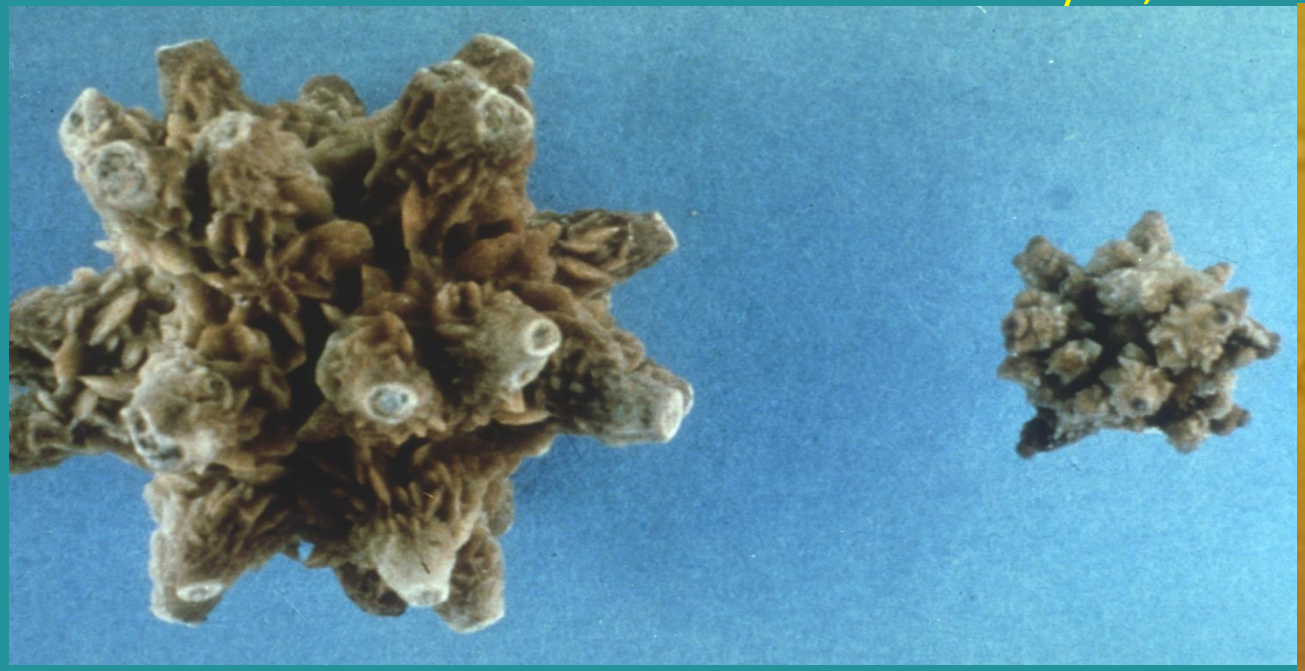
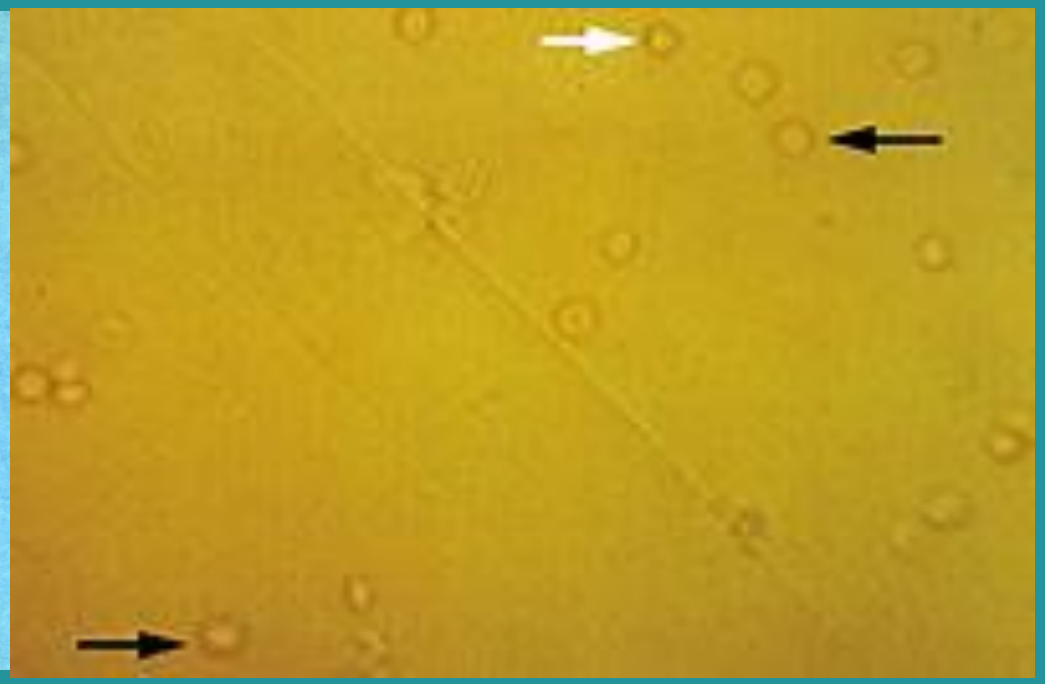
Nephrolithiasis and Hematuria

Academic Half Day
January 4, 2021





LEARING OBJECTIVES: Nephrolithiasis

1. Describe the five categories of kidney stones and their prevalence.
2. Know the clinical presentation and evaluation of the patient with suspected kidney stone, and its medical management and role of the urology consultant in the management 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

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Epidemiology

- Prevalence: 10%
- 20 years ago ratio 1:2 women:men, now 1:1.3
- Peak age 20-30 years old
- Southeastern geography (Most likely due to higher ambient temperatures rather than increased vitamin D)

Predisposing Conditions

METABOLIC SYNDROME

- Diabetes
- Obesity
- Gout

Predisposing Conditions

- Genetic factors: 15% pts in stone clinics have genetic disorders:
  - Renal tubular acidosis
  - Bartter syndrome
  - Primary hyperoxaluria
  - Cystinuria

Howles, S.A., Thakker, R.V. Genetics of kidney stone disease. *Nat Rev Urol* **17,** 407–421 (2020).

Predisposing Conditions

- Family history 20%
- Occupational exposure – jobs with limited access to water or bathroom facilities
- Intestinal disorders causing malabsorption – Crohns or bariatric surgery (increased oxalate absorption)
- Urinary tract infections

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

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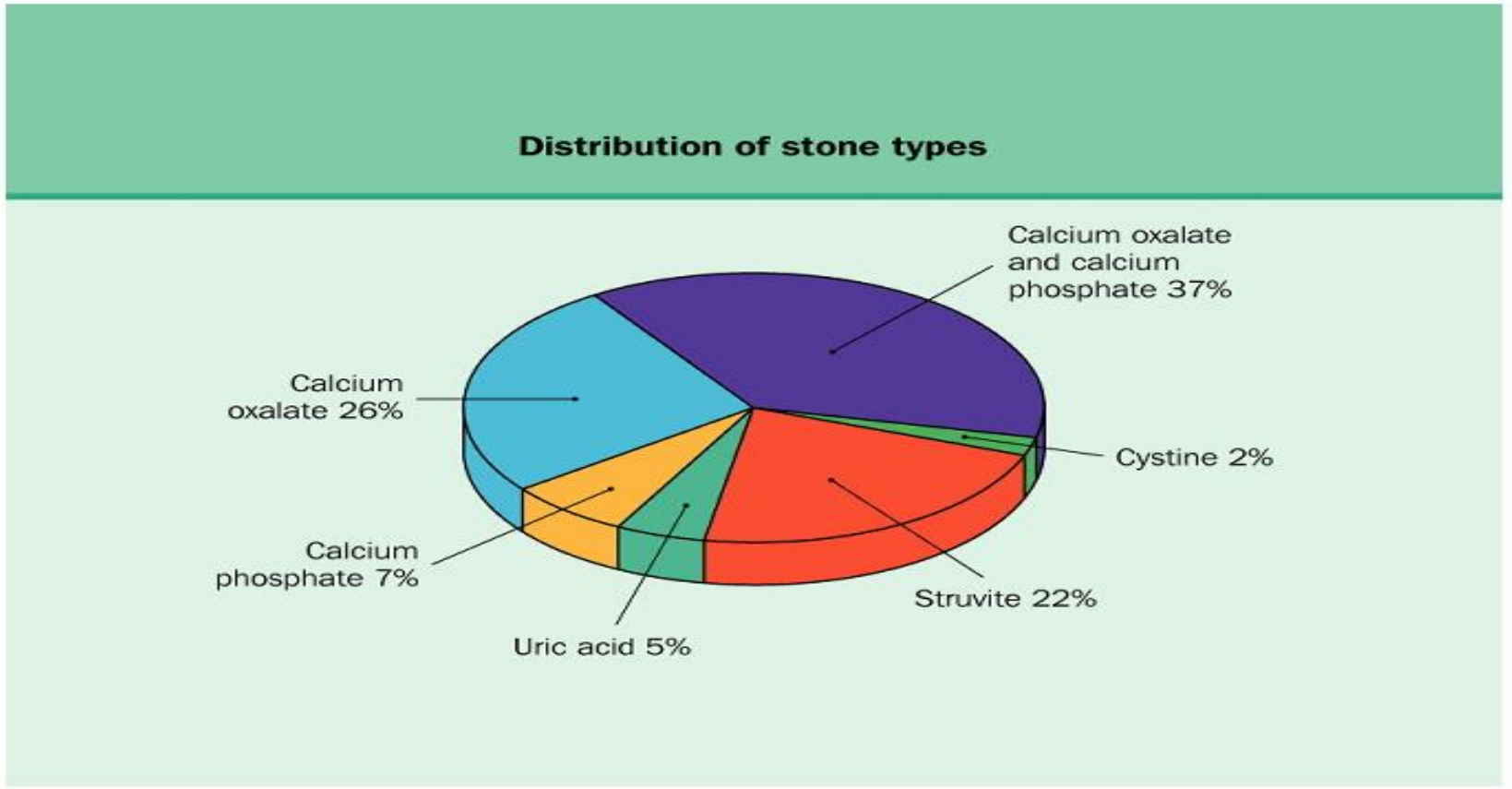
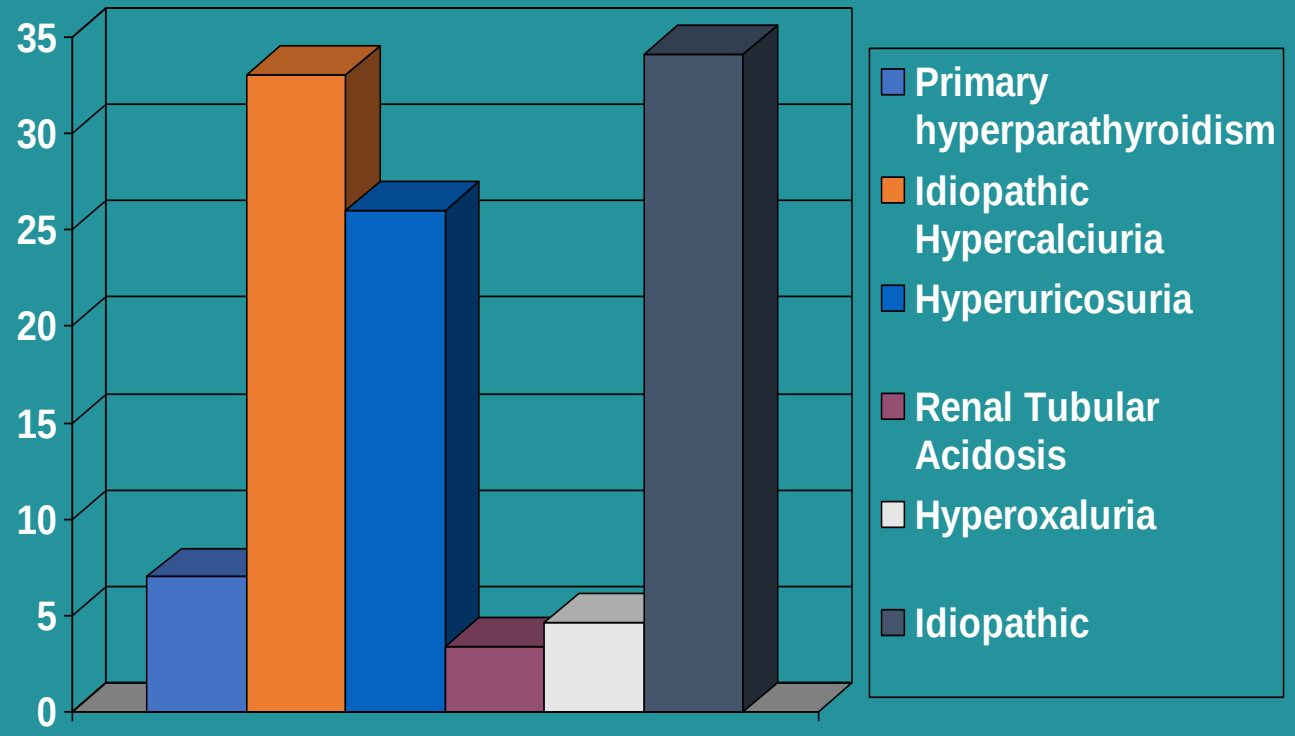
Frequency in US Population



