



Brigham and Women's Hospital
Founding Member, Mass General Brigham

NEPHROLOGY BOARD REVIEW

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University of New England College of Osteopathic
Medicine

MPH and MS @ Boston University

Medicine Residency @ Maine Medical Center

Nephrology Fellowship @ BWH/MGH

Instructor of Medicine @ HMS

- Clinical focus: Geriatric Nephrology
- Research focus: Supportive and palliative care for older adults with prevalent end stage kidney disease on dialysis



DISCLOSURES

I have no relevant financial relationships with ineligible companies.



OBJECTIVES

1. Review high-yield topics in nephrology relevant to the ABIM certification exam
2. Strengthen diagnostic reasoning and clinical decision-making in nephrology
3. Highlight evidence-based management strategies
4. Reinforce the interpretation of laboratory, imaging, and clinical findings in the evaluation of complex medical conditions in nephrology



Question 1

Which of the following conditions is most likely to cause an increase in serum creatinine WITHOUT a true reduction in glomerular filtration rate (GFR)?

- A. Bilateral hydronephrosis
- B. Severe extracellular volume contraction caused by diarrhea
- C. Severe congestive heart failure
- D. Increase in serum creatinine one day post arteriogram
- E. Cimetidine treatment of peptic ulcer disease



Question 1

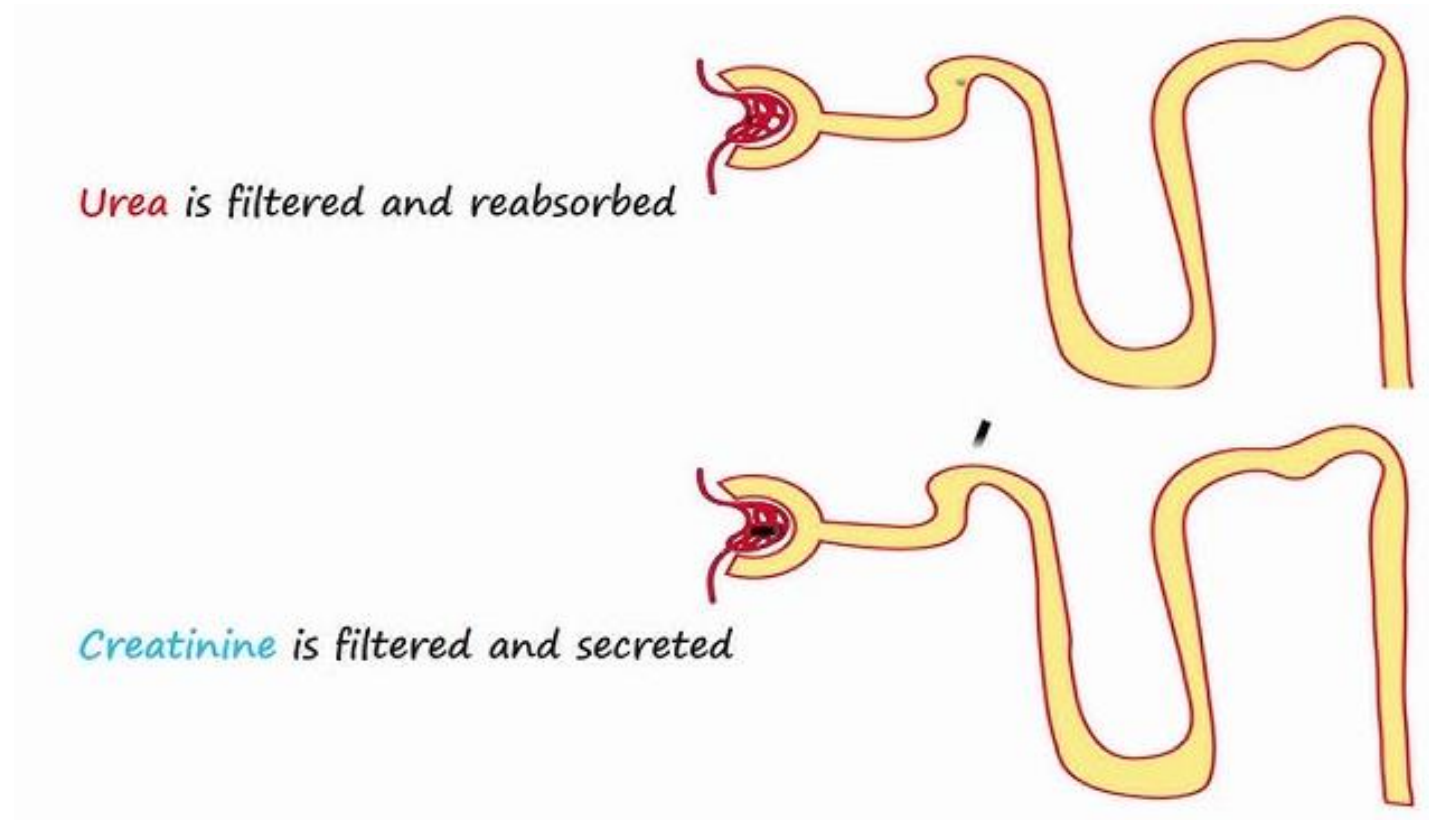
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Creatinine

- Use of creatinine as a marker of GFR dates back to the 1920s
- Creatinine is a 113-Da amino acid derivative that is the product of nonenzymatic breakdown of creatine in muscle
- Generated from muscle mass and diet (primarily animal protein intake)
- Not metabolized in the kidney, freely filtered in the glomerulus and secreted by the renal tubules



Limitations of serum creatinine



Freely filtered, secreted, and extra-renal degradation



Increases late after AKI



Between-person variability in creatinine generation rate (e.g. age, sex, muscle mass, race)

Breakdown of Question 1

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Cimetidine

- Creatinine Clearance (ml/min)

$$CrCl = \frac{U_{Cr} \times V_u}{S_{Cr}} \times \frac{1.73}{A}$$

CrCl: Creatinine Clearance (ml/min)

U_{Cr} : Urine Creatinine (mg/dL)

V_u : Volume of Urine (ml/min) [24 h Volume in ml / 1440 min]

S_{Cr} : Serum/Plasma Creatinine (mg/dL)

A: Patient's Surface Area (m^2) [from nomogram or formula]

Inhibits tubular secretion
of creatinine



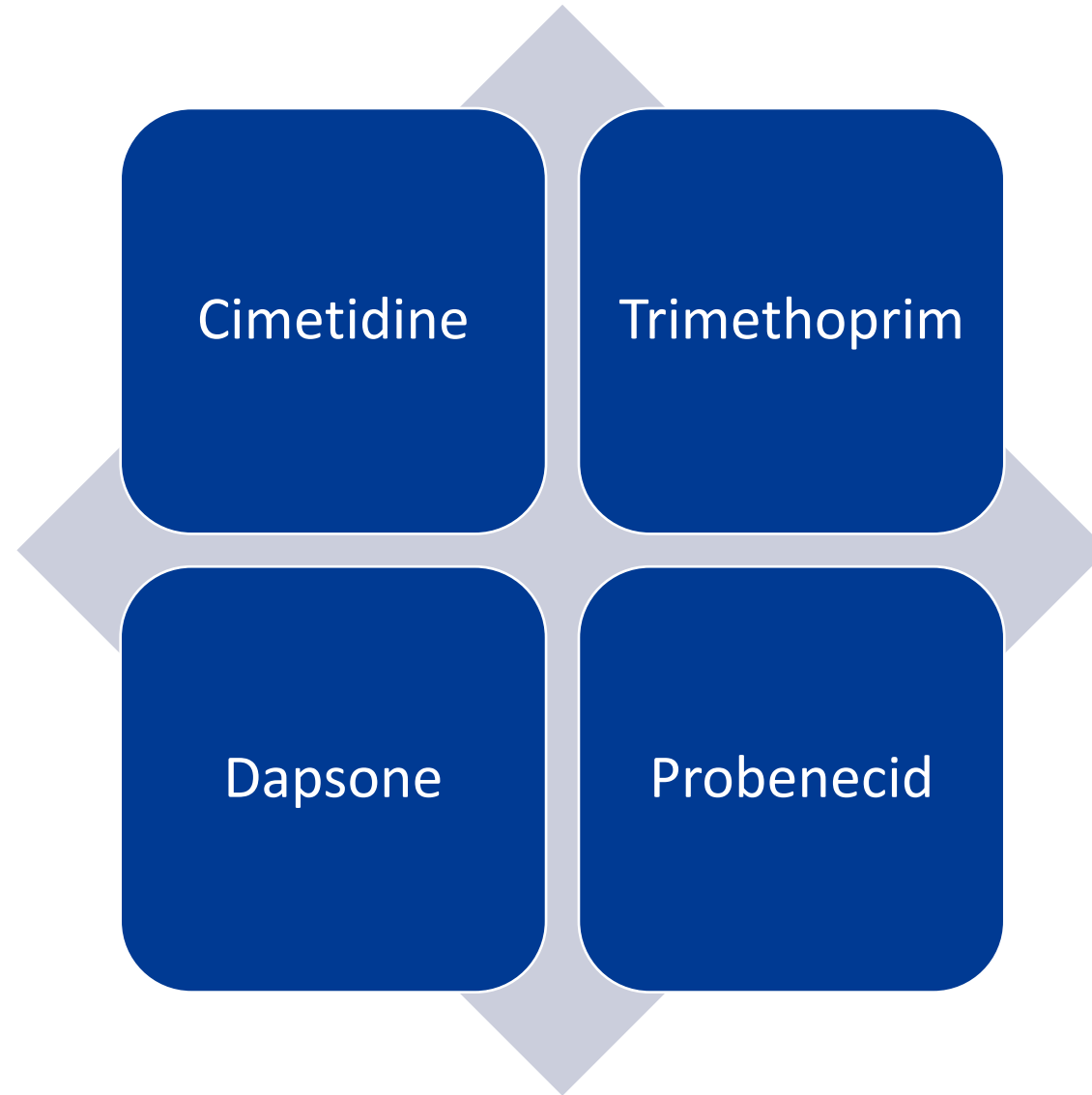
Increase in serum
creatinine levels



Creatinine clearance is
calculated by serum and
urine creatinine levels,
the inhibition of tubular
secretion leads to a
decreased calculated
creatinine clearance



