**Epidemiology**

Uncommon presentation of renal or urinary tract pathology, but increased by a third 1980 to 1995 with lifetime risk of 12% for males and 5% for females.

Males predominate in most studies: M:F = 1.5 to 4:1, except in children who have had bladder reconstruction.

Average age between 5 to 9 years.

Family history in 22%.

**Countries have variable**

1. **Incidence**
2. **Composition**
3. **Clinical characteristics**

Dependent upon:

1. Population genetic factors
2. Socio-economic factors
3. Diet
4. Climate

**1. Endemic Calculi**


Bladder 90%

Male 75%

Cereal diet (rice)

Comp: = calcium oxalate 80%

ammonium urate 57%

calcium phosphate 42%

*Angwafo et al Eur Urol 2000

**2. Infective Calculi**

Incidence 1:100,000 children/y*

Comp. Struvite Mg NH₄ PO₄ triple phosphate organic matrix.

Upper tract 90%

Proteus UTI.


**3. Metabolic Calculi**

Hypercalciuria

“Stone Belt” Southeastern USA

Most common metabolic cause

Hyperoxaluria

1: 60-120 thousand children

Tunisia – 13% ESRF

Cystinuria

1: 7-15 thousand children

Disorders of Purine Metabolism

Uric acid

dihydroxyadenine

xanthinuria

**4. Bladder abnormalities**

Cause of majority of lower urinary tract stones in developed countries.
**PAEDIATRIC UROLITHIASIS**

**Presentation***
- Abdominal pain 50%
- Haematuria microscopic 90%
- macroscopic 10%
- Investigation of UTI
- Renal failure
- Adult “classic acute flank colic” 7%

* Tekin et al J Urol 2000

**Categorisation and Size**

Chance of spontaneous passage:
- <5mm high
- 5-7mm 50%
- >7 urological treatment usually

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**PAEDIATRIC UROLITHIASIS**

**Investigation**

- Confirmation of urinary calculi
- Complications
- Cause

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**PAEDIATRIC UROLITHIASIS**

1. **Confirmation of Urinary Calculi**

   (a) Renal ultrasound*

   cf AXR equally sensitive ~ 60%
   more specific detects radio lucent calculi
   (urate acid)
   may miss small calculi
   cannot identify ureteric calculi
   standard for follow-up

   *Smith et al Clin Rdiol 2000

   (b) AXR

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**PAEDIATRIC UROLITHIASIS**

1. **Confirmation of Urinary Calculi (continued)**

   (c) CT/Spiral CT –

   Imaging of choice in adults
   less experience in children
   young require anaesthetic

   Onen* 59 children investigated
   20 ureteric calculus
   13 calyceal calculus
   12 non urologic cause
   14 no diagnosis
   2 US +ve were –ve

   * Onen et al BJU Int 2000

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PAEDIATRIC UROLITHIASIS

2. Complications

UTI urine culture
Obstruction Renal ultrasound DTAP/MAG III
Function DTPA/MAG III/DMSA
Renal injury DMSA/US

3. Cause

(i) Store analysis*

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Crystal structure</th>
<th>Implication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca PO4</td>
<td>Apatite(Ca5(PO4)3(OH))</td>
<td>hypercalciuria</td>
</tr>
<tr>
<td></td>
<td>brushite(CaHPO4)</td>
<td>post SWL &amp; citrate</td>
</tr>
<tr>
<td>Mg NH4 PO4</td>
<td>struvite</td>
<td>infection (proteus-urease)</td>
</tr>
<tr>
<td>Ca O</td>
<td>whewellite</td>
<td>hypercalciuria</td>
</tr>
<tr>
<td>Purine</td>
<td>urate</td>
<td>hyperoxaluria</td>
</tr>
<tr>
<td>Cystine</td>
<td>sartine</td>
<td>xanthine oxalate def</td>
</tr>
<tr>
<td></td>
<td>cylexinurina</td>
<td>xanthine oxalate def</td>
</tr>
</tbody>
</table>

*Leusmann, BJU Int, 2000

Three Pathways for Kidney Stone Formation and Growth

1. "Free particle" formation, either in the collection system of the kidney or along the nephron (uric acid), with supersaturation

2. Crystal nuclei form in the lumen of a nephron at sites of cell injury (e.g. high [oxalate]) such as at the opening of a duct of Talhott

3. Crystalline deposits of interstitial calcium phosphate followed by loss of the normal urothelial covering allowing crystals in the urine to become attached

3. Cause

(ii) Urine microscopy
Cystine crystals

(iii) Urine excretion
(a) calcium
(b) uric acid
(c) citrate

(iv) Urine excretion of uric acid
HVE

(v) Identified abnormality leads to further definitive tests
PAEDIATRIC UROLITHIASIS

