Disorders of Plasma Sodium

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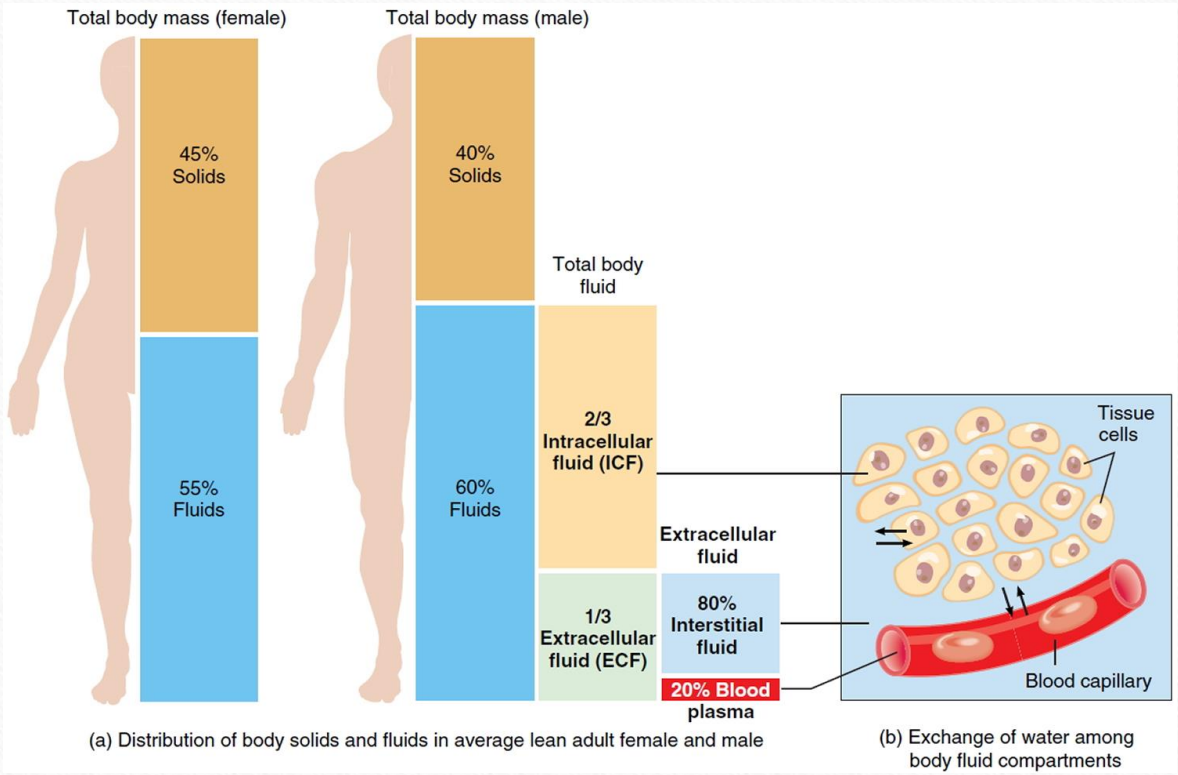
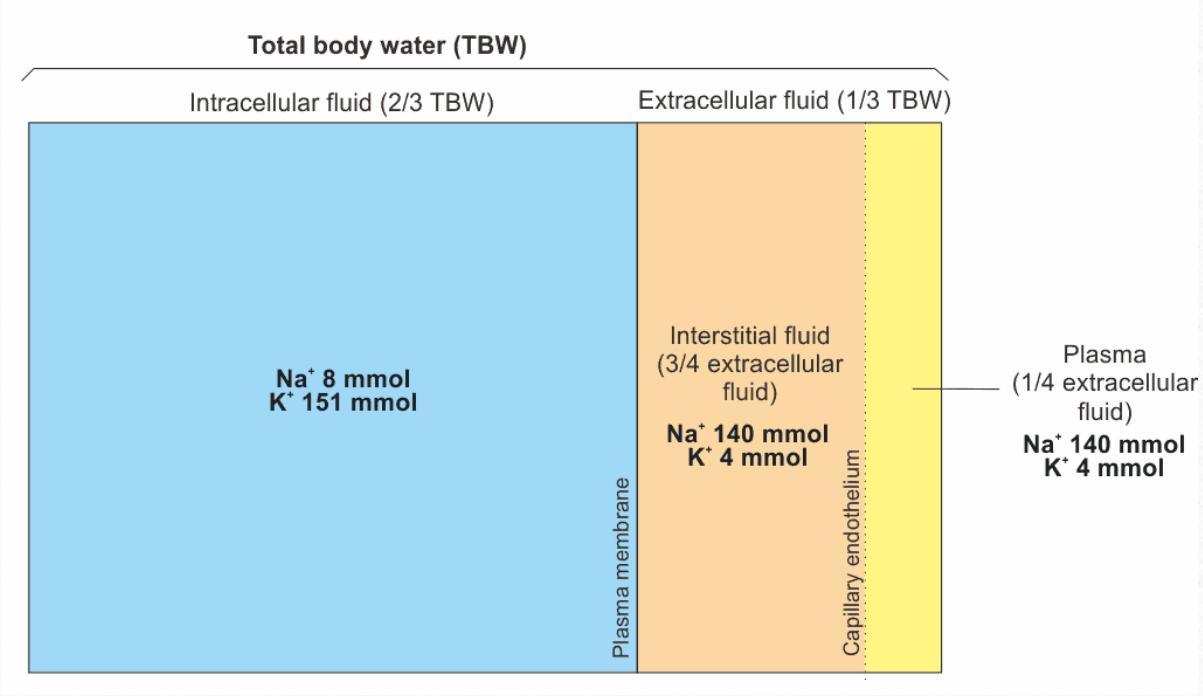
Objectives of the presentation

- Short review on the body regulation of the plasma sodium.
- Discuss various etiologies of sodium disorders.
- Understand the diagnostic approach to hyponatremia and hypernatremia.
- Learn the basic management of sodium disorder.

