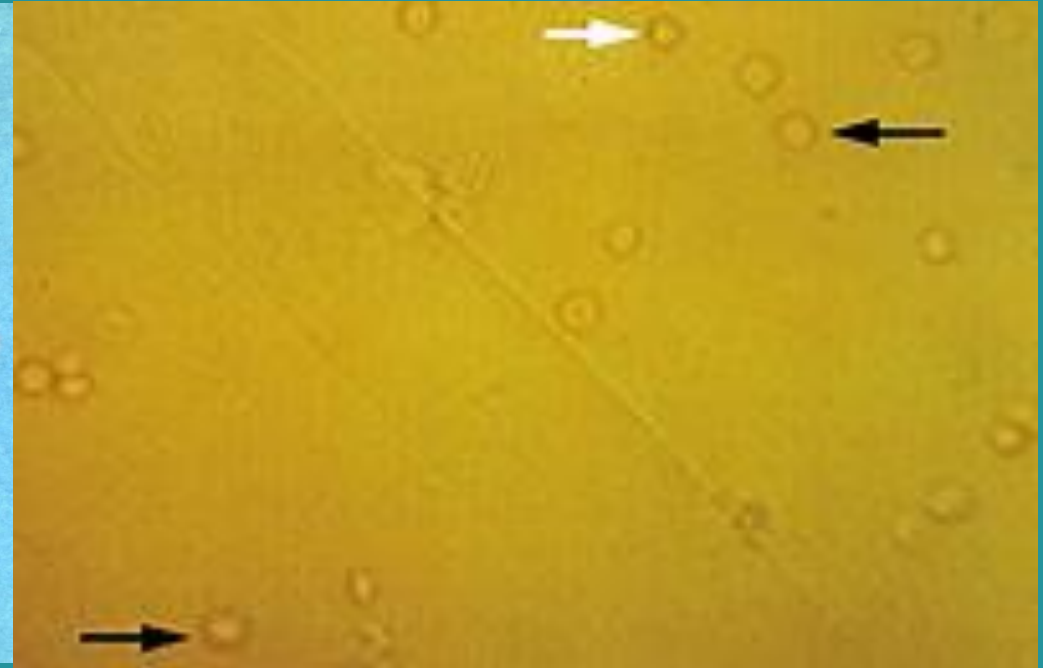
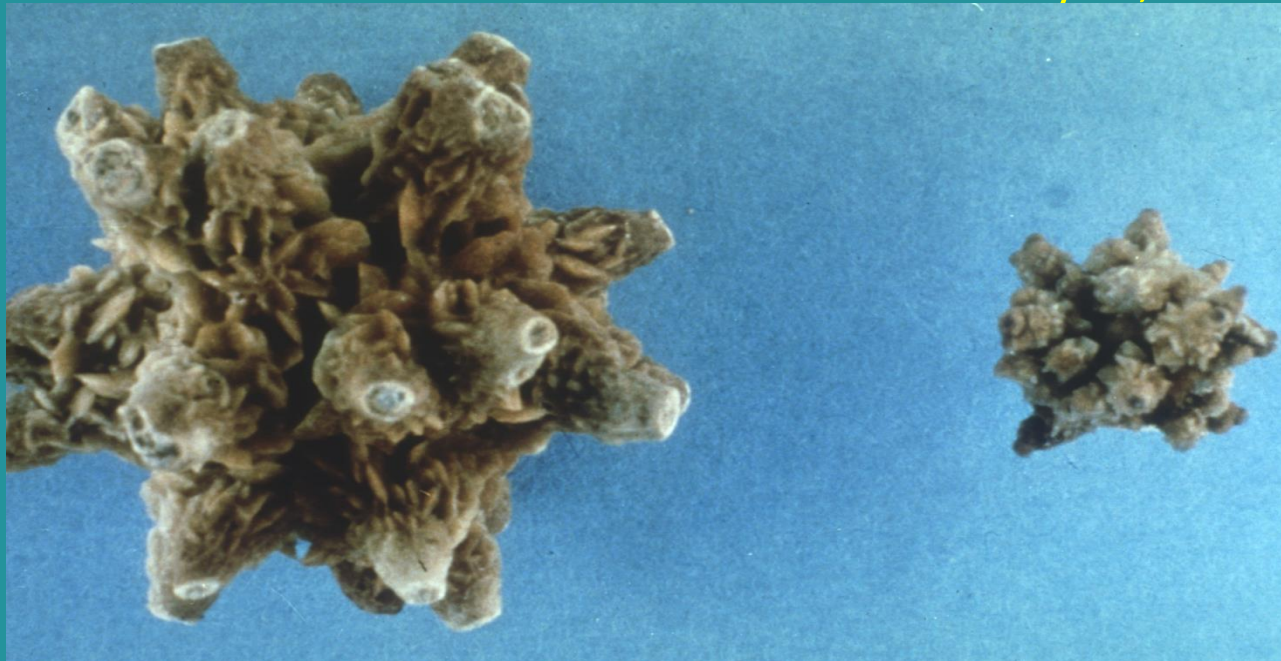


Nephrolithiasis and Hematuria

Academic Half Day
January 7, 2020



LEARNING OBJECTIVES: Nephrolithiasis

1. Explain what happens during each of the the stages of stone formation.
2. Understand the qualities of the 5 most common types of stones including precipitating factors, radiology findings, crystal appearance, and clinical associations.
3. Recommend methods of prevention and treatment of kidney stones.

NEPHROLITHIASIS

- Epidemiology
- Pathogenesis
- Clinical course
- Prevention of stones
 - Predisposing factors
 - Evaluation
 - Treatment

Epidemiology

Which of the following is not a predisposing factor for developing kidney stones?

- A. Vitamin D supplementation
- B. Low Body Mass Index
- C. Southeastern geography
- D. Urinary tract infections
- E. Gout

Epidemiology

Which of the following is not a predisposing factor for developing kidney stones?

- A. Vitamin D supplementation
- B. Low Body Mass Index
- C. Southeastern geography
- D. Urinary tract infections
- E. Gout

Epidemiology

- Prevalence: men 4-9%; women 1.7%-4.1%
- Hospital admissions: 7-10 of every 1000
- Hospitalization rates
 - 12% increase in # admissions for kidney stones in men
 - 21% increase in # admissions for kidney stones in women
- Historically ratio 1:3 women:men, now 1:1
- Increase in women possibly due to obesity and diet
- Rate of kidney stones has doubled from 1970s-1990s
- Peak age 20-30 years old
- Southeastern geography (More sunlight/vitamin D/heat/dehydration)

Predisposing Conditions

- Family history 20%
- Dehydration
- High protein diet
- Gout
- Metabolic syndrome
- Intestinal disorders causing malabsorption – Crohns or bariatric surgery (increased oxalate absorption)
- Medications (Topamax)
- Vitamin D and C
- Urinary tract infections
- Southwestern geography
- Hyperparathyroidism
- Cystinuria
- Renal tubular Acidosis

Epidemiology

What are the most common kidney stones in the United States?

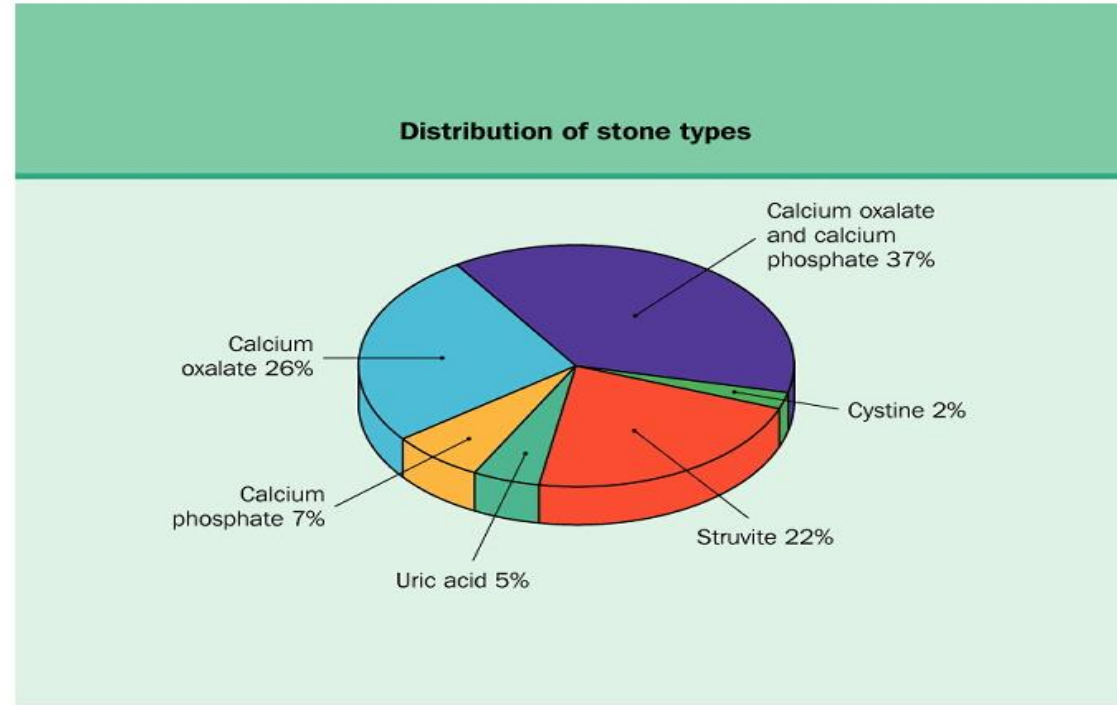
- A. Calcium oxalate
- B. Calcium phosphate
- C. Struvite
- D. Uric acid
- E. Cystine

Epidemiology

What are the most common kidney stones in the United States?

