NEPHROLOGY REVIEW

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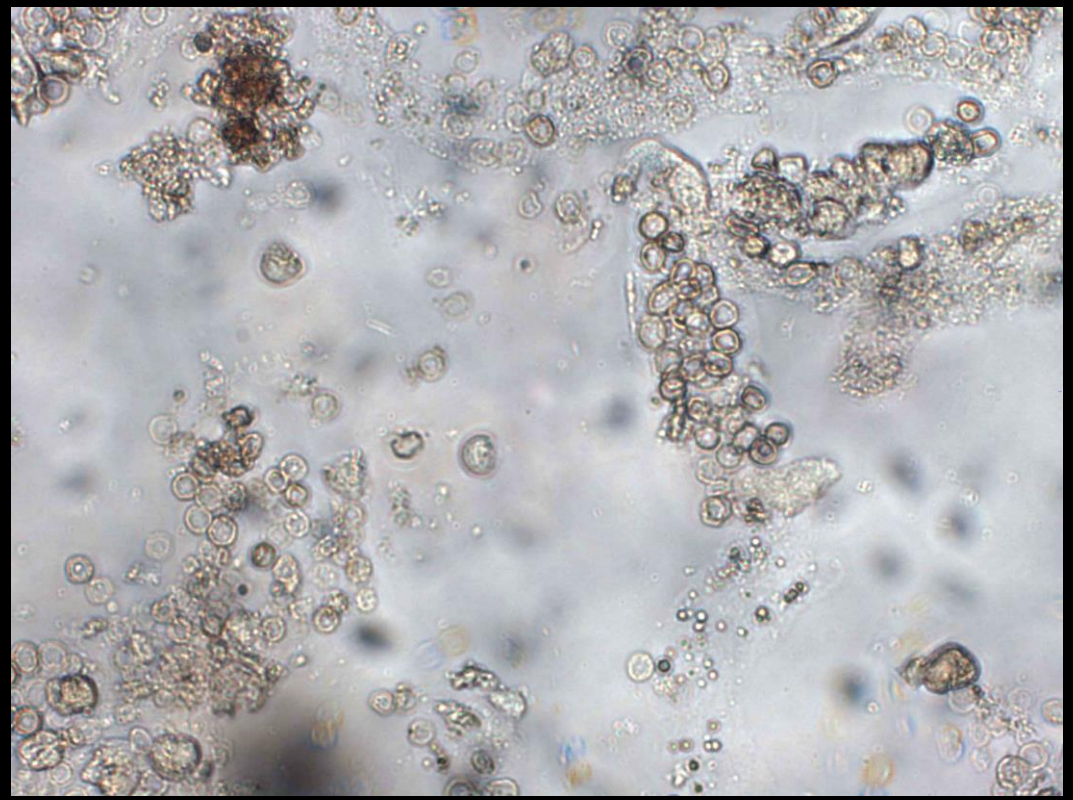
QUESTION 5 IMAGE



CORRECTION TO QUESTION 15 LABS

Laboratory studies:	
Potassium	5.6 mEq/L (5.6 mmol/L)
Sodium	Normal
Estimated glomerular filtration rate	90mL/min/1.73m^2

1) A 38-year-old man is evaluated in the emergency department for acute abdominal pain. Medical history is significant for excessive alcohol use and recurrent acute pancreatitis. He drinks six beers daily. He takes no medications.

On physical examination, the patient is in acute distress and indicates epigastric pain. Temperature is 38.0 °C (100.4 °F), blood pressure is 160/88 mm Hg, pulse rate is 88/min, and respiration rate is 20/min. BMI is 25. Chest and heart examinations are normal. The abdomen is slightly distended, with tenderness to minimal palpation in the epigastric area. There is no peripheral edema.

Which of the following is the most likely cause of this patient's hyponatremia?

Laboratory studies:	
Leukocyte count	10,000/μL (10 × 10^9/L)
Blood urea nitrogen	15 mg/dL (5.4 mmol/L)
Creatinine	1.2 mg/dL (106.1 μmol/L)
Electrolytes:	
Sodium	128 mEq/L (128 mmol/L)
Potassium	4.0 mEq/L (4.0 mmol/L)
Chloride	99 mEq/L (99 mmol/L)
Bicarbonate	24 mEq/L (24 mmol/L)
Glucose	90 mg/dL (5 mmol/L)
Lipase	620 U/L
Plasma osmolality	290 mOsm/kg H_2O
Urine osmolality	400 mOsm/kg H_2O

#1 PSEUDOHYPONATREMIA

PSEUDOHYPONATREMIA

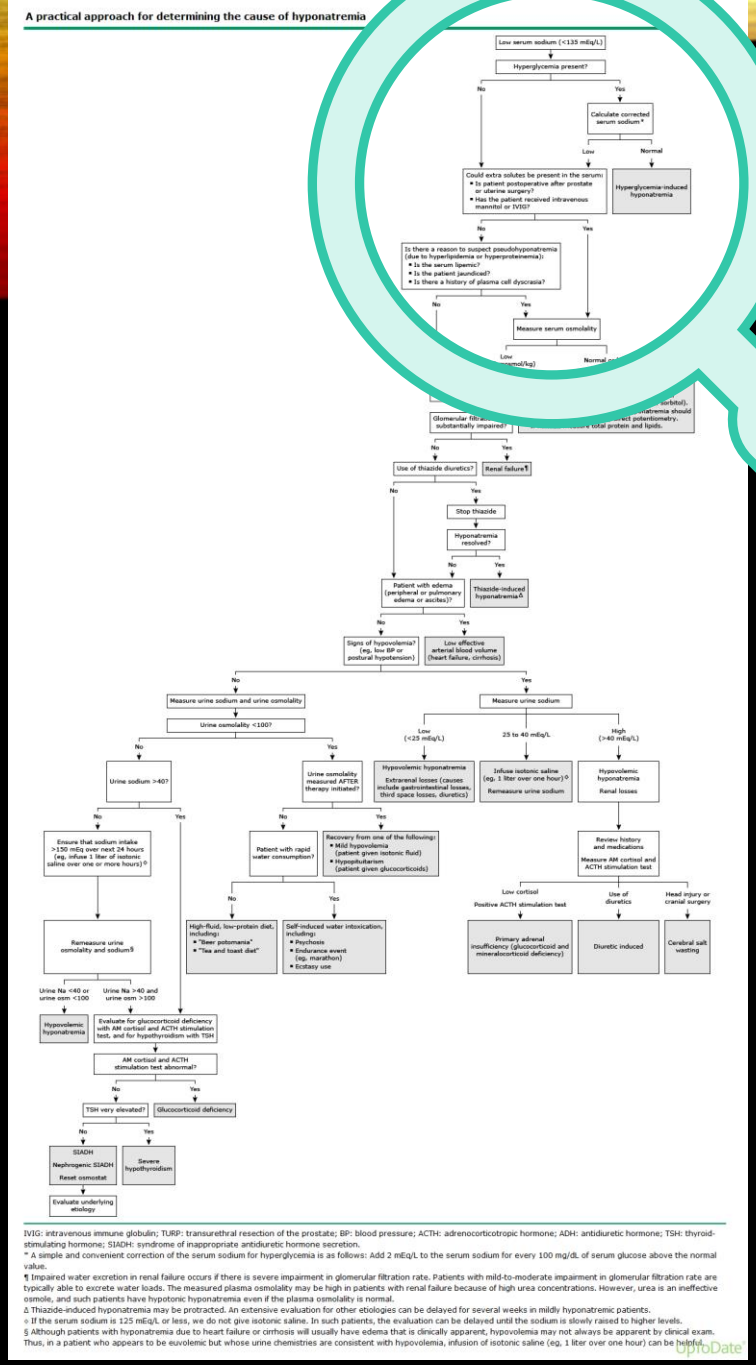
- Pseudohyponatremia is caused by a laboratory error in the measurement of serum sodium due to the presence in the serum of other material. The lab measures the proportion of sodium in PLASMA. Normally, plasma is 93% water. However, foreign substances decrease the proportion of plasma that is water, causing the concentration to look off. Common causes of paraproteins like myeloma proteins, and triglycerides, which this patient may have from his pancreatitis.

$$2Na\ (mEq/L) + 2K\ (mEq/L) + \frac{glucose\ (mg/dL)}{18} + \frac{BUN\ (mg/dL)}{2.8}$$

that is,

$$2(Na + K) + \frac{BUN}{2.8} + \frac{glucose}{18}$$

- Calculated = 266, but measured = normal (275-295)
- This means he either ingested other uncalculated osmoles like methanol or ethylene glycol, OR has pseudohyponatremia!
- Importantly – all of the other choices on this question should have LOW osms!



Low serum sodium (<135 mEq/L)
Hyperglycemia present?
No
Yes
Calculate corrected serum sodium*
Low
Normal
Could extra solutes be present in the serum:
• Is patient postoperative after prostate or uterine surgery?
• Has the patient received intravenous mannitol or IVIG?
Hyperglycemia-induced hyponatremia
No
Yes
Is there a reason to suspect pseudohyponatremia (due to hyperlipidemia or hyperproteinemia):
• Is the serum lipemic?
• Is the patient jaundiced?
• Is there a history of plasma cell dyscrasia?
No
Yes
Measure serum osmolality

This is actually step number one in almost every hyponatremia algorithm, but very easy to forget!

2) A 65-year-old woman is evaluated in the emergency department for dysuria, urgency, and polyuria occurring for 4 days. She has no neurologic symptoms. Medical history is significant for depression. Her only medication is fluoxetine, which was started 8 weeks ago.

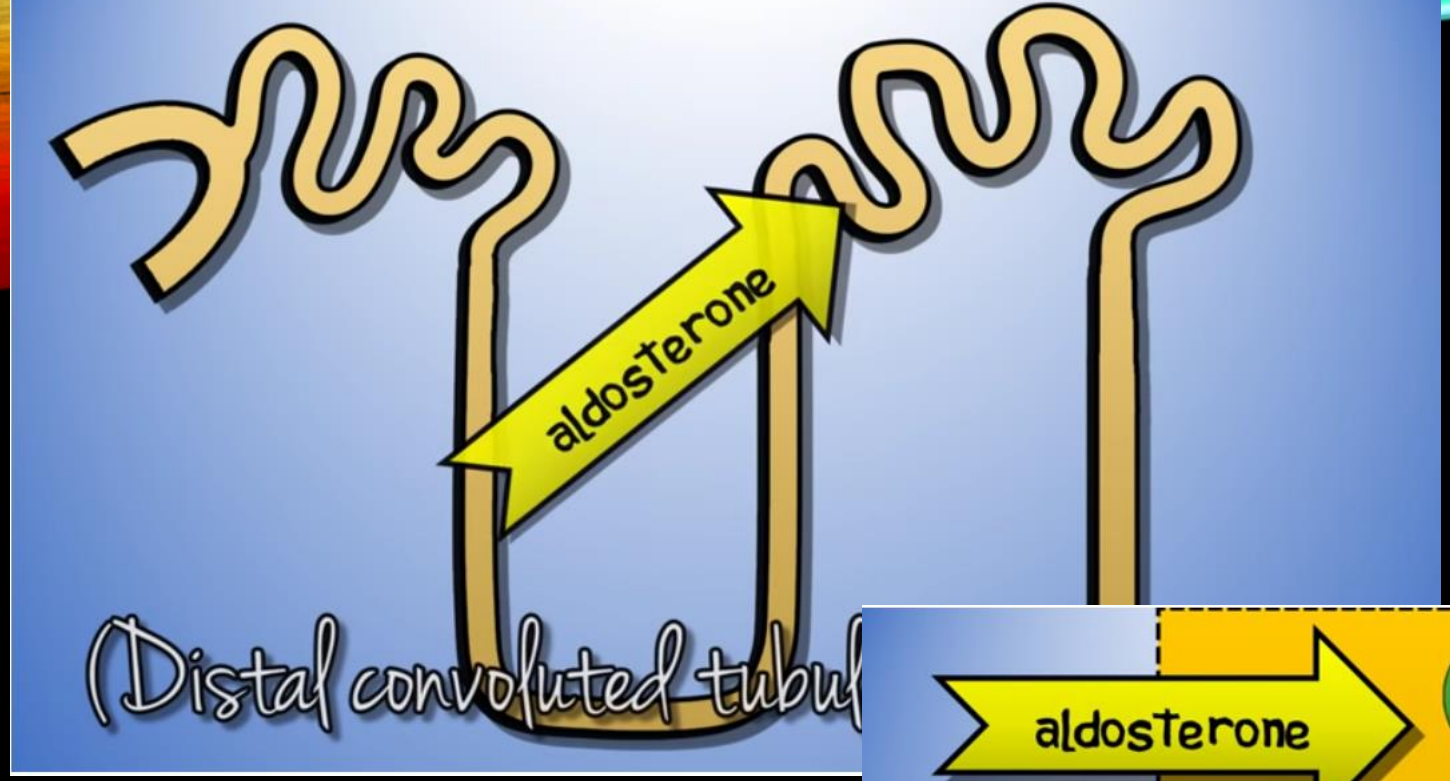
On physical examination, temperature is 38.0 °C (100.4 °F), blood pressure is 140/90 mm Hg, pulse rate is 85/min, and respiration rate is 15/min. BMI is 30. Cardiovascular, pulmonary, and neurologic examinations are normal. Mild tenderness to palpation of the mid lower abdomen is noted. There is no costovertebral angle tenderness.

Antibiotics for a urinary tract infection are started.