Drugs that inhibit tubular secretion of creatinine



Question 2

A 69 year old obese woman with malaise, generalized pain, and weakness for the past 3 months. Laboratory studies reveal a serum creatinine of 3.8 mg/dL (baseline 1.2 mg/dL a year ago), hemoglobin 8.9 g/dL, serum albumin 3.0 g/dL, urinalysis: trace protein, no hematuria. Urine albumin to creatinine ratio: < 30 mg/g

A renal biopsy is performed. Which of the following is the most likely diagnosis?

- A. Diabetic nephropathy
- B. Phosphate nephropathy
- C. Uric acid nephropathy
- D. Cast nephropathy
- E. Fibrillary glomerulonephritis



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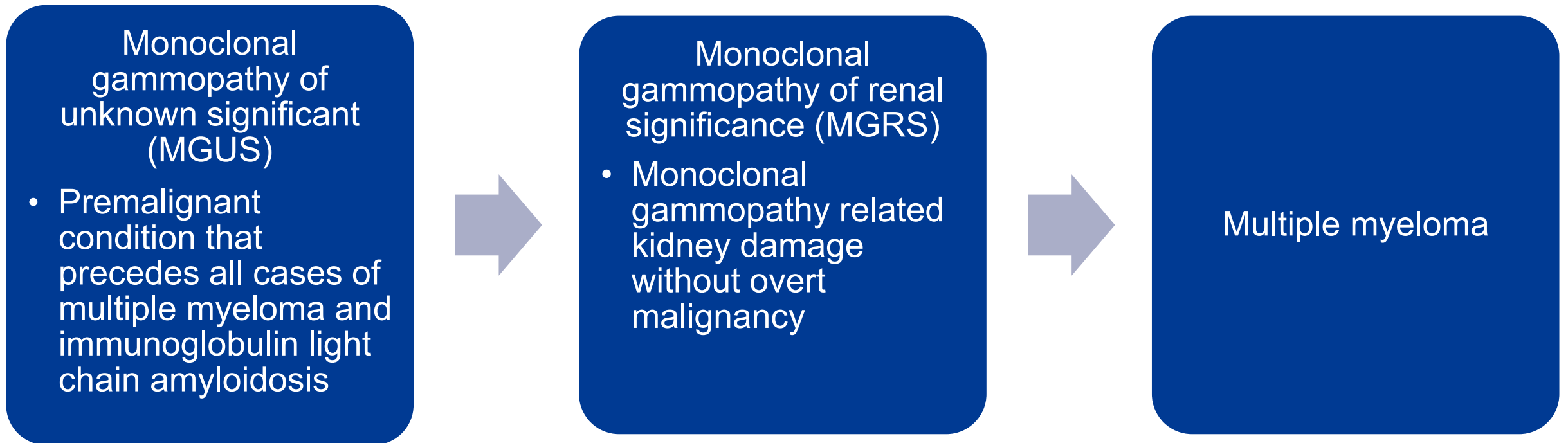
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Monoclonal Gammopathy

- Monoclonal protein may be toxic due to its ability to bind other proteins, misfold, or deposit in tissues



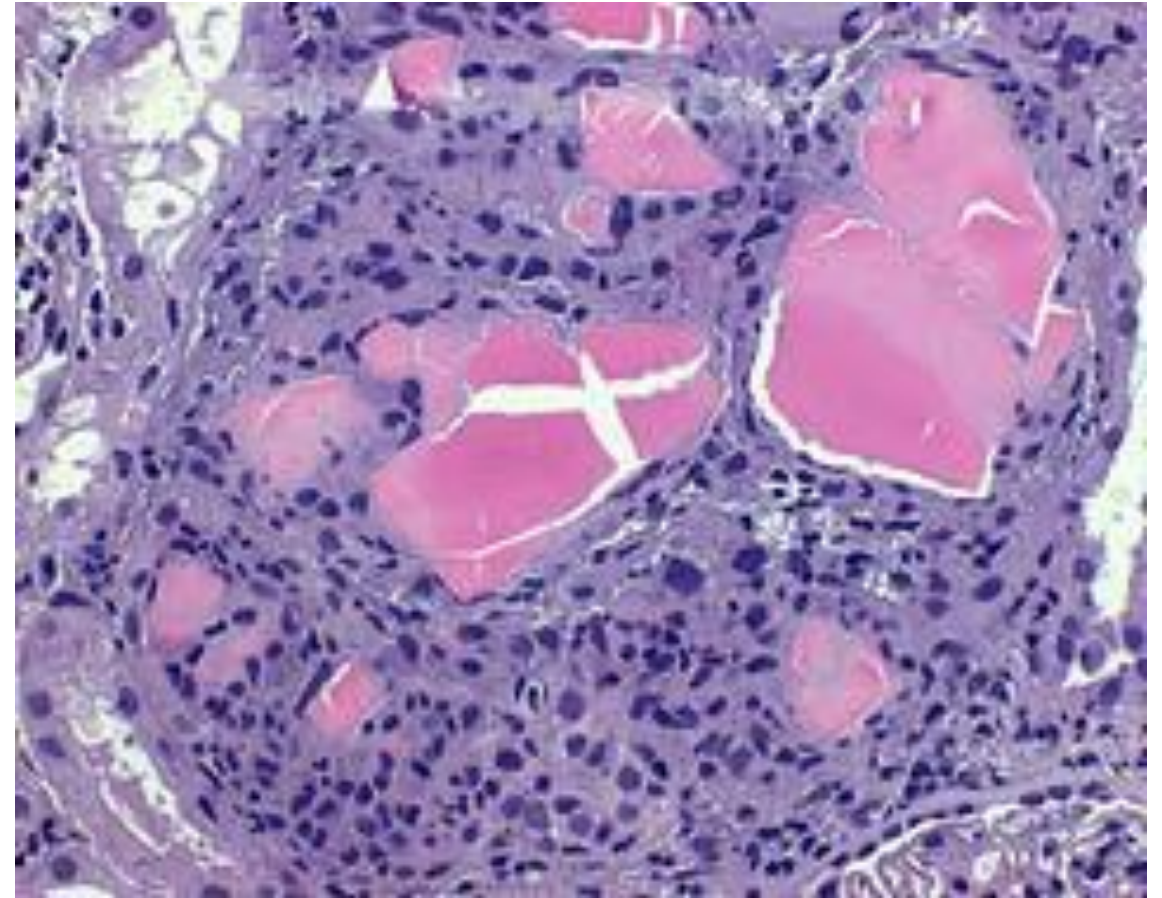
Multiple Myeloma in Nephrology

- In patients with MM newly diagnosed, 20-30% will present with estimated GFR <30 mL/min/1.73 m² at the time of diagnosis
- Dialysis is required in up to 5% of patients
- Most common cause of decreased GFR in patients with multiple myeloma is light chain cast nephropathy
 - In an autopsy series, $> 66\%$ of patients with myeloma with renal involvement had cast nephropathy



Cast Nephropathy

- Overproduction of light chains → tubular capacity for reabsorption is exceeded
- Filtered light chains and immunoglobulins then bind Tamm-Horsfall glycoprotein in the distal nephron
- Cast formation causing tubular obstruction in the distal nephron that elicits an inflammatory response
- Gold standard for diagnosis: kidney biopsy



Kidney biopsy: hypereosinophilic fractured casts within tubules

Question 3

A 58 year old man with a 12-year history of T2DM (HbA1C of 8.2), HTN, HLD, and CKD3B with urine albumin to creatinine ratio of 0.5g/g (normal <0.03 g/g). Currently managed with lisinopril 40 mg/d, amlodipine 10 mg/d, and empagliflozin 25 mg/d. On exam: BP 132/60 mmHg, HR 70 bpm. Trace to 1+ edema.

Which of the following is the most appropriate next step in management?

