

# Preventing Recurrent Renal Calculi: Best Practices, Pitfalls and Prescribing

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## Course outline

- ▶ Key resources
- ▶ Incidence and population trends
- ▶ Principles of stone formation
- ▶ Prevention and prescribing per urinary abnormality
- ▶ Case studies



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## Recurrence rates

- ▶ Generally quoted as 50% lifetime
- ▶ 2239 first time stone formers
  - ▶ 2 years 11%
  - ▶ 5 years 20%
  - ▶ 10 years 31%
  - ▶ 15 years 39%



Rule AD, et al. J Am Soc Nephrol Epub April 2014

## Morbidity and “The Why” of Prevention

- Pain (physical, psychological and financial)
- Nausea/vomiting/dehydration
- Loss of productivity, income
- Stress/anxiety for individual and family
- Excessive radiation exposure
- AKI
- CKD/Loss of kidney function from chronic or repeat obstruction
- Urosepsis
- Death

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# Key Resources and Guidance

## AUA Guideline: Medical Management of Kidney Stones (2014)

27 guidelines in four categories

- ▶ Evaluation
- ▶ Diet therapies
- ▶ Pharmacologic therapies
- ▶ Follow up

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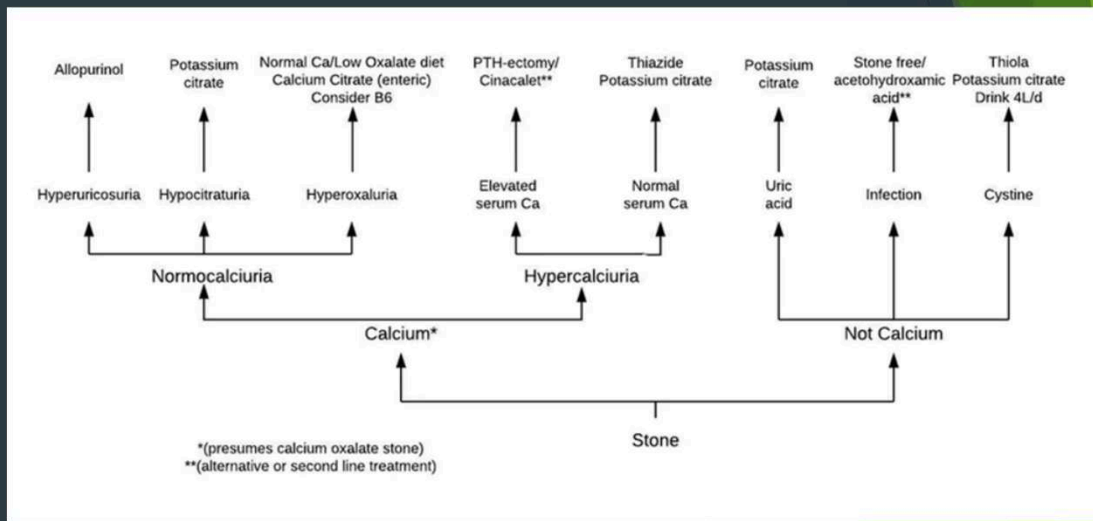
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## Stone Prevention: Moral Imperative

*“A clinician should perform a screening evaluation consisting of a detailed medical and dietary history, serum chemistries and urinalysis on a patient newly diagnosed with kidney or ureteral stones.”  
(Clinical Principle)*

*“Clinicians should perform additional metabolic testing in high-risk or interested first-time stone formers and recurrent stone formers.”  
(Standard; Evidence Strength: Grade B)*

## “Stone Tree” paper, 2018 Clayman, Patel, and Pearle

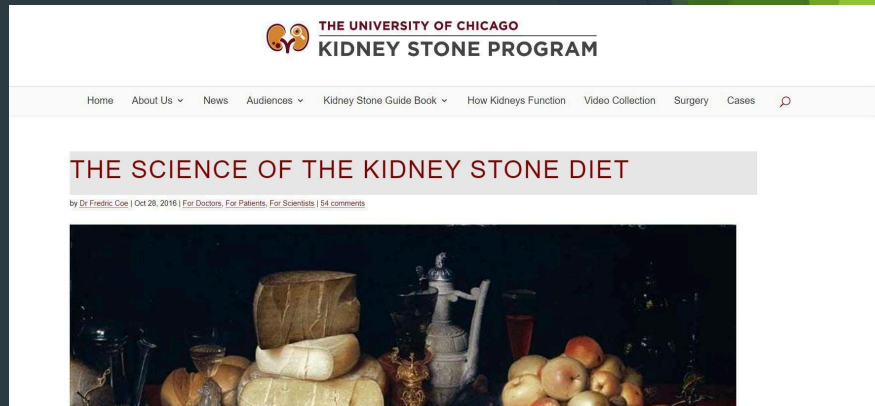


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## University of Chicago's Frederic Coe