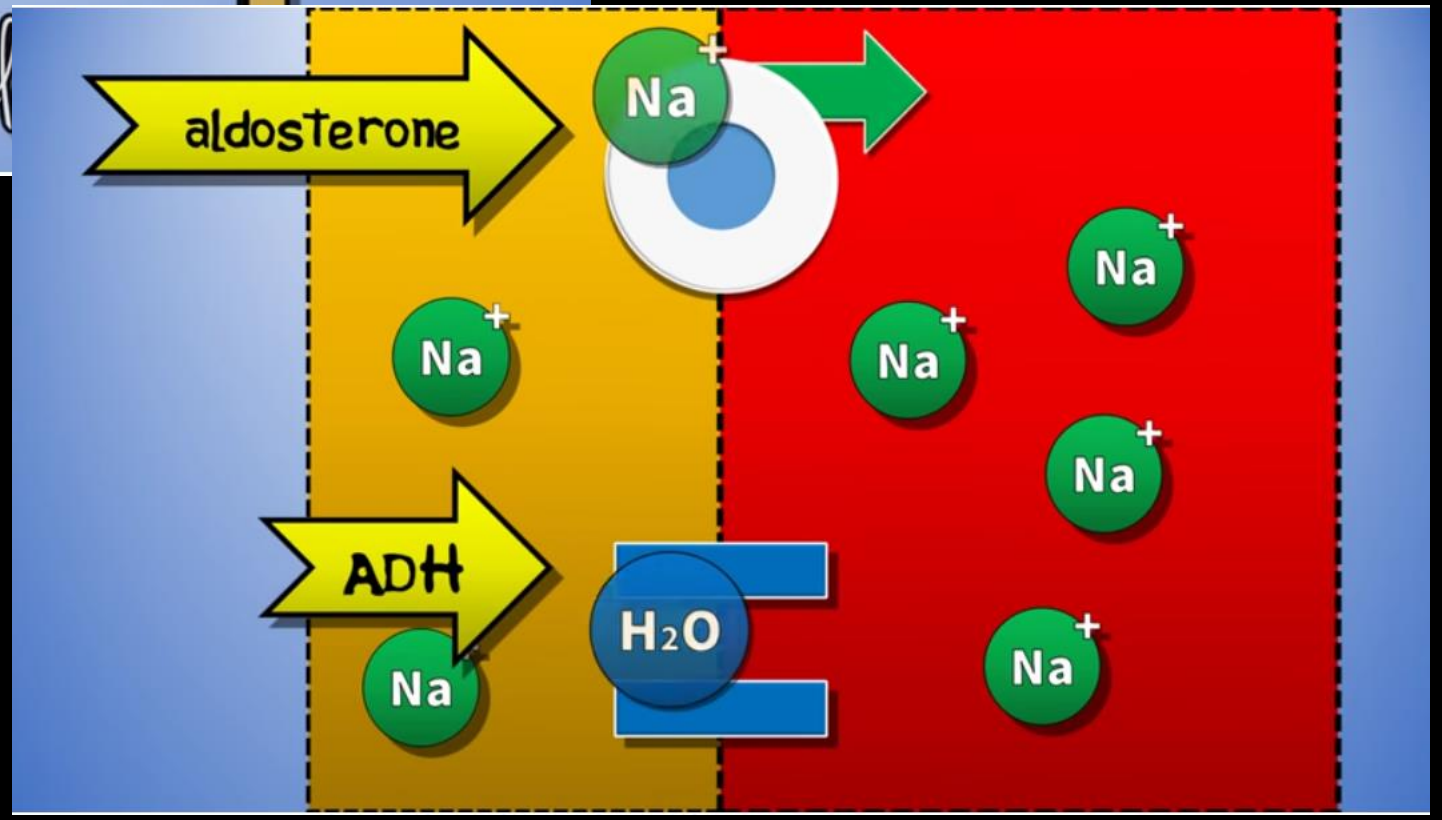
In addition to discontinuing fluoxetine, which of the following is the most appropriate management of this patient's hyponatremia?

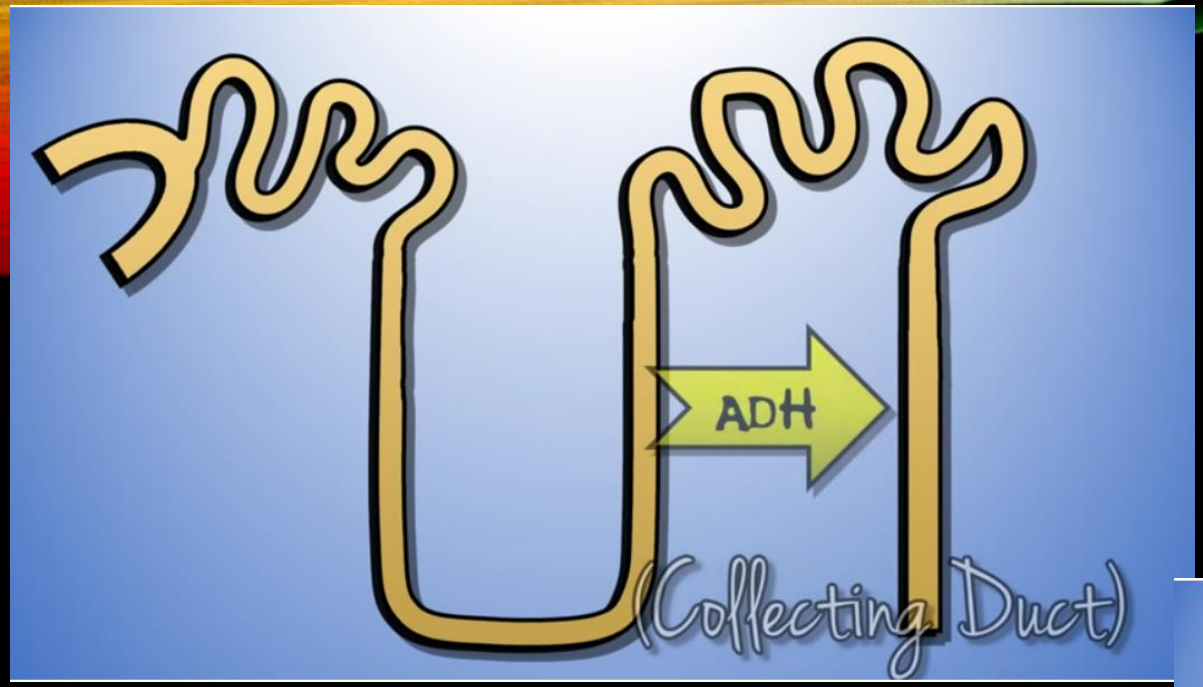
Laboratory studies:	
Blood urea nitrogen	10 mg/dL (3.6 mmol/L)
Creatinine	1.0 mg/dL (88.4 µmol/L)
Electrolytes:	
Sodium	123 mEq/L (123 mmol/L)
Potassium	4.0 mEq/L (4.0 mmol/L)
Chloride	91 mEq/L (91 mmol/L)
Bicarbonate	24 mEq/L (24 mmol/L)
Glucose	120 mg/dL (6.7 mmol/L)
Plasma osmolality	260 mOsm/kg/H_2O
Urine sodium	40 mEq/L (40 mmol/L)
Urine osmolality	600 mOsm/kg/H_2O
Urinalysis	Too numerous to count leukocytes/hpf

#2
FLUID RESTRICTION

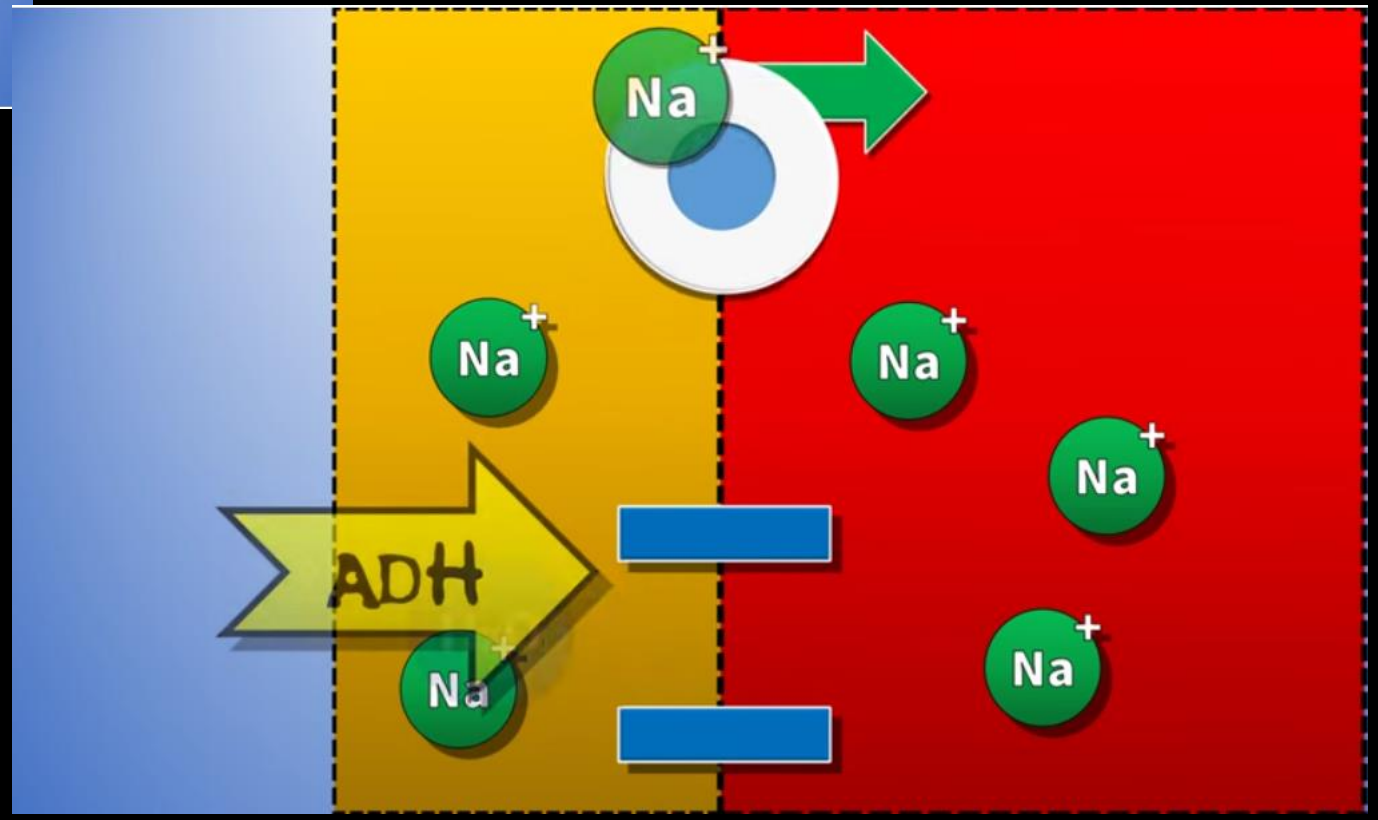


Aldosterone works in the DCT to increase Sodium-Potassium transports, effectively pumping sodium from the urine into the blood and bringing water and volume with it.





ADH works in the collecting duct to up-regulate aquaporins, which allow water to return to the blood stream (causing dilution).

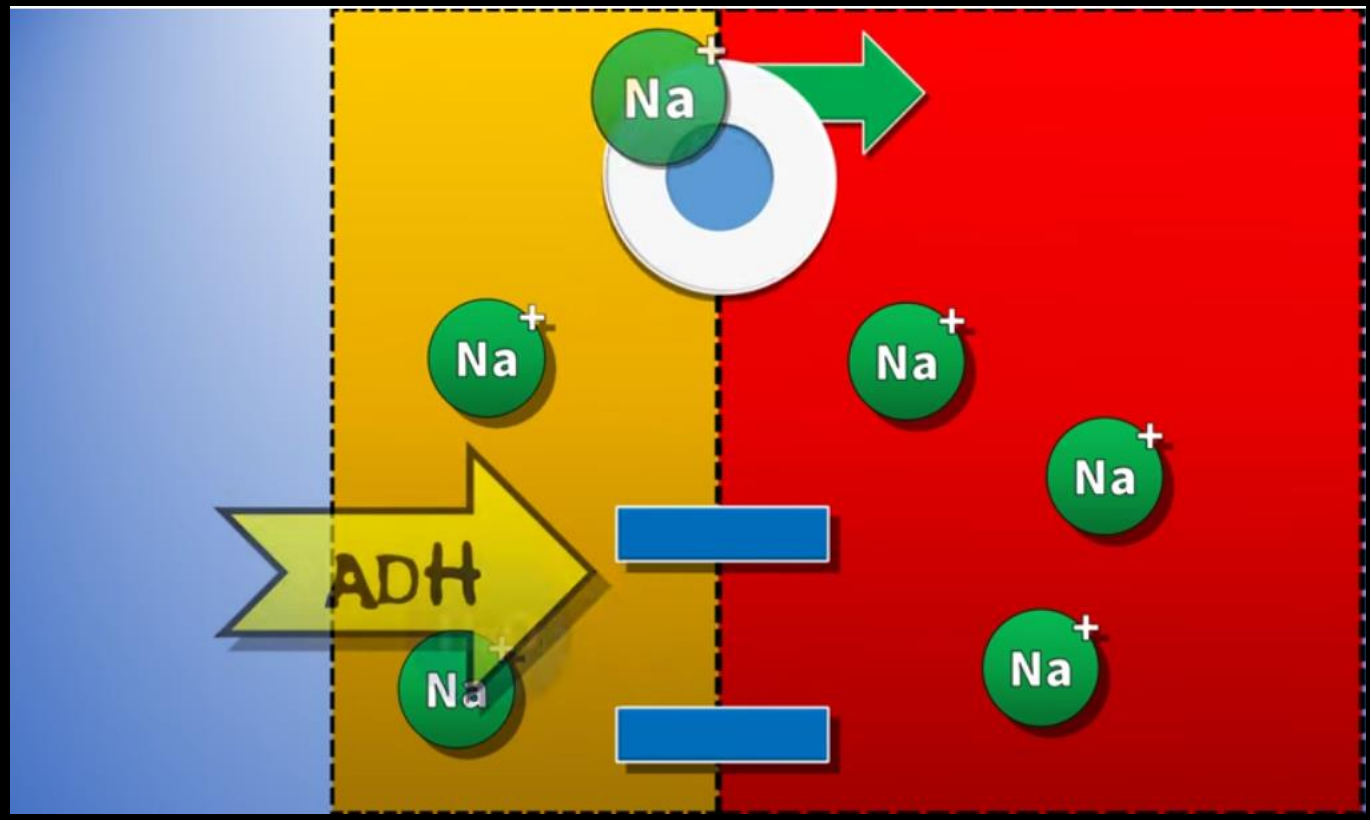


What is SIADH?

