



The Nuts and Bolts of Kidney Stones

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UHW
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Urinary Calculi

- **Prevalence and incidence of kidney stones increasing across the world**
- **Environmental factors**
 - **Diet and climate changes (high fructose consumption, sodium, animal protein, global warming)**
- **Recurrence rate – 25-40% over 10 years in treated patients**
- **Higher recurrence risks**
 - **Multiple stones**
 - **Metabolic abnormality**

Supersaturation & Modulators

- Crystalluria is universal but stone formation is not.
- Supersaturation (Ca, oxalate) in healthy individuals is common leading to formation of crystals but for crystals to form stones they need to grow and be retained in the kidney (crystals-nucleation-aggregation and retention)
- Crystallisation is modulated by various inhibitors and promoters which determine whether a crystal will nucleate and grow into a stone or get excreted as crystals in urine

Risk factors

- **Non Urinary Factors**
- **Urinary Factors**



Risk factors

- **Non dietary factors**
 - Family history (two fold higher)
 - Race/ethnicity
 - Systemic disorders (obesity, gout, DM)
 - Environmental (occupations)
- **Dietary factors**
 - Calcium
 - Oxalate
 - Other nutrients and supplements (animal protein, potassium, sodium, sucrose, vit C)
 - Fluid intake

Urinary Factors

24Hr urine collection

- **Urine Calcium**

- Men- >7.5 mmol/24hr, Women- >6.25 mmol/24hr

- **Urine oxalate**

- >0.5 mmol/24hr

- **Urine urate**

- >4.0 mmol/24hr

- **Urine volume**

- <1.5 L/day (12-25% of stone formers)

- **Urine citrate**

- <1.67 mmol/24hr

Investigations

Leave No Stone Unturned

Investigations for Recurrent Stone former

- **Blood sample**
 - Renal, Bone profiles and uric acid.
- **Urine sample**
 - pH, nitrites
 - Qualitative cystine screen
- **24hr urine collection (acidic and alkaline)**
- **Stone analysis**

Evaluation of Results

- **Stone composition is known**
 - Treatment for the different stone types
- **Stone composition is not known**
 - Treatment will be based on results of urine and serum
 - Urine calcium >6.5 mmol/L-Dietary history
 - Urine urate >4 mmol/L- dietary history
 - pH >6 on several occasions when infection was excluded-proceed for an ammonium chloride test

General Advice

Fluid Intake

- One of the most important measures
- Fluid intake >2.5L is associated with ~30% lower risk than <1.3/L day.
- Fluid intake should be evenly distributed over the day
- Fluids:
 - Water
 - Citrus juices; lemon contains higher citric acid than oranges
 - Apple juice
 - Coffee and tea
 - Soft drinks
 - Alcohol
 - Neutral beverages (tap water, fruit and herbal teas)

General Advice

Dietary habits

- Eat varied diet and avoid excessive amount of calories
- Different forms of fresh fruits, vegetables and salads, low fat dairy products
- A high intake of animal protein can increase urinary Ca
- *Avoid too much salt*
- *Check OTC*

Cases from Metabolic Stone Clinic

Case 1, Uric acid stones

38 y old male

- Type II DM, BMI 33
- Urine volume 2.2L/24hr
- Urine urate 4.0 mmol/24hr (1.5-4.5)
- Normal serum urate

Why does he form stones?

