

ELECTROLYTE AND ACID BASE: Challenging Questions and Answers Part 2 (Questions 9-24)

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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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No conflict of interest to disclose.

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
 3. Acid/Base-interpret labs; identify compensation; assess for additional disorders
-

Case 9

An 18 year-old female is brought in with change in mental status and suspected toxic ingestion. Her blood pressure is 100/73 mm Hg, pulse rate 89, respiratory rate 40, temperature 100.5° C. She vomited once in the emergency room and is poorly responsive.

Laboratory studies:

Serum sodium	142 mEq/L
Serum potassium	3.6 mEq/L
Serum chloride	102 mEq/L
Serum bicarbonate	16 mEq/L
Blood urea nitrogen	21 mg/dL
Serum creatinine	1.8 mg/dL
Serum glucose	62 mg/dL

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Case 9

Acetest	Negative
Serum lactate	1.8 mmol/L
Serum osmolality	295 mOsm/kg

Arterial blood studies on room air:

pH	7.39
PCO ₂	25 mm Hg

Case 9

Which of the following treatments would be most likely to be effective in the management of this patient?

- (A) Breathe into a bag
- (B) Insulin drip
- ☒ (C) Forced alkaline diuresis
- (D) 5% dextrose
- (E) Fomepizole

Clues to high anion gap acidosis syndromes

- Tinnitus/deafness
- Fever, tachycardia, hyperventilation
- Associated respiratory alkalosis and metabolic acidosis

Salicylate intoxication

Case 9

pH 7.39, PCO_2 25 mm Hg, HCO_3 16 mEq/L

Primary metabolic acidosis, & probably respiratory alkalosis

Predicted PCO_2 from Winter's formula = $(1.5 \times 16) + 8 = 32$

Concomitant respiratory alkalosis

Na 142 mEq/L, Cl 102 mEq/L

Anion gap = $142 - 102 - 16 = 24$ (normal 8-12)

Anion gap metabolic acidosis

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

$$\Delta\text{HCO}_3 = 24 - 16 = 8$$

$$\Delta/\Delta = 14/8 = 1.8$$

Vomiting induced metabolic alkalosis: bicarb higher than expected for degree of elevation of AG

Serum osmolal gap=0

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

Calculated S_{osm} :

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

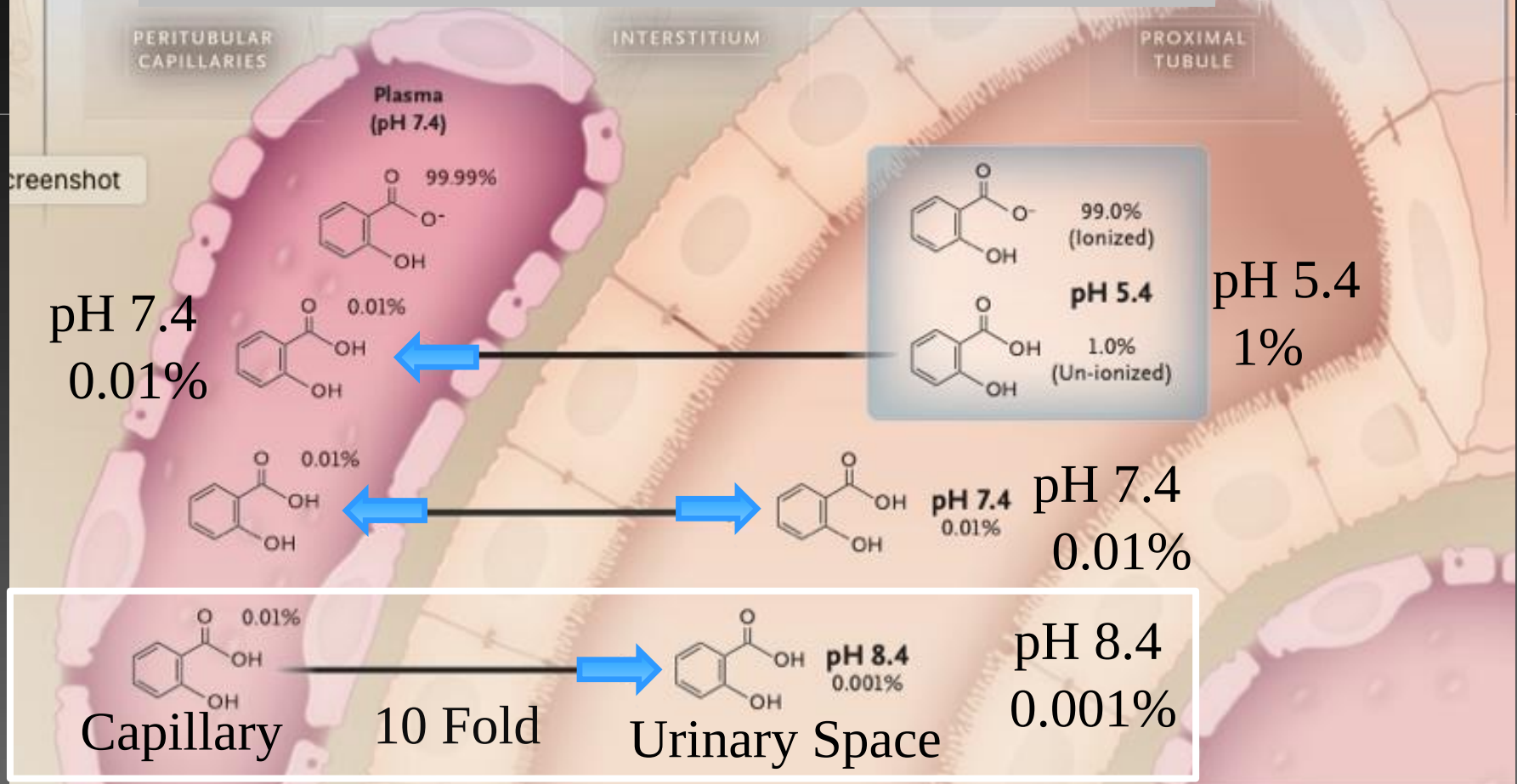
$$(2 \times 142) + (62/18) + (21/2.8) = 295$$

$$\text{Osmolal gap} = 295 - 295 = 0$$

Anion and osmolar gap in diagnosis of intoxications

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

Urine Alk Leads to Favorable HS gradient in Urinary Space



Ions not able to cross membranes; HS diffuses.

Increasing pH leads to *less* HS in tubular lumen which creates favorable gradient for diffusion out of tissue/plasma in urinary space.

(modified from Palmer; N Engl J Med 2020;382:2544-55. DOI: 10.1056/NEJMr2010852)

Case 9

Which of the following treatments would be most likely to be effective in the management of this patient?