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

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

Why does primary hyperparathyroidism cause nephrolithiasis?

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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.

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%

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B. 30%
C. 50%
D. 75%

Pathogenesis – Stages of Stone development

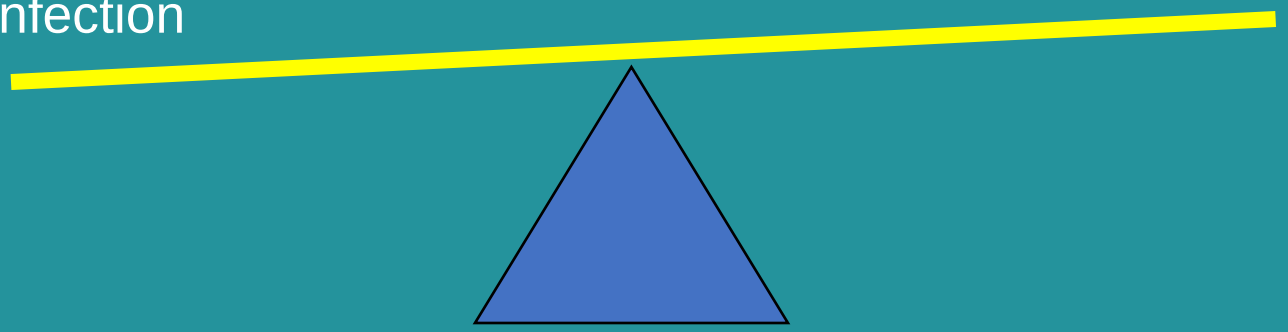
- Supersaturation
- Nucleation (ions join together in more stable, solid phase)
- Aggregation (small crystals bond together)
- Anchoring (via stone-epithelial cell interactions) facilitates aggregation in limited time

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 heterogenious 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

- Appendicitis
- Ovarian cysts
- Peritonitis
- Ectopic pregnancy
- UTI
- Diverticulitis

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, amphoteracin 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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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	

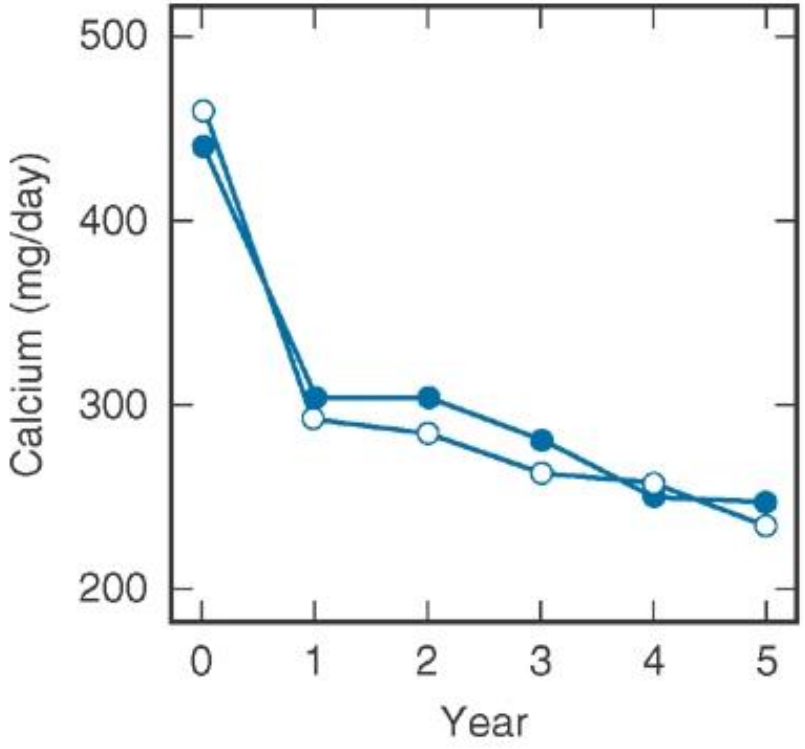
*Group 1 had intake values below the first quintile for the group (lowest intake), group 2 values between the first and second quintiles, group 3 values between the second and third quintiles, group 4 values between the third and fourth quintiles, and group 5 values above the fourth quintile (highest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

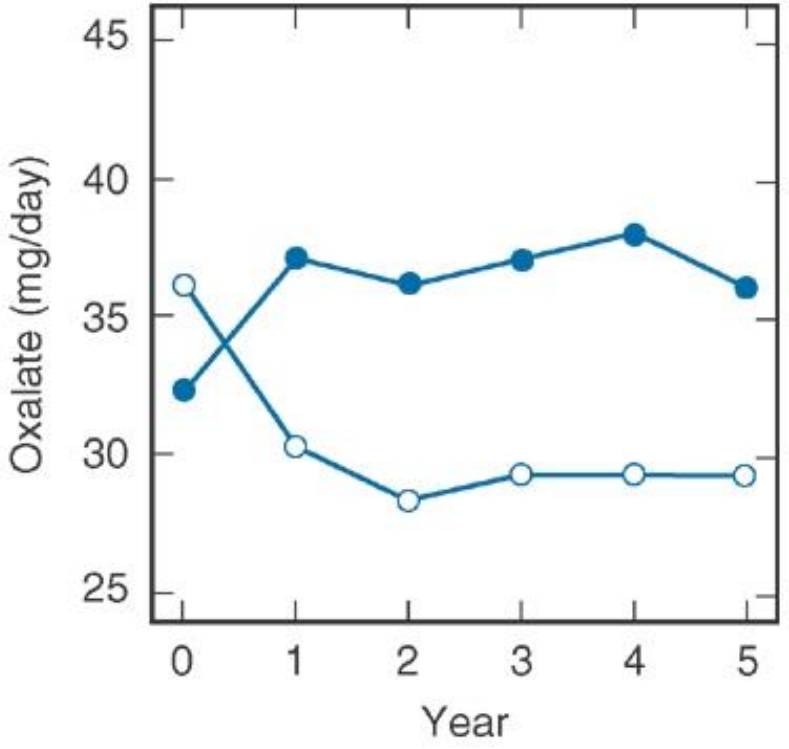
†A chi value of more than 1.96 denotes a P value of less than 0.05. The sign of the chi value indicates the direction of the trend.

‡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).

Curhan GC. Willett WC. et al. *New England Journal of Medicine.* 328(12):833-8, 1993 Mar 25.

