Evaluation of the Child with Urolithiasis

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• Pathophysiology
• Imaging
• Metabolic evaluation
Aetiology

• **Infection**: majority of stones.
  – These located in the upper urinary tract,
  – *struvite* (magnesium, ammonium, phosphate),
  – frequently related to *proteus* infection.

• **Metabolic** stones. Increasing trend
  – Hypercalciuria is the most common metabolic cause of stones in Western children.

• **Dietary**: inadequate protein and dehydration,
  “Stone Belt”. Bladder stones

• **Idiopathic**: 
• Urinary calculi are composed of varying proportions of:
  – **Matrix** gelatinous glycoprotein.
  – **Crystalline**

• Matrix is a particular feature of infective stones, which are typically soft and crumbly.

• Metabolic stones, e.g. cystine and xanthine, are predominantly crystalline and harder.
Pathophysiology of stone formation

• Complex process and depends on the interaction of several factors:
  – concentration of stone forming ions
  – pH of urine
  – flow of urine
  – balance between crystallisation promoters and inhibitory factors of; citrate, magnesium, pyrophosphate, macromolecules and glycosaminoglycans
  – Infection: Proteus, Klebsiella and Pseudomonas, are capable of the enzymatic splitting of urea to produce NH3 and high urinary pH and precipitation of ammonium salts. Infection is also a key factor in the production of the proteinaceous matrix component of calculi.
  – Anatomic factors that encourage urinary stasis; VUR, PUJO
  – Others: Prematurity, Formula feeding and diuretics
Urine containing crystals flowing down renal tubules

Crystals growing and agglomerating

Critical particle forms and is trapped in tubule

Particle adheres to damaged site on tubule wall and other crystals agglomerate with it

Free-Particle Model of Stone Initiation

Fixed-Particle Model of Stone Initiation
Clinical presentation

- **Age**  higher prevalence in early childhood (<5 years) due to Infections as early as 2–3 mo

- **Infection**  - infants deceptively non-specific, vague ill health, low-grade fever -older children show features of UTI.
  - *Proteus* MUST prompt inv.

- **Haematuria**  -common regardless of severity -Absence does not exclude stones

- **Passage of stone material:**
  Occasionally
  streaks of blood in the nappy may be incorrectly ascribed to balanitis.

- **Pain:** Acute renal colic of adults is not a prominent feature in children.
  Often a poorly localised symptom

- **Abdominal mass**  Xanthogranulomatous pyelonephritis (XGPN)
  general ill health may resemble Wilms’ tumour.
• **Urinalysis**: identify haematuria, pyuria, and bacteria.

• **microscopy** of fresh urine may also identify crystals of Oxalate, cystine. The

• **culture and sensitivity** should be sent for to identify bacteria

• who are subsequently found to have an

• underlying metabolic cause for the renal stone
Two levels;

I. Initial screening for possible calculi

1. Ultrasound

- First line
- Sensitive modality for the detection of renal calculi.
- Easy, no radiation
- Define stone size, location and dilatation
- Color doppler can assess severity of obstruction
  
  - Ureteric and small bladder calculi may be missed.
imaging

2. *Abdominal X-ray*
   - Currently used in conjunction with US
   - Detect radiopaque stones
   - Good for follow up

3. *NCCT*
   - accurate diagnosis within minutes,
   - avoids the potential risk of adverse contrast media
   - Positively demonstrate the presence of radiolucent calculi
     - radiation hazard
     - difficulty in interpreting images of the collecting system.

The role of CT as front-line modality in children requires further evaluation.
ii. Evaluation prior to treatment of proven stone disease

1. **DMSA**
   Pre and post operative evaluation of differential renal function

2. **Intravenous urography: limited but imp. role**
   - permitting visualisation of nonopaque stones
   - calyceal anatomy is important in planning (PCNL/ESWL)
   - Ureteric calculi are best localised by IVU
   - identifying any underlying anatomical abnormality predisposing to urolithiasis
   - Give idea about renal function.
Additional inv

1. *Micturating cystography (MCU)*:
   - not routinely required.
   - when ureteric dilatation and/or infection persists postoperatively

2. *Dynamic renography (MAG3/DTPA)*
   - if obstruction is suspected. following the complete removal of the stone.
Inherited metabolic diseases are identified more frequently in children than in adults and therefore investigations to identify such disorders are indicated.

**STONE ANALYSIS; Why important?**
- helpful in elucidating the underlying cause
- metabolic evaluation can be modified according to the specific stone type
- Infection does NOT rule out metabolic cause.

**But**
- Less important than urine composition.
- Stone composition is not necessarily reflect urine composition

**Methods of stone analysis:**
- polarizing microscopy,
- X-ray diffraction,
- infrared spectroscopy
- chemical analysis. Not useful

North American data of analysed stones:
- Calcium oxalate: 70–80%
- Calcium phosphate: 5–10%
- Uric acid: 5–10%
- Struvite: 5–10%
- Cystine: 1–5%.
Algorithm for metabolic investigations and prevention in urinary stone disease in children

Paediatric stone patient

Elimination of stones by spontaneous passage or active removal (SWL, surgery)

Stone analysis

Mg Ammonium phosphate (struvite)
- urine culture
- possibly urease producing bacteria
- total elimination of stone (surgery/SWL) antibiotics

Uric acid stone
- urine pH
- urine and serum uric acid levels
- acidic urine hyperuricosuria hyperuricemia

Cystine
- urine pH
- urine cystine level
- cystinuria
- high fluid intake
- potassium citrate 3-4 mEq/kg/d
- mercaptopropionylglycine 10-15 mg/kg/d

