Renal Stone Analysis
my side of the story......

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This presentation will,

- Present a case
- Examine briefly the basis of stone formation
- Suggest a protocol for metabolic investigations
- Briefly discuss regional variation
The Case

- 6 year old girl
- Investigated for headaches and abdominal pain
- UTI discovered, successfully treated with trimethoprim
- Crystalluria observed
Urine amino acid analysis

- Cystine $401 \mu \text{mol/mmol creat} \ (\text{ref <8})$
- Ornithine $826 \mu \text{mol/mmol creat} \ (\text{ref <9})$
- Lysine $1037 \mu \text{mol/mmol creat} \ (\text{ref <36})$
- Arginine $187 \mu \text{mol/mmol creat} \ (\text{ref <8})$

Results consistent with stone forming cystinuria
Clinical course

- Staghorn calculus identified in right kidney
- Surgically removed following year
  - DTPA clearance showed significant impairment of function in right kidney
  - Abdominal X-ray demonstrated no growth of the residual stone
- UTIs were recurrent
- Treatment: diuresis and trimethoprim
Second Stone

- At age 6.5 she passed a stone
- Analysis of whole stone showed:
  - Calcium 30%
  - Magnesium 10%
  - Phosphate 25%
  - Oxalate 20%
  - Ammonium 10%
  - Cystine *not detected*
Why do stones form?

Precipitation of material due to
• increased concentration of poorly soluble material
• change in pH
• reduction in natural inhibitors
Stone growth may be epitaxial

nidus of nascent stone
Stone growth may be epitaxial
Stone growth may be epitaxial

The bulk of a stone may not be the same material as the original nidus
Stone analysis may miss the original nidus

As many as 10% of the stones formed by cystinurics contain no detectable cystine

Milliner DS, 1990, Endocrinol Metab Clin North Am 19; 889
Infection

• strong association between stone disease and urinary tract infection
• either one increases the risk of occurrence of the other
• infections change the urinary environment, esp if urease secreted
• urease splits urea, releasing ammonia which:
  - increases the pH, and decreases solubility of calcium salts
  - increases ammonium ion conc, causing precipitation of ammonium magnesium phosphate (struvite)
The presence of stones in the urinary tract increases the likelihood of infection because:

- there may be local urine pooling and stasis
- bacteria can colonise the stone surfaces and penetrate crevices

30% of cystinuric patients, in a multi-centre study, were reported to suffer from repeated UTIs.
Absence of Bacterial Imprints on Struvite-containing Kidney Stones

Bazin et al
*Urology* 2012; 79, 786-90
Published Protocols

All Wales Clinical Biochemistry Audit Group

Standards for the Laboratory Investigation of Renal Stone Disease

INTRODUCTION
In industrialised communities the incidence of stones is rising; up to 10% of men and 3% of women have identifiable renal stones at some time in their life. Approximately 65 to 70% of individuals undergoing surgery for stones do so for recurrent stones.

A survey of Welsh laboratories, presented at an audit meeting in October 2000, showed significant variations in laboratory strategies for investigating renal stone disease. The following standards have been prepared in the light of these findings and also of published evidence, in consultation with clinical and laboratory colleagues with a special interest in renal stone disease.

STANDARDS
1. Investigation Strategy
   a) Each laboratory should have a written protocol, agreed locally with relevant clinicians, for the initial biochemical investigation of renal stone disease in both the adult and adolescent populations.
Adult Protocol

- examine history for risk factors
- take fasting blood for u&e, calcium, phosphate, albumin, urate,
- collect two 24h urine samples,
  - alkaline for urate
  - acid for creatinine, sodium, calcium, magnesium, phosphate, oxalate, cystine
  - measure pH in early morning sample
Paediatric Protocol

- examine history for risk factors
- take fasting blood for u&e, calcium, phosphate, albumin, urate,
- collect untimed morning urine, divide into three aliquots:
  - measure pH
  - alkalise for measurement of urate
  - acidify for calcium, magnesium, oxalate, cystine

express results as creatinine ratio
# Renal Stone Investigations

**Name of Patient:**

**D.o.B.:**

**Consultant:**

**Unit No.:**

## SERUM

<table>
<thead>
<tr>
<th>Date: .../.../...</th>
<th>Urea</th>
<th>mmol/L</th>
<th>(2.2-7.7)</th>
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<tbody>
<tr>
<td></td>
<td>Sodium</td>
<td>mmol/L</td>
<td>(135-145)</td>
</tr>
<tr>
<td></td>
<td>Potassium</td>
<td>mmol/L</td>
<td>(3.7-5.1)</td>
</tr>
<tr>
<td></td>
<td>Bicarbonate</td>
<td>mmol/L</td>
<td>(20-28)</td>
</tr>
<tr>
<td></td>
<td>Creatinine</td>
<td>μmol/L</td>
<td>(male 70-120, female 50-100)</td>
</tr>
<tr>
<td></td>
<td>Adjusted Calcium</td>
<td>mmol/L</td>
<td>(2.20-2.60)</td>
</tr>
<tr>
<td></td>
<td>Phosphate</td>
<td>mmol/L</td>
<td>(0.8-1.3)</td>
</tr>
<tr>
<td></td>
<td>Urate</td>
<td>μmol/L</td>
<td>(male 0.2-0.45, female 0.14-0.38)</td>
</tr>
<tr>
<td></td>
<td>Albumin</td>
<td>g/L</td>
<td>(37-49)</td>
</tr>
<tr>
<td></td>
<td>Alk. Phos.</td>
<td>U/L</td>
<td>(70-300)</td>
</tr>
</tbody>
</table>

## URINE (random early morning)

<table>
<thead>
<tr>
<th>Date: .../.../...</th>
<th>pH</th>
<th>fasting</th>
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</thead>
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<table>
<thead>
<tr>
<th>Date: .../.../...</th>
<th>Volume</th>
<th>mls</th>
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</thead>
</table>

<table>
<thead>
<tr>
<th>24h URINE Acidified</th>
<th>Creatinine</th>
<th>mmol/24h</th>
<th>(male 13.2-17.6, female 7.04-13.2)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Calcium</td>
<td>mmol/24h</td>
<td>(male 1.25-10.0, female 1.25-9.0)</td>
</tr>
<tr>
<td></td>
<td>Magnesium</td>
<td>mmol/24h</td>
<td>(3.3-4.9)</td>
</tr>
<tr>
<td></td>
<td>Oxalate</td>
<td>mmol/24h</td>
<td>(0.2-0.5)</td>
</tr>
<tr>
<td></td>
<td>Cystine</td>
<td>μmol/24h</td>
<td>(45-250)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date: .../.../...</th>
<th>Volume</th>
<th>mls</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>24h URINE Alkaline</th>
<th>Creatinine</th>
<th>mmol/24h</th>
<th>(male 13.2-17.6, female 7.04-13.2)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Urate</td>
<td>mmol/24h</td>
<td>(1.2-3.9)</td>
</tr>
</tbody>
</table>

**Signed:** Dr M J Henderson  
**Consultant Biochemist**

**Telephone enquiries:** Dr M J Henderson: ext 66381  
**Duty Biochemist:** ext 64293  

MJH/LMC
Regional Variations

- Collecting only one 24h sample
- Measuring cystine in the alkaline sample
- Measuring u citrate
- Warming urine samples prior to taking aliquot
- Decisions on when to analyse stones
- Investigate after 1st episode or wait for 2nd
- When to include 'very rare compounds