Renal Stones in Children

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Aetiology

- Differs from adults
- Varies with geography & over time
- Most have primary ‘metabolic’ risk factors
- Some have ‘other’ risk factors
Aim to discuss

- Stones in the UK children
- Stones in Australian Aboriginal children
- Stones in other geographical settings
- Management Strategies
- Local examples
  - Infection Stones
  - Urate Stones
  - Cystine Stones
  - Standing Stones

Calcium oxalate stones
Paediatric Stones in the UK

- Incidence seems to be increasing, esp. in young females (F ≤ M)
- Younger age at 1st stone
- In children, commoner in younger patients (esp. 0-5 yrs)
- Associated with sub-optimal growth
- ‘Metabolic’ & ‘Idiopathic’ ↑-ing proportions, ‘Infective’ ↓-ing

Van’t Hoff W. Aetiology of Paediatric Renal Stones. ICH, London, March 2009 (Lecture)
Paediatric Stones in the UK

- Approx 50% have identifiable metabolic abnormality (GOS 1997-2005, n=250)

- Hypercalciuria 27%
- Cystinuria 10%
- Primary Hyperoxaluria 3%
- Other Oxaluria (e.g. Enteric) 6%

- Risk of metabolic cause greater if bilateral stones (OR 2.7)

Van’t Hoff W. Aetiology of Paediatric Renal Stones. ICH, London, March 2009 (Lecture)
Presenting Features

- Haematuria 60%
- Abdominal Pain 55%
- UTI 44%
- Vomiting 22%
- Asymptomatic 16%

- Note 40% didn’t have haematuria
  45% didn’t have abdo. pain

Van’t Hoff W. Aetiology of Paediatric Renal Stones. ICH, London, March 2009 (Lecture)
Theories about Lifestyle & Stones

- Diet changes relate to ↑-ed stone frequency
e.g. ↑ protein, refined sugars, purines & sodium
  → ↑-ed urine Ca, uric acid, oxalate & Na
  ↓ urine citrate

- Increased antibiotic use → altered gut flora
  ↓ Oxalobacter formigenes (consumes oxalate)
  → ↑-ed oxalate absorption from colon

→ increased formation of CaOx type stones

Robertson WG. Lifestyle & Risk of Stones, ICH, London, March 2009 (Lecture)
Stones in Australian Aboriginal Children

- 1977

- Do Australian Aborigines suffer from renal tract calculi?

  - Bateson EM. Aust NZ J Med, 380-381
Where & how do stone-forming Aboriginal Australian children live?

- Often, though by no means exclusively
- Hot
- Dry or humid
- Social disadvantage
- Inadequate diet
- Recurrent infections & poor health
Stones in Australian Aboriginal Children

- 1994
- 36 Aboriginal children reported
- Mostly boys
- 70% 2 yrs or less
- Urate & oxalate main constituents
- Known metabolic disorders not seen
- Diet, dehydration & recurrent diarrhoea incriminated

Stones in Australian Aboriginal Children

- 2003 – Hypothesis
  - recurrent diarrhoeal illness
  - → secondary lactose intolerance
  - → chronic metabolic acidosis
  - → increased urine urate excretion
  - → stone formation

Personal Observations

- Recurrently unwell young children
- Dx-ed when admitted ‘sick’
- Metabolic acidosis, acid urine, hypercalciuria, uricosuria
- Seen on US, not seen on x-ray
- Often multiple & small
- Usually asymptomatic
- Most get better with time, good health and nutrition +/- urinary alkalinisation
- Low recurrence rate (=> unlikely due to persistent metabolic or anatomical factors)
Personal Postulation

- ? Enteric hyperoxaluria
- Diarrhoea → reduced GIT Ca for binding with Oxalate
  → ↑ GI Ox absorption
  → Hyperoxaluria
- Diet rich in animal protein can → hyperoxaluria
- Low dietary calcium can also → hyperoxaluria
- Altered GIT flora due to illness & antibiotics
  → ↓ Oxalobacter → hyperoxaluria
Oxalate

- Kidneys are 1\textsuperscript{st} route of excretion & site of only known function → uptake of H\textsubscript{2}O, Na\textsuperscript{+} & Cl\textsuperscript{-} from PCT.
‘Set-up’ for hyperuricosuria / urate cystaluria

