

ELECTROLYTE AND ACID BASE: Challenging Questions and Answers Part 1 (Questions 1-8)

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Clinical Chief

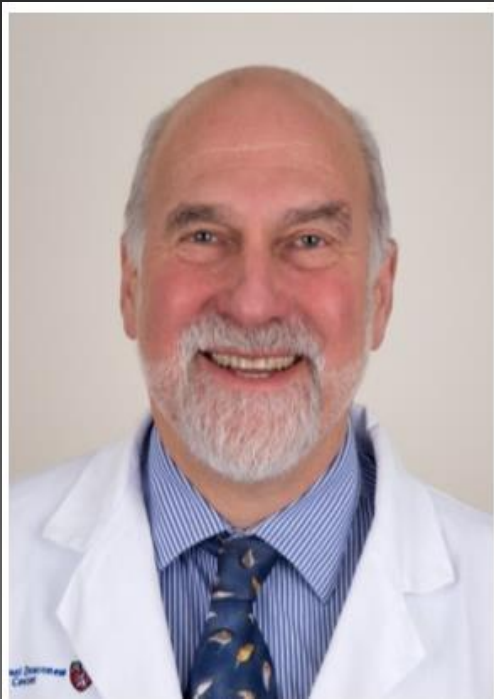
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**CONTINUING MEDICAL EDUCATION
DEPARTMENT OF MEDICINE**



**HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL**

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Financial disclosures

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Objectives

1. Use physiologic approach to identify dysregulated physiology of:
 1. Sodium Concentration
 2. Potassium Concentration
 2. Identify appropriate treatment for disorder based on physiology
-

Case 1

A 35 year-old man with bipolar disorder treated on lithium, is referred to you for chronic polyuria and polydipsia. He complains that he has to void once every hour.

Laboratory studies:

Serum sodium	146 mEq/L
Blood urea nitrogen	35 mg/dL
Serum creatinine	1.9 mg/dL
Serum osmolality	305 mOsm/kg
24-hr urine volume	5 L
Urine sodium	28 mEq/L
Urine osmolality	190mOsm/kg

Case 1

Which of the following might be appropriate in the management of this patient?

- ☒ (A) Discontinue lithium
- ☐ (B) Demeclocycline
- ☐ (C) Vasopressin V2 receptor antagonist
- ☐ (D) Fluid restriction
- ☐ (E) Furosemide

Choices B-E are all potential treatment options for **Hyponatremia** but will worsen hypernatremia

Hypernatremia

Urine Osmolality
[mOsm/kg]

Low
< 300

Intermediate
300-600

High
> 800

Renal H₂O loss

Diabetes
insipidus

CDI

NDI

ADH
Deficiency

ADH
Resistance

Osmotic
diuresis

Glucose,
urea, mannitol

- **Insensible H₂O loss**

- **GI H₂O loss**

+

↓ **Water intake**

- **Na⁺ Intoxication**

Nephrogenic diabetes insipidus

- Hypokalemia
 - Hypercalcemia
 - Tubulointerstitial nephropathies
 - Sickle cell disease
 - Myeloma
 - Obstructive uropathy
 - Recovery from ATN or obstruction
 - Lithium
 - Chronic renal failure
-

Distinguishing central from nephrogenic DI

Water deprivation test



DDAVP (desmopressin)



↑ U_{Osm}

CDI



No Δ in U_{Osm}

NDI

Case 1

Which of the following might be appropriate in the management of this patient?

- (A) Discontinue lithium
- (B) Demeclocycline; interferes with ADH action in collecting duct-*increased* water excretion
- (C) Vasopressin V2 receptor antagonist-blocks V2 receptor and ADH action in collecting duct-*increased* water excretion
- (D) Fluid restriction; more free water needed
- (E) Furosemide; blocks ability to concentrate urine; dilute urine output (*increased water excretion*)

Case 2

An 85 year-old woman, who lives alone, fell in her bedroom and broke her hip. She was unable to get up and had no access to water. She was found 2 days later and brought into the ER. On examination, she is drowsy but responsive. The blood pressure is 88/51 mm Hg, pulse rate 90 per minute supine, weight 70 kg, mucous membranes are very dry and skin turgor is decreased.

Laboratory studies:

Serum sodium	164 mEq/L
Blood urea nitrogen	54 mg/dL
Serum creatinine	1.2 mg/dL
Hematocrit	56%
Urine osmolality	820 mOsm/kg

Case 2

Which of the following statements is most accurate?

- A. She has intracellular fluid volume depletion but normal extracellular volume
- B. 3% saline should initially be used to minimize the plasma sodium gradient
- C. Her serum Na^+ should be lowered to 140mEq/L in the next 24 hours
- D. Overly rapid correction of her hypernatremia could cause osmotic demyelination syndrome
-  E. Rapid correction of her hypernatremia could cause cerebral edema

Hypernatremia

Urine Osmolality
[mOsm/kg]

Low
< 300

Intermediate
300-600

High
> 800

Renal H₂O loss

Diabetes
insipidus

CDI

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Osmotic
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Glucose,
urea, mannitol