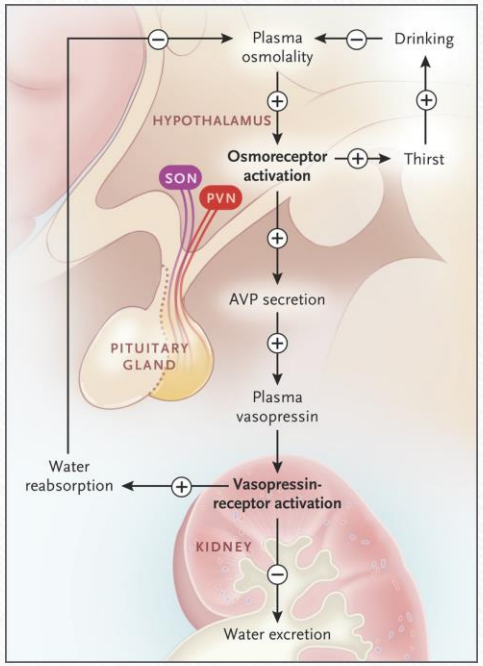
Plasma Sodium Concentration and the Electrolyte and Water Content of the Body



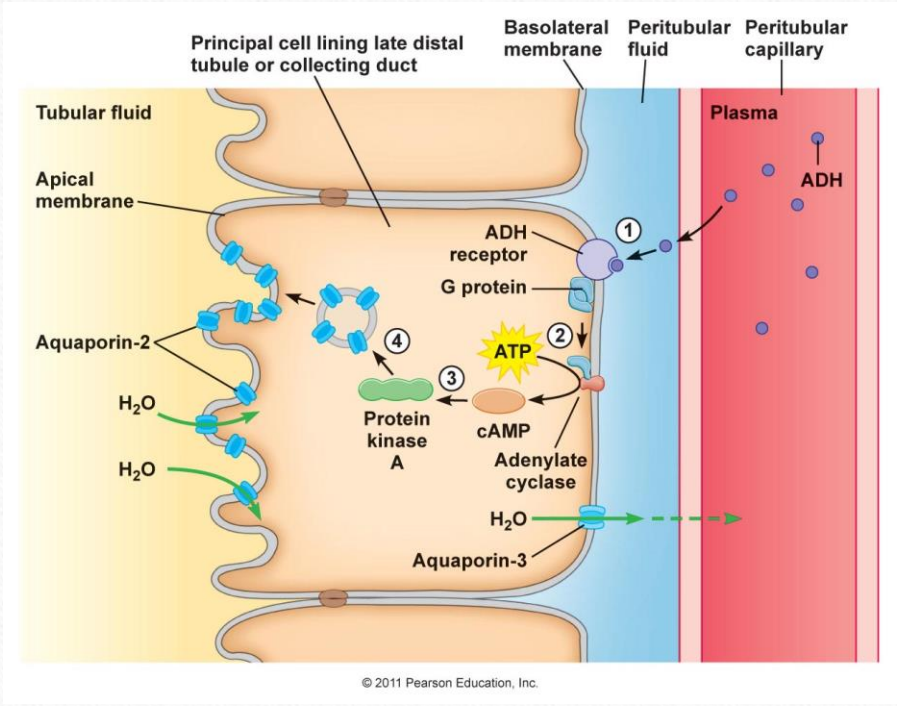
Plasma Sodium Concentration and the Electrolyte and Water Content of the Body



Hypothalamic-pituitary axis to influence water intake through thirst and water excretion via the effect of vasopressin, or antidiuretic hormone, on renal collecting duct water permeability



Paraventricular nucleus (PVN), Supraoptic nucleus (SON)



Hypo/Hypernatremia- how does it happen?

Normal sodium concentration = $\frac{Na}{H_20}$

Hyponatremia = $\frac{Na}{H_2O}$ Or $\frac{Na}{H_2O}$

Hyponatremia

- Hyponatremia is common findings in the elderly.
  - Inpatient (15-20%)
  - Outpatient (7-11%) settings.

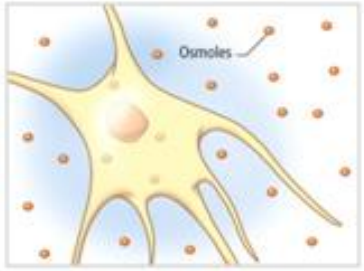
Plasma osmolality (mosm/kg) = 2 serum Sodium + Serum Urea (mmol/l) + plasma glucose (mmol/l)

Adverse Outcomes Associated With Chronic Mild to Moderate Hyponatremia

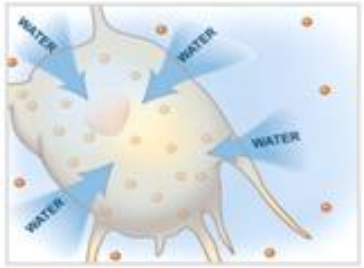
- Cognitive impairment and decline
- Falls
- Fractures and osteoporosis
- Gait instability
- Mortality
- Calcium-forming kidney stones

Hyponatremia Importance

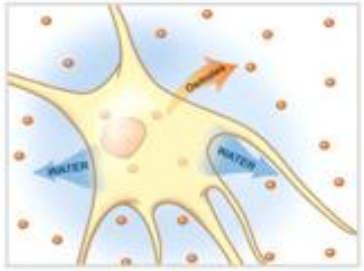
- The most common electrolyte disorder encountered in clinical practice
- Two kinds of problems?
  - Complications due to hyponatremia
  - Complications due to overly rapid correction of hyponatremia