- A. No changes to therapy are needed other than optimizing glycemic control
- B. Finerenone
- C. Refer for kidney transplant evaluation
- D. Furosemide
- E. Add an angiotensin receptor blocker to his current regimen



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Question stem breakdown

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- Longstanding history of T2DM
- Uncontrolled T2DM
- Hypertension and hyperlipidemia
- Moderate albuminuria
- On max dose of lisinopril and SGLT2i



Guide to frequency of monitoring (number of times per year) by GFR and albuminuria category

				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
GFR categories (ml/min per 1.73 m ²) Description and range	G1	Normal or high	≥90	1 if CKD	1	2
	G2	Mildly decreased	60–89	1 if CKD	1	2
	G3a	Mildly to moderately decreased	45–59	1	2	3
	G3b	Moderately to severely decreased	30–44	2	3	3
	G4	Severely decreased	15–29	3	3	4+
	G5	Kidney failure	<15	4+	4+	4+

GFR and albuminuria grid to reflect the risk of progression by intensity of coloring (green, yellow, orange, red, deep red). The numbers in the boxes are a guide to the frequency of monitoring (number of times per year).



Diabetic Kidney Disease (DKD)

- First line therapy for DKD with albuminuria
 - Maximally dosed ACEi or ARB
 - Combination of ACEi and ARB are associated with increased risk of hyperkalemia and AKI
- SGLT2i (e.g. empagliflozin, dapagliflozin) are strongly recommended in DKD with albuminuria (≥ 200 -300 mg/g), regardless of glycemic control (EMPA-KIDNEY and DAPA-CKD)
- Nonsteroidal MRAs (e.g. finerenone) offer additional renal and cardiovascular protection in patients with T2DM and DKD (FIDELIO-DKD and FIGARO-DKD)



Question 4

A 62-year-old man is hospitalized for acute on chronic kidney disease attributed to diabetic nephropathy. He underwent a contrast-enhanced CT scan the day prior. Routine labs reveal an AKI and potassium of 8.2 mg/dL.

Which of the following ECG findings is LEAST likely to be associated with severe hyperkalemia:

- A. Peaked T waves
- B. Prolonged QRS interval
- C. Flattened p wave
- D. Sine wave-like QRS complex
- E. U wave



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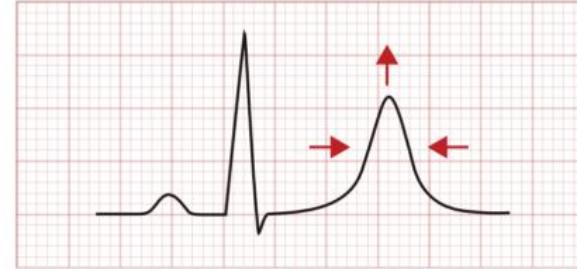
EKG changes in hyperkalemia

- Hyperkalemia leads to a depolarizing effect on the heart
- Early:
 - Tenting/peaked of T waves
 - Prolonged PR interval
 - ST segment depression
- Moderate/Later
 - Progressive widening of QRS
- Late
 - Appearance of sine wave pattern (P wave disappears, further widening of QRS)
 - Ventricular fibrillation and asystole

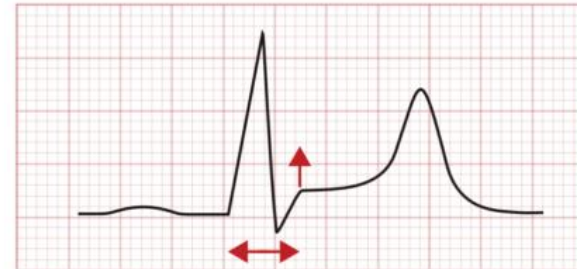
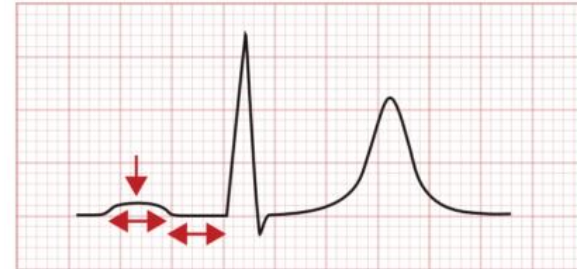
Normal potassium



K⁺ 5,5 mmol/L



Increasing serum potassium



Sine wave pattern



Mathematical sine wave



Question 5

A 72 year old woman with a history of hypertension and depression is admitted with confusion and unsteady gait. Her medications include hydrochlorothiazide and sertraline. On exam, she appears confused but is hemodynamically stable. Laboratory results are as follows:

Sodium: 119 mEq/L

Creatinine: 0.8 mg/dL

Glucose: 98 mg/dL

Serum osmolality: 260 mOsm/kg

Urine sodium: 48 mEq/L

Urine osmolality: 520 mOsm/kg

Which of the following is the MOST likely cause of her hyponatremia?

- A. Syndrome of inappropriate antidiuretic hormone secretion (SIADH)
- B. Primary polydipsia
- C. Hypervolemic hyponatremia
- D. Pseudohyponatremia



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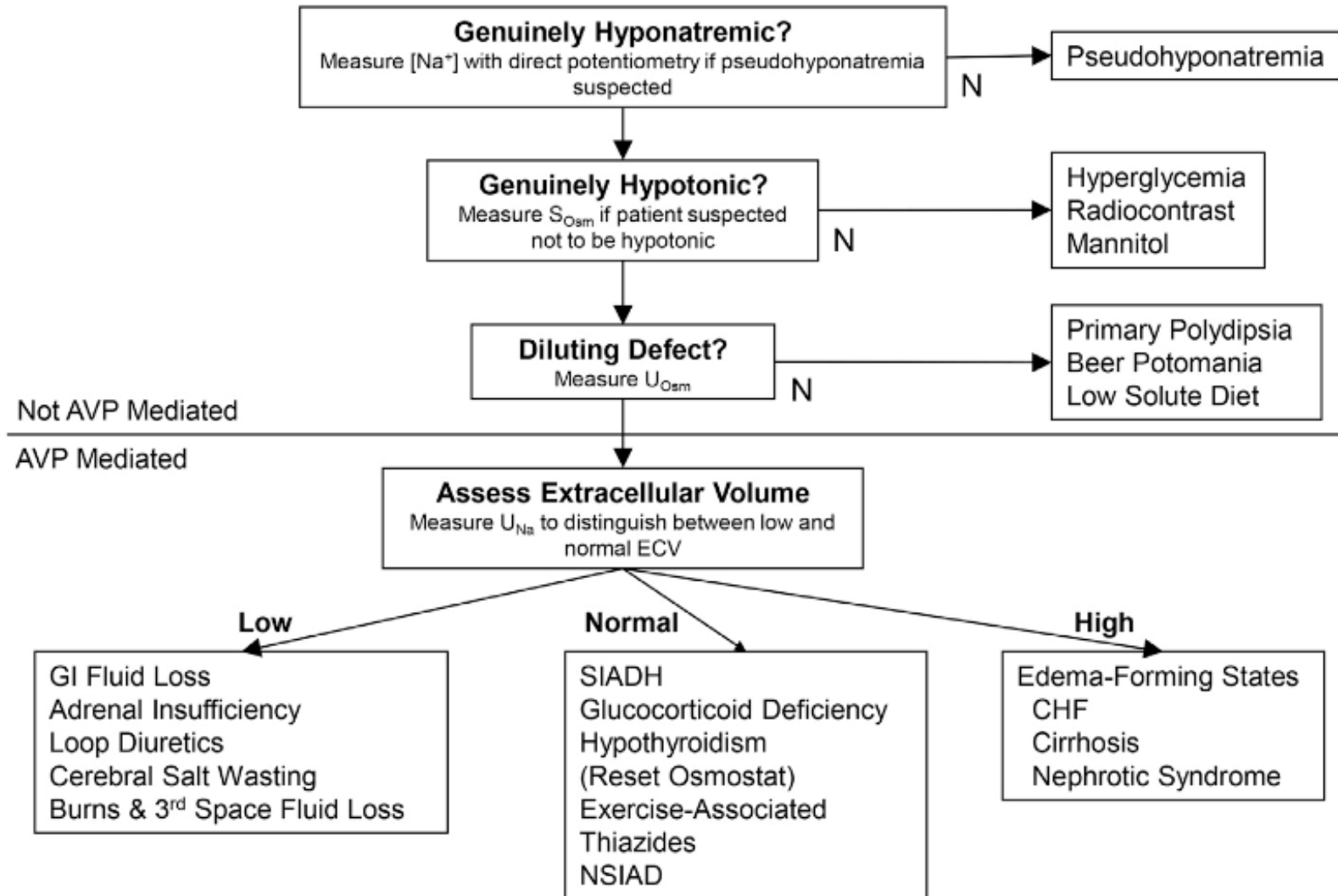


Adverse outcomes associated with chronic mild to moderate hyponatremia

- Cognitive impairment and decline
- Falls
- Fractures and osteoporosis
- Gait instability
- Mortality
- Calcium-forming kidney stones



