Endocrinology cases

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GLMS symposium

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Mr Salt

- 76 yo male presented to hospital with failure to thrive
- Several months of anorexia, malaise, anhedonia – treated with Mirtazipine with some improvement
- 1 month prior to admission was noticed to be withdrawn, poor diet, stopped antidepressants, mood swings
- Reviewed by GP and noted to be confused, fall, vomiting and too weak → referred to ED

Background

- Depression (15 years), worse in the last year
- Type 2 diabetes
- Hyperlipidemia
- GORD
- Non smoker, non drinker

Medications

- Metformin 1000 mg twice daily
- Simvastatin 40 mg nocte
- Omeprazole 40 mg daily (not taking)
- Mirtazepine 15 mg daily (not taking)

Examination

- T 36.3, BP 165/69 mmHg, HR 63 bpm
- Pale
- Flat affect, awake and oriented. Unable to recall phone number
- JVP 1 cm
- Cardiac, respiratory and abdominal findings NAD
- No focal neurology
- No peripheral oedema

- CXR, CT head and abdomen – normal

Lab results

Na 112, K 4.2, Cl 77; glucose 4.8

Plasma osmolality 246 mOsm/kg (275 – 290)

Creatinine 71 umol/L; Urea 3.2 mmol/L (3.2 – 7.7)

Urate 0.2 mmol/L (0.23 – 0.42)

Albumin 30 g/L; LFTs normal

Lipid profile normal

FBC normal

Hypotonic hyponatraemia

Spot urine investigations

- Urine Na = 53 mmol/L
- Urine K = 25 mmol/L
- Urine Creatinine = 4.14 mmol/L
- Urine Osmolality = 255 Osm/kg

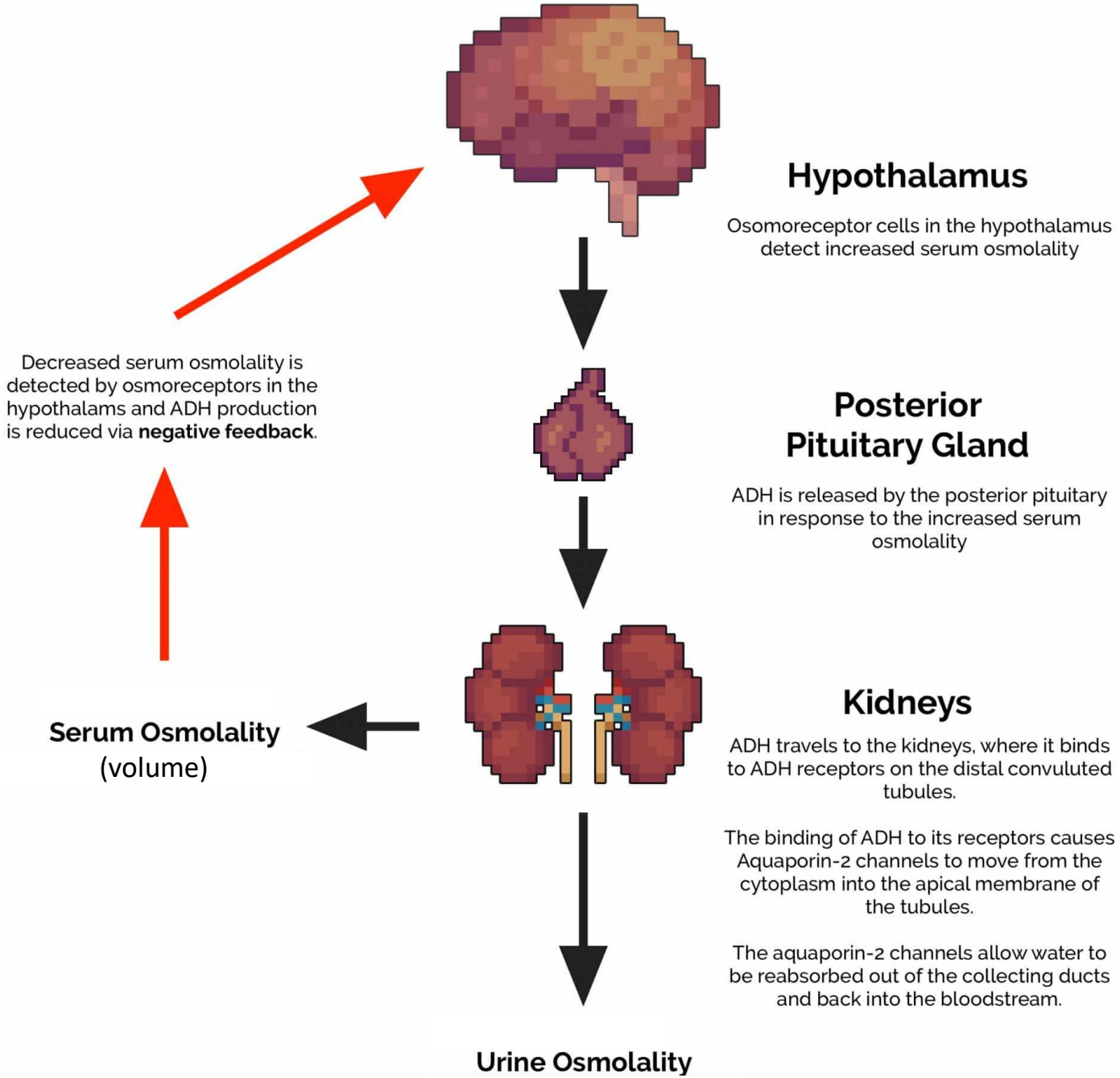
Which cause of hyponatraemia is most consistent with the findings?

