

Kidney stones Medical Management and Prevention

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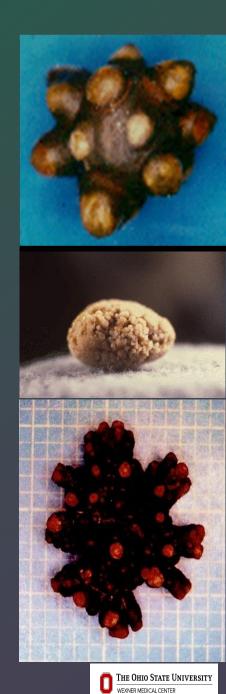


Associate Professor Division of Nephrology Metabolic Stone Clinic



Outline...

- 1. Epidemiology
- 2. Pathogenesis
- 3. Types of stones
- 4. Etiology/Risk factors
- 5. Evaluation
- 6. Medical management



Renal Colic: The Experience

- It felt like I was trying to give birth to an elephant, but all that finally came out was a little speck of blood.
- as if someone took a pair of vise grips to my side and started clamping it down without letting up.
- hot needle-like pain radiating down to the end of my penis.
- it felt like a white hot poker was sticking into my side.
- dull ache over the kidney area.



Events before and during medical Treatment

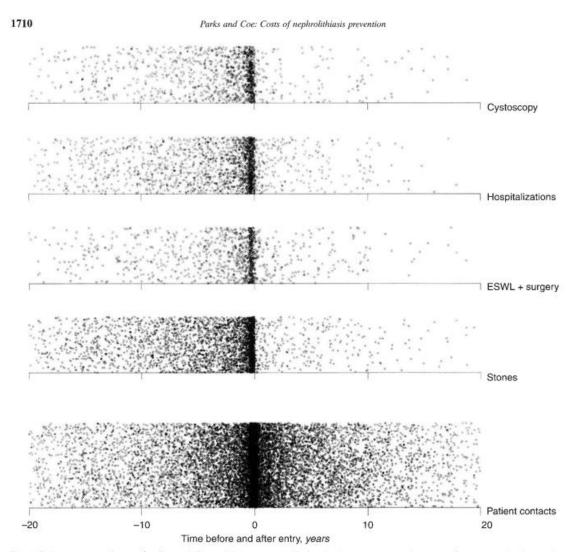


Fig. 1. Patient contacts and stone related events before and during treatment. Each point shows one contact (lowest panel), or stone related event (upper panels); time before entry is shown as negative numbers. Despite large numbers of contacts, stone related events fell in all categories.

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Epidemiology:

- In 1994 prevalence : 1 in 20 (5.2%)
- In 2010 prevalence : 1 in 11 (10.6%)
- Demographics

-Men > Women (2 or 3 : 1)

- Cost in 2000 \$2.1 billion (Pearl, 2005)
- Cost in 2012 \$10 Billions (Litwin MS et)
- Projected rise in cost 1.24 Billion/year by 2030
- Loss of wages/productivity

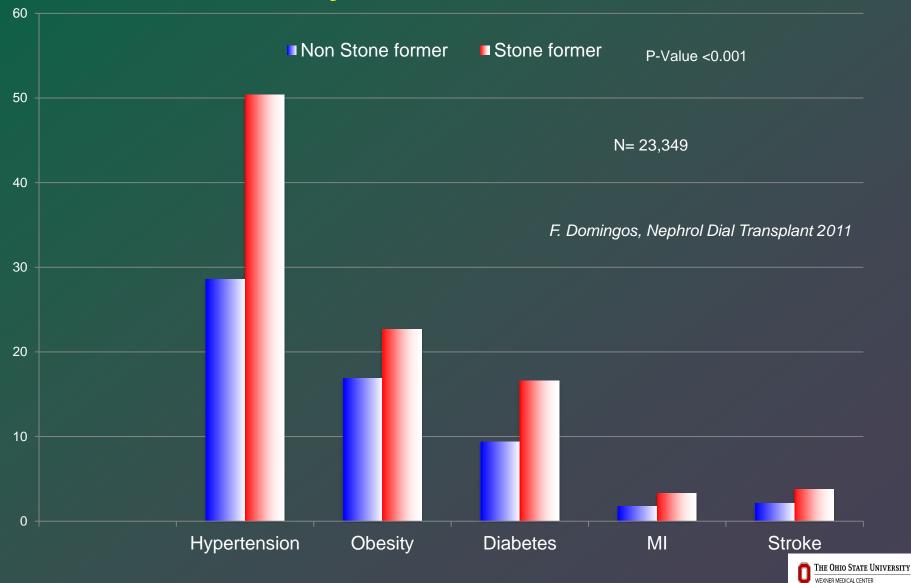
Treatment aimed at prevention of stones is critical to decrease cost and morbidity

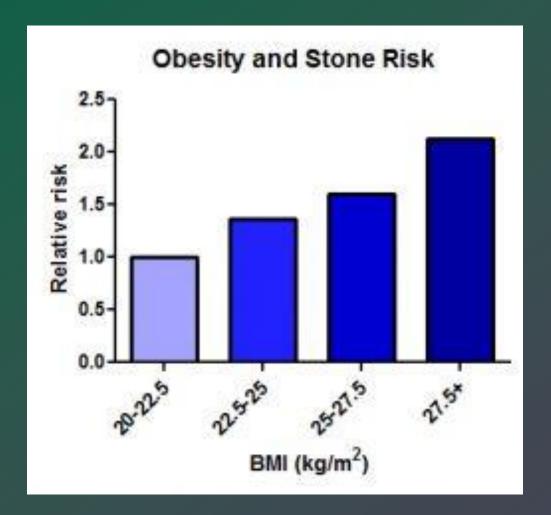
Lotan, Adv in Chr Kid dis 2009;