- **Insensible H₂O loss**

- **GI H₂O loss**

+

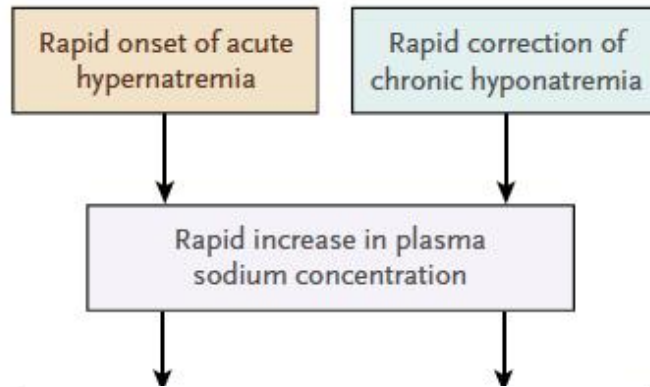
↓ **Water intake**

- **Na⁺ Intoxication**

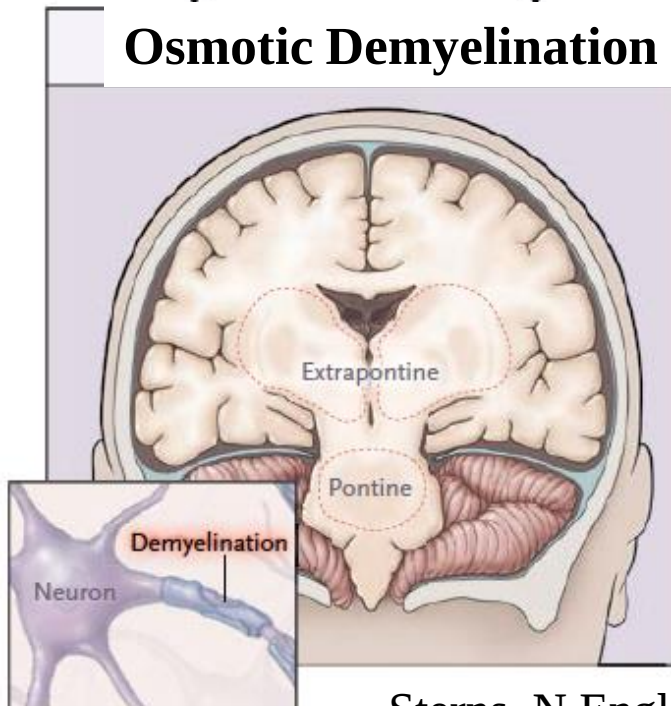
Management of hypernatremia

- Replace free water deficit (50% in first 24 hr, no more than 0.5 mM/hr); Observational studies show no increase of cerebral edema or death with faster correction
 - Replace ongoing free water losses
 - Treat underlying cause
 - Desmopressin for CDI
 - No specific Rx for NDI (attempt to reduce urine output with Na restriction, thiazides or give supratherapeutic dose of desmopressin)
-

Rapid Increase in Na



Osmotic Demyelination



Sterns, N Engl J Med 2015;372:55-65.

140

160

H₂O

Case 2

Which of the following statements is most accurate?

- A. She has intracellular fluid volume depletion but normal extracellular volume-**water is lost from all compartments**
- B. 3% saline should initially be used to minimize the plasma sodium gradient-**3% saline contains 512mEq/L so this will worsen the condition**
- C. Her serum Na^+ should be lowered to 140mEq/L in the next 24 hours-**correcting to this level would require 6 L of water (too much too fast!)**
- D. Overly rapid correction of her hypernatremia could cause osmotic demyelination syndrome-**this is risk in treating hyponatremia**
-  E. Rapid correction of her hypernatremia could cause cerebral edema

Case 3

A 64 year-old woman with coronary artery disease, multiple prior MI and ischemic cardiomyopathy, with a LV EF of 15%, is admitted with pulmonary edema. Her medications include aspirin, metoprolol, furosemide, spironolactone, digoxin, isosorbide dinitrate, and lisinopril. On examination, the blood pressure is 97/54 mm Hg, pulse rate 85 per minute, jugular venous pressure 9 cm, moist mucous membranes, lungs with diffuse inspiratory crackles, heart with an S3 gallop, and cool, clammy extremities with 1+ peripheral edema.

Serum sodium 128 mEq/L

Serum potassium 3.6 mEq/L

Serum chloride 87 mEq/L

Serum bicarbonate 34 mEq/L

Blood urea nitrogen 46 mg/dL

Serum creatinine 1.2 mg/dL

Arterial pH 7.48

Case 3

Urine electrolytes (6 hrs after last diuretic dose):

Urine sodium 15 mEq/L

Urine chloride < 5 mEq/L

Urine osmolality 220 mOsm/kg

Case 3

Which of the following is the most appropriate management for this patient's hyponatremia?

- (A) Intravenous 0.9% saline
- (B) Start Tolvaptan
- (C) Discontinue furosemide
- ☒ (D) Fluid restrict to 1.5L
- (E) Add Acetazolamide

Hyponatremia

P_{osm}

$> 290 \text{ mOsm/kg}$

$\uparrow$ Glucose*
Mannitol

Normal
“Pseudohyponatremia”

Lipid $\uparrow$
Protein $\uparrow$

$< 275 \text{ mOsm/kg}$

Hypoosmolar
hyponatremia

*Correct serum Na^+ by 1.6 for every 100 mg/dL Δ in glucose

Next Slide

Hypoosmolar hyponatremia

Volume status

Hypovolemic

Dehydration*
Addison's
Diuretics

Euvolemic

U_{Osm}

> 100

SIADH
Hypothyroid

< 100

Polydipsia

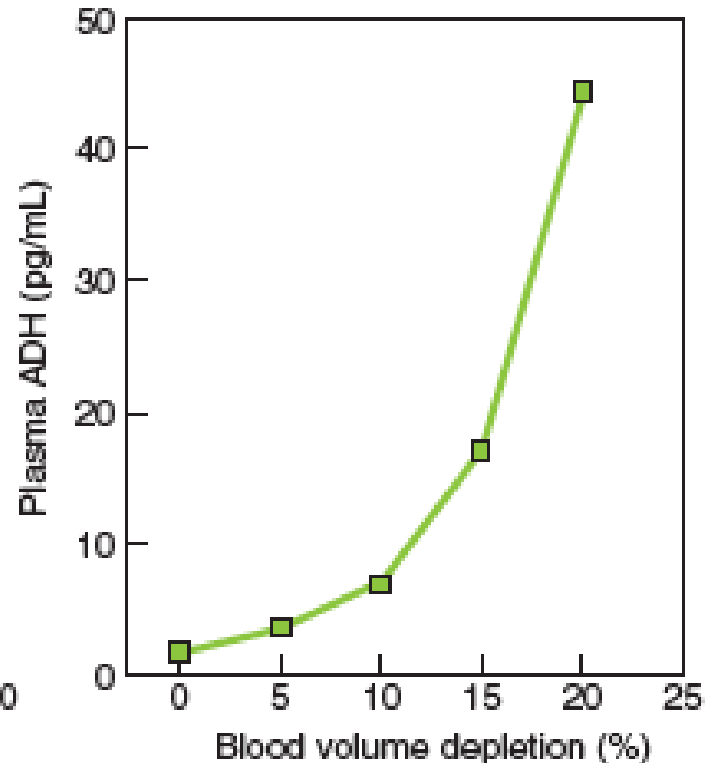
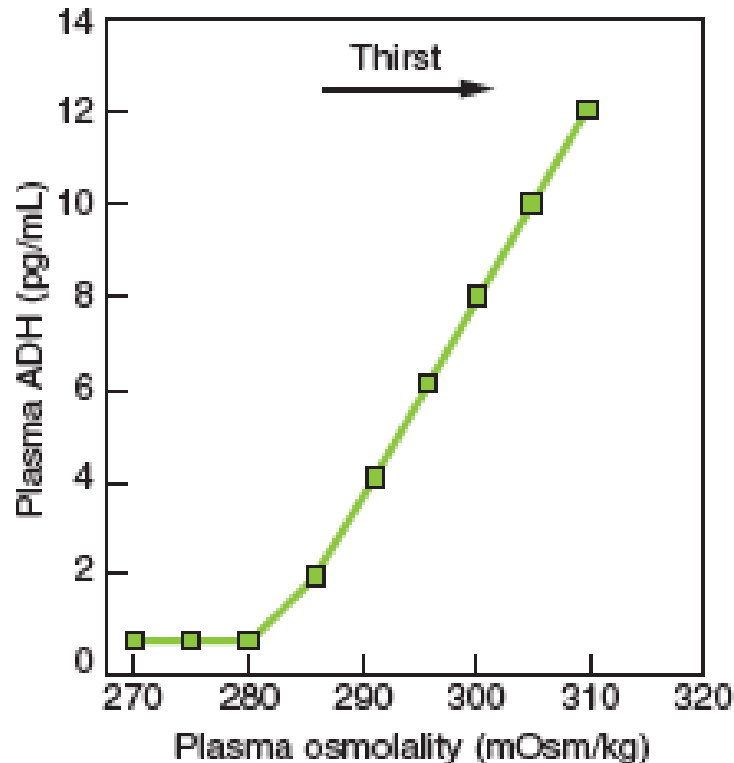
Edematous