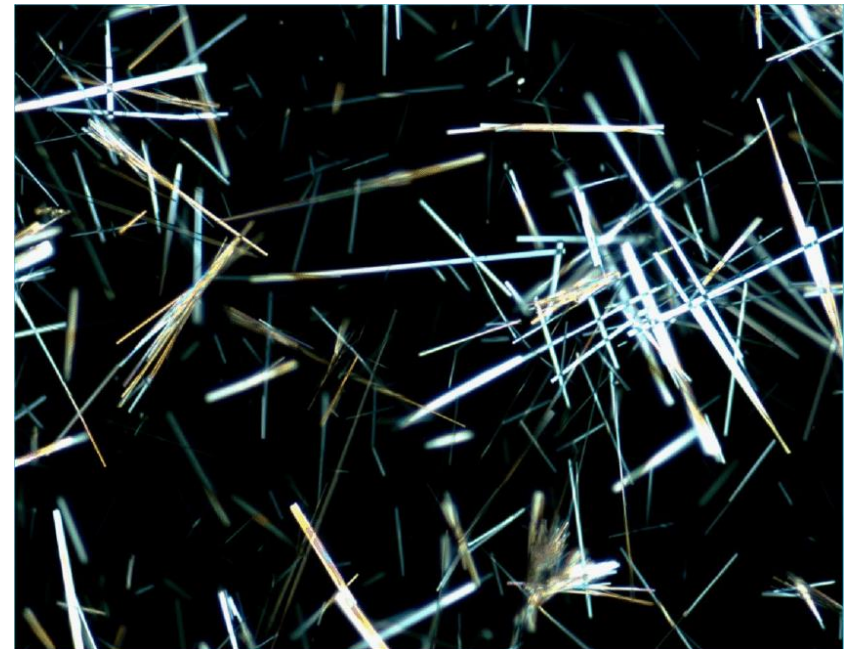
Approach to hyponatremia



Question 6

A 62-year-old man with T2DM and HTN is hospitalized for disseminated herpes zoster and is started on intravenous acyclovir. On hospital day 2, he develops nausea and right flank discomfort. Vital signs are stable. Urine output has decreased. Repeat labs show serum creatinine of 2.4 mg/dL (baseline creatinine is 1.0 mg/dL). A urine sample is sent for microscopy. Which of the following is the most likely cause of this patient's acute kidney injury?

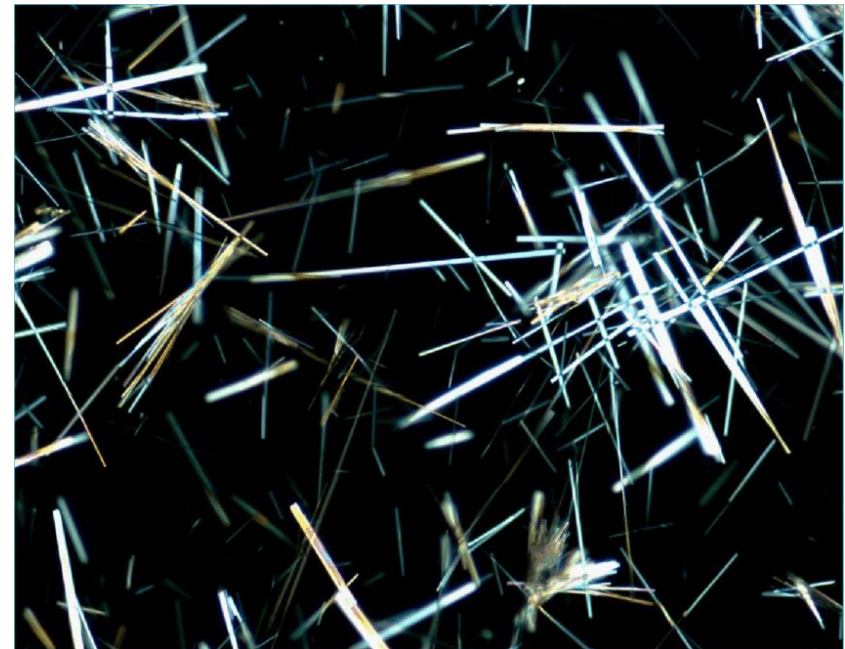
- A. Acute interstitial nephritis
- B. Acute tubular necrosis
- C. Obstructive crystal-induced tubulopathy
- D. Pre-renal azotemia due to volume depletion
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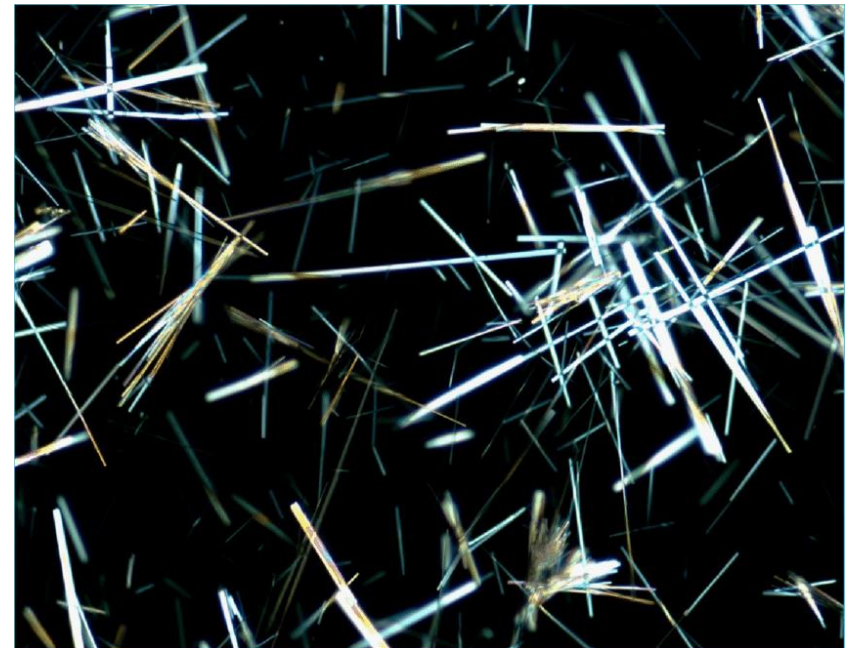
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Acyclovir induced nephropathy

- Acyclovir is renally excreted (65-90%) via glomerular filtration and tubular secretion
- With low urine flow or volume depletion, the drug can precipitate as needle-shaped crystals leading to tubular obstruction and AKI



Question 7

A 45-year-old man is evaluated for recurrent episodes of flank pain and hematuria. A non-contrast CT scan confirms the presence of a renal calculus. He has no significant past medical history and takes no medications. His diet is unremarkable.

Which of the following is the MOST common type of kidney stone identified in patients in the United States?

- A. Cystine stone
- B. Triple phosphate stone
- C. Struvite stone
- D. Calcium oxalate stone
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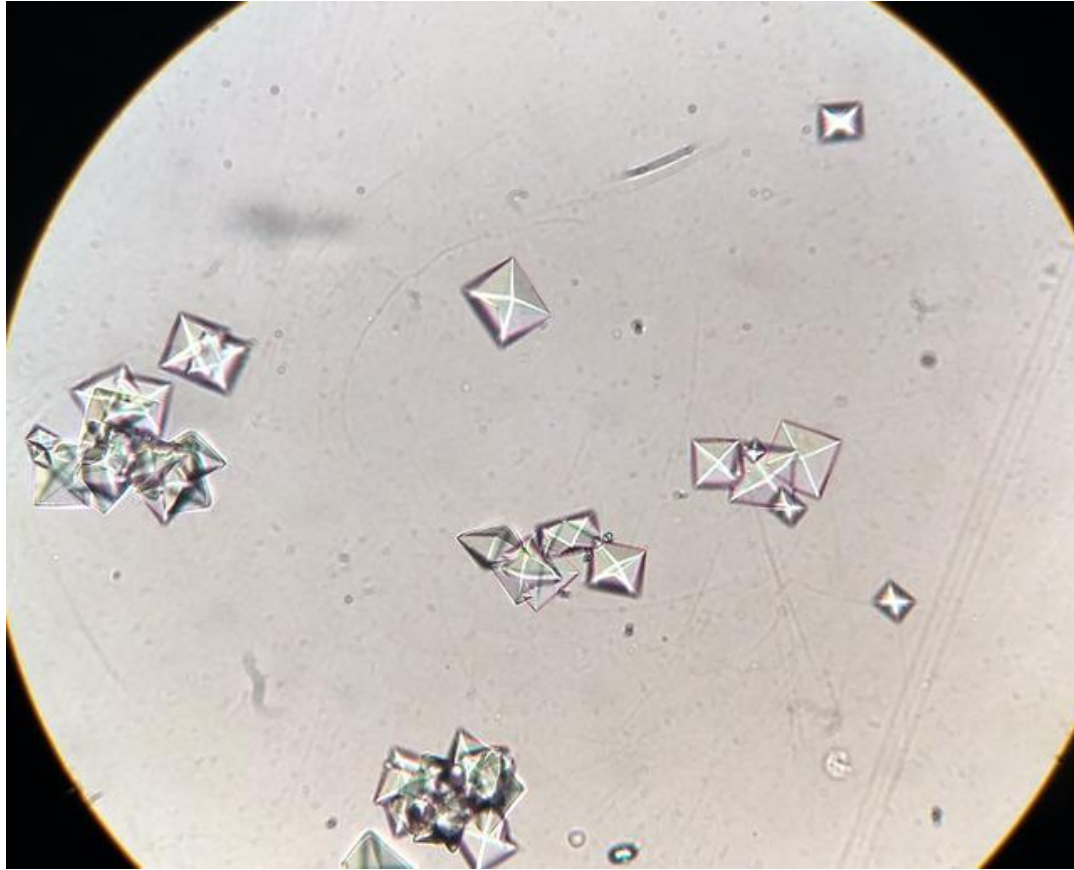


