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
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Medicine Residency @ Maine Medical Center
Nephrology Fellowship @ BWH/MGH
Instructor @ HMS

- Clinical focus: Geriatric Nephrology
- Research focus: Supportive care of older adults with prevalent end stage kidney disease

DISCLOSURES

None

OBJECTIVES

- Review high-yield topics in Nephrology relevant to ABIM certification exam
- Strengthen diagnostic reasoning and clinical decision-making in Nephrology
- Highlight evidence-based management strategies aligned
- 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 1 day post arteriogram
E. Cimetidine treatment of peptic ulcer disease

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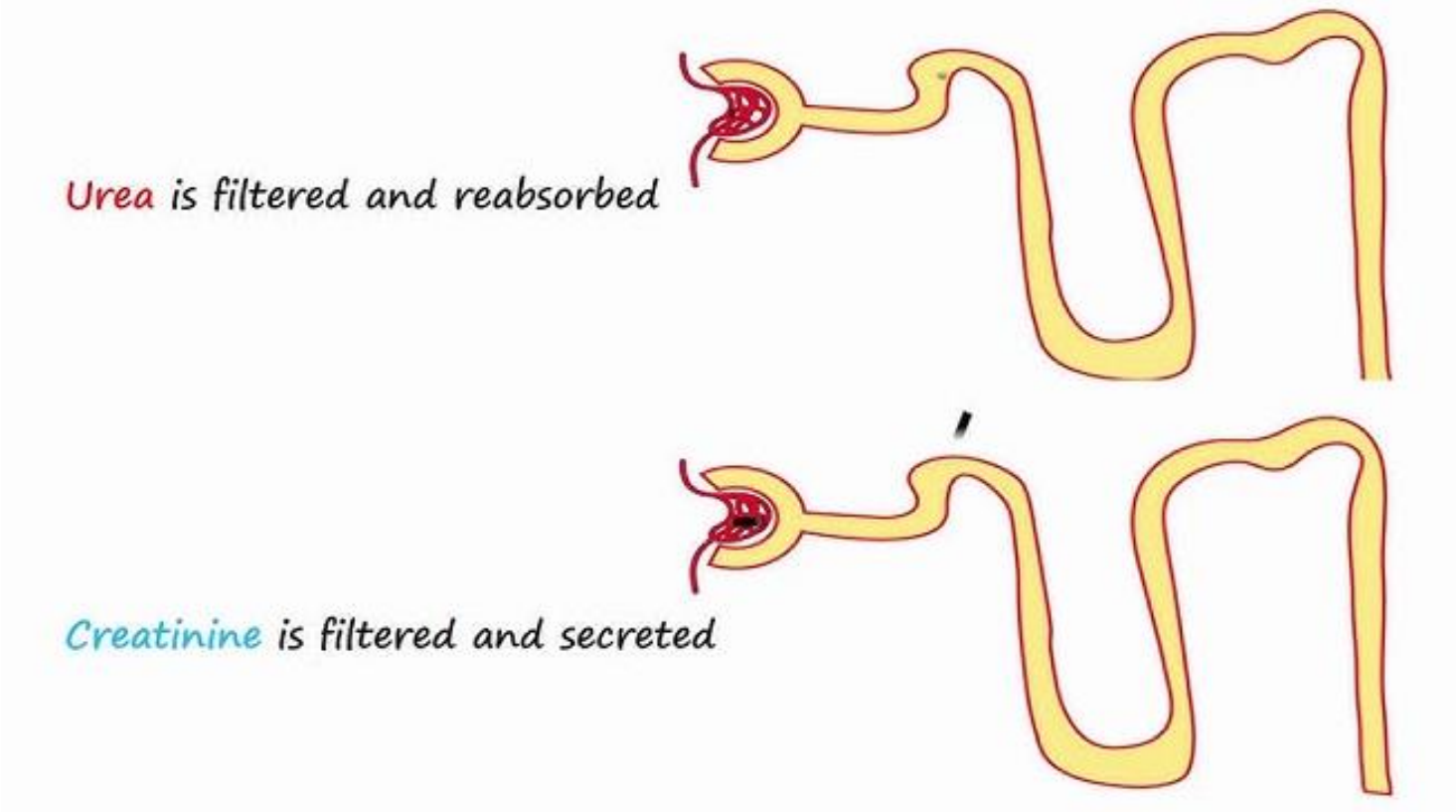
Creatinine

- 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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E. Cimetidine treatment of peptic ulcer disease