Calcium intake

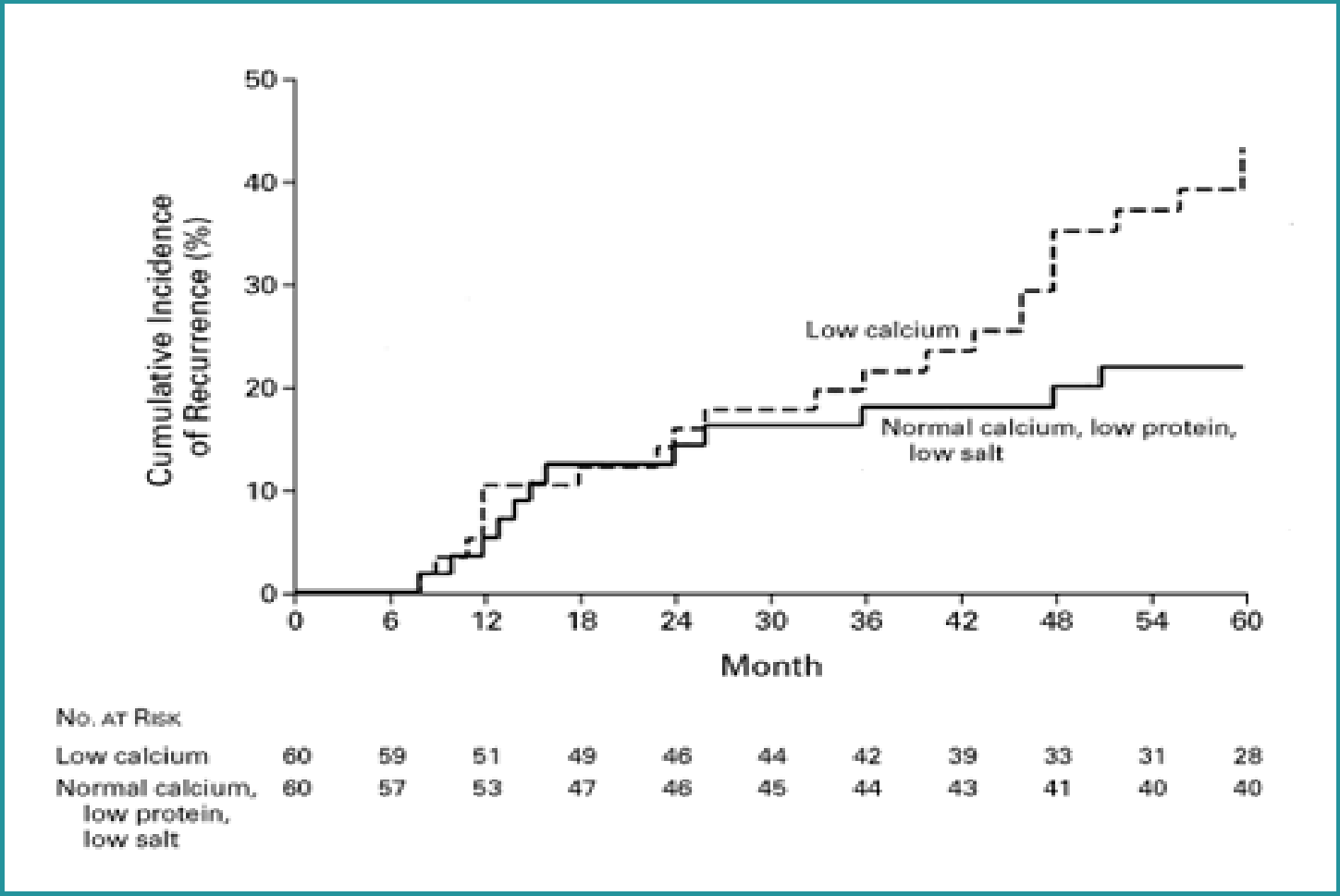




The effects of a low-calcium diet vs. a normal-calcium, low-sodium, low-protein diet on urine chemistries. In a 5-year randomized prospective study of the effects of dietary intervention on stone formation, patients treated with a normal-calcium, low-sodium, low-protein diet (*open symbols*) had a similar 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



No. at Risk											
Low calcium	60	59	51	49	46	44	42	39	33	31	28
Normal calcium, low protein, low salt	60	57	53	47	48	45	44	43	41	40	40

Borghi L. Schianchi T. et al. New England Journal of Medicine. 346(2):77-84, 2002 Jan 10.

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

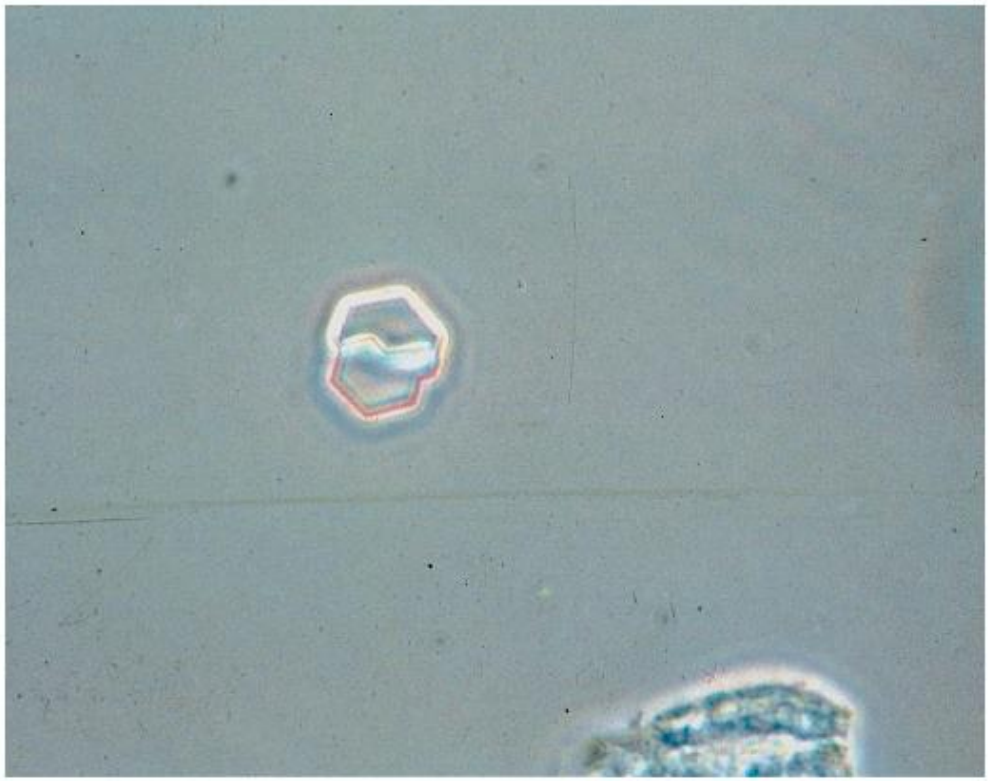
Calcium Oxalate

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

Uric Acid

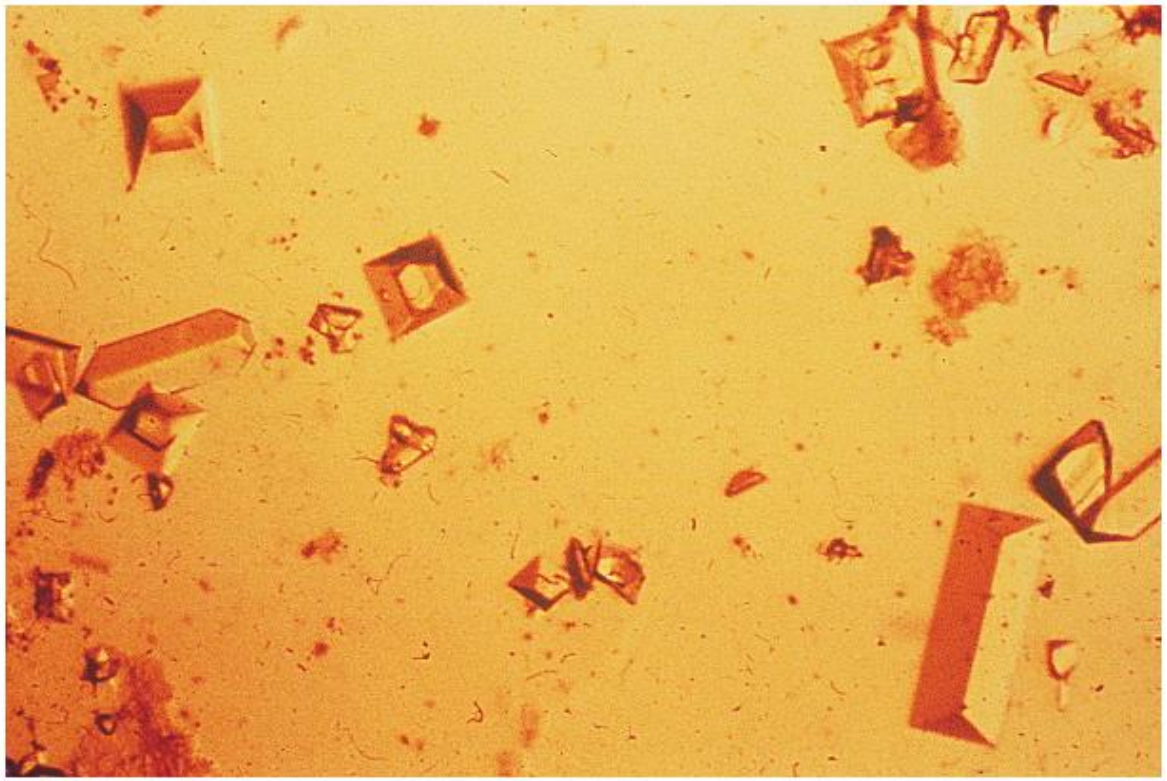
Johnson J and Feehally J, *Comprehensive Clinical Nephrology,* 2nd ed.

