practice.

c. Duties and Responsibilities

All healthcare professionals responsible for the care of all children 0-18years should be aware of practice according to this guideline.

d. Approval and Ratification

This guideline will be approved and ratified by the Paediatric Guidelines Group.

e. Dissemination and Implementation

i. This guideline will be uploaded to the trust intranet 'Paediatric Guidelines' page and thus available for common use.
ii. This guideline will be shared as part of ongoing education within the Paediatric Department for both medical and nursing staff.
iii. All members of staff are invited to attend and give comments on the guideline as part of the ratification process.

f. Review and Revision Arrangements

a. This policy will be reviewed on a 3 yearly basis by the appropriate persons.
b. If new information comes to light prior to the review date, an earlier review will be prompted.
c. Amendments to the document shall be clearly marked on the document control sheet and the updated version uploaded to the intranet. Minor amendments will be ratified through the Paediatric Guidelines Group. A minor amendment would consist of no major change in process, and includes but is not limited to, amendments to documents within the appendices.

g. Equality Impact Assessment

Background • Who was involved in the Equality Impact Assessment
Author and the supervising consultants.
Methodology • A brief account of how the likely effects of the policy was assessed (to include race and ethnic origin, disability, gender, culture, religion or belief, sexual orientation, age) • The data sources and any other information used • The consultation that was carried out (who, why and how?)
All groups of staff and patients were taken into consideration and there is no bias towards or against any particular group.
Key Findings • Describe the results of the assessment • Identify if there is adverse or a potentially adverse impacts for any equalities groups
There is no evidence of discrimination.
Conclusion • Provide a summary of the overall conclusions
There is no evidence of discrimination.
Recommendations • State recommended changes to the proposed policy as a result of the impact assessment • Where it has not been possible to amend the policy, provide the detail of any actions that have been identified • Describe the plans for reviewing the assessment
This guideline is appropriate for use.

h. Document Checklist

To be completed (electronically) and attached to any document which guides practice when submitted to the appropriate committee for approval or ratification.

Title of the document:

Policy (document) Author:

Executive Director: N/A

		Yes/No/ Unsure/NA	Comments
1.	**Title**		
	Is the title clear and unambiguous?		
	Is it clear whether the document is a guideline, policy, protocol or standard?		
2.	**Scope/Purpose**		
	Is the target population clear and unambiguous?		
	Is the purpose of the document clear?		
	Are the intended outcomes described?		
	Are the statements clear and unambiguous?		
3.	**Development Process**		
	Is there evidence of engagement with stakeholders and users?		
	Who was engaged in a review of the document (list committees/ individuals)?		
	Has the policy template been followed (i.e. is the format correct)?		
4.	**Evidence Base**		
	Is the type of evidence to support the document identified explicitly?		

		Yes/No/ Unsure/NA	Comments
	Are local/organisational supporting documents referenced?		
5.	**Approval**		
	Does the document identify which committee/group will approve/ratify it?		
	If appropriate, have the joint human resources/staff side committee (or equivalent) approved the document?		
6.	**Dissemination and Implementation**		
	Is there an outline/plan to identify how this will be done?		
	Does the plan include the necessary training/support to ensure compliance?		
7.	**Process for Monitoring Compliance**		
	Are there measurable standards or KPIs to support monitoring compliance of the document?		
8.	**Review Date**		
	Is the review date identified and is this acceptable?		
9.	**Overall Responsibility for the Document**		
	Is it clear who will be responsible for coordinating the dissemination, implementation and review of the documentation?		
10.	**Equality Impact Assessment (EIA)**		
	Has a suitable EIA been completed?		

Committee Approval (Paediatric Guidelines Group)			
If the committee is happy to approve this document, please complete the section below, date it and return it to the Policy (document) Owner			
Name of Chair		**Date**	
Ratification by Management Executive (if appropriate)			
If the Management Executive is happy to ratify this document, please complete the date of ratification below and advise the Policy (document) Owner			
Date: n/a			