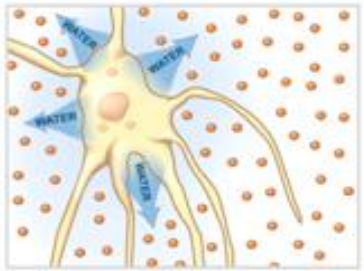
Normal State



Acute Hyponatremia

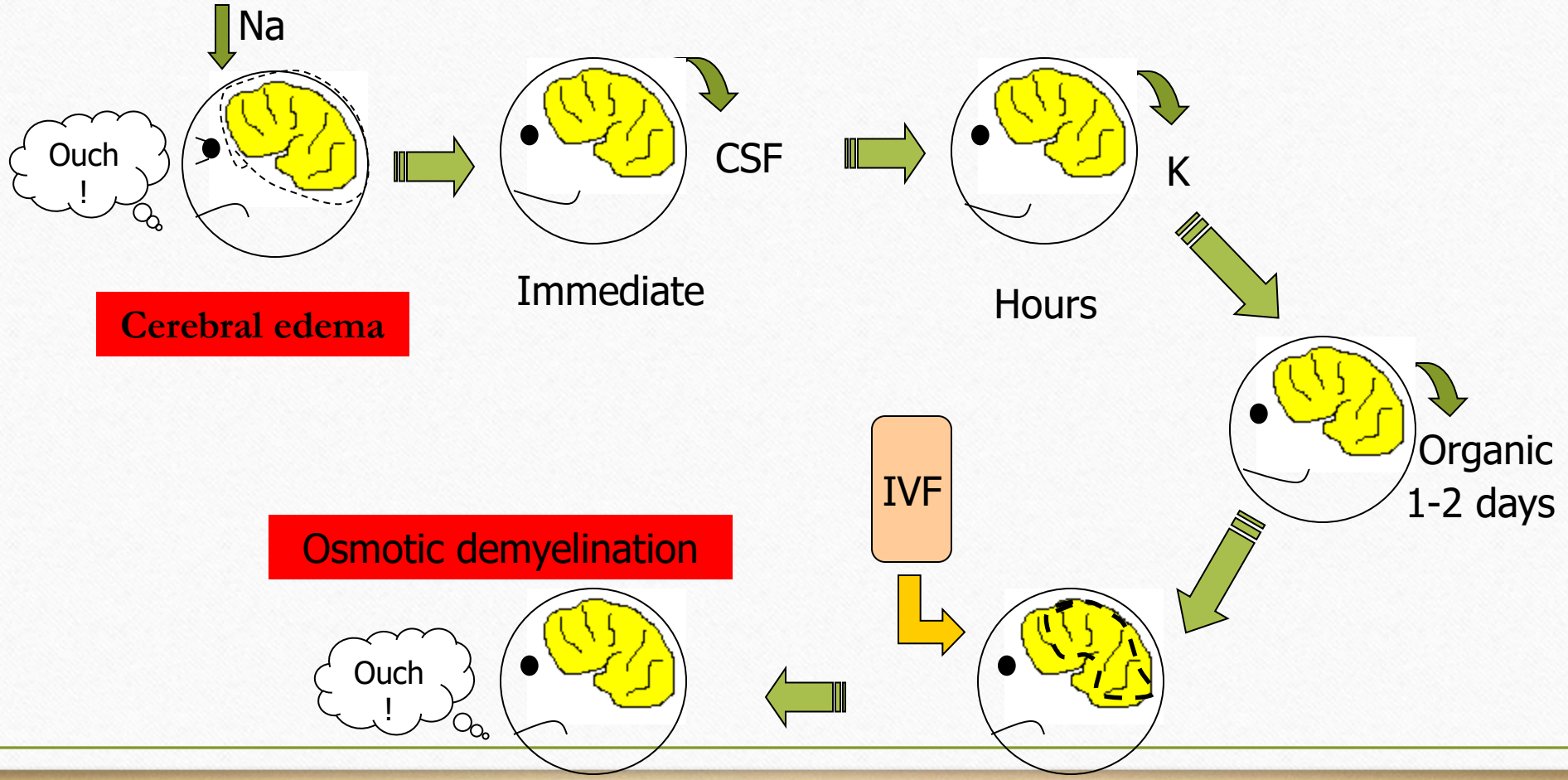


Adaptation



Overly aggressive Rx

Adaptations to hyponatremia



Classification Based on Severity of Hyponatremia

- **Mild:** Serum sodium concentration of 130-135 mEq/L
- **Moderate**: Serum sodium concentration of 120-129 mEq/L
- **Severe:** Serum sodium concentration of <120 mEq/L; may occur at <125 mEq/L

Classification Based on Tonicity

- **Hypotonic Hyponatremia (True Hyponatremia)**
  - **Serum osmolality of <275 mOsm/kg H2O**
- **Isotonic Hyponatremia**
  - **Serum osmolality of 275-295 mOsm/kg H2O**
- **Hypertonic Hyponatremia**
  - **Serum osmolality of >295 mOsm/kg H2O**