Scales, Eur Urology 2012



Kidney stones and associations – a Systemic disease







Recurrence of Stones Recurrence rate <u>after first</u> kidney stone

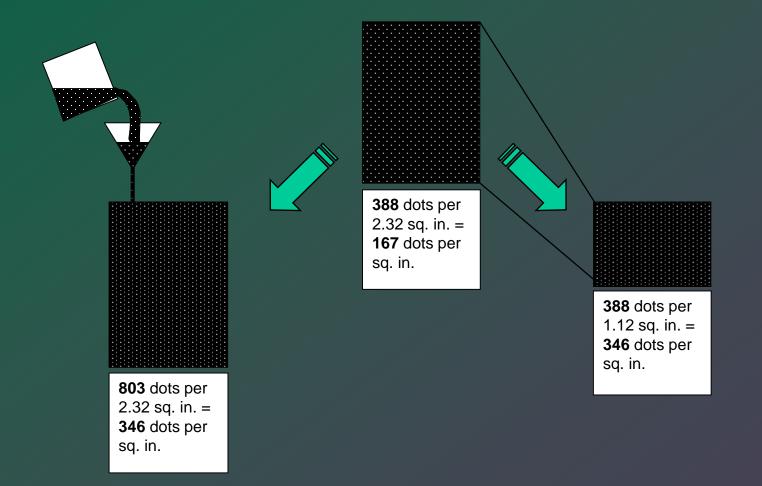


Recurrence 5% per year if untreated

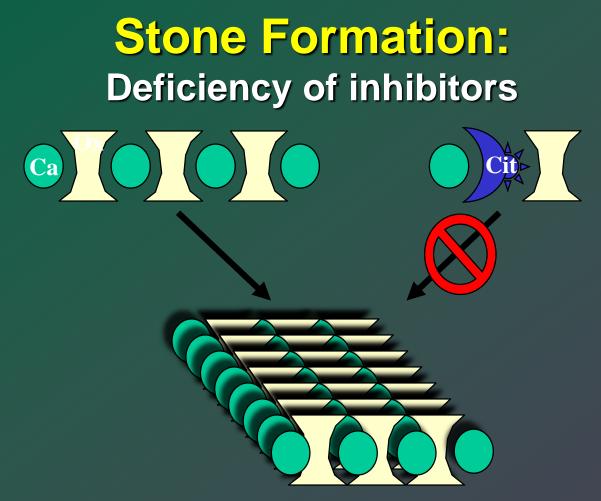
Uribarri, et al, Ann Intern Med 1989; 111;1006



Stone Formation : SuperSaturated urine





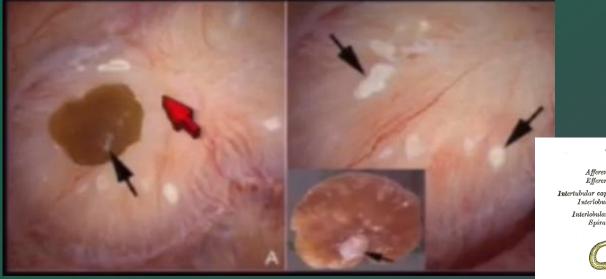


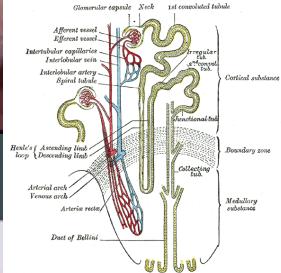
Inhibitors of crystal nucleation, growth and aggregation-

Mg, citrate, macromolecules like glycosaminoglycan, RNA, acidic glycoproteins, Tamm-Horsfall protein, nephrocalcin, uropontine

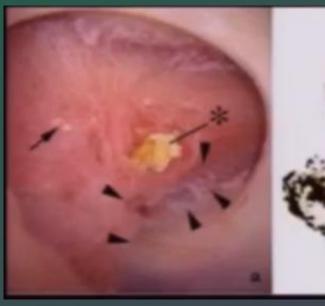
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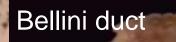
Papillary Interstitium





Intraductal





D



Types of Kidney Stones

Туј	pe	Pe	Percentage		
1.	Calcium stones - Calcium Oxalate - Calcium Phosphate - Calcium oxalate & phosphate	26 7 37	70-75		
2. 3. 4. 5.	Struvite Uric acid Cystine		15-20 10-15 1		

Rare types of stones: Xanthine, Oxypurinol, triamterene, indinavir, ephedrine, matrix stones.



