Renal stone disease: medical management

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21 April 2021

Green Lane Medical Specialists

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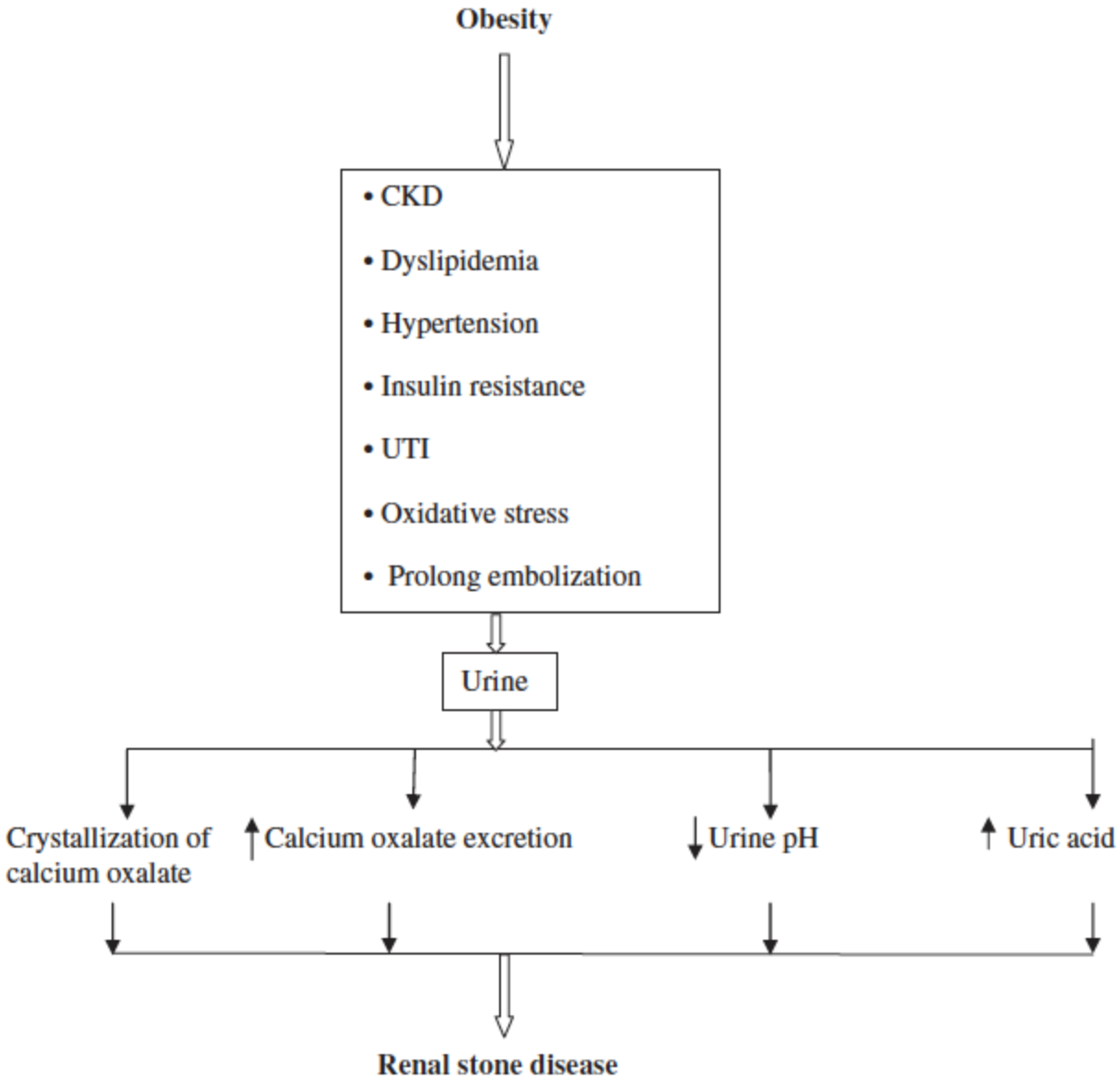
Increased incidence of renal stone disease