- (A) Breathe into a bag; increasing PCO₂ will worsen acidosis
- (B) Insulin drip; used for DKA
- ☒ (C) Forced alkaline diuresis
- (D) 5% dextrose; no benefit
- (E) Fomepizole; inhibits alcohol dehydrogenase

Case 10

A 35 year-old male with HIV infection is maintained on HAART therapy, with his most recent regimen being raltegravir (INSTI), tenofovir (NRTI) and emtricitabine (NRTI). He has been doing well, but on a routine clinic visit was found to have abnormal chemistries.

Serum sodium	135 mEq/L		
Serum potassium	2.8 mEq/L	Serum glucose	91 mg/dL
Serum chloride	109 mEq/L	Serum calcium	8.8 mg/dL
Serum bicarbonate	18 mEq/L	Serum phosphate	1.8 mg/dL
Blood urea nitrogen	13 mg/dL		
Serum creatinine	1.7 mg/dL		

Urinalysis: Specific gravity 1.015, pH 6, trace protein, 3+ glucose, no blood, leukocyte esterase negative

Case 10

Which of the following would be the most appropriate next step in the management of this patient?

- (A) Stool microbiology and colonoscopy
- ☒ (B) Discontinue tenofovir
- (C) Discontinue raltegravir
- (D) Send autoantibody panel
- (E) Magnetic resonance imaging of the adrenal glands