Evaluation Lab Studies

- Stone analysis
- Blood profile
- 24 hr Urine metabolic evaluation:

-Metabolic abnormalities in 96% (Levy et al)

- Urine Microscopy crystals
- Imaging:
 - CT scan with stone protocol (most sensitive and specific)
 - US kidney



Evaluation 24-Hour Urine Testing

- Volume
- Calcium
- Sodium
- Citrate
- pH
- Oxalate
- Uric Acid

- Potassium
- Creatinine
- Urea Nitrogen
- Sulfate
- Ammonia
- Phosphorus

SuperSaturation calculation SS CaOx SS CaP SS UA



Urinary Risk factors for Calcium Stone Formation

- Low U Vol
- Hypercalciuria
- Hypocitraturia
- Hyperuricosuria
- Idiopathic
- Hyperoxaluria

> 70-90% 40-75% 10-50% 30% 20% 5%



Kidney Stones Treatment

- Acute Renal colic ER/PCP/Urology
 - Stone <4 mm: Pain Control and Fluids
 - Stone >5 mm: Obstruction OR infection: Urologic Intervention
- Currently Asymptomatic: Chronic Recurrent Disease:
 - Identify risk factors
 - Medical Rx for Prevention of recurrent stones
 - Int Medicine /FM/ Nephrology



Medical Management



Myths about Kidney stone treatments

- Dr Google
- Advice from friends and relatives
- Advice from physicians unaware of Rx
- Myth- Not to drink milk if stone is made of calcium
- Kidney stone cleanser, herbals etc

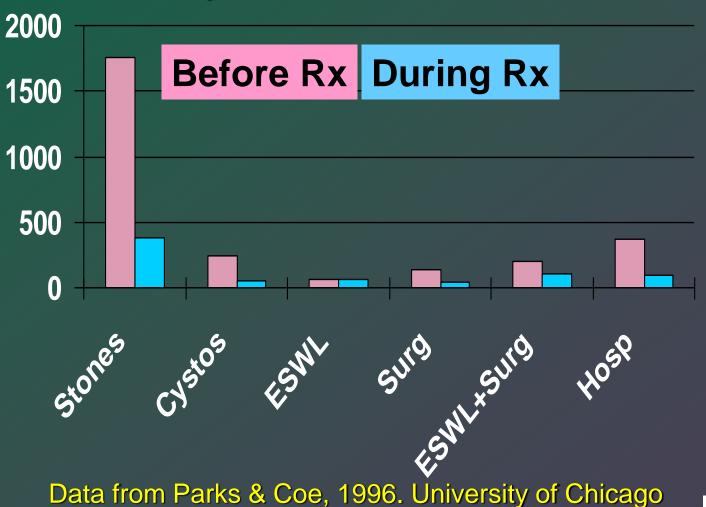
Truth is:

"Treatment advice should be personalized to specific metabolic risk factors"



Before and During Medical Treatment

Rates per 1000 Pat-Yrs of Stones



THE OHIO STATE UNIVERSITY WEXNER MEDICAL CENTER Urine volume: Concentrated Urine



27 WM, obese. 2 visits to ER for renal colic. CT abd shows 2-3 mmNon-obstructing stones. Stone analysis not available.Has not needed any urology procedures.Significant family history of kidney stones.

DATE	SAMPLE	Not 24	SS CaOx	Ca 24	0x 24	Cit 24	SS CaP	pH	SS UA	UA 24
07/10/18	\$256203		11.05	74	50	525	0.65	5.756	2.49	0.637
07/09/18	\$256203	69 0.81	8.19	93	33	404	0.41	5.385	3.49	0.542
	ENCE RANGE		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 <0.75
Dieta	ry Fact	ors								
DATE	SAMPLE ID	Na 24	K 24	Mg 24	P 24	Nh4 24	CI 24	Sul 24	UUN 24	PCR
	\$25620370	115	49	76	0.733	53	130	38	10.34	0.9
07/09/18	525620369	114	48	84	0.822	58	137	43	10.25	0.8
	ICE RANGE	50 - 150	20 - 100	30 - 120	0.6 - 1.2	15 - 60	70 - 250	20 - 80	6 - 14	0.8 - 1.4
	alized \									
DATE	SAMPLE ID	WEIGHT	Cr 24	Cr 24/Kg	Ca 24/1	(g Ca 24,	/Cr 24			
07/10/18	\$25620370	97.5	1541	15.8	0.8	4	2011 C			
7/09/18	\$25620369	97.5	1580 *	16.2	0.9	5	9			
REFEREN	CE RANGE			male 11.9-24.4 emale 8.7-20.3	<4	maie 3		*****		

Low Urine Volume: Concentrated urine

- Definition: Urine output < 1 It per day
- Goal: Urine output > 2.5 Lt per day and decrease supersaturation of urine
- Etiology:
 - -Chronic diarrhea, Colon resection
 - Excessive sweating, warm climate, foundry/factory work in high temperatures
 Habitual low fluid intake. Decreased thirst.
 Work limitations



Low Urine Volume: Concentrated urine

• Recommendations:

- -Drink 16 Oz water every 2.5 to 3 hrs. Goal 100 Oz fluid/day.
- -"Drink water Reminder" app
- -Type of fluid: Best- water/flavored water.
- -Avoid sugar containing beverages/juices.
- -Coffee, Tea, Alcohol in moderation. Too much caffeine can cause HyperCalciuria
- -Cranberry juice- no studies to support its use in stone prevention