Uric acid stones

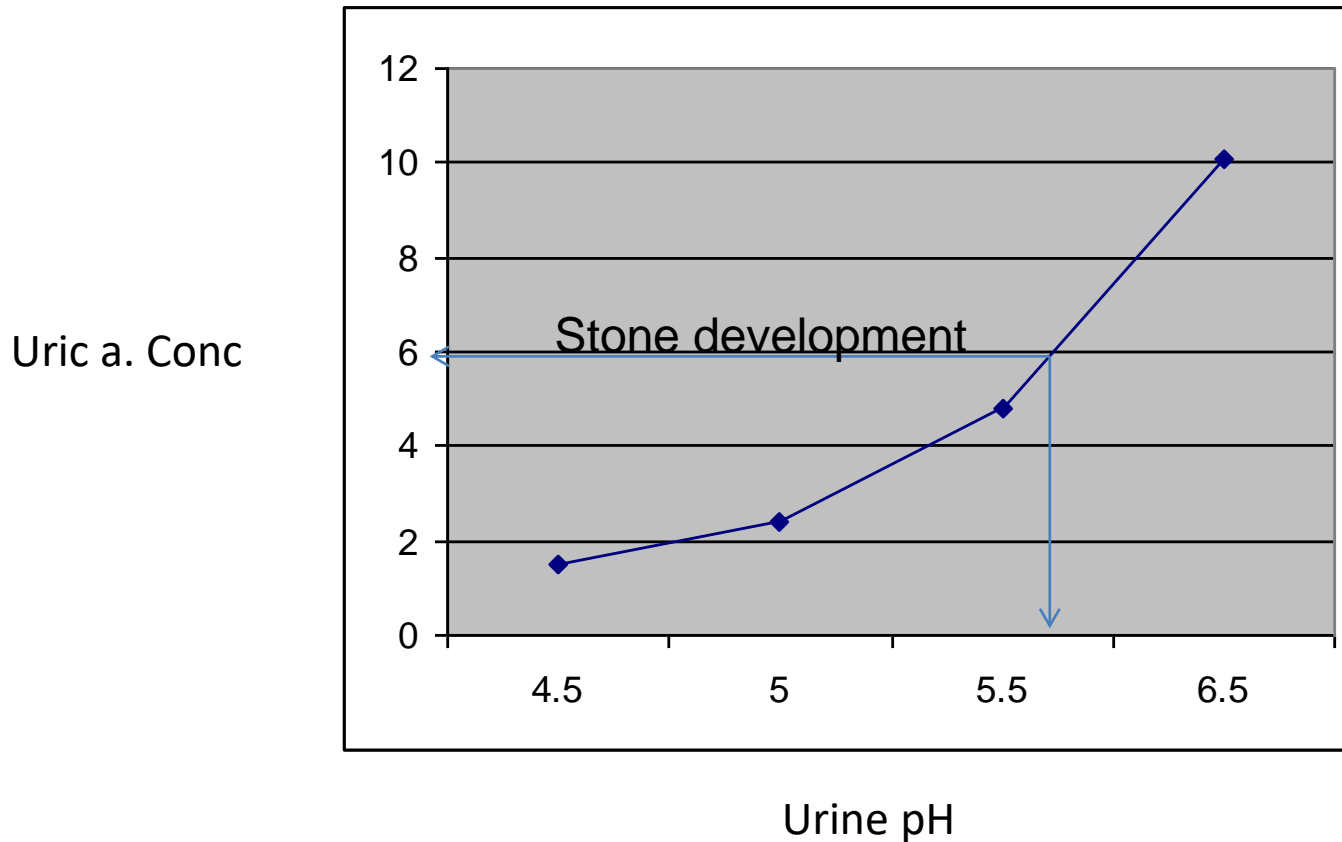
- 8-10% of patients with kidney stones
- Formed in acid urine \pm high conc of uric acid
- Radiolucent
- Susceptible to medical dissolution