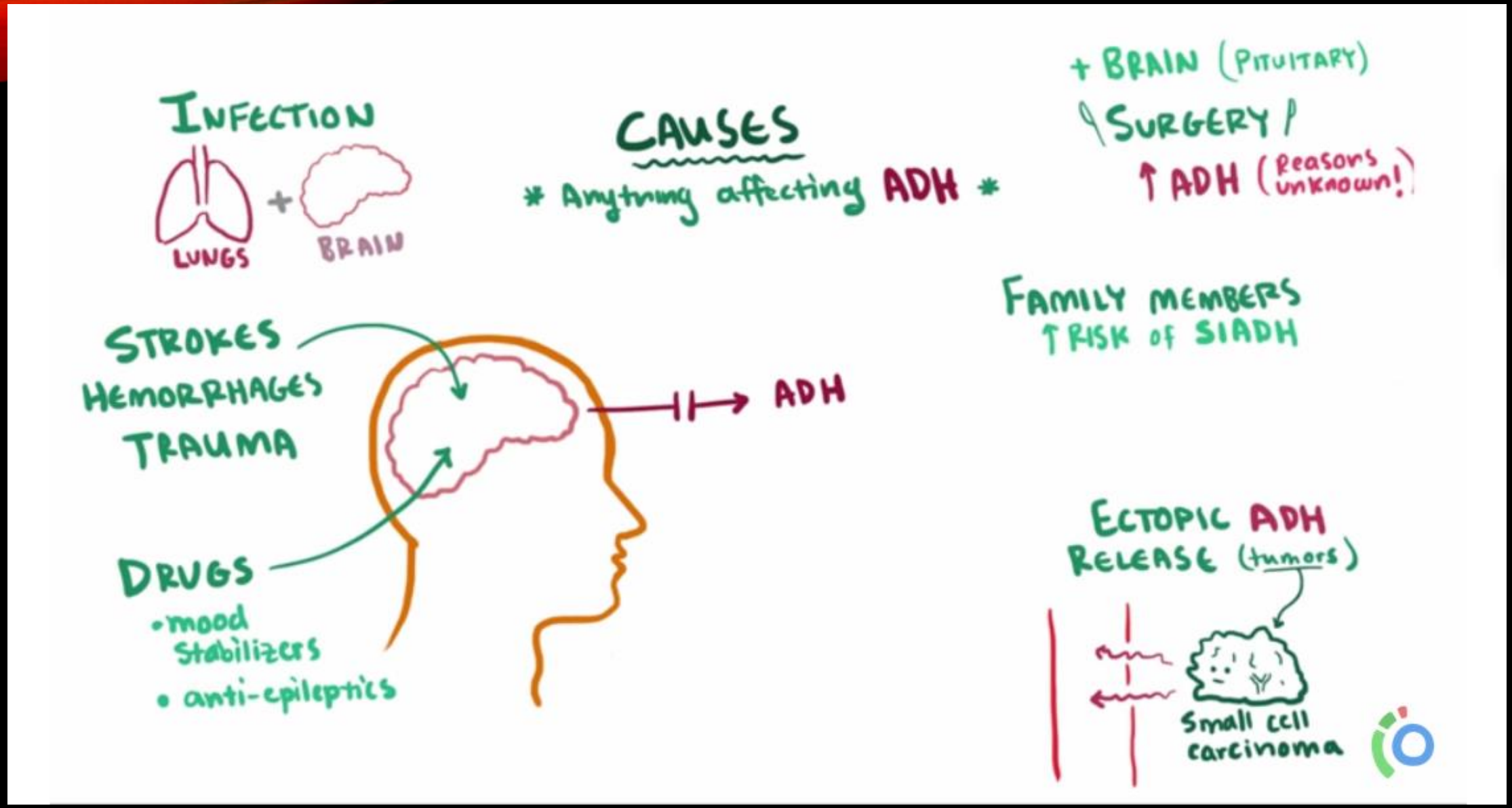
SIADH is simply unregulated ADH, which pumps too much water back into the blood stream, diluting the blood, and concentrating the urine.

But wait – why are they EUVOLEMIC?

As the renal tubule starts to see a higher volume of water/plasma, it regulates the RAAS syndrome, and decreases aldosterone production, which results in not seeing sodium and water return to the blood from the urine. Thus the volume gets managed appropriately and you stay euvolemic, but the upregulated aquaporins result in progressive dilution and hyponatremia.



Causes of increased ADH production:



LAB CRITERIA:

- You must have a low serum sodium <135
- A low serum osm <165
- A HIGH urine osm >100
- Normal TSH and adrenal function
- And be euvolemic on exam

Treatment:

- When asymptomatic, treatment is to restrict free water intake and overcome the ADH drive
- ALWAYS try to treat the underlying cause (Stop Fluoxetine!)
- If symptomatic, hypertonic solutions are appropriate, but pose risk of rapidly overcorrecting.
- Demeclocycline is reserved because of it's potential to cause kidney injury, and vaptans are reserved because of inconsistent responses between patients.

3) A 37-year-old man is evaluated in the emergency department for nausea and vomiting of 12 hours' duration. The patient states that he has been drinking large amounts of alcohol for several weeks and has eaten very little for the past week. His last alcoholic drink was more than 24 hours ago. He also reports intermittent diarrhea for the past 2 months. History is notable for chronic alcoholism. He takes no medications.

On physical examination, the patient is cachectic. Blood pressure is 100/65 mm Hg, and pulse rate is 105/min. BMI is 17. Proximal muscle wasting is noted. There is no evidence of jaundice or ascites. The liver is enlarged and mildly tender. There is no asterixis. Neurologic examination is unremarkable.

While awaiting the results of laboratory studies, the patient is given intravenous saline with dextrose and vitamins. His respiration rate becomes markedly diminished, and he requires intubation. His laboratory studies return and show the following:

Which of the following is the most likely cause of this patient's respiratory failure?

Laboratory studies:	
Albumin	3.0 g/dL (30 g/L)
Calcium	8.0 mg/dL (2.0 mmol/L)
Electrolytes:	
Sodium	132 mEq/L (132 mmol/L)
Potassium	3.4 mEq/L (3.4 mmol/L)
Chloride	90 mEq/L (90 mmol/L)
Bicarbonate	32 mEq/L (32 mmol/L)
Magnesium	1.7 mg/dL (0.7 mmol/L)
Phosphorus	1.5 mg/dL (0.48 mmol/L)

#3 HYPOPHOSPHATEMIA

REFEEDING SYNDROME

- The refeeding syndrome is defined as the clinical complications that can occur as a result of fluid and electrolyte shifts during aggressive nutritional rehabilitation of malnourished patients. These complications are potentially fatal.
- Hypophosphatemia - This is the hallmark feature that leads to physiological manifestations
- Hypokalemia
- Vitamin (e.g. thiamine) deficiencies
- Congestive heart failure
- Peripheral edema
- Rhabdomyolysis
- Seizures
- Hemolysis

- Symptoms rarely occur unless the serum phosphate concentration is <2.0.
- Symptoms include weakness, myalgia, rhabdomyolysis, arrhythmias, heart failure, respiratory failure, seizures, coma, and hemolysis.

MECHANISM OF HYPOPHOSPHATEMIA

- When nutritional replenishment starts and patients are fed carbohydrates, glucose causes release of insulin, which triggers cellular uptake of phosphate (and potassium and magnesium).
- Insulin also causes cells to produce a variety of depleted molecules that require phosphate (eg, adenosine triphosphate and 2,3-diphosphoglycerate), which further depletes the body's stores of phosphate.
- The lack of phosphorylated intermediates causes tissue hypoxia and resultant myocardial dysfunction and respiratory failure due to an inability of the diaphragm to contract.

4) A 54-year-old woman is evaluated during a follow-up visit for chronic osteomyelitis. She has type 2 diabetes mellitus complicated by nephropathy and peripheral neuropathy and was recently diagnosed with osteomyelitis of the left foot associated with a chronic neuropathic ulcer. Bone biopsy and culture demonstrated methicillin-sensitive *Staphylococcus aureus*, and 1 week ago she was started on oral high-dose trimethoprim-sulfamethoxazole and rifampin based on sensitivity data for a planned 6-week course of therapy. Medical history is also significant for hypertension. Medications are trimethoprim-sulfamethoxazole, rifampin, glipizide, and atorvastatin.

On physical examination today, temperature is 37.2 °C (99.0 °F), blood pressure is 126/66 mm Hg, and pulse rate is 78/min. Chest, heart, and abdominal examinations are unremarkable. There is loss of sensation to light touch on the feet bilaterally to the ankles. The ulcer overlying the first metatarsal head on the plantar aspect of the left foot is clean and dry.

Which of the following is the most appropriate management?

Current laboratory studies:	
Blood urea nitrogen	28 mg/dL (10 mmol/L) (pretreatment baseline: 26 mg/dL [9.3 mmol/L])
Creatinine	1.8 mg/dL (159.1 µmol/L) (pretreatment baseline: 1.4 mg/dL [123.8 µmol/L])
Potassium	4.7 mEq/L (4.7 mmol/L)

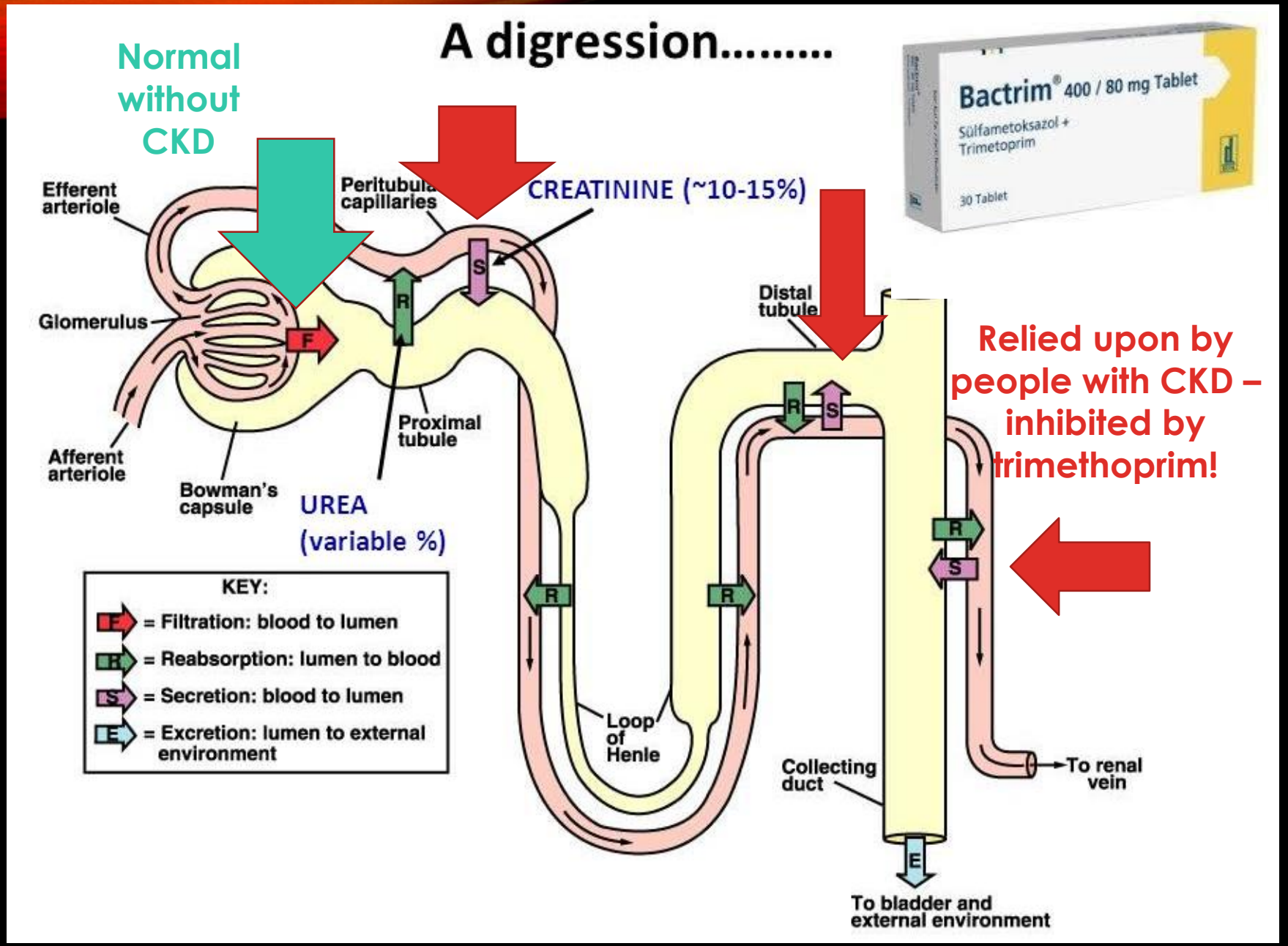
#4
CONTINUE CURRENT THERAPY

TRIMETHOPRIM AND CREATININE

- Trimethoprim is known to interfere with creatinine secretion without affecting the glomerular filtration rate and can cause increases in serum creatinine of **up to 0.5 mg/dL** – this is not a kidney injury!