- ▶ Free and accessible internet articles
- ▶ Nephrologist milieu
- ▶ Coe's meta-analysis
- ▶ Pragmatic
- ▶ Funny



# Risk Factors and Population Trends

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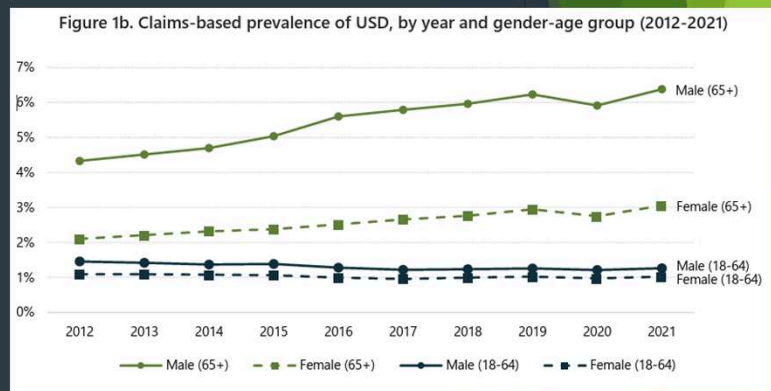
## Risk Factors: Social, Dietary, Medical and Family Histories

- ▶ Dehydration
- ▶ Diet: purines, salt, oxalate
- ▶ Environmental factors: occupation, climate change, urban heat island
- ▶ Family history (Cysteine, calcium oxalate)
- ▶ Medical conditions and medications
- ▶ Aging
- ▶ Obesity

## Population Trends

Date range	US Stone prevalence
2015-2016	10.1%
2007-2010	8.8%
1988-1994	5.2%
1976 - 1980	3.8%

Chewcharat, Curhan 2020



NIDDK, 2024

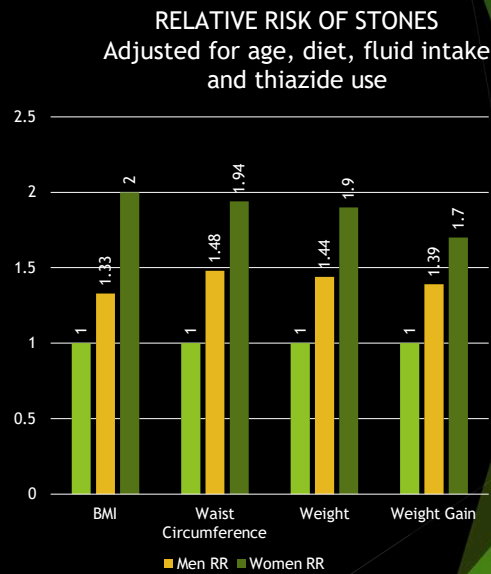
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## Population Trends

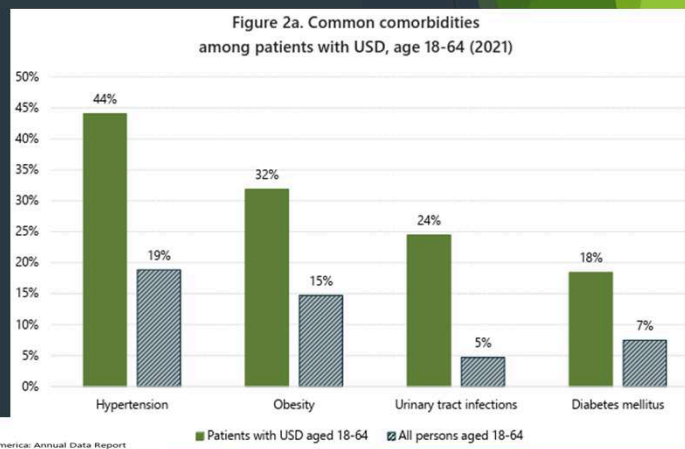
Obesity relative risk compared to healthy cohort