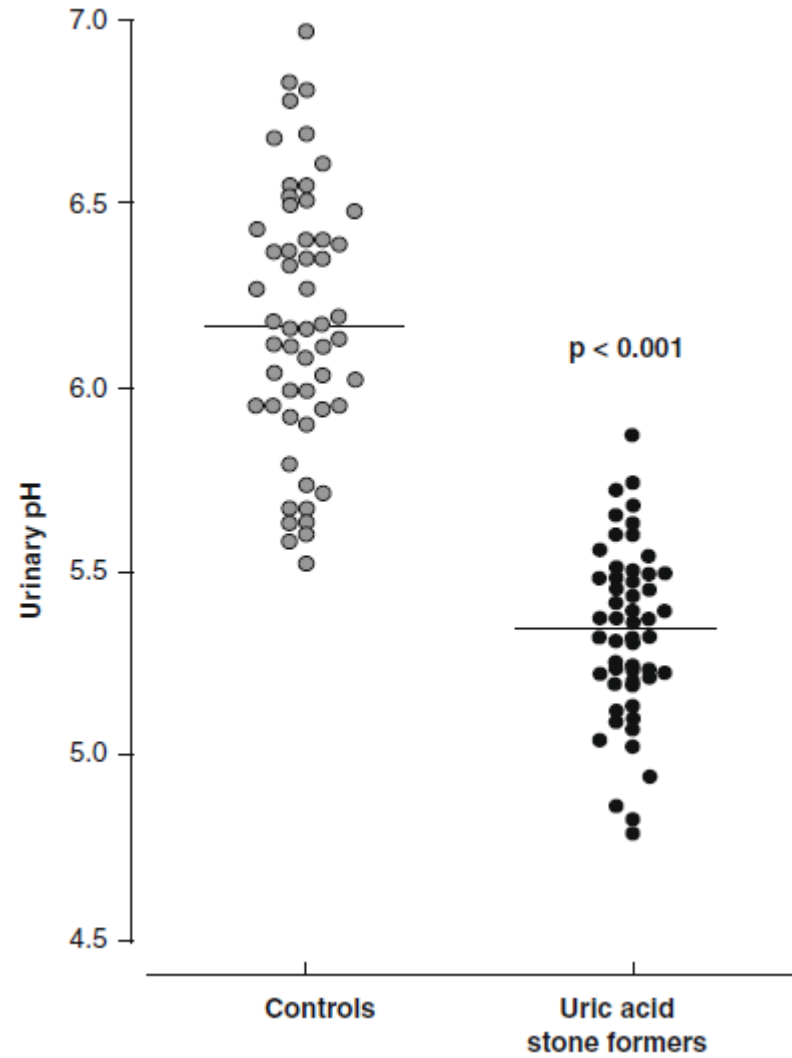
Uric acid stone former

- Overweight patient
- Metabolic syndrome – Insulin Resistance
- Type II DM
- Conditions associated with increased tissue catabolism eg thalassaemia