- Creatinine is normally filtered by the kidney from the serum, although a smaller amount is also secreted by the proximal tubule (and tiny amounts in Distal Conv. Tubule and Collecting Duct).
- With more advanced chronic kidney disease (CKD), up to 50% of urine creatinine may be secreted instead of filtered through the glomerulus.
- Reversible upon discontinuation of the medication!
- Trimethoprim also inhibits the epithelial sodium channel in the collecting tubule, effectively acting as a potassium-sparing diuretic and potentially increasing the serum potassium level.

TRIMETHOPRIM AND CREATININE



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With more advanced chronic kidney disease (CKD), up to 50% of urine creatinine may be secreted instead of filtered through the glomerulus.

Reversible upon discontinuation of the medication!

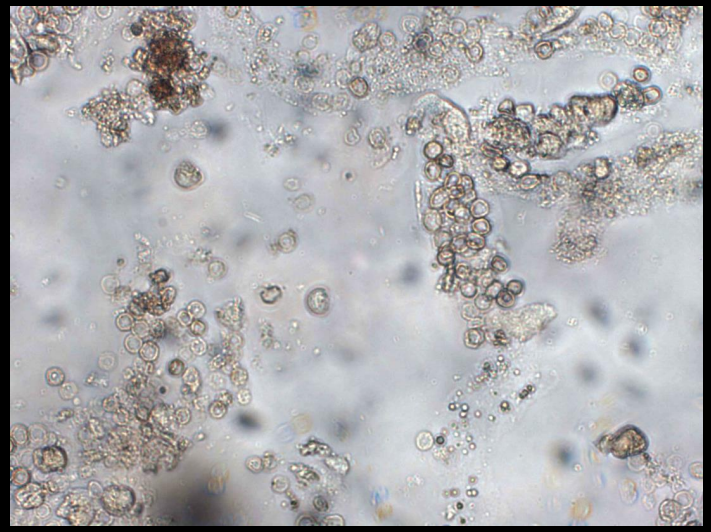
Trimethoprim also inhibits the epithelial sodium channel in the collecting tubule, effectively acting as a potassium-sparing diuretic and potentially increasing the serum potassium level.

5) A 37-year-old woman is evaluated for an episode of blood in her urine. She notes the passage of red-colored urine that resolved spontaneously and was not associated with her menstrual cycle. She reports having had several similar episodes in the past. She has no other symptoms such as abdominal pain or dysuria. Medical history is otherwise unremarkable, and she takes no medications.

On physical examination, the patient is afebrile. Blood pressure is 128/78 mm Hg, pulse rate is 82/min, and respiration rate is 13/min. Cardiopulmonary and abdominal examinations are normal. There is no flank tenderness to palpation. The remainder of the examination is unremarkable.

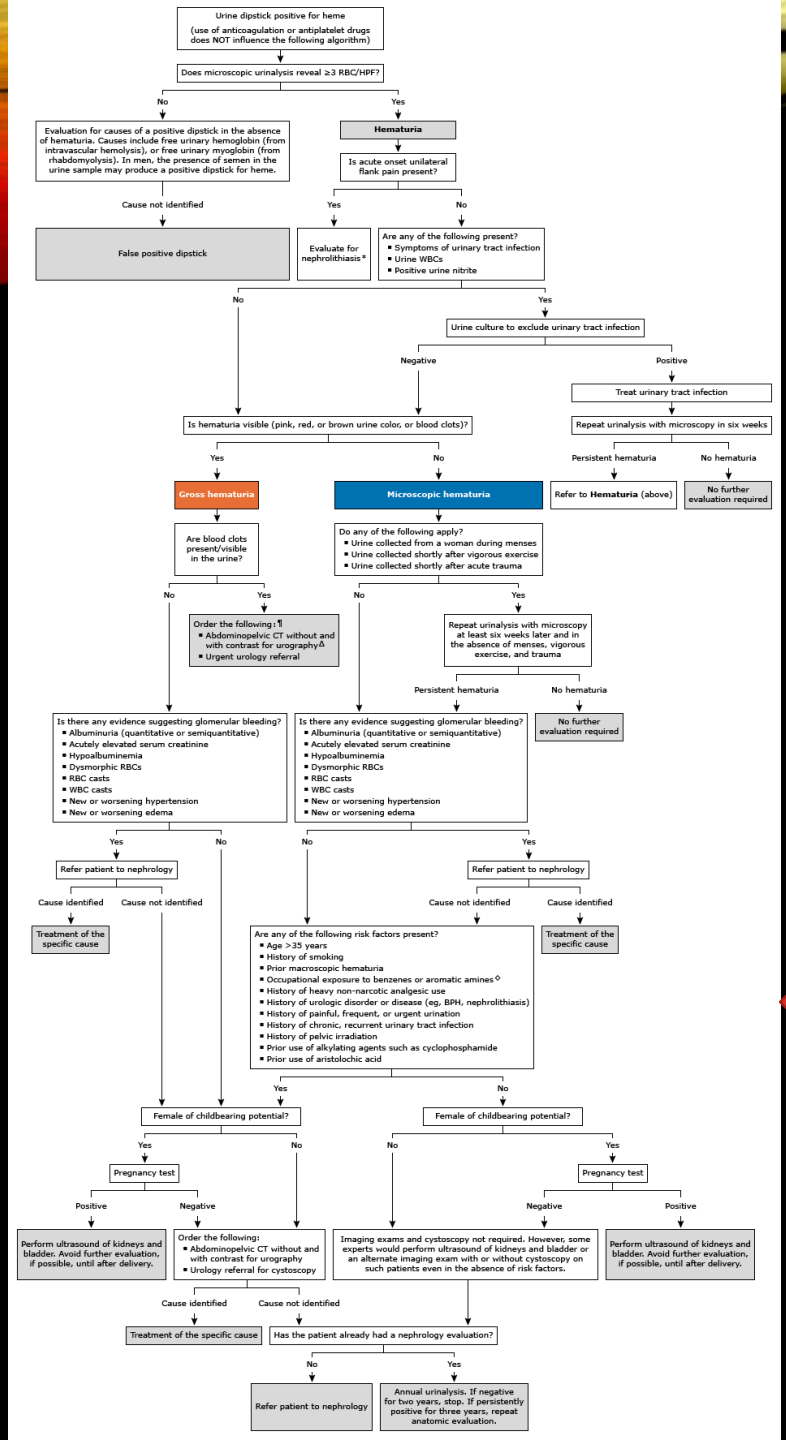
Laboratory studies show a normal complete blood count and metabolic profile and a serum creatinine level of 0.9 mg/dL (79.6 µmol/L). Dipstick urinalysis is positive for blood and protein but is negative for leukocyte esterase and nitrites.

Microscopy of the urine sediment is shown.



Which of the following is the most appropriate next step in evaluation of this patient?

#5
EVALUATION FOR GLOMERULAR DISEASE



HEMATURIA

MEMORIZE THIS!

6) A 26-year-old woman is evaluated for muscle weakness developing over the past several months. She has no focal symptoms and states that she otherwise feels well. Medical history is unremarkable, and there is no pertinent family history. She takes no medications.

On physical examination, blood pressure is 98/62 mm Hg, pulse rate is 98/min, and respiration rate is 16/min. BMI is 19. There is no lower extremity edema. The remainder of the examination is unremarkable.

Which of the following is the most likely cause of this patient's acid-base and electrolyte abnormalities?

ANION GAP = 7

Laboratory studies:	
Serum electrolytes:	
Sodium	142 mEq/L (142 mmol/L)
Potassium	3.1 mEq/L (3.1 mmol/L)
Chloride	120 mEq/L (120 mmol/L)
Bicarbonate	15 mEq/L (15 mmol/L)
Serum creatinine	1.2 mg/dL (106.1 µmol/L)
Urine electrolytes:	
Sodium	18 mEq/L (18 mmol/L)
Potassium	8.0 mEq/L (8.0 mmol/L)
Chloride	32 mEq/L (32 mmol/L)
Urine pH	5.0
Urine dipstick	No blood or protein

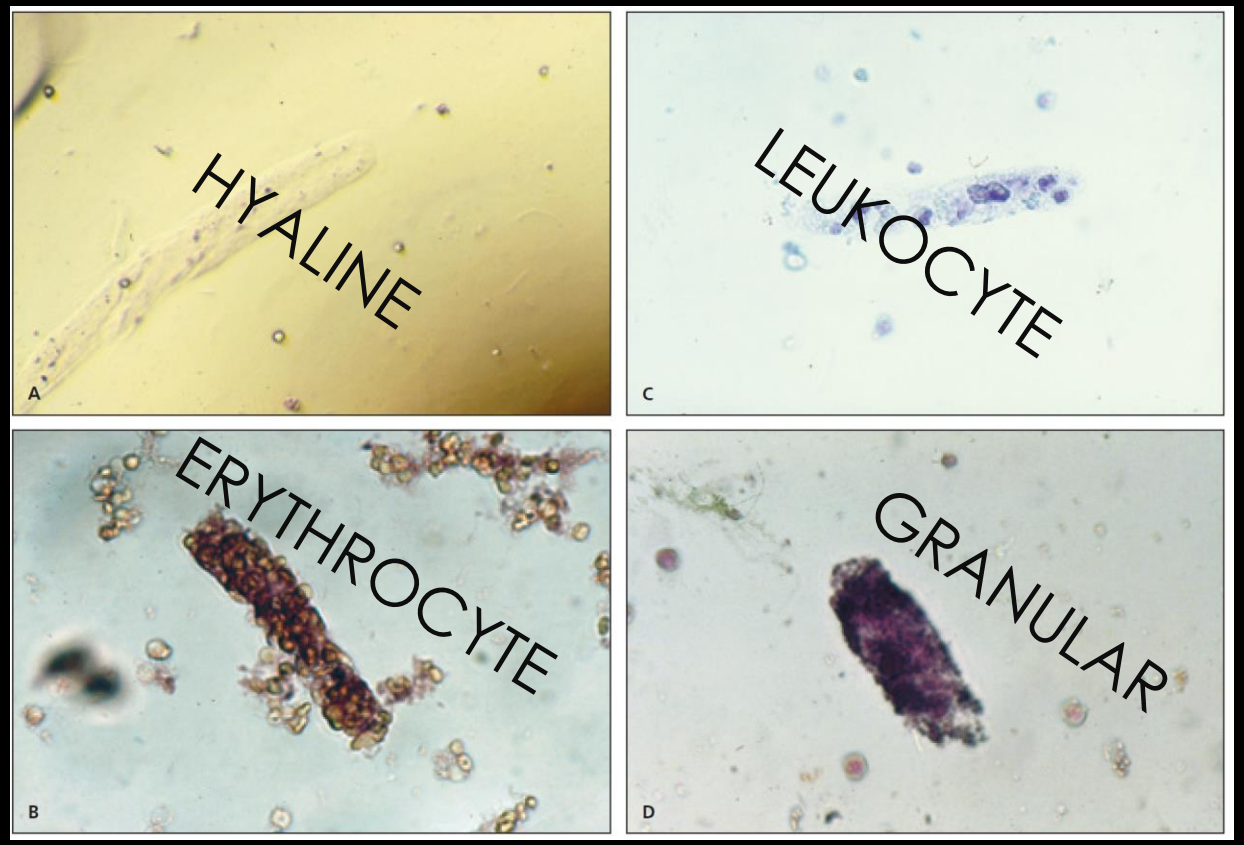
Hematuria = ≥3 RBC/hpf

- Dipstick + but no RBCs?
  - Hemoglobinuria (PNH or hemolysis)
  - Myoglobinuria (Rhabdomyolysis)

- Exclude stones and UTI
  - Need to make sure hematuria clears after UTI

- Exercise induced hematuria
  - Repeat UA in 6 weeks without exercising beforehand

NAME THAT CAST!



GLOMERULAR HEMATURIA

"ACTIVE UA"

- Erythrocyte casts
- Proteinuria
- Dysmorphic RBCs

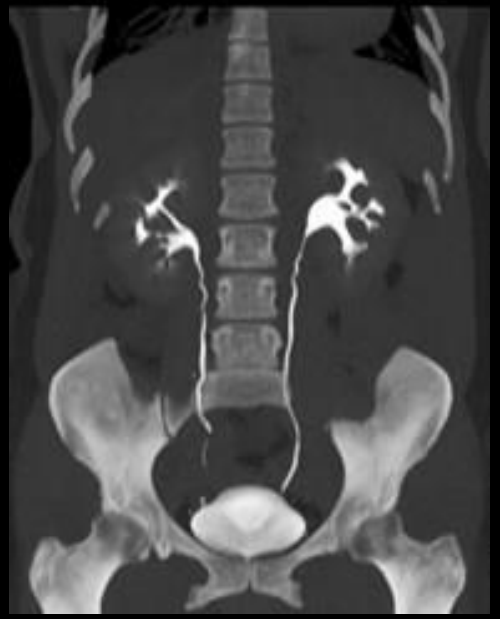
What does evaluate for glomerular disease even mean?

- Complement levels
- ANA, dsDNA
- ANCA
- Strep ASO
- Anti-GBM antibody
- Kidney biopsy

NONGLOMERULAR HEMATURIA

- MUST RULE OUT MALIGNANCY

1) CT urogram
2) Cystoscopy



6) A 26-year-old woman is evaluated for muscle weakness developing over the past several months. She has no focal symptoms and states that she otherwise feels well. Medical history is unremarkable, and there is no pertinent family history. She takes no medications.