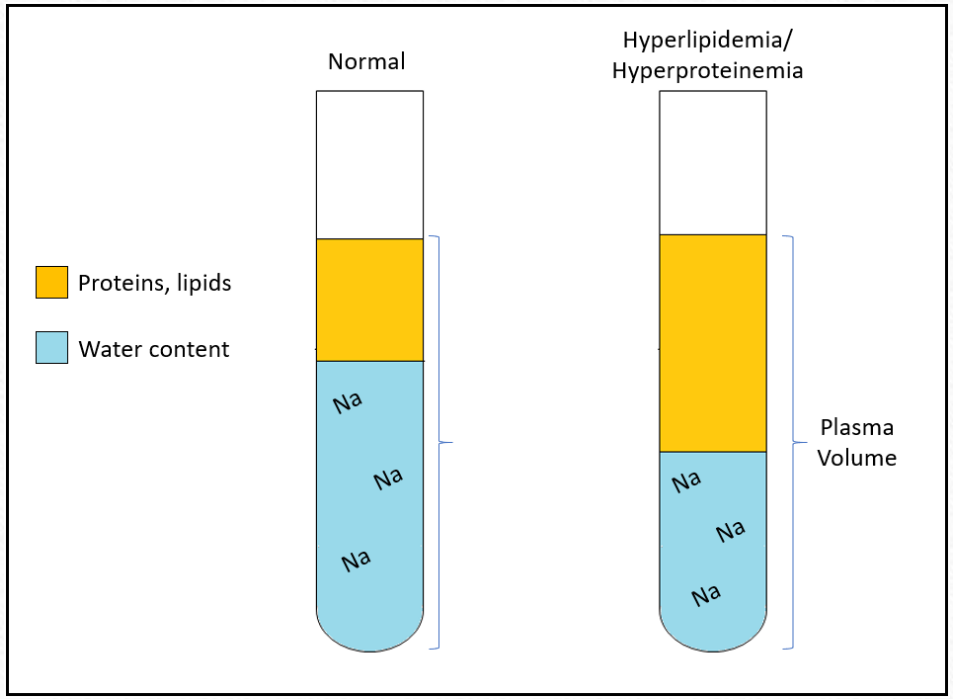
Classification Based on Duration

- **Acute:**
  - Hyponatremia that has developed over a period of <48 hours
  - The main pathologic consequence is the development of cerebral edema that may lead to raised intracranial pressure, cerebral herniation, hypoxia and even death
- **Chronic**
  - Hyponatremia that has been present for ≥48 hours or the duration is unclear
  - Due to the presence of cerebral adaptive mechanisms, many patients exhibit no or minor symptoms

Symptoms and signs of hyponatremia

- None
- Headache
- Lethargy
- Dizziness and ataxia
- Confusion
- Psychosis
- Seizure
- Coma

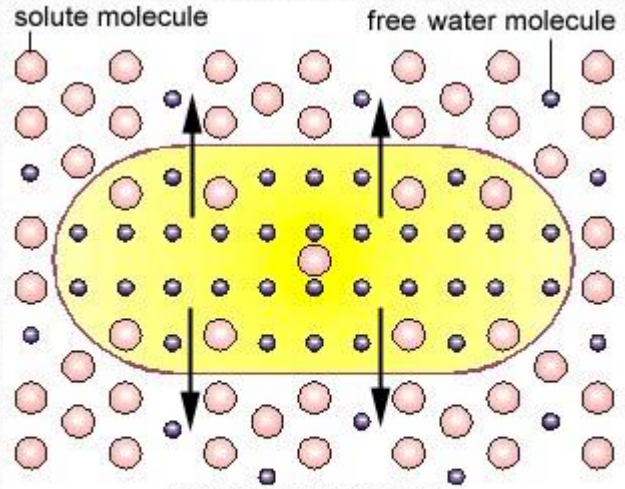
Isotonic hyponatremia or Pseudo-hyponatremia



- Serum multianalyzers measure [Na+] using indirect potentiometry and specimen dilution.
- assumes that water constitutes 93% of plasma.
- High plasma lipid or protein con. will lower the aqueous contribution to plasma volume, leading to a falsely decreased calculated [Na+] value.

Hypertonic hyponatremia (Translocational hyponatremia)

- Hyponatremia combined with plasma tonicity > 295
- Most commonly observed in hyperglycemia
- The correction factor is a 1.6 mmol/L decrease in serum Na for every 5.6 mmol per L increase in glucose.
- Other causes: Mannitol and radiocontrast.