- Radiological detection
- Obesity (females > males)
  - HR 2.6 for stone recurrence in first time stone formers
  - 2-fold risk in those with ≥ 4 traits present (abdominal obesity, increased TG, decreased HDL, hypertension, or diabetes/IGT)

- Diabetes and renal stones
  - Incident risk of nephrolithiasis in older women with DM 1.29 (95% CI: 1.05–1.58); younger women 1.60 (95% CI: 1.16–2.21) and in men 0.81 (95% CI:0.59–1.09)1
  - Similarly high rates of diabetes within 5 years of diagnosis of renal stone disease

1. Renal Failure, 2012; 34(10): 1348–1354
Am J Kidney Dis (2008) 51: 741–747
Eur J Epidemiol (2018) 33: 1033–1047



Renal Failure, 2012; 34(10): 1348–1354

Renal stone disease and CKD risk

- Absolute risk for ESRD is small
  - ESRD HR 2.16
  - CKD stage 3b-5 HR 1.74
  - At risk: stone formers with cystinuria, uric acid or struvite stones, RTA, chronic bowel disorders

J Nephrol (2016) 29:715 – 734

Renal stone disease and osteoporosis risk

- 4-fold cumulative risk of vertebral fractures compared to general non-stone-forming population
  - Higher associations for fractures in men> women
  - Low BMD present in both hypercalciuric and normocalciuric stone-forming subjects
  - Greater reduction in BMD in patients with hypercalciuria

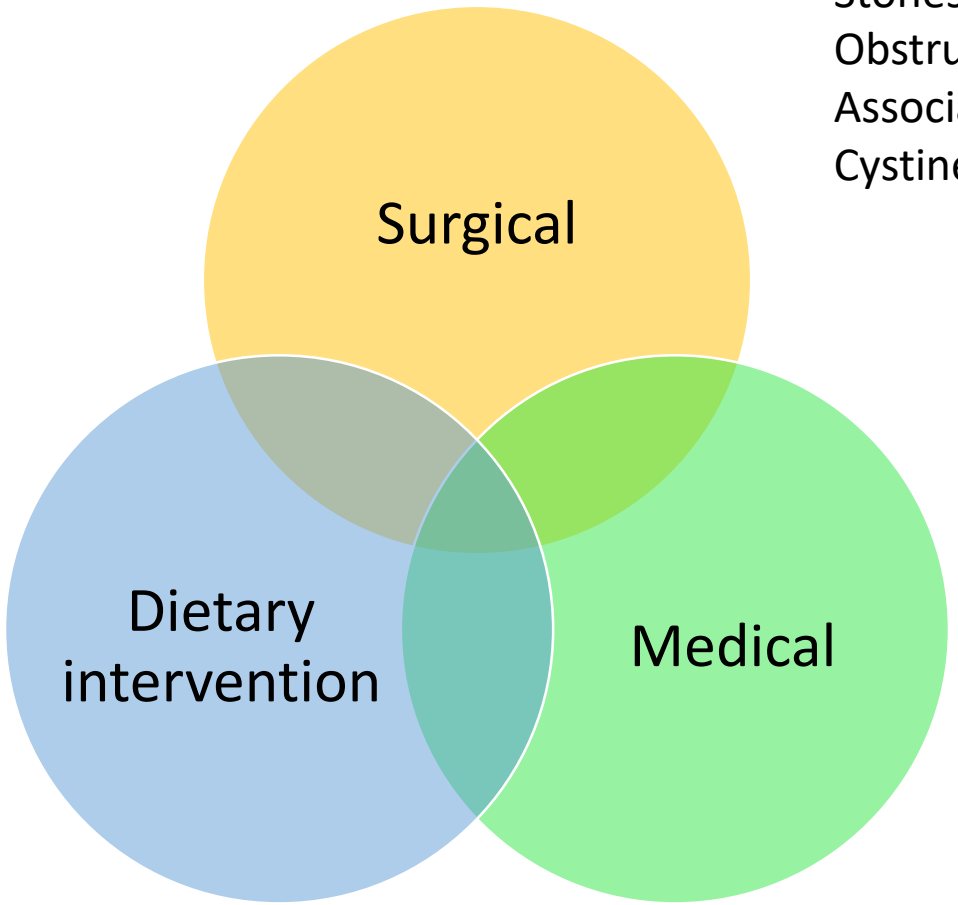
Table 2 | Prevalence of low BMD at various skeletal sites in kidney stone formers (cumulative data from Table 1)