Cystine



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

Magnesium ammonium phosphate (struvite)



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

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

Creatinine 1.0 mg/dL
Potassium 4.6 meq/L
Bicarbonate 26 meq/L
Calcium 10.1 mg/dL
Phosphorus 2.1 mg/dL
Uric acid 9.0 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

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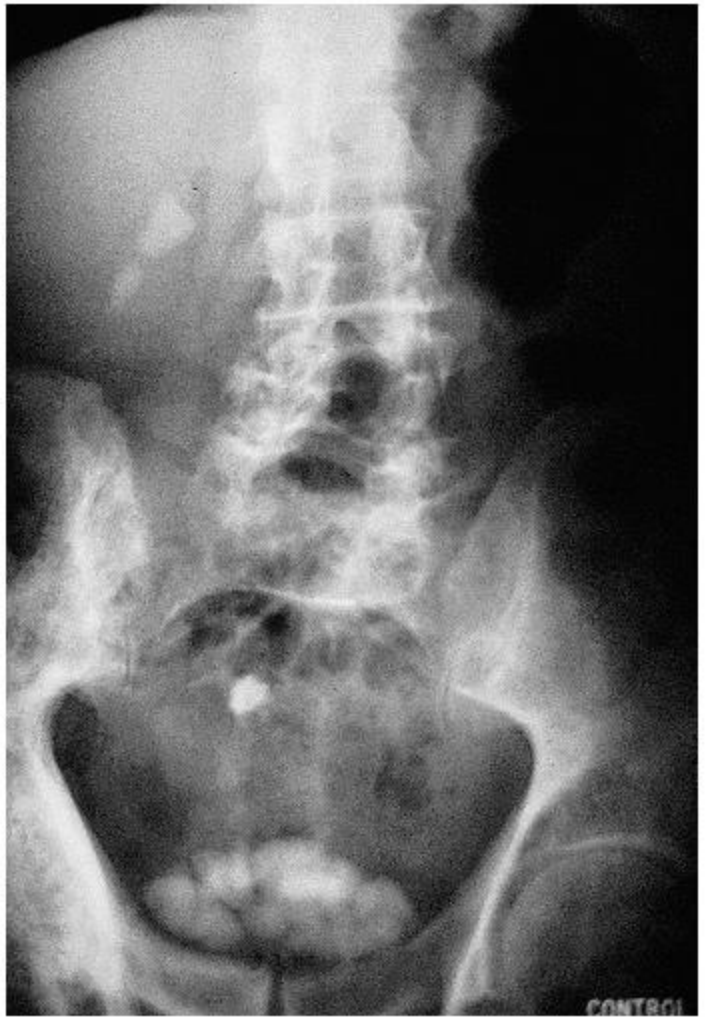
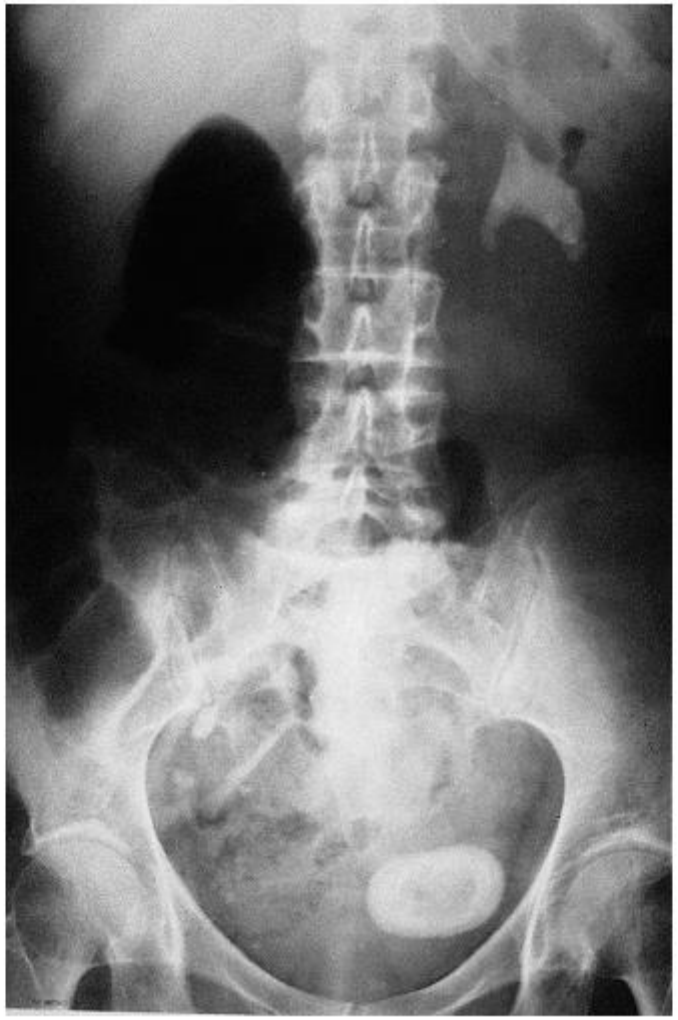
Radiologic evaluation

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



Multiple cystine stones in r kidney, ureter, and bladder

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



Struvite stones; L staghorn calculus; single bladder stone

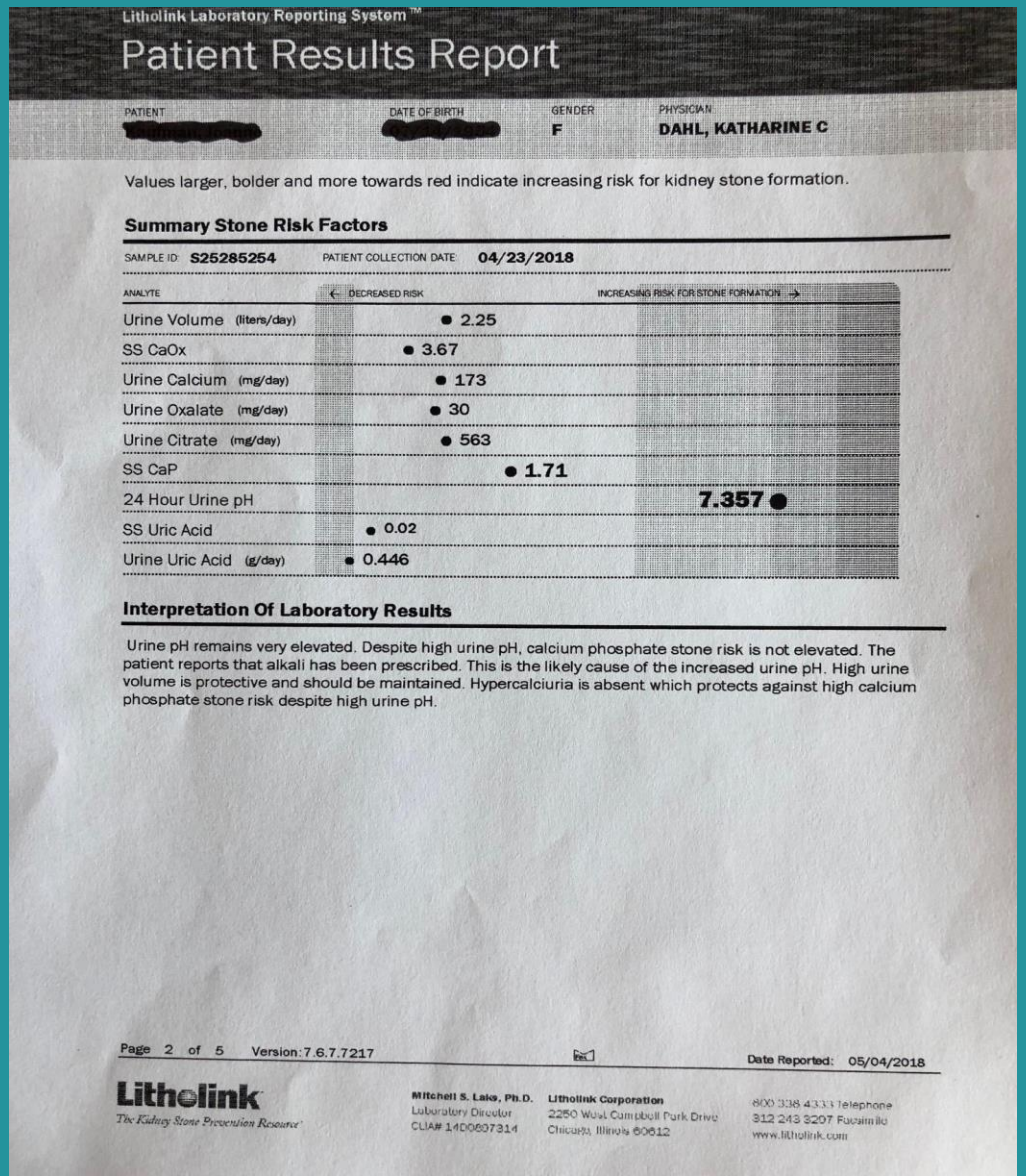
Johnson J and Feehally J, *Comprehensive Clinical Nephrology,* 2nd ed.

Complete Evaluation (for >1 stone)

24 hour urine for:

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

Stone Risk Profile



Litholink Laboratory Reporting System™

Patient Results Report

PATIENT	DATE OF BIRTH	GENDER	PHYSICIAN
[redacted]	[redacted]	F	DAHL, KATHARINE C

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

Summary Stone Risk Factors

SAMPLE ID: **S25285254** PATIENT COLLECTION DATE: **04/23/2018**

ANALYTE	← DECREASED RISK	INCREASING RISK FOR STONE FORMATION →
Urine Volume (liters/day)	● 2.25	
SS CaOx	● 3.67	
Urine Calcium (mg/day)	● 173	
Urine Oxalate (mg/day)	● 30	
Urine Citrate (mg/day)	● 563	
SS CaP	● 1.71	
24 Hour Urine pH		**7.357** ●
SS Uric Acid	● 0.02	
Urine Uric Acid (g/day)	● 0.446	

Interpretation Of Laboratory Results

Urine pH remains very elevated. Despite high urine pH, calcium phosphate stone risk is not elevated. The patient reports that alkali has been prescribed. This is the likely cause of the increased urine pH. High urine volume is protective and should be maintained. Hypercalciuria is absent which protects against high calcium phosphate stone risk despite high urine pH.