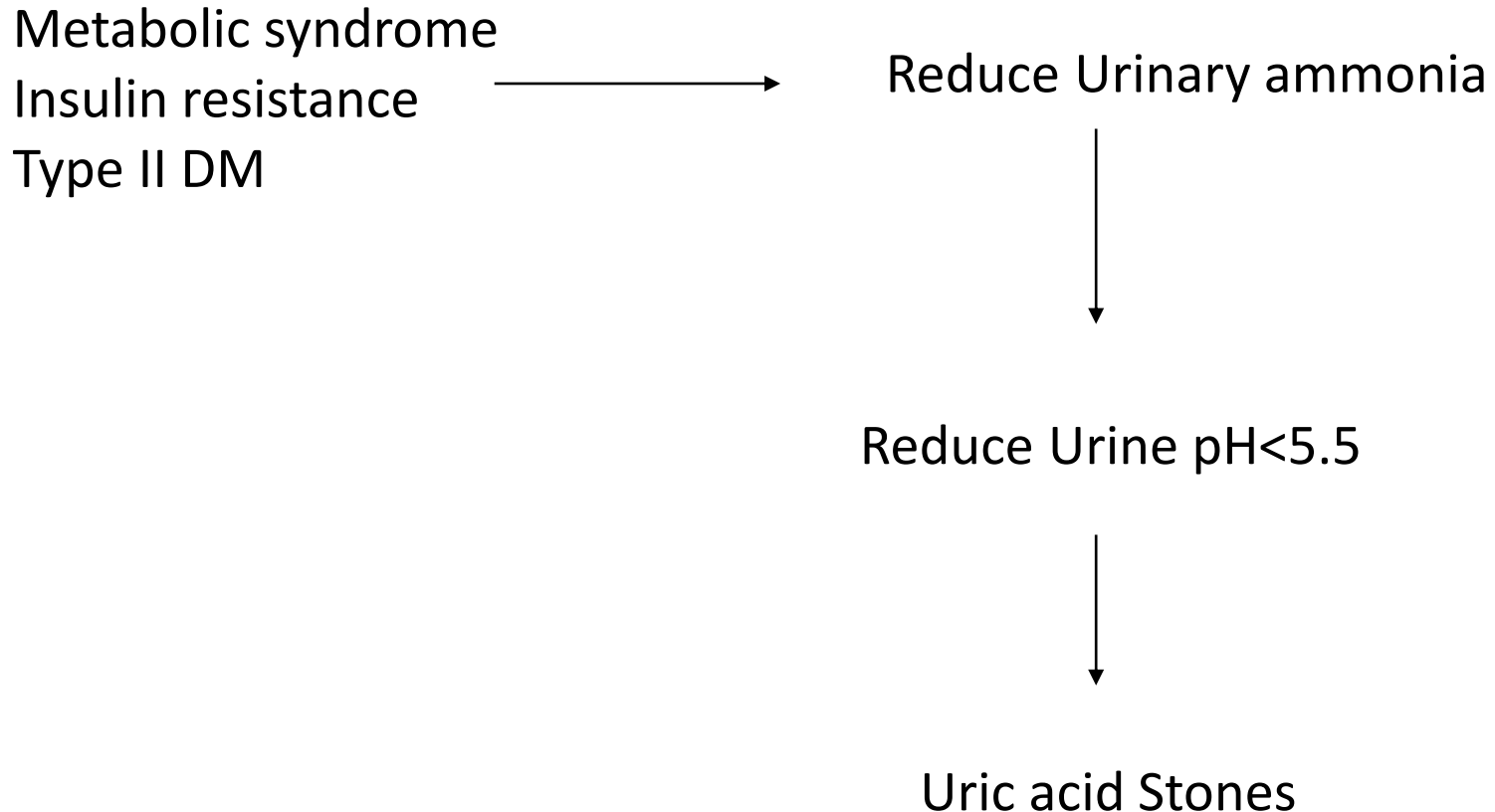
Investigations

Urine pH and uric acid conc-the most important determinants of uric acid stone formation





Pathogenesis of uric acid stones



Risk Factors

- **Serum analysis**
 - Serum uric acid > 380 μ mol/L (Diet \pm Medication)
- **24hr Urine analysis**
 - Volume <2L /24 hr
 - pH <6.0
 - Uric acid >4.0 mmol/24hr

Management

Chemolysis

- Urine alkalization-pH 6.5-6.8
 - K-citrate, NaHCO₃
 - Alkaline Beverages (mineral water rich in bicarbonate, citrus juice)
- Decrease uric acid excretion
 - Allopurinol
 - Reduced intake of purines (max 500mg of uric a./day)
- Increase urine dilution
 - Fluid intake of 2.5-3.0 L/day

Case 2, 62 y old gentleman

Recurrent bilateral small renal stones over the last 8 years
Calcium phosphate stones

Urine biochemistry

Urine Ca	12.6 mmol/24hr	(2.5-7.5)
Urine PO ₄	47.0 mmol/24hr	(12.9-42)
Urine citrate	0.9 mmol/24hr	(1.60-4.5)

Any thoughts?