Case 10

HCO_3^- 18 mEq/L, no ABG

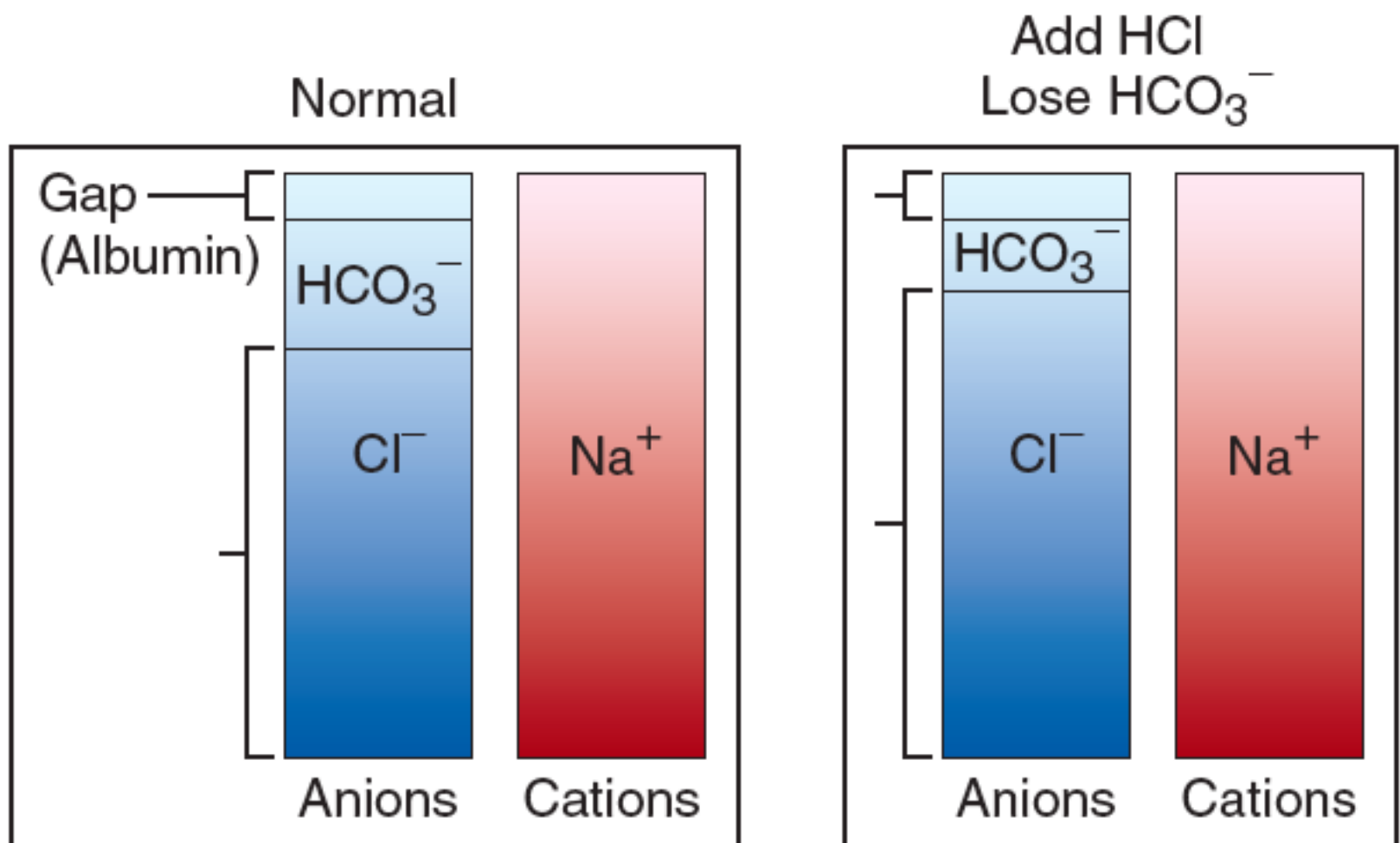
Probable metabolic acidosis

Na 135 mEq/L, Cl 109 mEq/L

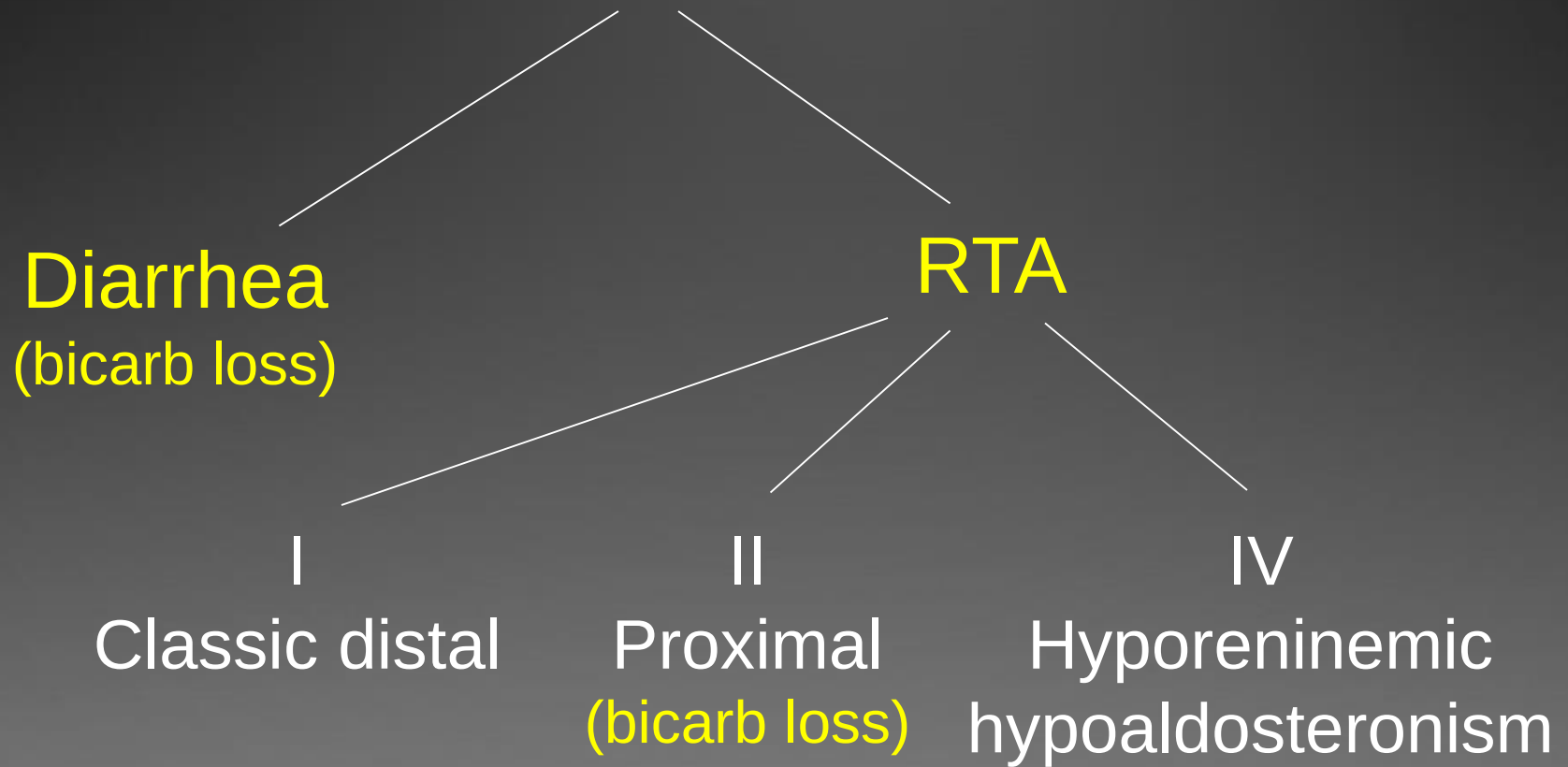
Anion gap = $135 - 109 - 18 = 8$ (normal 8-12)

Non-gap metabolic acidosis

DDx of a non-gap metabolic acidosis



DDx of a non-gap metabolic acidosis



Case 10

HCO_3^- 18 mEq/L, no ABG

Probable metabolic acidosis

Na 135 mEq/L, Cl 109 mEq/L

Anion gap = $135 - 109 - 18 = 8$ (normal 8-12)

Non-gap metabolic acidosis

Urine pH 6 is inappropriately high

Renal tubular acidosis, Type I or II

Hypokalemia, hypophosphatemia, glycosuria with normoglycemia

Fanconi syndrome, most likely with Type II (proximal) RTA

DDx of RTA

	Proximal	Classic distal	Hyporenin hypoaldo
Serum K	Low	Low	High
Urine pH	Variable	> 5.5	< 5.5
Other features	Fanconi (low PO ₄ , glycosuria)	Nephrocalcinosis ± CaPO ₄ stones	

Causes and Rx of RTA

	Proximal	Classic distal	Hyporenin hypoaldo
Common causes	Ifosfamide NRTI (tenofovir, adefovir, cidofovir) Myeloma	Sjogren's SLE Amphotericin	CKD plus: DbM Obstruction Sickle cell dz SLE NSAIDs
Rx	Bicarbonate (lots) -tenofovir disoproxil fumarate (TDF); newer alafenamide (TAF) is effective at 1/30 th dose so less renal toxicity anticipated/seen to date	Bicarbonate (1 mEq/kg/day)	K ⁺ lowering Rx: Diuretics Kayexalate Low K diet Mineralocorticoid

Case 10

Which of the following would be the most appropriate next step in the management of this patient?

- (A) Stool microbiology and colonoscopy; diarrhea leads to non-gap acidosis but intact renal acidification (urine pH-6)
- ☒ (B) Discontinue tenofovir
- (C) Discontinue raltegravir; not associated with RTA
- (D) Send autoantibody panel; consider for distal RTA and Sjogren's syndrome
- (E) Magnetic resonance imaging of the adrenal glands; hyperaldo should cause HTN

Case 11

A 47 year-old female with known peptic ulcer disease presents with a 3 day history of epigastric pain, profuse vomiting and inability to tolerate oral fluids. On examination, she is in moderate pain. Blood pressure is 88/42, pulse rate 97, and mucous membranes are dry.

Serum sodium	124 mEq/L
Serum potassium	3.0 mEq/L
Serum chloride	65 mEq/L
Serum bicarbonate	40 mEq/L
Blood urea nitrogen	56 mg/dL
Serum creatinine	2.1 mg/dL
Serum lactate	8.3 mmol/L

Arterial blood studies on room air:

pH 7.65	PCO ₂ 38 mm Hg
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Case 11

Which of the following best describes the acid-base disorder in this patient?

- (A) Metabolic alkalosis and respiratory acidosis
- (B) Metabolic alkalosis and respiratory alkalosis
- (C) Metabolic alkalosis, respiratory acidosis and respiratory alkalosis
- ☒ (D) Metabolic alkalosis, respiratory alkalosis and metabolic acidosis
- (E) None of the above

Case 11

pH 7.65, PCO_2 38 mm Hg, HCO_3 40 mEq/L

Metabolic Alkalosis

Case 11

pH 7.65, PCO_2 38 mm Hg, HCO_3 40 mEq/L

Metabolic Alkalosis

$\uparrow \text{PCO}_2$ - 0.6-0.7mm/1Meq change in bicarb or
 $16(0.6)=9.6$ so predicted $\text{PCO}_2 \sim 50\text{mmHg}$