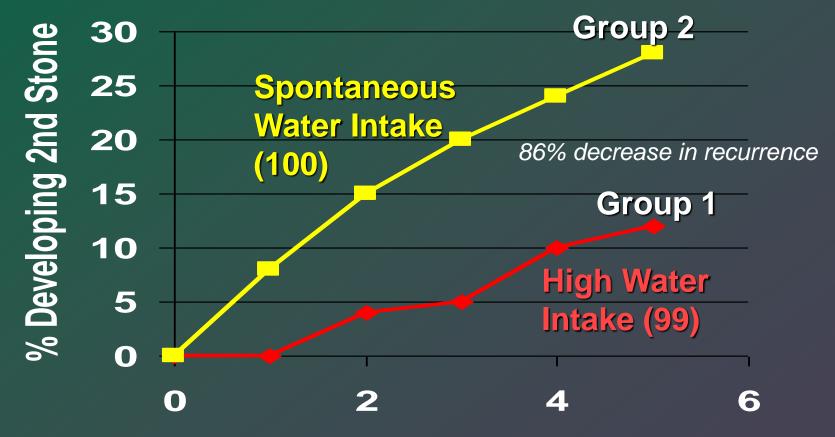


Urine Volumes in Kidney Stone Patients



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Effect of Increased Water on Stone Recurrence



Follow-Up, Years

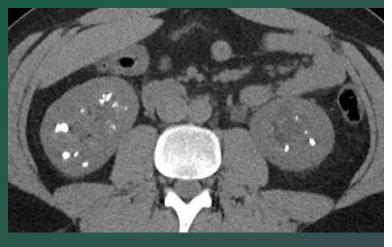
(Borghi, L. et al, J Urology 1996)



Urine Calcium: HyperCalciuria



34 yrs WM. H/O kidney stones since 2006. Recently presented with obstructing left ureteral stone, L hydronephrosis and needed Left Ureteroscopy and laser Lithotripsy. *Stone analysis: CaOx 80%, CaP 20%.*



DATE	SAMPLE	ID Vol 2	4 SS CaOx	Ca 24	0x 24	Cit 24	SS CaP	pH	SS UA	UA 24
07/06/1	8 5255976	2.63	2 5.56	394	41	520	2.05	6.240	0.43	0.904
07/05/1	8 \$255976	2.69	3.79	316	28	658	1.68	6.459	0.23	0.786
04/24/1		153 2.3 4	4 4.51	286	27	316	1.62	6.313	0.40	0.843
REFER	ENCE RANGE		L 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
DATE	SAMPLE ID	Na 24	K 24	Mg 24	P 24	Nh4 24	CI 24	Sul 24	UUN 24	PCR
DATE	SAMPLE ID	Na 24	K 24	Mg 24	P 24	Nb4 24	CI 24	Sul 24	1000.24	BOB
07/06/18	3 525597671	176	88	274	1.581	61	180	74	15.07	1.1
	\$25597670	179	71	206	1.013	37	192	34	12.81	0.9
04/24/18	\$25542353	112	47	163	0.976	50	119	43	11.94	0.9
	NCE RANGE	50 - 150	20 - 100	30-120	0.6 - 1.2	15 - 60	70-250	20-80	6-14	0.8 - 1.4
Norm	alized	Values	s lista							
DATE	SAMPLE ID	WEIGHT	Cr 24	Cr 24/Kg	Ca 24/	Kg Ca 24	/Cr 24			
	\$25597671	106.6	3456	32.4	3.7	11	.4			
	\$25597670	106.6	2036 *	19.1	3.0	15				
4/24/18	\$25542353	106.6	2196	20.6	2.7	13	0			

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HyperCalciuria

- Definition: 200 mg/day (risk is continuous)
- Goal: U Calcium < 150 mg/day
- Risk Factor: seen in 40-75% cases
- Etiology:
 - A. With hypercalcemia

Hyperparathyroidism

Granulomatous diseases

Hyperthyroidism

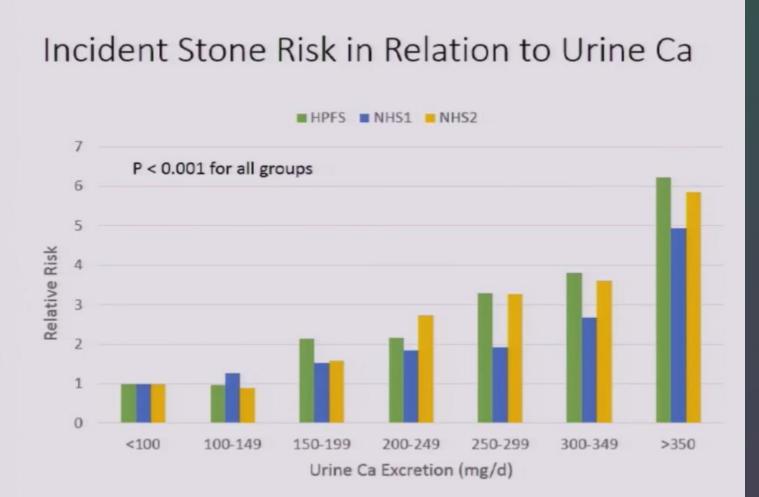
Malignancies, Immobilization

B. Without Hypercalcemia

<u>High salt intake</u>, High protein intake,
Excess Refined sugar, Caffeine in excess
Type 1 RTA *Idiopathic Hypercalciuria (most common)*