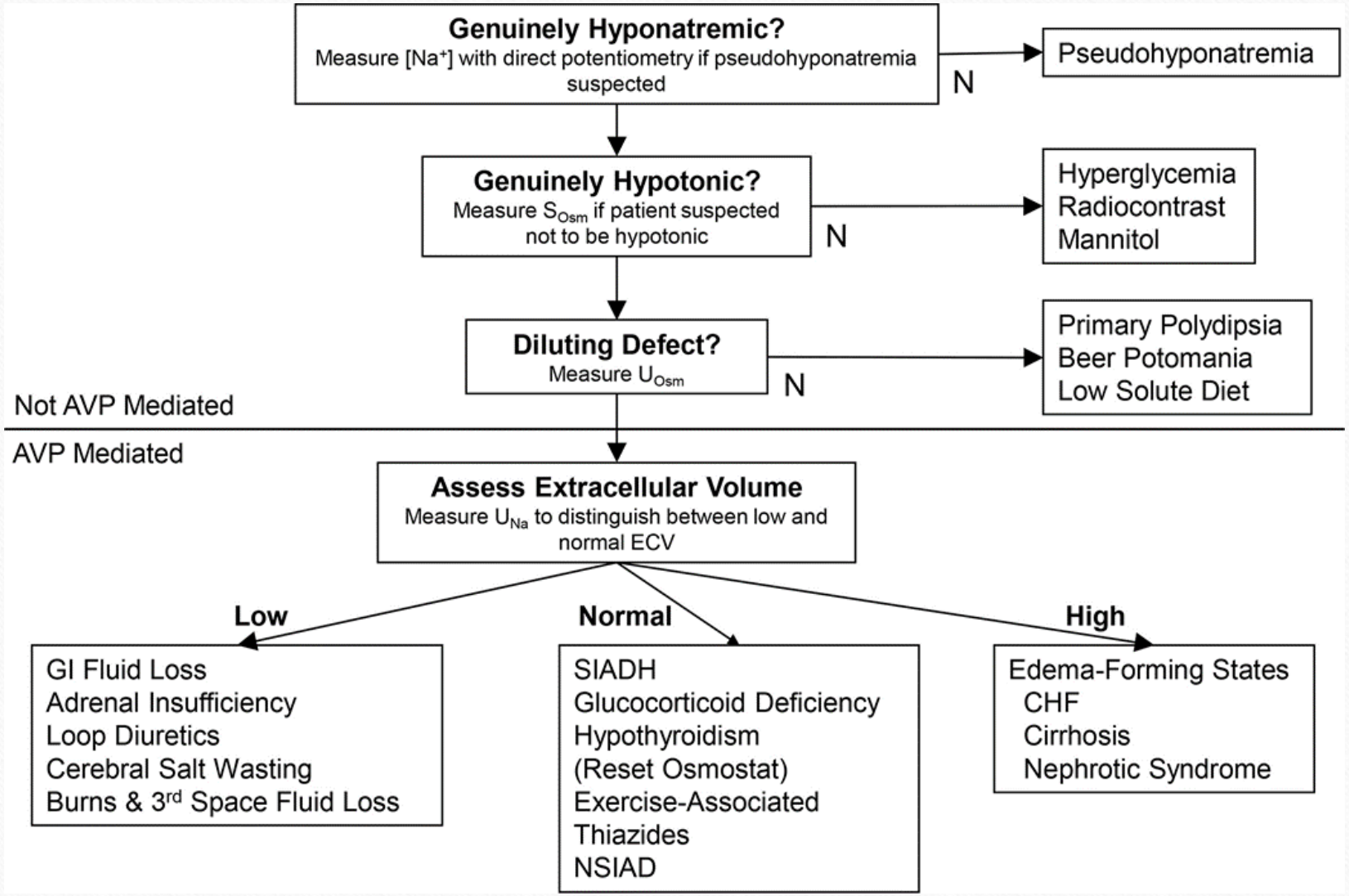
Hypertonic Environment:
The solute concentration is greater outside the cell; the free water concentration is greater inside. Free water flows out of the cell.

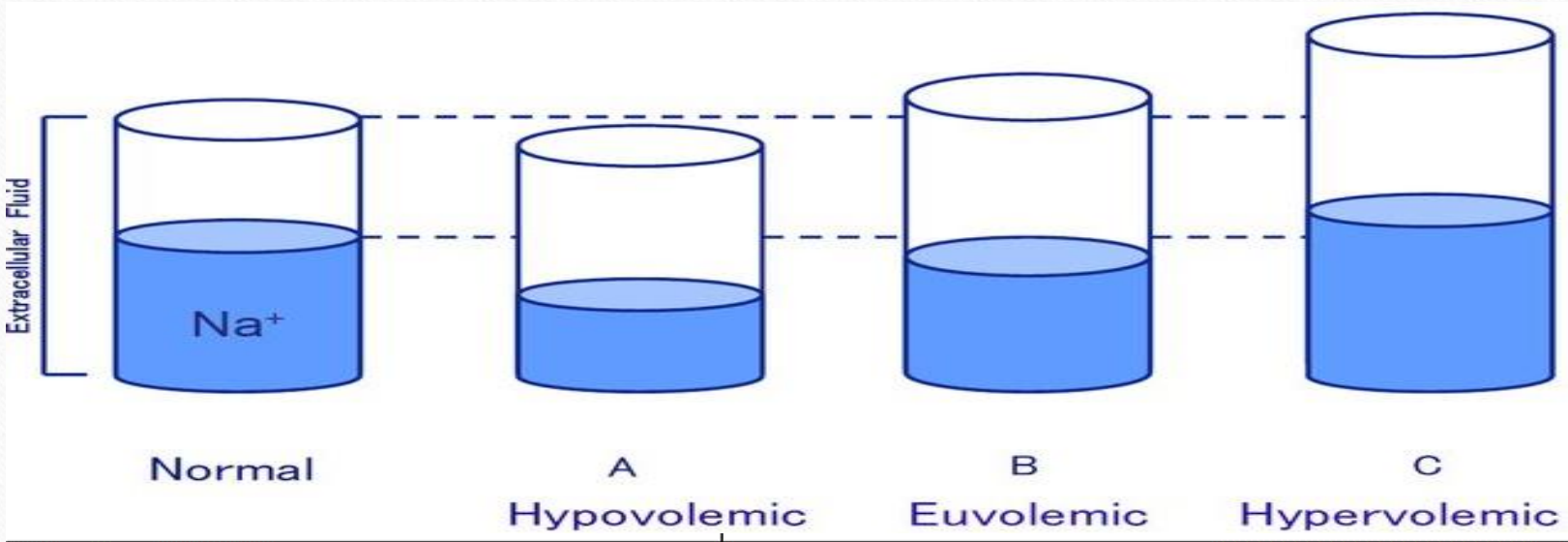
Hypotonic hyponatremia

- Serum osmolality < 275 mOsm/kg H2O

Hypotonic Hyponatremia and Preserved Urinary Dilution

- **Low Urine osmolality** indicative of maximally dilute urine—typically <100 mOsm/kg H2O
- Vasopressin is appropriately suppress.
- Causes:
  - Primary polydipsia
  - "tea-and-toast" diet
  - Beer potomania: excessive intake of alcohol, particularly beer, together with poor dietary solute intake that leads to fatigue, dizziness, and muscular weakness.


