Electrolytes and Acid-Base Practice for the Boards I

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  - Clinical focus: Nephrology
  - Research focus: Kidney physiology, PKD

Disclosures

- I have no financial disclosures

Objectives

- Use ABIM-style MCQs to:
  - Review the diagnostic approach to common electrolyte disorders, including hypernatremia, hyponatremia and hypokalemia
  - Review the approach to management of common electrolyte disorders

A 35-year-old man with bipolar disorder, maintained on lithium for 10 years, is referred to you for chronic polyuria and polydipsia. He complains that he has to void once every hour.

Serum sodium	144 mEq/L
Blood urea nitrogen	35 mg/dL
Serum creatinine	1.9 mg/dL
Serum osmolality	292 mOsm/kg
24-hr urine volume	5 L
Urine sodium	28 mEq/L
Urine osmolality	190 mOsm/kg

Case 1

All of the following might be appropriate in the management of this patient EXCEPT:

(A) Thiazide diuretic

(B) Dietary salt reduction

(C) Discontinuation of lithium

(D) Fluid restriction

(E) Amiloride

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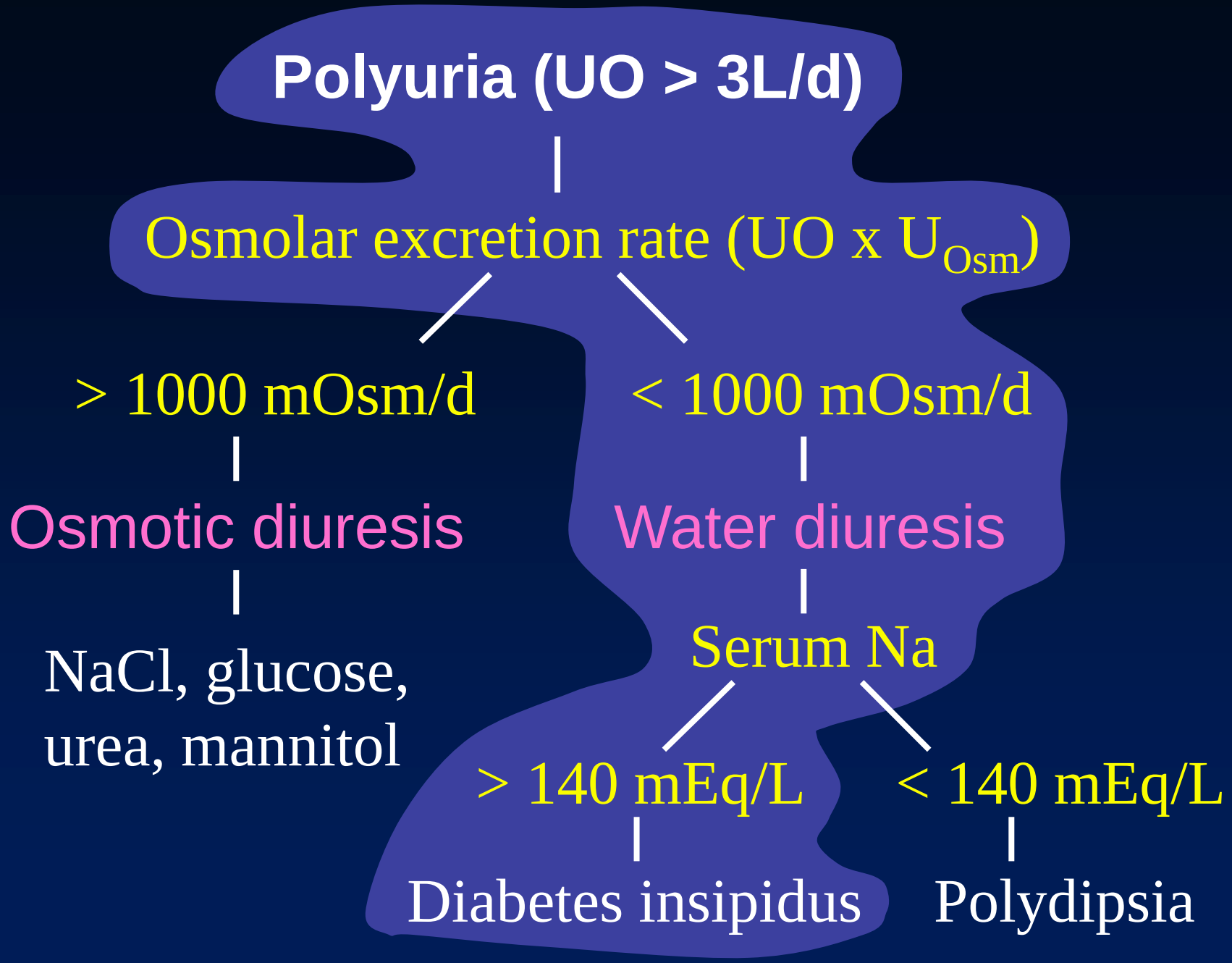
Polyuria (UO > 3L/d)
Osmolar excretion rate (UO x U_{Osm})
> 1000 mOsm/d
< 1000 mOsm/d
Osmotic diuresis
Water diuresis
NaCl, glucose, urea, mannitol
Serum Na
> 140 mEq/L
< 140 mEq/L
Diabetes insipidus
Polydipsia

Causes of nephrogenic DI

- Electrolyte disorders
  - Hypercalcemia
  - Hypokalemia
- Drugs
  - Lithium
  - Demeclocycline
  - Amphotericin B, cidofovir, tenofovir, foscarnet
  - Cisplatin, cyclophosphamide, ifosfamide
- Tubulointerstitial diseases
  - Obstructive uropathy
  - Sickle cell disease
  - Amyloidosis
  - Polycystic kidney disease
- Chronic kidney disease
- Genetic

Treatment of nephrogenic diabetes insipidus

- Treat the underlying cause, if possible
- Desmopressin (supraphysiological dose)
- Indomethacin, celecoxib
- Low salt diet, thiazide diuretic, amiloride
  - ↓Delivery of NaCl to IMCD

A 55 year-old man with colonic carcinoma undergoes resection of his tumor and diverting colostomy. Post-operatively he has prolonged ileus and is therefore started on intravenous total parenteral nutrition with 25 kCal/kg/day, and 1.6 g protein/kg/day. Four days later, a renal consult is called for hypernatremia. On examination, the patient is clinically euvolemic.

Serum sodium	151 mEq/L
Blood glucose	138 mg/dL
Blood urea nitrogen	33 mg/dL
Serum creatinine	0.9 mg/dL
Urine osmolality	480 mOsm/kg
Urine sodium	30 mEq/L
Urine volume (24 h)	3700 mL

Case 2

Which of the following is the MOST LIKELY cause of his hypernatremia?

(A) Central diabetes insipidus

(B) Nephrogenic diabetes insipidus

(C) Osmotic diarrhea

(D) Osmotic diuresis

(E) Excess intravenous saline

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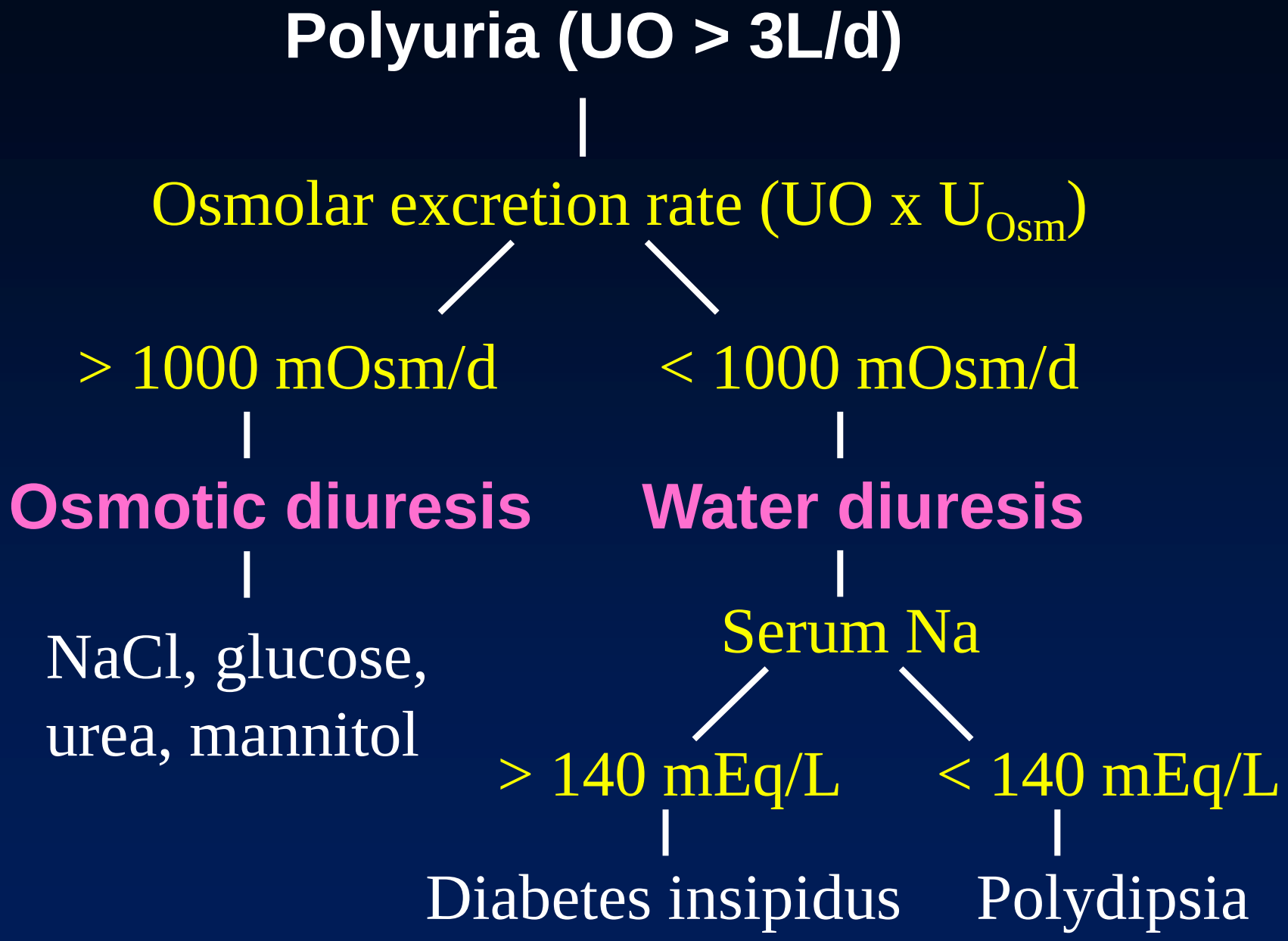
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> 1000 mOsm/d
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Water diuresis
NaCl, glucose, urea, mannitol
Serum Na
> 140 mEq/L
< 140 mEq/L
Diabetes insipidus
Polydipsia