INFECTION STONES

Clinical
- Age: median 2y
- Sex: 80% male
- Infection: 90% at time of diagnosis
- Site: left 66%
  - Upper tract 85%
  - Bilateral 15%
- Associated: FTT common
- Proteus – urease

Composition
- Struvite and apatite hence, triple phosphate
- Organic matrix

Urologic Abnormalities
- 33% VUR (later 11%)
- 33% other abnormality
- Lumbar ureter dilation

Calcium Excretion
- Often transiently raised acutely

Treatment
- Removal essential
- If not:
  - Xanthogranulomatous pyelonephritis
  - Pyonephrosis
  - Renal scarring
  - Nephrectomy

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URINE CALCIUM EXCRETION

99% filtered calcium is reabsorbed

Calcium Excretion
- Often transiently raised acutely

HYPERCALCIURIA

Causes
1. Nephrocalcinosis
   - Look for
     - Hypercalcaemia
     - RTA
     - Hyperoxaluria
2. Urinary Calculi
Exclude hypercalcaemia

Causes:
- Hyperparathyroidism
- Vitamin D excess
- Immobilisation
- Hyperphosphatasia

Normocalcaemia hypercalciuria

Idiopathic hypercalciuria

1. Acid base disorders
- (a) Distal RTA
  - \( \uparrow \text{U}_{\text{Ca}} \)
  - \( \downarrow \text{Ucitrate} \)
  - High urine pH
  - Associated nephrocalcinosis, osteoporosis, poor growth, deafness

Normocalcaemia hypercalciuria (continued)

Idiopathic hypercalciuria

Polygenic
- Some families autosomal dominant
- Classified in past as renal: thiazide absorptive: diet Ca restriction

Problems
- Difficulty in classification
- Dietary Ca restriction
- Oxalate absorption
- Reduced bone mineralisation

Clinical
- Haematuria
- Leucocyturia
- Decreased bone mineralisation
- Nephrocalcinosis, calculi

Stone Development in Idiopathic Calcium Oxalate Stone Formers

1. Apatite deposits develop in the BM of the thin loops of Henle.
2. Extension into the interstitial space and are embedded in matrix, forming islands of interstitial plaque termed Randall’s plaque.
3. Loss of urothelial covering.
4. Urine proteins and ions coat the exposed interstitial plaque.
5. A layer of amorphous apatite forms on top of the interstitial plaque, and this new mineral layer is coated with urine matrix molecules.
6. A layer of biological apatite with matrix coating forms on the amorphous apatite.
7. A layer of both apatite and CaOx forms, and, at the outer margin of this small stone, only CaOx is found.

Stone Development in Idiopathic Calcium Oxalate Stone Formers

- Endoscopic image of CaOx stone (arrows) on a papilla from an idiopathic calcium oxalate stone former.
- The stone had been attached and attached to a site of Randall’s plaque (arrowhead): interstitial calcium phosphate plaque forming in the BM’s of thin loops.

Treatment

Diet
1. Fluid increase
2. Dietary Na decrease
3. Dietary K+ increase: \( \downarrow \text{U}_{\text{Ca}}, \text{U}_{\text{Ox}} \)
4. \( \downarrow 1.25(\text{OH})_2\text{D}_3 \)
5. Citrate chelates urine Ca
6. Thiazides
DISORDERS OF PURINE METABOLISM

Uric acid over production
1. Leukaemia/lymphoma tumor lysis
2. Lesch-Nyhan syndrome HXG PRTase hypoxanthine guanyl phosphoribosyl transferase deficiency
3. 1x Gout
4. Type 1 GSD
5. Ketogenic or high protein diet
6. Drugs - salicylates
Treatment: Alkalinize urine
           Allopurinol
           Uricase

1. Dihydroxyadeninuria
   APRTase deficiency
   May cause renal failure
   Alkalisation makes worse
   Allopurinol blocks production of dihydroxyadenine
2. Xanthinuria
   Failure of XO to convert xanthine to uric acid
   Plasma uric acid low

DISORDERS OF PURINE METABOLISM

CYSTINURIA
Defective re-absorption of cystine in renal tubule
Cystine precipitates
Hexagonal crystals

Genetics
1992 SLC3A1 (rBAT) 2p21
   i.e. parents cystine excretion normal
1997 SLC7A9 199
   encodes for light subunit of aa transporter

Molecular basis
Transport channel
SLC 7A9
Transporter subunit r BAT
“key to unlock”