Genuinely Hyponatremic?
Measure [Na+] with direct potentiometry if pseudohyponatremia suspected
N
Pseudohyponatremia
Genuinely Hypotonic?
Measure SOsm if patient suspected not to be hypotonic
N
Hyperglycemia
Radiocontrast
Mannitol
Diluting Defect?
Measure UOsm
N
Primary Polydipsia
Beer Potomania
Low Solute Diet
Not AVP Mediated
AVP Mediated
Assess Extracellular Volume
Measure UNa to distinguish between low and normal ECV
Low
GI Fluid Loss
Adrenal Insufficiency
Loop Diuretics
Cerebral Salt Wasting
Burns & 3rd Space Fluid Loss
Normal
SIADH
Glucocorticoid Deficiency
Hypothyroidism
(Reset Osmostat)
Exercise-Associated
Thiazides
NSIAD
High
Edema-Forming States
CHF
Cirrhosis
Nephrotic Syndrome



AVP Mediated

Assess Extracellular Volume
Measure U_{Na} to distinguish between low and normal ECV

Low

GI Fluid Loss
Adrenal Insufficiency
Loop Diuretics
Cerebral Salt Wasting
Burns & 3rd Space Fluid Loss

Normal

SIADH
Glucocorticoid Deficiency
Hypothyroidism
(Reset Osmostat)
Exercise-Associated
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High

Edema-Forming States
CHF
Cirrhosis
Nephrotic Syndrome

Hypotonic Hyponatremia With Impaired Urinary Dilution (High U.Osmol)

Classification Based on Extracellular Volume Status

- Hypovolemic hyponatremia
- Euvolemic hyponatremia
- Hypervolemic hyponatremia

Hypovolemic Hyponatremia

- Decreased total body water with greater decrease in sodium level
- Extracellular fluid losses can occur from kidney, gastrointestinal tract or the skin
- Most common cause is thiazide diuretic therapy; other causes are Addison's disease and cerebral salt wasting
- Signs and symptoms associated with volume depletion:
  - Dry mucous membranes, . Decreased skin turgor . Vomiting . Diarrhea
  - Tachycardia . Hypotension
- Elevated blood urea nitrogen-to-creatinine ratio and uric acid level
- Urinary sodium usually <20 mEq/L unless the kidney is the site of sodium loss

Hypervolemic Hyponatremia

- Increased total body water compared with sodium that occurs when kidneys cannot excrete water efficiently
- Common causes include heart failure, liver cirrhosis and kidney injury
- Clinical signs include:
  - Peripheral edema
  - Ascites
  - Raised jugular venous pressure
  - Pulmonary edema
  - Underlying illness
- Useful diagnostic lab findings are elevated plasma levels of brain natriuretic peptide and spot urine of <20-30 mEq/L

Euvolemic Hyponatremia

- Increased total body water with normal sodium level
- Accounts for the majority of hyponatremia cases
- Most commonly caused by syndrome of inappropriate antidiuretic hormone (SIADH)
- Other causes are hypothyroidism and glucocorticoid deficiency
- Clinical signs depend on the underlying illness
- Diagnostic lab findings:
  - Low serum uric acid levels
  - Normal blood urea nitrogen-to-creatinine ratio
  - Spot urinary sodium >20 mEq/L

Diagnostic criteria for SIADH

Essential features

- **Decreased serum osmolality (<275 mOsm/kg)**
- **Urinary osmolality >100 mOsm/kg during hypotonicity of the serum**
- **Clinical euvolaemia**
- **Urinary sodium >40 mmol/L with normal dietary salt intake**
- **Normal thyroid and adrenal function**
- **No recent use of diuretics**

Supplemental features

- Low Serum uric acid
- Low normal Serum urea & serum creatinine
- Fractional sodium excretion >1%, fractional urea excretion >55%
- Failure to correct hyponatraemia after 0.9% saline infusion
- Correction of hyponatraemia through fluid restriction
- Abnormal water loading test (excretion <80% of a 20 mL/kg water load in 4 h)
- Elevated vasopressin levels despite hypotonicity and clinical euvolaemiaa

Causes of SAIDH

- Other stimuli (≈ SIADH)
  - CNS disease (virtually any)
  - Lung disease (virtually any)
  - Neoplasm
    - Small cell Ca lung, renal cell Ca, thymoma, etc.
  - Drugs
    - Long list (e.g., anti-depressant, anti-psychotic, anti-epilepetic……)
  - Endocrinopathies
    - Deficiency of thyroid hormone and cortisol
  - "Stress"
    - Pain, surgery, nausea

How to approach a case of hyponatremia?

- Called by ER doctor to asses a patient with serum sodium of

123 mmol/l

Approach to hyponatremia

1. Confirm the patient truly has a hypo-osmolar state by checking serum osmolality
2. Assess for serious signs or symptoms suggesting cerebral edema
3. Determine the duration of development of hyponatremia (less or more than 48 hours)
4. Assess the patient's extracellular fluid volume status using clinical examination and laboratory testing
5. Check the urine osmolality to see if the urine is appropriately dilute (< 100 mOsm/kg) or inappropriately concentrated (≥ 100 mOsm/kg)
6. Assess for underlying causes of hyponatremia
7. Look for drugs the patient is taking that potentiate antidiuretic hormone action (e.g., selective serotonin uptake inhibitors)

History

- Inquire from patient's history possible causes of hyponatremia
- History of cardiac, cancer, pulmonary, endocrine, gastrointestinal, neurologic and renal diseases
- History of electrolyte-rich fluid loss (eg vomiting, diarrhea or diuretic therapy)
- History of low protein intake and/or high fluid intake
- Medications used (eg diuretics, Carbamazepine, selective serotonin reuptake inhibitors)
- Alcohol and illicit drug use (eg beer, 3,4-methylenedioxymethamphetamine/"Ecstasy")
- For athletes, training regimens because high-endurance activities can cause hyponatremia
- History of very recent surgery

Physical Examination

- The patient should be examined to determine volume status
- Polyuria is most common in primary polydipsia
- Signs of volume depletion include:
  - Low urine output . Weight loss . Orthostatic hypotension . Decreased jugular venous pressure
  - Poor skin turgor, Dry mucus membranes . Absence of axillary sweat . Absence of edema.
- Signs of volume overload include:
  - Edema and/or ascites . Rales or crackles on lung auscultation
  - Significant weight gain . Raised jugular venous pressure.