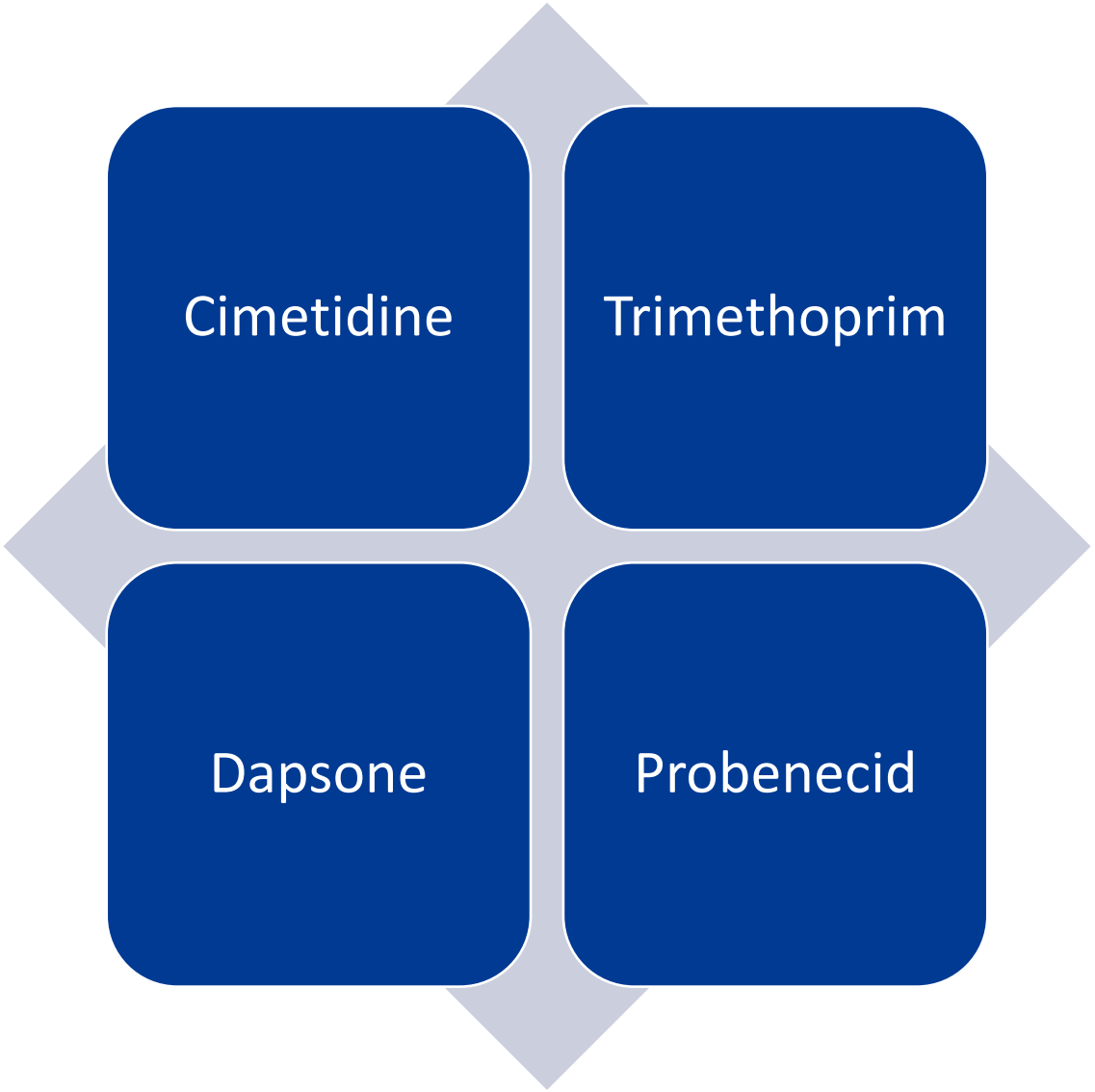
Cimetidine

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



Andreev et al. Journal of Internal Medicine 1999

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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Monoclonal Gammopathy

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

Monoclonal gammopathy of unknown significant (MGUS)

- Premalignant condition that precedes all cases of multiple myeloma and immunoglobulin light chain amyloidosis

Monoclonal gammopathy of renal significance (MGRS)