CHF*

Nephrotic*
Liver failure*
Renal failure

* $U_{Na} < 20$ = Extrarenal cause of ECV depletion

Intravascular Volume Depletion Will Predominate Over Hypo-osmolality



Underfilled Arterial
Circulation

Case 3

Which of the following is the most appropriate management for this patient's hyponatremia?

- (A) Intravenous 0.9% saline- NO will worsen CHF
- (B) Start Tolvaptan-aquaretic; will “fix” Na but no evidence for benefit in CHF
- (C) Discontinue furosemide- NO will worsen CHF
- ☒ (D) Fluid restrict to 1.5L
- (E) Add Acetazolamide-carbonic anhydrase inhibitor

Case 4

A 45 year-old male smoker presents with confusion and drowsiness. His only medications are bronchodilator and steroid inhalers. On examination, his BP is 125/86, HR 78, moist mucous membranes, good skin turgor, jugular venous pressure 4 cm, lung fields clear to auscultation, no peripheral edema. Chest radiograph shows emphysematous changes but is otherwise normal. Laboratory studies:

Serum sodium 116 mEq/L

Serum osmolality 256 mOsm/kg

Urine sodium 85 mEq/L

Urine potassium 78 mEq/L

Urine osmolality 670 mOsm/kg

Case 4

Appropriate steps in the management of this patient might include:

- (A) Order serum protein and lipid panel
- ☒ (B) Computed tomography scan of the chest
- (C) Psychiatry consult for psychogenic polydipsia
- (D) Administer thiazide diuretic
- (E) Order echocardiogram

Hyponatremia

P_{osm}

$> 290 \text{ mOsm/kg}$

$\uparrow$ Glucose*
Mannitol

Normal
“Pseudohyponatremia”

Lipid $\uparrow$
Protein $\uparrow$

$< 275 \text{ mOsm/kg}$

Hypoosmolar
hyponatremia

*Correct serum Na^+ by 1.6 for every 100 mg/dL Δ in glucose

Next Slide

Hypoosmolar hyponatremia

Volume status

Hypovolemic

Dehydration*
Addison's
Diuretics

Euvolemic

U_{Osm}

> 100

SIADH

Hypothyroid

< 100

Polydipsia

Edematous

CHF*

Nephrotic*

Liver failure*

Renal failure

* $U_{Na} < 20$ = Extrarenal cause of ECV depletion

Case 4

Appropriate steps in the management of this patient might include:

- (A) Order serum protein and lipid panel; this is pseudohyponatremia
- ☒ (B) Computed tomography scan of the chest
- (C) Psychiatry consult for psychogenic polydipsia; would expect appropriately dilute urine
- (D) Administer thiazide diuretic; no effect on urine dilution; Na loss will worsen hyponat
- (E) Order echocardiogram; No evidence for CHF

Case 5

A 45 year-old woman with hypertension and type 2 diabetes mellitus presents with leg swelling and recent worsening of BP. Her medications are insulin, amlodipine, enalapril, furosemide, aspirin.

Laboratory studies:

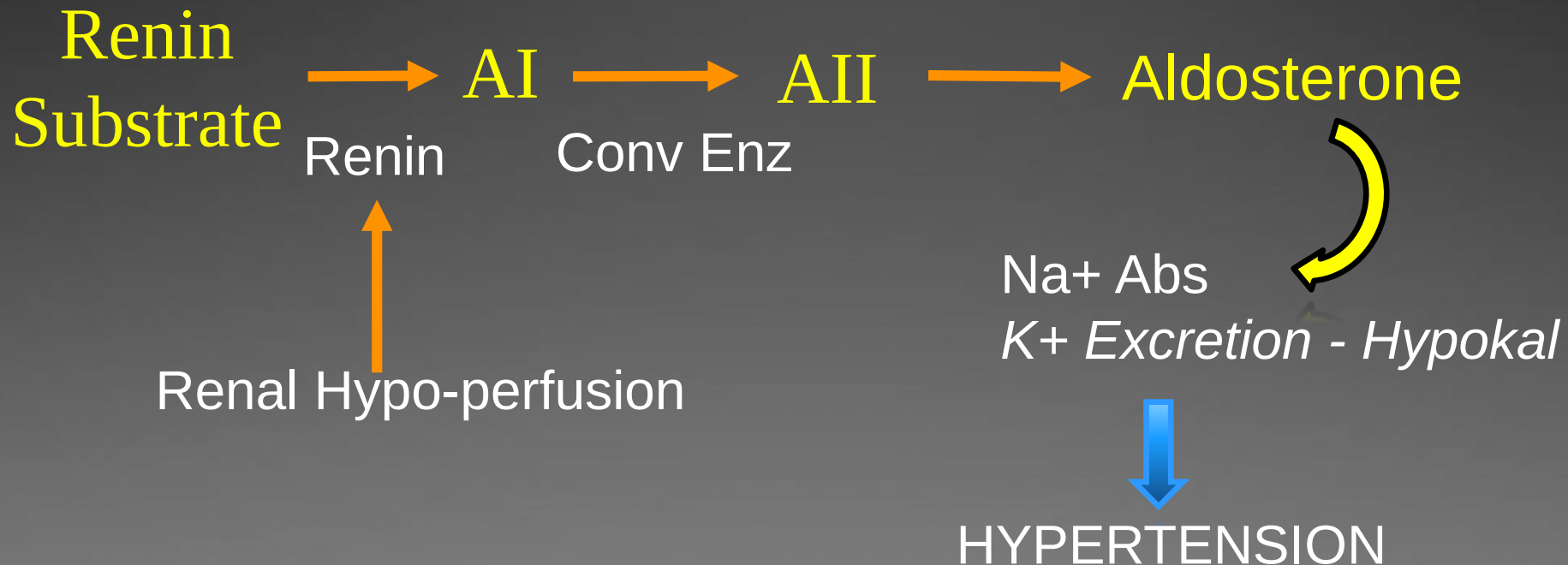
Serum sodium	136 mEq/L
Serum potassium	6.2 mEq/L
Serum bicarbonate	20 mEq/L
Blood urea nitrogen	32 mg/dL
Serum creatinine	1.9 mg/dL (eGFR-45)
24 hr urine total protein	4.8 g