Calcium Phosphate Stones

- **Types**

- **Carbonate apatite (hydroxyapatite)**

- Urine pH >6.8
 - +ve nitrite
 - With CaOx or struvite

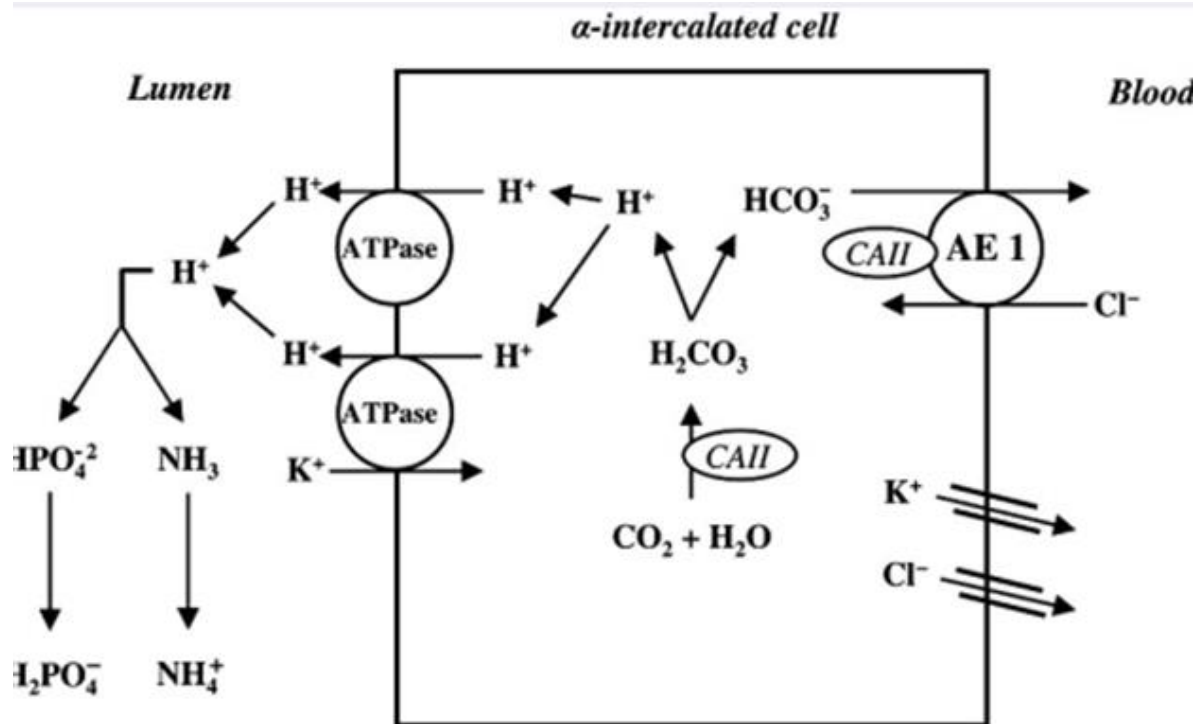
- **Brushite (Calcium hydrogen phosphate)**

- Urine pH >6.5
 - -ve nitrite
 - With small amount of CaOx
 - Very high recurrence rate
 - Low urine citrate

Calcium Phosphate Stones

- Most common causes are disturbance of calcium phosphate balance
 - UTI
 - 1ry HyperPTH
 - RTA
- Need to exclude the different causes

Renal acidification Process and RTA



Distal RTA

- **Complete**

- Occurs in 0.5% of stone formers
- Systemic hyperchloremic acidosis
- Hypokalaemia
- Low urine citrate
- High urine phosphate and calcium

- **Incomplete**

- Occurs in 3-5% of all patients with stones
- No acidosis
- Normokalaemia
- High urine Calcium
- Low urine citrate

Investigations Ca Phosphate Stones

- Hypercalciuria- Urine Ca ≥ 8 mmol/L
- Hyperphosphaturia- urine PO₄ ≥ 35 mmol/L
- Hypocitraturia- Urine Citrate ≤ 2.5 mmol/L
- Urine pH-alkaline
 - Exclude UTI
 - Ammonium Chloride loading test to exclude RTA

Ammonium Chloride test

Time	Urine pH	Serum pH
0	6.80	7.44
1hr	6.68	7.28
1hr30	6.03	
2hr30	6.16	
3hr30	6.16	
4hr30	6.23	

Treatment

- If CaOx is a major component of the stone so treat as CaOx stone
- If RTA- potassium citrate
- If Brushite
 - sufficient urine dilution
 - Urine acidifying beverages (mineral water with low calcium and bicarbonate, Cranberry juice)
 - Avoid citrus juices and lemonade

Case 3- 16y old female

- First episode of renal colics at the age of 13
- 4 stones in the left kidney-left nephrectomy
- 2 more stones in right kidney
- Stone analysis-cystine

Cystinuria

- Defect in the luminal transporter for dibasic amino acids in the epithelial cells of proximal renal tubules
 - cystine, ornithine, arginine, lysine (**COAL**)
- Homozygotes will excrete >4 mmol/24hr (RR < 0.3 mmol/day)
- If concentration exceeds threshold for cystine solubility (1.3 mmol/L), crystals (hexagonal) and stones may be formed.
- 6-8% of renal stones in childhood; 1-3% in adulthood
- High index of suspicion in relatively young stone formers or positive family history

Genetics

- Average incidence 1:2000

autosomal recessive (over 60% of cases)

SLC3A1 gene on chromosome 2p
more than 80 mutations reported

autosomal dominant with incomplete penetrance

SLC7A9 gene on chromosome 19q,
more than 50 mutations described.