Nephrolithiasis

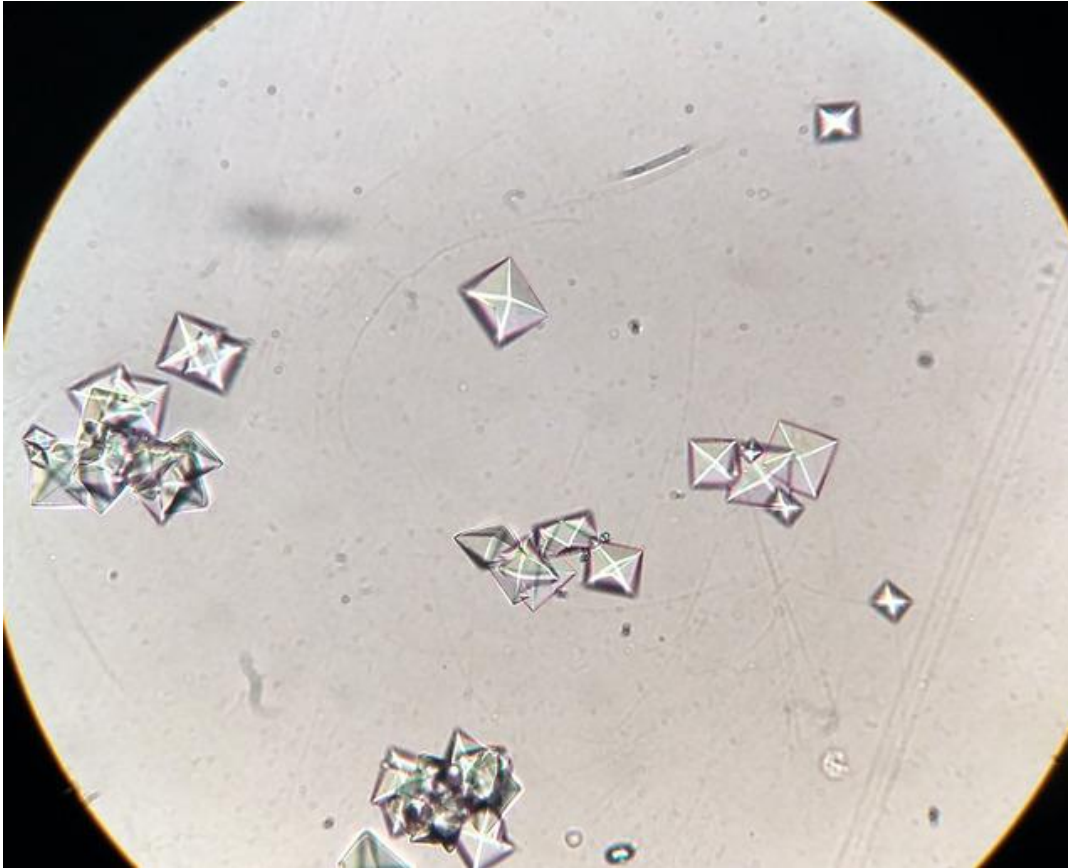
- Affects approximately 1 in 11 people in the U.S.
- By age 70, 19.1% of men and 9.4% of women report ever having a kidney stone
- Risk of stone recurrence is high, with a relapse rate of 50% in 5-10 years and 75% in 20 years
 - Risk factors: younger age of onset, male gender, family history of kidney stones, higher BMI
- Increased risk of developing CKD compared to non-stone formers



High yield crystals



High yield crystals



Calcium oxalate dihydrate crystals

- Most common cause of nephrolithiasis in the U.S.
- Causes: oxalate rich diets
- Key characteristics: bipyramidal shape, octahedral shape, "envelope shape"

High yield crystals



High yield crystals



Calcium oxalate monohydrate crystals

- Key characteristic: dumbbell shaped, ovoid (less common)
- Clinical context: ethylene glycol ingestion, primary hyperoxaluria, or enteric hyperoxaluria (e.g. chronic pancreatitis, IBD)

High yield crystals



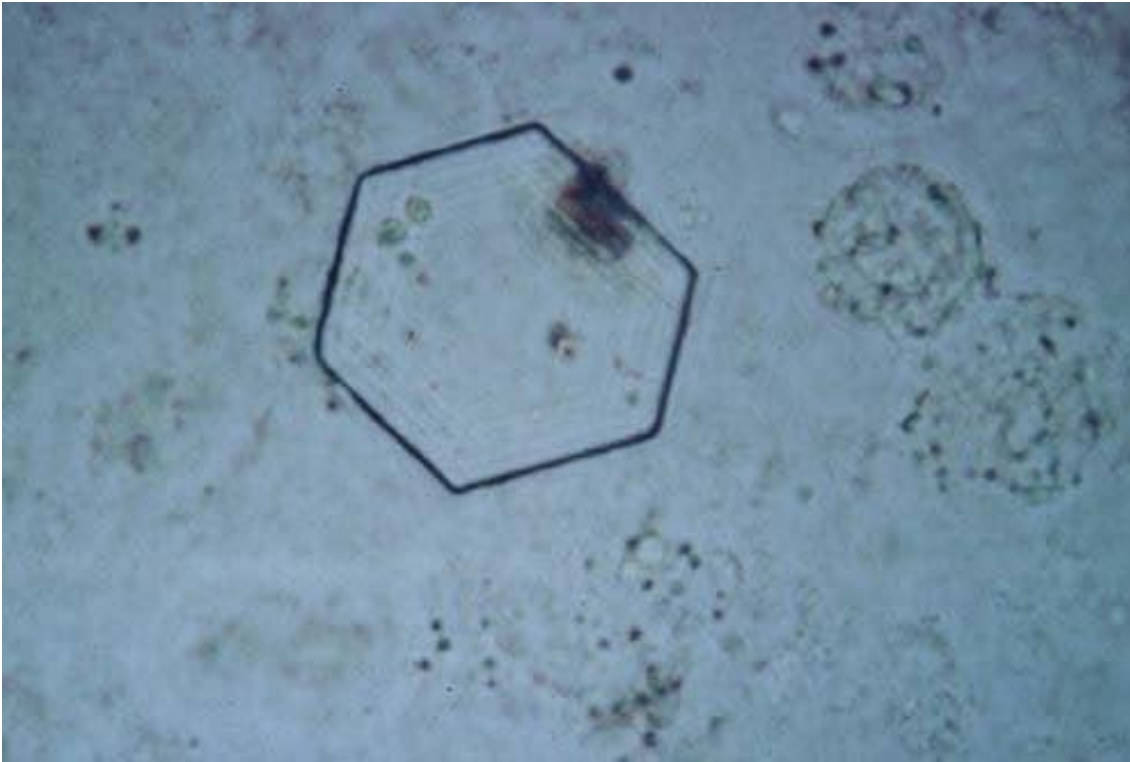
High yield crystals



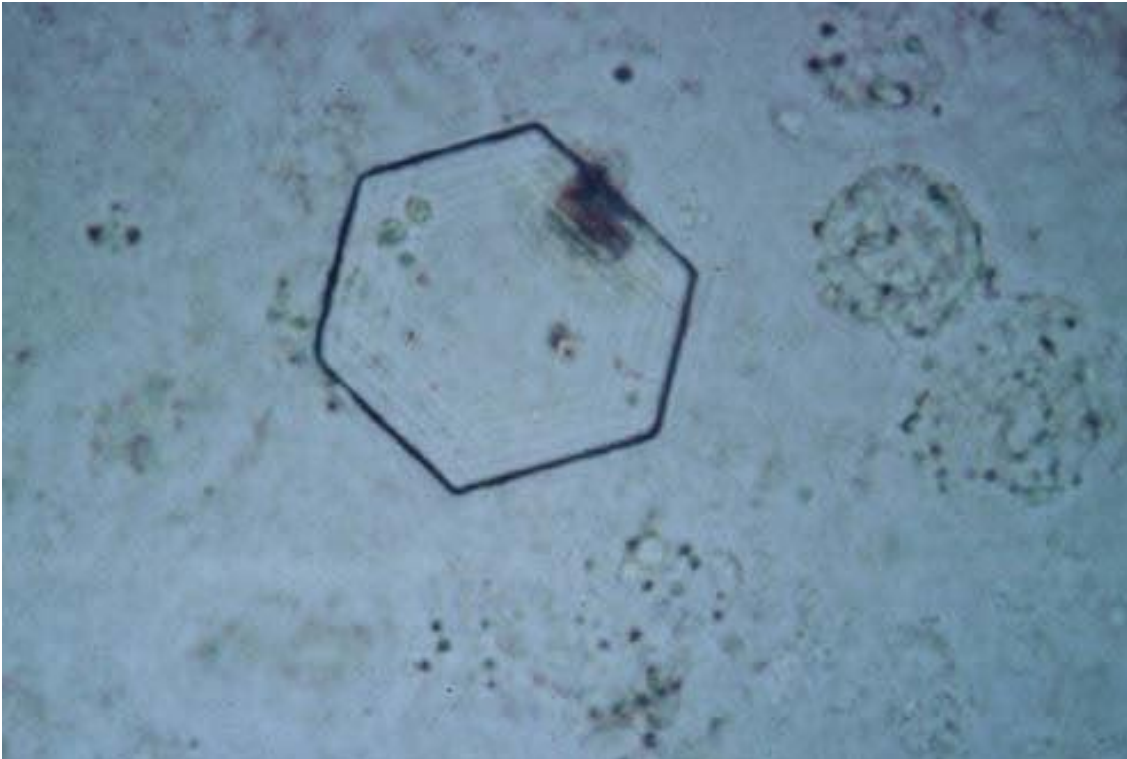
Struvite (triple phosphate) crystal

- Characteristic: coffin-lid
- Clinical context: alkaline urine, urea-splitting bacteria in upper urinary tract, recurrent UTIs