	Prevalence		
Skeletal sites	Total number of patients	Number of patients with low BMD	Percentage (%)
Vertebral spine	975	388	40
Hip	450	141	31
Radius	627	410	65

Abbreviation: BMD, bone mineral density.

Kidney Int (1998) 53: 450 – 465
Kidney Int (2011) 79, 393–403

Approach to renal stone disease



Stones > 4mm
Obstructive uropathy
Associated urosepsis
Cystine, staghorn calculi

Patient education
Accurate and focused dietary advice
Weight loss

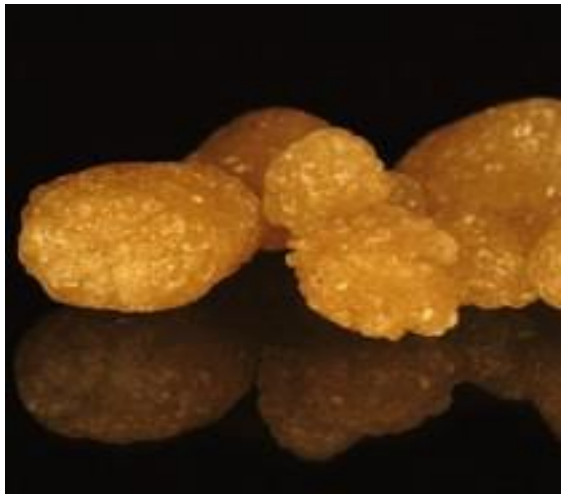
Metabolic evaluation
Assessment for secondary causes
Pharmacological therapy

Composition and prevalence of main renal stone types

Calcium-based stones
60 – 80%
Predominantly calcium oxalate

Struvite/infection stones
10 - 15%
“triple phosphate stones”
(Calcium/magnesium and ammonium phosphate)
Urease splitting bacteria
Alkaline urine from ammonia
Staghorn calculi - large