Case 5

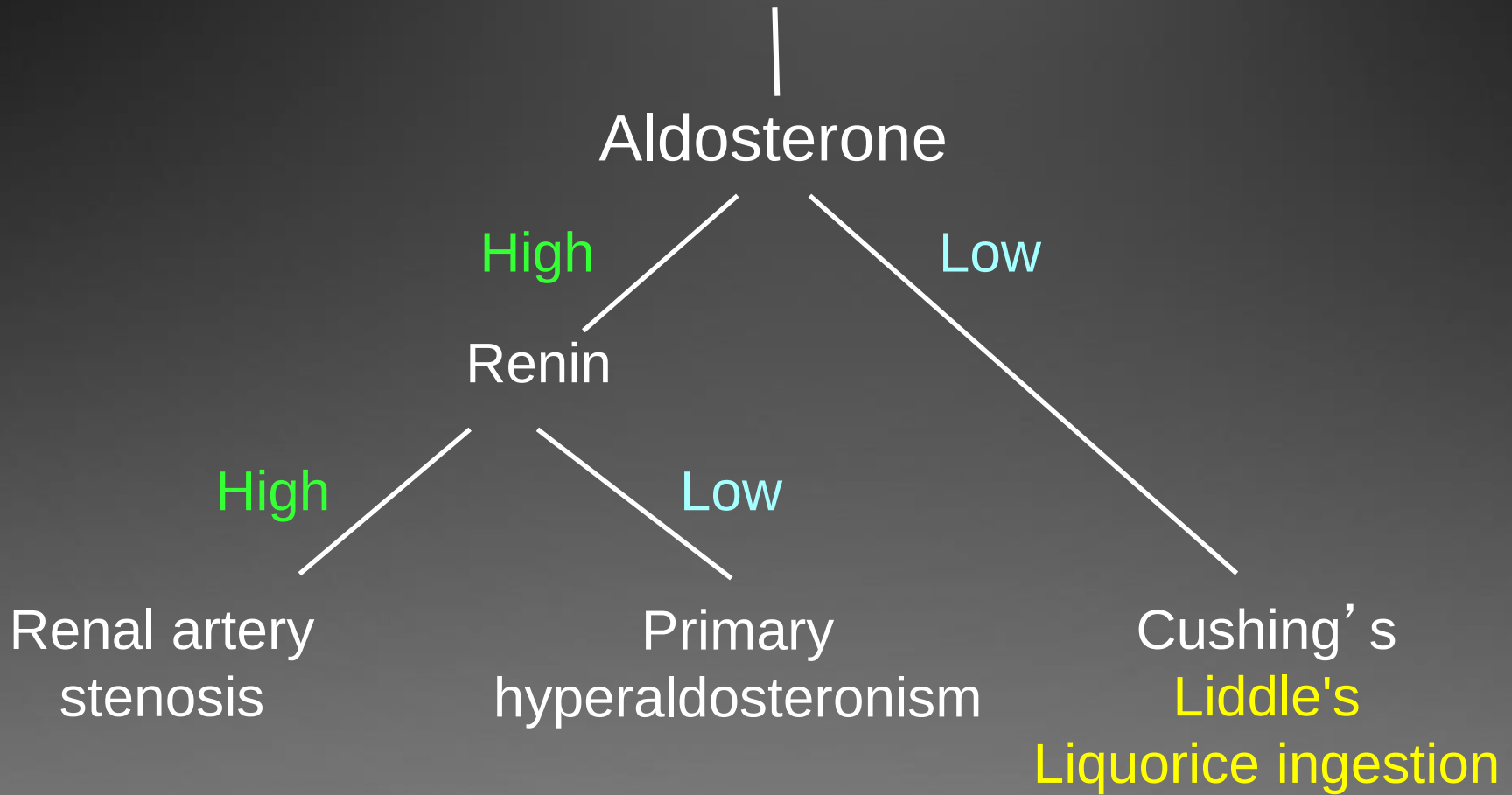
Which of the following is the most likely explanation for her hyperkalemia?

- (A) Primary hyperaldosteronism
- (B) Renal artery stenosis
- ☒ (C) Type 4 renal tubular acidosis
- (D) Type 2 (distal RTA)
- (E) Excess dietary K intake

Hypokalemia/Renal K⁺ wasting & hypertension



Hypokalemia/Renal K⁺ wasting & hypertension



Hyperkalemia

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graph TD; H[Hyperkalemia] --- I[↑ Intake]; H --- D[Decreased urinary K+ excretion]; H --- C[Cell shift]; I --- I1[↑ Intake]; D --- D1[24 hr urine K+ < 40 mEq]; C --- C1[Metabolic acidosis]; C --- C2[Hyperglycemia]; C --- C3[β-blocker]; C --- C4[Digitalis]; C --- C5[Hyperkalemic periodic paralysis]; C --- C6[Cell lysis];
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↑ Intake