Osmolar excretion rate

Osmolar excretion rate

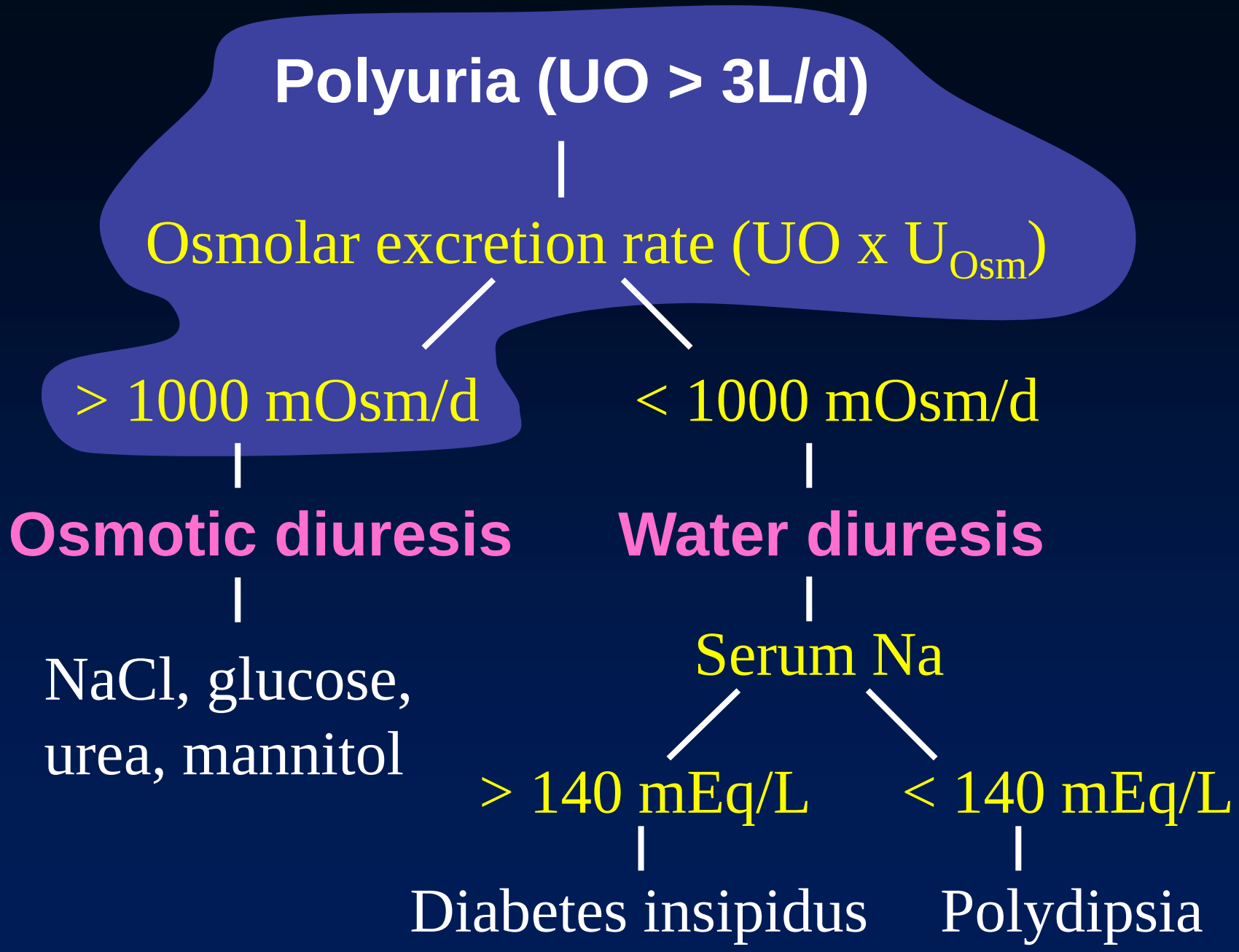
= Urine osmolality x Urine volume

(mOsm/kg) *(L/day)*

Normal 500-1000 mOsm per day

In this patient:

OER = 480 mOsm/kg x 3.7L/day = 1776 mOsm/day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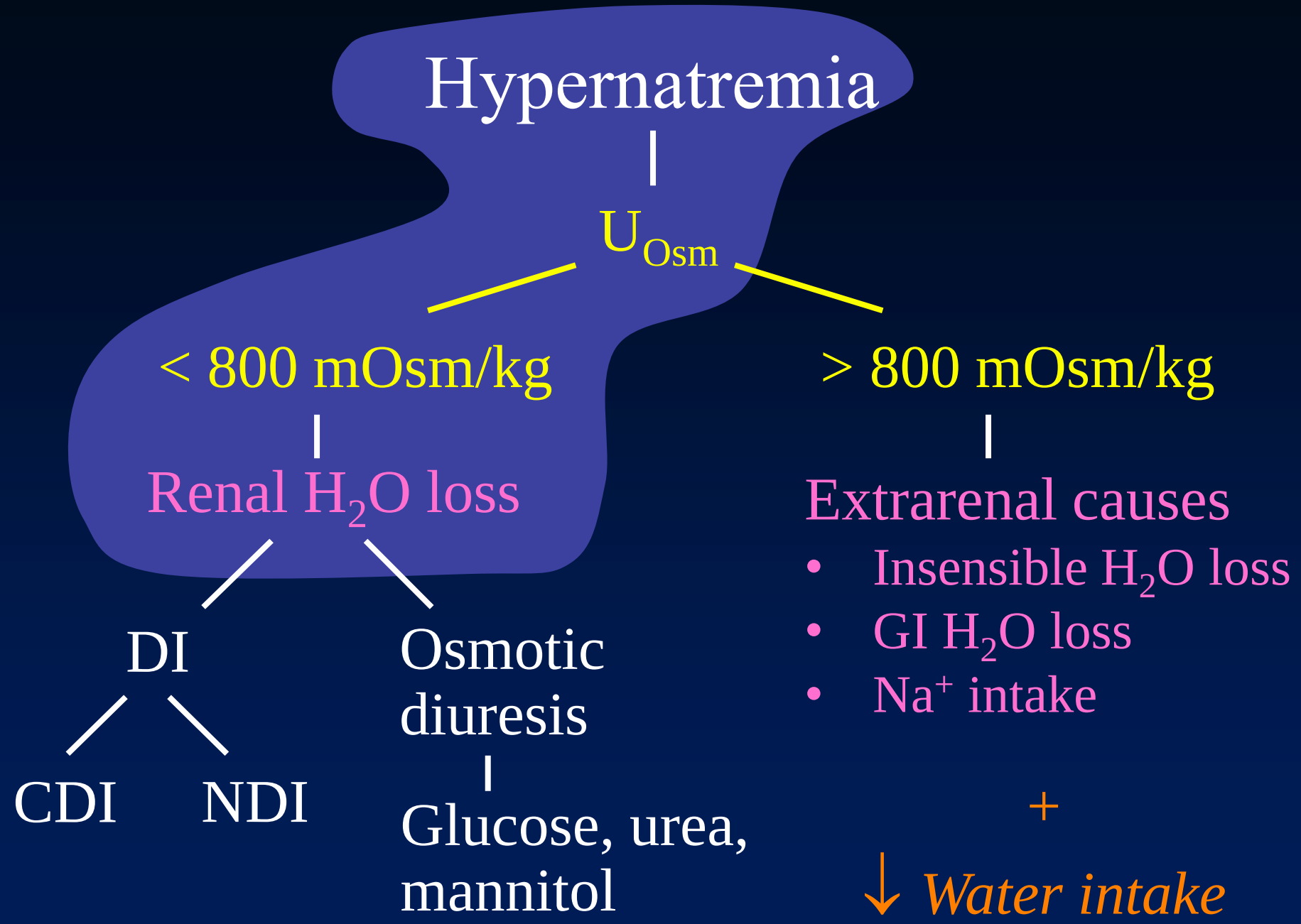
Hypernatremia
U_{Osm}
< 800 mOsm/kg
Renal H_2O loss
DI
CDI
NDI
Osmotic diuresis
Glucose, urea, mannitol
> 800 mOsm/kg
Extrarenal causes
• Insensible H_2O loss
• GI H_2O loss
• Na^+ intake
+
↓ Water intake

A 17-year-old woman who is otherwise fit and well, and on no medications, presents with a history of polyuria since early childhood.