Uric acid stones
5 – 10 %
Acidic urine
Associated with metabolic syndrome



Cystine stones
1 %
Hereditary
Young patients
Often recur

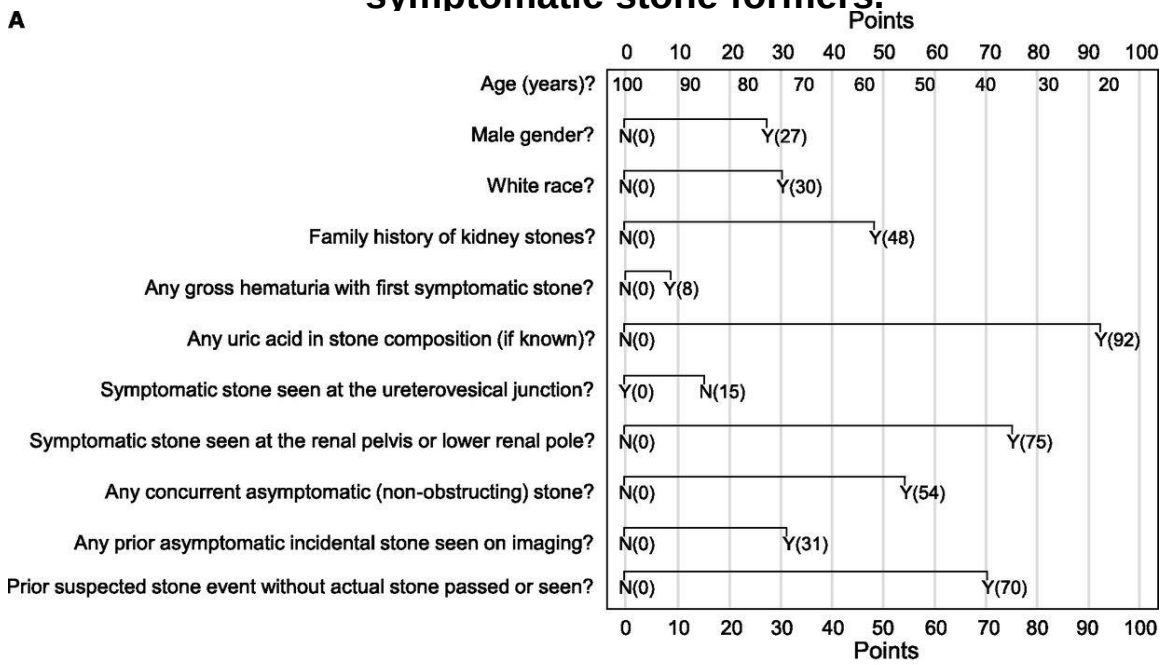
Other stones
1 %
Drug stones
Xanthine crystals

Recurrent stone formers

- Indication of metabolic activity
- No markers to distinguish between single and recurrent stone formers
- In a population cohort study (N=2,239), developed as a prediction tool for assessing risk in first-time stone formers
  - 10-year recurrence of symptomatic stone disease was 30% on the whole
  - 56% risk for second symptomatic episode in high risk patients
  - *Recurrence of Kidney Stone (ROKS) nomogram*

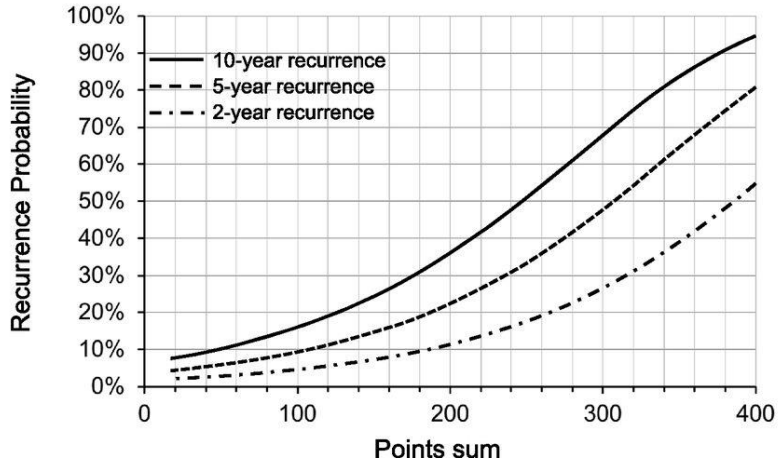
The Recurrence of Kidney Stone (ROKS) nomogram can be easily applied in first time symptomatic stone formers.

A



Sum the points from each question. If no imaging performed, use 0 points for imaging questions (ureterovesical junction, concurrent asymptomatic, and renal pelvis/lower pole) and add 38 to the points sum.

B



Andrew D. Rule et al. JASN 2014;25:2878-2886

QxMD calculator

ROKS – Recurrence Of Kidney Stone (2018)

Predict the risk of a future symptomatic kidney stone after the last symptomatic stone.

Questions

1.How many confirmed symptomatic kidney stone episodes with a passed or obstructing stone on imaging has this patient had (including the last episode)?

2.Number of years since last confirmed symptomatic kidney stone episode?

3.Age in years at last confirmed symptomatic stone episode?

4.Body mass index in kg/m2 at last confirmed symptomatic stone episode?