Decreased urinary
K⁺ excretion

24 hr urine K⁺ < 40 mEq

Cell shift

Metabolic acidosis

Hyperglycemia

β-blocker

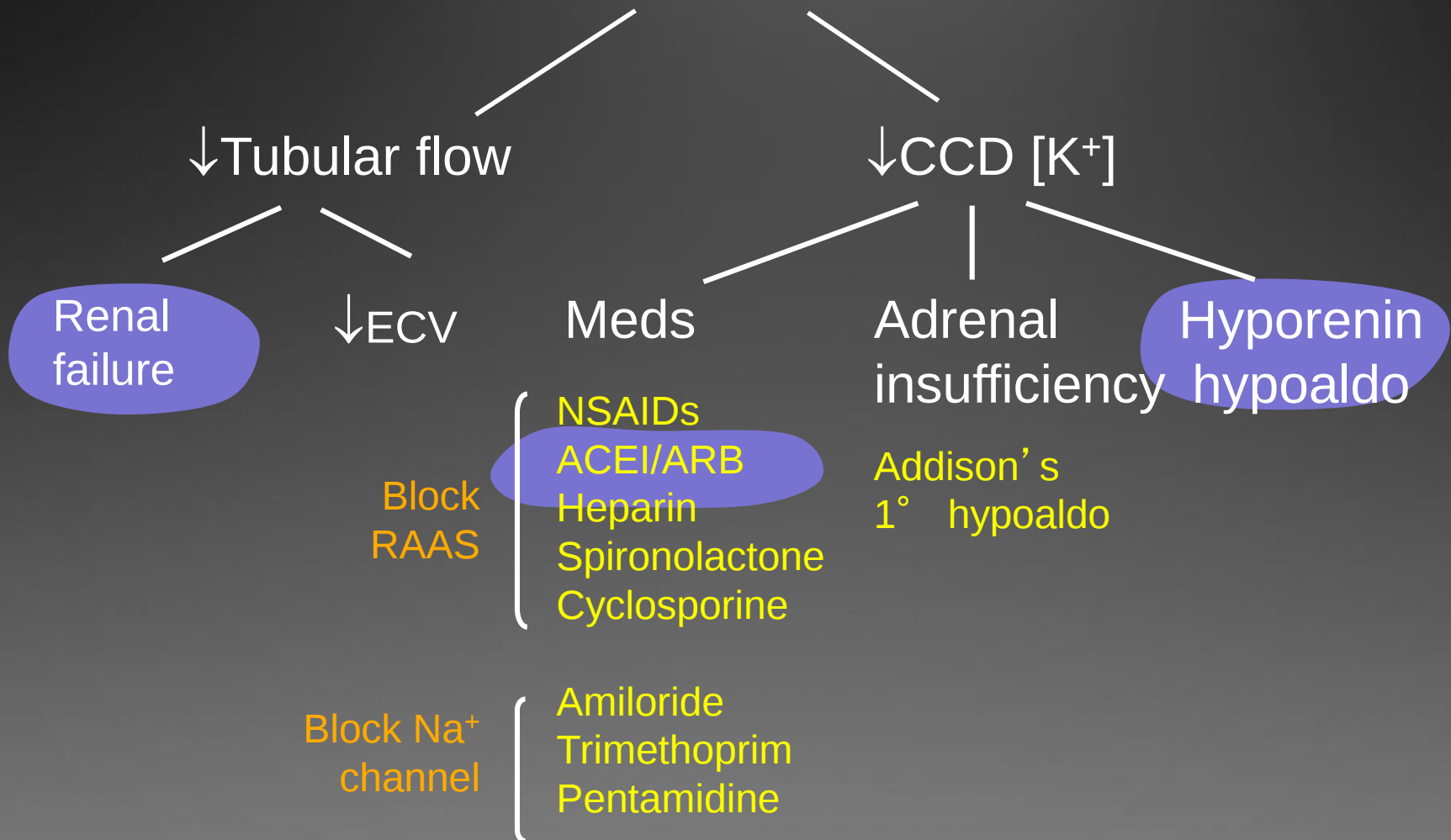
Digitalis

Hyperkalemic

periodic paralysis

Cell lysis

Decreased urinary K⁺ excretion



Type IV RTA (hyporeninemic hypoaldosteronism)

- Hyperkalemia (disproportionate to level of GFR)
- Non-gap metabolic acidosis with normal urine acidifying ability
- Mild CRF
- Often underlying tubulointerstitial disease:
 - DM
 - SLE, obstruction, myeloma/amyloid, HIV etc.
 - *NSAIDs*

Case 5

Which of the following is the most likely explanation for her hyperkalemia?

- (A) Primary hyperaldosteronism-hypertension and *hypokalemia*
- (B) Renal artery stenosis- ditto
- ☒ (C) Type 4 renal tubular acidosis
- (D) Type 2 (distal RTA)-impaired urinary acidification; K usually low
- (E) Excess dietary K intake-often a contributor but K elevation out of proportion to reduction in GFR decline

Case 6

An 18 year-old female presents with acute muscle weakness. She has had several previous episodes that resolved spontaneously. BP 96/54. Rest of the exam was unremarkable.

Laboratory studies:

Serum sodium	135 mEq/L
Serum potassium	2.9 mEq/L
Serum chloride	99 mEq/L
Serum bicarbonate	28 mEq/L
Blood urea nitrogen	8 mg/dL
Serum creatinine	0.5 mg/dL

24 hr urine studies:

Sodium	80 mEq/d
	(range 50-150mEq)
Potassium	105 mEq/d
	(range 50-100mEq/d)
Chloride	150 mEq/Ld

Case 6

Which one of the following diagnoses are compatible with this clinical picture?

- ☒ (A) Gitelman's syndrome
- ☐ (B) Primary hyperaldosteronism
- ☐ (C) Surreptitious amiloride use
- ☐ (D) Surreptitious laxative abuse
- ☐ (E) Hypokalemic periodic paralysis