On presentation:

Serum sodium	141 mEq/L
Serum osmolality	285 mOsm/kg
Urine osmolality	210 mOsm/kg
Urine volume	4 L

Case 3

After 4 hrs of water deprivation:

Serum sodium	146 mEq/L
Serum osmolality	298 mOsm/kg
Urine osmolality	250 mOsm/kg

1 hr after administration of 10 µg intranasal DDAVP:

Serum sodium	143 mEq/L
Serum osmolality	292 mOsm/kg
Urine osmolality	585 mOsm/kg

Case 3

Which of the following statements could be TRUE?

(A) She is entirely normal since her baseline serum sodium is normal

(B) The water deprivation test is non-diagnostic because water deprivation was not continued for long enough

(C) She has central diabetes insipidus

(D) She has nephrogenic diabetes insipidus

(E) She has an osmotic diuresis with washout of her medullary interstitium concentrating gradient

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(D) She has nephrogenic diabetes insipidus

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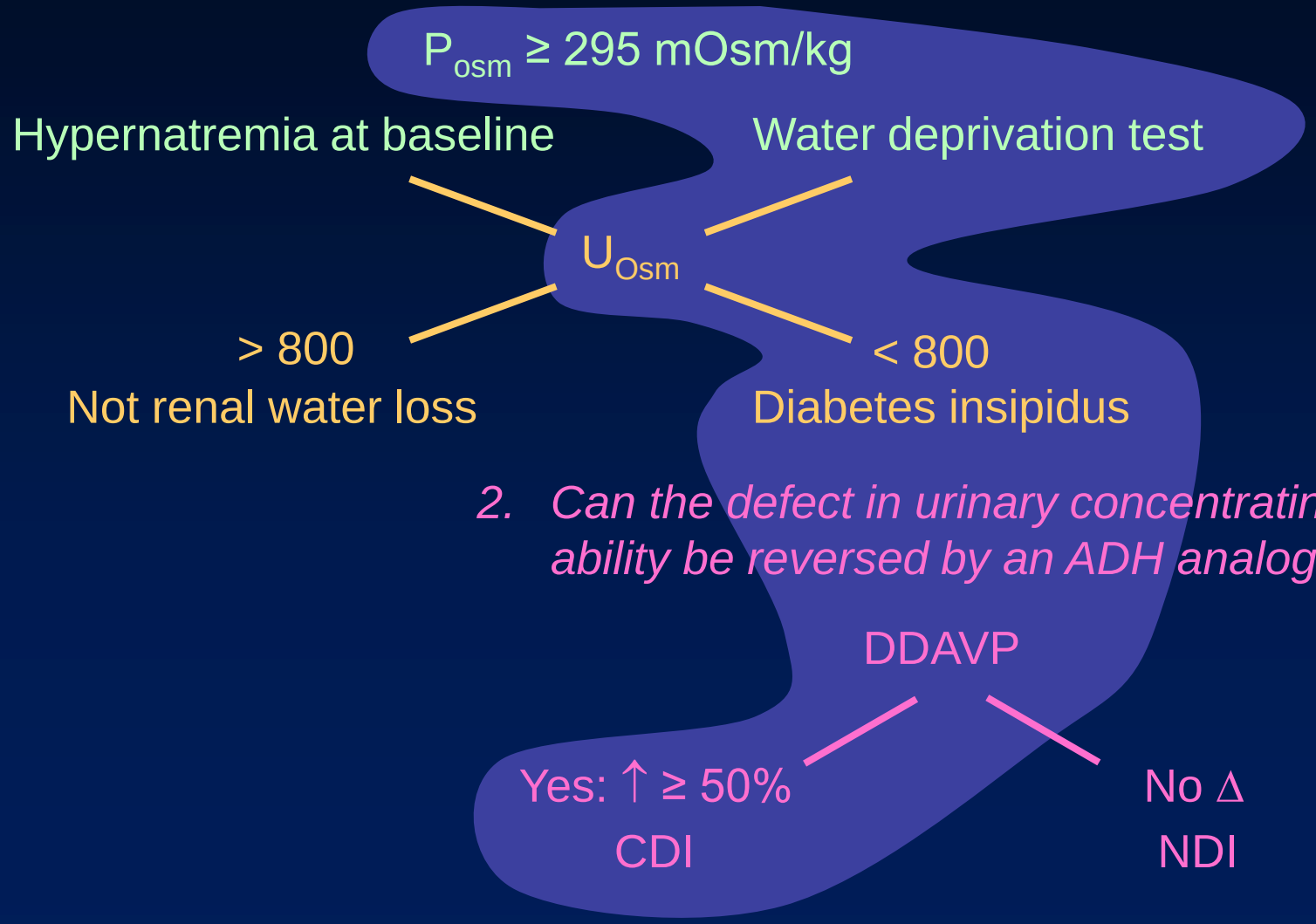
DDX of renal water loss

1. *Is there a defect in urinary concentrating ability when ADH release is maximally stimulated?*



2. *Can the defect in urinary concentrating ability be reversed by an ADH analog?*

A 45-year-old female underwent transsphenoidal resection of a large pituitary adenoma 1 week ago. Immediately postoperatively she developed polyuria and was treated with DDAVP for 2 days and encouraged to increase po fluid intake. She returns with change in mental status, has a seizure in the emergency room, and is found to have a serum sodium of 120 mEq/L.

Case 4

Which of the following statements about her hyponatremia is TRUE?

(A) Her hyponatremia is caused by inappropriate treatment with DDAVP

(B) She has pseudohyponatremia

(C) She has central hypothyroidism

(D) She has psychogenic polydipsia

(E) Her hyponatremia is due to unregulated vasopressin release from the posterior pituitary

Which of the following statements about her hyponatremia is TRUE?

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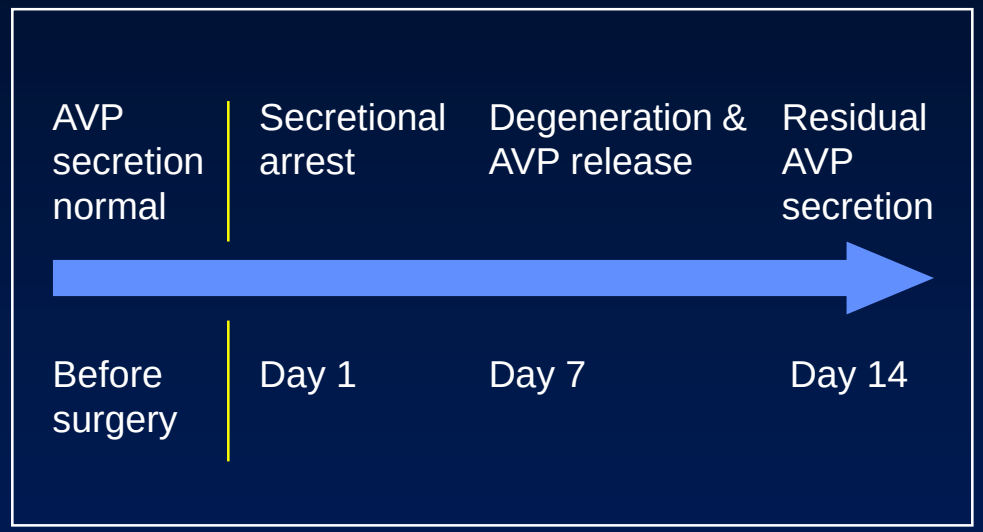
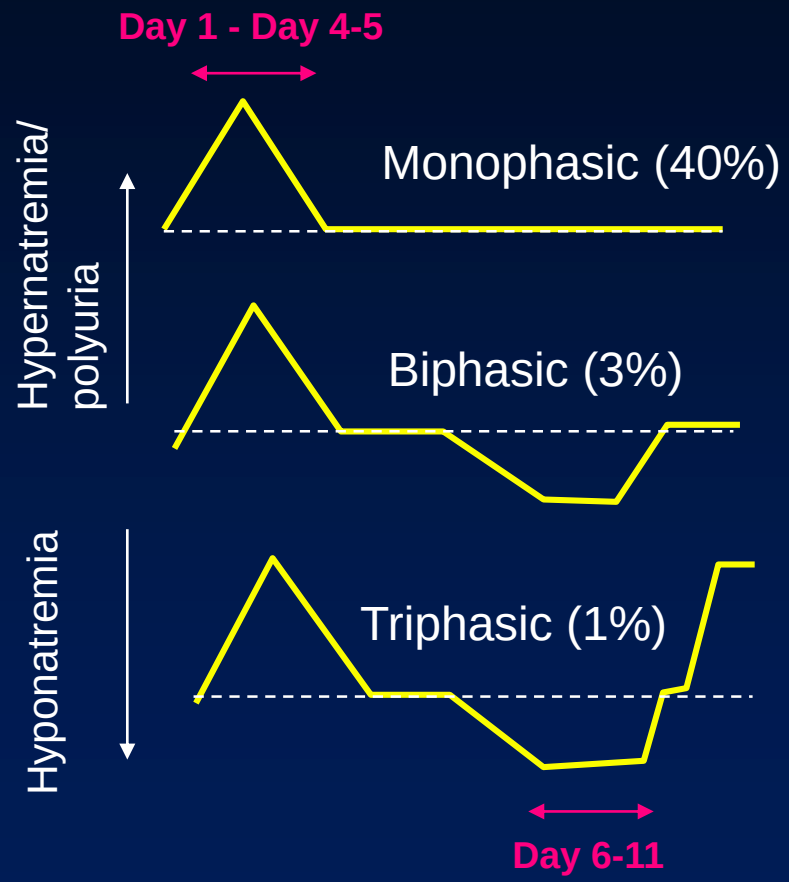
Pathogenesis of disordered water metabolism after transsphenoidal surgery





Hensen et al. Clin Endocrinol. 1999;50, 431

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.