A. Hypovolemia
B. Low solute intake
C. Cerebral salt wasting
D. SIADH

Osmolality

Osmolality = 2 X (Na + K) + urea + glucose

(Normal range 275 – 290)

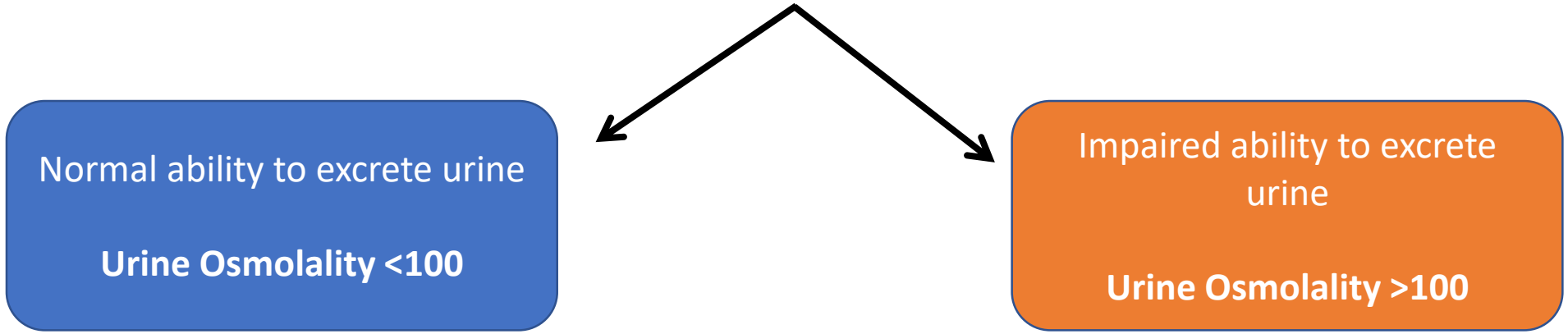


https://geekymedics.com/syndrome-of-inappropriate-antidiuretic-hormone-secretion-siadh/

Approach to hyponatraemia

Urine osmolality

HYPONATRAEMIA (Low plasma Na)



<u>No effect with water excretion</u>
Psychotic water intoxication

<u>Solute limited water excretion</u>
Beer potomania
Tea & toast diet with large water intake

<u>Abnormal diluting sites</u>
Severe renal failure
Thiazide diuretics

<u>Vasopressin mediated</u>
Underfilled arterial circulation
Inappropriate secretion of ADH

Approach to hyponatraemia

Spot urine sodium

- Urine sodium can be used to assess volume status

- Urine sodium < 20 mmol/L = Aldosterone drive ++
  (Hypovolemia or sodium deplete)
- Urine sodium > 40 mmol/L = Renal tubular damage (renal salt wasting)
  Thiazide diuretics
  SIADH

Which cause of hyponatraemia is most consistent with the findings?