- Monoclonal gammopathy related kidney damage without overt malignancy

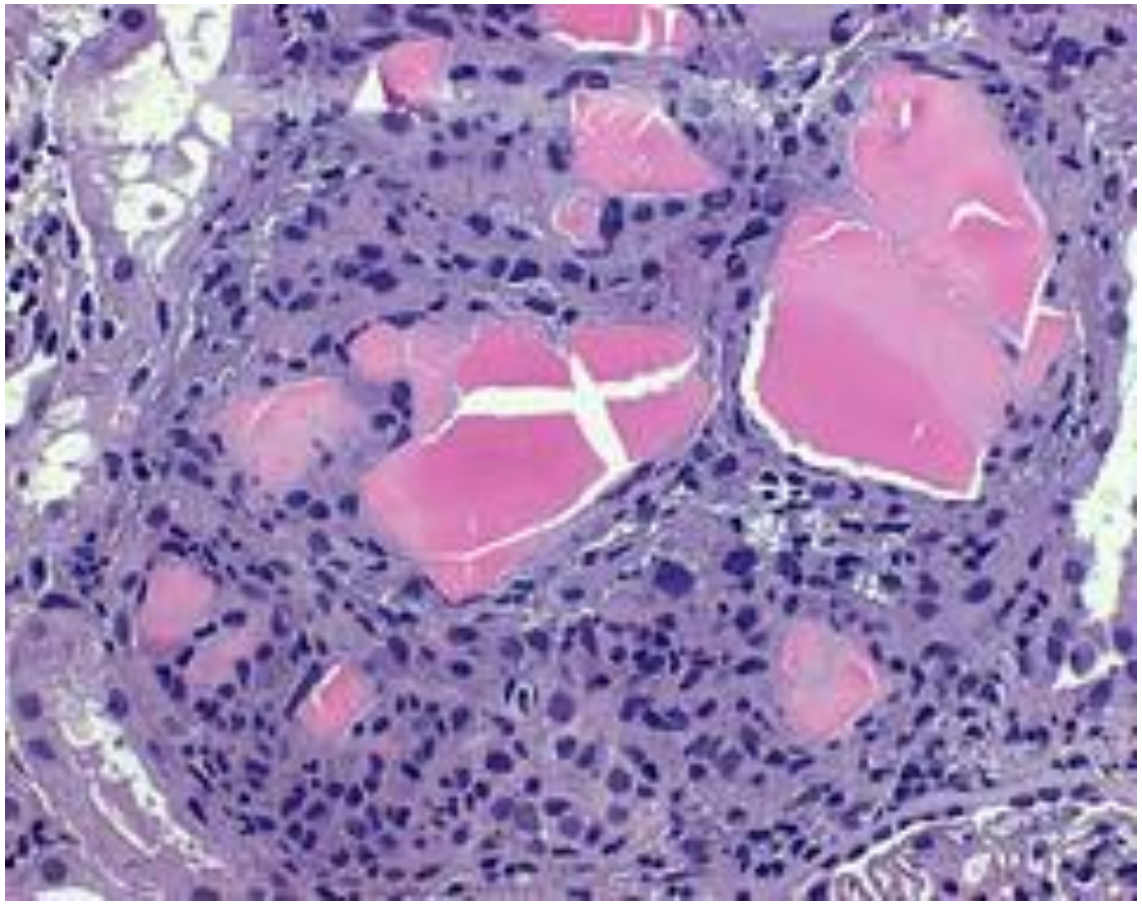
Multiple myeloma

Multiple Myeloma in Nephrology

- In patients with MM newly diagnosed, 20-30% will present with estimated GFR <30 mL/min/1.73 m^2 at the time of diagnosis
- Dialysis is required in up to 5% of patents
- 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 furosemide 40 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. Initiate an SGLT2 inhibitor and consider adding a non-steroidal mineralocorticoid receptor antagonist
C. Refer for kidney transplant evaluation
D. Intensify loop diuretic therapy to control edema
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

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

GFR categories (ml/min per 1.73 m²) Description and range				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
	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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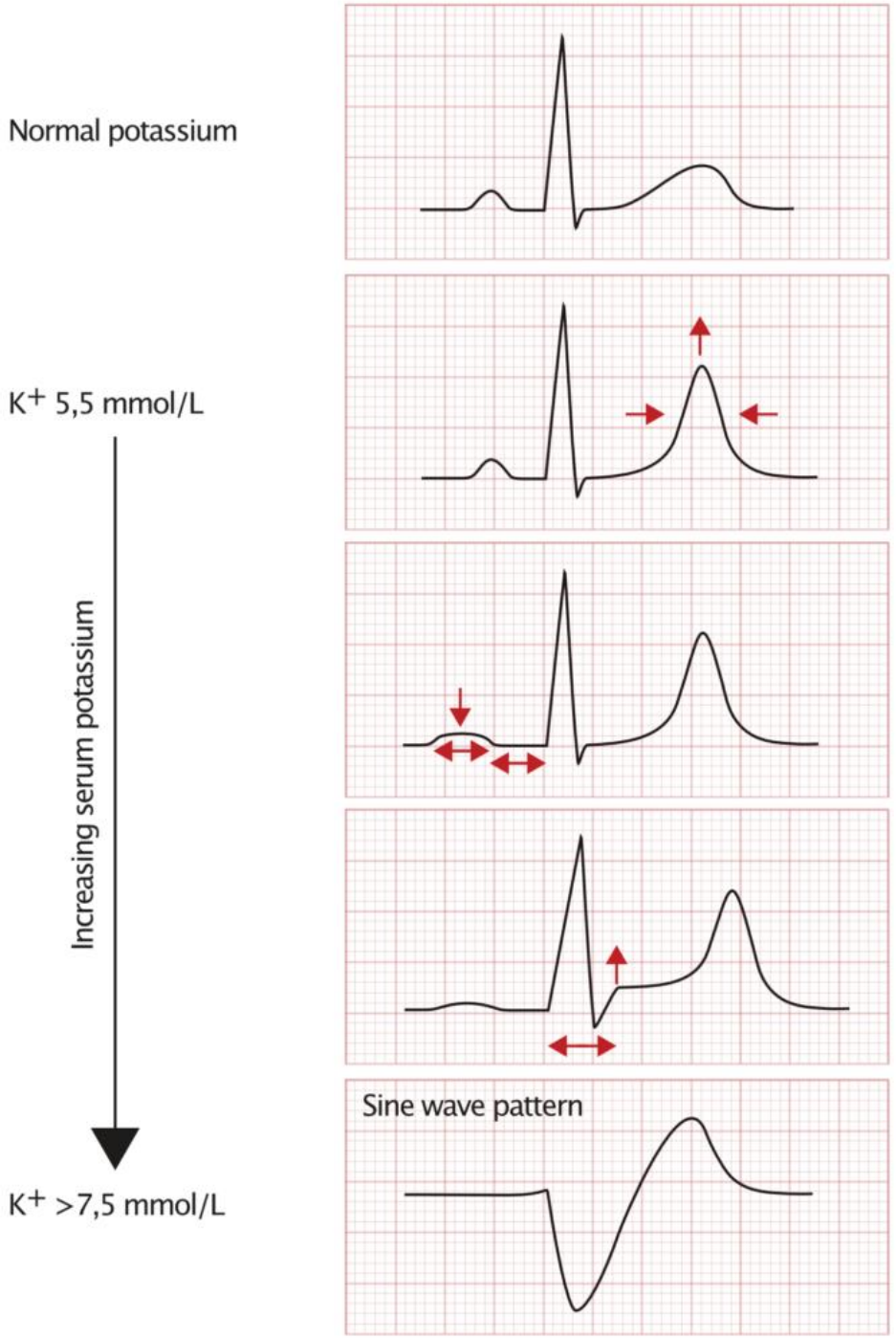
EKG changes in hyperkalemia