Calcium stones CaOx-CaPO

alkali replacement - K citrate
- Allopurinol (10 mg/kg)
- low purine diet
Stone screening

• Early morning urine sample (pH to exclude renal tubular acidosis)

• Blood sample for plasma levels of urea, electrolytes, creatinine, calcium, phosphate, uric acid

• ‘Spot’, i.e. untimed, urine sample 2–5 ml (divided into two aliquots)

• First aliquot acidified and analysed for:
  - creatinine, calcium, magnesium, cystine, oxalate

• Second aliquot alkalinised and analysed for:
  - creatinine and uric acid

• Compare the concentration of substance to urine creatinine conc

• Fairly representative of a 24 hour
24 hrs urine collection

- Not easy to do in a young child
- After stone clearance
- Child to be on routine diet.
- **Serum**: urea, creatinine, Na, K, Ca, Ox, P
- Collect urine for 2 days; start after morning void and include next day morning void
- **Urine**
  - volume
  - calcium, phosphorus, magnesium, oxalate, uric acid, citrate, cystine, protein, and creatinine clearance.
Calcium stones
- calcium oxalate or calcium phosphate.

Hypercalciuria
A. Idiopathic
B. Secondary to hypercalcaemia due to: bone resorption, hyperparathyroidism, hyperthyroidism, immobilization, acidosis, metastatic disease or hyperabsorption (hypervitaminosis D)

= 24-hour urinary Ca > 4 mg/kg/day (infants < 3 mo 5 mg/kg/day)

- Screening: Ca:creat ratio > 0.2

Hyperoxaluria
- School children excrete < 50 mg (0.57 mmol)/1.73m2/day (infants 4 X)

- Idiopathic: ‘mild’ hyperoxaluria majority
- 1ry : enzymes deficiency that play a role in the metabolism of oxalate
- 2ry: high dietary intake (spinach, tea), hyperabsorption (short bowel syndrome), inborn error of metabolism
- Treatment: high urine flow, restriction of dietary oxalate and regular calcium intake. Pyridoxine may be useful especially in primary hyperoxaluria
Hypocitraturia.

- Usually no symptoms
- bind to calcium and inhibit growth and aggregation of ca ox & CaP
- adults < 320 mg/day (adjusted for children)
- Found in 30-60% of children with calcium stone disease.
- Cause: high protein and salt intake
- Treat: potassium citrate 1 mEq/kg, given in two divided doses

Uric acid stones

- Hyperuricosuria is the main cause in children. A daily output of uric acid > 10 mg/kg/day
- pH < 5.8 favour stone formation
- Either
  1. familial or idiopathic: normal serum uric
  2. uric acid overproduction: inborn errors of metabolism, myeloproliferative disorders, high purine and protein intake (nuts, chockolates)
Cystine stones

- 2-6% of all urinary stones in children.
- recessive autosomal disorder \( \rightarrow \) failure of renal tubules to reabsorb amino acids: cystine, ornithine, lysine and arginine. (COLA)
- cystine has poor solubility in urine \( \rightarrow \) stones at pH levels < 7.0.
- faintly radiolucent, Hard

Infection stones (struvite stones)

- urease enzyme bacteria (Proteus, Klebsiella, Pseudomonas) are responsible
- Urease converts urea \( \rightarrow \) ammonia and bicarbonate, \( \rightarrow \) alkalinizing the urine and further converting bicarbonate into carbonate.
- In the alkaline environment, triple phosphates form-\( \rightarrow \) supersaturation magnesium ammonium phosphate and carbonate apatite, leading to stone formation.
- Elimination of both bacteria and stone is essential for treatment, as stones will harbour infection and antibiotic treatment will not be effective.
### Conclusions and recommendations

#### Conclusions

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<td>The incidence of stone disease in children is increasing.</td>
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<td>Any child with urinary stone disease deserves metabolic and anatomical evaluation.</td>
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<td>Treatment should be supported with medical treatment for the underlying metabolic abnormality if detected.</td>
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<td>Open surgery for stone disease in children is an exceedingly rare requirement.</td>
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<td>Surgical treatment is based on minimally invasive modalities.</td>
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#### Recommendations

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<td>In most cases, plain abdominal X-ray and ultrasonography is sufficient for diagnosis and follow-up.</td>
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<td>Non-contrast CT may be required in cases with a doubtful diagnosis or complex cases requiring surgery.</td>
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<td>The use of appropriate-size instruments will decrease the number of complications in surgical treatment.</td>
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Thank you
• Particular attention must be paid to the method of urine collection for oxalate analysis.
• The patient must not be receiving vitamin C supplements, as the latter falsely elevate oxalate values. A fresh sample must be collected and sent immediately to the laboratory for analysis
• unless the urine is collected in a container acidified with hydrochloric acid. Delays will
• cause false elevation of oxalate concentration by oxidation. Urinary L-glyceric acid estimation
• is required to diagnose primary hyperoxaluria type II, but special handling of the
• urine collection is not necessary as this forms part of a urinary organic acid screen
METABOLIC REVIEW

- Inherited metabolic diseases are identified more frequently in children than in adults and therefore investigations to identify such disorders are indicated. The yield from a metabolic screen in a child with Proteus urine infection and a stone is often small, but any child with recurrent stones, a family history, or sterile urine requires adequate assessment.
- All children with urolithiasis must be screened for cystinuria as medical therapy improves long term outcome. Conditions such as hyperoxaluria, which have hitherto been considered very rare, may be identified more frequently if the appropriate tests are requested.
- Figure 1 presents a suggested protocol for investigations.