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- B. Calcium phosphate
- C. Struvite
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- E. Cystine

Frequency in US Population

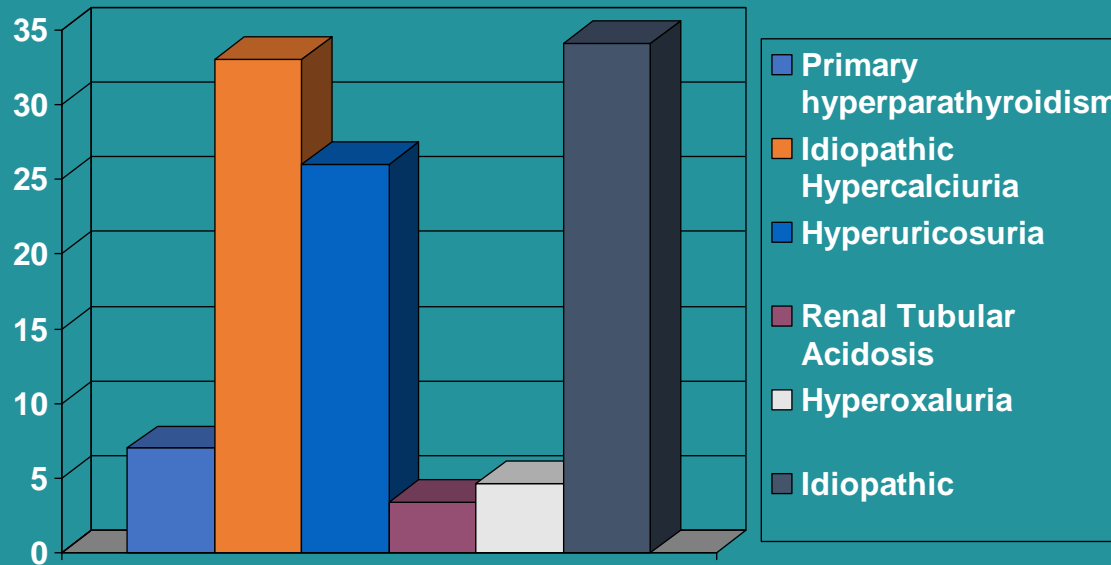


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Types of Stones: Frequency in Mediterranean and Middle Eastern countries

- 75% uric acid

Diseases Associated with Calcium Containing Renal Stones (n=1650)



Causes of Kidney Stones

Why does primary hyperparathyroidism cause nephrolithiasis?

- A. Increased calcium absorption in the gut
- B. Increased calcium absorption in the thick ascending loop of Henle
- C. Decreased distal tubular calcium absorption from the urine
- D. Decreased filtered load of calcium

Causes of Kidney Stones – PGY 3

Why does primary hyperparathyroidism cause nephrolithiasis?

- A. Increased calcium absorption in the gut
- B. Increased calcium absorption in the thick ascending loop of Henle
- C. Decreased distal tubular calcium absorption from the urine
- D. Decreased filtered load of calcium

Primary Hyperparathyroidism

- Increased calcium absorption in gut
- Increased distal tubular urinary absorption, but marked hypercalciuria because of
 - the increased filtered load of calcium
 - reduced calcium reabsorption in the thick ascending limb of the loop of henle.
- Treatment: surgical removal of adenoma – most patients don't get more stones, but up to half of them still have residual renal disease (calculi, nephrocalcinosis, uti, azotemia)

Idiopathic Hypercalciuria

- Diagnosis of exclusion - requires no sarcoidosis, no renal tubular acidosis, no hyperparathyroidism, no malignant tumors, no rapidly progressive bone disease, no immobilization, no paget disease, cushing disease, or furosemide administration.
- Polygenic disorder with regulation by 2 codominant alleles.

Idiopathic Hypercalciuria

- Pathogenesis involves excessive intestinal calcium absorption and depressed renal tubule calcium reabsorption
- Patients are in net negative calcium balance, suggesting bone loss of calcium.
- Increased activity of Ca-Mg-ATPase in the intestine and distal tubule
- Stone formers have decreased bone mineral density, compared to non-stone formers, suggesting bone demineralization as an etiology.

Hyperuricosuria

- Uric acid crystals plug the lumen of renal collecting duct and act as a nucleus for calcium stone formation.
- Treatment with allopurinol
 - 3 year prospective randomized trial of hyperuricosuric, normocalciuric calcium oxalate stone formers: 70% allopurinol patients remained stone free at 3yrs, vs. 40% placebo.

Type 1 Distal Renal Tubular Acidosis

- Stones result from hypercalciuria, hypocitraturia, and alkaline urine pH; stones are usually calcium phosphate.
- High urine pH increases the availability of phosphate.
- Metabolic acidosis, hypokalemia, and renal insufficiency decreases citrate excretion.
 - Hypokalemia reduces urine citrate by generating an intracellular acidosis in the proximal tubular cell.

Natural History

A 25 year old woman comes to the office for evaluation after she was recently in the emergency room for renal colic. She passed the kidney stone and KUB showed no more visible stones.

What is the likelihood that she will form another stone sometime during her life?

- A. 10%
- B. 30%
- C. 50%
- D. 75%

Natural History

A 25 year old woman comes to the office for evaluation after she was recently in the emergency room for renal colic. She passed the kidney stone and KUB showed no more visible stones.

What is the likelihood that she will form another stone sometime during her life?

- A. 10%
- B. 30%
- C. 50%
- D. 75%

Natural History: Will the first stone recur?

YES

Recurrence is the rule after the 1st stone

- 40-50% recur by 5 years
- 50-60% recur by 10 years
- 75% recur by 20-30 years

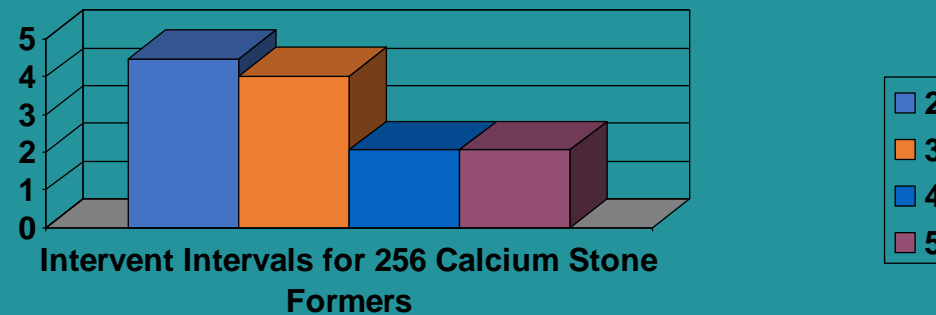
There is no way to distinguish by laboratory evaluation who will recur.

Natural History:

Will stone disease get better over time?

NO, in general.

Stone disease accelerates over time in the majority of patients (stone-free intervals shorten over time)



Pathogenesis – Stages of Stone development

- Supersaturation
- Nucleation (ions join together in more stable, solid phase)
- Aggregation (small crystals bond together)
- Anchoring (via stone-epithelial cell interactions) facilitates aggregation in limited time

Supersaturation: factors

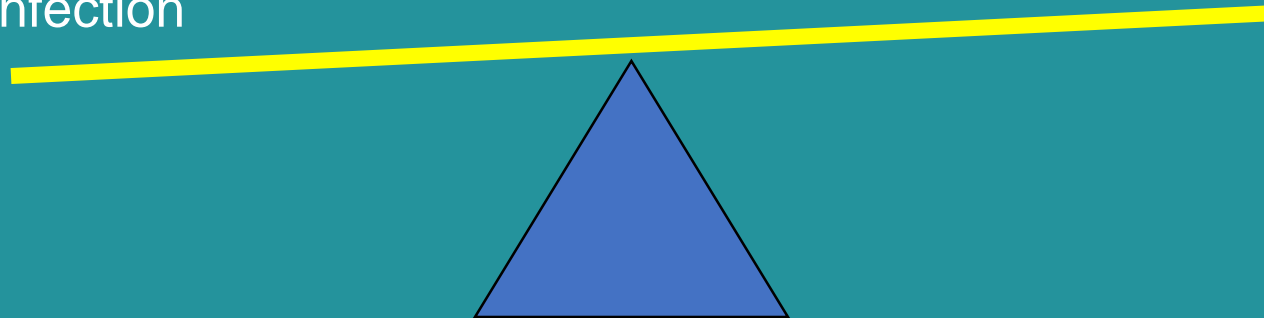
- Ion excretion
 - Calcium
 - Oxalate
 - Phosphate
- Water excretion
- Interaction with other solutes
 - Citrate binds calcium
 - Magnesium complexes oxalate
- pH alters free ion concentration by adding hydrogen ion to the circulating free ion
 - i.e. mono vs dihydrogen phosphate

Pro-Stone Forces

- Calcium
- Uric Acid
- Oxalate
- Cystine
- Infection

Stone Inhibitors

- Volume (dilution)
- Citrate
- Alkaline urine



Nucleation

- Ions join together in a more stable solid phase
- Surface irregularities create a surface on which crystal nuclei start to form.
- Some crystals are efficient at matching together
 - Monosodium urate/uric acid are good heterogenous nuclei for calcium oxalate.
 - Brushite nuclei nucleate calcium oxalate
 - Calcium phosphate nucleates calcium oxalate

Aggregation

- Small crystals aggregate into larger crystalline masses by electrostatic attraction.

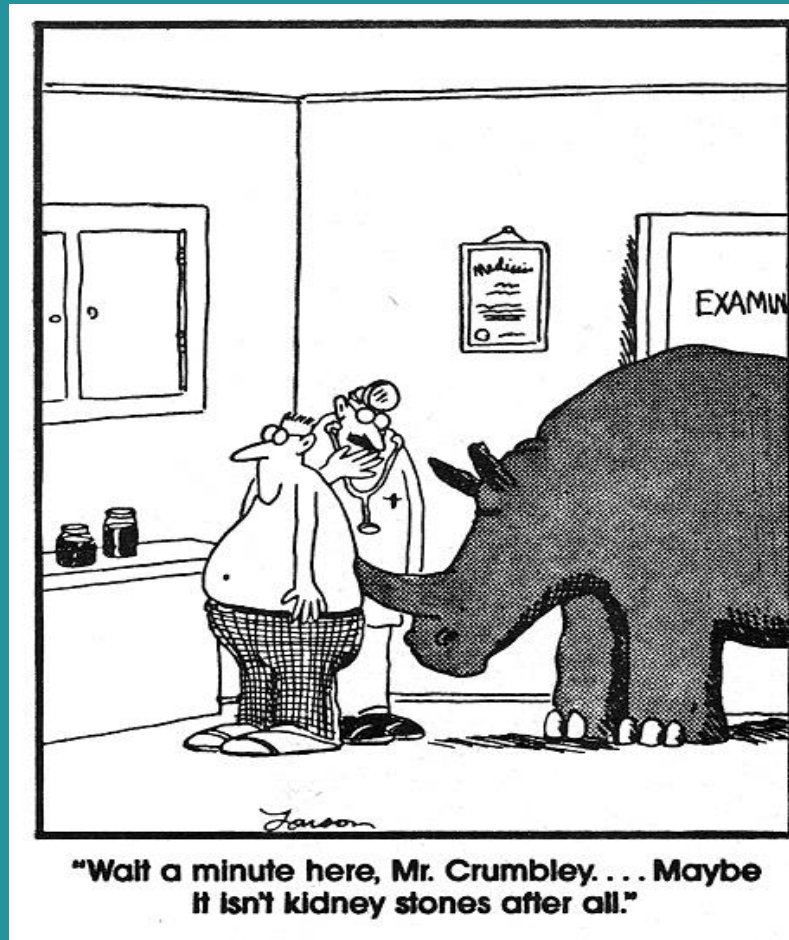
Anchoring

- Cell-Crystal interactions
 - crystals cannot form fast enough to wedge into the tubules and cause obstruction, they must anchor to renal tubular epithelium or urothelium
 - these cells can act as nucleating sites