High yield crystals



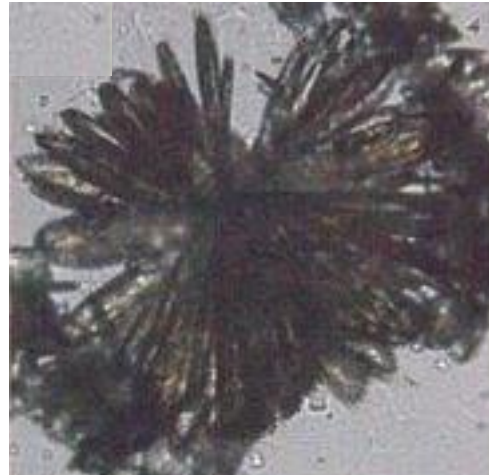
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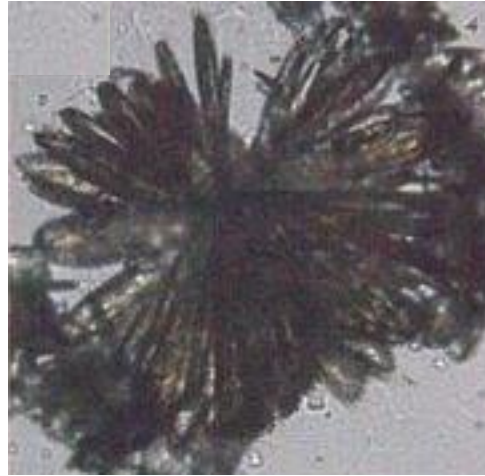
Cystine

- Characteristic: hexagonal shaped plates
- Cause: mutation in SLC7A9 and SLC3A1 affected patients excrete high amounts of cystine in urine
- Clinical context: young patient, +family history

High yield crystals



High yield crystals



Uric acid crystals

- Characteristic: polymorphous (barrel, rosette, rhomboid), yellow/amber colored, birefringent in polarized light
- Clinical context: TLS, hyperuricemia

Imaging Workup

- **Non-Contrast helical CT: imaging modality of choice**
 - High sensitivity and specificity
 - Ability to detect nearly all types of stones (EXCEPT those caused by protease inhibitors)
 - Accurate delineation of size and location
- **Ultrasound:**
 - Good specificity but poor sensitivity
 - Used in patients needing avoidance of radiation (pregnant, pediatric)
- **Plain abdominal X-ray**
 - Can be used for patients with documented radiopaque stones to assess stone clearance, recurrence or growth
 - Will miss radiolucent stones, small stones, stones with overlying bony structures.



Management of stones

- **If stone <5 mm**
 - > 60% of passing spontaneously
 - Supportive treatment, hydration, and strain urine
- **If stone 5-10 mm**
 - ~50% chance of passing
 - Supportive care, hydration, alpha blocker (more effective for distal stones), strain urine
- **If stone > 10 mm :**
 - ~25% chance of passing
 - Urology evaluation and strain urine
- For ANY size with
 - Urosepsis, AKI, anuria, unyielding N/V/Pain → admission with urgent urology evaluation
 - Failed conservative management and stone did not pass spontaneously -> Inpatient or Outpatient urology evaluation depending on severity



Question 8

A 24 year old man presents with 3 days of dark-colored urine, facial puffiness, and mild shortness of breath. He had a sore throat 2 weeks ago that resolved without antibiotics. On physical exam, he has periorbital edema and hypertension (BP 148/92). There are no rashes or joint findings. Serum creatinine: 2.0 mg/dL (unknown baseline), C3: low, C4: normal. Urinalysis reveals: 2+ protein, numerous RBCs, red blood cell casts.

Which of the following is the most likely diagnosis?

- A. Minimal change disease
- B. Post-infectious glomerulonephritis
- C. IgA nephropathy
- D. Acute interstitial nephritis
- E. Lupus nephritis



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Infectious organisms associated with GN

Bacterial

- Gp A-beta strep
- Staph aureus
- Staph epi
- Gram neg bacilli
- Strep pneumoniae
- Treponema pallidum
- Salmonella typhi
- Meningococcus
- Leptospirosis

Viral

- Hep B and C
- CMV
- Enterovirus
- Measles
- Parvovirus
- Oncovirus
- Mumps virus
- Rubella
- Varicella

Parasitic

- Plasmodium malariae
- Toxoplasma
- Filaria
- Schistosomia
- Trichenella
- Trypanosome

Rickettsial

- Scrub typhus

Fungal

- Coccidioides immitis



Postinfectious Glomerulonephritis

- Presents as an acute nephritic syndrome with low complement C3 in serum
- Commonly follows 10-14 days after pharyngeal or skin infection
- Most commonly occurs in children or young adults
- Presentation: hematuria (70%), proteinuria (usually $<2\text{g}/24\text{H}$), RBC casts periorbital edema, weight gain, HTN, oliguria
- Pathogenesis: antigens of infectious agent activate the alternate complement pathway. Immune complexes may be circulating or antigens can bind within the glomerulus with antibody and complement activation
- Serology
 - Antistreptolysin Ab (ASO)
 - Antideoxyribosenuclease B (anti-DNAse B)
 - Antinicotyladenine dinucleotidase (anti-NAD)



Question 9

A 42 year man with no past medical history completes the Boston Marathon in 4 hours. Shortly after finishing the race, he develops severe muscle cramps. Later that evening, he notes low urine output that appears tea-colored and presents to the emergency department. His vital signs are normal except for HR 102. Labs show: creatinine 4.0 mg/dL, BUN: 18 mg/dL, potassium: 5.8 mEq/L, pH 7.38. Urinalysis: 3+ blood, 0-2 RBCs per high power field on microscopy.

Which of the following is the MOST appropriate next step in management?

- A. Perform renal ultrasound
- B. Begin pulse dose methylprednisolone
- C. Immediate initiation of hemodialysis
- D. Aggressive IV hydration with isotonic saline



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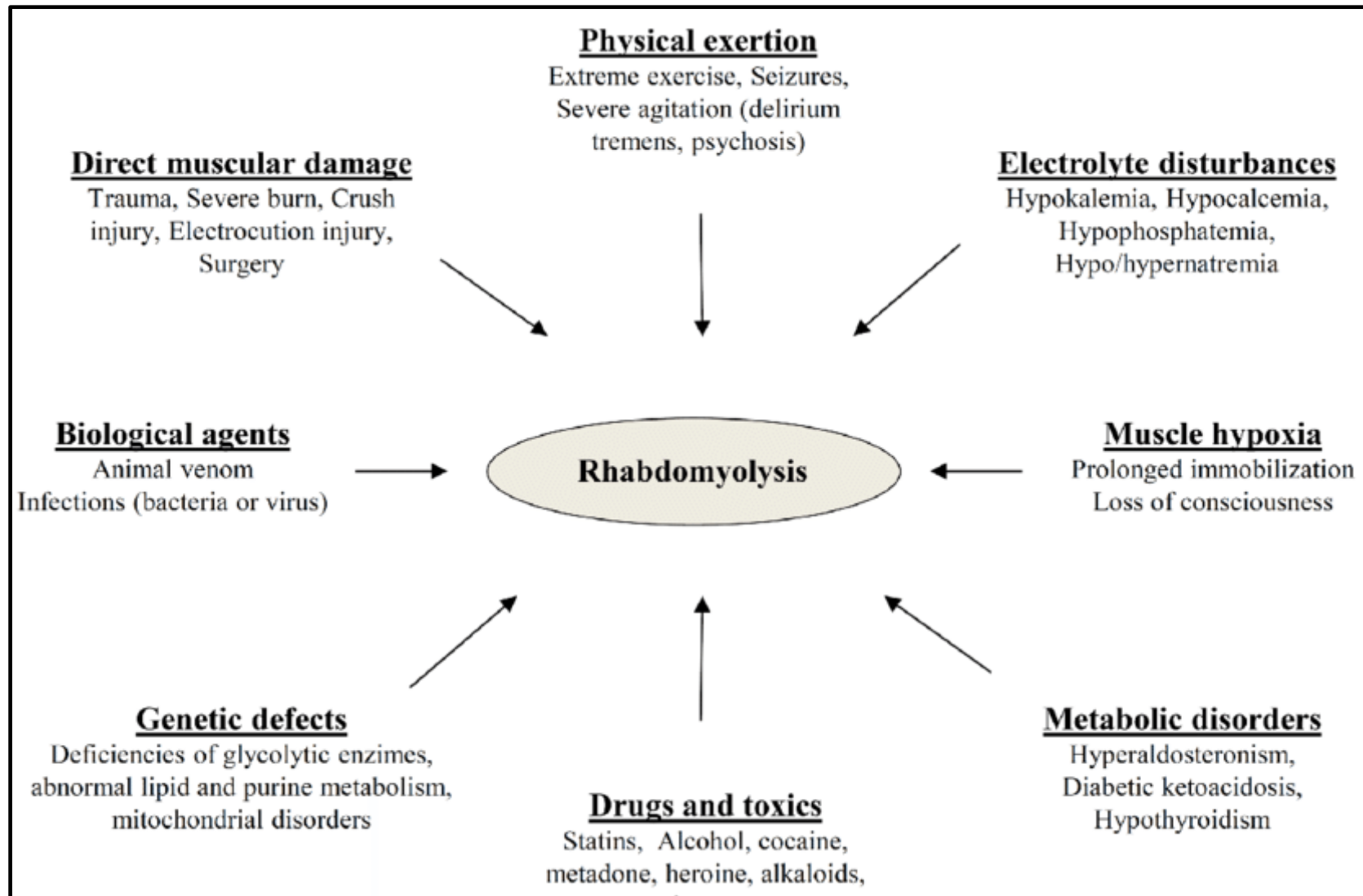
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Causes of Rhabdomyolysis