Taylor et al JAMA 2005, 293(4): 455-469



## Comorbidities: Stone disease

- ▶ Bowel disease (malabsorption, chronic diarrhea, Crohn's disease, Roux-en-Y, laxative abuse)
- ▶ Bone disease
- ▶ Renal Tubular Acidosis
- ▶ Hyperparathyroidism
- ▶ Diabetes
- ▶ Obesity
- ▶ Gout
- ▶ Hypertension



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## Clinical Pearls: Hypertensive Comorbid, Osteopenia Comorbid

If the patient has calcium stones and hypertension, consider a thiazide to treat both conditions

Thiazides can also improve bone health, so use in osteopenia/osteoporosis

## GLP-1 potential? (2025)

### Clinical Research

#### The Effect of Sodium-Glucose Cotransporter 2 Inhibitors and Glucagon-Like Peptide-1 Receptor Agonists on 24-Hour Urine Parameters

##### A Retrospective Cohort Study

Jennifer A. Schaub<sup>1</sup>, Mary K. Oerline<sup>2</sup>, Joseph J. Crivelli<sup>3</sup>, Naim M. Maalouf<sup>4</sup>, Sara L. Best<sup>5,6</sup>, John R. Asplin<sup>6</sup>, John M. Hollingsworth<sup>7</sup>, Vahakn Shahinian<sup>1,2</sup> and Ryan S. Hsi<sup>8</sup>

##### Key Points

- In a cross-sectional study, sodium-glucose cotransporter 2 inhibitors were associated with a significant increase in urine volume and urine citrate.
- Glucagon-like peptide-1 receptor agonists were not associated with any significant changes in 24-hour urine parameters that affect stone formation.

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# Principles of Stone Formation

## Three categories of causes (Clayman, Patel, Pearle 2018)

1. What makes stones (calcium, oxalate, uric acid)
2. What inhibits stones (citrate)
3. What promotes stone growth  
(pH, sodium excess, metabolic syndrome, supersaturation)

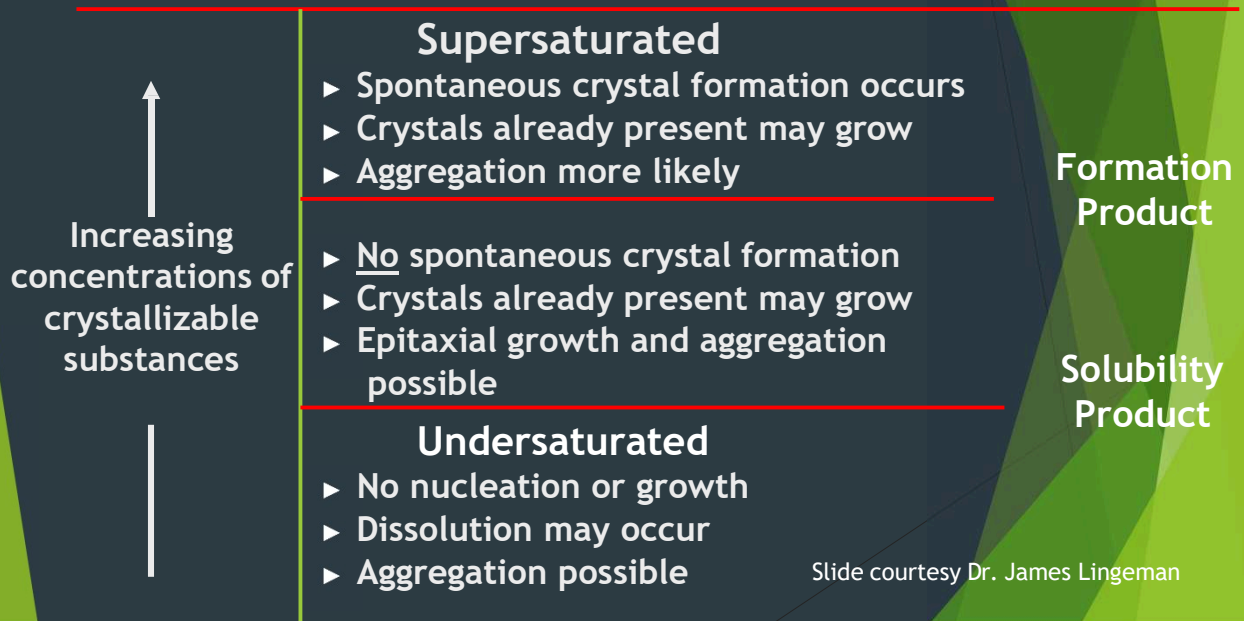


Super  
Saturation

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# Zones of Urine Saturation



## Interrupting Crystal Formation

- ▶ Increase solvent
- ▶ Decrease solute
- ▶ Introduce inhibitors
- ▶ Create pH unfavorable to stone formation
- ▶ Fix problem of stasis (?beneficial?)