Clinical Presentations

- Pain (ureteral colic, loin pain, dysuria)
- Hematuria
- Urinary tract infection (recurrent, chronic infection)
- Asymptomatic urine abnormality (microscopic hematuria, proteinuria, sterile pyuria)
- Interruption of urinary stream
- Calculus anuria

Differential Diagnosis of Flank Pain



Basic Evaluation of Stone Formers (1st stone)

- Stone history
- Medical history
 - Diseases leading to hypercalcemia (malignancy, hyperparathyroidism, sarcoidosis)
 - Malabsorptive GI disorders (Crohn's, celiac sprue)
 - Gout
- Family History
 - Idiopathic hypercalciuria (multiple genes identified)
 - Cystinuria (AR)
 - Hyperuricosuria
 - X-linked causes of calcium stones and nephrocalcinosis
 - Primary hyperoxaluria (AR)

Basic Evaluation of Stone Formers (1st stone)

- Medications
 - Loop diuretics, vitamin D, glucocorticoids, antacids, theophylline, acetazolamide, amphotericin B (calcium)
 - Salicylates, probenecid (uric acid)
 - Allopurinol (xanthine)
 - Acyclovir, triamterene, indinavir (precipitation into stones)
- Social history (jobs resulting in volume depletion)
- Dietary history

Dietary History

High oxalate foods

- green beans
- Beets
- Celery
- Green onions
- Leeks
- Leafy greens
- Cocoa/chocolate
- Black tea
- Berries
- Orange & lemon peel
- Dried figs
- Summer squash
- Nuts, peanut butter
- Tofu

High purine foods

- Organ meats
- Shellfish
- Meat
- Fish
- Meat extracts
- Gravies
- Asparagus
- Cauliflower
- Peas
- Spinach
- Mushrooms
- Beans (lima, kidney, lentils)

Risk Reduction

A 44-year-old man with a history of nephrolithiasis requests nonpharmaceutical interventions for stone prevention.

His last symptomatic kidney stone was 2 years ago. He does not recall the exact type of stone that he formed but believes that it contained calcium. Previous laboratory studies have showed normal renal function and normal levels of calcium, phosphorus, and uric acid.

A plain abdominal radiograph performed 1 year ago revealed no genitourinary calcifications.

He does not have a family history of nephrolithiasis wishes to reduce his chances of developing further kidney stones.

In addition to increasing fluid intake, which of the following recommendations is warranted?

- A. Calcium intake >1 g/d
- B. A high sodium diet
- C. A high protein diet
- D. Furosemide
- E. Reducing potassium intake

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- E. Reducing potassium intake

VARIABLE	DIETARY INTAKE*					CHI (P FOR TREND)†
	GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 5	
Animal-protein intake (g/day)	≤50	51–58	59–66	67–76	≥77	—
Incidence/100,000 person-yr	293	264	370	271	326	—
No. of cases	98	85	130	86	106	
Age-adjusted RR‡	1.0	0.90	1.26	0.92	1.11	0.80 (0.68)
95% CI		0.68–1.21	0.97–1.64	0.69–1.24	0.85–1.47	
Multivariate RR‡	1.0	0.97	1.41	1.07	1.33	1.99 (0.05)
95% CI		0.73–1.31	1.08–1.85	0.79–1.44	1.00–1.77	
Potassium intake (mg/day)	≤2895	2896–3252	3253–3592	3593–4041	≥4042	—
Incidence/100,000 person-yr	432	365	291	262	184	—
No. of cases	142	116	99	89	59	
Age-adjusted RR‡	1.0	0.83	0.68	0.60	0.43	–6.21 (<0.001)
95% CI		0.65–1.06	0.52–0.87	0.46–0.79	0.32–0.58	
Multivariate RR‡	1.0	0.88	0.74	0.69	0.49	–4.35 (<0.001)
95% CI		0.68–1.14	0.56–0.97	0.52–0.92	0.35–0.68	
Fluid intake (ml/day)	<1275	1275–1669	1670–2049	2050–2537	≥2538	—
Incidence/100,000 person-yr	372	386	307	270	192	—
No. of cases	117	129	101	90	68	
Age-adjusted RR‡	1.0	1.05	0.82	0.72	0.52	–4.87 (<0.001)
95% CI		0.81–1.34	0.63–1.07	0.55–0.95	0.39–0.70	
Multivariate RR‡	1.0	1.16	0.95	0.89	0.71	–2.95 (0.003)
95% CI		0.90–1.49	0.72–1.25	0.67–1.18	0.52–0.97	

*Group 1 had intake values below the first quintile for the group (lowest intake), group 2 values between the first and second quintiles, group 3 values between the second and third quintiles, group 4 values between the third and fourth quintiles, and group 5 values above the fourth quintile (highest intake).

†A chi value of more than 1.96 denotes a P value of less than 0.05. The sign of the chi value indicates the direction of the trend.

‡RR denotes relative risk as compared with the group with the lowest intake, and CI confidence interval. The multivariate model included age (in five-year age categories), profession, use of thiazide diuretics (yes or no), alcohol (eight categories), and dietary intake of calcium, animal protein, potassium, and total fluid (quintile groups).

Calcium intake

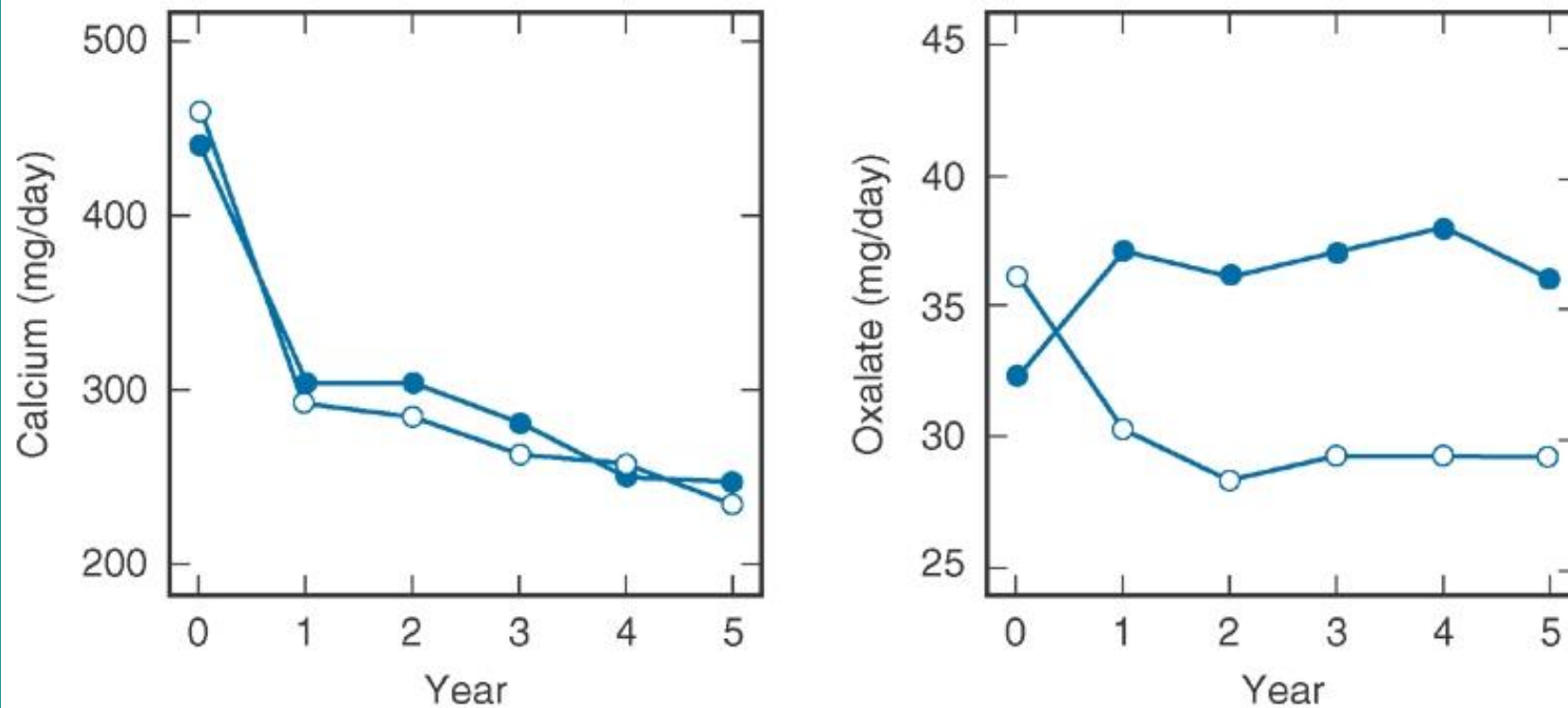
VARIABLE*	DIETARY CALCIUM†					CHI (P FOR TREND)‡
	GROUP 1 (N = 8861)	GROUP 2 (N = 9029)	GROUP 3 (N = 9106)	GROUP 4 (N = 9184)	GROUP 5 (N = 9330)	
Dietary calcium intake (mg/day)	<605	605–722	723–848	849–1049	≥1050	—
Incidence/100,000 person-yr	435	310	279	266	243	—
No. of cases	139	102	93	89	82	
Age-adjusted RR	1.0	0.71	0.64	0.61	0.56	–4.37 (<0.001)
95% CI		0.55–0.92	0.50–0.83	0.47–0.80	0.43–0.73	
Multivariate RR	1.0	0.74	0.68	0.68	0.66	–2.38 (0.018)
95% CI		0.57–0.97	0.52–0.90	0.51–0.90	0.49–0.90	

*RR denotes the relative risk as compared with the group with the lowest calcium intake, and CI confidence interval. The multivariate model included age (in five-year age categories), profession, use of thiazide diuretics (yes or no), alcohol (eight categories), and dietary intake of animal protein, potassium, and fluid (quintile groups).

†Group 1 had dietary calcium values below the first quintile for the group (lowest intake), group 2 values between the first and second quintiles, group 3 values between the second and third quintiles, group 4 values between the third and fourth quintiles, and group 5 values above the fourth quintile (highest intake).

‡A chi value of more than 1.96 denotes a P value of less than 0.05. The sign of the chi value indicates the direction of the trend.