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C. Cerebral salt wasting
D. SIADH

Mr Salt
Serum Na = 112 mmol/L
Urine Na = 53 mmol/L
Urine Osmolality = 255 mOsm/kg water

Urine is not dilute in setting of hyponatraemia
Urine Na is not low
Euvolemic clinically

Which cause of hyponatraemia is most consistent with the findings?

A. Hypovolemia → *BP 165/69 mmHg, low uric acid, urine sodium > 20*
B. Low solute intake → *urine sodium 53 mmol/L*
C. Cerebral salt wasting → *normal CT head*
D. SIADH

What feature is not observed in SIADH?

A. High urine osmolality
B. Increased levels of natriuretic peptides
C. High renin and aldosterone levels
D. Low uric acid

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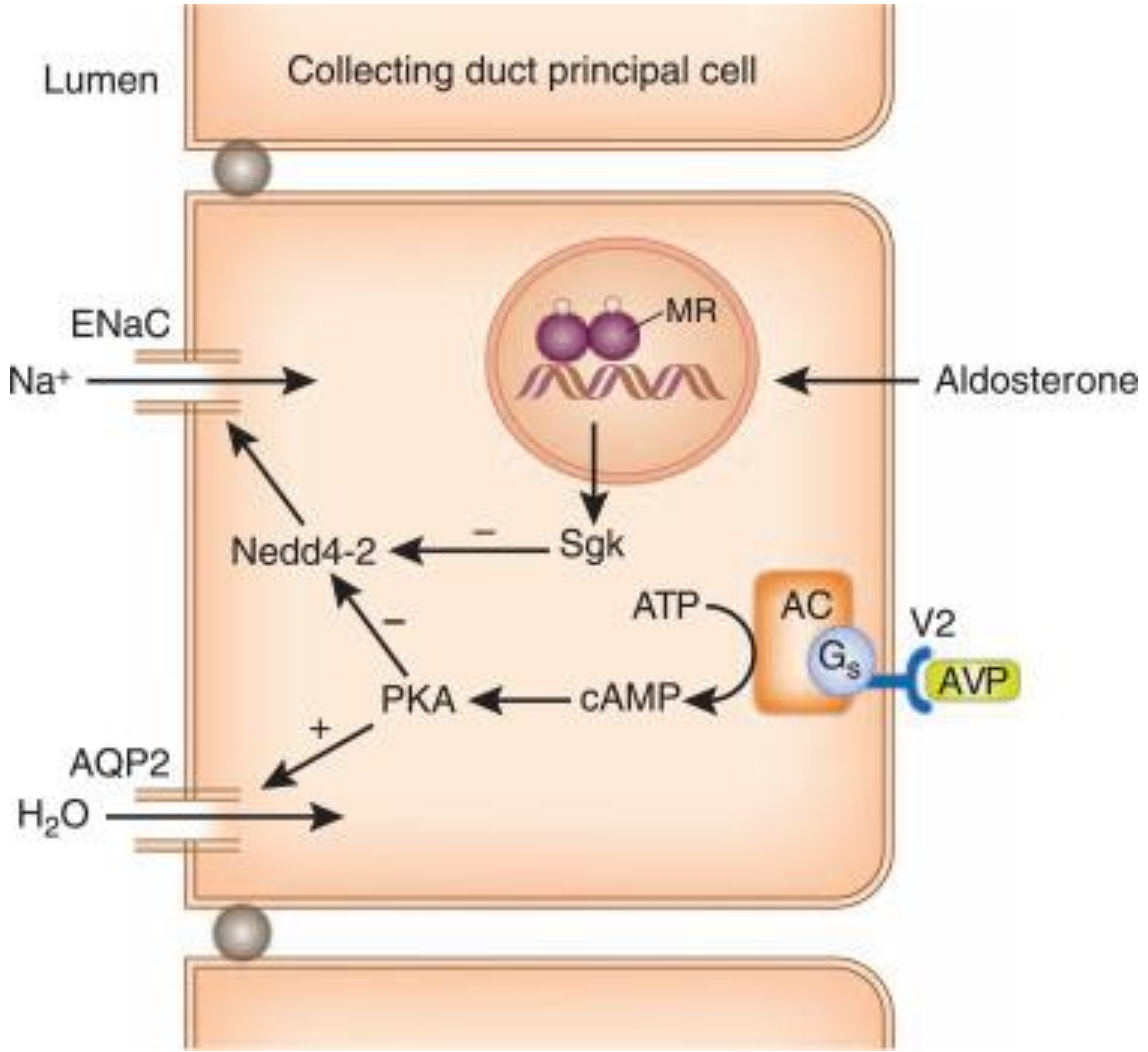