Serum sodium	116 mEq/L
Serum osmolality	256 mOsm/kg
Urine sodium	96 mEq/L
Urine potassium	87 mEq/L
Urine osmolality	670 mOsm/kg

Case 5

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

(A) Water deprivation test

(B) Computed tomography scan of the chest

(C) Serum protein electrophoresis

(D) Echocardiogram

(E) Assessment of daily fluid intake

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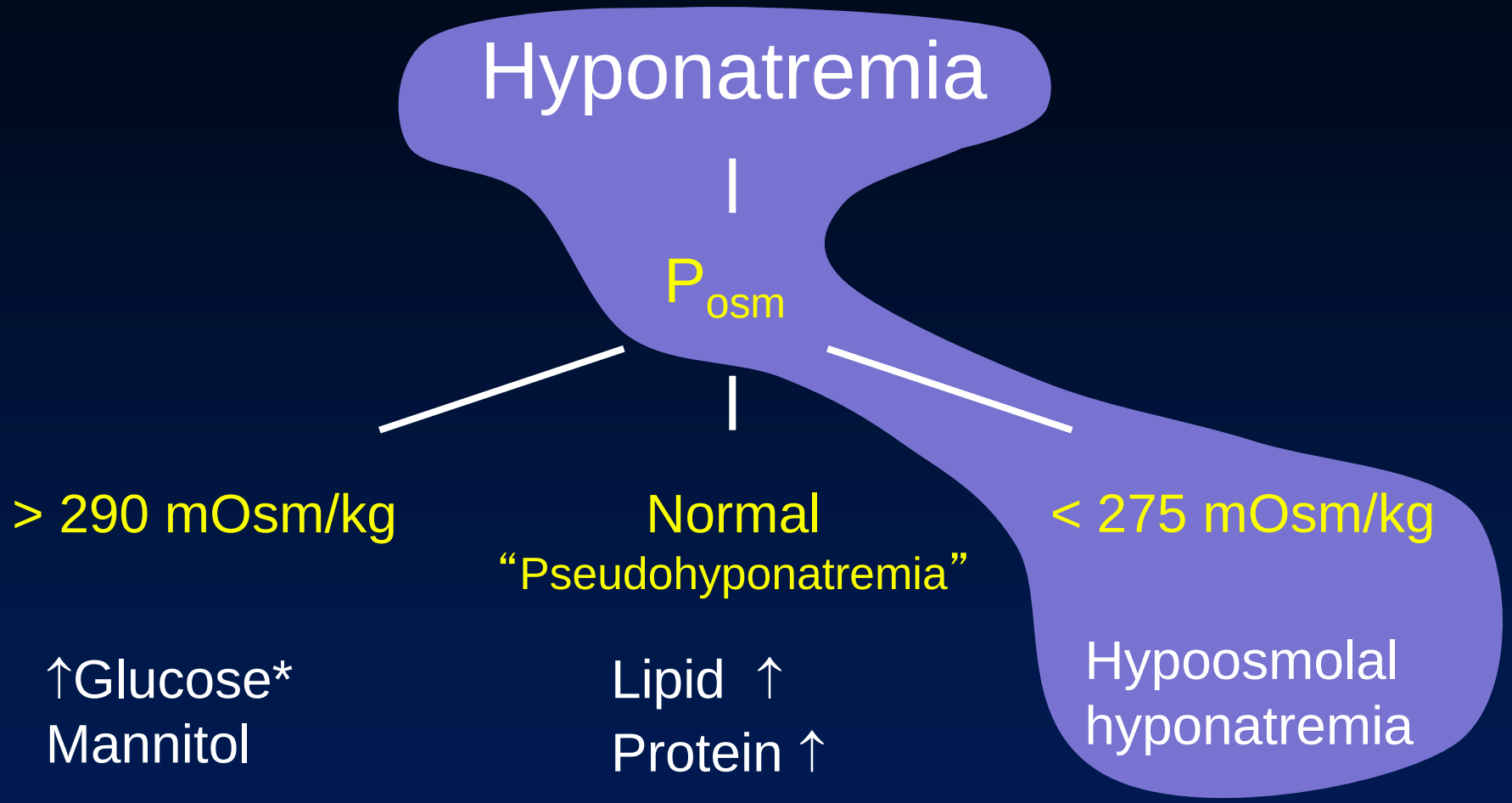
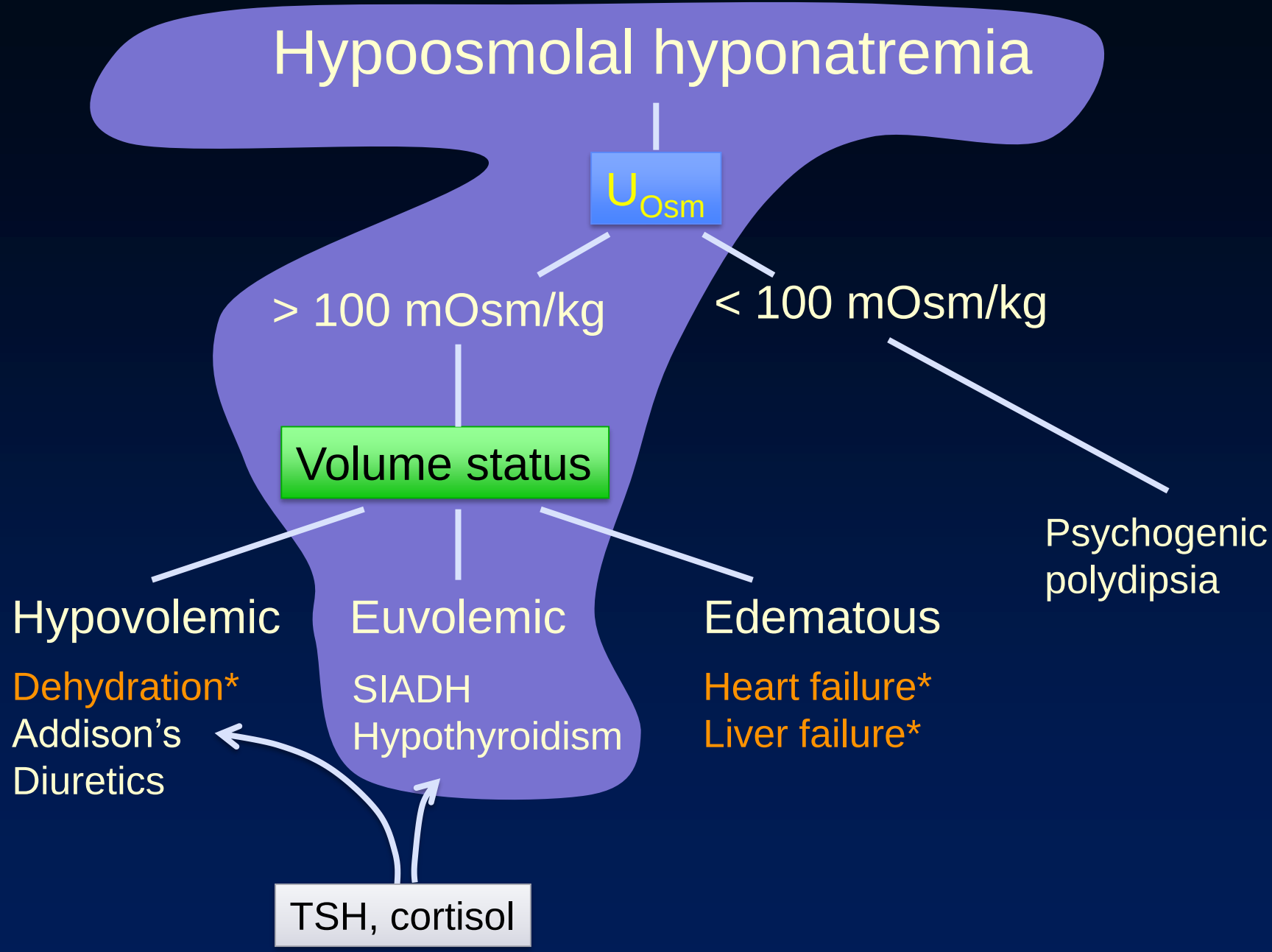


*Correct serum Na^+ by 1.6 for every 100 mg/dL Δ in glucose



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

Causes of SIADH

1. Ectopic production by tumors
   - Small cell carcinoma of the lung
2. Neurological
   - Meningoencephalitis, CVA, neoplasm
3. Pulmonary disease (uncommon)
   - Pneumonia & TB
4. Drugs
   - SSRI and other psychoactive drugs, chlorpropamide, cyclophosphamide, vincristine
5. Postoperative patient
6. Exercise-associated hyponatremia

An 18-year-old woman with schizophrenia, maintained on risperidone, presents with a generalized seizure.

Serum sodium	120 mEq/L
Serum osmolality	252 mOsm/kg
Urine sodium	20 mEq/L
Urine osmolality	90 mOsm/kg

Case 6

Which of the following is the best treatment for this patient?