Lack of respiratory compensation indicates

Respiratory Alkalosis

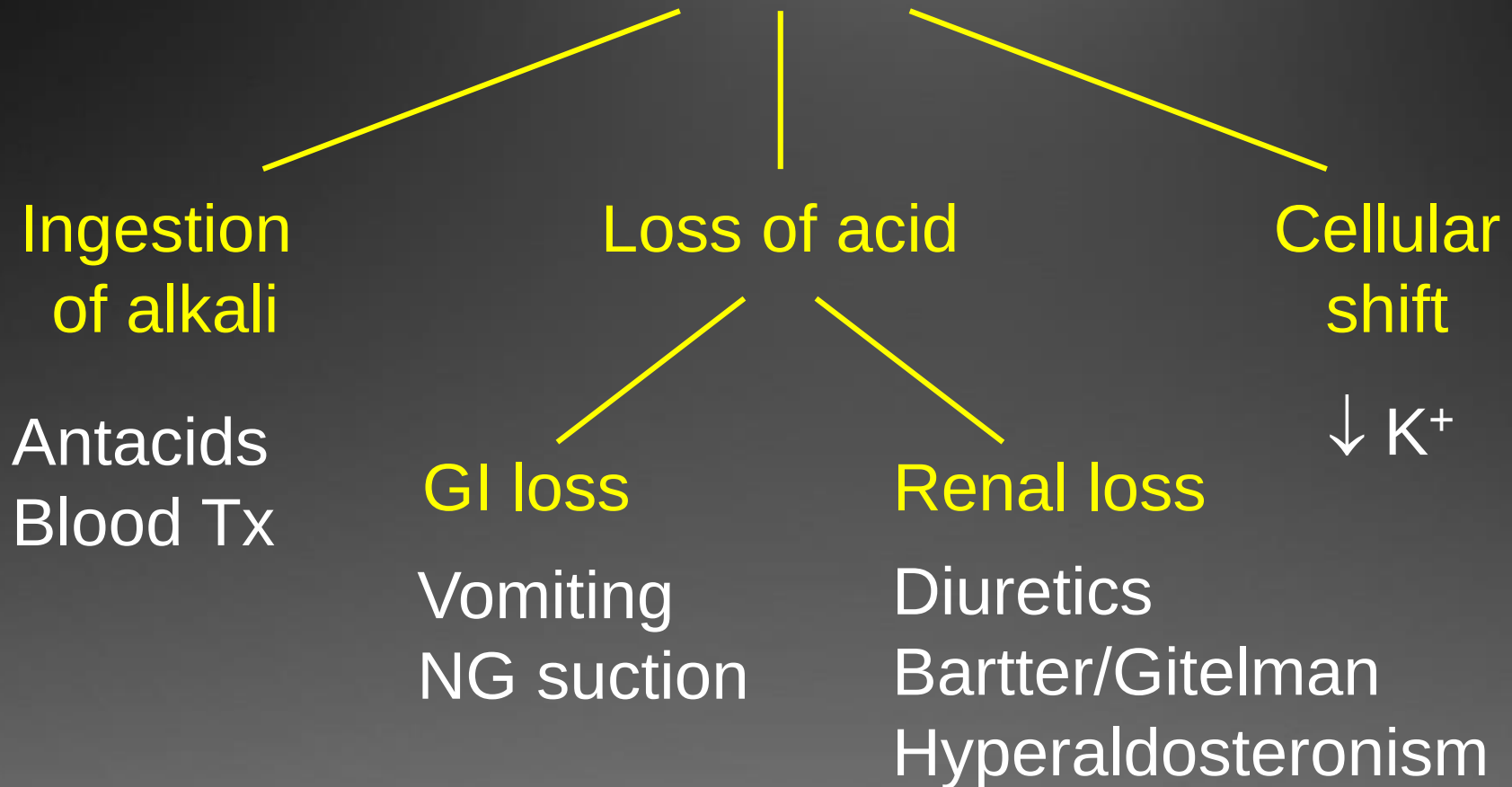
Na 124 mEq/L, Cl 65 mEq/L

Anion gap = $124 - 65 - 40 = 19$ (normal 8-12)

Lactate level = 8.3 mmol/L

Superimposed **anion gap Metabolic Acidosis** (lactic acidosis)

Induction of metabolic alkalosis



Case 11

Which of the following best describes the acid-base disorder in this patient?

- (A) Metabolic alkalosis and respiratory acidosis
- (B) Metabolic alkalosis and respiratory alkalosis
- (C) Metabolic alkalosis, respiratory acidosis and respiratory alkalosis
- ☒ (D) Metabolic alkalosis, respiratory alkalosis and metabolic acidosis
- (E) None of the above

Case 12

22 year-old male with no past medical history presents with confusion. His serum sodium is 106 mEq/L, serum osmolality 240 mOsm/kg, urine sodium 45 mEq/L and urine osmolality 40 mOsm/kg.

Select the best option (A-E) for treatment of the serum sodium.

- (A) 0.9% NaCl
- (B) 3% NaCl
- ☒ (C) Free water restriction
- (D) Hydrocortisone
- (E) No treatment

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 13

52 year-old female with chronic obstructive pulmonary disease and 2 month history of worsening dyspnea presents with a seizure. On examination she appears confused. BP 125/90, HR 74, mucous membranes moist, no peripheral edema. Her serum sodium is 110 mEq/L, serum osmolality 251 mOsm/kg, urine sodium 150 mEq/L and urine osmolality 710 mOsm/kg.

Select the best option (A-E) for treatment of the serum sodium.

- (A) 0.9% NaCl
- ☒ (B) 3% NaCl
- (C) Free water restriction
- (D) Hydrocortisone
- (E) No treatment

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

Rate of correction of hyponatremia

- Acute (< 48 hr, usually due to hypotonic fluid intake) or *severely symptomatic (seizures)*
 - 100 mL of 3% saline bolus to increase S_{Na} by 2-3 mEq/L
 - Chronic (> 48 hr) including SIADH and asymptomatic
 - 0.5 mEq/l per hour
 - Do not exceed $\Delta 8-10$ mEq/L in 1st day
-

Case 14

67 year-old male with fatigue and low back pain. Serum values were: sodium 124 mEq/L, glucose 76 mg/dL, total protein 13 g/dL, albumin 3.6 g/dL, hemoglobin 9 g/dL.

Select the best option (A-E) for treatment of the serum sodium.

- (A) 0.9% NaCl
- (B) 3% NaCl
- (C) Free water restriction
- (D) Hydrocortisone
- ☒ (E) No treatment

Hyponatremia

P_{osm}

$> 290 \text{ mOsm/kg}$

$\uparrow$ Glucose*
Mannitol

Normal
“Pseudohyponatremia”

Lipid $\uparrow$
Protein $\uparrow$

$< 275 \text{ mOsm/kg}$

Hypoosmolar
hyponatremia*

**Requires ADH+
Water Intake*

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

Case 15

45 year-old male with diabetes mellitus, hypertension and ischemic cardiomyopathy maintained on aspirin, carvedilol, captopril, glipizide and furosemide. On examination, BP is 135/94, HR 80, mucous membranes moist, jugular venous pulsations are visible to the angle of the jaw, and there is 3+ pitting edema of the legs and thighs. His serum sodium is 123 mEq/L, urine sodium 10 mEq/L and urine osmolality 570 mOsm/kg.

Select the best option (A-E) for treatment of the serum sodium.