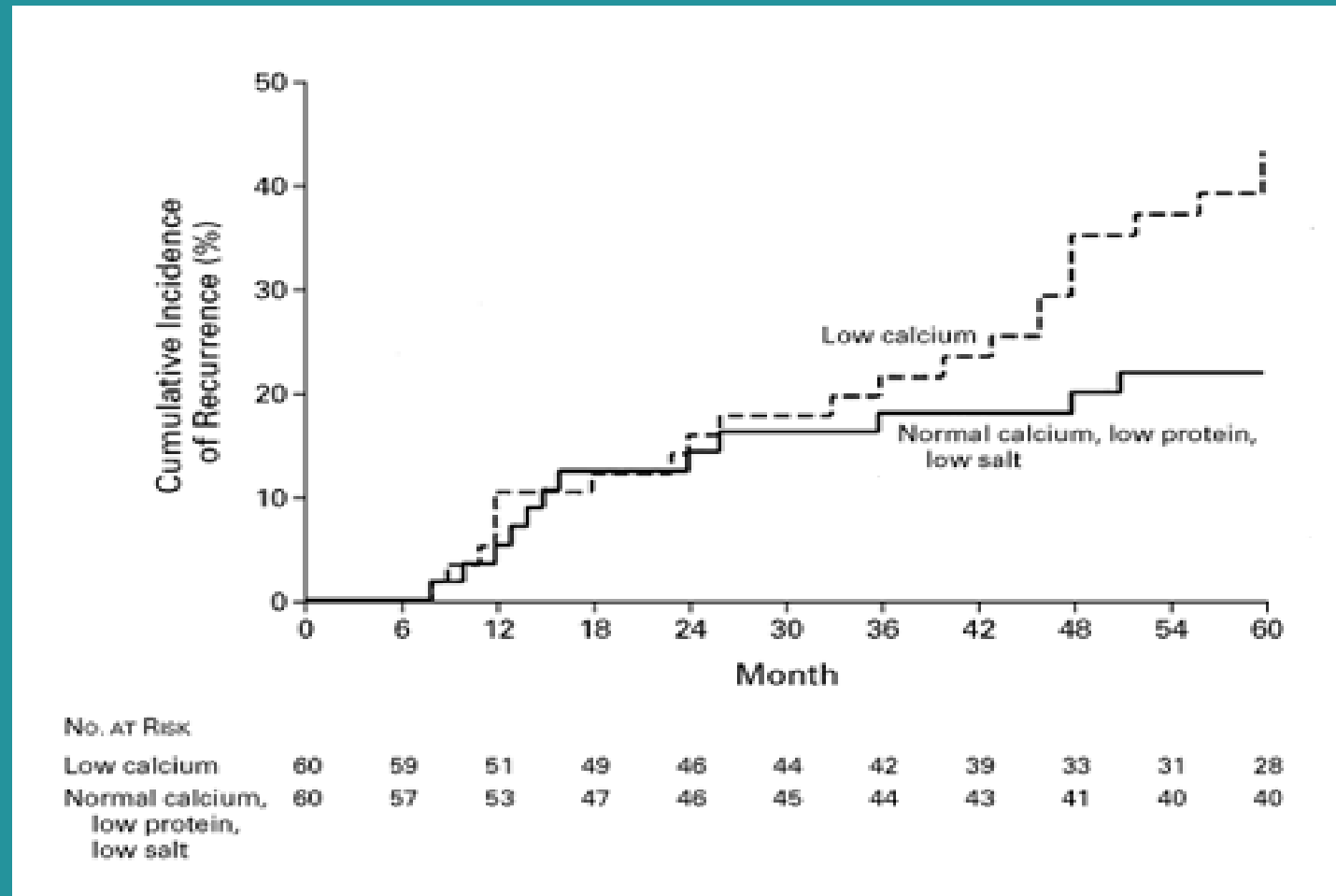
Calcium intake



The effects of a low-calcium diet vs. a normal-calcium, low-sodium, low-protein diet on urine chemistries. In a 5-year randomized prospective study of the effects of dietary intervention on stone formation, patients treated with a normal-calcium, low-sodium, low-protein diet (*open symbols*) had a similar reduction in urine calcium compared with patients given a low-calcium diet (*closed symbols*). However, the subjects on the low-calcium diet had an increase in urine oxalate, whereas those on the normal-calcium, low-sodium, low-protein diet had a decrease in urine calcium.

(Data from Borghi L, Schianchi T, Meschi T, et al: Comparison of two diets for the prevention of recurrent stones in idiopathic hypercalciuria. *N Engl J Med* 346:77-84, 2002.)

Calcium, protein, and salt intake



Laboratory evaluation

- Urinalysis
 - pH
 - High with struvite/calcium phosphate stones
 - Low with uric acid and calcium oxalate stones
 - Specific gravity to assess adequacy of fluid intake
 - RBCs
 - Characteristic crystals

Calcium Oxalate



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Uric Acid



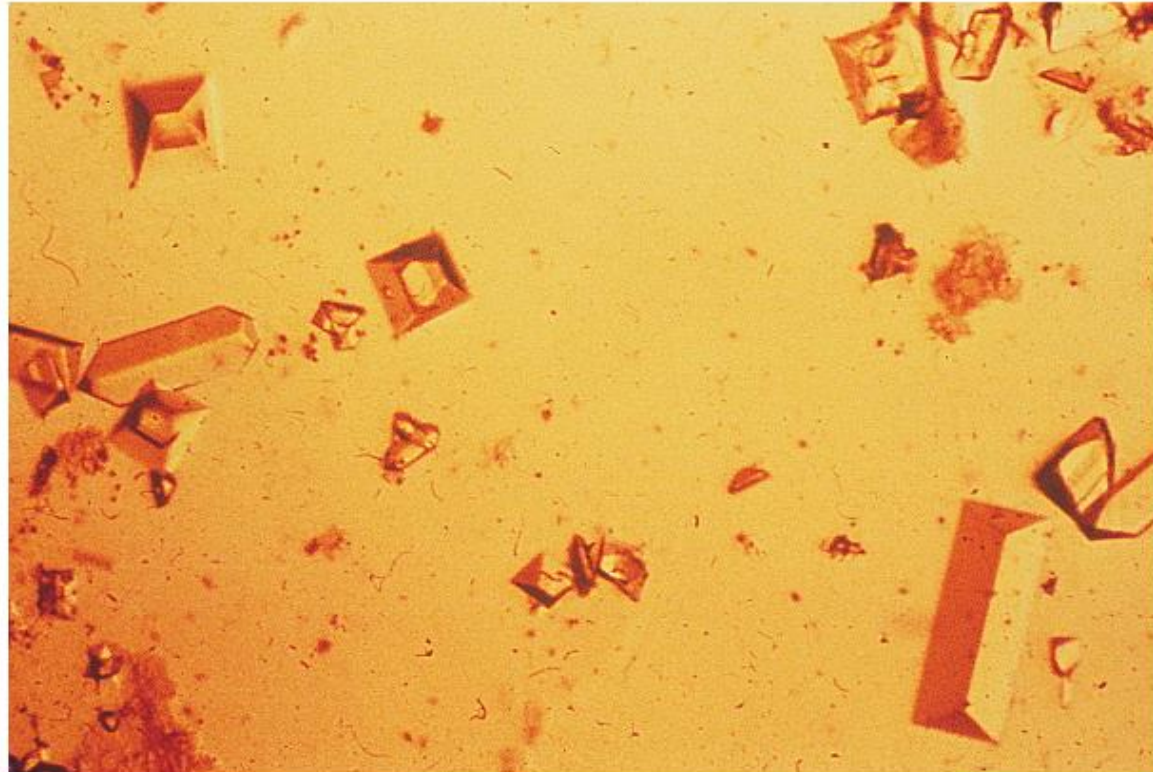
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Cystine



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Magnesium ammonium phosphate (struvite)



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Laboratory evaluation

- Blood test (electrolytes, calcium, uric acid, phosphorus, creatinine)
- Stone analysis when possible

Evaluation

A 49-year-old man with a history of gouty arthritis comes for a follow-up evaluation. One week ago, he was evaluated in the emergency department for left-sided flank pain and hematuria.

A plain abdominal radiograph is unremarkable. After radiography is performed, the patient urinates debris and his pain is immediately relieved.

He has had no further symptoms.

Laboratory Data

Blood urea nitrogen 12 mg/dL

Uric acid 9.0 mg/dL

Creatinine 1.0 mg/dL

Sodium 138 meq/L

Potassium 4.6 meq/L

Bicarbonate 26 meq/L

Albumin 4.0 mg/dL

Calcium 10.1 mg/dL

Phosphorus 2.1 mg/dL

Urinalysis pH 5, 3+ blood, 10–15 erythrocytes/hpf

Which of the following is the most likely diagnosis?

- A. Calcium oxalate stones
- B. Uric acid stones
- C. Calcium phosphate stones
- D. Struvite calculi
- E. Cystine stones

Which of the following is the most likely diagnosis?

- A. Calcium oxalate stones
- B. Uric acid stones
- C. Calcium phosphate stones
- D. Struvite calculi
- E. Cystine stones

Radiologic evaluation

- KUB (uric acid and xanthine calculi are radiolucent)
- IV urogram (can show anatomic abnormalities in GU tract)
- CT scan (high sensitivity and specificity)
- Renal ultrasound (misses ureteral stones)



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Multiple cystine stones in r kidney, ureter, and bladder

Johnson J and Feehally J, *Comprehensive Clinical Nephrology*, 2nd ed.



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Struvite stones; L staghorn calculus; single bladder stone

Johnson J and Feehally J, *Comprehensive Clinical Nephrology*, 2nd ed.