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How do we know which factors need correction?

Stone analysis &  
24-hour urine chemistry studies

Metabolic  
stone type  
and urine  
findings

#### Calcium Oxalate

- Associated with low volume and hypocitraturia
- Associated with hypercalciuria, hyperoxaluria and hyperuricosuria

#### Calcium phosphate, including brushite

- Alkaline urine pH
- Hypercalciuria

#### Uric Acid

- Acid urine pH
- With or without hyperuricosuria

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## Infection and cysteine stones and urine findings

### Struvite (magnesium ammonium phosphate)

- Fast growing, staghorn
- Urine infected with urea splitting organisms
  - Proteus, pseudomonas, some klebsiella
- The only treatment is complete stone-free status plus antibiotic

### Cysteine - hereditary

- Prevention measured by “capacity”
- Goals are to reduce cystine (tiopronin), dilution, elevate pH above 7

# Dietary Therapy for Stone Prevention

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How do we tailor dietary factors for each patient?

Stone analysis &  
Social History &  
24-hour urine chemistry studies

### AUA “Dietary Therapy” Guidelines #8-13

Stone type	24-hour urine findings	Dietary counseling
All types	independent	Achieve urine volume over 2.5 L
Calcium	<i>with elevated urine sodium</i>	limit sodium to 1000-1200 mg/day
Calcium	<i>with elevated urine oxalate</i>	limit high oxalate foods and consume adequate calcium
Calcium	<i>with low urine citrate</i>	increase fruits and vegetables, limit non-dairy animal protein
Calcium or uric acid	<i>with elevated urine uric acid</i>	limit intake of non-dairy animal protein
Cysteine	independent	limit sodium and intake of non-dairy animal protein

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## Low urine volume

- ▶ Achieve urine OUTPUT of >2.5 Liters
- ▶ Reduces supersaturation of any stone type - rarely harmful
- ▶ No clear evidence that water “hardness” plays a role in stone formation
- ▶ Avoid grapefruit juice
- ▶ Strategies to increase:
  - ▶ Visual reminder (clear water bottle, in plain sight)
  - ▶ Smart water bottle
  - ▶ Smartphone app



## Sodium

- ▶ Many studies have correlated high sodium diets with stone risk
  - ▶ And low bone density
- ▶ Likely factor in increase in stone disease world wide
- ▶ Consensus goal is < 2500 mg/day (<100 mEq)
- ▶ Restriction is difficult
- ▶ Education is key
- ▶ Consider referral to dietician



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## Hyperoxaluria

- ▶ Reference range output 20-40 mg/D
- ▶ Diet accounts for 10-40% of urine oxalate
  - ▶ The liver produces the rest
- ▶ Calcium and oxalate bind in gut
- ▶ Enteric hyperoxaluria secondary malabsorption
  - ▶ Small bowel absent or bypassed
  - ▶ Fat malabsorption, eg pancreatic insufficiency, celiac
- ▶ Primary hyperoxaluria rare (>100 mg/day)
- ▶ Oxalate content of foods varies by season/conditions

What happens  
in the gut,  
stays in the  
gut.

I should have  
had cheese  
on my  
spinach salad



## Calcium Intake

**NEWS FLASH:** Calcium restriction does not reduce stone risk!

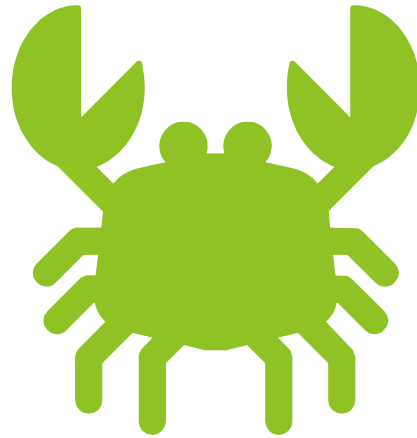
- ▶ Meet RDA for calcium, 1000-1200 mg/day
- ▶ Dairy and non-dairy sources
- ▶ Calcium supplements MAY increase stone risk, so mitigate by
  - ▶ Use of calcium citrate
  - ▶ Taking with meals