On physical examination, blood pressure is 98/62 mm Hg, pulse rate is 98/min, and respiration rate is 16/min. BMI is 19. There is no lower extremity edema. The remainder of the examination is unremarkable.

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Chloride	120 mEq/L (120 mmol/L)
Bicarbonate	15 mEq/L (15 mmol/L)
Serum creatinine	1.2 mg/dL (106.1 µmol/L)
Urine electrolytes:	
Sodium	18 mEq/L (18 mmol/L)
Potassium	8.0 mEq/L (8.0 mmol/L)
Chloride	32 mEq/L (32 mmol/L)
Urine pH	5.0
Urine dipstick	No blood or protein

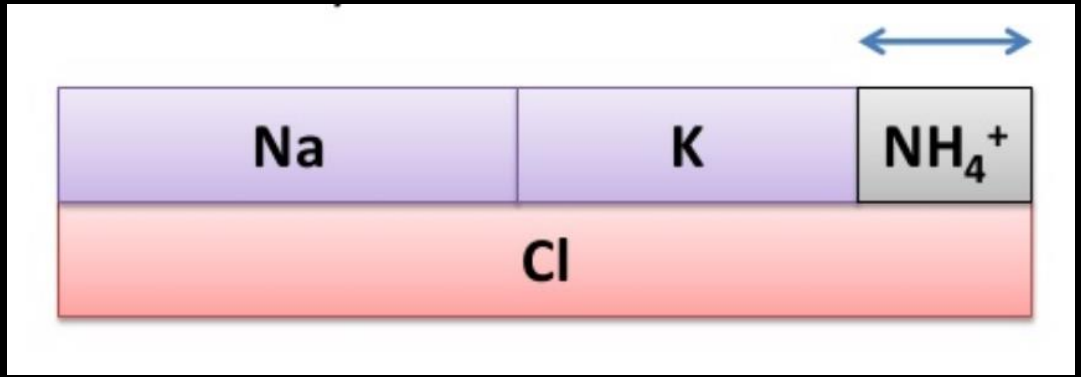
#6
LAXATIVE ABUSE

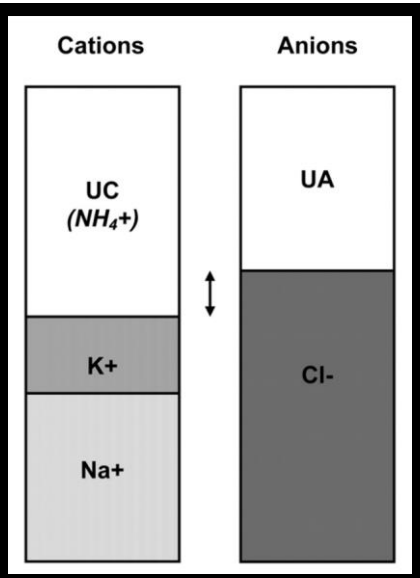
NORMAL ANION GAP METABOLIC ACIDOSIS

1) URINE ANION GAP

- Na + K – Cl = UAG
- Positive = renal
  - Typically an RTA
- Negative = GI (neGUTive)
  - Bicarb loss in GI tract

Calculates unmeasured ammonium (NH4+) in urine, which is how the kidney excretes excess acid





7) A 34-year-old woman is evaluated for laboratory abnormalities discovered as part of an evaluation for joint pain. She describes the pain as being diffuse and associated with chronically dry eyes and mouth. She also notes recent-onset mild nocturia. Medical history is otherwise negative, and she takes acetaminophen daily for her joint pain.

On physical examination, vital signs are normal. BMI is 23. Mucous membranes and conjunctivae are dry, and mild parotid enlargement is present. There is no evidence of joint inflammation. The remainder of the examination is unremarkable.

Which of the following is the most likely cause of this patient's laboratory findings?

ANION GAP = 8

Laboratory studies:	
Creatinine	0.9 mg/dL (79.6 µmol/L)
Electrolytes:	
Sodium	138 mEq/L (138 mmol/L)
Potassium	3.1 mEq/L (3.1 mmol/L)
Chloride	118 mEq/L (118 mmol/L)
Bicarbonate	12 mEq/L (12 mmol/L)
Glucose	74 mg/dL (4.1 mmol/L)
Urinalysis	pH 7.0

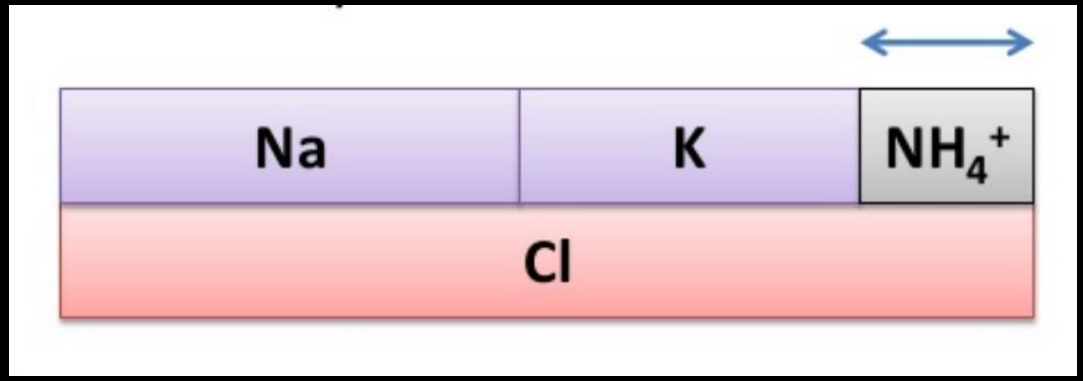
#7
TYPE 1 (HYPOKALEMIC DISTAL) RENAL TUBULAR ACIDOSIS

NORMAL ANION GAP METABOLIC ACIDOSIS

1) URINE ANION GAP

- Na + K – Cl = UAG
- Positive = renal
  - Typically an RTA
- Negative = GI (neGUTive)

Calculates unmeasured ammonium (NH4+) in urine, which is how the kidney excretes excess acid



	Hypokalemic RTA		Hyperkalemic RTA	
	Type 1 RTA	**Type 2 RTA**	**Hypoaldosteronism (Type 4 RTA)**	**Distal tubule sodium transport defects**
Primary defect	Impaired distal acidification.	Reduced proximal HCO_3 reabsorption.	Decreased aldosterone secretion or aldosterone resistance.	Reduced sodium reabsorption.
Plasma HCO_3	Variable. May be below 10 mEq/L.	Usually 12 to 20 mEq/L.	Usually greater than 17 mEq/L.	Usually greater than 17 mEq/L.
Urine pH	Greater than 5.3.	Variable. Greater than 5.3 if the serum HCO_3 exceeds the proximal tubule's HCO_3 reabsorptive threshold. Less than 5.3 when the serum HCO_3 is reduced to levels that can be reabsorbed despite defective proximal tubule HCO_3 reabsorption.	Variable. Usually greater than 5.3.	Variable. Usually greater than 5.3.
Plasma potassium	Usually reduced, but hyperkalemic forms exist; hypokalemia largely corrects with alkali therapy.	Normal or reduced; made worse by bicarbonaturia induced by alkali therapy.	Increased; correcting the hyperkalemia alone will improve the acidosis by increasing ammonium availability.	Increased; correcting the hyperkalemia alone will improve the acidosis by increasing ammonium availability.
Urine anion gap	Positive	Negative	Positive	Positive
Urine calcium/creatinine ratio	Increased	Normal	Normal	Normal
Nephrolithiasis/nephrocalcinosis	Yes	No	No	No

Type I RTA

- Distal
- Impaired acid secretion
- High urine pH
- Hypokalemia
- Causes: Sjogrens, autoimmune hepatitis, lithium, amphotericin, kidney stones, amyloidosis/cryoglobulinemia, NSAIDs

Type II RTA

- Proximal
- Impaired bicarbonate reabsorption
- Variable urine pH
  - Low if normal bicarb intake
  - High if high bicarb intake
- Hypokalemic
- Causes: Fanconi syndrome, multiple myeloma, acetazolamide, topiramate

Type IV RTA

- Distal
- Think hypoaldosteronism
- Hyperkalemic
- Diabetes, Lupus, AIDs, hypoaldosteronism

8) A 46-year-old woman is evaluated in the emergency department for fatigue and weakness of 5 days' duration. The patient also reports recurrent lower extremity swelling. She is vague when asked about medication or drug use.

On physical examination, blood pressure is 108/62 mm Hg, pulse rate is 98/min, and respiration rate is 16/min. Upon standing, systolic blood pressure decreases by 15 mm Hg, and pulse rate increases by 10/min. BMI is 26. The remainder of the examination is unremarkable, with no evidence of lower extremity edema.

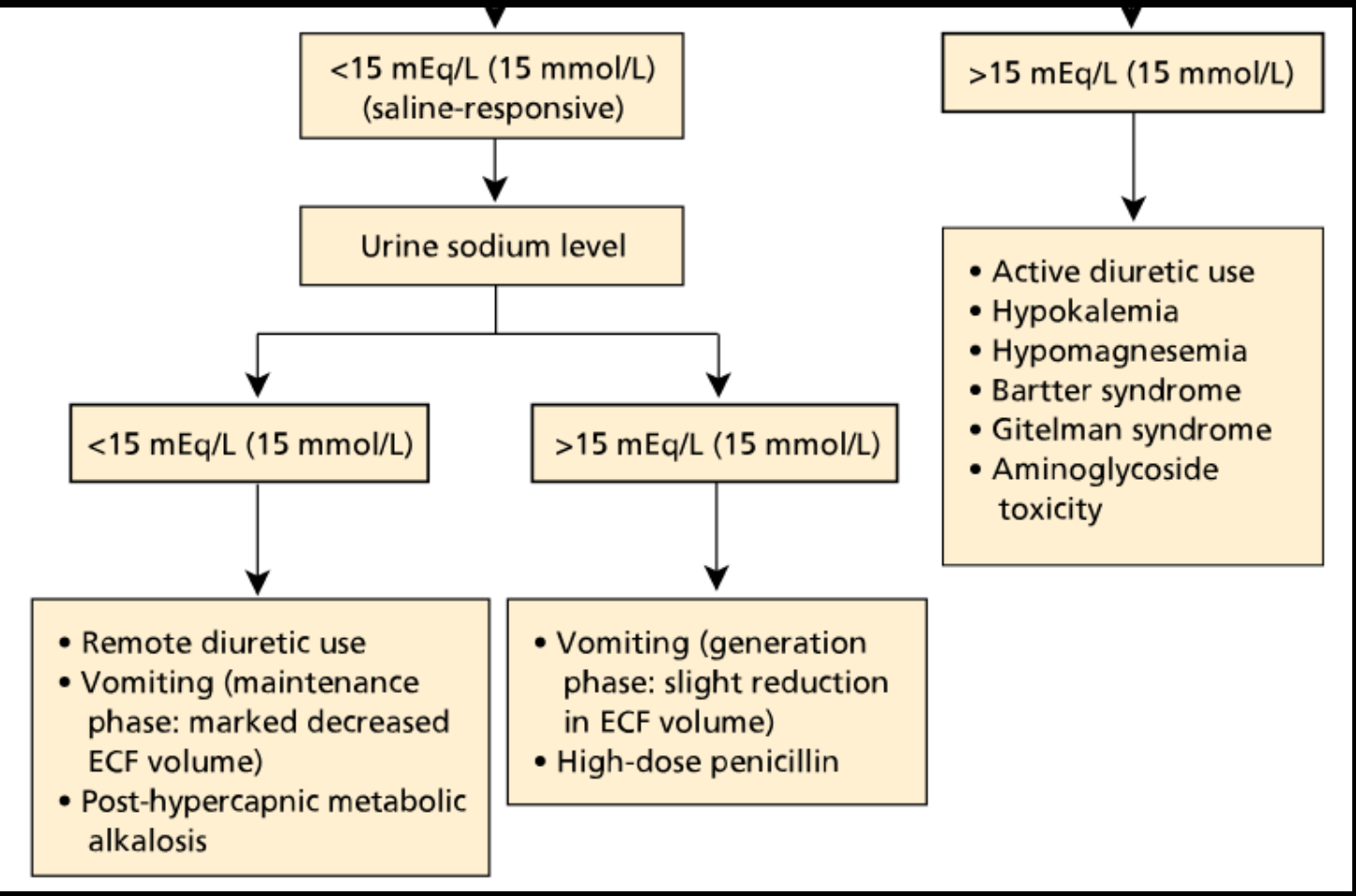
Which of the following is the most appropriate diagnostic test to perform next?

Laboratory studies:	
Serum bicarbonate	29 mEq/L (29 mmol/L)
Serum creatinine	1.2 mg/dL (106.1 µmol/L)
Serum potassium	3.1 mEq/L (3.1 mmol/L)
Urine chloride	53 mEq/L (53 mmol/L)
Urine potassium	25 mEq/L (25 mmol/L)
Urine sodium	42 mEq/L (42 mmol/L)

#8
URINE DIURETIC SCREEN

METABOLIC ALKALOSIS

SALINE RESPONSIVE
Measure urine chloride



1. Check volume status
   - Saline resistant (hypervolemia & hypertension
   - Saline responsive (hypovolemia & low urine chloride)
2. Check urine chloride
   Why chloride?