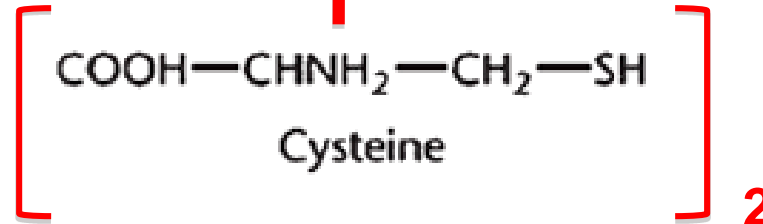
Cysteine and Cystine



Cystine



Oxidation



Cysteine



Penicillamine



α -Mercaptopropionylglycine



Penicillamine-cysteine complex

Urine Dilution

- Reduce urine cystine conc to below solubility limit (<1.3 mmol/L)
- Fluid intake should be evenly distributed over the 24hr period.
- Alkalisating beverages
- Neutral beverages are also suitable
- Limit tea and coffee
- Less suitable-soft drinks containing sugar and alcoholic beverages, cranberry juice

Treatment

(i) Excessive Urine Dilution: Increase daily fluid intake to 3-4L, particularly at night – to maintain cystine below its saturation point

(ii) Urine Alkalinisation: (pH >7.0) to increase cystine solubility

e.g. potassium citrate

(iii) Thiol-chelating agents: form soluble mixed disulphide with cysteine → reduced concentration of cystine in urine

e.g. D-penicillamine
Tiopronin (alpha-mercaptopropionylglycine)
Captopril

Case 4

- 51y old gentleman-stones over the last 24 years.
- Calcium oxalate stones
- 24hr urine metabolic stone screen, random urine pH and blood profiles

Results

Urine Calcium= 14.8 mmol/24 hr (2.5-7.5)

Urine citrate= 5.3 mmol/24hr (1.60-4.50)

Urine oxalate= 0.31 mmol/24hr (0.08-0.49)

Urine sodium= 300 mmol/24hr

Urine volume= 1.6L/24hr

Blood profiles are all normal

Calcium Oxalate Stones

Calcium Oxalate Stones

- Most frequent stones (70-75%)
- Men are two times more common than women
- Develop due to multifactorial process
 - Reduction of inhibitory activity
 - Low urine volume
 - Low urine citrate and magnesium
 - Increased lithogenic activity
 - Low urine pH
 - High urine uric acid, oxalate, calcium

Biochemical Investigations

- **Serum analysis**
 - Calcium
 - Uric acid
- **24 hr Urine analysis**
 - 56% of patients have hypercalciuria
 - 20-50% of patients have hyperoxaluria
 - High Uric acid can decrease solubility of CaOx
 - Low citrate and magnesium
- Urine pH-variation has no effect

Metaphylactic Treatment

- **Urine dilution**

- Alkaline beverages are preferred- increases excretion of citrate
- Limited amount of coffee and black tea because caffeine increase excretion of uric. Black tea contains considerable amount of oxalate. Milk contains calcium and phosphate.
- Avoid beverages rich in sugar because of their effect on excretion of calcium

Metaphylactic Treatment

- **Calcium intake**

- General population: 1000-1200 mg/day
- CaOx stone formers: 800- 1000 mg/day

- A normal diet without milk products contains about 500 mg of calcium

- Except patients with intestinal hyperoxaluria

Metaphylactic Treatment

- **Oxalate intake**

- 8% of urinary oxalate is derived from diet, the remainder is from endogenous sources.
- 44% of patients with CaOx stones have increased absorption of oxalate
- Vegetables contain very high conc of oxalate
- Wheat bran is rich in oxalate

- **Purine intake**

- Avoid food rich in purines such as sardines, anchovies, herring, mackerel, skin of fish and poultry.

Medical treatment

- If calcium excretion is not reduced by dietary means then medical treatment is indicated
 - Thiazides- only in patients with pronounced hypercalciuria
 - Alkaline citrate
- Dietary fibres
 - Reduces absorption of calcium and oxalate

Thank you