- 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



Palmer et al. Physiology and Pathophysiology of Potassium. AJKD 2019.
Image: ECGWaves

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. Thiazide-induced hyponatremia
C. Primary polydipsia
D. Hypervolemic hyponatremia
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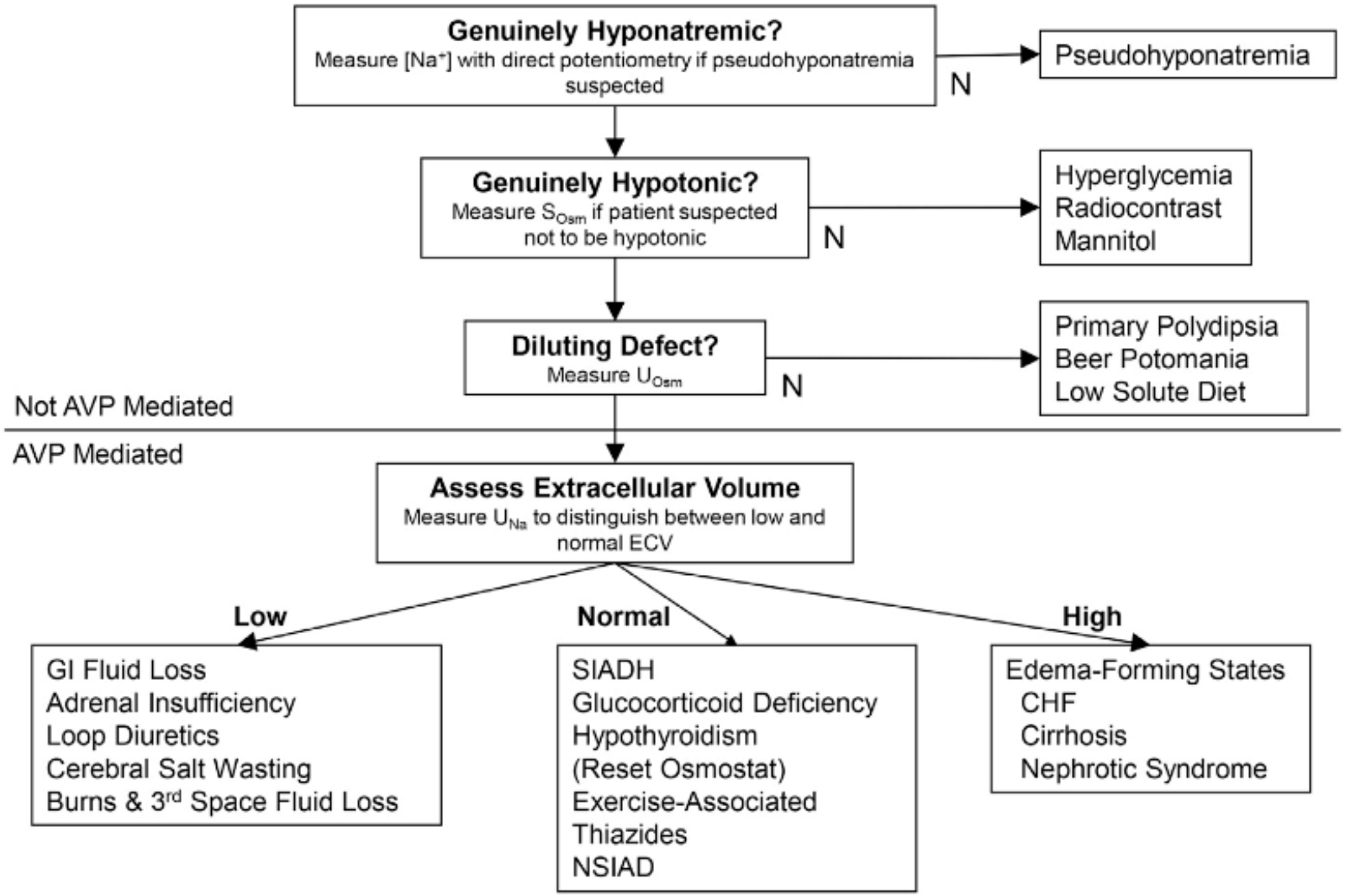
Adverse outcomes associated with chronic mild to moderate hyponatremia