Bartter syndrome – loop diuretic
Gitelman – thiazide diruetics

- Severe metabolic alkalosis can lead to hypoventilation, seizures, delirium, stupor.
  - Treatment in this case:
    - Fluid replacement
    - Potassium replacement if low
    - Mechanical ventilation
    - Dialysis

SALINE RESPONSIVE

- Blood pressure and ECF increased
- Urine sodium and chloride >15 mEq/L (15 mmol/L) (saline-resistant)

- Renin-secreting tumor
- Malignant hypertension
- Renovascular hypertension
- ...mary hyperaldosteronism
- ...ineralocorticoid
- ...ible hyperaldosteronism
- Syndrome... ...corticoid excess:
  - Glycyrrhetinic acid... ...acco)
  - Familial syndrome of appar... excess (11-β-HSD deficiency)
  - Increased nonaldosterone mineralocorticoid receptor agonist (congenital adrenal hyperplasia; Cushing syndrome; deoxycorticosterone-producing tumor; 5-α-reductase deficiency)
  - Ectopic ACTH syndrome
  - Liddle syndrome

THINK HYPERALDOSTERONISM

9) A 35-year-old man is evaluated in the emergency department for dyspnea of 24 hours' duration. He also reports progressive lower extremity edema for 1 month. He has no other pertinent personal or family medical history, and he takes no medications.

On physical examination, the patient is afebrile, blood pressure is 120/78 mm Hg, pulse rate is 100/min, and respiration rate is 22/min. Oxygen saturation on ambient air is 88%. BMI is 25. The chest is clear. Examination of the heart is unremarkable. There is bilateral lower extremity pitting edema to the knees. The remainder of the examination is normal.

Chest radiograph is normal. CT angiogram of the chest shows a right pulmonary artery embolism.

The patient is started on supplemental oxygen and heparin.

Which of the following is the most likely underlying diagnosis?

Laboratory studies:	
Albumin	1.8 g/dL (18 g/L)
Creatinine	1.1 mg/dL (97.2 µmol/L)
Urinalysis	3+ protein
Urine protein-creatinine ratio	5500 mg/g

#9 MEMBRANOUS GLOMERULOPATHY

NEPHROTIC SYNDROME

Features

- Proteinuria >3500 mg/g
  - "Nephrotic proteinuria"
- Hypoalbuminemia
- Hypercholesterolemia
- Edema/Anasarca

- Infection
- Blood clots

Types:

- Membranous glomerulopathy
- Minimal Change disease
- Focal segmental glomerulosclerosis
- Diabetic nephropathy

None of these end in –itis!

MEMBRANOUS GLOMERULOPATHY

- Primary: PLA2R antigen (75%)
- Secondary:
  - Hepatitis B
  - Solid organ tumors
- Spikes on glomerular BM
- Blood clots (renal vein thrombosis) and solid organ tumors
- Treatment:
  - 6 months: Monitor, ACE/ARB, diuresis
  - High risk or > 6 months: steroids, cyclophosphamide, calcineurin inhibitors

FSGS

- Most common cause in black patients.
- Idiopathic or secondary (DM, HTN, obesity)
- Treat: steroids and immunosuppression

MINIMAL CHANGE

- Most common cause in children
- Associated with lymphoma
- Treat: Steroids and immunosuppression

DIABETIC NEPHROPATHY

10) A 24-year-old woman is evaluated for fever, lower extremity edema, and worsening malar rash. She was diagnosed with systemic lupus erythematosus 2 years ago. Her initial evaluation showed normal kidney function, trace proteinuria, and an otherwise normal urinalysis; periodic monitoring of her kidney function and urinalysis has been unchanged. She has been treated with hydroxychloroquine and prednisone, 5 mg/d, since the time of her diagnosis with good control of her symptoms. Medical history is otherwise unremarkable, and she takes no additional medications.

On physical examination, blood pressure is 140/92 mm Hg. A malar rash is present. Mild erythema and effusion in the left knee and bilateral wrist joints are noted. The remainder of the examination is unremarkable.

A kidney biopsy shows a diffuse proliferative glomerulonephritis with immunofluorescence microscopy showing granular deposits in the subendothelial, mesangial, and subepithelial areas (IgG, IgM, IgA, C3, and C1q), which are confirmed by electron microscopy, and is classified as class IV lupus nephritis.

Which of the following is the most appropriate treatment?

Laboratory studies:	
Hemoglobin	9.2 g/dL (92 g/L)
C3	Low
C4	Low
Creatinine	1.0 mg/dL (88.4 µmol/L)
Liver chemistry tests	Normal
Anti–double-stranded DNA antibodies	Elevated
Urinalysis	3+ blood; 2+ protein; 20-30 erythrocytes/hpf; 5-10 leukocytes/hpf
Urine protein-creatinine ratio	2200 mg/g

#10
INCREASE PREDNISONE AND ADD MYCOPHENOLATE MOFETIL

LUPUS NEPHRITIS

- Most patients with class III lupus nephritis and all patients with class IV lupus nephritis benefit from aggressive combination immunosuppressive therapy.
- This patient has class IV, and thus warrants immunosuppressive therapy.
- Group III vs IV = focal vs. diffuse

WHO Classification of Lupus Nephritis

CLASS I	**Minimal Mesangial Glomerulonephritis** - histologically normal on light microscopy but with mesangial deposits on electron microscopy
CLASS II	**Mesangial Proliferative Lupus Nephritis** - typically responds completely to treatment with corticosteroids
CLASS III	**Focal Proliferative Nephritis** - often successfully responds to treatment with high doses of corticosteroids
CLASS IV	**Diffuse Proliferative Nephritis** - mainly treated with corticosteroids and immunosuppressant drugs
CLASS V	**Membranous Nephritis** - characterized by extreme edema and protein loss
CLASS VI	**Glomerulosclerosis**

LUPUS NEPHRITIS

- Occurs in up to 70% of SLE patients
- dsDNA antibodies are marker for risk
- Check everybody for LN at the time of SLE diagnosis
- Patients with class I or II LN may have minimal or no kidney findings, and those with classes III and IV present with varying degrees of the nephritic syndrome.
- Patients with class V LN present predominantly with proteinuria. Class VI is the end stage of long-standing LN.

11) A 65-year-old man is hospitalized for an ischemic, nonhealing right lower extremity ulcer with associated biopsy-proven osteomyelitis. On hospital day 1, he was started on cefazolin and underwent angiography and stenting of the iliac artery using a low osmolar contrast agent. On day 2, he became febrile and was switched to vancomycin and gentamicin based on culture sensitivity data. On day 3, his fever resolved and his serum creatinine was at baseline (1.5 mg/dL [132.6 µmol/L]). On day 10, his serum creatinine increased to 3.0 mg/dL (265.2 µmol/L) with a urine output of 0.5 mL/kg/h. Medical history is notable for type 2 diabetes mellitus, hypertension, dyslipidemia, coronary artery disease, and chronic kidney disease. Medications are rosuvastatin, amlodipine, carvedilol, aspirin, insulin, vancomycin, and gentamicin.

On physical examination, blood pressure is 150/78 mm Hg, and pulse rate is 72/min. There is no rash. The lower extremities have decreased peripheral pulses. The right foot has a 1-cm clean-appearing ulcer on the tip of the second toe. The remainder of the physical examination is normal.

Kidney ultrasound is normal.

Which of the following is the most likely cause of this patient's acute kidney injury?

Laboratory studies on day 10:	
Hemoglobin	11.2 g/dL (112 g/L)
Leukocyte count	8500/µL (8.5 × 10^9/L) with 58% polymorphonuclear leukocytes, 20% lymphocytes, 3% eosinophils
Creatinine	3.0 mg/dL (265.2 µmol/L) (baseline, 1.5 mg/dL [132.6 µmol/L])
Urine sodium	40 mEq/L (40 mmol/L)
Fractional excretion of sodium	2.1%
Urinalysis	trace blood trace protein granular casts tubular epithelial cells

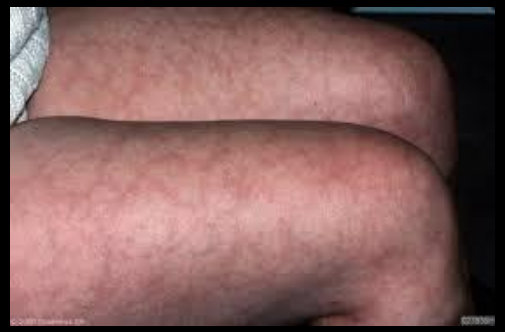
#11
GENTAMICIN

AMINOGLYCOSIDE INDUCED ATN

…TIMING IS EVERYTHING

Aminoglycosides

- Cause nonoliguric ATN
  - Granular casts, high FENa
- Renal potassium and magnesium wasting
- Timing: 5-10 days
- Stop aminoglycoside



Contrast induced nephropathy

- Timing: 1-2 days

Acute interstitial nephritis

- Beta-lactams, PPI, NSAIDs
- Urine WBC, WBC casts, rash, eosinophilia
- Timing: 3-5 days after 2nd exposure

Cholesterol emboli

- Typically following vascular procedure
- Livedo reticularis
- Eosinophilia/eosinophiluria

11) A 69-year-old woman is evaluated during a follow-up visit for stage G4/A1 chronic kidney disease due to hypertensive nephrosclerosis. History is also significant for peripheral arterial disease with right femoral-popliteal bypass 1 year ago. Medications are metoprolol, atorvastatin, aspirin, and calcium acetate.

On physical examination, temperature is 37.0 °C (98.6 °F), blood pressure is 132/89 mm Hg, pulse rate is 61/min, and respiration rate is 13/min. BMI is 27. There is an audible S_4 gallop and reduced pedal pulses. The lungs are clear. The lower extremities are warm with normal capillary refill. There is no peripheral edema.

Review of a previous chest radiograph is remarkable for a heavily calcified aorta but is otherwise clear.

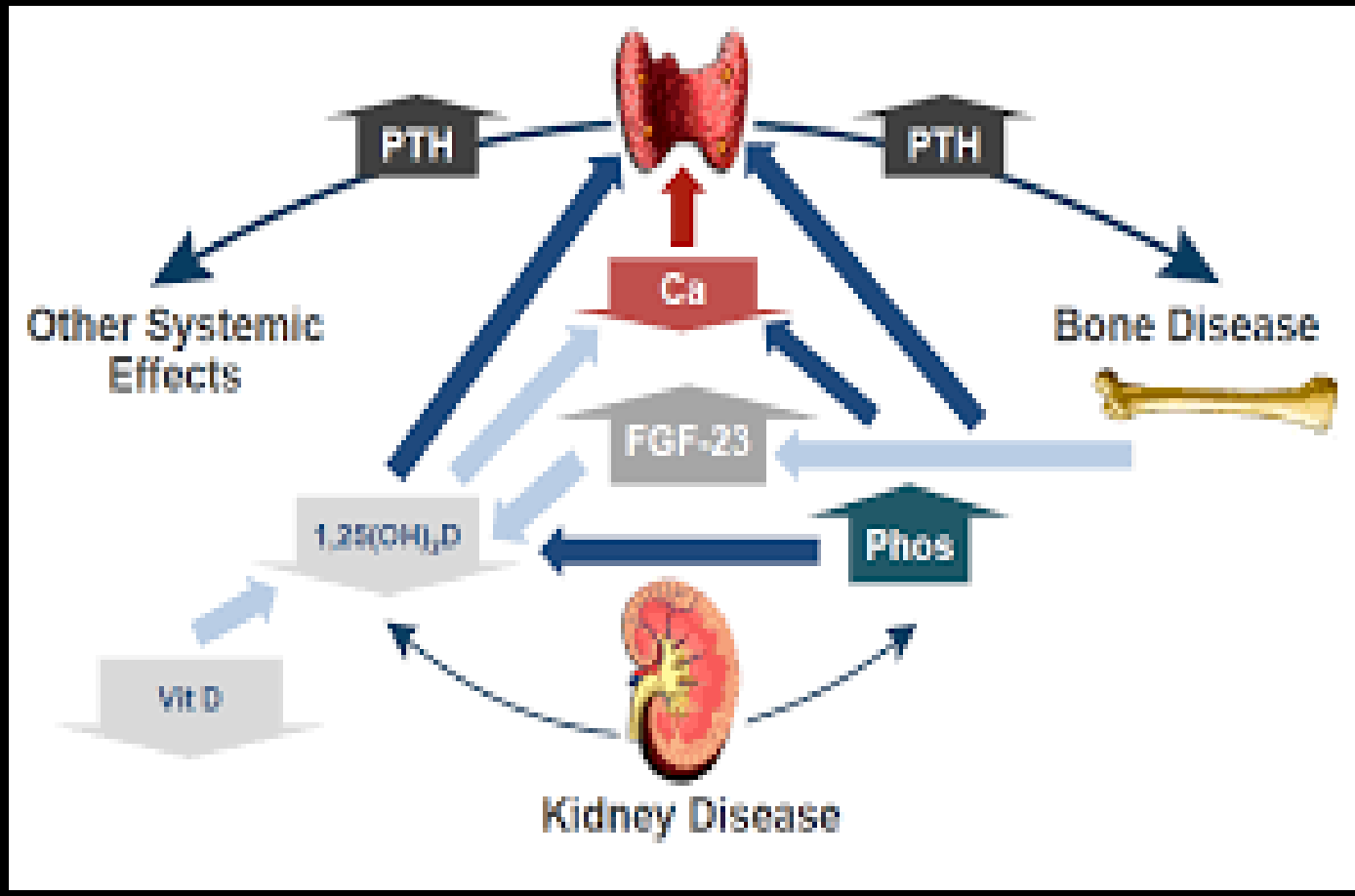
In addition to dietary counseling regarding a low phosphate diet, which of the following is the most appropriate treatment?

Laboratory studies:	
Albumin	4.2 g/dL (42 g/L)
Calcium	8.3 mg/dL (2.1 mmol/L)
Creatinine	2.6 mg/dL (229.8 µmol/L)
Phosphorus	6.9 mg/dL (2.23 mmol/L)
Intact parathyroid hormone	95 pg/mL (95 ng/L)
Estimated glomerular filtration rate	22 mL/min/1.73 m^2

#12
SEVELAMER

HYPERPHOSPATEMIA

- 3 hormones
  - PTH
  - Vitamin D
  - FGF-23
- CKD leads to increased FGF-23, decrease renal conversion of 25-hdyroxy-D to 1,25 dihydroxy-D
- Calcium and phos absorption decreases
- PTH increase
  - Increases calcium and phos excretion by kidney
  - Increases bone resorption
- Eventually kidney function is bad enough, it can't keep up with phos excretion.