5.Gender?

6.Any family history of kidney stones?

7.Incidental (asymptomatic) stone on imaging prior to first confirmed symptomatic stone episode?

8.Suspected kidney stone event (no stone seen) before first confirmed symptomatic kidney stone episode?

9.Pregnant during last confirmed symptomatic stone episode?

10.Any prior stone found to contain any uric acid, brushite or struvite?

11.Any prior stone found to be mostly calcium oxalate monohydrate with or without calcium oxalate dehydrate or hydroxyapatite?

12.Was imaging (CT scan, abdominal X-ray, or ultrasound) performed at the last symptomatic stone episode?

13.Number of stones in both kidneys?

14.Diameter of largest kidney stone?

15.Symptomatic stone seen at the ureterovesical junction?

16.Stone seen in the renal pelvis or in the lower renal pole?

Vaughn LE et al. Mayo Clin Proc. 2019 Feb; 94(2): 202–210.

Case 1

40 yo lady with recent AKI

History of renal colic and haematuria, managed conservatively.

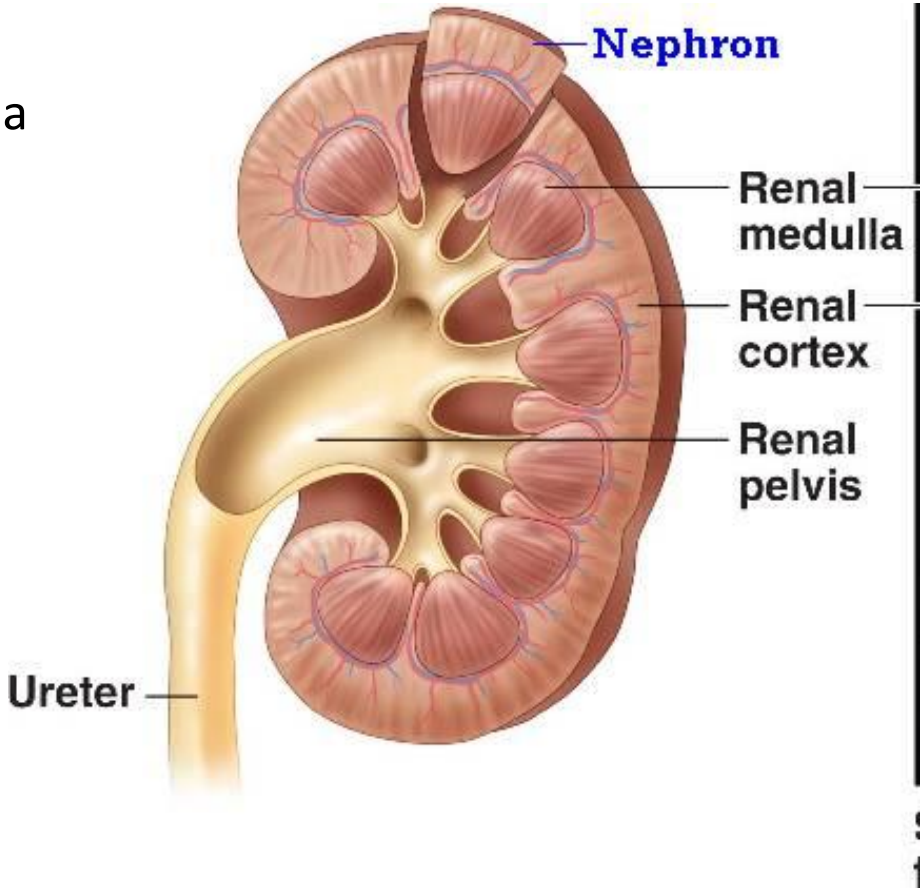
No fevers, no flank tenderness

What is your next investigation?

a. CT KUB
b. Urine microscopy &
c. Spot urine calcium/creatinine ratio
d. Renal biopsy