Complete Evaluation (for >1 stone)

24 hour urine for:

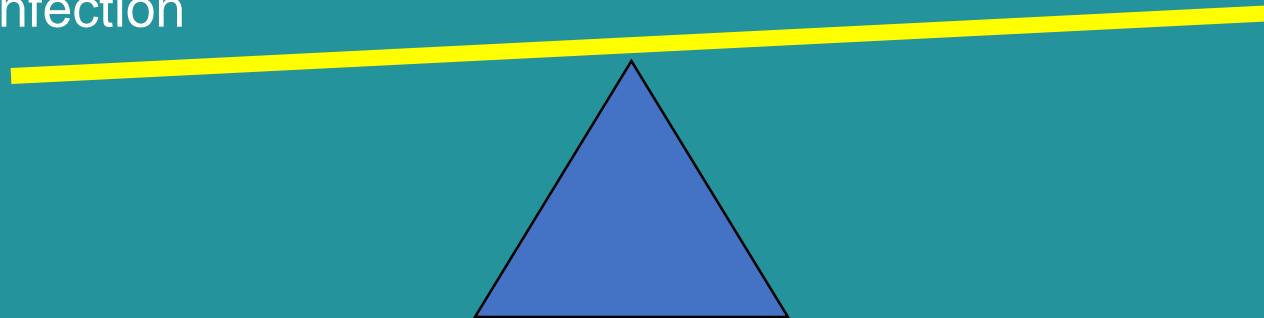
- Volume
- pH
- Calcium
- Phosphate
- Sodium
- Uric acid
- Oxalate
- Citrate
- Creatinine

Pro-Stone Forces

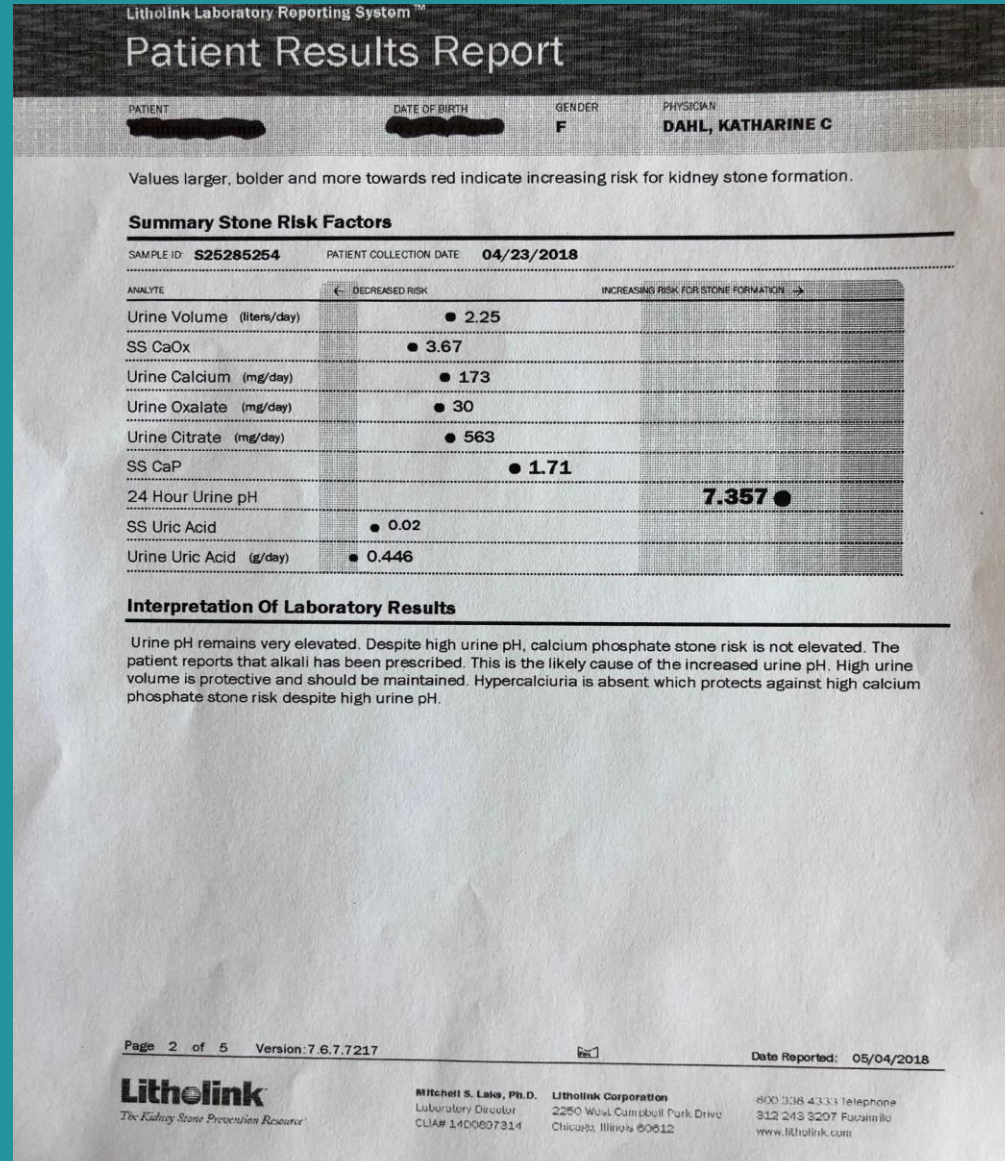
- Calcium
- Uric Acid
- Oxalate
- Cystine
- Infection

Stone Inhibitors

- Volume (dilution)
- Citrate
- Alkaline urine



Stone Risk Profile



Stone Risk Profile

Patient Results Report

PATIENT: [REDACTED] DATE OF BIRTH: [REDACTED] GENDER: [REDACTED] PHYSICIAN: **DAHL, KATHARINE C**

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 (10/18/2010)

DATE	SAMPLE ID	Vol 24	SS CaOx	Ca 24	Ox 24	Cit 24	SS CaP	pH	SS UA	UA 24
04/23/18	S25285254	2.25	3.67	173	30	563	1.71	7.357	0.02	0.446
02/04/11	S807099	2.38	6.28	391	29	621	3.30	6.603	0.11	0.426
10/15/10	S736850	3.03	3.49	373	21	432	1.30	6.248	0.21	0.503
10/14/10	S736849	2.50	3.63	294	18	290	0.79	5.942	0.32	0.350
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
04/23/18	S25285254	133	99	130	0.663	7	125	27	7.54	
02/04/11	S807099	117	102	98	1.133	14	129	40	9.38	1.1
10/15/10	S736850	143	68	108	0.984	20	155	46	9.32	1.1
10/14/10	S736849	111	51	93	0.836	18	123	35	7.50	0.9
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
04/23/18	S25285254		1150			150
02/04/11	S807099	63.5	961	15.1	6.2	407
10/15/10	S736850	63.5	1022	16.1	5.9	365
10/14/10	S736849	63.5	939	14.8	4.6	312
REFERENCE RANGE			male 18-24 female 15-20	<4	<4	<140

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Litholink
The Kidney Stone Prevention Resource

Mitchell S. Lake, Ph.D.
Laboratory Director
CLIA# 14D0607314

Litholink Corporation
2250 West Cuneen Hill Park Drive
Chicago, Illinois 60612

800.338.4333 Telephone
312.248.8207 Facsimile
www.litholink.com

Evaluation

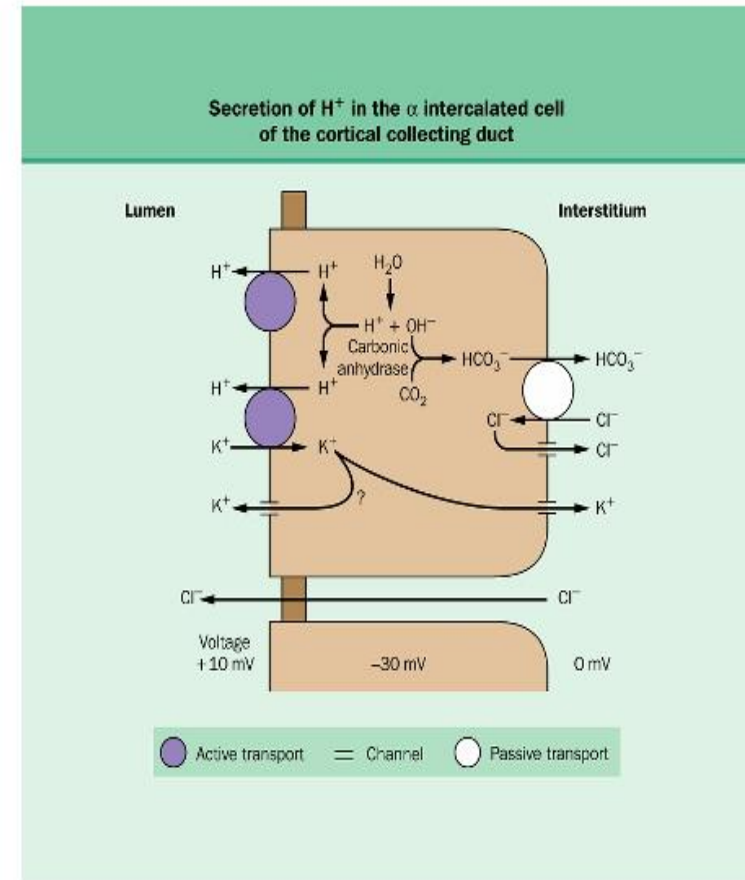
A 54 year old woman with Sjogren Syndrome comes to the office for evaluation of nephrolithiasis. Her potassium is 3.2, bicarbonate 12. You diagnose her with a distal type 1 renal tubular acidosis. What will her urine pH will be?

- A. 4.5
- B. 6.0
- C. 7.5

In a Type 1 Distal Renal Tubular Acidosis, there is a failure of the α -intercalated cell to secrete H^+ ions and reclaim K^+ ions.

A 54 year old woman with Sjogren Syndrome comes to the office for evaluation of nephrolithiasis. Her potassium is 3.2, bicarbonate 12. You diagnose her with a distal type 1 renal tubular acidosis. What do you think her urine pH will be?