SECONDARY HYPERPARATHYROIDISM

- eGFR <60: Goal is normal PTH level
  - First treat 25-OH vit D deficiency, normalize calcium and phosphorus levels
  - Second: calcitriol to suppress PTH
    - Only if normal Ca and Phos
    - Risk of hyperphosphatemia or hypercalcemia (increases gut absorption)

TERTIARY HYPERPARATHYROIDISM

- Due to prolonged PTH stimulation needed to maintain normal calcium levels
- Causes parathyroid hyperplasia with elevated PTH levels not responding to phosphate binders and calcitriol
- Treat: parathyroidectomy

PHOSPHATE BINDERS

Calcium containing

- Calcium carbonate
- Calcium acetate

- Avoid if hypercalcemia

No calcium

- Sevelamer
- Lanthanum
- Ferric citrate

13) A 72-year-old man is evaluated for a 3-month history of slowly progressive anemia and fatigue. He has a 3-year history of end-stage kidney disease and receives hemodialysis three times weekly. Prior to starting hemodialysis, he was able to maintain adequate iron stores with oral iron therapy. Erythropoietin for symptomatic anemia was initiated 3 years ago with the onset of dialysis; he responded well, with an increase in his hemoglobin level to 11 g/dL (110 g/L) and a decrease in symptoms. There have been no changes in his medications, which consist of erythropoietin, three times weekly; oral iron sulfate, 325 mg three times daily; lisinopril; metoprolol; nifedipine; sevelamer; and aspirin.

On physical examination, the patient is afebrile. Blood pressure is 144/94 mm Hg, pulse rate is 76/min, and respiration rate is 16/min. The lungs are clear. There is no edema.

Which of the following is the most appropriate management?

Laboratory studies:	
Hemoglobin	9.8 g/dL (98 g/L)
Ferritin	80 ng/mL (80 µg/L)
Transferrin saturation	12%

#13
ADMINISTER IV IRON

ANEMIA OF CKD

Normocytic anemia
Diagnosis of exclusion
EPO level will be low, but not useful for testing

Start ESAs for Hgb <10
Avoid if Hgb >11.5, history of stroke, active malignancy

Monitoring:
- CKD III: yearly
- CKD IV-V: Every 6 months
- Dialysis: Every 3 months
- Iron studies every 3 months while on ESA

- KDIGO goals
  - Hemoglobin
  - Transferrin saturation level
  - Ferritin

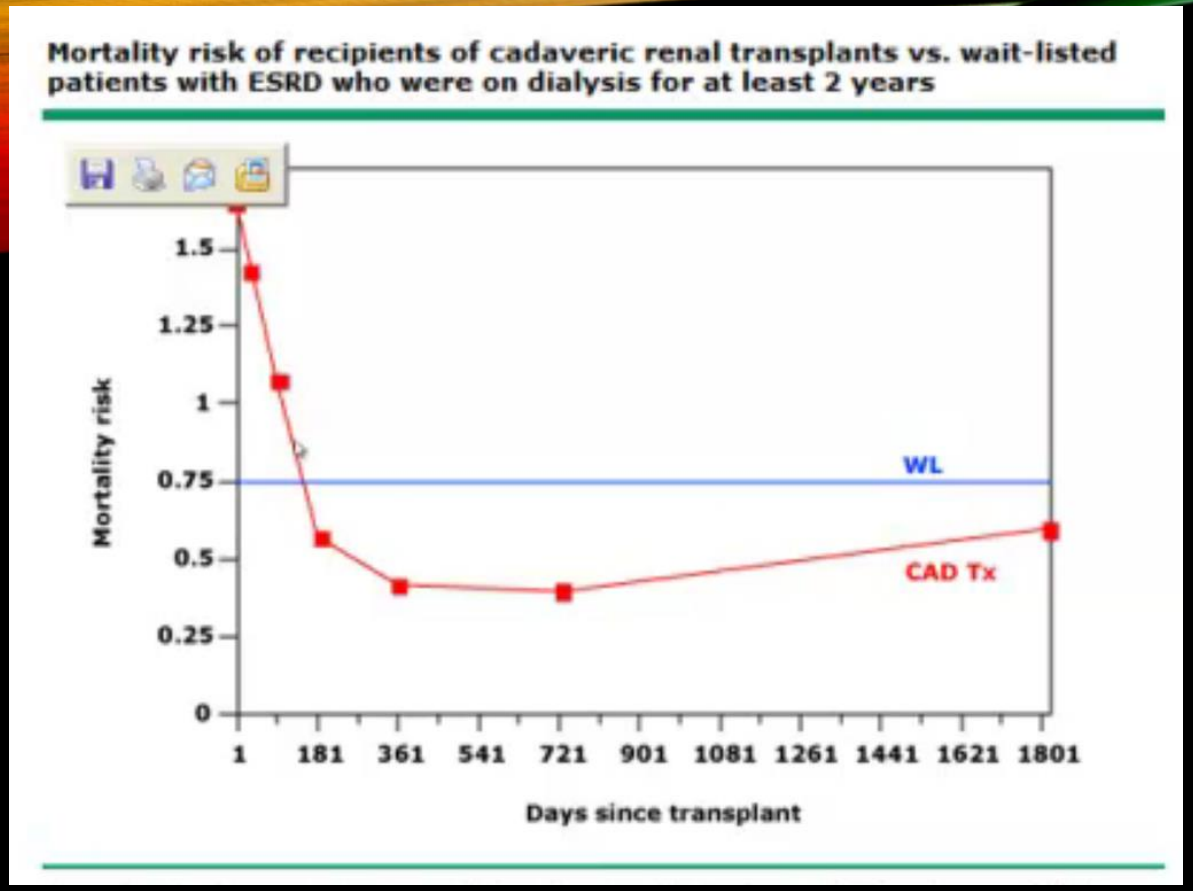
- 10.0-11.5 mg/dL
- >30%
- >500 ug/L

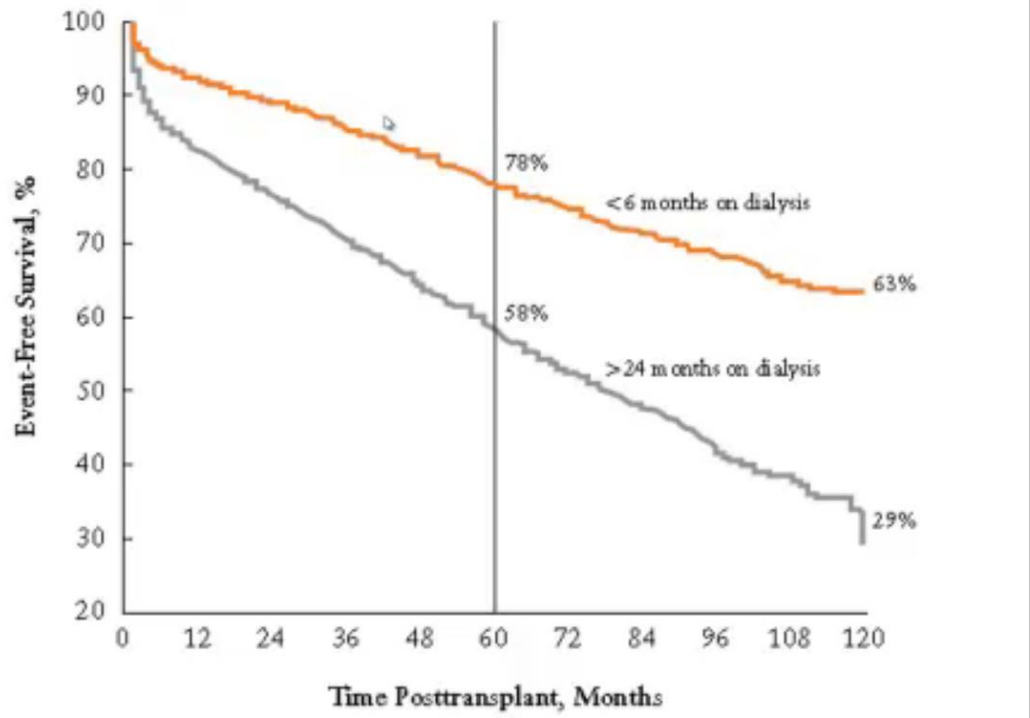
14) A 65-year-old woman is evaluated during a follow-up visit. She has end-stage kidney disease due to IgA nephropathy; she started peritoneal dialysis 3 months ago. She also has a 10-year history of hypertension. She has done well since starting dialysis, is without current complaints, and has recently resumed exercising regularly. She has three adult children who are encouraging her to explore kidney transplantation and are willing to be evaluated as kidney donors; however, the patient feels that she is "too old." Medications are amlodipine, ramipril, calcitriol, epoetin alfa, and calcium acetate.

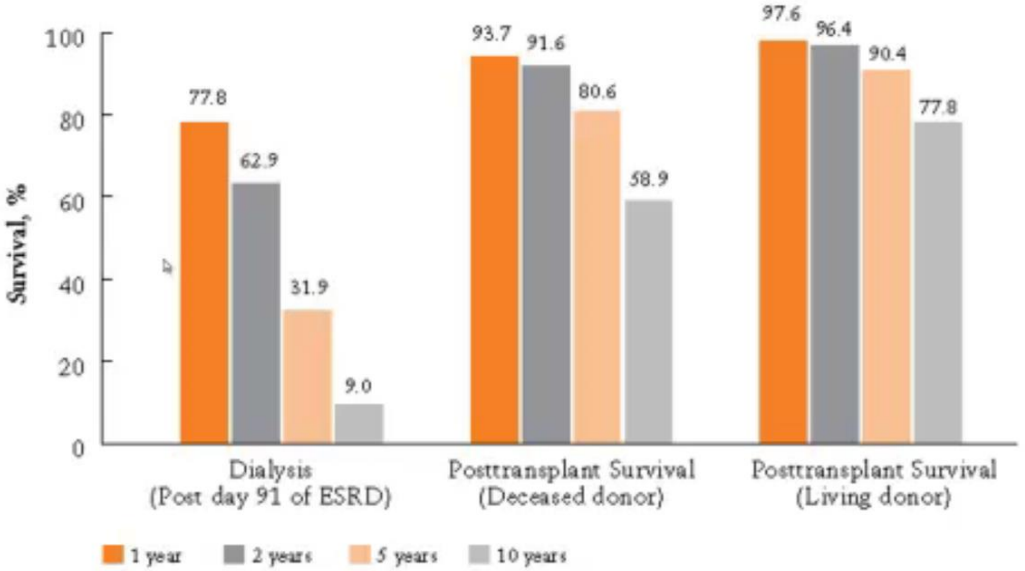
On physical examination, temperature is 37.0 °C (98.6 °F), blood pressure is 135/75 mm Hg, pulse rate is 72/min, and respiration rate is 14/min. BMI is 27. The peritoneal dialysis catheter site is nontender without induration or exudate. Cardiac examination reveals normal heart sounds. The lungs are clear. The abdomen is nontender. There is no peripheral edema.

Which of the following kidney replacement strategies is most likely to provide this patient with the best long-term survival?

#14
REFER FOR TRANSPLANTATION NOW







- Kidney transplant improves long term mortality
- Mortality improves if transplanted prior to initiating dialysis
- Long term survival is better in patients receiving living donor transplants

15) A 40-year old man is evaluated during a follow-up visit for a kidney transplant he received 2 years ago. History is also significant for hypertension. Medications are tacrolimus, mycophenolate mofetil, prednisone, and nifedipine.

On physical examination, blood pressure is 150/95 mmHg; other vital signs are normal. BMI is 26. The cardiovascular and pulmonary examinations are normal. The abdomen and renal allograft are nontender to palpation. Trace pedal edema is noted.

Duplex ultrasound of the kidneys shows no evidence of transplant renal artery stenosis.

Which of the following is the most appropriate treatment?

Laboratory studies:	
Potassium	5.6 mEq/L (5.6 mmol/L)
Sodium	Normal
Estimated glomerular filtration rate	90mL/min/1.73 m^2

#15 CHLORTHALIDONE

CALCINEURIN INHIBITORS

- Tacrolimus and cyclosporine
- Side effects: Hypertension, hyperkalemia, increased creatinine, GI upset
- Activate sodium chloride cotransporter in distal convoluted tubule, causing sodium and chloride reabsorption and hypertension.
- Decreased distal tubular flow impairs potassium secretion in the connecting tubule and collecting duct

Table 1. Drugs Used in Maintenance Immunosuppression of Kidney Transplant Recipients

Drug	Mechanisms of Action	Adverse Effects	Common Signs of Acute Toxicity	How Drug Dose is Monitored/Adjusted	Important Drug Interactions
Glucocorticoids	Blockade of cytokine gene transcription in lymphocytes, antigen-presenting cells, and other immune cells	Glucose intolerance, hypertension, hyperlipidemia, osteoporosis, osteonecrosis, myopathy, cosmetic defects, growth suppression in children	Multiple	Standard center protocol	Cyclosporine and tacrolimus potentiate diabetogenic effects
Cyclosporine	Inhibits calcineurin and ultimately lymphocyte synthesis of IL-2	Nephrotoxicity (acute and chronic), hyperlipidemia, hypertension, glucose intolerance, hirsutism, gum enlargement	Rising plasma creatinine, tremor	Trough blood concentrations or 2 hours after dosing	Inducers and inhibitors of cytochrome P450 decrease and increase blood concentrations, respectively
Tacrolimus	Inhibits calcineurin and ultimately lymphocyte synthesis of IL-2	Broadly similar to those of cyclosporine; diabetes mellitus more common; hypertension, hyperlipidemia and cosmetic defects less common	Rising plasma creatinine, tremor, GI upset	Trough blood concentrations	Same as for cyclosporine
Azathioprine	Inhibits leukocyte proliferation	Bone marrow suppression; rarely, hepatitis and/or pancreatitis	Marrow suppression	Initially, 1-2 mg/kg per day; dose reduced in case of marrow suppression	Allopurinol inhibits metabolism of drug, thereby greatly increasing toxicity
Mycophenolate mofetil	Inhibits leukocyte proliferation; relatively more selective for lymphocytes than azathioprine	Bone marrow suppression, nausea, abdominal pain, diarrhea; invasive CMV disease more common than with azathioprine	Marrow suppression, diarrhea	Initially 500-1000 mg bid; dose reduced in case of marrow suppression or GI adverse effects	GI symptoms exacerbated by tacrolimus
Sirolimus	Inhibits leukocyte proliferation	Bone marrow suppression, hyperlipidemia, diarrhea, interstitial pneumonitis (rare)	Marrow suppression, diarrhea	Trough blood concentrations	Inducers and inhibitors of cytochrome P450 decrease and increase blood concentrations, respectively; sirolimus enhances nephrotoxicity of cyclosporine and tacrolimus

16) A 65- year old man is evaluated for a 2-month history of low back pain. The pain is worse with movement, but it does not radiate. He reports associated fatigue and a 4.5-kg (10-lb) weight loss. He has osteoarthritis and gastroesophageal reflux disease. He has been taking ibuprofen without any pain relief. His only other medication is omeprazole.