Medullary nephrocalcinosis

- Diffuse calcium deposits in localized at the renal medulla
- Increased risk of calcium stone formation
- Associated with underlying conditions which cause hypercalcemia and/or hypercalciuria
- Treat underlying cause



- Further investigations

Urine calcium/Cr ratio 0.73 (normal 0.06 – 0.4)

Creatinine 91 umol/L; eGFR 68 ml/min/1.73m^2

Adjusted calcium 2.83 mmol/L (2.1 – 2. 55); PTH 9.6 pmol//L (1.7 – 7.3)

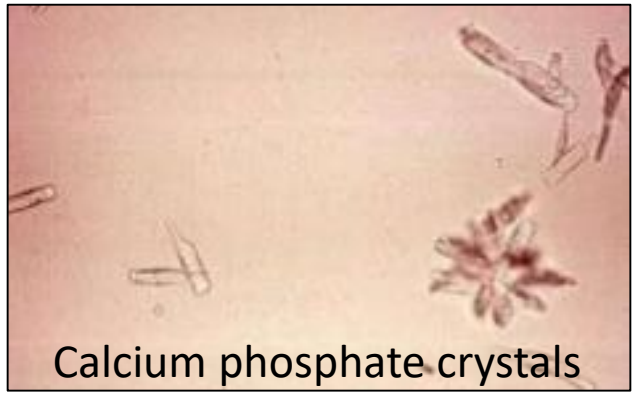
ALP 186 U/L (40 – 120)

Parathyroid scintiscan: localized left inferior parathyroid adenoma

Q2

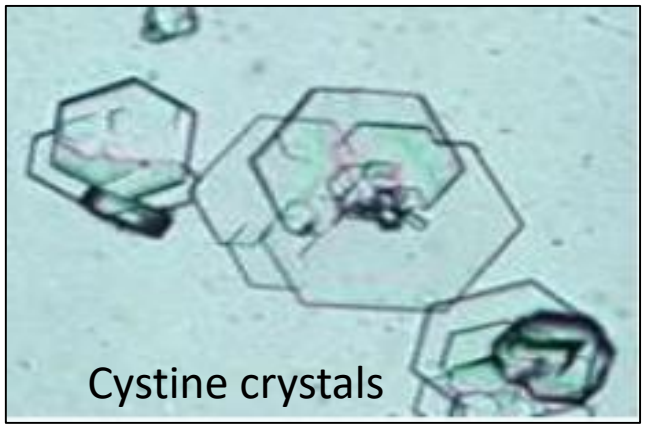
- Which crystals are characteristic for struvite stones?

a.



b.

c.



d.

Struvite stones

- Associated with UTIs
  - Urease-producing bacteria leads to the hydrolysis of urea into ammonium and hydroxyl ions.
  - Alkalotic urine (pH >7.2) secondary to increase in ammonium & phosphate concentrations
  - More frequent in woman and older people

Gram-positive bacteria	Gram-negative bacteria	Yeasts
Staphylococcus aureus *Staphylococcus epidermidis* *Corynebacterium* species (ie, *C ulcerans, C renale, C ovis, C hofmannii, C murium, C equi*) *Mycobacterium rhodochrous* group *Micrococcus varians* *Bacillus* species *Clostridium tetani* *Peptococcus asaccharolyticus*	*Bacteroides corrodens* *Helicobacter pylori* *Bordetella pertussis* *Bordetella bronchiseptica* *Haemophilus influenzae* *Haemophilus parainfluenzae* *Proteus* species (ie, *P mirabilis, P morganii, P rettgeri*) *Providencia stuartii* *Klebsiella* species (*K pneumoniae, K oxytoca*) *Pasteurella* species *Pseudomonas aeruginosa* *Aeromonas hydrophilia* *Yersinia enterocolitica* *Brucella* species *Flavobacterium* species *Serratia marcescens* *Ureaplasma urealyticum* *Mycoplasma* T-strain	*Cryptococcus* species *Rhodotorula* species *Sporobolomyces* species *Trichosporon cutaneum* *Candida humicola*

https://emedicine.medscape.com/article/439127-overview#a8

Management

- Complete removal key as residual stone material serve as nidus
  - Recurrence up to 85%
- Suppressive antibiotic therapy – prophylaxis and inhibiting stone growth
- Urease inhibitors - acetohydroxamic acid (not available in NZ)
  - Reduces urine alkalinity and urinary ammonium concentration
  - Impaired effectiveness and increased toxicity in renal impairment
- Low phosphorus, low calcium diet