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

Kinsella, S et al. CJASN 2010

Approach to hyponatremia

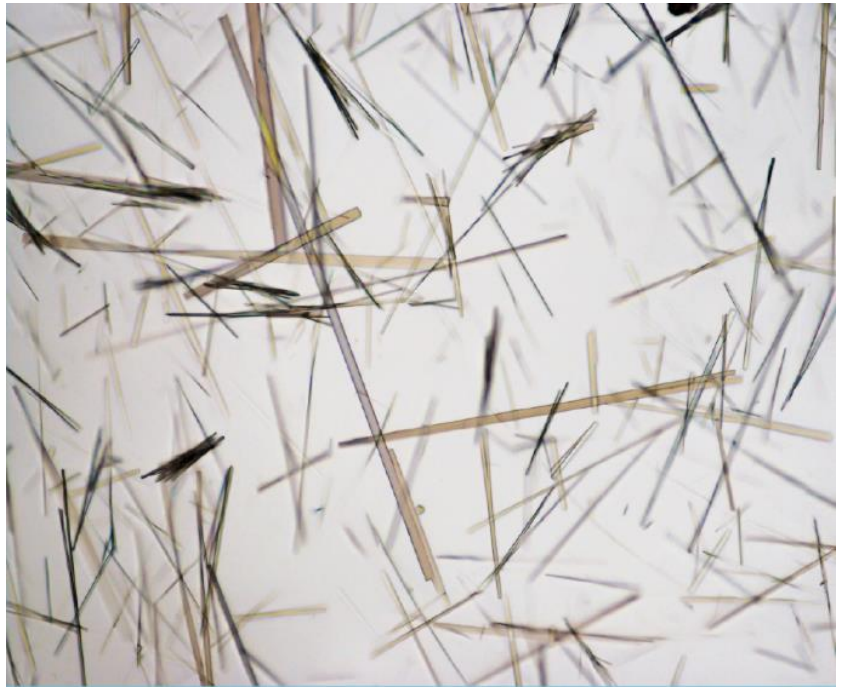


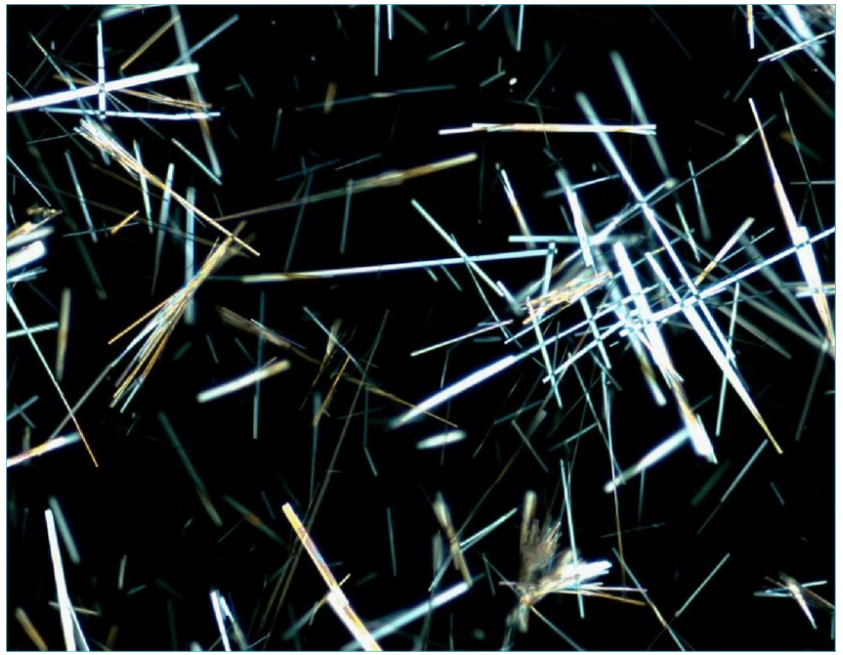
Seay et al. AJKD 2019

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
E. Uric acid nephropathy





Andrews et al. eJIFCC 2020

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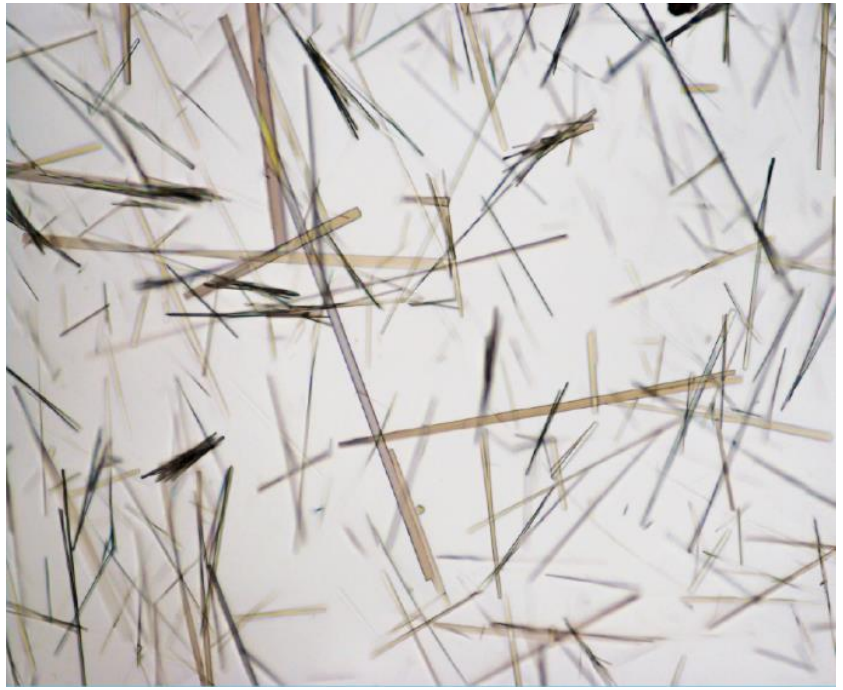
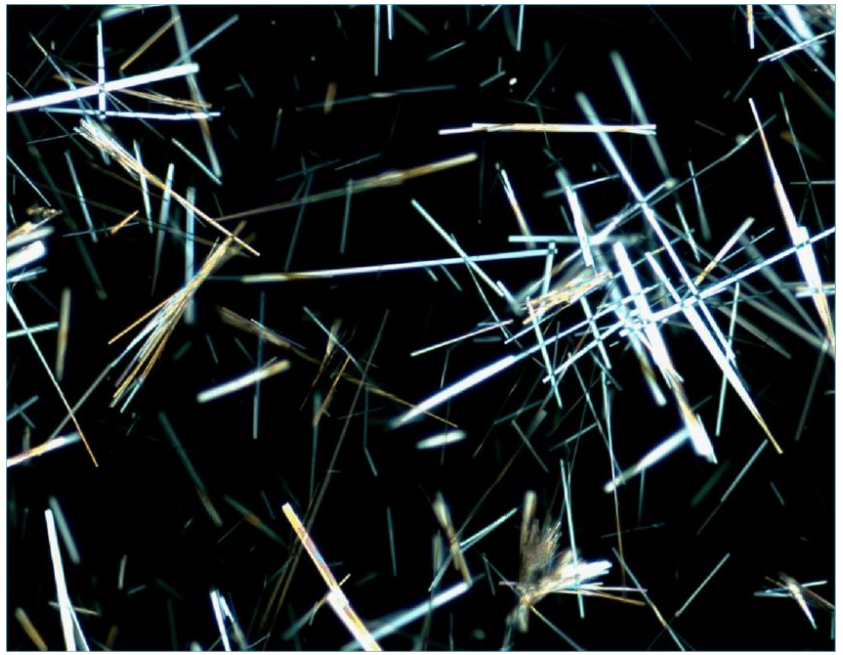
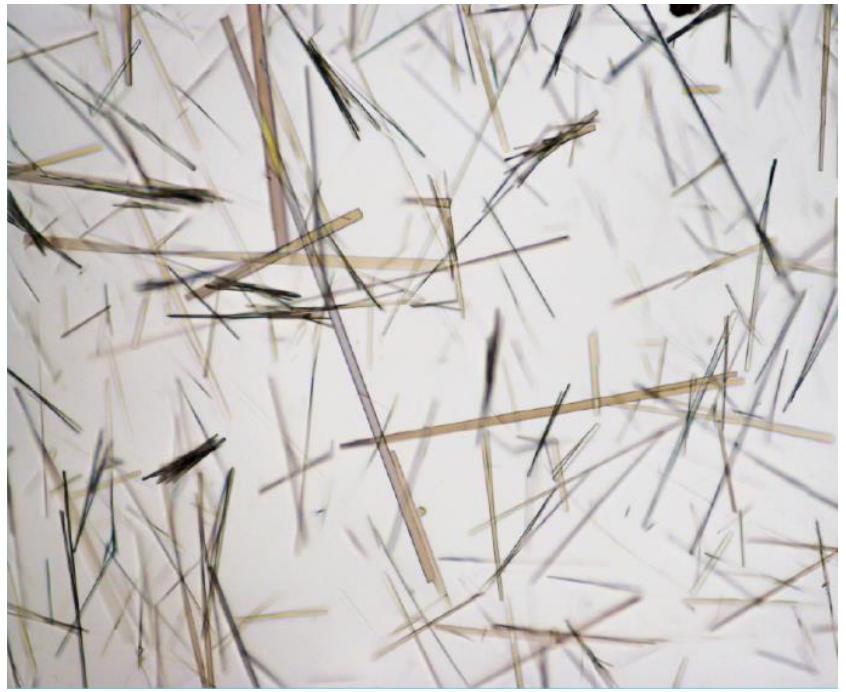