(A) 3% NaCl at 100 mL/hr

(B) 0.9% NaCl, 500 mL IV bolus

(C) Tolvaptan

(D) Stop risperidone

(E) Fluid restriction

Which of the following is the best treatment for this patient?

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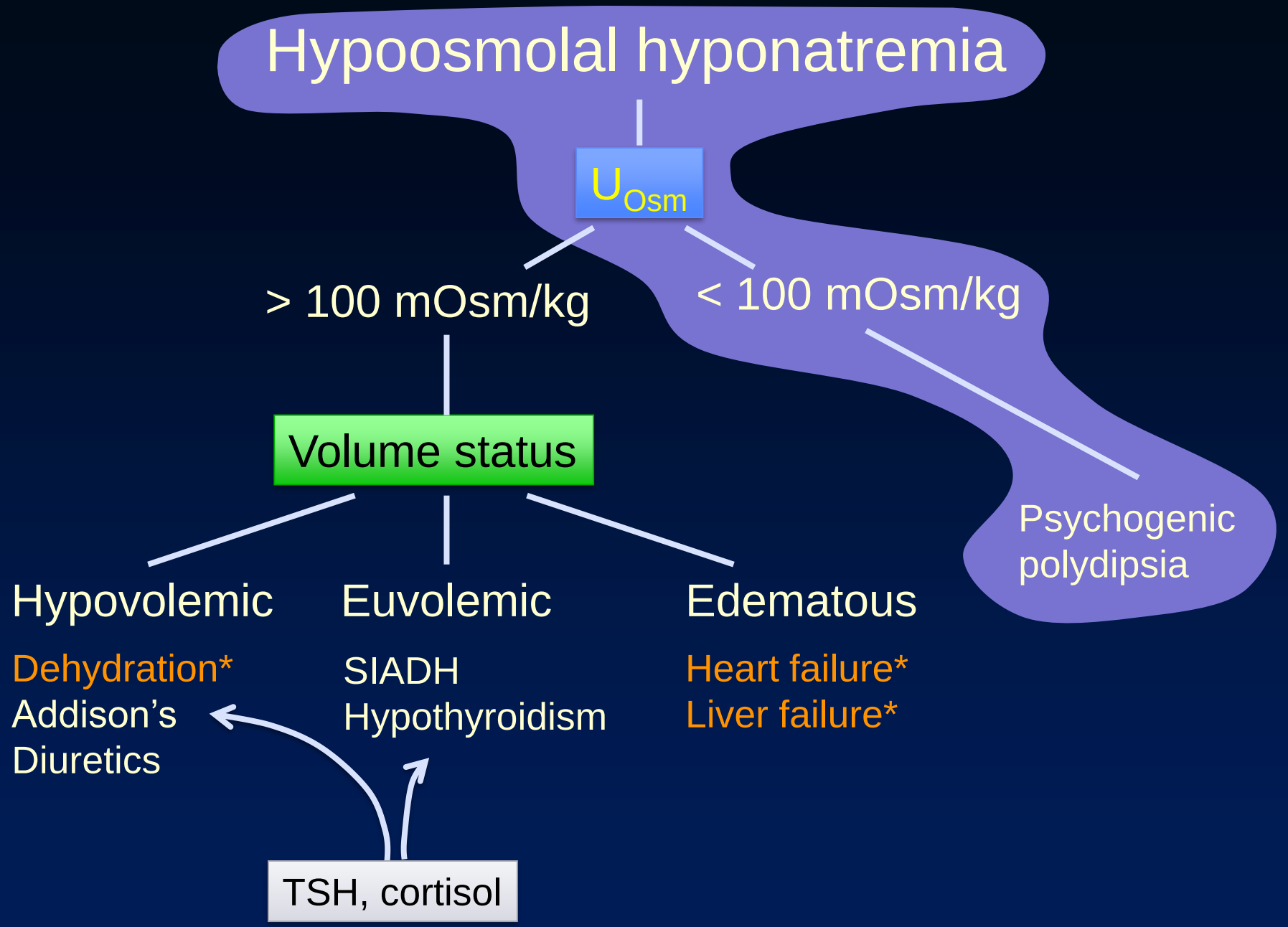

* U_{Na} < 20 = Extrarenal cause of ECV depletion

A 38 year-old man was diagnosed with squamous cell carcinoma of the head and neck 2 months ago and has known chronic SIADH. On a routine clinic visit he is alert, oriented and feels fine but reports subtle impairment in his ability to think clearly.

Serum sodium	116 mEq/L
Serum potassium	3.4 mEq/L
Serum chloride	85 mEq/L
Serum bicarbonate	23 mEq/L
Urine sodium	90 mEq/L
Urine potassium	23 mEq/L
Urine osmolality	464 mOsm/kg

Case 7

Which of the following would be appropriate in the management of this patient:

(A) Hypertonic saline to raise serum Na by 14 mEq/L in the first day

(B) 0.5 L fluid restriction and salt tablets

(C) Tolvaptan to raise serum Na by 2 mEq/L per hour over the next 12 hr

(D) 0.9% NaCl at 125 mL/hr

(E) DDAVP 1 mcg SQ

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(D) 0.9% NaCl at 125 mL/hr

(E) DDAVP 1 mcg SQ

Case 7

Treatment of SIADH

- Water restriction
- Isotonic saline
- Hypertonic saline / NaCl tablets
- Urea powder
- Furosemide
- Vasopressin antagonist (e.g. tolvaptan) or demeclocycline

Avoiding Osmotic Demyelination Syndrome (ODS) in Patients with Chronic Hyponatremia

Population at risk:

- Hyponatremia with serum Na < 120 mmol/L of > 48 hours' duration

Limits not to exceed:

- For high risk of ODS: 8 mmol/L in any 24-hour period
- For normal risk of ODS: 10-12 mmol/L in any 24-hour period; 18 mmol/L in any 48-hour period.

Verbalis et al., Diagnosis, evaluation, and treatment of hyponatremia: Expert panel recommendations. AJM 2013 126 (10 Suppl 1):S1-42

An 18 year-old female college student runs the Boston marathon. It is her first marathon and so she is careful to keep well hydrated before and during the race. At the finish line, she feels severely nauseated, dyspneic and has generalized headache. On exam, she is lethargic, dyspneic and confused, but looks well hydrated. BP 102/64, HR 95.

Her POC blood sodium concentration is 112 mEq/L.

Case 8

Which of the following would be the best initial treatment for this patient:

(A) 1 liter of intravenous 0.9% NaCl

(B) Fluid restriction and observe for 1 hour

(C) Salt tablets orally

(D) 100 mL intravenous 3% NaCl

(E) 1 liter of sports drink

Case 8

Which of the following would be the best initial treatment for this patient:

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(D) 100 mL intravenous 3% NaCl

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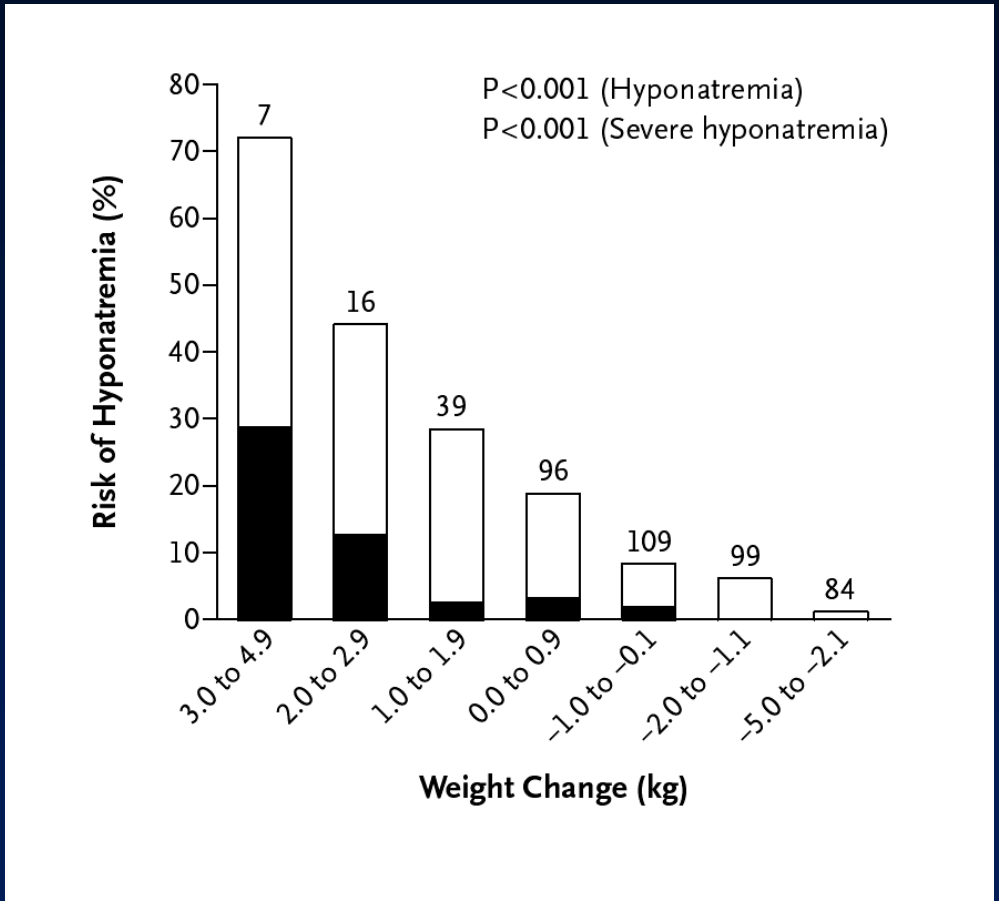
Case 8

Exercise-associated hyponatremia (EAH)

Pathogenesis of EAH

- EAH is dilutional due to excessive water or sports drink consumption, **not** due to salt loss/dehydration
- In addition, ADH levels are inappropriately elevated and U_{osm} is high



Almond et al.(2005) NEJM 352:1550

Consensus Statement of the 1st International Exercise-Associated Hyponatremia Consensus Development Conference, Cape Town 2005:

- Any athlete with EAH and respiratory insufficiency, confusion, obtundation, N/V can be treated on-site with **100 mL of 3% NaCl over 10 min** (expected Δ [Na^+] ~ 2-3 mmol/L)
- If symptomatic EAH persists, repeat 100 mL 3% NaCl hourly at a rate of 100 mL/h and monitor serum Na hourly

Hew Butler et al. (2005) Clin J Sport Med 15:208

A 66 yr old female with NIDDM presents with several days of malaise, lethargy, polyuria and decreased oral intake. Physical examination reveals tachycardia, orthostatic hypotension and dry mucous membranes.