- (A) 0.9% NaCl
- (B) 3% NaCl
- ☒ (C) Free water restriction
- (D) Hydrocortisone
- (E) No treatment

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

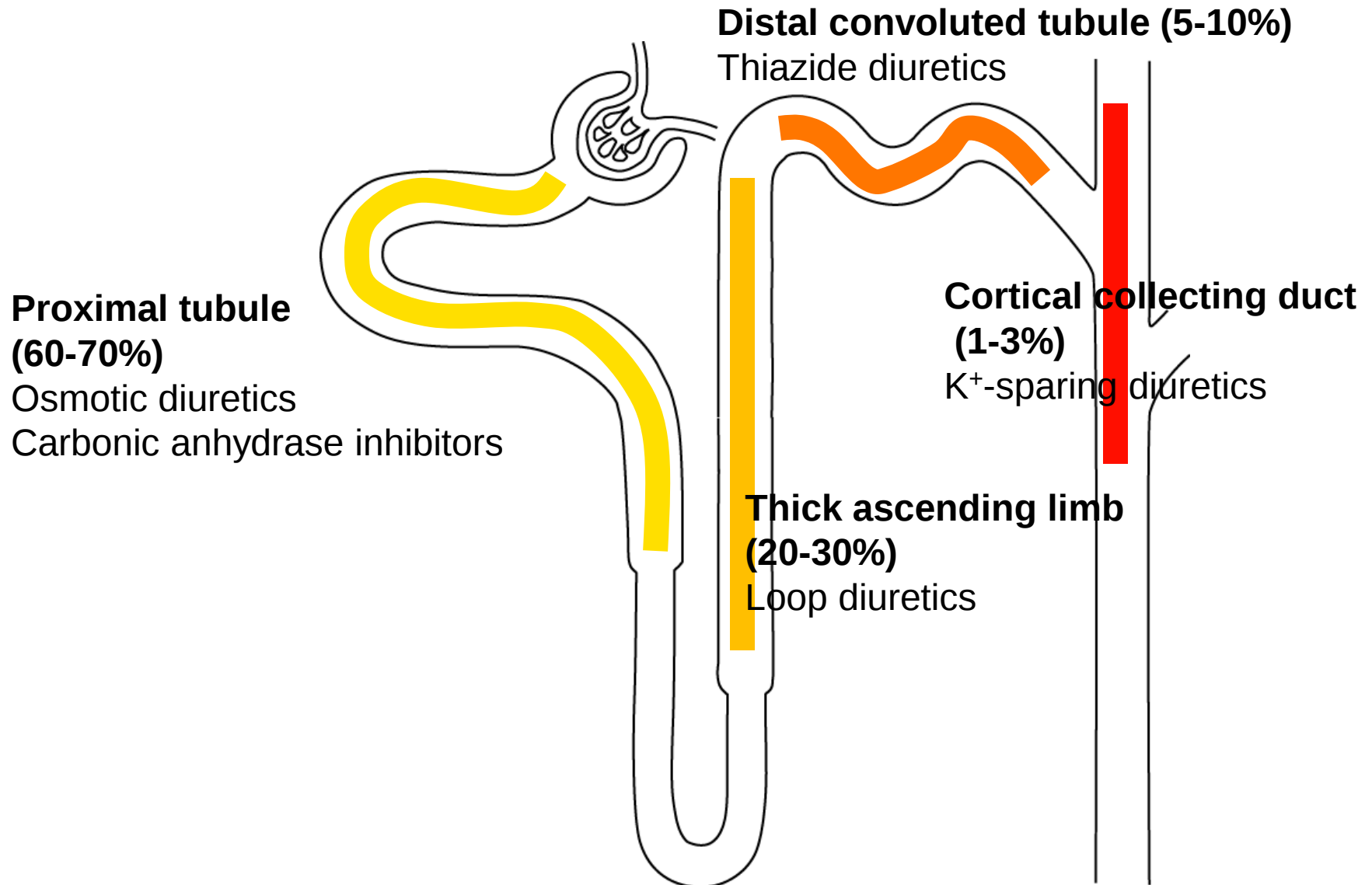
Case 16

43-year-old man with Type II diabetes mellitus, hypertension, congestive cardiac failure, nephrotic-range proteinuria, peripheral edema and a serum creatinine of 1.6 mg/dl. His serum potassium has been in the range of 5.3-5.6 mEq/L since starting captopril, despite adhering to a potassium-restricted diet.

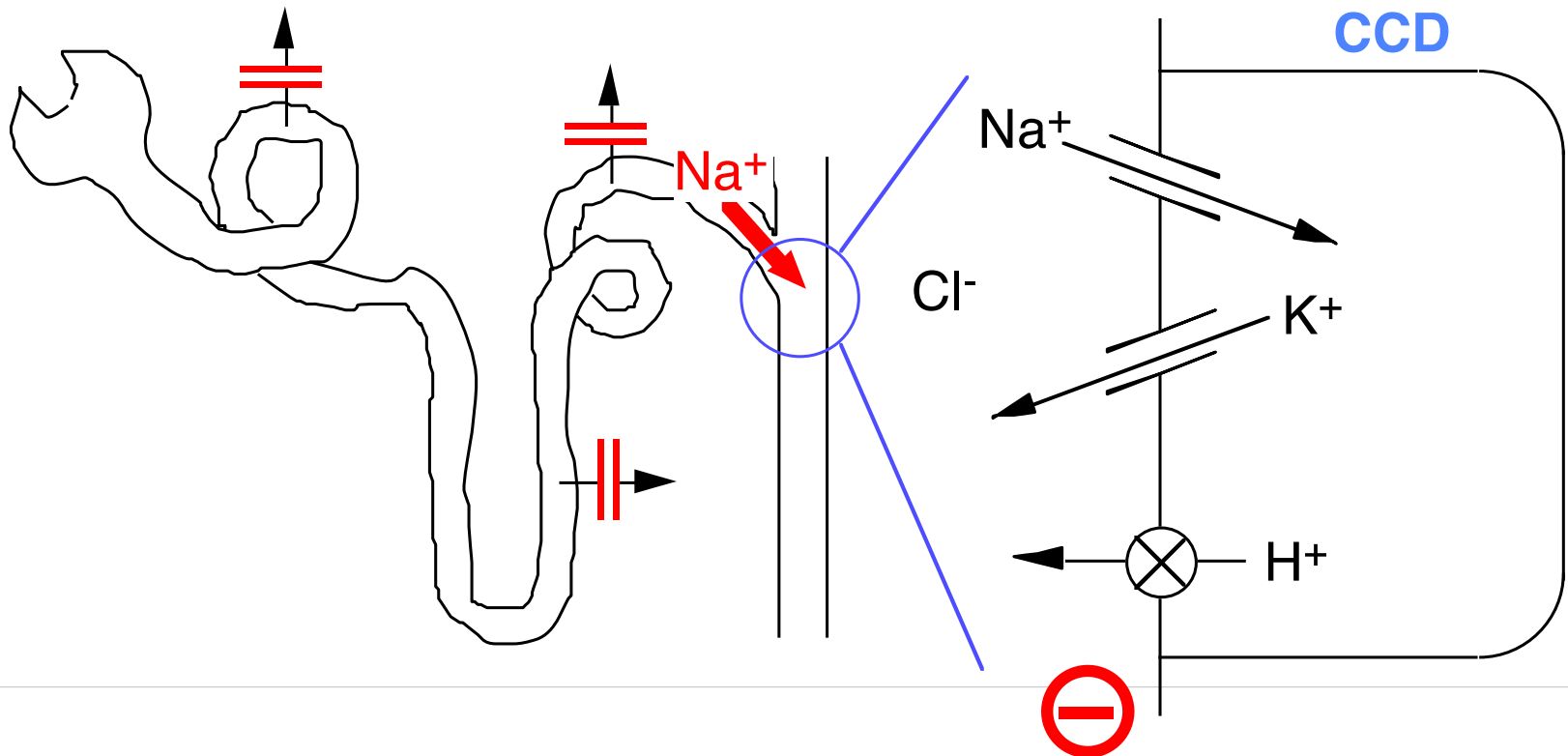
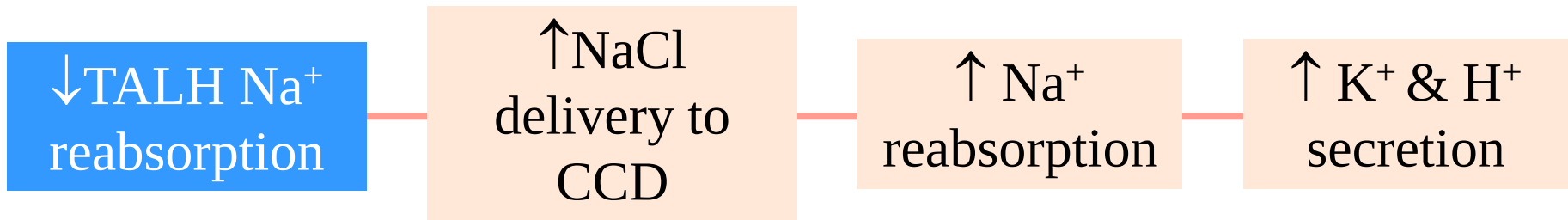
Select the best option (A-E) for treatment of the serum potassium.