ADH activates V1 and V2 transmembrane G-protein receptors

Promotes aquaporin channels at luminal membrane

Increased free water reabsorption

Increases Na reabsorption via ENaC

Kidney International 2010 78849-856DOI: (10.1038/ki.2010.276)

SIADH

- In SIADH, ability to excrete dilute urine is impaired
- ADH is not adequately suppressed with ingestion of water
- Increased urinary sodium excretion and ADH mediated sodium and water retention at the DCT increases total body water → lowering serum Na concentration

- Associated with CNS disorder, pulmonary diseases, ectopic ADH secretion (malignancy associated), drugs, hypopituitarism, use of dDAVP

Further investigations

- Free T4 = 10.3 (12 – 22)
- TSH = 1.46 mU/L (0.27 – 4.2)
- 9am cortisol = 149 nmol/L (>170)
- FSH 2.3 mU/L (3 – 55), LH 0.9 mU/L (10 – 60)
- Total testosterone 2.1 nmol/L (6.7 – 26); fT 1.2 (179 – 520)

Panhypopituitarism

- 250 mcg synacthen stimulation test

0 min	cortisol 140 nmol/L	ACTH 3.3 pmol/L (2 - 11)
30 min	cortisol 438 nmol/L	
60 min	cortisol 618 nmol/L	

Which of the following statements is true?

A. Adrenal insufficiency is unlikely because the serum potassium is normal
B. Adrenal insufficiency is unlikely because the patient is euvolemic
C. Adrenal insufficiency has been ruled out by ACTH stimulation test
D. All of the above
E. None of the above

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- Synacthen stimulation test: At 30 min > 400 is in keeping with normal response and < 400 suggests adrenal insufficiency
- Normal results can be observed in partial or recent onset ACTH deficiency

- Relative hyperkalaemia is seen in adrenal insufficiency
- Hypovolemia is less common in secondary adrenal insufficiency compared to Addison’s

Hyponatraemia and cortisol deficiency

- SIADH is associated with:
  - Cortisol deficiency → reduced feedback to hypothalamus → stimulated CRH → increases ADH/AVP secretion
  - Reduced arterial circulation

  - Aldosterone deficiency → renal salt wasting & hypovolemia → increases ADH

Progress

- Mr Salt was diagnosed with secondary adrenal insufficiency, and started on hydrocortisone 10mg mane and 5 mg 5pm

- 1 day after
  - Clinically improved with improved appetite
  - Na increased from 126 → 132 mmol/L

- After 3 days of hydrocortisone replacement, urine osmolality <100 after 1 L water load

Case 2

- 30 yo female with T1D and bipolar disorder presents with 3/52 or pruritis, pale stools, dark urine and abdominal pain
- Her medications include quetiapine, lithium and insulin
- On examination

She had scleral icterus

Normal skin turgor

JVP not raised and no peripheral oedema

Clear lung fields and HSD no added

No organomegaly

Laboratory results

- AST 144 (0 – 45), ALT 212 (0 – 45), ALP 2,056 (40 – 110), bilirubin 205 (<25)
- Na 119, K 4.4, urea 4.3, creatinine 88 umol/L, glucose 13.2
- Serum osmolality 285 (normal 275 - 290)
- Urine osmolality 434, urine Na 62
- Total serum proteins 51 (66 – 84)
- Ethanol level negative
- No lipemia

Non-hypotonic hyponatraemia
Obstructive liver dysfunction

Which one of the following will most likely reveal the cause of hyponatraemia?

A. Plasma lithium level
B. Repeat serum sodium after stopping quetiapine
C. Serum triglycerides
D. Serum cholesterol
E. Abdominal ultrasound

Non-hypotonic hyponatraemia

- Serum Na 119; plasma osmolality 285
- urea 4.3, glucose 13.2

- Calculate osmolality:

  2 (Na + K) + urea + glucose

  2 X (119 + 4.4) + 4.3 + 13.2 = 264.3 (difference of -21)

Osmolar gap is the difference between the measured and calculated serum osmolalities. The normal range is 0 – 15.