The physical examination, including vital signs and neurologic examination, is normal.

Ultrasound reveals normal-sized kidneys with slightly increased echogenicity; no hydronephrosis or abnormalities of the collecting system are seen.

In addition to discontinuing ibuprofen, which of the following is the most appropriate next step in management?

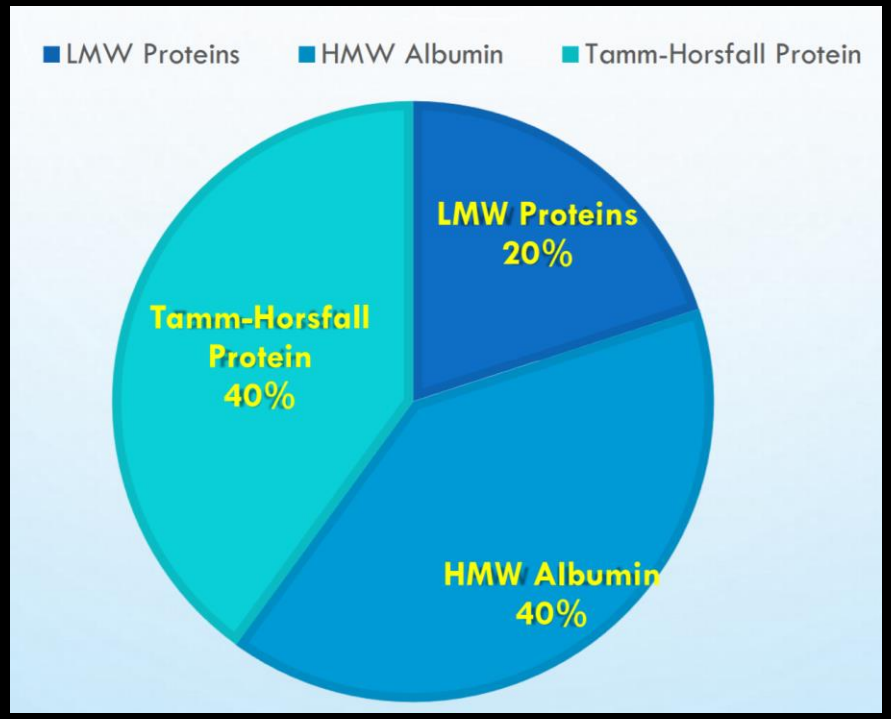
Laboratory studies:	
Hemoglobin	9.2g/dL (92g/L)
Creatinine	3.0 mg/dL (265.2 umol/L)
Urinalysis	Trace protein
Urine protein-creatinine ratio	2500 mg/g

#16
OBTAIN URINE PROTEIN ELECTROPHORESIS

PROTEINURIA

- Urine dip stick is more sensitive to albumin than other proteins such as Bence-Jones proteins or immune globulins.

Urine Dipstick Protein Reading	Urinalysis Protein Excretion mg/dL	Protein Excretion mg/ 24 Hours
Negative	< 10	< 100 mg
Trace	15	100 - 300
+1	30	200 – 500
+2	100	500 - 1500
+3	300	2000 - 5000
+4	> 1000	> 5000



17) A 36-year-old man is evaluated following his second episode of nephrolithiasis. His initial kidney stone occurred 6 months ago and passed spontaneously. The stone was recovered and on analysis was found to be a pure uric acid stone. He was advised to increase his urine output to at least 2 L/d and has been adherent to this recommendation. His second episode occurred last week. He again passed the stone spontaneously, which was submitted for analysis and shown to be a pure uric acid stone. Medical history is significant for type 2 diabetes mellitus, but he has never had evidence of gout. Medications are metformin and rosuvastatin.

On physical examination, temperature is 36.9 °C (98.5 °F), blood pressure is 135/87 mm Hg, pulse rate is 78/min, and respiration rate is 12/min. BMI is 31. There is no costovertebral angle tenderness. No joint abnormalities or gouty tophi are noted.

In addition to continuing oral hydration, which of the following is the most appropriate next step in therapy?

Laboratory studies:	
Electrolytes	Normal
Kidney function studies	Normal
Urate	7.6 mg/dL (0.45 mmol/L)
Urinalysis	pH 5.8; no blood; no cells or crystals
24-Hour uric acid excretion	850 mg/24 h (5 mmol/24 h)

#17
URINE ALKALINIZATION

KIDNEY STONES

Calcium oxalate

- Most common form
- Causes
  - Hypercalciuria – hyperparathyroidism, sarcoidosis, vitamin D excess
  - Hyperoxaluria – increased dietary oxalate, malabsorption , low dietary calcium, high vitamin C intake, Orlistat.
- Treatment: fluids, thiazide diuretics, potassium citrate or bicarbonate (urine alkalinization)
- Do not decrease dietary calcium intake

Calcium phosphate

- Common with alkaline urine
  - Distal RTA
  - Acetazolamide
  - Topiramate
  - Hyperparathyroidismm

Struvite

- Caused by urea splitting bacteria
  - Proteus
  - Klebsiella
- Urea is split into ammonium, increasing urine pH – magnesium ammonium phosphate precipitates
- Treatment: treat infection, lithotripsy

Uric acid

- Causes: gout, chronic diarrhea, metabolic syndrome
- Radiolucent stones! (X-ray)
- Treatment
  - Alkalinize urine first
  - Allopurinol second

Cystine

- Caused by cystinuria
  - Autosomal recessive disorder
- Hexagonal crystals

HIGH URINE Ph

- Calcium phosphate
- Struvite

LOW URINE pH

- Uric acid
- Cystine

18) A 44-year old man is evaluated during a follow up visit for treatment of persistently elevated blood pressure. He takes no medications.

Physical examination reveals a well-developed muscular man in no apparent distress. Blood pressure is 165/98 mmHg, and pulse rate is 70/min; other vital signs are normal. BMI is 26. Jugular venous pressure is normal. Cardiac examination is unremarkable.

Electrocardiogram reveals normal sinus rhythm; voltage criteria for left ventricular hypertrophy are present.

Which of the following is the most appropriate treatment?

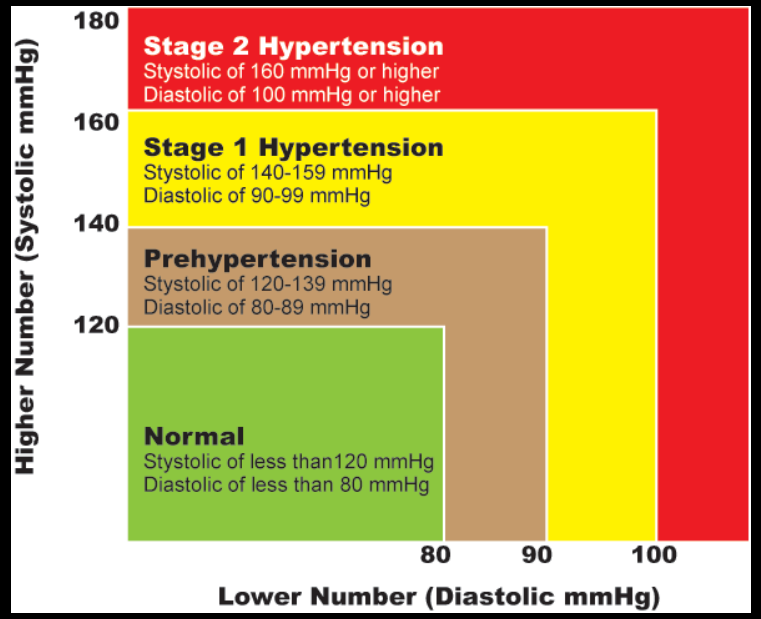
Laboratory studies:	
Bicarbonate	27 mEq/L (27 mmol/L)
Creatinine	1.3 mg/dL (114.9 umol/L)
Potassium	4.5 mEq/L (4.5 mmol/L)
Estimated glomerular filtration rate	>60 mL/min/1.73m^2
Urine toxicology screen	Negative

#18 AMLODIPINE/BENAZEPRIL COMBINATION ONCE DAILY

ACC/AHA recommends combination of 2 first line antihypertensives for stage 2 hypertension

There is a nonlinear diminishing blood pressure-lowering effect when titrating antihypertensive medication doses above 50% maximum dose.

- Addition of a second medication will achieve greater blood pressure reduction.



- First line antihypertensives
  - Thiazide diuretics
  - Calcium channel blockers
  - ACE inhibiters

Not Recommended:

- Beta-blockers: higher rate of cardiovascular related events and mortality compared to ARBs
- Alpha-blockers: Higher rate of cardiovascular related events and mortality compared to thiazides.
- ACE and ARB combination has higher rates of hyperkalemia, hypotension, AKI without proven cardiovascular or renal benefits.

19) A 45-year old man is seen for a routine evaluation of his blood pressure. He has gained 1.5 kg (3.3 lb) since his last visit 3 weeks ago. History is significant for stage G4 chronic kidney disease, hypertension, type 2 diabetes mellitus, and coronary artery disease. Medications are amlodipine, lisinopril, carvedilol, chlorthalidone, basal and prandial insulin, atorvastatin, and low-dose aspirin.

On physical examination, blood pressure is 165/100 mmHg, pulse rate is 58/min, and respiration rate is 16/min. There is 1+ bilateral leg edema. The remainder of the physical examination is noncontributory.

In addition to maintaining a low sodium diet, which of the following is the most appropriate treatment of this patient's blood pressure?

Laboratory studies:	
Blood urea nitrogen	44mg/dL (15.7 mmol/L)
Creatinine	2.8 mg/dL (247.5 umol/L)
Potassium	5.4 mEq/L (5.4 mmol/L)
Estimated glomerular filtration rate	26 mL/min/1.73 m^2
Urinalysis	Normal

#19
STOP CHLORTHALIDONE; BEGIN FUROSEMIDE

CKD AND HYPERTENSION

SECONDARY HYPERTENSION

- CKD
- Renovascular hypertension
  - Atherosclerotic (older)
  - Fibromuscular dysplasia (younger)
- Primary hyperaldosteronism
- Pheochromocytoma
- OSA
- Thyroid disease
- Hyperparathyroidism
- Cushing syndrome
- Liddle syndrome

- ACC/AHA goal BP <130/80 mmHg
- ACE inhibitor or ARB first line
- Diuretic resistance increases as GFR decreases.
- When GFR falls below 30, switch to loop diuretic
- Volume overload will precipitate uncontrolled hypertension. BP control improves when euvolemic.

20) A 45-year old woman is evaluated for the recent onset of resistant hypertension. During her last visit, chlorthalidone was added to her medication regimen. She reports no symptoms, and review of the systems is otherwise unremarkable. Current medications are metoprolol, amlodipine, hydralazine, and chlorthalidone.

On physical examination, blood pressure is 160/96 mmHg, and pulse rate is 65/min; other vital signs are normal. BMI is 24. There is no proptosis. The thyroid gland is not enlarged. The remainder of the examination is unremarkable.

Which of the following is the most appropriate diagnostic test to perform next?

Laboratory studies:	
Bicarbonate	34mEq/L (34mmol/L)
Creatinine	0.8 mg/dL (70.7 umol/L)
Potassium	2.9 mEq/L (2.9 mmol/L)
Urine albumin-creatinine ratio	10mg/g

#20
PLASMA ALDOSTERONE CONCENTRATION/PLASMA RENIN ACTIVITY RATIO

RESISTANT HYEPRTENSION
- BP above goal despite 3 antihypertensives
- 1 must be a diuretic

Interventions
- Addition of spironolactone
- Taking one of the medications at night.

SECONDARY HYPERTENSION
- Hyperaldosteronism
    1. Stop diuretics, aldosterone antagonists, ACE-I
    2. Check PAC/PRA ratio
        - High ratio is suggestive (PRA<1, PAC>10)
        - Ratio >20 and hypokalemia is diagnostic
    3. Confirmatory testing
        1. Salt load
            - 3 days salt load should suppress urine aldosterone below 12 mcg/24 hours
        2. Fludrocortisone suppression test
        3. Captopril challenge test
            - Single dose should suppress aldosterone levels below 15 ng/dL

SALINE NONRESPONSIVE METABOLIC ALKALOSIS