Date Reported: 05/04/2018

Litholink
The Kidney Stone Prevention Resource

Mitchell S. Lais, Ph.D.
Laboratory Director
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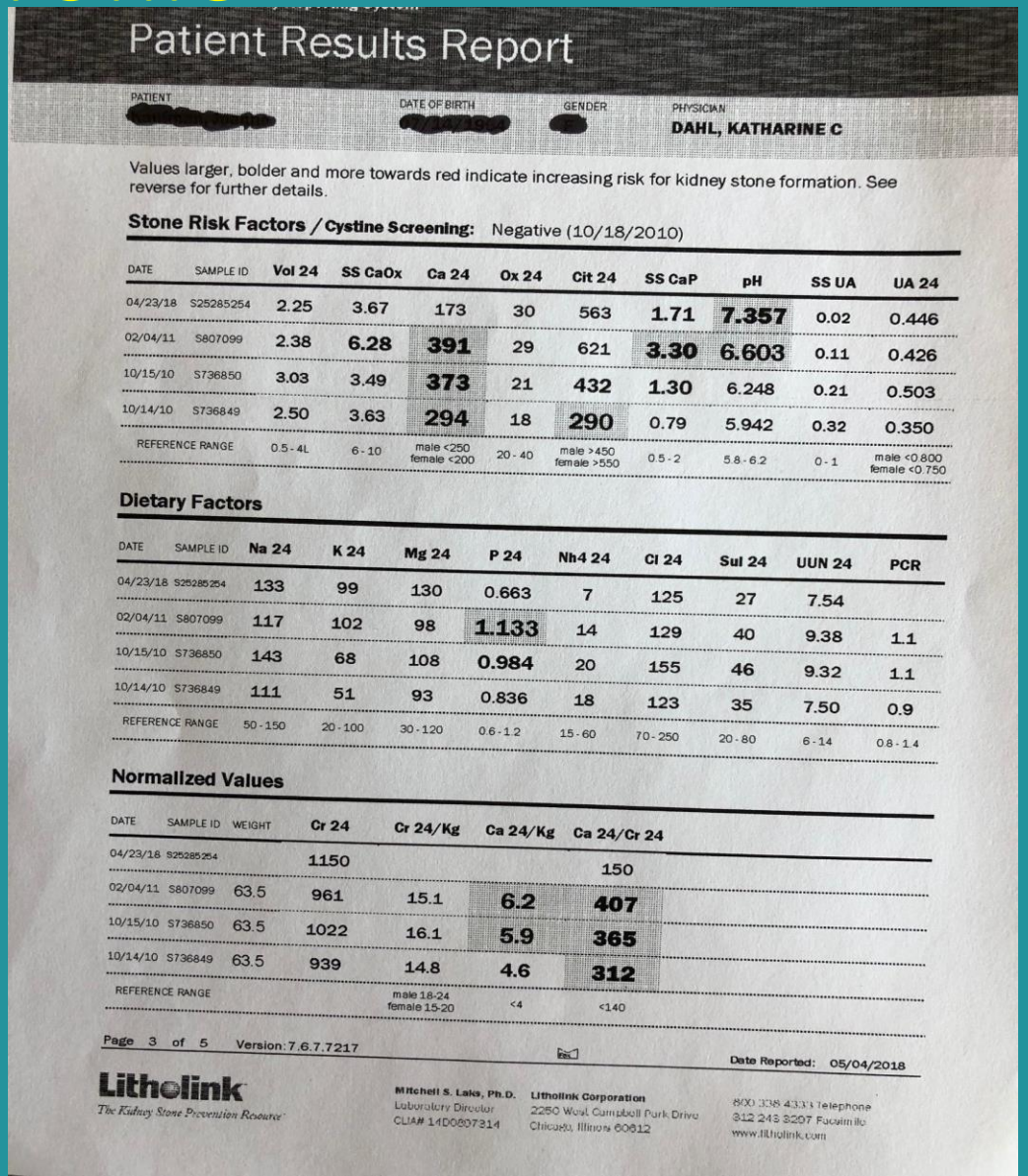
Stone Risk Profile



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	<140

 Version: 7.6.7.7217 Date Reported: 05/04/2018

Litholink
The Kidney Stone Prevention Resource
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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

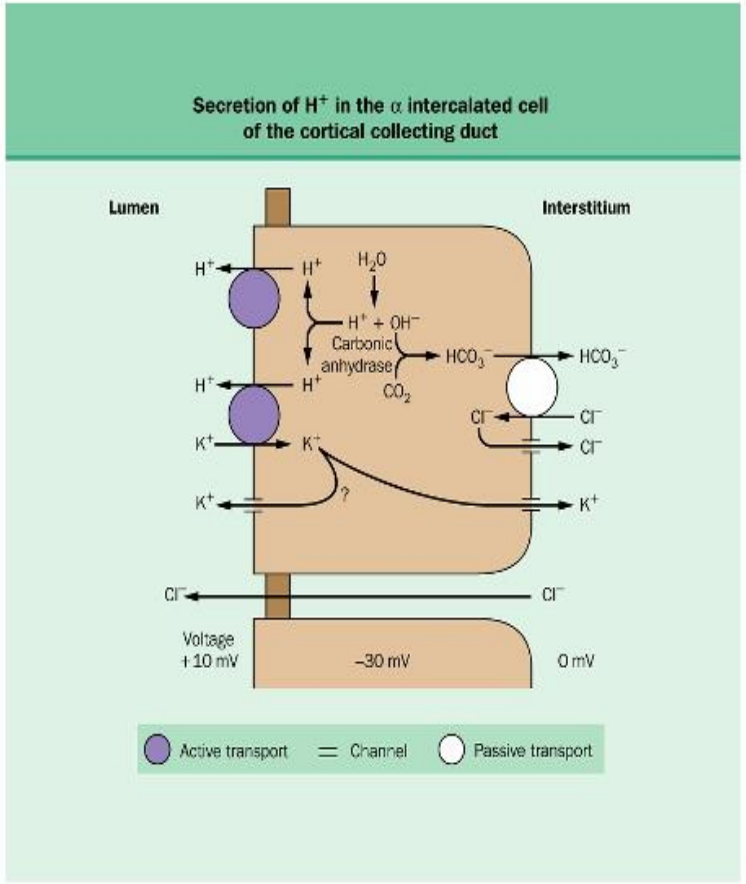
In a Type 1 Distal Renal Tubular Acidosis, there is a failure of the α-intercalated cell to secrete H+ ions and reclaim K+ ions.

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



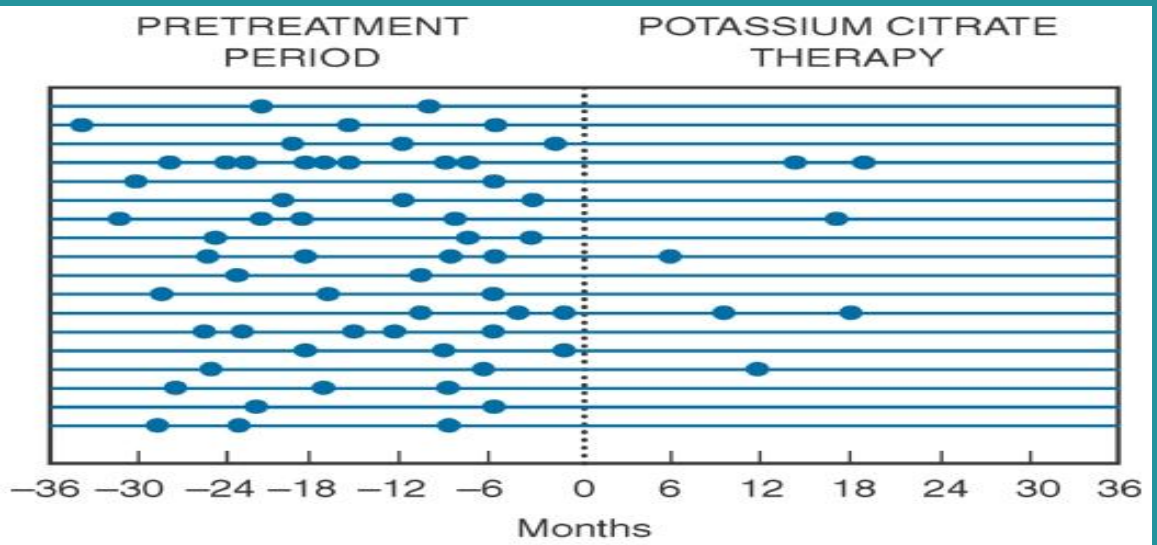
Prevention - Dietary Modifications

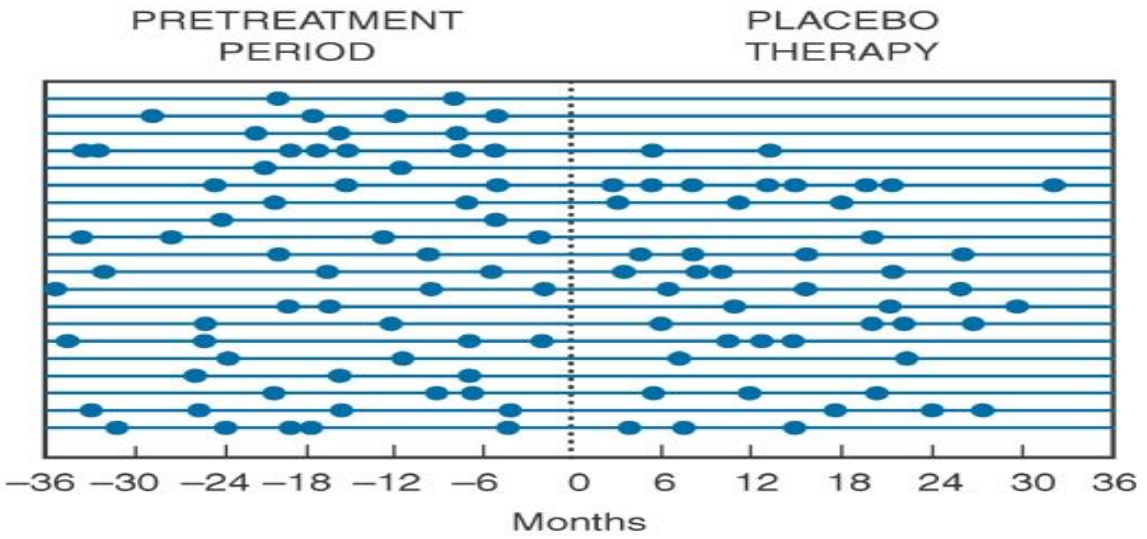
- Fluid intake urine output > 2L/day
- Calcium intake > 1gm/day
- Sodium intake avoid excess (2g/day)
- Protein intake moderation(0.8-1g/kg/day)