- A. 4.5
- B. 6.0
- C. 7.5



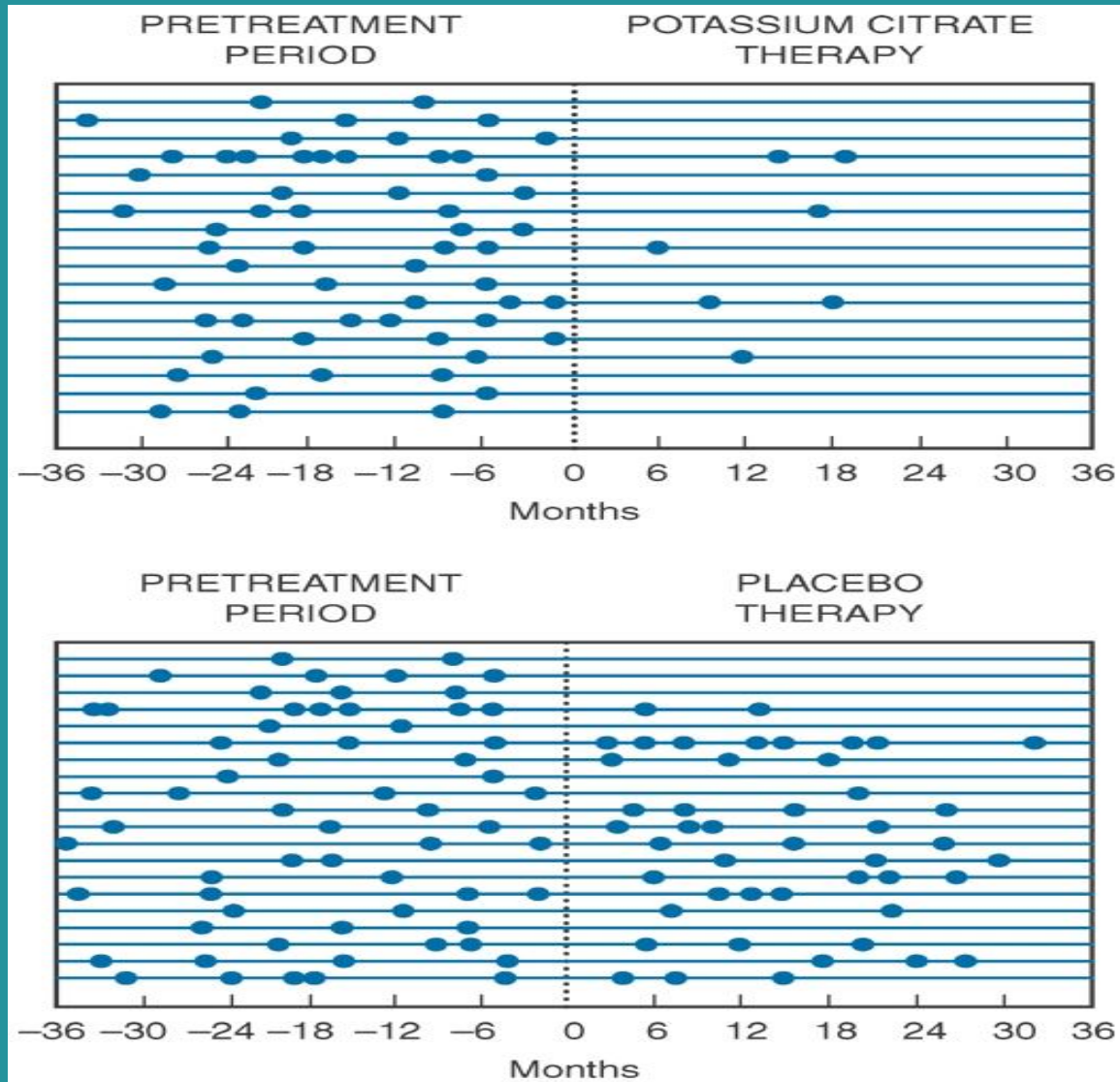
Prevention - Dietary Modifications

- Fluid intake urine output > 2L/day
- Calcium intake > 1gm/day
- Sodium intake avoid excess (2g/day)
- Protein intake moderation(0.8-1g/kg/day)

Treatment of Specific Forms of Stone Disease: hypercalciuria

- Thiazide diuretic
- Potassium citrate (Urocit-K 20-40mmol daily)

Of note: both therapies have been effective in patients that are not hypercalciuric or hypocitraturic.



Effect of potassium citrate therapy (upper panel) vs. placebo (lower panel) on hypocitraturic calcium oxalate stone disease. Each line represents a single patient and each dot represents a new stone formation.

(From Barcello P, Wuhl O, Servitge E, et al: Randomized double-blind trial of potassium citrate in idiopathic hypocitraturic calcium nephrolithiasis. *J Urol* 150: 1761-1764, 1993.)

Prevention

A 25-year-old man with a history of active Crohn's disease with several small-bowel resections is evaluated for recurrent calcium oxalate kidney stones. He typically passes three to four stones each year and he becomes incapacitated during acute attacks. He requests further therapy for stone prevention.

A plain abdominal radiograph is obtained in the office and reveals no calcifications in the genitourinary tract.

Laboratory data

Uric acid 6.8 mg/dL

Blood urea nitrogen 10 mg/dL

Creatinine 0.8 mg/dL

Sodium 139 meq/L

Potassium 4.3 meq/L

Bicarbonate 25 meq/L

Calcium 9.9 mg/dL

Phosphorus 2.2 mg/dL

Urinalysis pH 5.0, no blood or protein

In addition to increasing fluid intake, which of the following recommendations is warranted?

- A. Calcium intake >1 g/d
- B. A high sodium diet
- C. A high protein diet
- D. Furosemide, 40mg/day

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Treatment of Specific Forms of Stone Disease: hyperoxaluria

Humans cannot metabolize oxalate, so renal excretion is the major form of oxalate elimination.

Dietary/enteric hyperoxaluria

- Avoid high oxalate foods
- Calcium carbonate with meals to bind oxalate
- Magnesium gluconate or magnesium oxide serves as urinary stone inhibitor

Primary hyperoxaluria

- Liver transplant (replace defective enzyme)
- Pyridoxine (vit B6) – decreases production of oxalate
- Raise urinary pH
- Magnesium, potassium citrate, orthophosphate – decrease supersaturation of phosphate

Treatment of Specific Forms of Stone Disease: hypocitraturia

- Avoid/treat things that cause hypocitraturia
 - Excess protein intake
 - Hypokalemia
 - Metabolic acidosis
 - Exercise
 - Hypomagnesemia
 - Infections
 - Androgens
 - Starvation
 - Acetazolamide
- Potassium citrate 15-25mmol, 2-3 tabs/day

Treatment of Specific Forms of Stone Disease: Distal RTA

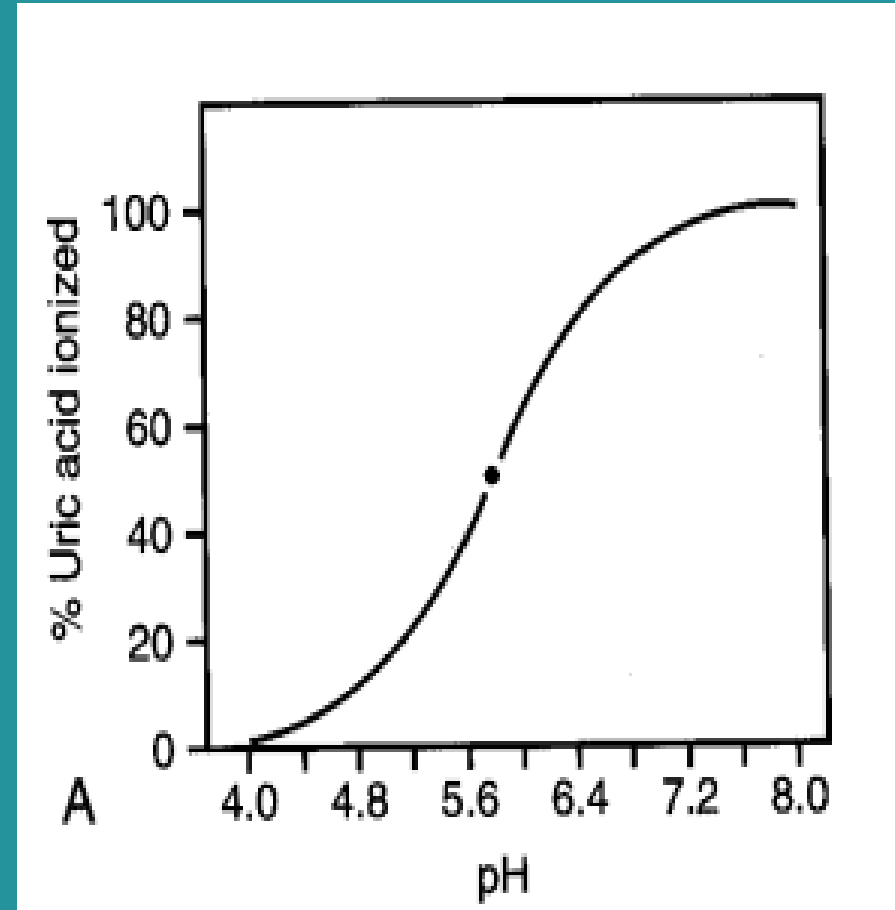
- In distal renal tubular acidosis – defect in distal tubular excretion of hydrogen ions
 - results in non-anion gap metabolic acidosis
 - Causes calcium/phosphate to be released from the bone
 - Increase in citrate reabsorption in proximal tubule
 - High urine pH, hypocitraturia, increased renal excretion of calcium and phosphate
- Treatment: Large amounts of base (1-2mmol/kg daily)
 - Sodium citrate/bicarbonate
 - Potassium citrate/bicarbonate

Treatment of Specific Forms of Stone Disease: Hyperuricosuria

- Hyperuricosuria contributes to calcium oxalate nephrolithiasis in 10-15% calcium stones.
- Increased fluid intake
- Low-purine diet
- If uric acid level high, allopurinol

Uric Acid Stones

- Difference between stone formers and non-former is urine pH (low=stone formation)
- There is no difference in uric acid excretion



Uric Acid Stones: treatment

- Increase urine volume, pH
- Alkaline urine can even result in stone dissolution
- Acetazolamide
- Avoid pH above 7; it may result in calcium phosphate precipitation
- Low-purine, low protein diet
- May need allopurinol

Prevention

A 56-year-old woman is evaluated for recurrent urinary tract infections. Three weeks ago, she had a urinary tract infection with *Klebsiella*, and she has had four previous *Proteus* urinary tract infections over the past 6 months.

Physical examination is unremarkable. Urinalysis is significant for leukocyte esterase and 2+ blood, and urine pH is 7.5. Abdominal CT reveals a 5-cm staghorn calculus in the left kidney.

In addition to increasing fluid intake, which of the following is the most appropriate therapy in this setting?

- A. Potassium citrate
- B. Allopurinol
- C. Antibiotics
- D. Low calcium diet

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Struvite Stones

- Grow rapidly, develop staghorn calculi
- Require the presence of urease-producing bacteria in the urine (protease, e. coli, are the most common but even mycoplasma can cause)

Struvite Stones: treatment

- Antibiotic, may need chronic suppression
- Early urological intervention
- Stones <2cm can try ESWL
- Percutaneous nephrolithotomy for larger stones.
- Urease inhibitors (acetohydroxamic acid)
- Preferred treatment – surgical removal
- Nephrectomy is required in 50% of untreated staghorn calculi.

Cystine Stones

- Cystinuria; rare hereditary disorder
 - Prevalence: 1 in 15,000
 - Accounts for 1% of stones.
 - Stone recurrence common: a stone forms every 1-4yrs.
 - Defect in tubular transport protein, resulting in increased cystine excretion and accumulation in the renal tubules.
- Cystine is poorly soluble
- Urinary tract obstruction and infection are common.

Cystine Stones: treatment

- UOP > 4L day
- Alkalinization of the urine
- Low sodium diet
- D-Penicillamine or tiopronin both bind cystine and reduce urinary supersaturation
- Staghorn calculi common – lithotripsy often needed.

Summary: Evaluation

- 1st stone: history, urinalysis, chemistries, imaging
- Recurrent stone: 24 hour analysis of urine for risk factors
- Treat based on results of 24 hour urine

Summary of Preventative Treatments

- Dietary modification.
 - Increase fluids, low sodium, low protein, high potassium, normal calcium intake
- Thiazides for hypercalciuria.
- Potassium citrate for hypocitraturia.
- Allopurinol for hyperuricosuria.
- Tiopronin for cystinuria.

Management

A 45 year old man comes to the ER with renal colic. A CT scan shows a 5mm stone in his mid-ureter. What is the approximate likelihood that his stone will pass without intervention?