DDX of hypokalemia

Cellular shift

Alkalemia

Insulin

β -agonist

Hypokalemic periodic
paralysis

GI loss

Vomiting*

Diarrhea

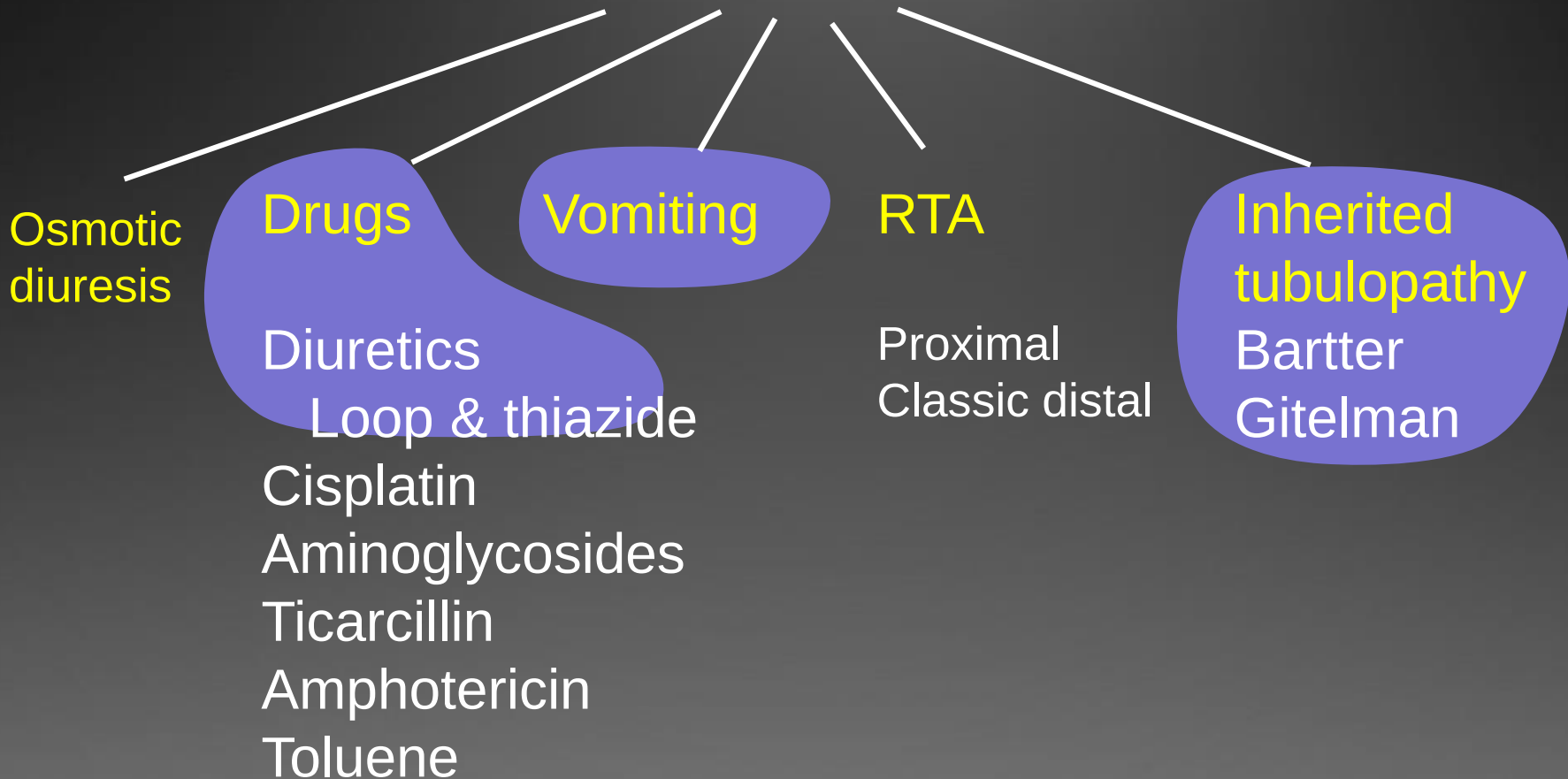
Urinary K wasting

24 hr $U_K > 25$ mEq

Random $>10-15$ mEq

*Also renal K^+ wasting

Renal K wasting with normal or low BP



Cryptogenic hypokalemic metabolic alkalosis

	Volume status/BP	Urine Cl ⁻	Urine diuretics
Hyperaldosteronism	↑	> 40 mEq/L	-
Surreptitious vomiting	NI or ↓	< 25 mEq/L	-
Diuretic abuse	NI or ↓	> 40 mEq/L	+
Bartter/Gitelman syndrome	NI or ↓	> 40 mEq/L	-

Case 6

Which one of the following diagnoses are compatible with this clinical picture?

- (A) Gitelman's syndrome-recessive mutation in thiazide sensitive transporter
- (B) Primary hyperaldosteronism; Hypokalemia + HTN
- (C) Surreptitious amiloride use; K sparing diuretic; expect low urine K and high serum K
- (D) Surreptitious laxative abuse; causes low K but urine K should be very low
- (E) Hypokalemic periodic paralysis; cellular K shifts, urine K not elevated

Case 7

A 74 year-old woman diagnosed with hypertension at the age of 40 presents with worsening blood pressure control over the past 3 years. She is now on amlodipine, lisinopril, hydrochlorothiazide, atenolol and clonidine. Her current BP is 156/78.

Laboratory studies:

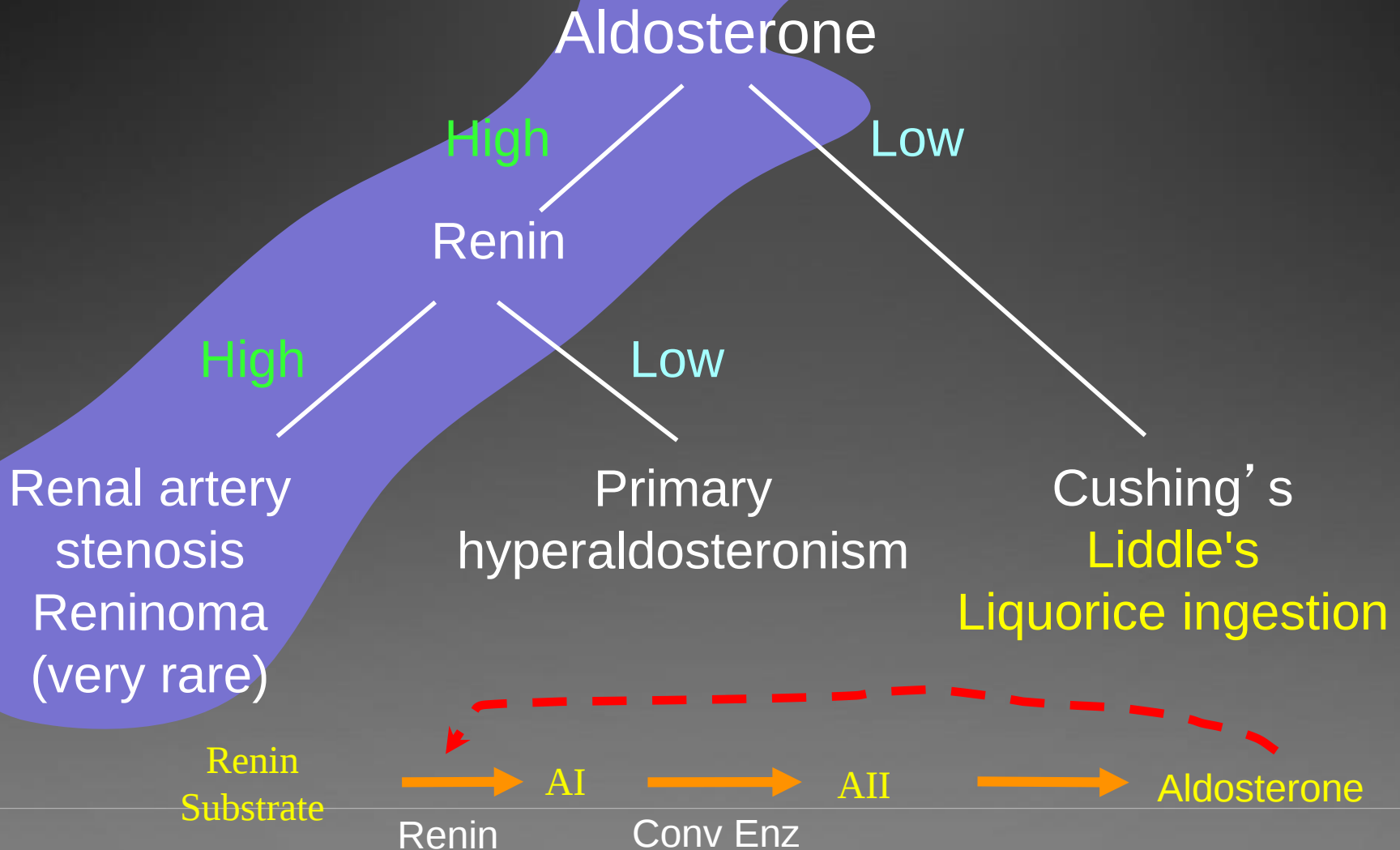
Serum sodium	136 mEq/L	
Serum potassium	3.0 mEq/L	
Serum chloride	101 mEq/L	
Serum bicarbonate	26 mEq/L	
Blood urea nitrogen	18 mg/dL	
Serum creatinine	2.0 mg/dL	
Plasma renin activity	8.5 ng/mL/hr	(Normal range 1-6)
Plasma aldosterone	24 ng/dl	(Normal range 5-20)

Case 7

Which of the following tests would be the most appropriate next step?