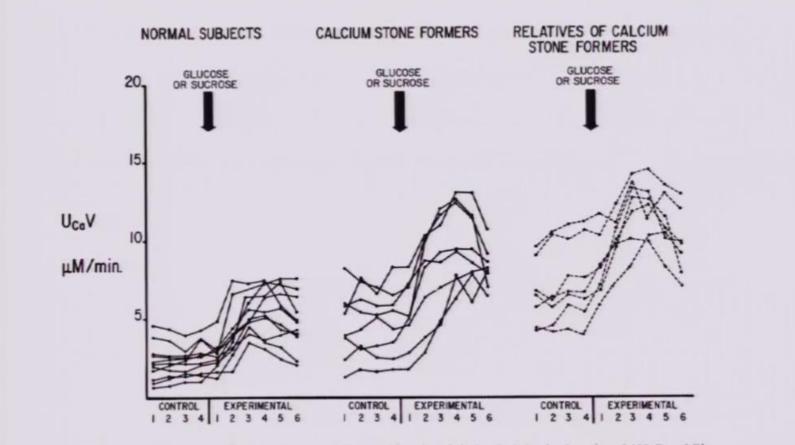
U Calcium and Risk for Ca Kidney stones

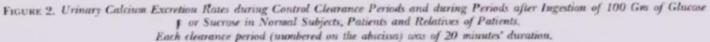


Curhan GC and Taylor EN Kidney Int 73:489, 2008



Refined sugars and U Calcium





N Engl J Med 1969 Jan 30;280(5): 232-7



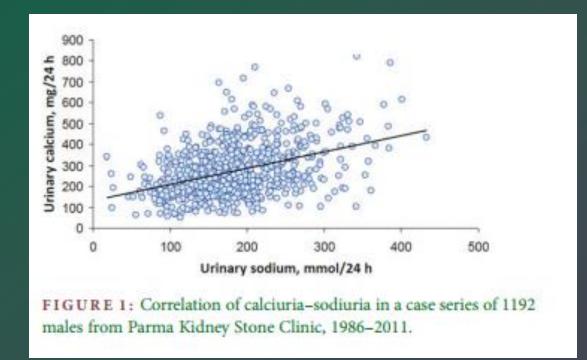
Sucrose intake and Risk of stone formation

Median sucrose intake gm/d	31	40	47	54	66
No. of stones	210	209	263	223	318
RR	1.00	1.01	1.25	1.0	1.31

Curhan GC et al. Arch Int Med 2004;164:885-891



Urine Sodium and Urine Calcium



For every additional 100 mmol Na, U Ca increases by 140 mg in Idiopathic Hypercalciuria Salt and Nephrolithiasis. Nephr Dial Trans, 2016, 31: 39-45

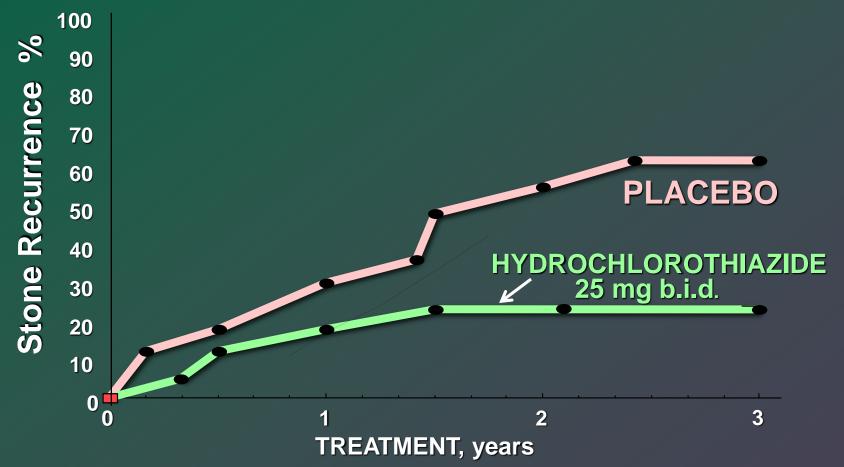


Hypercalciuria: Treatment

- 1. Urine output >2.5 L/day
- 2. Low salt diet 2 gm Sodium ~(24 hr U Na <100 mmol)
- 3.Chlorthalidone 25-50 mg qd or HCTZ 25 mg bid or Indapamide (↓ Urine Ca by 40-60%)
- 4. Avoid Hypokalemia
 - (causes Hypocitraturia and Hypercalciuria)
- 5. Maintain normal Ca diet
- 6. Avoid refined sugars
- 7. Dietary protein 1 gm/kg/day



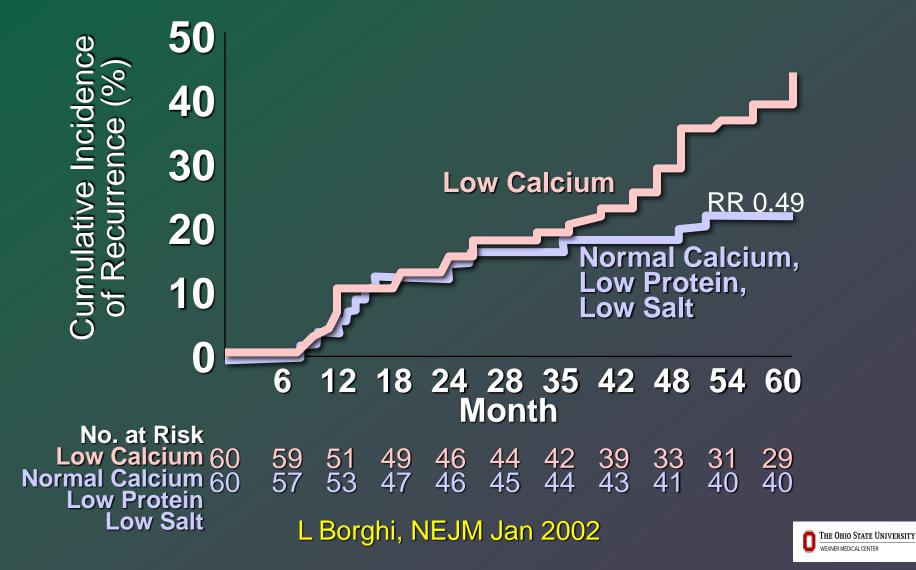
Hypercalciuria: Thiazides & Stone Recurrence