- A. 25%
- B. 50%
- C. 75%
- D. 100%

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The Patient in the ER...

Indication for surgical intervention

- Size
 - 80% of stones <4mm will pass
 - 50% of stones 5mm will pass
 - If stone >7mm, unlikely to pass
- Location
 - 70% distal ureteral stones will pass
 - 45% mid ureteral stones will pass
 - 25% proximal ureteral stones will pass
- If active pain >72 hrs despite analgesia
- Persistent obstruction with risk of renal impairment
- Urinary tract sepsis

Shock Wave Lithotripsy

- Highly effective.
- Persistent stone fragments (larger/more stones).
- Reversible impairment in RPF and GFR.
- Permanent damage after 3 lithotripsies
- Subcapsular hemorrhage and hematoma.
- Hypertension?

Pig Kidney Post-ESWL



Willis et al., JASN, 1999.

Ureteroscopy with laser lithotripsy

- Higher rate of stone fragmentation and passage
- Don't have the GFR impairment of ESWL
- Complications of procedure (perforation, etc)

HEMATURIA LEARNING OBJECTIVES

1. Know the differential diagnosis for hematuria
2. Distinguish between glomerular hematuria, extraglomerular hematuria, and heme-positive urine without hematuria.
3. Understand the workup for incidentally found hematuria

Differential Diagnosis of Hematuria

- Nephrolithiasis
- Infection
- Malignancy (renal cell carcinoma, transitional cell carcinoma, prostatic carcinoma, Wilms' tumor)
- Trauma
- Glomerular disease
- Interstitial nephritis
- Polycystic kidney disease
- Papillary necrosis
- Medullary sponge kidney
- Coagulopathy
- Miscellaneous (loin pain hematuria syndrome, avm's, chemical cystitis)

Hematuria

- Presence of blood or intact cells in the urine
- A very alkaline urine or a urine with very low specific gravity can cause RBC to lyse
- RBC can enter the urine anywhere from the glomerulus to the urethra
- Reagent strips can detect 1-2 RBC/hpf
- Greater than 2 RBC/hpf considered abnormal

Hemoglobinuria

- Hemoglobinuria –presence of free hemoglobin in the urine as a result of intravascular hemolysis

May lead to kidney damage – Acute Tubular Necrosis from heme pigment

Blood

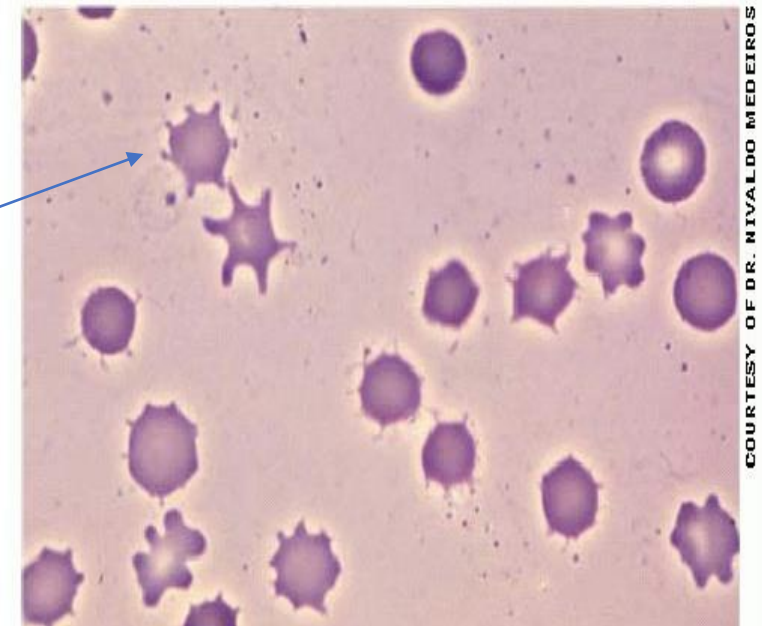
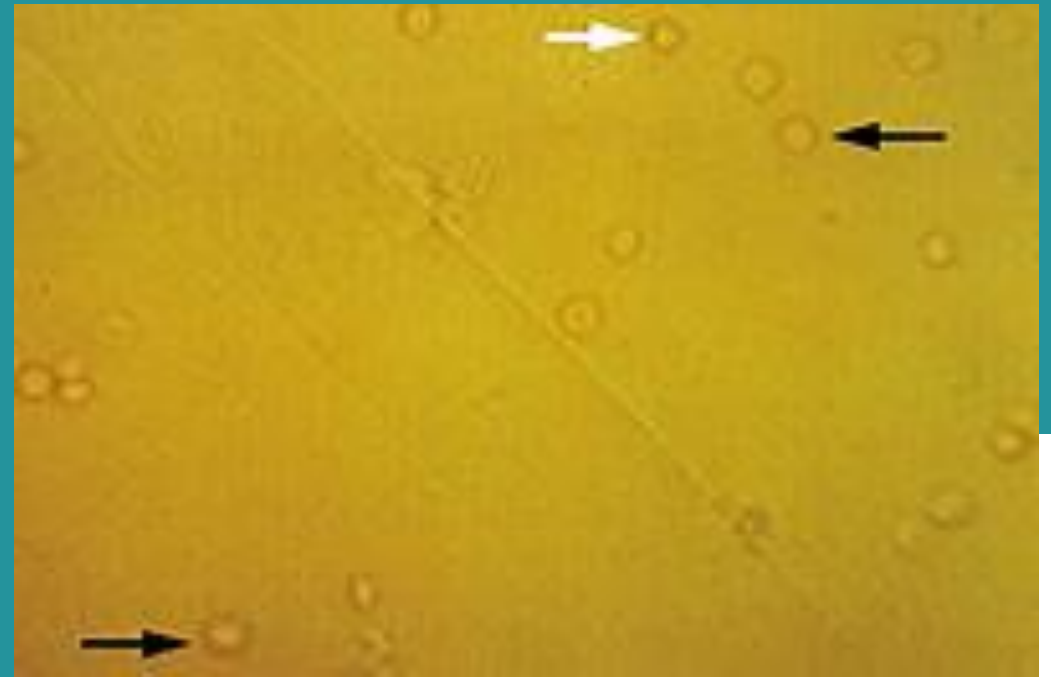
- Dipstick measures peroxidase activity
 - **Free hemoglobin – hemolysis**
 - Intact erythrocytes
- 1-3 erythrocytes/hpf needed for positive result
- False positives
 - **Myoglobin**
 - Bacteria that express pseudoperoxidase activity: Enterobacter, Staphylococci, Streptococci species
 - Hypochlorite
 - Rifampin
 - Chloroquin
 - Iodine
 - Alkaline urine
 - Low specific gravity
 - Semen
 - Oxidizing agents to clean the perineum
- False negatives
 - Ascorbic acid
- Blood on urine dipstick with no RBCs on microscopy raises suspicion for:
 - **Rhabdomyolysis (myoglobin) positive for blood with no erythrocytes**
 - **Hemolysis**

Myoglobinuria

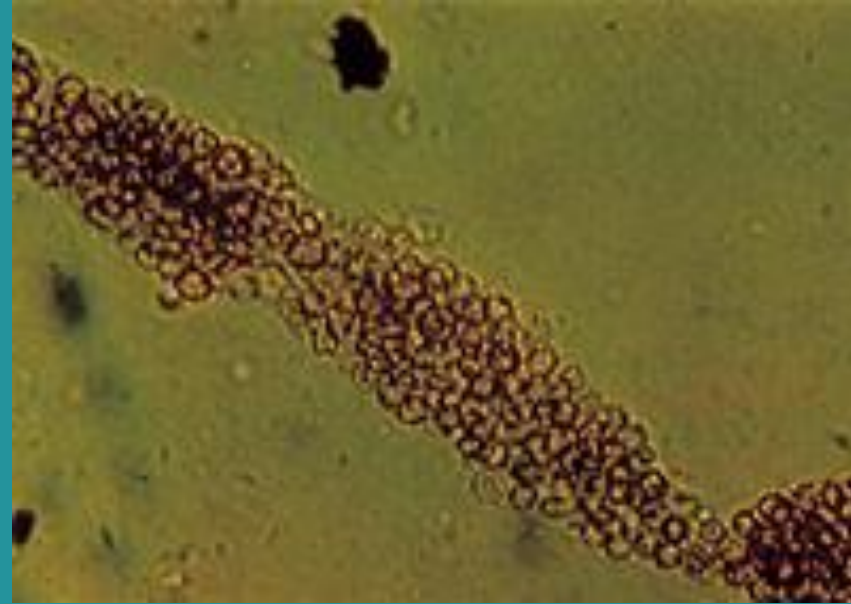
- Myoglobinuria-small molecular weight heme protein of striated muscle found in urine
- Reacts to same reagent for hemoglobin
- Toxic to renal tubules, may cause acute renal failure
- Cleared from plasma in the first pass, therefore serum is clear of myoglobin

Erythrocytes

- Causes:
 - Glomerular injury
 - Genitourinary tract bleeding
- Isomorphic – urologic process
 - Stone
 - Tumor
 - Infection
- Dysmorphic – glomerular process
 - Acanthocytes – have vesicle-shaped protrusions – highly specific for glomerulonephritis