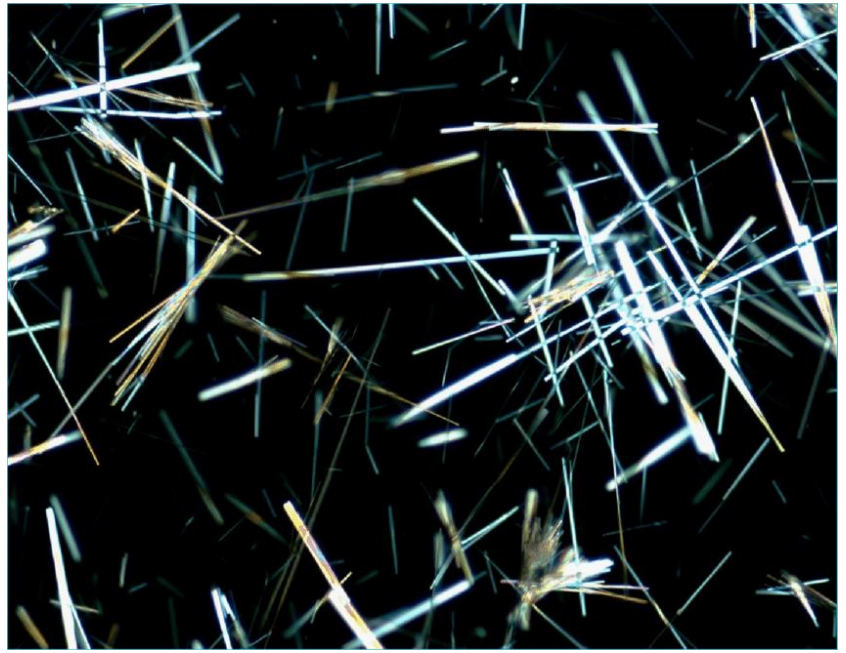


Andrews et al. eJIFCC 2020

Acyclovir induced nephropathy

- Acyclovir is renally excreted (65-91%) 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





Andrews et al. eJIFCC 2020

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?