- (A) Thiazide diuretic
- (B) Hydrocortisone
- (C) Insulin
- (D) Hemodialysis
- (E) Sodium polystyrene sulfonate

Sites of action of natriuretics



Loop and thiazide diuretics cause K^+ wasting and alkalosis



Case 17

88-year-old woman who had partial sigmoid colectomy for perforated diverticular abscess and septicemia two days previously, and has been anuric since the operation. Her serum potassium is 6.5 mg/dL but there are no electrocardiographic changes.

Select the best option (A-E) for treatment of their serum potassium.

- (A) Thiazide diuretic
- (B) Hydrocortisone
- (C) Insulin
- ☒ (D) Hemodialysis
- (E) Sodium polystyrene sulfonate

Hyperkalemia

```
graph TD; H[Hyperkalemia] --- I[↑ Intake]; H --- D[Decreased urinary K+ excretion]; H --- C[Cell shift]; I --- I1[↑ Intake]; D --- D1[Decreased urinary K+ excretion]; D --- D2[24 hr urine K+ < 40 mEq]; C --- C1[Cell shift]; C --- C2[Metabolic acidosis]; C --- C3[Hyperglycemia]; C --- C4[β-blocker]; C --- C5[Digitalis]; C --- C6[Hyperkalemic periodic paralysis]; C --- C7[Cell lysis];
```

↑ 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

↓GFR

Renal
failure

↓CCD [K^+]

Meds

Block
RAAS

NSAIDs
ACEI/ARB
Heparin
Spironolactone
Cyclosporine

Block Na^+
channel

Amiloride
Trimethoprim
Pentamidine

Adrenal
insufficiency

Addison's

Hyporenin
hypoaldo

Treatment of hyperkalemia

- Stabilize membrane excitability
 - Calcium chloride or gluconate, 1 g IV
- Increase K^+ entry into cells
 - Glucose 25 g and insulin 10 U
 - β_2 -adrenergic agonist (albuterol 10-20 mg inh)
 - $NaHCO_3$
- Removal of excess K^+
 - Cation exchange resin (Kayexalate)
 - Diuretics
 - Dialysis
- Dietary K^+ restriction

Case 18

18-year-old man with no prior medical history who presents with one week of polyuria and polydipsia.

Labs:

Na 132, K 5.9, Cl 91, HCO₃ 16, BUN 30, Cr 1.2, glucose 330

Select the best option (A-E) for treatment of their serum potassium.

- (A) Thiazide diuretic
- (B) Hydrocortisone
- ☒ (C) Insulin
- (D) Hemodialysis
- (E) Sodium polystyrene sulfonate

Hyperkalemia

```
graph TD; H[Hyperkalemia] --- I[↑ Intake]; H --- D[Decreased urinary K+ excretion]; H --- L[Cell shift<br/>Metabolic acidosis<br/>Hyperglycemia<br/>β-blocker<br/>Digitalis<br/>Hyperkalemic periodic paralysis<br/>Cell lysis];
```

↑ Intake

Decreased urinary
 K^+ excretion

24 hr urine $K^+ < 40$ mEq

Cell shift
Metabolic acidosis
Hyperglycemia
 β -blocker
Digitalis
Hyperkalemic
periodic paralysis
Cell lysis

Case 19

26-year-old woman with acquired immune deficiency syndrome, fatigue, weight loss, low-grade fever, and orthostatic hypotension. Na-129; K-5.9

Serum cortisol level:

Baseline at 8 a.m. 7 $\mu\text{g/dL}$ (nl 5-24 $\mu\text{g/dL}$)

30 minutes after 250 μg cosyntropin i.m. 10 $\mu\text{g/dL}$

60 minutes after 250 μg cosyntropin i.m. 11 $\mu\text{g/dL}$

Select the best option (A-E) for treatment of their serum potassium.

- (A) Thiazide diuretic
- ☒ (B) Hydrocortisone
- (C) Insulin
- (D) Hemodialysis
- (E) Sodium polystyrene sulfonate

Decreased urinary K^+ excretion

↓GFR

Renal
failure

↓CCD [K^+]

Meds

Block
RAAS

NSAIDs
ACEI/ARB
Heparin
Spironolactone
Cyclosporine

Block Na^+
channel

Amiloride
Trimethoprim
Pentamidine

Adrenal
insufficiency
Addison's

Hyporenin
hypoaldo

Case 20

For the following cases of hypokalemic metabolic alkalosis, select the most likely cause (A-E):

16-year-old girl with amenorrhea, body mass index of 13, and a urine chloride concentration of 5 mEq/L.