1. Diet rich in animal protein can → high purine load → nitrogen waste → uricosuria

2. Recurrent (or persistent) dehydration → ↓ urine production

3. ? recurrent illness (e.g. diarrhoea → GI bicarbonate loss) → metabolic acidosis → acid urine
Stones in Tunisian Children

- Retrospective 12 year study (n=133 overall)
- Males > Females (difference ↓-ed)
- Urate stones ↑-ed. (now 25%)
- Struvite (Triple Phosphate) ↑-ed (15.6% to 37.5%)
- UTI rate increasing
- Calcium oxalate remains the most frequent component, but frequency ↓-ed

Stones in Turkish Children

- Males ≈ Females (n=179 overall)
- Family History (22% consang.) 55%
- Abdominal or flank pain 65%
- Radio-opaque ≈ radio-lucent
- Positive urine culture 20%
- Hyperuricosuria 55%
- CaOx stones 60%

*Dursun et al. Int Urol Nephrol. 2008 20: pp3-9*
Stones in Icelandic Children

- Commoner in girls (n=26 overall)
- Abdominal pain 69%
- Haematuria on urinalysis 81%
- Sterile pyuria 65%
- Positive urine culture 23%
- Hypercalciuria 78%
- Recurrence 29%

Stones in Argentinean Children

- Slightly commoner in boys (n=90 overall)
- Biochemical abnormalities 84%
- Single metabolic urine risk factor 52%
- Multiple risk factors 31%
- Idiopathic hypercalciuria 40%
- Hypocitraturia 38%
- Family Hx in 1° relatives 46%

Stones in US Children

- Incidence seems to be increasing (New York) (? population, ? referral patterns, ? real increase)
- Blood tests generally normal
- 24-hr urine - 76% have 1 or more abnormalities
- Hypocitraturia commonest (52%)
- Hypercalciuria next commonest
- Recurrent in 39%

CHINA MILK PRODUCT SCARE

- Four baby deaths
- More than 50,000 children made ill

EU ban on China-made baby food

Deaths/illness
Products withdrawn/banned
Melamine found
Melamine Stones in Chinese Children

- Recent epidemic related to contaminated baby milk
  4 reported deaths in China by September 2008
- 15 patients from Hong Kong, aged 3-31 months
- 2/3 were asymptomatic (Dx-ed on US)
- Stones varied from 2.5 - 18mm, 9/15 bilateral, soft & friable
- None had UTI
- 8/14(?) had predisposing lithogenic factors e.g. hyperuricosuria (commonest), hypercalciuria, hyperoxaluria and acid urine.

Melamine Stones in Chinese Children

- Urine melamine levels correlated with stone size
- Most responded well to non-invasive Mx (fluids +/- urine alkalinisation)
- Young children have immature excretory mechanisms for melamine
- Multifactorial e.g. high urinary uric acid in infancy
- Melamine → central nidus & other metabolic factors (e.g. uric acid) produce stone

Clinical Management

1. Diagnose Stone
2. Clear Stone
3. Investigate for cause
4. Prevent future stones
Diagnose Stone

- Clinical (pain, haematuria etc)
- then imaging

1. **US is the principal imaging mode**
2. **X-rays**
3. **DMSA (baseline function)**
4. **CT (occasionally helpful in children)**
5. **IVU (for planning Rx only)**
Clear Stones

- Stones up to 4 or 5mm may pass spontaneously

- Shock Wave Lithotripsy (Edinburgh)
  - stones up to 2cm, young children need GA

- Minimally invasive surgery may include:
  PCNL, Uretero-reno-scroscopy, Laparoscopy, Vesico-lithotomy (augmented bladders)
  - Choice based on location, hardness or softness

- Open surgery occasionally
Investigate for cause
RHSC-Yorkhill stone workup

1. Ultrasound and abdominal x-ray

2. Biochemical stone analysis when possible.
   - If the biochemical stone analysis suggests a cystine stone, the key investigation is urinary amino acid chromatography.
   - If analysis suggests a uric acid stone the key investigations are urinary urate/creatinine ratio, plasma urate, plasma HGPRT and APRT (enz. def.s).
   - If analysis suggests a struvite stone, metabolic evaluation is unnecessary.