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B. Triple phosphate stone
C. Struvite 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

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 immites

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 <2g/24H), 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 dinucleaotidase (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

E. Initiate hemodialysis

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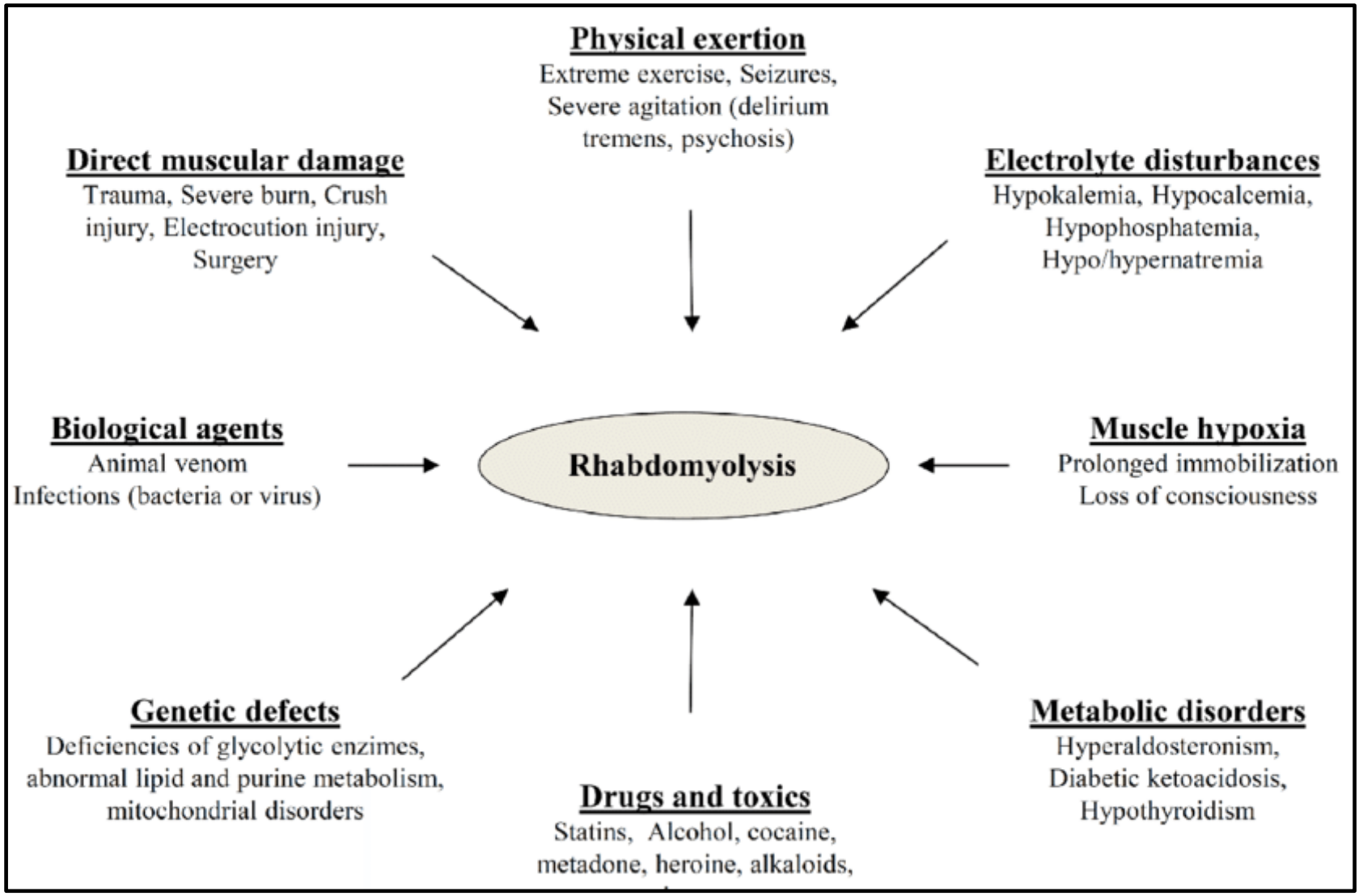
Causes of Rhabdomyolysis



Panizio et al 2015

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

Harriston S. A review of rhabdomyolysis. Dimensions Of Critical Care Nursing:. 2004
Chatzizisis et al. Eur J Intern Med. 2008

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.

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

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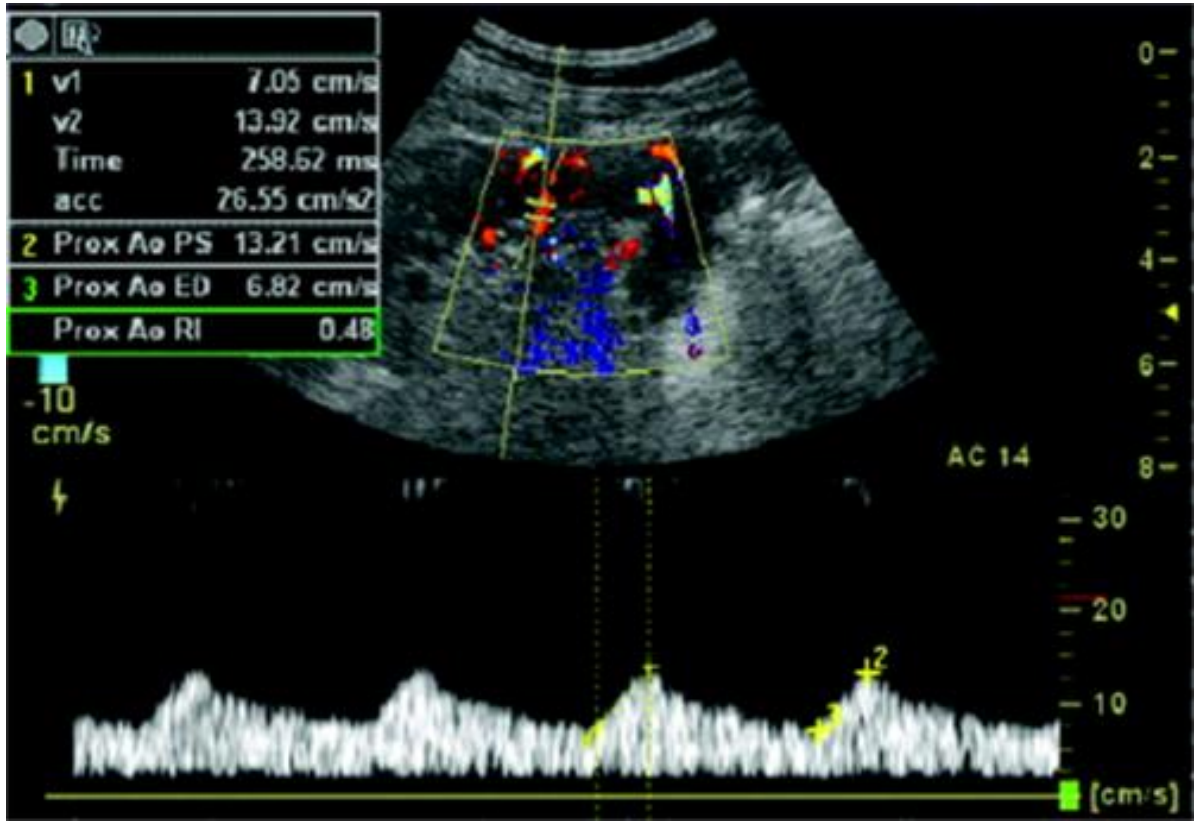
Resistant Hypertension