Osmolar gap in non-hypotonic hyponatraemia
Causes

Within the normal osmolar gap of 0 – 15

- Endogenous
  - High urea
  - Hyperglycaemia

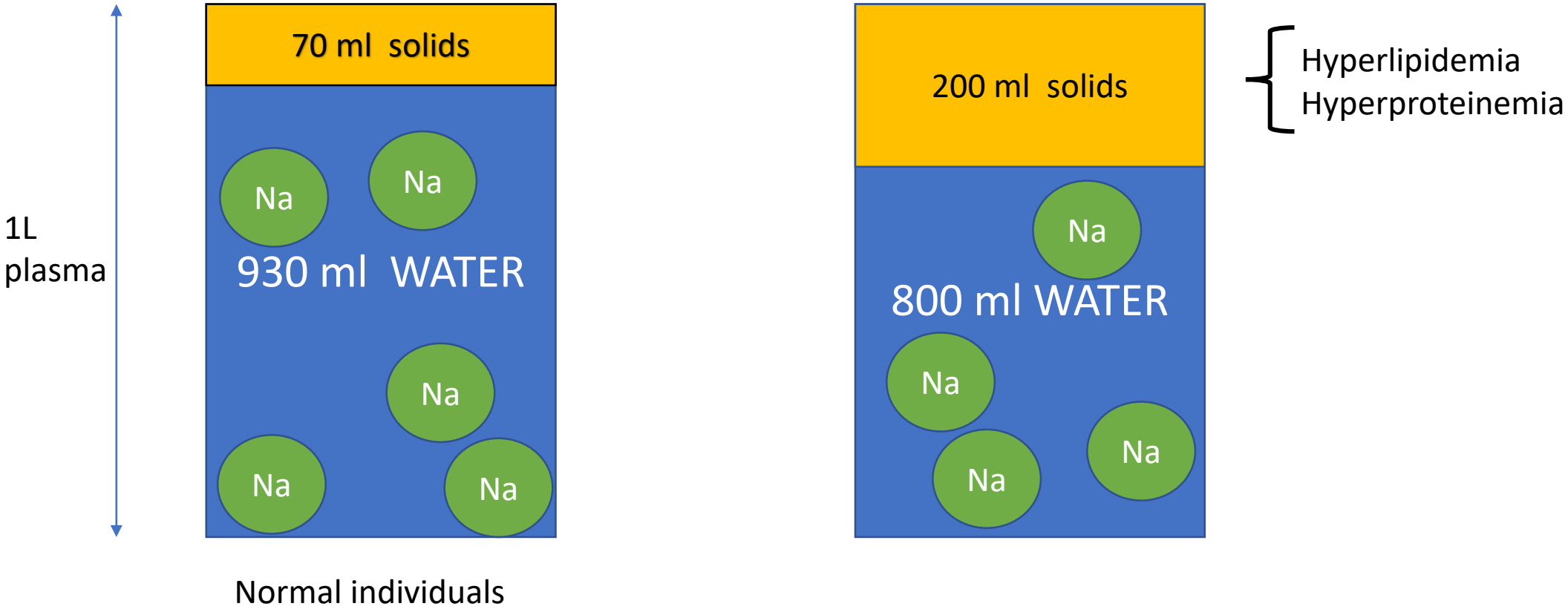
Increased osmolar gap >15

- Extra solutes
  - Ethanol
  - Methanol
  - Ethylene glycol
  - Acetone
  - Mannitol
  - IgG infusion

- Pseudohyponatraemia in the setting of hyperlipidemia or hyperprotenemia

Pseudohyponatraemia

- Serum sodium concentration is measured per L of serum, not serum water (Indirect ISE)