- (A) Diuretic use
- ☒ (B) Surreptitious vomiting
- (C) Hypokalemic periodic paralysis
- (D) Gitelman's syndrome
- (E) Conn's syndrome

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	-

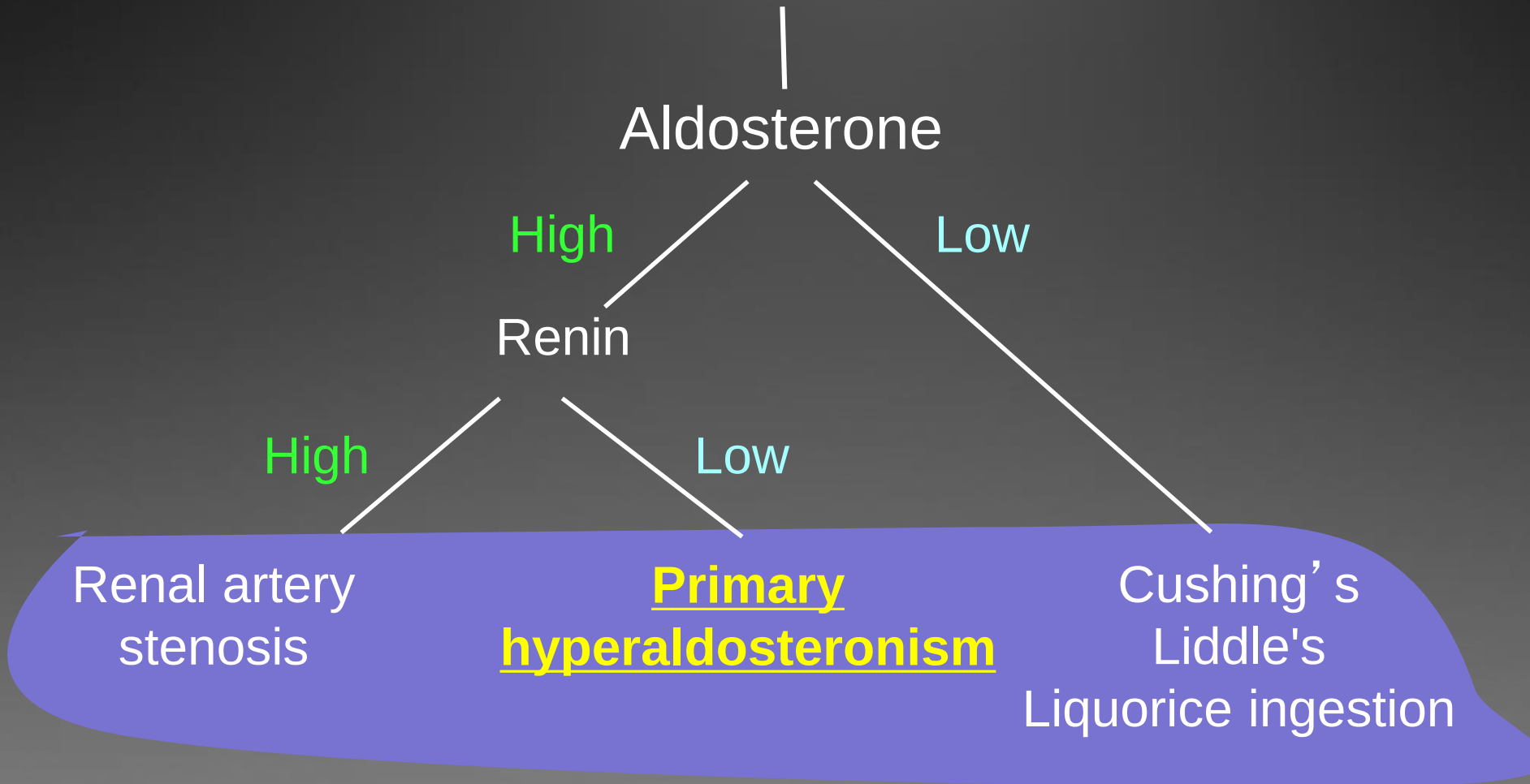
Case 21

For the following cases of *hypokalemic* metabolic alkalosis, select the most likely cause (A-E):

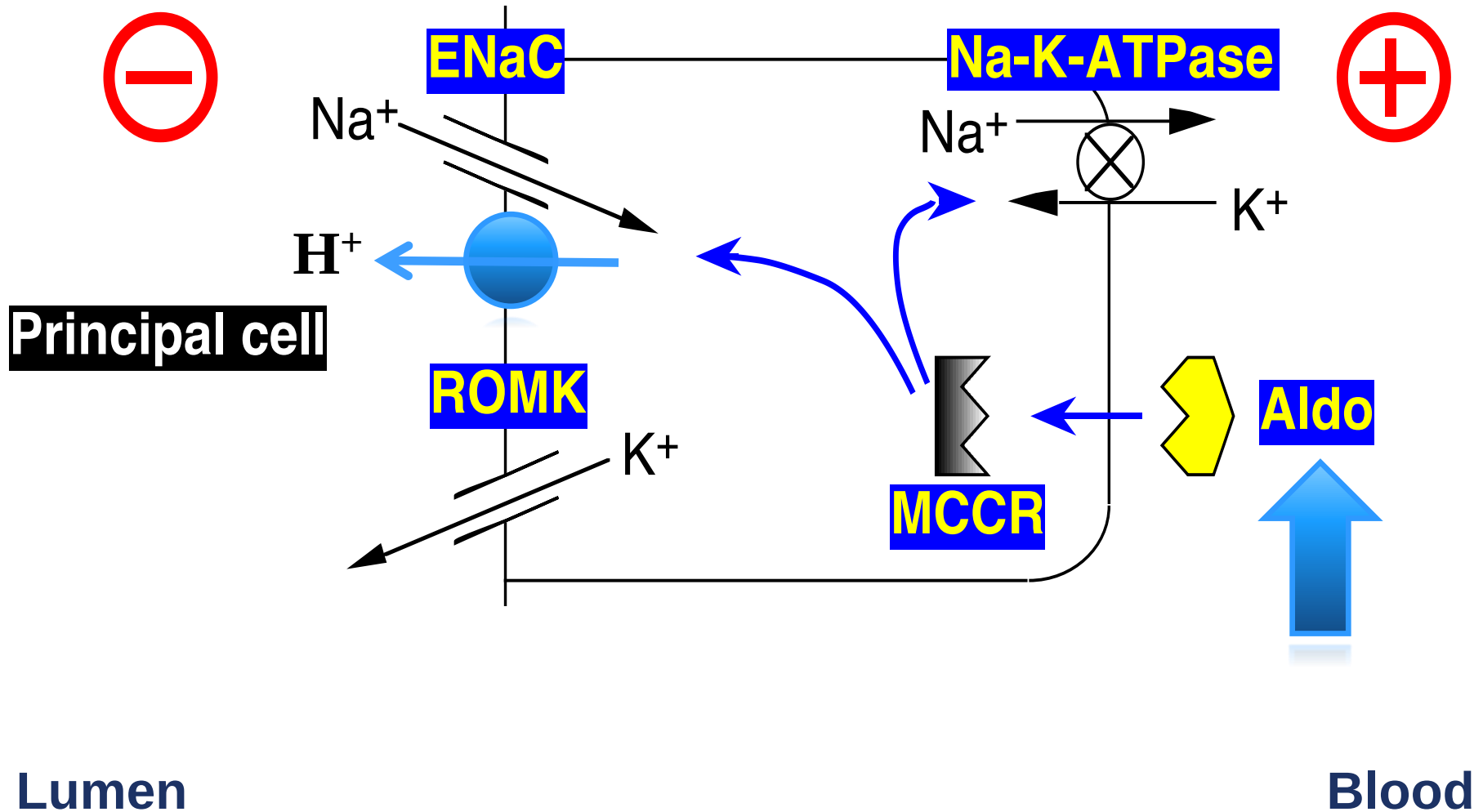
35-year-old man presenting for the first time with new-onset hypertension.