- 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

Acelajado et al. Circ Res. 2019

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



MOC REFLECTIVE STATEMENT

In approaching nephrology questions, consider clinical context and targeted testing that is critical to accurately diagnose and treat acute and chronic kidney conditions

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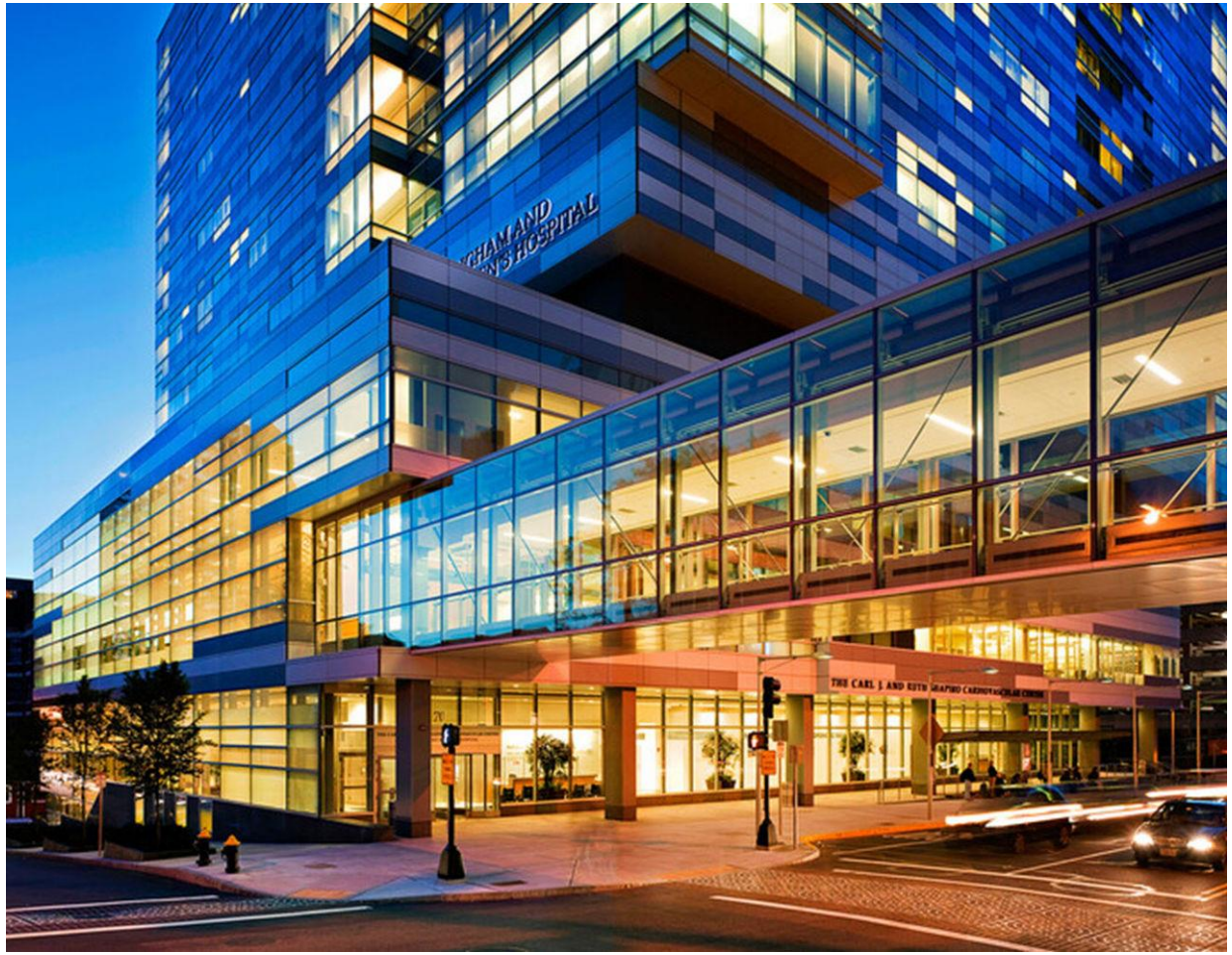
Thank you!



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