Management of hyponatremia

Acute symptomatic hyponatremia

- The rate of sodium correction should not exceed 6 to 8 mEq/L in 24 hours or 12 to 14 mmol/L in 48 hours
- Hypertonic Saline
- Supportive care: ICU admission and close monitoring
- Treat the underlying cause

Chronic (>48hours)

1. Hypovolemic Hyponatremia
    - 1st isotonic fluid infusion
    - plus treat underlying cause
2. Hypervolemic Hyponatremia
    - Fluid restriction
    - plus treat underlying cause
    - adjunct loop diuretic or spironolactone
    - Vasopressin receptor antagonist +

Euvolemic Hyponatremia

- Careful monitoring during treatment
- Fluid restriction
- Loop diuretics plus salt tablets to replace urinary sodium losses
- Demeclocycline
- Vasopressin receptor antagonists
- Enhance solute intake if poor nutrition
- Discontinue medications associated with syndrome of inappropriate antidiuretic hormone secretion (SIADH)
- Treatment of underlying carcinoma if ADH-secreting tumor
- Treatment of underlying condition associated with SIADH (eg, antibiotics for pneumonia)
- Treatment of endocrinopathy (eg, hypothyroidism)

Hypernatremia

Hypernatremia

Hypernatremia, serum sodium concentration of 145 mmol/L a state of total body water deficiency absolute or relative to total body sodium.

Pathophysiology

- Hypernatremia is caused by:
  - Net water loss (increased loss or decreased intake) (e.g., diabetes insipidus [DI], osmotic diarrhea)
  - Rarely, sodium gain (Sodium containing fluids e.g., IV Fluid)
- Patients at increased risk:
  - Impaired thirst mechanism or
  - Restricted access to water (e.g., those with altered mental status, intubated patients, infants, older adults).

Hypernatremia

- Hypernatremia is common in ICU, the older nursing home resident, usually with dementia and infant.
  - Inpatient (1%)
  - Outpatient (2%)

- Clinical presentation:
  - Often asymptomatic
  - Irritability, nausea, weakness, altered mental status
  - Brain shrinkage, resulting in vascular rupture and intracranial bleeding.

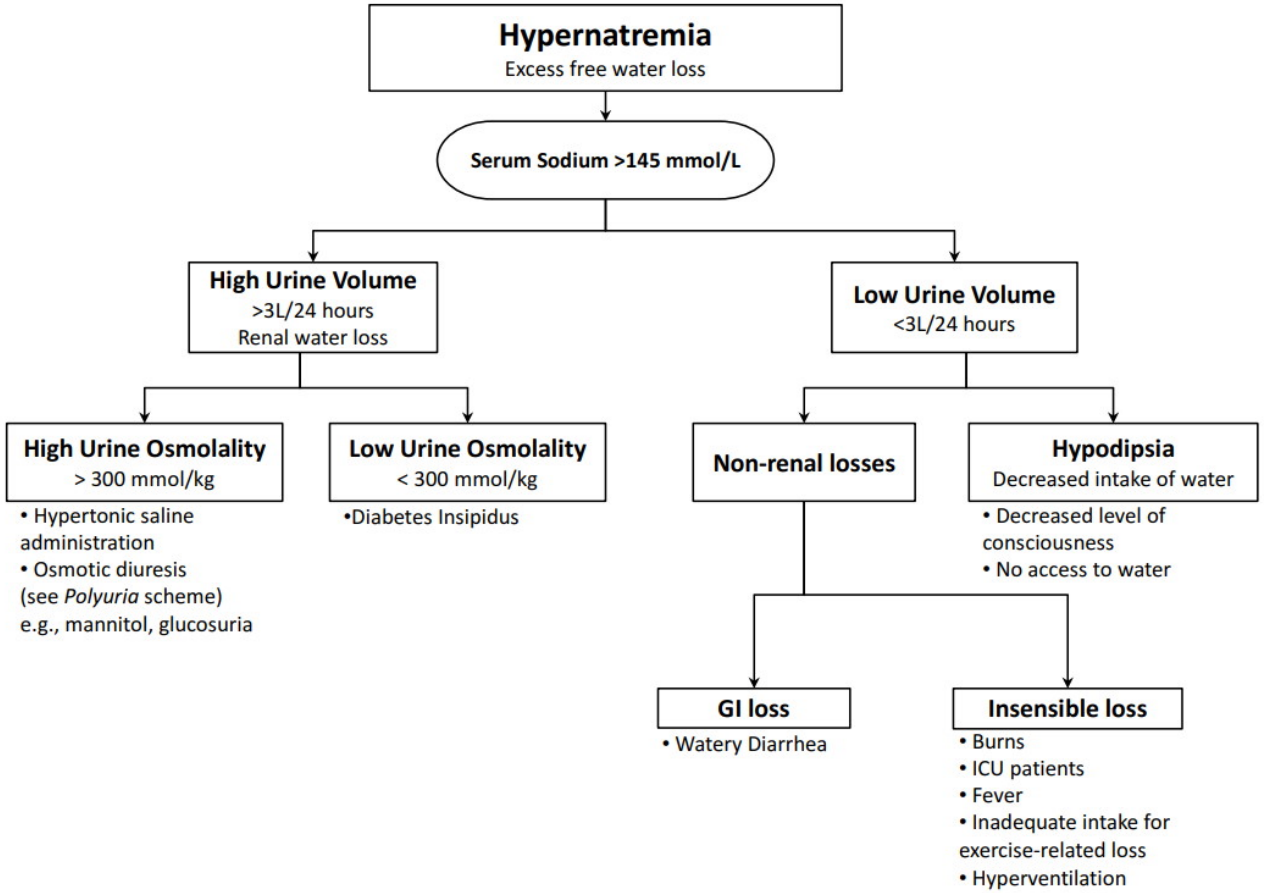
Approach

- Detailed History AND Urine Osmolality can reveal most of the cases:
  - Water loss (GI loss or Insensible loss or Polyuria)