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## Purine content of animal products

- ▶ High purine 0.15g/3 ounce
  - ▶ anchovies, sardines, herring, mackerel, scallops and mussels, water-fowl, organ meats, glandular tissue, gravies and meat extracts.
- ▶ Moderately-high sources of purines
  - ▶ shellfish and fish, game meats, mutton, beef, pork, poultry and meat-based soups and broths



## Hypocitraturia: Causes

- ▶ Metabolic acidosis
- ▶ High acid-load diet
  - ▶ High in meats, grains
  - ▶ Low in fruits/vegetables
  - ▶ Dairy and fats - neutral
- ▶ RTA (profound!)
- ▶ UTI
- ▶ Chronic diarrhea/bowel disease
- ▶ Idiopathic
- ▶ Hypokalemia, including thiazide-induced



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## DASH Diet (Dietary Approaches to Stop Hypertension)

- ▶ Plant based diet
  - ▶ Vegetables
  - ▶ Fruits
  - ▶ NUTS
- ▶ Includes low and non-fat dairy
- ▶ Healthy fats
- ▶ Lean meats in moderation
- ▶ Whole grains



## DASH Diet offers protection

- ▶ Diet analysis for over 240,000 US health care and nurse health study participants
  - ▶ 50 year follow up!!
- ▶ Higher DASH score individuals have lower incidence of stones (relative risk 0.55-0.60), even when calcium intake was lower
- ▶ Higher intakes of calcium, potassium, magnesium, oxalate, and vitamin C
- ▶ Lower intakes of sodium

Taylor, E., Fung, T, Curhan, G. (2009) DASH-style diet associated with reduced risk for kidney stones. J Am Soc Nephrol.20(10):2253-9. doi: 10.1681/ASN.2009030276. Epub 2009 Aug 13.

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## How do we tailor medical therapies for each patient?

Stone analysis &  
Medical/medication history &  
24-hour urine chemistry studies

## Medical Therapy Based on Urine Chemistry Studies

- Hypercalciuria → thiazide diuretics
- Hypocitraturia → citrate supplementation
- Hyperuricosuria → xanthine oxidase inhibitors  
vs. alkalinization

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## Hypercalciuria

- ▶ Urine calcium >4mg/kg/day
- ▶ A factor in at least 30% of those with Calcium oxalate stones
- ▶ Types
  - ▶ Resorptive: from bone, as in hyperparathyroidism
  - ▶ Absorptive: too much absorbed from the gut
  - ▶ Renal loss/idiopathic: decreased renal tubular reabsorption
    - ▶ Can be driven by excess sodium intake

## Thiazide diuretics for hypercalciuria

*AUA says: "Clinicians should offer thiazide diuretics to patients with high or relatively high urine calcium and recurrent calcium stones." Standard; Evidence Grade B*

Long acting preferred:

- ❖ Chlorthalidone: daily dosing, 12.5, 25 or 50 mg/day
- ❖ Indapamide: 1.25 to 2.5 mg/day

Twice daily dosing:

- ▶ Hydrochlorothiazide: 25 mg twice daily
- ▶ Modurectic = HCTZ + amiloride: ½ to 1 tab twice daily
  - ▶ Use in intractable hypokalemia

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## Thiazide Diuretics for Hypercalciuria

Increases calcium reabsorption in distal tubule  
- active resorption

Stimulates proximal tubule calcium reabsorption - passive resorption

- Helping body retain calcium → increased serum calcium
- Potassium wasting
- Sodium overrides effectiveness

Side effects:

- hypokalemia
- hypotension
- sexual dysfunction
- hypercalcemia

Monitoring:

- Serum K, renal function at one to two weeks and periodically
- Check 24-hour urine 4-6 weeks

## Thiazide Pitfalls and a Pearl

- Pitfall: Rarely causes uricemia and gout
- Pitfall: Unmanaged hypokalemia can result in hypocitraturia via intracellular acidosis

→ Pearl: Unless you need to alkalinize, correct hypokalemia with potassium chloride before turning to potassium citrate