Rhabdomyolysis on kidney function

- Rhabdo + AKI have a mortality of 20%
- Mechanism of kidney injury:
 - Massive release of myoglobin into the circulation with myoglobinuria
 - Urine myoglobin excretion exceeding 100-300 mg/dL causes cast formation and accumulation of iron in proximal tubules with intratubular obstruction and proximal tubular injury
 - Volume depletion due to sequestration of fluids into injured muscles
 - Release of cellular contents from damaged muscles leads to HAGMA, hyperkalemia, hyperphosphatemia, and hyperuricemia



Management of patients with AKI from rhabdomyolysis

- Saline solutions to expand/restore intravascular volume
 - Goal to increase urine flow (200-300 mL/h)
- Sodium bicarbonate infusion to alkalinize the urine to potentially avoid myoglobin precipitation and inhibit reduction-oxidation cycling of myoglobin and lipid peroxidation
 - Risk for metastatic tissue calcification and ionized hypocalcemia
 - No studies have compared bicarbonate therapy with IV fluid therapy alone
- Dialytic therapy



Question 10

A 55 year old woman with hypothyroidism presents for evaluation of hypertension that has been difficult to control. Her medications include chlorthalidone 25 mg daily, verapamil ER 240 mg daily, carvedilol 25 mg BID, and valsartan, recently increased from 160 mg daily to twice daily. Her baseline creatinine level is 1.1 mg/dL but has gradually increased to 1.8 mg/dL. Her electrolyte panel is notable for potassium of 4.9 mEq/L and bicarbonate of 22 mEq/L. She denies any symptoms. Blood pressure in clinic is 164/94.

Which of the following is the MOST appropriate next step?

- A. Abdominal CT scan with adrenal protocol
- B. Polysomnography
- C. Renal angiography
- D. Renal duplex ultrasonography



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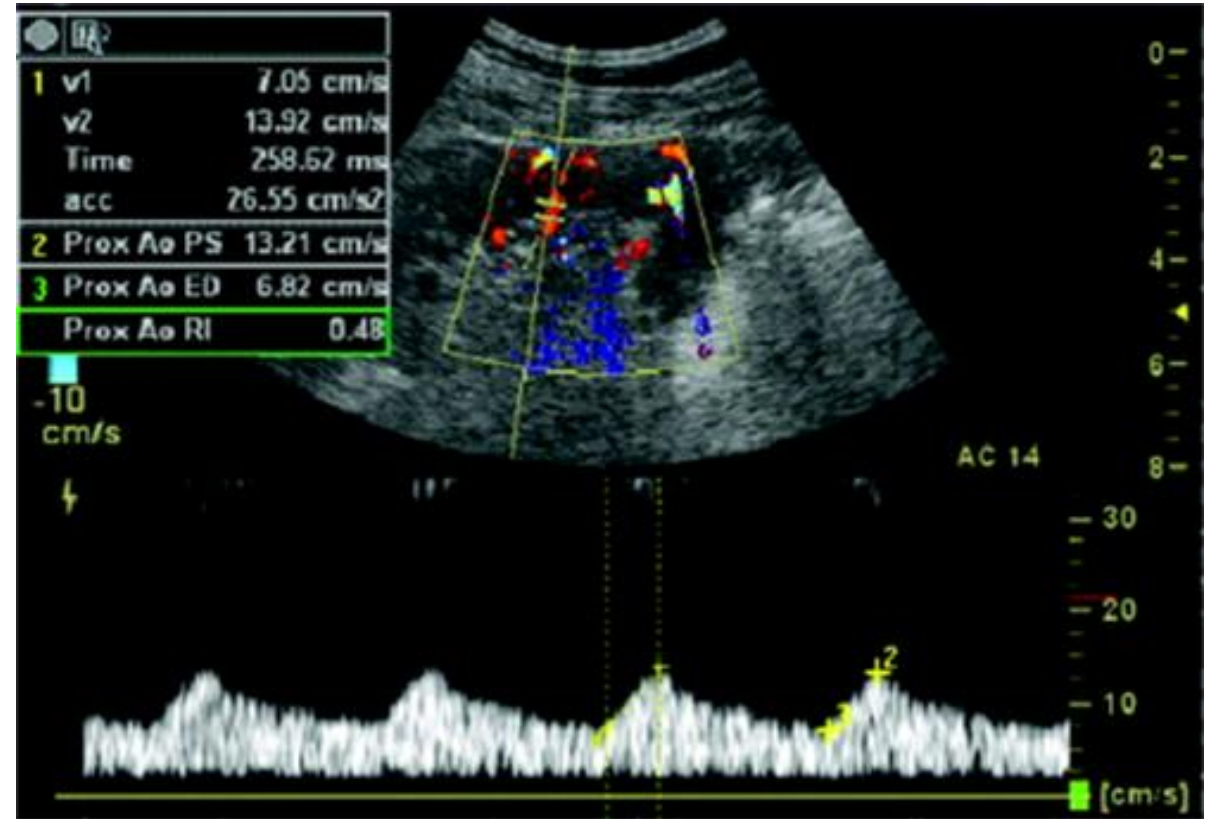
Resistant Hypertension

- Definition: BP is not at goal despite 3 different classes of antihypertensives at the highest tolerated dose with one being a diuretic
- Patients with resistant HTN are nearly 50% more likely to have a cardiovascular event and 25% more likely to develop kidney failure than those with HTN that is not resistant



Renal artery stenosis (RAS)

- RAS is common among those with resistant HTN, especially older adults with known vascular disease, smoking history, diabetes, and CKD
- Duplex ultrasound imaging is the most common initial imaging test performed in those with a high pretest probability of a RAS diagnosis
- Elevated peak systolic velocity is the most sensitive and specific ultrasound criterion for a RAS diagnosis
 - Most common abnormality is a tardus-parvus waveform



Question 11

A 58 year old man on hemodialysis presents with bone pain and proximal muscle weakness.

Lab studies: serum calcium 7.2 mg/dL, phosphate 6.8 mg/dL, iPTH 680 pg/mL.

Which complication of mineral bone disease is he most likely experiencing?