- (A) Computed tomography scan of the adrenal glands
- (B) Dexamethasone suppression test
- (C) Urine diuretic screen
- ☒ (D) Doppler ultrasound of the renal arteries

Hypokalemia/Renal K⁺ wasting & hypertension



Case 7

Which of the following tests would be the most appropriate next step?

- (A) Computed tomography scan of the adrenal glands; hyperaldo causes HTN and low K but renin should be suppressed
- (B) Dexamethasone suppression test; Rule out Cushing's but aldo usually normal/low
- (C) Urine diuretic screen; not typical scenario/ taking diuretic
- ☒ (D) Doppler ultrasound of the renal arteries

Case 8

A 28 year-old man is found unconscious in the street and brought into the emergency room. No medical history is available. His blood pressure is 120/75 mm Hg, respiratory rate 12 per minute. He appears dishevelled and is comatose and responsive only to pain. His pupils are reactive to light and he has a non-focal neurological examination. No fetor is noted. He is intubated, undergoes gastric lavage, and activated charcoal is administered via a nasogastric tube.

Serum sodium	132 mEq/L
Serum potassium	3.5 mEq/L
Serum chloride	98 mEq/L
Serum bicarbonate	10 mEq/L
Blood urea nitrogen	32 mg/dL
Serum creatinine	1.6 mg/dL
Serum glucose	75 mg/dL

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Case 8

Serum ethanol	None detected
Acetest	Negative
Serum β -hydroxybutyrate	Negative
Serum lactate	< 1 mmol/L
Serum salicylate	None detected
Serum creatine kinase	10 mU/mL
Serum osmolality	308 mOsm/kg

Arterial blood studies on room air:

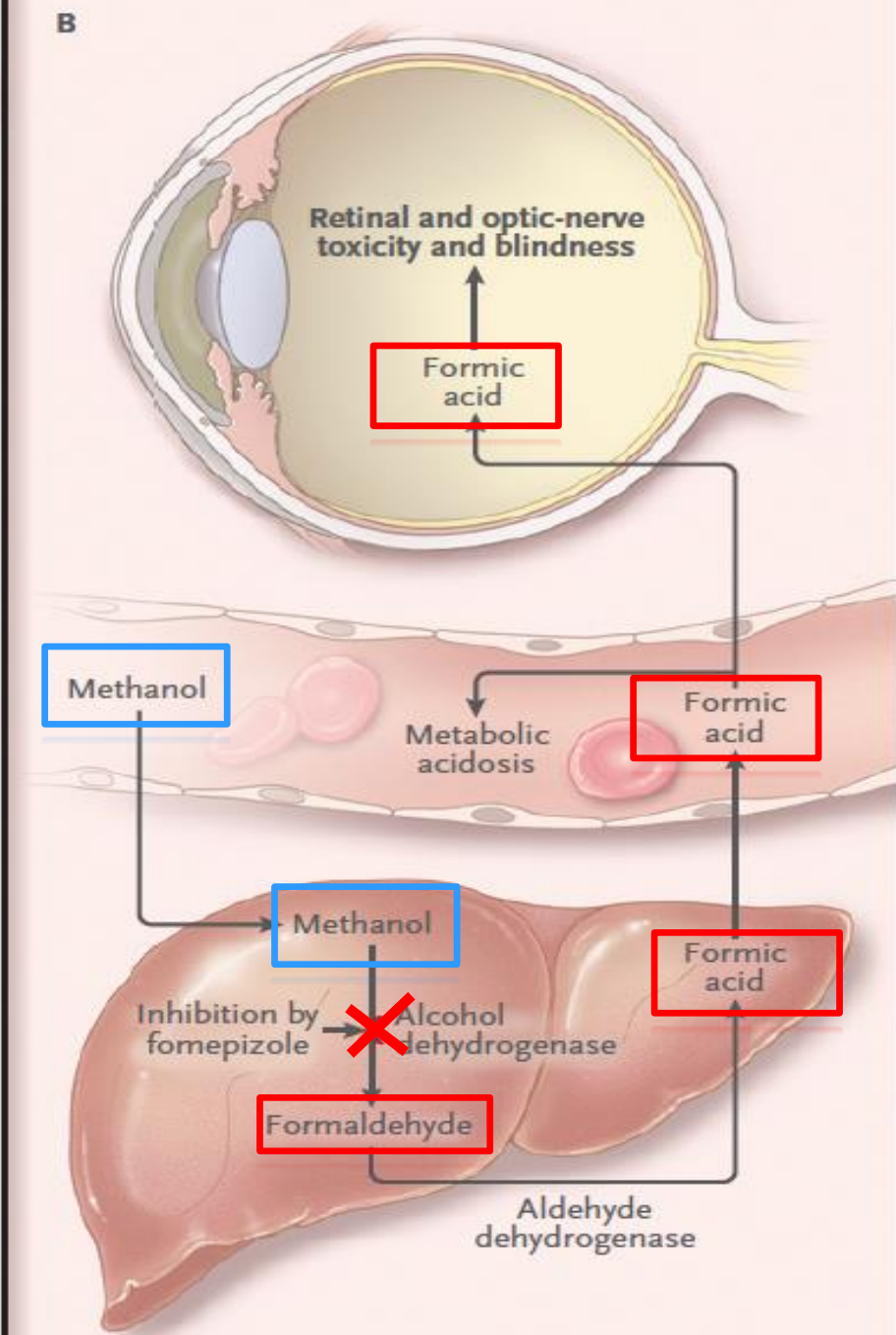
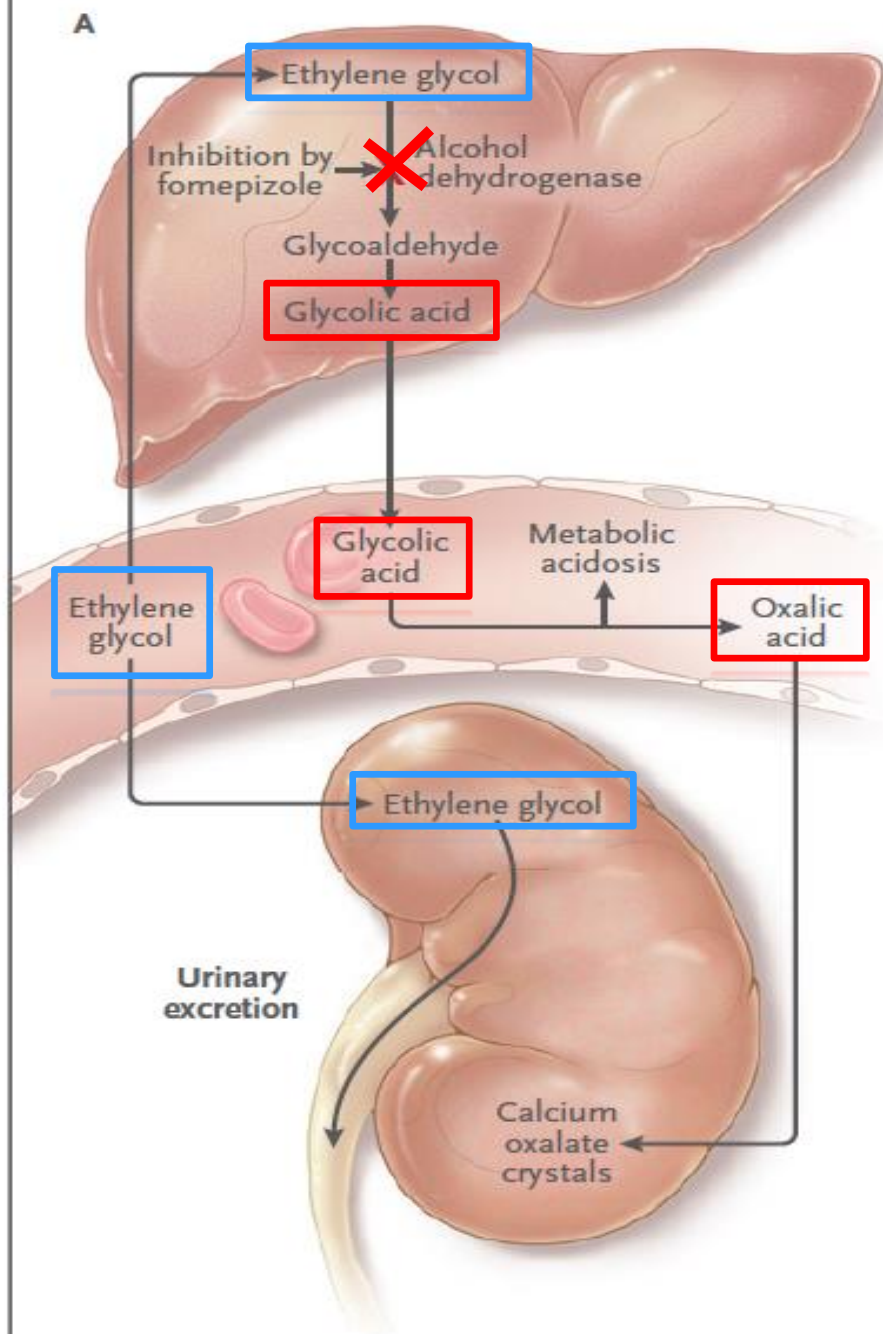
pH	7.22
PCO ₂	24 mm Hg