Serum sodium	135 mEq/L
Serum potassium	5.2 mEq/L
Serum chloride	96 mEq/L
Serum bicarbonate	25 mEq/L
Blood urea nitrogen	42 mg/dL
Serum creatinine	1.8 mg/dL
Serum glucose	975 mg/dL

Case 9

After initiating insulin and with 2L of isotonic saline, which of the following would be the best treatment to normalize the patient's serum sodium concentration:

(A) Hypertonic saline

(B) Oral fluid restriction

(C) Hypotonic saline

(D) Tolvaptan

(E) Salt tablets

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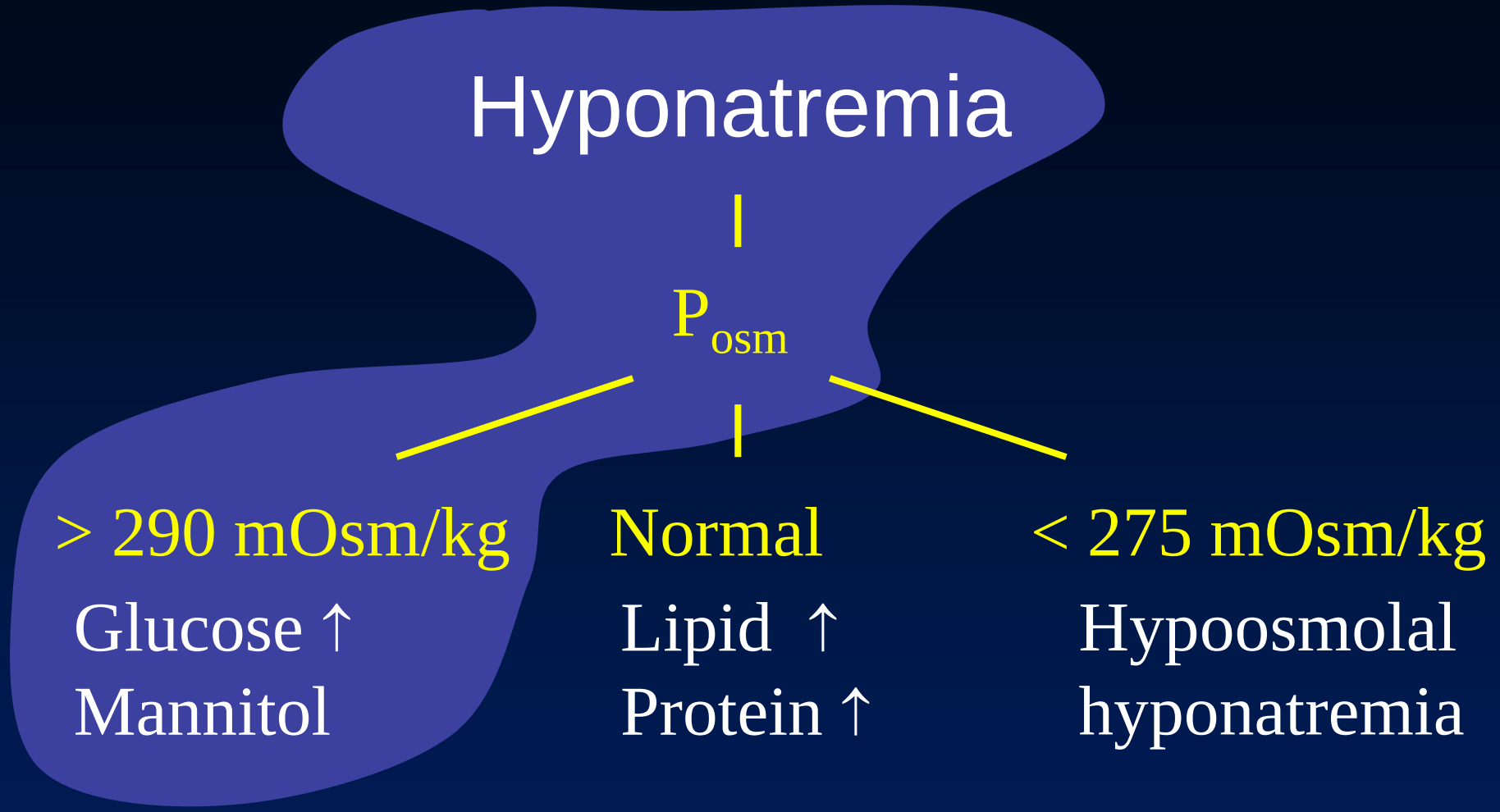

Correction for hyperglycemia:

For every 100 mg/dL increase in glucose, add 1.6 mEq/L to Na^+

Correction of serum Na for hyperglycemia

Increase in glucose = 975 – 100 = 875

Na correction = 8.75 x 1.6 = 14

Corrected Na = 135 + 14 = 149

A 74 yr old female with a history of hypertension, hyperlipidemia and depression is admitted with unsteady gait and a fall at home. Medications: Hydrochlorothiazide, lisinopril, simvastatin, sertraline. On exam she appears euvolemic.

Serum sodium	117 mEq/L	
Serum potassium	4.6 mEq/L	
Serum chloride	92 mEq/L	
Serum total cholesterol	220 mg/dL	
Serum triglycerides	345 mg/dL	
Serum cortisol	15 µg/dL	(NR 5-15 µg/dL)
Serum free T4	0.9 ng/dL	(NR 0.7-2.0 ng/dL)
Urine sodium	58 mEq/L	
Urine osmolality	230 mOsm/kg	

Case 10

What is the most likely cause of her hyponatremia

(A) Pseudohyponatremia

(B) Adrenal insufficiency

(C) Hypothyroidism

(D) ADH-secreting tumor

(E) Adverse effect of medications

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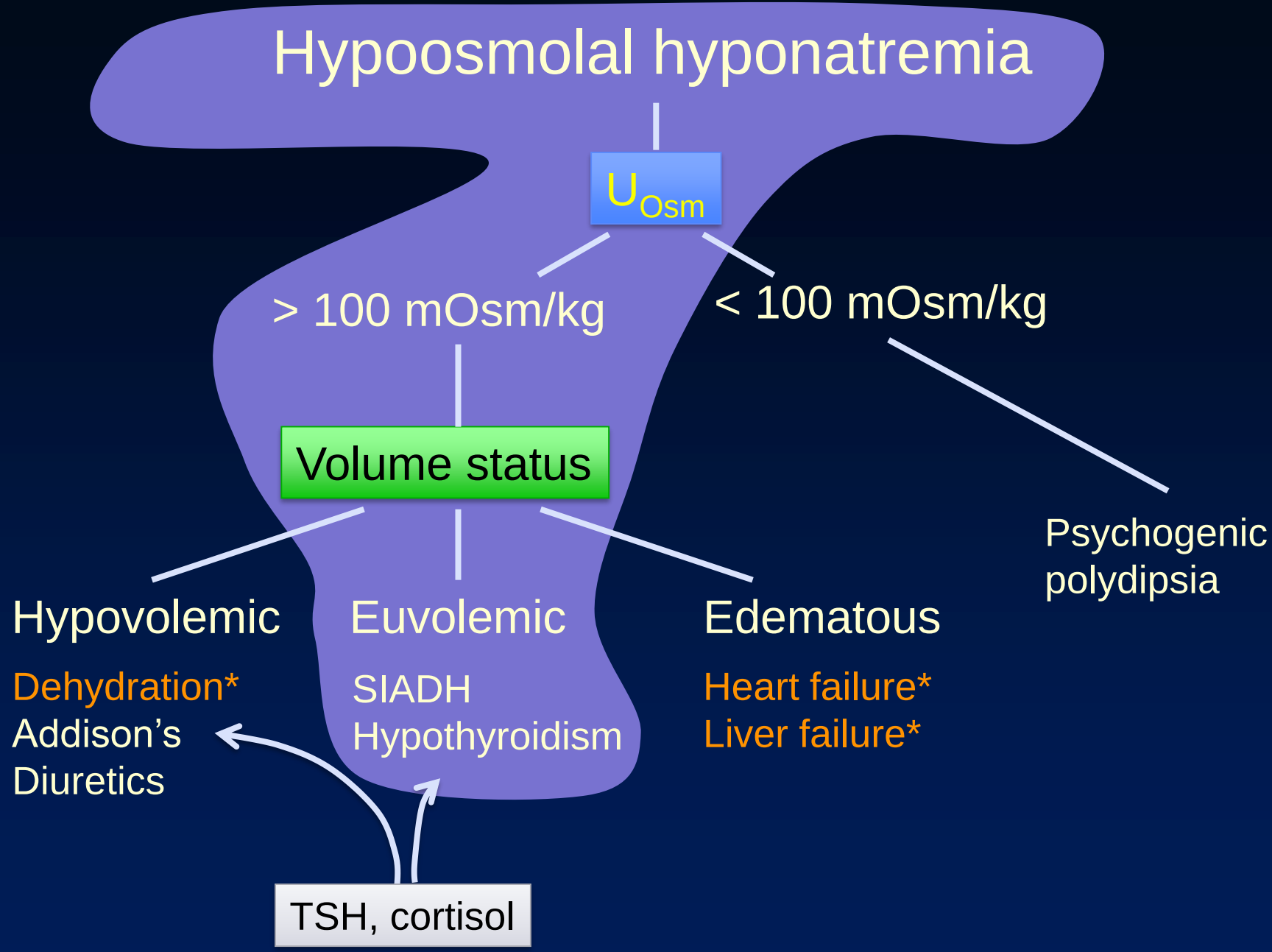

* U_{Na} < 20 = Extrarenal cause of ECV depletion

A 63 yr old female with hypertension was started on hydrochlorothiazide 2 months ago and presents with drowsiness, confusion and hyponatremia.