CYSTINE SOLUBILITY
pH  Solubility Product*  Metastable zone+  Uric Acid
     mmol/L (mg/L)          mmol/L (mg/L)        (mmol/L)
5     3.0 (720)          1
6     1.3 (312)          3.2 (768)        4
6.5   -                  -                  10
7     1.4 (336)          3.5 (8.40)       10
8     2.5 (600)          6 (1440)         10
8.5   6 (1440)

* Solubility product: above level aggregates of crystals, growth about aidas
+ Metastable zone: to this concentration spontaneous precipitate without aids do not occur
CYSTINURIA

Epidemiology

Incidence: 1:7000 to 1:15,000
1-3% nephrolithiasis
6-8% of all nephrolithiasis in children
Age of presentation: 50% < 10y
90% < 20y
Stone free interval: 3-6 months

Diagnosis

1. Flat hexagonal crystals
   Microscopy
   morning urine
   +/- acidification
2. Cyanide – nitropresside test:
   +ve at 35-60 µm/MM Cr (75-125mg/g/Cr)
   (heterozygote 120 µm/MM Cr (250mg/g/Cr))
   not specific – acetone, homocystine +ve
3. Urinary concentration
   HVE and/or urine as chromatography
   Raised concentration of L, O, A & C

Treatment

Principle: raise solubility of cystine
1. Increase urine volume
2. Alkalize urine
3. Reduce diet sodium content
4. Form mixed disulphides more soluble than cystine using penicillamine

PRIMARY HYPEROXALURIA

Endogenous overproduction of oxalic acid
PH1
PH2
Others?
2
Enteric disease
Dietary

OXALATE METABOLISM
**GENETICS OF PH1**

AGXT 2q37.3
Consanguinity – homozygotes
Many – compound heterozygotes
50% no activity
50% residual activity 2-48%
60% 630G→A
Gly170 - Arg aa sub
enzyme directed to mitochondria
some pyridoxine responsive

**CLINICAL**

1. Infantile nephrocalcinosis & ESRF rare
2. Recurrent nephrolithiasis
    Nephrocalcinosis
    Progressive loss of renal function
    most common child or adol
3. Elderly occ stone

**EPIDEMIOLOGY**

Incidence
1:60,000-120,000 (Tunisia 13% ESRF),
ESRF 20% 15 y 50% 25y
infantile 80% at 3 y
50% 1st symptom <5y
1m to 60y
diagnosis usually >5y later
M=F
Complete clinical heterogeneity even with identical mutation

**CLINICAL**

Systemic Oxalosis
Occurs when saturation point reached
= plasma oxalate >30µM in early renal
insufficiency -40ml/min/1.73m²
Deposition in all tissues except liver
Bones – radio dense metaphyseal bands
diffuse demineralization
replaces marrow
pain, fracture
EPO resistant anaemia

**CLINICAL**

System oxalosis
Deposition (cont.)
Retinal
Media of vessels
Peripheral nervous system
Myocardium – AV block
Thyroid
Skin-livido reticularis
Conservative
Aim: ↓ oxalate production ↑ urinary solubility

ESRF Treatment:

Common Incidence of calculi
Barros et al 400 children
Mathoera+ 89 children augmented bladders 16% developed bladder calculi

70% asymptomatic 70% solitary 33% recur after removal

Risk factors
- female sex
- Urinary tract infection
- Bowel mucosa used in bladder augmentation
- Vaginal reconstruction
- Bladder neck surgery
Routine radiological or endoscopic evaluation

Primary: ? Distinct entity
Secondary: Hypokalaemia metabolic acidosis ketogenic diet UTI

In General
SURGICAL MANAGEMENT

Multiple approaches often used:
1. Extracorporeal shock wave lithotripsy - method of choice
2. Ureteroscopy - difficult in smaller children
3. Percutaneous nephrolithotomy - larger stones
4. Open / laparoscopic surgery - anatomical abnormalities

ESWL

Indications:
- renal pelvic or calyceal calculi up to 2cm diameter

Relative Contraindications:
- cystine stores
- dilated obstructed kidneys
- large stone burden
- radiolucent stones

Technique:
- lung protection – not with newer machines
- General anaesthetic – young children
- Pre-operative ureteric stenting used with obstructed upper tract

Results:
Stone-free rates variable from study to study: often need more than one treatment

immediate: 50%
3 months: 60-90%
2y: 60-90%
4y: 70% with 56*
more stone regrowth and stone recurrence

Complications
Common: skin haemorrhage
haematuria
obstruction

Rare: lung contusion
perirenal haematoma
renal injury

PCNL

Relative indications
- larger calculi >2cm
- lower pole calculi >1.5cm
- impaired urinary drainage
- softer stones (cystine or struvite)

* Schultz Lampel Urol A 1997