3. If the biochemical stone analysis suggests calcium oxalate/calcium phosphate or if there is no stone recovered, the following investigations should be carried out.
   1. Urinalysis and pH
   2. Urine Culture
   3. Urinary calcium, oxalate and urate / creatinine ratios
   4. Urinary amino acid and organic acid screen
   5. If spot urines are abnormal, a second voided EMU should be taken and subsequently a 12-14hr collection
Stone Types

North American data of analysed stones suggest the frequency and composition of urinary tract stones as:

1. Calcium oxalate 70-80%
2. Calcium phosphate 5-10%
3. Uric acid 5-10%
4. Struvite 5-10%
5. Cystine 1-5%
‘Metabolic’ risk factors

- Monogenic causes (uncommon)
  - cystinuria
  - hyperoxaluria
  - Lesch-Nyhan Syn.

- ‘General Metabolic’ risk factors (common)
  - Hypercalciuria
  - Hyperuricosuria
  - Hyperoxaluria
  - Hypocitraturia
Other risk factors include:

- Urinary tract Infection
- Prematurity
- Family history
- Ketogenic diet
- Neurological problems / immobility
- Reconstructed / augmented bladders
- Other renal tract anatomical abnormalities
Prevention Strategies

- Maintain high urine output (always)

- Dietary changes where appropriate
  (need care esp. with children)

- Specific therapies (sometimes)
  e.g. - thiazides for hypercalciuria
         - urinary alkalinisation for urate or
         cystine stones (usually potassium citrate)
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(Michelangelo mid C16, alkaline mineral water, still marketed today)
Beware of over-alkalinising

- Aim for urine pH not exceeding 7.5-8.0
- Above this precipitates calcium phosphate stones
UTI-related (Struvite or triple phosphate) Stones

- Struvite is composed of:
  - magnesium, ammonium, calcium phosphate

- Urinary saturation with struvite occurs when:
  1. supra-normal excretion of ammonia &
  2. alkaline urine occur together.

- Hydrolysis of urea by certain (urea splitting) bacteria
  → ammonia
  → alkalinisne urine.
  → formation of struvite stones.
UTI-related (Struvite or triple Phosphate) Stones

- Usually related to Proteus or other urea splitting organisms
  
  *(Klebsiella, Serratia & Mycoplasma)*

- generally located in the upper urinary tract
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**Struvite:** described from sewers in Hamburg (1845) & named for geographer & geologist Heinrich Christian Gottfried von Struve
HQ – 12 yrs ♂

- Presented with acute renal failure
- Unilateral loin pain & macrohaematuria
- US echogenic focus upper pole right kidney & lower pole left kidney with no hydronephrosis or hydroureter
- Passed a stone
HQ – 12 yrs ♂

- Plasma urate 1.14 mMol/mMol (<0.4)
- Urine urate/creatinine 0.81 mMol/L (<0.44)
- Serum creatinine came down
- Other Ix normal
- Stone analysis pending
- FHx – cousins on maternal side hyperuricaemia
- Rx – liberal fluids, Potassium Citrate
  ? low urate diet, ? Allopurinol
Cystinuria

- Autosomal recessive defect of transport of cystine & other dibasic AAs (COAL)
- Urolithiasis is the only clinical expression
- \(\approx 10\%\) of stones in children (GOS series)
- Stone formation is life long
- Doesn’t recur in renal Tx
Cystinuria Variants

- 3 types exist (as well as double heterozygotes)
- Type I (Classical) - AR behaviour, heterozygotes have normal cystine excretion
- Type II – Dominant behaviour, heterozygotes ↑-ed cystine excretion (need active Mx)
- Type III – Intermediate behaviour, heterozygotes moderately ↑-ed cystine excretion
- Types II & III may share variant genes on long arm Ch 19 (19q13.1)
- Type I is due to a defect on the short arm of Ch 2 (2p)
Cystinuria Mx principles

- High fluid intake (day & night)
- Aim for urine OP of 1.5L/m²/day
- Vegetarian(-ish) diet (↓ Methionine load)
- Alkalinise urine to around pH 7.5
- Regular follow up (compliance difficult)
- Chelating agents e.g. D-penicillamine if needed (lots of side effects), ?? Captopril (conflicting evidence)
- Minimally invasive surgery if possible (? ESWL resistant)
- Monitor urine pH, crystaluria, 24hr urine [cystine], US
To recap – kidney stones in childhood

- Tend to differ from adults
- Vary with geography & over time
- Most associated with primary ‘metabolic’ risk factors
- Some have ‘other’ risk factors
- There are a few inherited (AR) monogenic causes
- Prevention is be better than cure