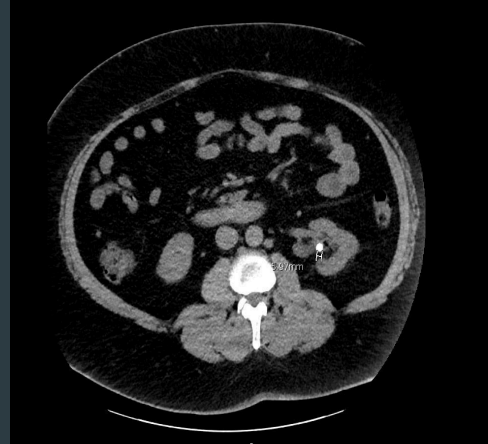


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## Case Study: J.B. 48 yo male

- ▶ Three episodes of gross painless hematuria
- ▶ CT urogram revealed bilateral renal stones, largest 6 mm
- ▶ No prior stones
- ▶ No FH stones
- ▶ BMI 55, BP 147/95
- ▶ PMH: PE, OSA
  - ▶ Coumadin



JAN 30, 2019 10:00 --		
Sodium SerPI QN	mmol/L	139
Potassium SerPI QN	mmol/L	4.4
Chloride SerPI QN	mmol/L	105
Carbon Dioxide Ser...	mmol/L	27
Anion Gap	mmol/L	7 *
BUN SerPI QN	mg/dL	17
Creatinine SerPI QN	mg/dL	1.01
Estimated GFR (CK...)	mL/min	↓ 88 *
Estimated CRCL (CG)	mL/min	>60
Glucose SerPI QN	mg/dL	↑ 106
Calcium Total SerPI...	mg/dL	9.1

Values larger, bolder and more towards red indicate increasing risk for kidney stone formation. See reverse for further details.

### Stone Risk Factors/ Cystine Serum Level; Negative (02/27/2019)

DATE	SAMPLE ID	Vol24	SSCaOx	Ca 24	Ox 24	C 24	SSCaP	pH	SS UA	UA 24
02/26/19	S25812544	1.91	S,SS	<b>488</b>	34	1191	<b>2.60</b>	5.932	1.16	<b>0.996</b>
02/24/19	S25812543	<b>1.72</b>	5.57	<b>355</b>	28	1005	<b>2.30</b>	6.149	0.71	0.832
REFERENCE RANGE		0.5-4L	6-10	male <250 female <200	20-40	male <450 female >550	0.5-2	5.8-6.2	0-1	male <0.800 female <0.750

### Dietary Factors

DATE	SAMPLE ID	Na 24	K 24	Mg 24	P 24	Nh4 24	Cl 24	Sul 24	UUN 24	PCR
02/26/19	S25812544	<b>312</b>	82	269	<b>1.846</b>	51	<b>297</b>	61	<b>20.fo</b>	0.9
02/24/19	S25812543	<b>301</b>	72	184	1.262	45	<b>285</b>	69	17.45	0.8
REFERENCE RANGE		50-150	20-100	30-120	0.6-1.2	15-60	10-250	10-80	6-14	0.8-1.4

### Normalized Values

DATE	SAMPLE ID	WEIGHT	C <sub>24</sub>	Cr <sub>24</sub> /Kg	Ca <sub>24</sub> /Kg	C <sub>24</sub> /C <sub>24</sub>
02/26/19	S25812544	167.8	2360	14.1	2.9	206
02/24/19	S25812543	167.8	2100	12.5	2.1	169
REFERENCE RANGE				male 11.9-24.4 female 8.7-20.3	<4	male 34-196 female 51-262

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## Hypocitraturia: Causes

- ▶ Metabolic acidosis
- ▶ High acid-load diet
  - ▶ High in meats, grains
  - ▶ Low in fruits/vegetables
  - ▶ Dairy and fats - neutral
- ▶ RTA (profound!)
- ▶ Hypokalemia, including thiazide-induced
- ▶ Chronic diarrhea
- ▶ Idiopathic
- ▶ UTI

## Hypocitraturia treatment



Urocit K 10 mEq, 15 mEq tablets

Wax matrix may not dissolve



Polycitra K syrup, 2 mEq/cc, 10 mEq/tsp.