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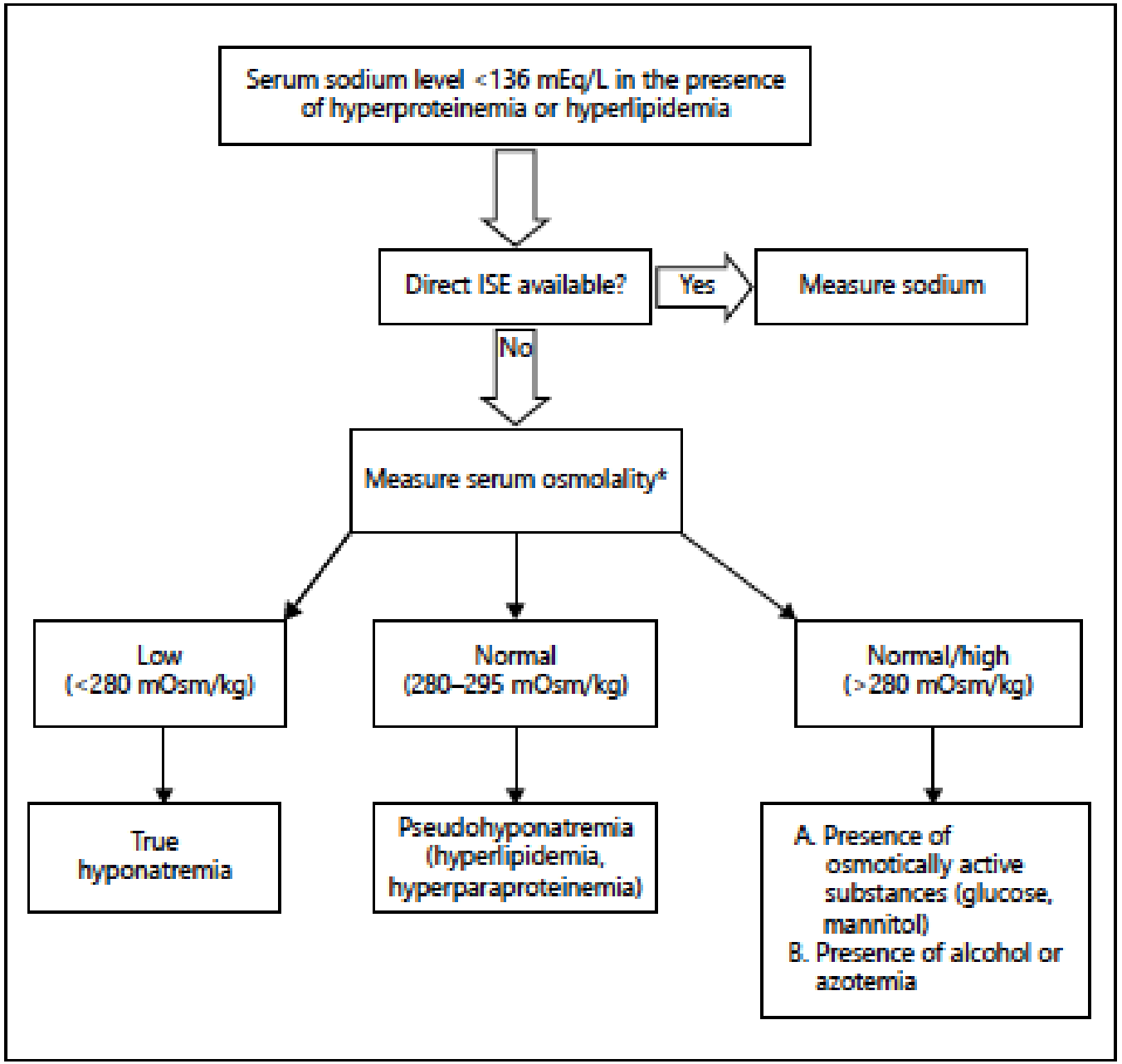
Which one of the following will most likely reveal the cause of hyponatraemia?

A. Plasma lithium level → *associated DI and hypernatraemia*
B. Repeat serum sodium after stopping quetiapine → *SIADH, hypotonic hyponatraemia*
C. Serum triglycerides
D. Serum cholesterol
E. Abdominal ultrasound → *identify cause of obstructive jaundice*

Pseudohyponatraemia & hyperlipidemia

- Associated with increased TG-rich chylomicrons, usually with visible turbidity
  - Direct potentiometry usually eliminates artifact
  - Ultracentrifuge before indirect potentiometry
- Hypertriglyceridemia observed in patients with pancreatitis and DKA

- In biliary obstruction/cholestatic disease, there is a reflux of unesterified cholesterol and phospholipids in the circulation.
- Liproprotein X contributes for high % of hypercholesterolemia
- Not usually associated with turbidity



Am J Nephrol 2013; 38: 50 -57

Summary

- SIADH hyponatraemia
  - Exclude inciting drugs
  - Important to exclude endocrine causes, particularly cortisol and severe thyroid deficiency
- Synacthen stimulation test can be misleading
- Recognize pseudohyponatraemia
  - Use direct potentiometry