Case 8

The most appropriate *next* step in the management of this patient is:

- (A) Dopamine
- (B) Hemodialysis
- (C) Forced alkaline diuresis
- (D) Thiamine
- ☒ (E) Fomepizole

Blocks alcohol dehydrogenase
which normally converts ethylene
glycol to glycolic acid and
methanol to formic acid



Case 8

pH 7.22, PCO_2 24 mm Hg, HCO_3^- 10 mEq/L

Primary metabolic acidosis

Predicted PCO_2 from Winter's formula = $(1.5 \times \{\text{HCO}_3^-\}) + 8$
= 23

Respiratory compensation is appropriate

Na 132 mEq/L, Cl 98 mEq/L

Anion gap = $132 - 98 - 10 = 24$ (normal 8-12)

Anion gap metabolic acidosis

$$\Delta\text{AG} = 24 - 10 = 14$$

$$\Delta\text{HCO}_3^- = 24 - 10 = 14$$

$$\Delta/\Delta = 14/14 = 1$$

Pure anion gap metabolic acidosis

Serum osmolal gap

$$\text{Osmolal gap} = \text{Measured } S_{\text{osm}} - \text{Calc } S_{\text{osm}}$$

Calculated S_{osm} :

$$2 [\text{Na}^+] + [\text{glucose}]/18 + [\text{BUN}]/2.8$$

$$(2 \times 132) + (75/18) + (32/2.8) = 280$$

$$\text{Osmolal gap} = 308 - 280 = 28 \text{ (normal } < 10)$$

Anion and osmolar gap in diagnosis of intoxications

Anion gap acidosis	Osmolal gap	
+	Normal	Salicylates
+	High	Ethanol Ethylene glycol Propylene glycol Methanol
-	High	Isopropanol

Clues to high anion gap acidosis syndromes

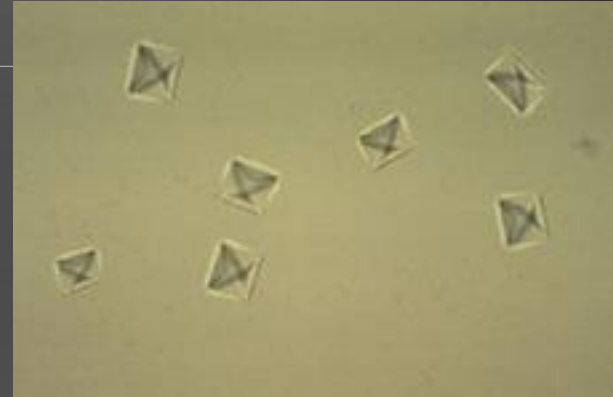
- Alcoholic fetor
- Papilledema
- Osmolar gap
- Undetectable serum ethanol

Methanol intoxication



Clues to high anion gap acidosis syndromes

- No fetor
- Osmolar gap
- Calcium oxalate dihydrate (envelope-shaped) crystalluria
- Urine fluoresces under Wood's (UV) lamp



Ethylene glycol intoxication

Case 8

The most appropriate *next* step in the management of this patient is:

- (A) Dopamine; not indicated
- (B) Hemodialysis; likely will be needed; takes time to initiate
- (C) Forced alkaline diuresis; indicated for salicylates; no utility for alcohol toxicities
- (D) Thiamine; Vitamin B1; deficient in alcoholics
- ☒ (E) Fomepizole; inhibits alcohol dehydrogenase to reduce toxic products

Take Home Messages

- Hypo- and Hyper-Natremia are usually *water imbalances*;
 - Volume depletion (Na loss) stimulates RAS
 - Water depletion (hypersomolality) stimulates ADH
 - Potassium Disorders
 - Most K is intracellular (intake/cellular shift)
 - Renal K excretion is regulated by GFR; Aldo and UNa
 - Calculate Osmolar Gap and AG in Acidosis
-

Suggested reading

- Rennke, H.G., Denker, B.M., **Renal Pathophysiology – The Essentials**, 5th Edition, Lippincott Williams & Wilkins, 2020
- Mount, D.B., **Fluid and Electrolyte Disturbances**. In Harrison's Principles of Internal Medicine, 18th Edition, Eds. Longo, Fauci, *et al.*, McGraw-Hill, p. 341-359
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