Laerum & Larsen, Acta Med Scand 1984



Hypercalciuria: Recurrent Stones According to Diet



Urine Oxalate: HyperOxaluria



HyperOxaluria

- Definition: U Oxalate > 40 mg/d (> 20% of U Ca) –Risk is continuous
- Goal: < 40 mg (Ideally < 25 mg/d)
- Risk Factor: seen in < 5% cases
- Etiology:
 - Enteric hyperoxaluria (Malabsorption, Bariatric surgery principally Roux-en-Y, Crohn's, small bowel resection, Irritable bowel, Celiac, lactose intolerance)
 - -Low dietary Ca
 - -Oxalate rich food- chocolate, cocoa, spinach, nuts, starfish fruit
 - -Ascorbic acid (6-13 mg U Oxalate for every 1 g Vit C above 500 mg)
 - Alteration in GI flora- abx, Cystic fibrosis loss of Oxalobacter formigenes which degrades oxalates
 - -Primary HyperOxaluria -enzyme def overproduction of oxalates



HyperOxaluria

Treatment:

- 1.Urine Output > 2.5 L
- 2.Low oxalate diet: 100-200 mg Oxalate/day
- 3. Avoid ascorbic acid or (upto 90 mg)
- 4.Dietary Calcium(1000-1200 mg)
- 5.Low sodium diet
- 6. Probiotics with antibiotics
- 7.Rx of Malabsorption- Cholestyramine, Tums with food
- 8. Treatment of Crohn's, Celiac, short gut.



Urine Citrate: Inhibitor of Kidney stones

HypoCitraturia



19 yr old OSU sophomore student, seen after
1 st kidney stone episode needing URS with HLL. He missed
4-5 weeks of college. He did not want to suffer more. He has h/o Pseudotumor Cerebri and was on Topamax.

DATE	SAMPLE ID	Vol 24	SS CaOx	Ca 24	0x 24	Cit 24	SS CaP	рН	SS UA	UA 24
11/23/18		3.31	1.85	114	31	436	0.43	6.389	0.22	0.768
10/15/17		2.86	3.11	215	30	303	0.50	5.838	0.92	0.958
04/18/17	\$25214666	2.79	3.43	215	30	301	0.46	5.846	0.90	0.922
1/25/16		2.40	4.57	235	36	387	0.56	5.764	1.19	0.938
08/12/16	520451874	4.03	3.67	222	43	279	0.62	6.438	0.13	0.617
06/08/16	519188124	4.70	2.43	293	33	<70	1.18	6.727	0.10	1.025
06/07/16	519188123	2.76	5.94	398	37	<41	2.72	6.903	0.12	1.125
REFER	ENCE 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 <0.75
Dieta	ry Facto	rs				_				_
DATE	SAMPLE ID	Na 24	K 24	Mg 24	P 24	Nh4 24	CI 24	Sul 24	UUN 24	PCR
	8 525617788	174	81	58	1.013	52	182	48	13.74	1.1
	525387470	198	60	104	1.385	68	198	55	16.59	
		169	46	113	1.145	55	150	59	14.24	1.2
04/18/17	7 525214666	Rest Street								
04/18/17	5 522111720	231	61	106	1.348	68	242	68	16.98	1.4

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Hypocitraturia

- Definition: U Citrate < 350 mg (Risk is continuous)
- Goal: U Citrate > 600-800 mg
- Risk factor: in 10-50% cases
- Etiology:
 - -Diarrhea
 - -Hypokalemia
 - -Metabolic acidosis
 - -Medications-(Carbonic anhydrase Inhibitor) Topamax, Diamox, Zonisamide, HIV meds (PI)
 - -High protein diet
 - -Type 1 RTA (Distal)- complete/incomplete



Hypocitraturia

• Treatment:

- -U Vol > 2.5 L/day
- -Discontinue offending agent
- -Alkali supplement promotes tubular excretion of Citrate
- -Normal protein diet
- -Normalize Serum Bicarb
- -Treat Hypokalemia



Hypocitraturia

• Treatment:

-Will need 60-80 meq of alkali:

- Pot Citrate 20 meq PO TID with food
- Crystal light 1 pack = 10 meq alkali
- Litholyte 1 pack = 10 meq citrate
- 1 It of Diet 7 UP =10 meq citrate
- Sod Bicarb 650 mg Tab = 7.7 meq Alkali
 - (Caution about Na -Can lead to high U Ca)
 - Baking soda 1 Teaspoon = 53 meq Alkali







potassium citrate (5 mEq), sodium bicarbonate (2.5 mEq) magnesium citrate (2.5 mEq)