Case 3

A 27-year-old woman has recurrent renal stones. Her serum electrolytes were normal. She has a history of Sjogren's syndrome.

Two 24-hour urine collections were similar:

Volume 1.7 L (> 2 – 2.5 L)

pH 6.9 (5.8 – 6.2)

Urinary calcium 5.6 mmol (<5)

Urinary phosphorus 36 mmol (<38)

Urinary oxalate 0.37 mmol (<0.45)

Urinary citrate 203 mmol (>2.6)

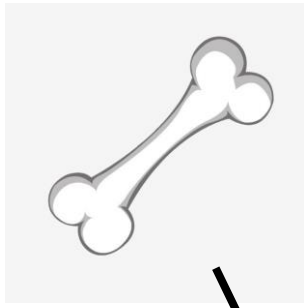
Urinary sodium 190 mmol (<100 - 150)

- What is the likely stone composition?

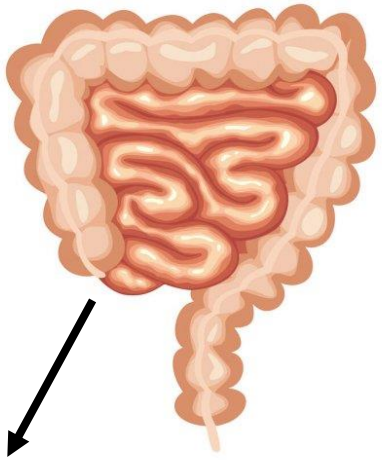
a. Calcium oxalate
b. Calcium urate
c. Calcium phosphate
d. Cystine stones

- Further investigations confirmed fasting urine pH 6.9 and venous bicarbonate 19 mmol/L and potassium 3.5 mmol/L = distal RTA
- Nephrocalcinosis and nephrolithiaisis are frequently associated with distal RTA (type 1)
- Associated with hypercalciuria and hypocitraturia
- Higher urine pH and hypocitraturia promote calcium phosphate supersaturation

Acidemia with distal RTA

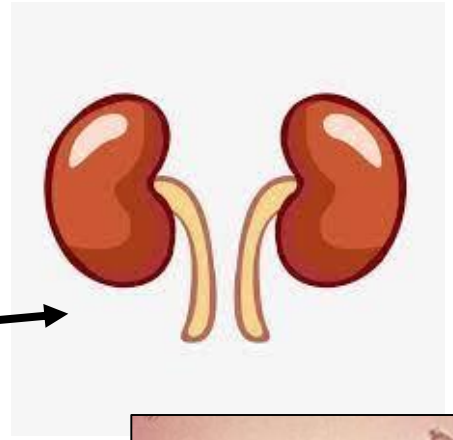


Ca^{2+}
$PO4^{2-}$



Increase absorption of Ca^{2+}

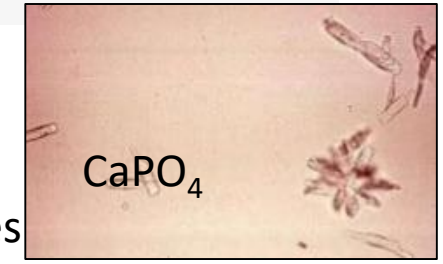
ECF calcium and phosphate



↑ urine Ca^{2+}

↓urine citrate

↑ urine pH



Management: Increase fluid intake; correction with potassium citrate; concomitant thiazides
DEXA scan

Q4.