- A. Adynamic bone disease
- B. Secondary hyperparathyroidism
- C. Osteomalacia
- D. Beta-2 macroglobulin amyloidosis



Question 11

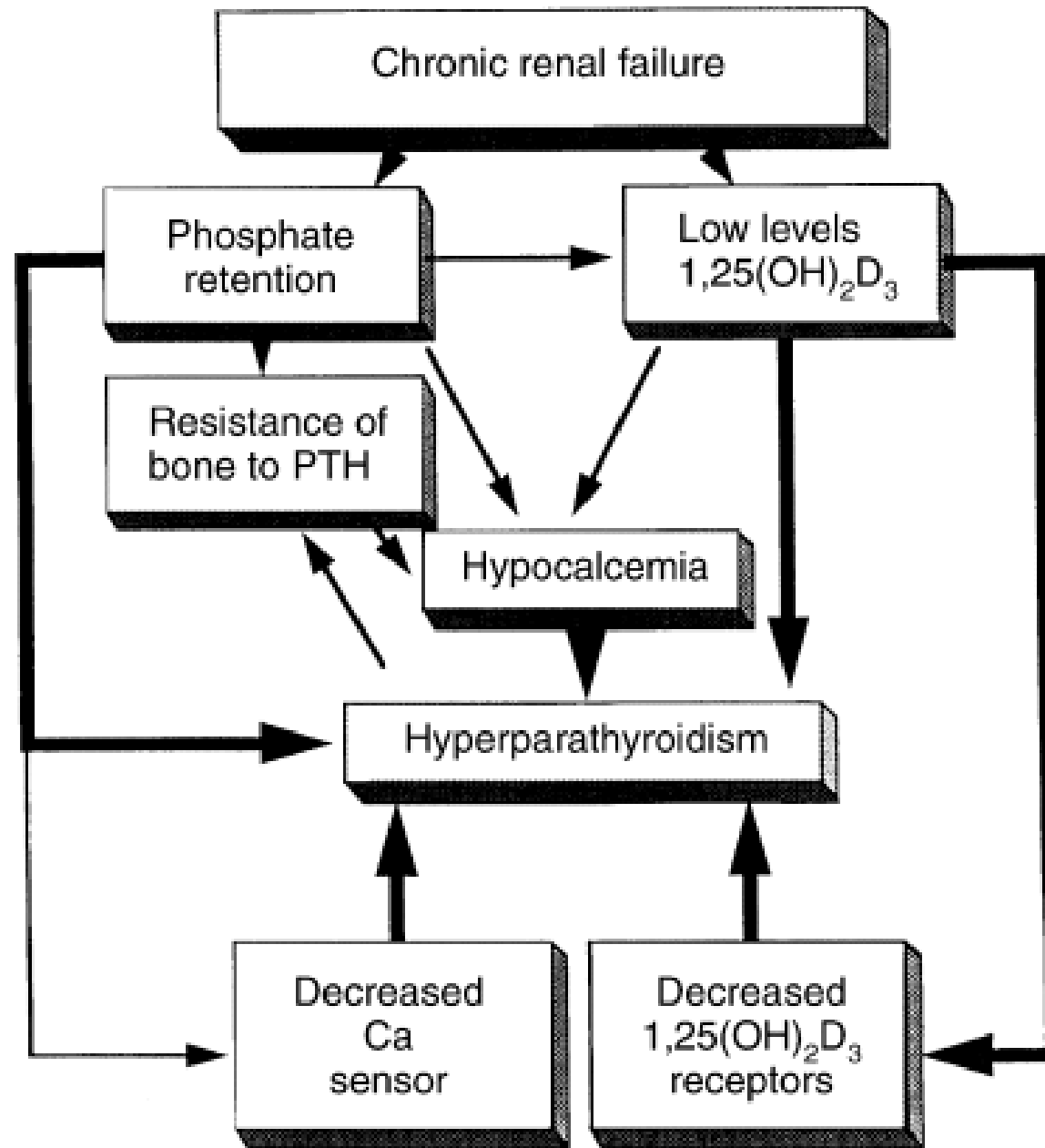
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Question 12

64 year old man on maintenance hemodialysis develops hypercalcemia (11.8 mg/dL) and hyperphosphatemia (7.2 mg/dL). He has been non-compliant with phosphate binders. What complication is at highest risk for developing?

- A. Calciphylaxis
- B. Renal osteodystrophy
- C. Hungry bone syndrome
- D. Osteitis fibrosa cystica



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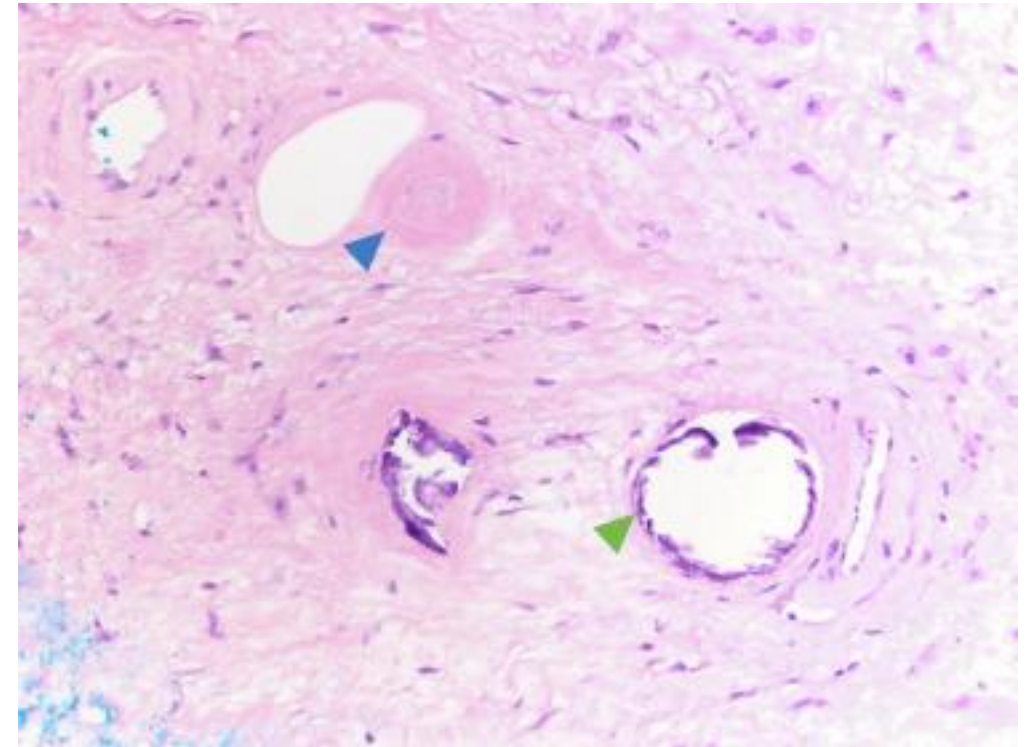
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Calciophylaxis (calcific uremic arteriolopathy)

- Life threatening complication associated with advanced kidney disease. Associated with 45-80% one-year mortality
- Deposition of calcium in the arteriolar microvasculature of the deep dermis and subcutaneous adipose tissue



Calciophylaxis continued

- Sx: painful evolving lesions
- Dx: skin biopsy
- Tx: wound care and symptom management
- Complications: sepsis from cutaneous wounds is the leading cause of death in patients with calciophylaxis



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Question 13

A 60 year old woman with autosomal dominant polycystic kidney disease (ADPKD) and hypertension is counseled about disease-modifying therapy. Which medication has demonstrated slowing of kidney disease progression in ADPKD?

- A. Enalapril
- B. Tolvaptan
- C. Verapamil
- D. Furosemide



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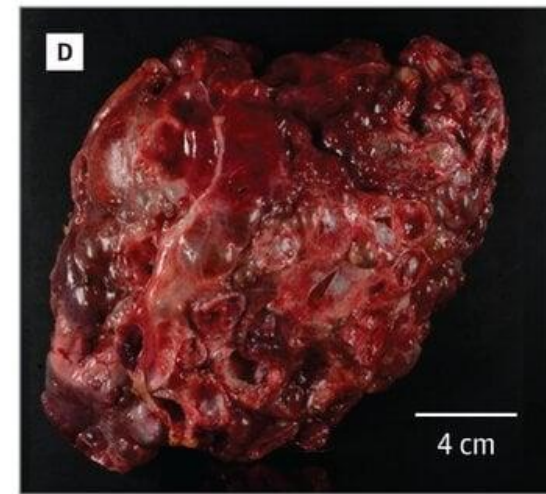
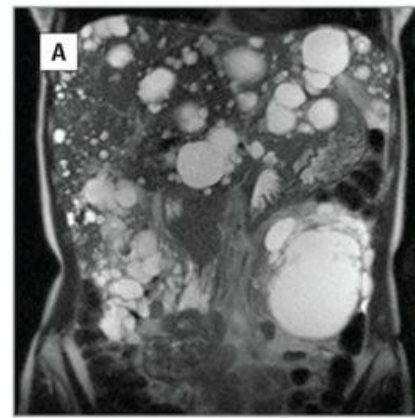


ADPKD

In 2018, V2R antagonist, tolvaptan was FDA approved for patients at risk for rapidly progressive disease following two pivotal clinical trials:

- TEMPO 3:4 demonstrated 50% reduction in the primary total kidney volume growth (2.8% in the tolvaptan vs 5.5% per year in the placebo arm, and a reduction in the rate of eGFR decline)
- REPRISE found 30-35% reduction in eGFR decline (2.34 mL/min/1.73 m² in the tolvaptan arm and 3.61 mL/min/1.73 m² in the placebo arm)

Side effects: polyuria, nocturia, and polydipsia
Severe liver toxicity*



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MOC REFLECTIVE STATEMENT

- In approaching nephrology questions, consider clinical context and targeted testing that is critical to accurately diagnose and manage acute and chronic kidney conditions.
- Serum creatinine is a useful marker for trending kidney function but it has important limitations
- POC urine dipstick may miss non-albuminuric proteinuria
- Nonsteroidal MRAs are an additional pillar of agents that can offer additional renal and cardiovascular protection in patients with T2DM and DKD
- In CKD-mineral and bone disorder, distinguish abnormalities in bone turnover from extraskeletal complication, as management differs.



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Thank you and good luck on your boards!



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