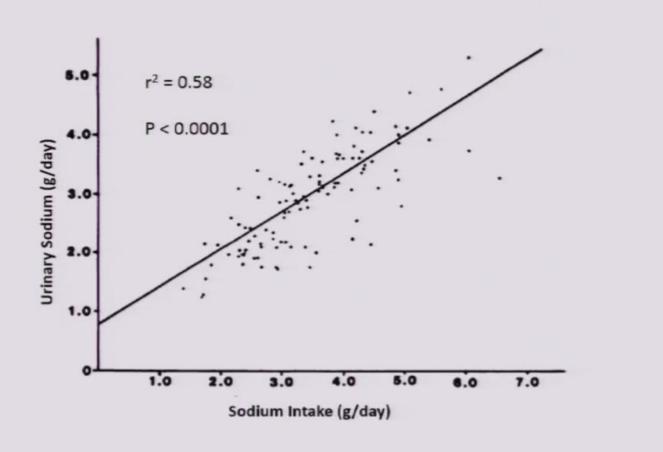
High U Sodium Leads to High U Ca



46 yrs old WM, H/O Kidney stones since 2014, needing 3 urology procedures. CaOx stones.

DATE	SAMPLE I	Vol 24	SS CaOx	Ca 24	0x 24	Cit 24	SS CaP	pН	SS UA	UA 24
06/06/18	\$255 4 450		9.02	351	41	801	0.42	5.301	1.26	0.382
06/05/18	\$2554450	a 1.77	10.47	257	56	786	0.58	5.627	1.32	0.624
	INCE RANGE	0.5-4L	6-10	mais <250 female <200	20 - 40	male >450 female >550	0.5 - 2	5.8 - 6.2	0 - 1	male <0.800 female <0.750
Dieta	ry Fact	ors								
DATE	SAMPLE ID	Na 24	K 24	Mg 24	P 24	Nh4 24	CI 24	Sul 24	UUN 24	PCR
06/06/18	\$25544504	310	81	112	1.067	50	346	59	13.80	1.0
	\$25544503	249	85	94	1.046	45	263	64	16.50	1.2
REFEREN	ICE RANGE	50-150	20 - 100	30 - 120	0.6 - 1.2	15.60	70 - 250	20 - 80	6-14	0.8-1.4
Norma	alized \	alues/								
DATE	SAMPLE ID	WEIGHT	Cr 24	Cr 24/Kg	Ca 24/1	Kg Ca 24	/Cr 24			
	\$25544504		1941	18.6	3.4	18	31			
06/05/18	\$25544503	104.3	1877	18.0	2.5	1:	37			
	ICE RANGE		******	maie 11.9-24.4 female 8.7-20.3	<4	male 3	34-196 51-262			

U Na as a marker of Dietary Na



Holbrook JT Am J Clin Nutr 40:786, 1984



High U Sodium

- Definition: U Na > 100 meq (2300 mg)/day
- Goal: U Na < 100
- Etiology: In steady state 24 hr urine sodium represents dietary sodium intake
- Risk: High U Na increases U Calcium
- Treatment:
 - -Low salt diet ~ 2 gm sodium per day
 - -Check Nutrition labels
 - -Check online sodium content of food
 - -Avoid processed food, Canned food, lunch meats etc



High Protein Intake:

High U Ca Low U Citrate High U Uric acid



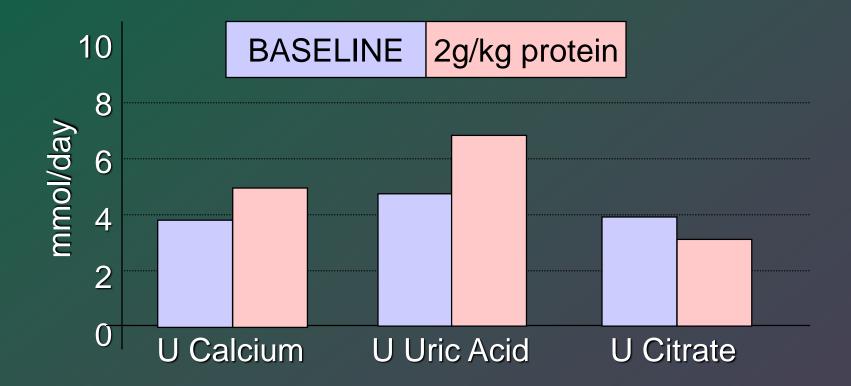
Case 3

44 yo man with recurrent kidney stones

DATE	SAMPLE ID	Vol 24	SS CaOx	Ca 24	0x 24	Cit 24	SS CaP	pH	SS UA	UA 24
10/31/0	7	4.21	4.21	409	53	542	0.54	5.748	1.48	1.976
09/05/0	7	4.49	4.39	545	55	774	1.42	6.206	0.54	1.806
ATE	SAMPLE IC	Na 24	К 24	Mg 24	P 24	Nh4 24	CI 24	Sul 24	UUN 24	PCR
ATE 0/31/07		Na 24 353	K 24 142		P 24 2.294	Nh4 24 107	CI 24 337	Sul 24		



Protein Load Increases Urine Stone Forming Tendency



J Cli Endocrinol Metab 1990;71:861



High protein intake

- Definition: Protein intake > 1.3 gm/kg/day, Sulfate > 70
- Goal: Protein intake < 1 gm/kg/d and Sulfates < 70
- Risk: HyperCalciuria, HypoCitraturia, HyperUricosuria
- Recommendations:
 - -Decrease animal protein and substitute with plant protein
 - -Protein intake ~ 1 gm/kg/day
- Monitor: U Sulfates, U PCR, U Ammonia