- Which is associated with an increased risk for calcium oxalate stone formation?

a. Roux-en-Y gastric bypass
b. Extracorporeal shock wave lithotripsy (ESWL)
c. Sleeve gastrectomy
d. Ileostomy

Calcium oxalate stones

- Idiopathic calcium oxalate stones most common
- Diseases affecting the small intestine or pancreas, including Crohn’s

disease, malabsorptive types of bariatric surgery, or chronic pancreatitis, lead to fat malabsorption and enteric hyperoxaluria

Table 2 Conditions to be excluded in idiopathic CaOx nephrolithiasis with hypercalciuria, hypocitraturia and hyperoxaluria

Conditions	Hypercalciuria	Hypocitraturia	Hyperoxaluria
Primary hyperparathyroidism	•		
Prolonged immobilization	•	•	
Incomplete dRTA	•	•	
Drugs and vitamin excess	• (vit. D)		• (orlistat, vit. C)
Chronic diarrhea		•	
Chronic pancreatitis, Crohn's disease, gastric bypass procedures, or small bowel resections		•	•
Nephrocalcinosis	•	•	•
Genetic conditions associated with stones (including primary hyperoxaluria)	•	•	•
MSK	•	•	

J Nephrol (2016) 29:715–734

24 hour urine interpretation

- Stone analysis still gold standard

Urine composition	Targets
Volume (L)	>2L
pH	5.8 – 6.2
Creatinine (mmol)	0.16 – 0.21 mmol/kg (males) 0.13 – 0.18 mmol/kg (females)
Calcium (mmol)	<6.25 (males) <5 (females)
Phosphate (mmol)	<38.8 (both)
Urate (mmol)	<4.76 (males) <4.46 (females)
Oxalate (mmol)	<0.45 (both)
Sodium (mmol)	<100 – 150 (both)
Magnesium	>1.23 (both)
Citrate	>2.34 (males) >2.6 (females)

Litholink
https://www.litholink.com/resources/kidney-stone-prevention-roi

Metabolic evaluation

- Renal stone composition for exclusion of cystinuria, APRT deficiency and struvite stones arising from urease-positive organism
- Initial urine microscopy and protein
- Serum biochemistry and bicarbonate
- Initial and follow up 24 hour urine biochemical evaluation
- Evaluation of GI diseases and systemic causes
- Periodic imaging to assess stone burden

Empiric therapies

- Increased oral fluids
- Dietary manipulation and low salt intake

Metabolic evaluation

Specific management of secondary cause

Targeted dietary manipulation

Pharmacological therapies

Dietary therapies

- Empiric dietary management for renal stone disease:
  - Fluids to produce 2 – 2.5L urine /day; appropriately spaced
  - Low dietary salt (<2,300 mg daily)
  - Normal dietary calcium (1,000 – 1,200 mg daily)
  - Citrate intake: 120ml lemon juice in 2L water

Pharmacological therapies

- Thiazides in hypercalciuria
  - Chlorthalidone 25–50 mg daily
  - Bendroflumethiazide 2.5 mg TDS
  - Hydrochlorothiazide 25 mg BD, 50 – 100 mg daily
  - Indapamide 2.5 mg daily
- Alkali therapy in hypocitriuira or recurrent calcium oxalate stone or uric acid stone formers
  - Potassium citrate 30 – 80 mmol/day
- Allopurinol in hyperuricosuria

Metabolic evaluation – Who to refer?

- Any patient with or at risk of recurrent stone disease
  - Positive family history
  - Recurrent UTIs
  - Obesity
  - Primary or secondary intestinal malabsorption disorder, or patients with malabsorptive type bariatric surgeries
  - Medical conditions predisposing to stone disease (eg cystinuria, struvite stones, Randall's plaques)
  - History of urinary tract abnormalities of reconstruction
- Any patient with solitary kidney
- Any patient who desires further information or insight into preventable and reversible causes