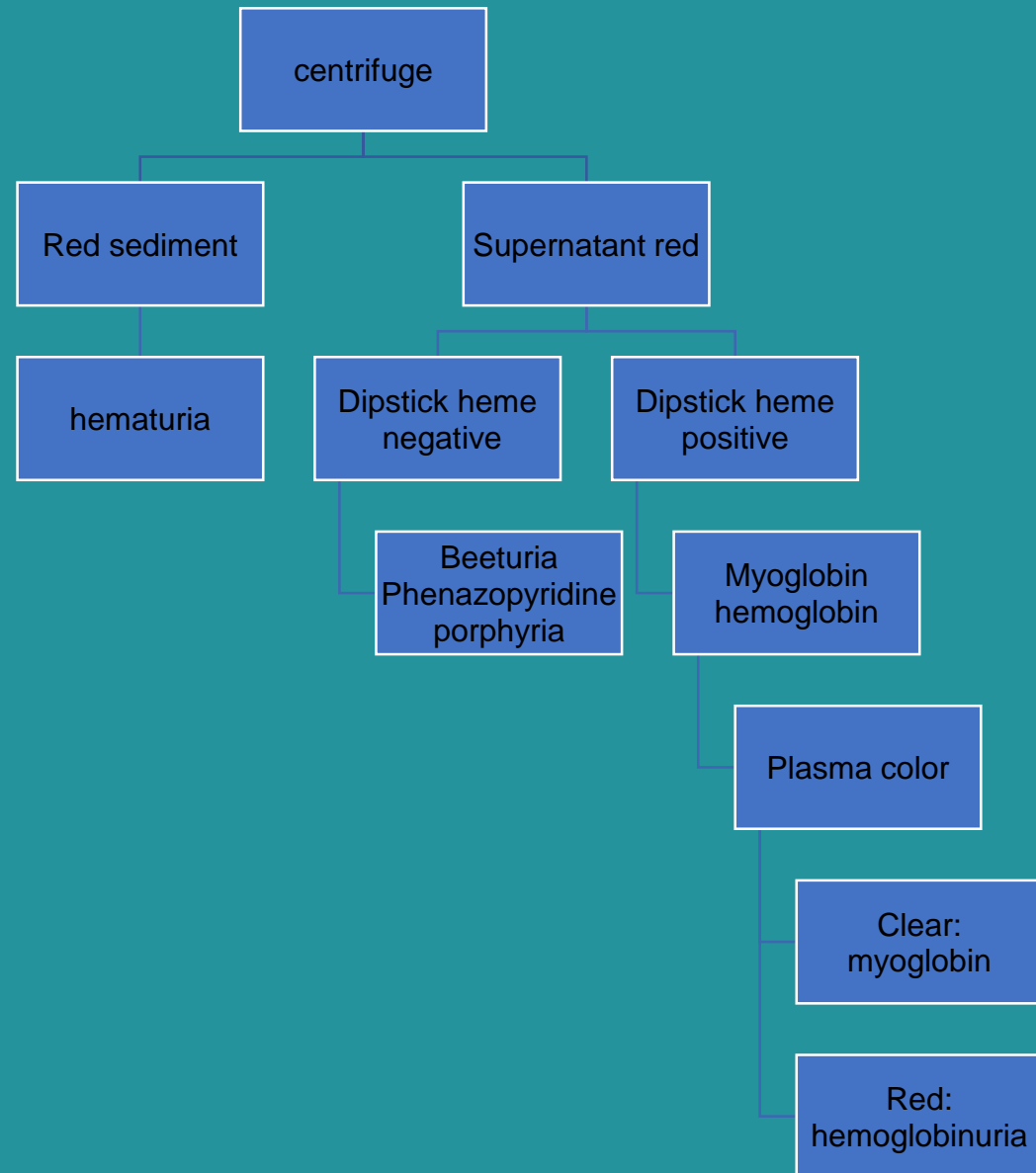


Red Blood Cell Casts



- Diagnostic of glomerulonephritis or vasculitis

Red Urine



Review: what will the plasma, urinalysis and micro look like for each of these patients?

- Has hemolytic anemia after a diarrheal illness
- Has been eating beets
- Has been exercising heavily and has severe muscle soreness
- Has leg swelling, hypertension, proteinuria, and acute renal failure
- Is passing a kidney stone

PRESENCE OF BLOOD			
	PLASMA	URINALYSIS	URINE MICRO
A	-	-	-
B	-	+	-
C	-	+	+
D	+	+	-

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CASE

A 30 year old man presents to the hospital with severe total body aches after a day of playing basketball outside in Phoenix. His creatinine is 5.6, potassium is 5.9. Hemoglobin is normal. Creatine kinase is 12,000. Urinalysis shows 3+ blood and no erythrocytes. What is the most likely diagnosis?

- A. Rhabdomyolysis with myoglobinuria
- B. Consumption of too many beets
- C. Acute renal colic from nephrolithiasis
- D. Renal cell carcinoma
- E. Lupus nephritis

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CASE

A 57-year-old man with no known past medical history comes to the office for evaluation of recurrent episodes of gross hematuria over the past 4 months. He has no flank pain or bladder pain.

SH: occupation: leather worker; 30-pack year tobacco

PE BP 130/70, exam otherwise normal

Labs: creatinine 1.2, urinalysis 2+ blood, >60 RBCs per HPF

You order a CT scan with contrast which is negative for renal mass.

What is the next diagnostic step?

- A. Check urine culture
- B. Repeat urinalysis in 3 months
- C. Cystoscopy
- D. Renal biopsy

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Bladder cancer

Most common cancer of the urinary tract

Almost all Transitional Cell Carcinoma

Risk factors: age, white ethnicity, smoking, occupational risk (metal workers, miners, textile workers, leather workers)

Presentation: painless hematuria

Evaluation: cystoscopy in patients >40 years old

Treatment: TURB + intravesical bacillus Calmette-Gjerin chemotherapy

Surveillance for recurrence is important

CASE

A 75 year old man with no known past medical history presents to the office complaining of facial flushing, headaches, blurred vision, and left flank pain.

PE: 148/92, facial plethora present, exam otherwise normal

Labs: Hgb 18, creatinine 0.9, urinalysis: 1+ blood >60 rbc/hpf

What is the next appropriate test?

- A. Renal biopsy
- B. Bone marrow biopsy
- C. Renal ultrasound
- D. Abdominal CT scan
- E. Cystoscopy

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Renal Cysts: Bosniak classification

Category I: Malignant risk less than 1%; no follow-up required

– uncomplicated, simple benign cyst – anechoic, posterior enhancement, round or oval shape, thin, smooth wall – homogeneous water content, sharp delineation with the renal parenchyma, no calcification, enhancement or wall-thickening

Category II: Malignant risk less than 3%; no follow-up required

Cystic lesion with some abnormal radiological features – <1 mm septations (hairline thin) – fine calcifications within the septum or wall – <3 cm in diameter – hyperdense cysts (>20 Hounsfield units)

Category IIF: Malignant risk 5-10%; follow-up recommended

Cystic lesion with increased abnormal findings – multiple thin septum – septa thicker than hairline or slightly thick wall – calcification, which may be thick – intrarenal, >3 cm – no contrast enhancement

Category III: Malignant risk 40-60%; surgical excision recommended

More complicated – uniform wall thickening/nodularity – thick/irregular calcification – thick septa – enhances with contrast

Category IV: Malignant risk greater than 80%; surgical excision recommended

Large cystic components – irregular margins/prominent nodules – solid enhancing elements, independent of septa

Renal Cell Carcinoma

CT scan is the test of choice for detecting renal cell carcinoma

Symptoms: hematuria, abdominal pain, abdominal mass, weight loss BUT, most patients are asymptomatic.

Classic triad of flank pain, hematuria and palpable abdominal mass occurs in only 9% of patients.

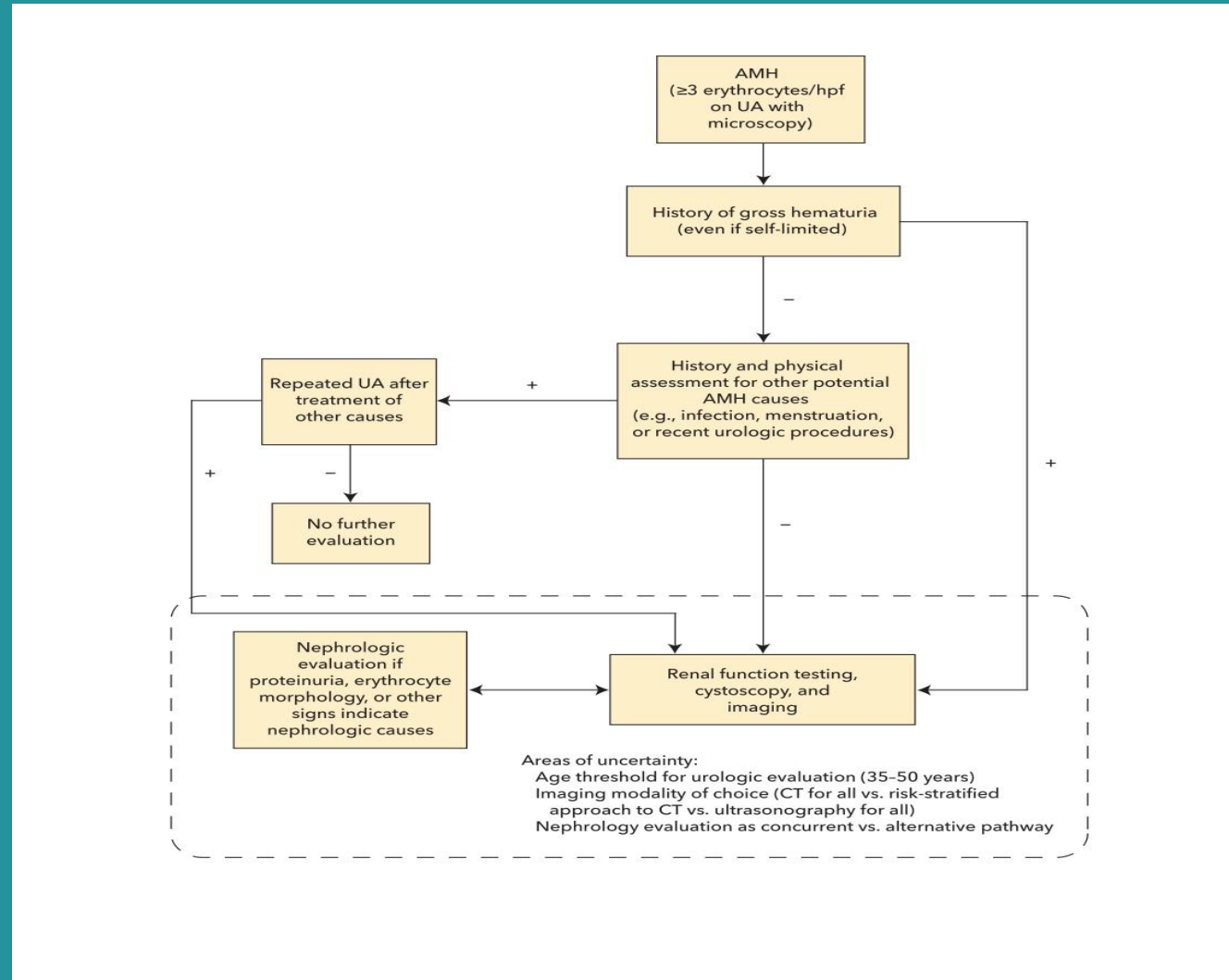
RCC is associated with paraneoplastic syndromes: erythrocytosis, AA amyloidosis, polymyalgia rheumatica, hepatic dysfunction.

Treatment:

Nonmetastatic – radical or partial nephrectomy or ablation

Metastatic – VEGF inhibitors or mTOR inhibitors

Summary: Workup of hematuria



Summary: Workup of hematuria

Evaluation of urine sediment to assess for false positives, glomerular disease, non-glomerular hematuria.

Repeat urine to r/o transitory cause (trauma, infection, menstrual period)

All unprovoked gross hematuria should be worked up even if resolves

Persistent microhematuria should be worked up

CT scan with IV contrast is the most sensitive for detecting renal masses <1cm

Cystoscopy should be performed in patients over 35 years old if no other cause found