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

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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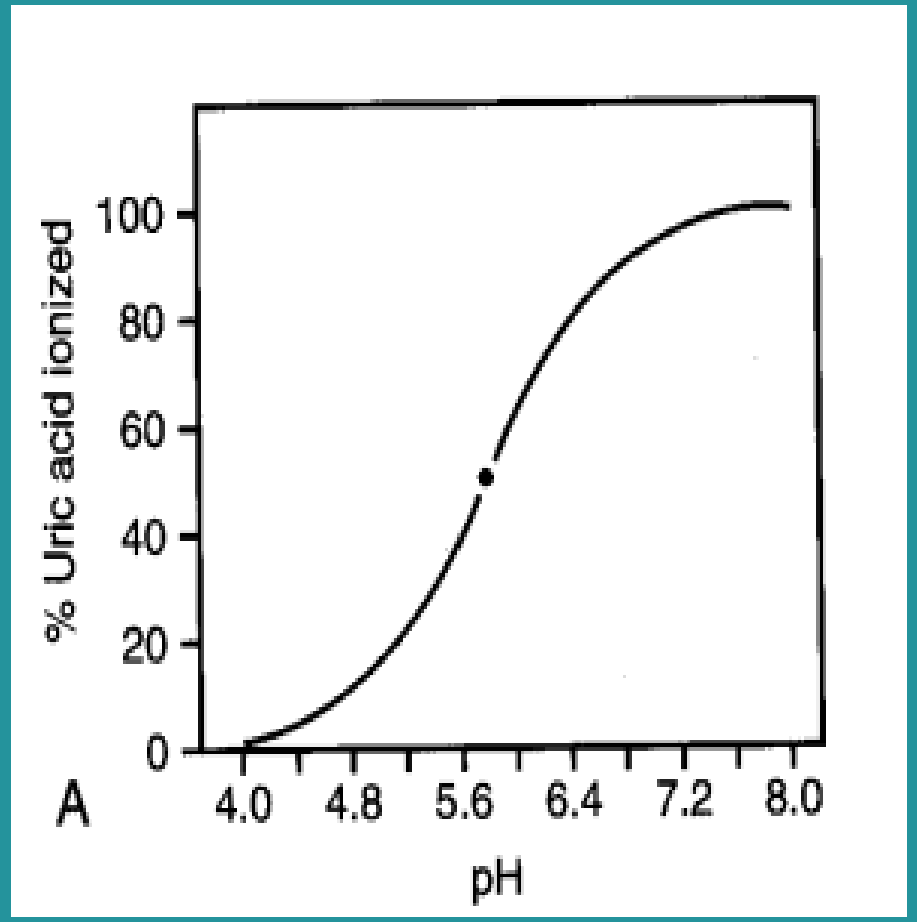
Treatment of Specific Forms of Stone Disease: Hyperuricosuria

- 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



Asplin, et al. Sem Neph. 16:412, 1996.

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 , 2+ blood, and coffin-shaped crystals shown below. Urine pH is 8.5. 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 (proteus, 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 – lithotrypsy 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 animal protein, moderate oxalate, normal calcium intake
- Thiazides empirically but especially for hypercalciuria.
- Potassium citrate empirically but especially for hypocitraturia.
- Allopurinol for hyperuricosuria
- Antibiotics for struvite stones

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%

Management

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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

Management

A 45 year old man comes to the ER with renal colic. A CT scan shows a 7mm stone in his mid-ureter. What therapies have been proven effective to facilitate stone passage?

A. Alpha blockers
B. NSAIDs
C. IV fluids
D. Extracorporeal Shock Wave Lithotripsy

Management

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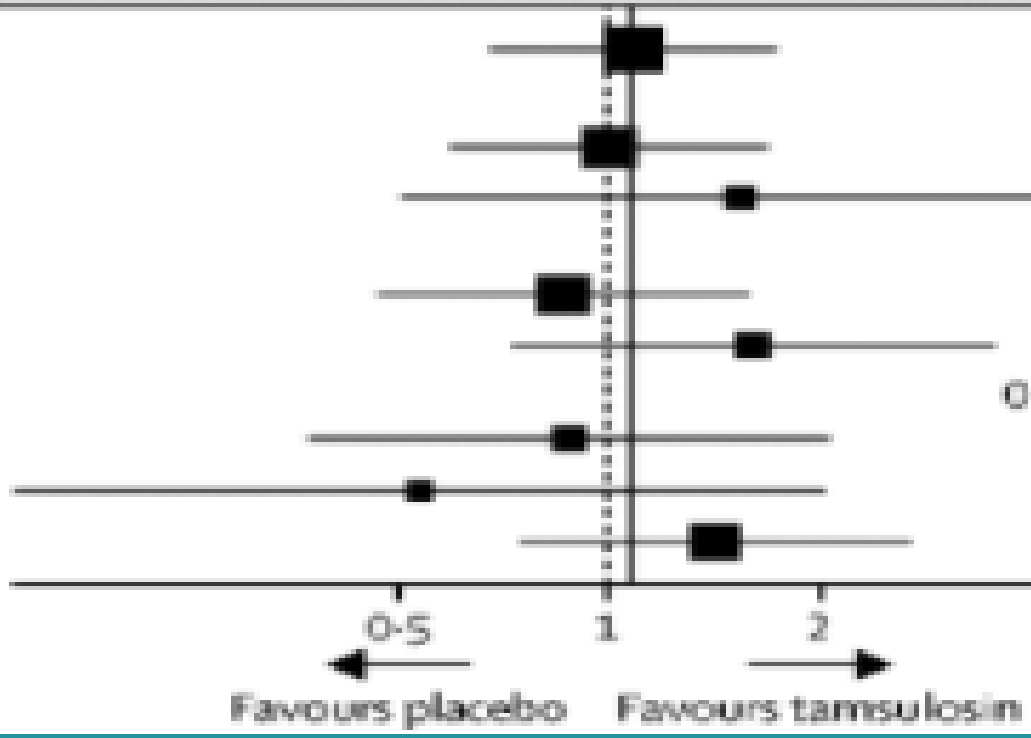
Tamsulosin

C Tamsulosin vs placebo

	Tamsulosin (n/N)	Placebo (n/N)	p value
All participants	307/378	303/379	
Sex			0·53*
Men	252/313	239/297	0·99
Women	55/65	64/82	0·32
Size			0·10*
≤5 mm	240/284	246/285	0·54
>5 mm	67/94	57/94	0·13
Location			0·37†/0·01‡
Upper	62/88	65/89	0·71
Middle	29/41	36/44	0·23
Lower	216/249	202/246	0·16



Picard R, et al. *Lancet.* 2015 Jul 25;386(9991):341-9.

IV fluids

Patients were randomized to 2L NS over 2 hours vs 20ml/hr continuous rate

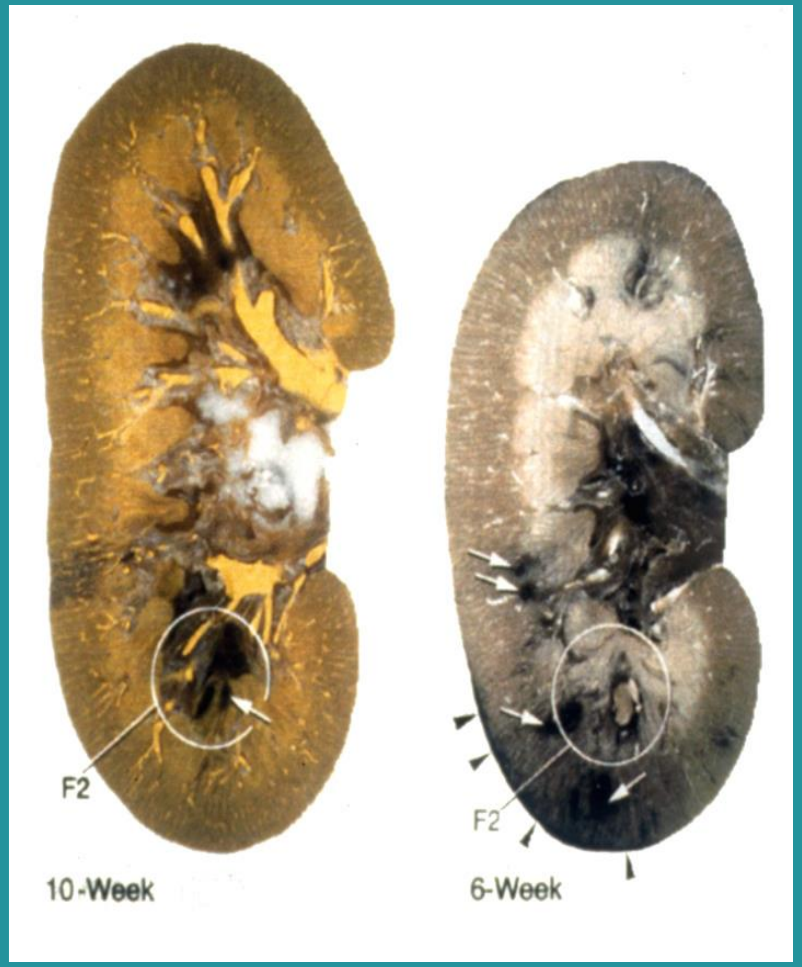
- No difference in analgesia requirements
- No difference in stone passage

Springhart WP, et al. J Endourol. 2006 Oct;20(10):713-6.