Admission:

Serum sodium	110 mEq/L
Urine osmolality	430 mg/dL

She is initiated on 3% NaCl at 200 mL/hr and kept NPO. Five hours later her serum sodium is 124 mEq/L. Her mental status is unchanged.

Case 11

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

(A) Change rate of 3% NaCl to 80 mL/hr

(B) Discontinue fluids and initiate tolvaptan

(C) Discontinue fluids and initiate 1 L daily oral fluid restriction

(D) Discontinue hypertonic saline and start 5% dextrose and DDAVP

(E) None of the above

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(E) None of the above

Case 11

Avoiding Osmotic Demyelination Syndrome (ODS) in Patients with Chronic Hyponatremia

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- Hyponatremia with serum Na < 120 mmol/L of > 48 hours' duration

Limits not to exceed:

- For high risk of ODS: 8 mmol/L in any 24-hour period
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Osmotic demyelination syndrome

- Central and extrapontine myelinolysis
- Risk factors :
  - Excessive rate or amount of correction of serum Na^+
  - Malnutrition and alcoholism
  - Severe liver disease
  - Hypoxia
- Classic CPM presents with dysphagia, quadriparesis, locked-in syndrome
- Can be permanent or fatal

A 30-year-old female with anorexia nervosa is found on routine laboratory examination to be hypokalemic. BP 95/45, HR 66.

Serum sodium	133 mEq/L
Serum potassium	3.2 mEq/L
Serum chloride	93 mEq/L
Serum bicarbonate	32 mEq/L
Blood urea nitrogen	6 mg/dL
Serum creatinine	0.6 mg/dL
24 hour urine	
Volume	1 L
Potassium	80 mEq/L
Chloride	54 mEq/L

Case 12

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

(A) Surreptitious vomiting

(B) Laxative abuse

(C) Bartter syndrome

(D) Licorice ingestion

(E) Diuretic abuse

Case 12

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

(A) Surreptitious vomiting

(B) Laxative abuse

(C) Bartter syndrome

(D) Licorice ingestion

(E) Diuretic abuse

Case 12

DDX of hypokalemia

Cellular shift

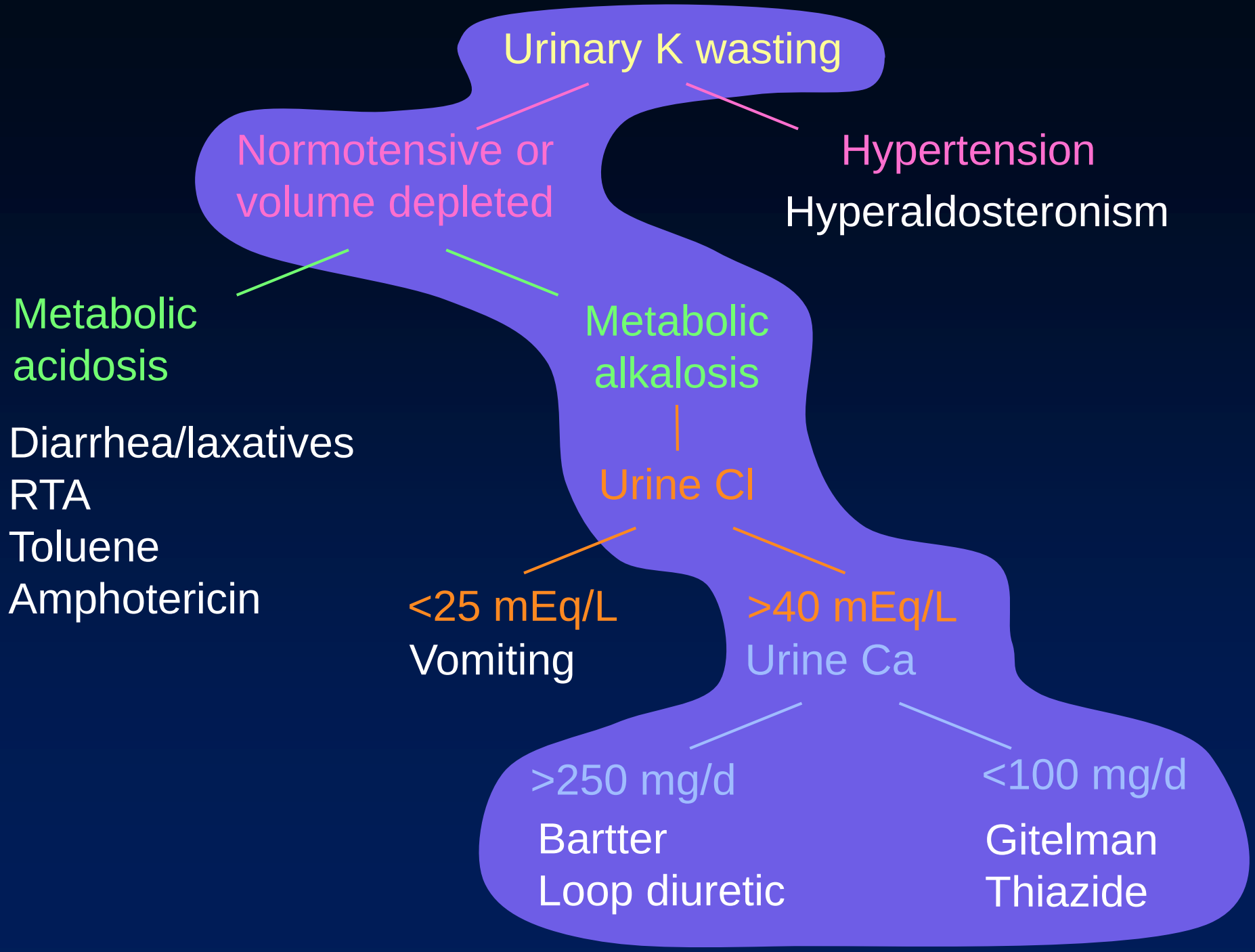
Alkalemia
Insulin
β-agonist
Hypokalemic
periodic paralysis

GI loss

Diarrhea
(Vomiting)

Urinary K wasting

24 hr U_K > 25 mEq
TTKG > 3


Urinary K wasting
Normotensive or volume depleted
Hypertension
Hyperaldosteronism
Metabolic acidosis
Diarrhea/laxatives
RTA
Toluene
Amphotericin
Metabolic alkalosis
Urine Cl
<25 mEq/L
Vomiting
>40 mEq/L
Urine Ca
>250 mg/d
Bartter
Loop diuretic
<100 mg/d
Gitelman
Thiazide

A 23-year-old male is referred for work-up of newly diagnosed hypertension. He is otherwise asymptomatic. Family history is non-contributory. BP 155/97. He is obese.

Serum sodium	143 mEq/L	
Serum potassium	3.0 mEq/L	
Serum chloride	106 mEq/L	
Serum bicarbonate	29 mEq/L	
Blood urea nitrogen	12 mg/dL	
Serum creatinine	1.2 mg/dL	
Plasma renin activity	0.7 ng/mL/hr	(NR 1-6)
Plasma aldosterone	3.9 ng/dl	(NR 5-20)
24 hour urine potassium	65 mEq	

Case 13

Which of the following tests would be most likely to be helpful in the diagnosis:

(A) Serum metanephrines

(B) Doppler ultrasound of the renal arteries

(C) 24 hr urine aldosterone

(D) 24 hr urine 18-hydroxycortisol and 18-oxocortisol

(E) 24 hr urine cortisol

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(A) Serum metanephrines

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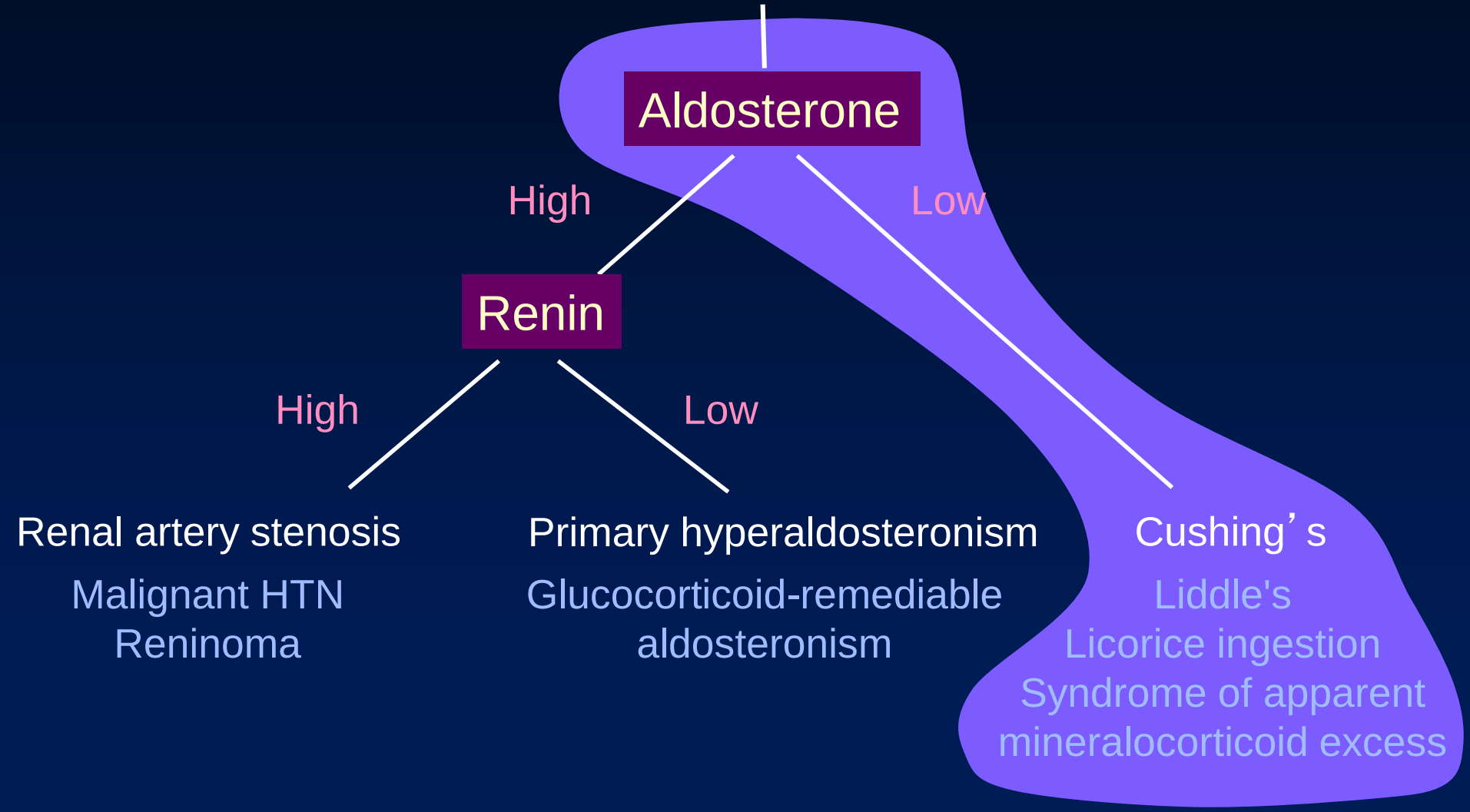
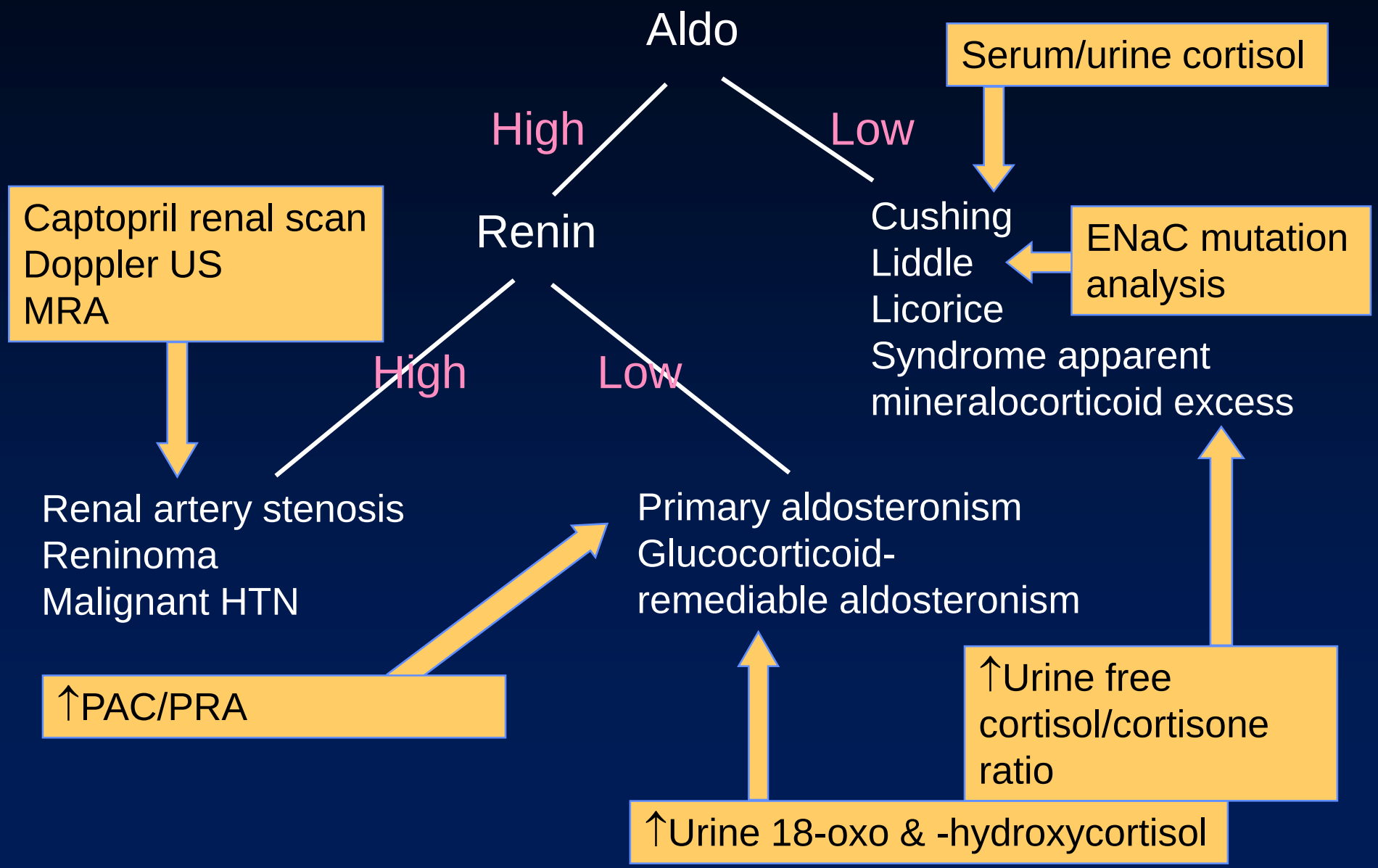
(D) 24 hr urine 18-hydroxycortisol and 18-oxocortisol

(E) 24 hr urine cortisol

HYPERALDOSTERONISM:
Hypokalemia metabolic alkalosis + hypertension



HYPERALDOSTERONISM:
Hypokalemia metabolic alkalosis + hypertension



A 19-year-old Asian male presents to the emergency room with acute onset of flaccid muscle weakness. He denies diarrhea or vomiting and is using no medications. BP 125/88, HR 95.

Serum sodium	139 mEq/L
Serum potassium	1.7 mEq/L
Serum chloride	105 mEq/L
Serum bicarbonate	25 mEq/L
Serum glucose	100 mg/dL
Blood urea nitrogen	11 mg/dL
Urine potassium	< 5 mEq/L

Case 14

Which of the following would be appropriate in the management of this patient:

(A) Repletion with KCl, 160 mEq daily

(B) Loperamide

(C) Indomethacin

(D) Check serum thyroid-stimulating hormone level

(E) None of the above

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DDX of hypokalemia

Cellular shift	GI loss	Urinary K wasting
Alkalemia	Vomiting	24 hr U_K > 25 mEq
Insulin	Diarrhea	TTKG > 3
β-agonist		
Hypokalemic periodic paralysis		

Thyrotoxic hypokalemic periodic paralysis

- Presents age 20-40 yr
- Predominantly Asians, mostly male (20:1 M:F ratio)
- Only with thyrotoxicosis (~2% of Asians with thyrotoxicosis) which may be asymptomatic
- Other clinical features identical to familial form
  - Precipitated by meals or exercise
  - Repetitive episodes of acute profound hypokalemia
  - Recovery of serum K^+ within hrs after each episode without repletion, either spontaneously or with propanolol (if Rx with KCl, give slowly ≤ 10 mmol/hr & avoid dextrose
  - Low urine K^+ and low TTKG (< 1)

A 67 year-old male with hypertension for 30 years has been having worsening blood pressure control over the past year. He had a myocardial infarction 2 years ago. His current medications include amlodipine, carvedilol and clonidine. On a clinic visit, his BP is 163/95.

Serum sodium	141 mEq/L	
Serum potassium	3.4 mEq/L	
Serum chloride	108 mEq/L	
Serum bicarbonate	27 mEq/L	
Serum creatinine	1.6 mg/dL	
Plasma renin activity	7.3 ng/mL/hr	(NR 1-6)
Plasma aldosterone	24 ng/dl	(NR 5-20)

Case 15

What is the most likely cause of this patient's hypokalemia?

(A) Reninoma

(B) Adrenal cortical adenoma

(C) Renal artery stenosis

(D) Ingestion of licorice

(E) Gordon's syndrome

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