Non Calcium stones

Uric Acid Cystine Infection – Triple phosphate - Carbonate



Non Calcium kidney stones

Uric Acid Stones



36 yrs WF, diagnosed with Staghorn kidney stone needing PNCL. Stone Analysis: Uric acid 90%, CaOx 10%

DATE	SAMPLE ID	Vol 24	SS CaOx	Ca 24	0x 24	Cit 24	SS CaP	PH	SS UA	UA 24
07/03/18	8 52561402	0.00	12.55	424	26	1332	0.99	5.001	3.00	0.376
07/02/18		1.00	10.78	251	26	686	0.68	5.146	4.51	0.665
	ENCE RANGE	0.5 - 4L	6-10	maie <250	20 - 40	male >450	0.5 - 2	1		male <0.800
	ry Facto	ors		female <200		female >550		5.8 - 0.2		
			K 24	1000000		rentaria - analia		Sul 24		
Dieta	SAMPLE ID	075 Na 24 97	к 24 43		P 24 1.605	Nh4 24 72	CI 24 84	Sul 24		
Dieta	SAMPLE ID 3 \$25614025	075 Na 24 97	к 24 43 48	Mg 24 183 129		Nh4 24 72	CI 24	Sul 24		PCR



Uric acid stones

Account for 10-15% of stones. 60% of Uric acid stones in diabetics

Risk factors-

Uric acid overproduction	Gout, myeloproliferative disorder
Hyperuricosuria >800 mg/day	High protein intake
Persistent acid urine < pH 5.5	Diarrhea, DM, Obesity
Concentrated urine < 1 L	Diarrhea, hot climate

Solubility of uric acid-Acidic urine - 100 mg/L At pH 7 – 1600 mg/L



Uric acid stones

Treatment -

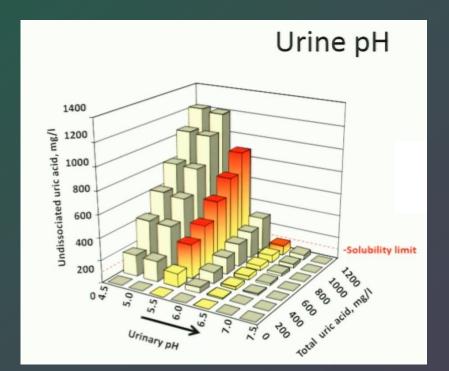
Purine rich food restricted

Drink water to make > 2.5 L of urine

Maintain alkaline urine pH ~ 6.5 K citrate 30-60 meq/d

If urine uric acid >800 mg/day Allopurinol

Normalize S Bicarbonate





Vitamin D Intake and Kidney stones

P Ferraro, G CurhanJ: Urology: Vol. 197, 405-410, February 2017

Participants: 193,551; Kidney stone incident events: 6,576

Table 3. Supplemental vitamin D intake and risk of kidney stones

	None	Less than 400 IU/Day	400—599 IU/Day	600—999 IU/Day	1,000 or Greater IU/Day	p Value for Trend
HPFS:						
No. cases	1,068	343	426	98	28	
Person-time	333,293	127,922	159,707	38,509	10,057	
Age adjusted HR	1.00 (Ref)	0.87 (0.77, 0.99)	0.91 (0.81, 1.02)	0.85 (0.69, 1.05)	1.12 (0.75, 1.66)	0.66
MV adjusted HR	1.00 (Ref)	0.90 (0.78, 1.04)	1.00 (0.86, 1.15)	0.93 (0.74, 1.18)	1.23 (0.81, 1.86)	0.34
NHS I:						
No. cases	671	250	340	62	8	
Person-time	480,572	214,937	252,492	53,291	9,150	
Age adjusted HR	1.00 (Ref)	0.83 (0.72, 0.96)	0.98 (0.87, 1.12)	0.90 (0.73, 1.12)	0.88 (0.61, 1.26)	0.70
MV adjusted HR	1.00 (Ref)	0.89 (0.76, 1.04)	1.09 (0.94, 1.27)	1.05 (0.83, 1.33)	1.03 (0.71, 1.51)	0.26
NHS II:						
No. cases	1,357	770	635	196	56	
Person-time	624,460	393,051	304,519	86,544	19,761	
Age adjusted HR	1.00 (Ref)	0.85 (0.78, 0.93)	0.92 (0.84, 1.02)	0.96 (0.82, 1.13)	1.18 (0.90, 1.56)	0.76
MV adjusted HR	1.00 (Ref)	0.94 (0.84, 1.04)	1.00 (0.89, 1.13)	1.10 (0.92, 1.32)	1.38 (1.03, 1.85)	0.02

Vitamin D intake in **typical amounts** was not statistically associated with risk of kidney stone formation.

However, higher risk with higher doses cannot be excluded

Take Home Messages -1

- Common disease causing fair amount of morbidity
 & large economic burden
- Systemic disease associated with HTN, Obesity, DM, CAD, Metabolic syndrome and bone disease
- Identifying risk factors is important
- Simple treatments –dietary & fluid modifications can slow or prevent stone development
- Increased fluid intake is first line of treatment for stone preventions



Take Home Messages -2

- Considerable variability in urine solute excretion, collection at home and work
- Stone risk increases even when chemistries are in "normal range"
- U chemistry can give insight in patients diet
- U pH is critical in management of Uric acid CaP, Cystine and Infection stones
- SS helps to identify type of stone and provide guidance for treatment



Questions?



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