Extracorporeal 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 LEARING 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

CASE

A 58yo man who works a truck driver who has a 30-pack-year smoking history presents with urinary frequency and nocturia.

Exam: normal except enlarged prostate

Urinalysis: SpGr 1.010, pH 6.5, 1+ blood

Microscopy: 1 wbc/hpf, 7 rbcs/hpf, no squamous epithelial cells

Based on his history , symptoms, and urinalysis findings, which of the following should be done next:

A. Repeat urinalysis in 6 months
B. Obtain BMP, CT scan, and cystoscopy
C. Treat with antibiotic and repeat UA with micro
D. Inform him that his enlarged prostate is causing microscopic hematuria
E. Perform urine cytology

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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

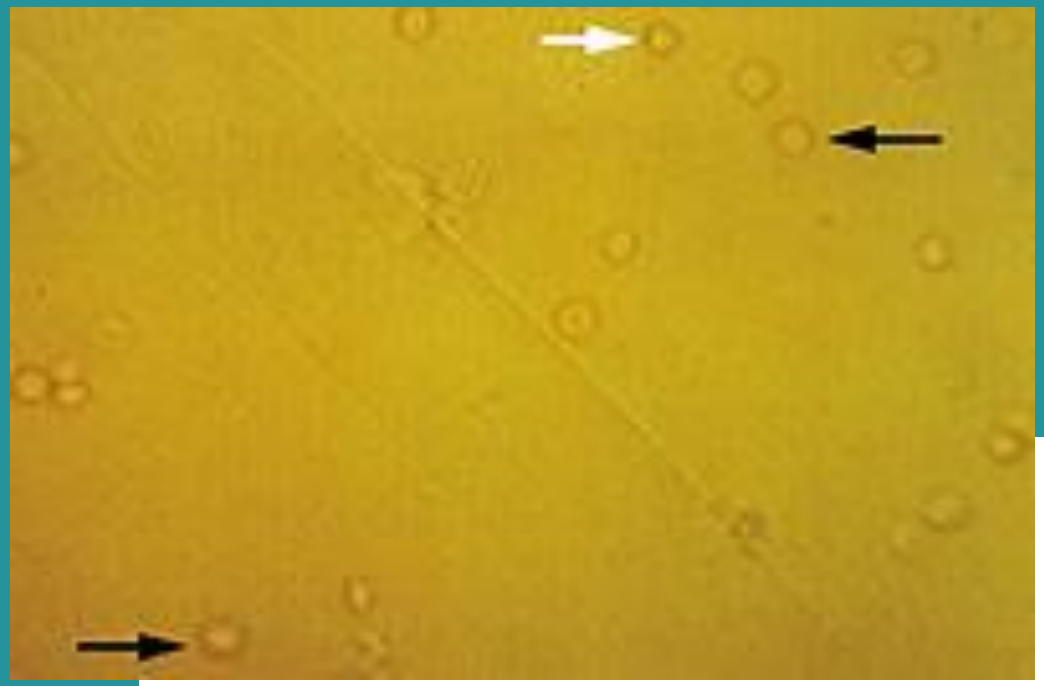
- Dipstick measures peroxidase activity
  - **Free hemoglobin – hemolysis**
  - Intact erythrocytes
- 1-3 erythrocytes/hpf needed for positive result
- False positives
  - **Myoglobin**
  - Bacteria that express pseudoperoxidase activity: Enterobacter, Staphyloccoci, Strebtococci species
  - Hypochlorite
  - Rifampin
  - Chloroquin
  - Iodine
  - Alkaline urine
  - Low specific gravity
  - Semen
  - Oxidiing 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**