Polycitra K crystals 30mEq/packet



Diet



OTC preparations are not created equal

Many contain both potassium citrate AND sodium bicarb  
Most also contain calcium, sodium, magnesium

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## Citrate: Dual Purpose Therapy

Inhibit crystal formation

Alkalinize the urine

## Citrates: a Pitfall and a Pearl

- ▶ Pitfall: Over-alkalization (pH>7) can cause CaP stone
- ▶ Pearl: Citrate can dissolve small uric acid stones
  - s-l-o-w-l-y
  - best for fragmented stone with great surface area

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## Citrate Pitfall: M.M. 68 yo male, 2nd opinion

- ▶ PMH arthritis, CKD3 secondary NSAIDS
- ▶ Chronic intermittent dysuria, hematuria, passage of debris and fragments for more than two years
- ▶ Multiple ESWL, multiple antibiotics
- ▶ Cultures negative
- ▶ Stone analysis “organic matter”
- ▶ No prior 24-hour urine testing
- ▶ Current medications
  - Tamsulosin 0.4mg daily
  - Potassium citrate 10 mEq TID
  - Tizanidine 4 mg q 8 hours
  - Gabapentin 600 mg TID

Values larger, bolder and more towards red indicate increasing risk for kidney stone formation. See reverse for further details.

**Stone Risk Factors / Cystine Screening:** Negative (09/21/2020)

DATE	SAMPLE ID	Vol 24	SS CaOx	Ca 24	Ox 24	Cit 24	SS CaP	pH	SS UA	UA 24
09/18/20	S26322940	<b>1.08</b>	<b>8.56</b>	153	21	453	<b>3.14</b>	<b>7.899</b>	0.01	0.254
09/17/20	S26322939	<b>0.99</b>	<b>7.14</b>	127	14	<b>318</b>	1.02	<b>8.105</b>	0.00	0.194
REFERENCE RANGE		0.5 - 4L	6 - 10	male >250 female <200	20 - 40	male >450 female >550	0.5 - 2	5.8 - 6.2	0 - 1	male <0.800 female <0.750

**Dietary Factors**

DATE	SAMPLE ID	Na 24	K 24	Mg 24	P 24	Nh4 24	Cl 24	Sul 24	UUN 24	PCR
09/18/20	S26322940	100	25	<b>47</b>	<b>0.323</b>	2	57	6	2.39	<b>0.4</b>
09/17/20	S26322939	101	25	<b>26</b>	<b>0.086</b>	1	68	4	1.72	<b>0.3</b>
REFERENCE RANGE		50 - 150	20 - 100	30 - 120	0.6 - 1.2	15 - 60	70 - 250	20 - 80	6 - 14	0.8 - 1.4

**Normalized Values**

DATE	SAMPLE ID	WEIGHT	Cr 24	Cr 24/Kg	Ca 24/Kg	Ca 24/Cr 24
09/18/20	S26322940	86.6	792	<b>9.1</b>	1.8	<b>193</b>
09/17/20	S26322939	86.6	534	<b>6.2</b>	1.5	<b>238</b>
REFERENCE RANGE				male 11.9-24.4 female 8.7-20.3	<4	male 34-196 female 51-262

## Uric acid stones With or without hyperuricosuria

- ▶ 5-10% of stones are uric acid
- ▶ Men > women
- ▶ Reference range < 0.8 g/d males, <0.75 g/d females
- ▶ Metabolic environment
  - ▶ Low pH urine (REQUIRED for crystal formation)
    - ▶ Soluble urate salt becomes insoluble uric acid in low pH
    - ▶ Suspect this in diabetics, metabolic syndrome
  - ▶ Hyperuricosuria: MAY be present, MAYBE NOT

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## Treating hyperuricosuria

Diet: increase fluids, reduce purine intake, reduce acid load

### Medications, consider

- Allopurinol 200 to 300 mg daily if total uric acid/24 hours > 0.800 in men, > 0.750 in women (and protein restriction fails).
- Mechanism: prevents conversion of xanthine to uric acid by inhibiting xanthine oxidase
- Side effects: Steven's Johnson syndrome, anemia, vasculitis, liver toxicity
- Monitor with annual LFT, CBC

## Conclusion

**Kidney stones are preventable!**

Awareness of co-morbid conditions associated with stones is beneficial to management

Diet change can be a powerful prevention measure

Patients unwilling or unable to complete a metabolic workup can follow DASH diet

The AUA Guideline on Medical Management of Stones states clinicians **SHOULD**

- Investigate causes of stones
- Counsel on prevention efforts

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## Thank you!

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Reach out to me about NP and RN Urology Certification



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