- (A) Diuretic use
- (B) Surreptitious vomiting
- (C) Hypokalemic periodic paralysis
- (D) Gitelman's syndrome
- ☒ (E) Conn's syndrome (hyperaldosteronism)

Hypokalemia/Renal K⁺ wasting & hypertension



Cortical Collecting Duct (CCD)



Case 22

For the following cases of hypokalemic metabolic alkalosis, select the most likely cause (A-E):

32-year-old woman with a history of bulimia. Random urine chloride concentrations on three separate clinic visits were 40, 67 and 26 mEq/L.

- (A) Diuretic use
- (B) Surreptitious vomiting
- (C) Hypokalemic periodic paralysis
- (D) Gitelman's syndrome
- (E) Conn's syndrome

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	-

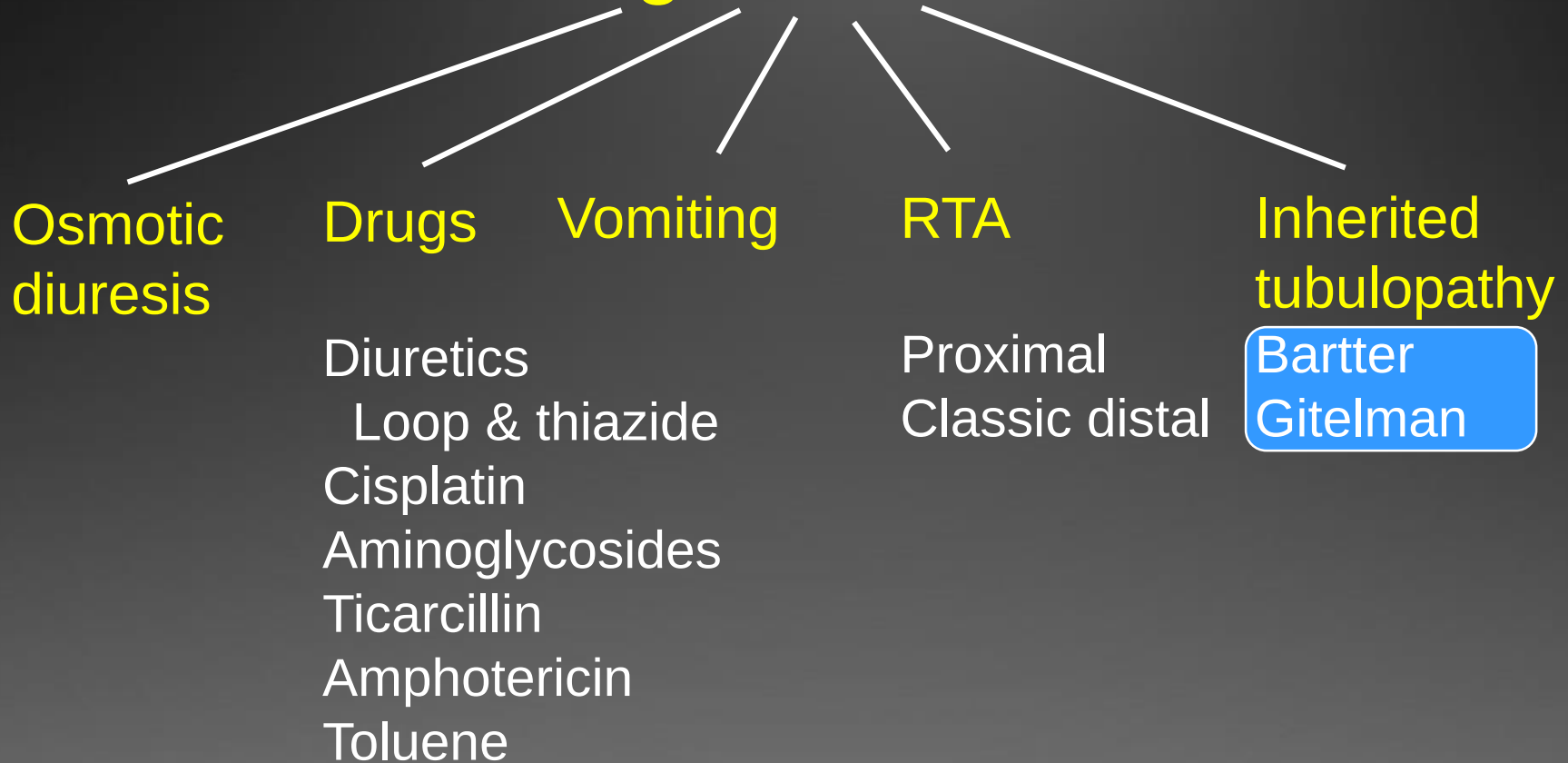
Case 23

For the following cases of hypokalemic metabolic alkalosis, select the most likely cause (A-E):

15-year-old girl with recurrent episodes of muscle weakness since childhood and a urine chloride concentration is 65 mEq/L and 24 hour urine K^+ is 60 mEq. Her brother has had similar symptoms.

- (A) Diuretic use
- (B) Surreptitious vomiting
- (C) Hypokalemic periodic paralysis
- ☒ (D) Gitelman's syndrome
- (E) Conn's syndrome

Renal K wasting with normal or low BP



How Can One Distinguish Bartter/Gitelman?

Urinary Calcium is Low with Na^+Cl^- Cotransporter Inhibition (Thiazides)

Case 24

For the following cases of hypokalemia, select the most likely cause (A-E):

20-year-old man with thyrotoxicosis and recurrent episodes of muscle weakness after meals.

- (A) Diuretic use
- (B) Surreptitious vomiting
- ☒ (C) Hypokalemic periodic paralysis
- (D) Gitelman's syndrome
- (E) Conn's syndrome

Features suggestive of hypokalemic periodic paralysis

- +FH or Asian male with thyrotoxicosis
- Precipitated by meal or exercise
- Repetitive episodes of acute profound hypokalemia
- Recovery of serum K^+ within hrs after each episode without repletion, either spontaneously or with propanolol
- Low urine K^+

Take Home Messages

- Hypo- and Hyper-Natremia are usually *water imbalances*;
 - Volume depletion (Na loss):RAS
 - Water depletion (hypersomolality):ADH
 - Exclude hypothyroid, adrenal insufficiency
- Potassium Disorders
 - Most K is intracellular (intake/cellular shift)
 - Renal K excretion is regulated by GFR; Aldo and UNa
- Identify Osmolar gap and AG vs Non-AG acidosis
- Compensation is in opposite direction and process but does not normalize pH

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
 - DuBose, T.D., Jr. **Acidosis and Alkalosis**. In Harrison's Principles of Internal Medicine, 18th Edition, Eds. Longo, Fauci, *et al.*, McGraw-Hill, p. 363-373
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