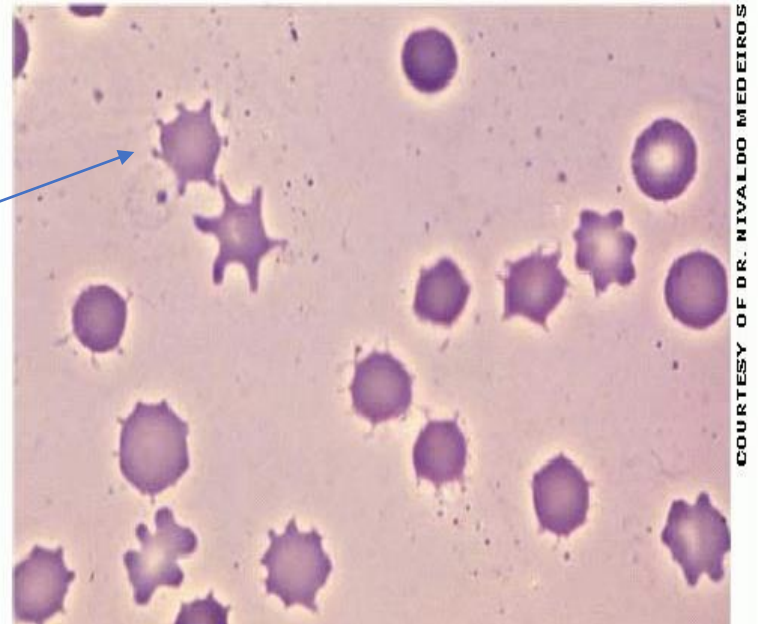
Myoglobinuria

- 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

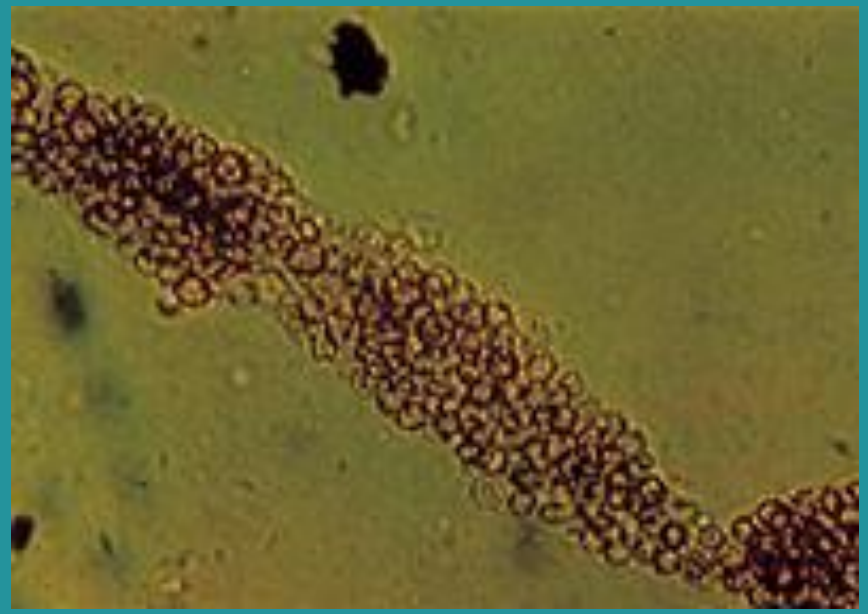
Erythrocytes

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



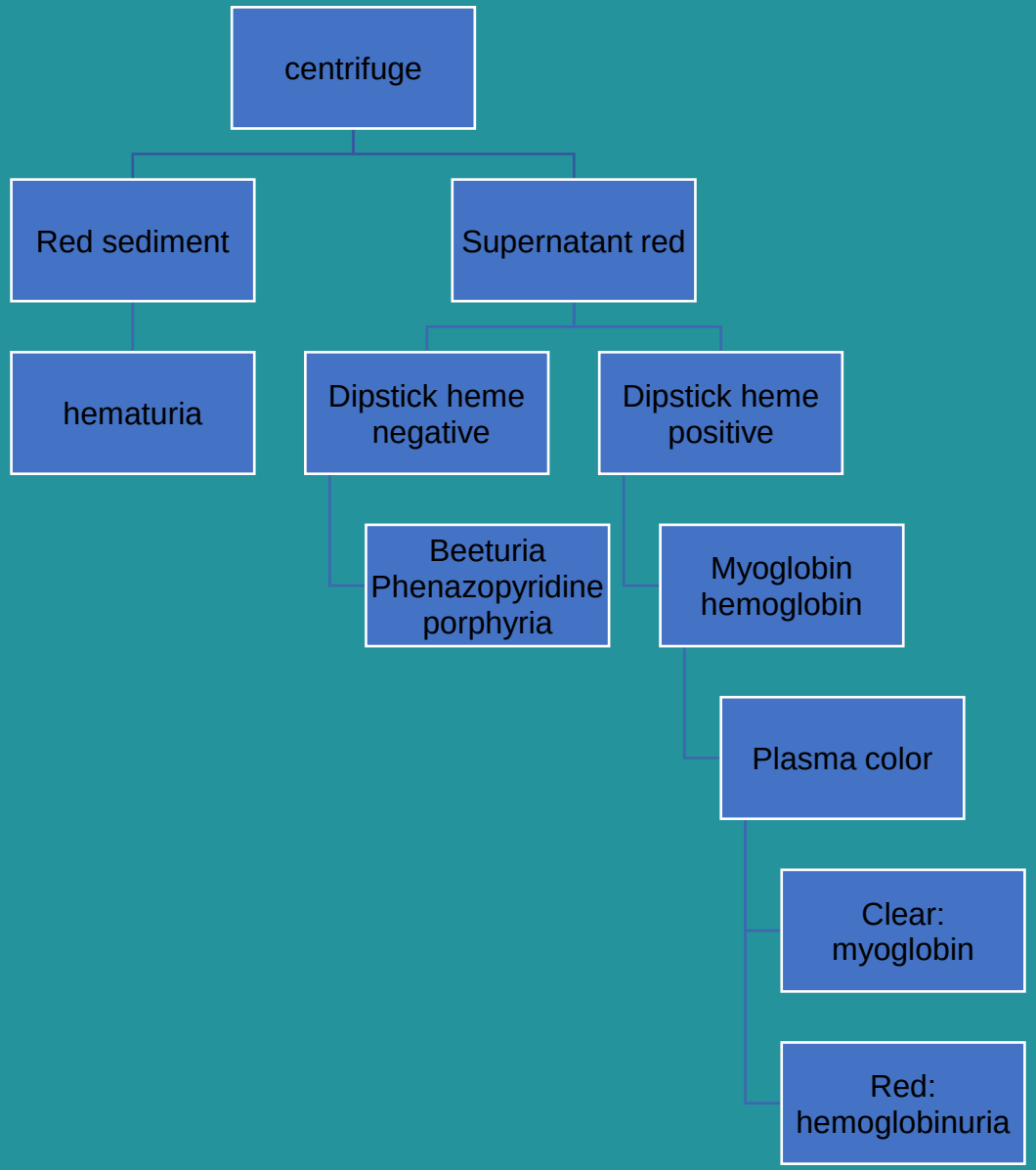


Red Blood Cell Casts



- Diagnostic of glomerulonephritis or vasculitis

Red Urine


centrifuge
Red sediment
Supernatant red
hematuria
Dipstick heme negative
Dipstick heme positive
Beeturia
Phenazopyridine
porphyria
Myoglobin
hemoglobin
Plasma color
Clear:
myoglobin
Red:
hemoglobinuria

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 57year 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; 30pack 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. Cystosopy
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, minors, textile workers, leather workers)

Presentation: painless hematuria

Evaluation: cystoscopy in patients >35 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

Whelan. Can Urol Assoc J2010;4(2):98-9

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.

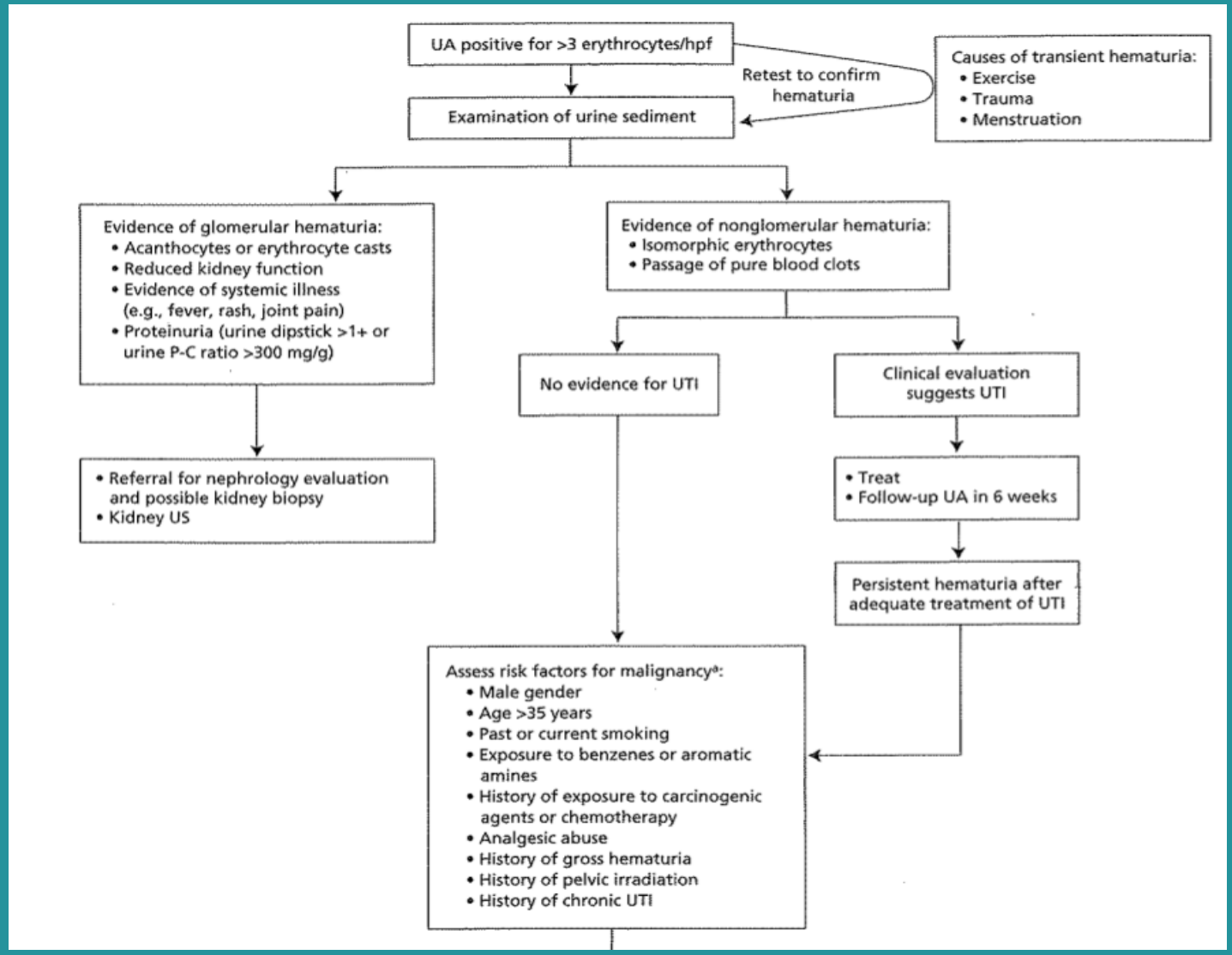
RCC is associated with paraneoplastic symdromes: erythrocytosis, AA amyloidosis, polymyalgia rheumatica, hepatic dysfunction.

Treatment:

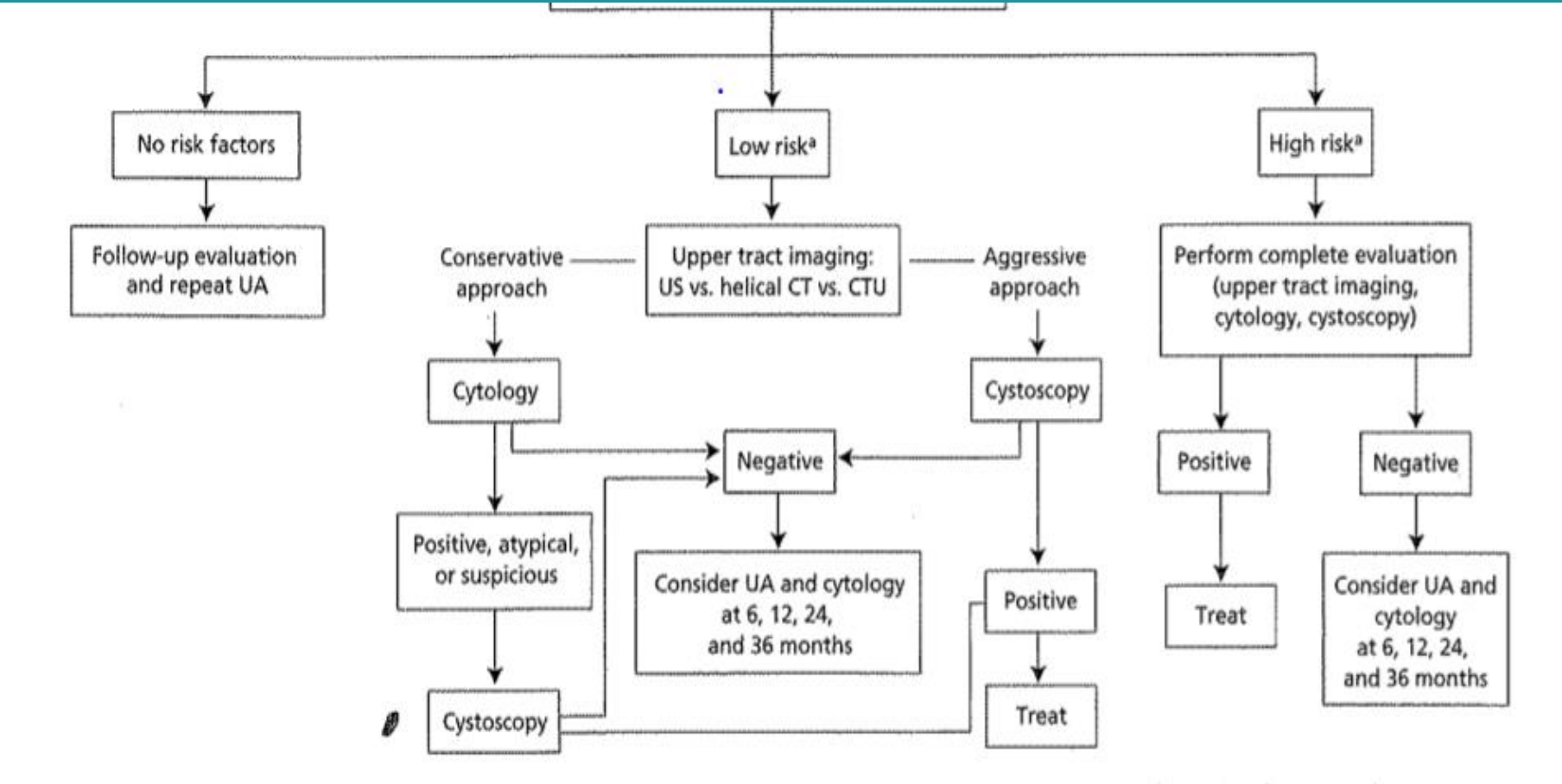
Nonmetastatic – radical or partial nephrectomy or ablation

Metastatic – VEGF inhibitors or mTOR inhibitors

Summary: Workup of hematuria



Summary: Workup of hematuria – risk stratification



MKSAP 19

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

Unprovoked microhematuria should be worked up in a patient with risk factors for malignancy

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