+

  - Lack of access to water or Primary neurological disease

Hypernatremia



Management

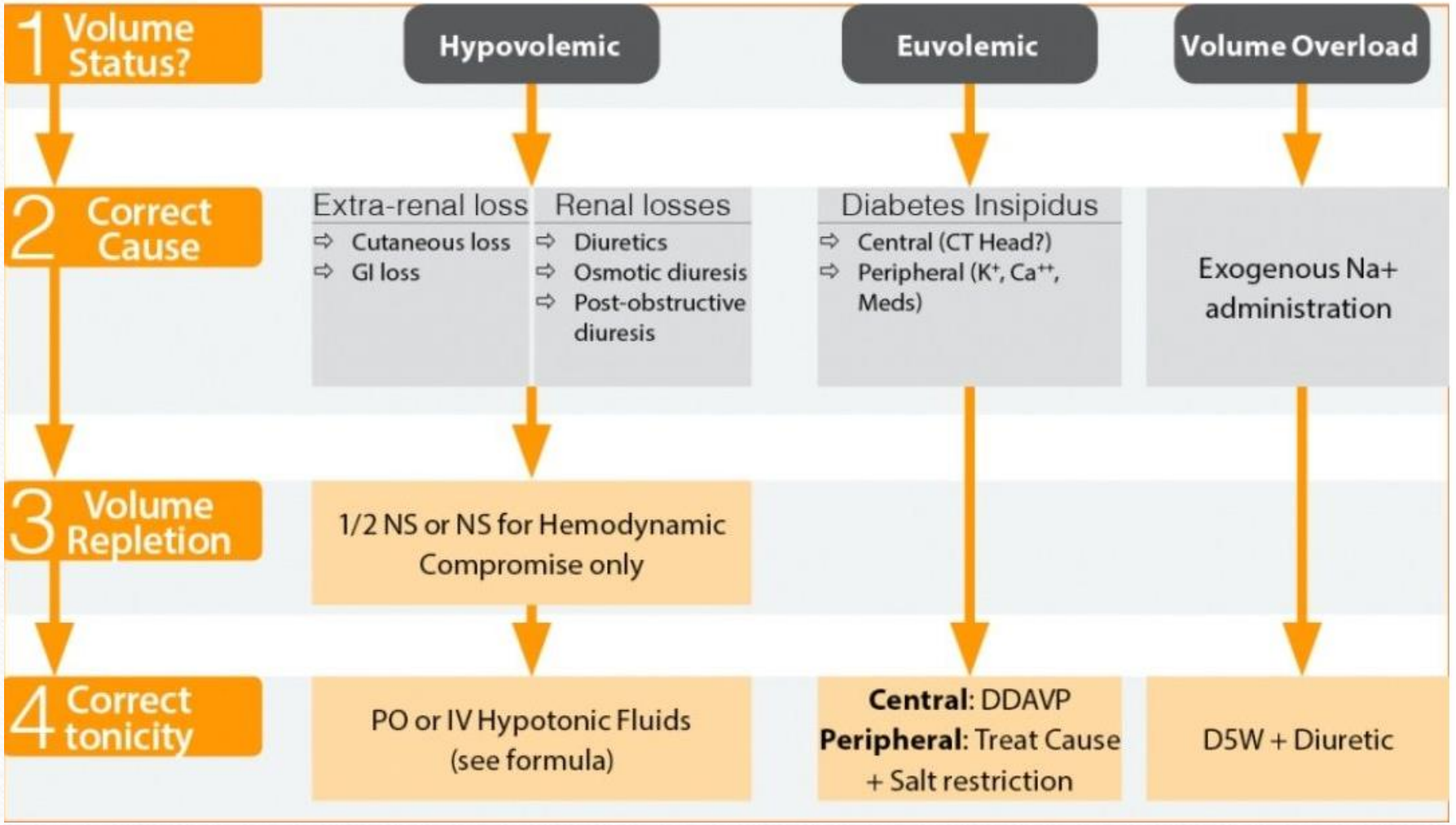
- Free Water Deficit (FWD) = TBW x (serum [Na] -140) / 140
  - TBW = wt (kg) x 0.6 (male) or 0.5 (female). If elderly use, 0.5 (male) and 0.45 (female)

  - **E.g. Serum Sodium 150 mmol/l in 70 Year old gentleman with a weight of 60 Kg**
    - TBW = 0.5 x 60 = 30 L
    - FWD = 30 L x (150 -140) /140)= 2,1 L

Management of Hypernatremia

- Hypernatremia for ,48 hours is considered acute; sodium correction rate can be up to 1 mEq/L per hour.
- Hypernatremia of 2 days or unknown duration is considered chronic and should be corrected gradually, ,0.5 mEq/L per hour (approximately 10 mEq/L per day).
- The initial step in management is **identification of the cause of hypernatremia** and its correction (Insulin, Anti-Pyretics, DDAVP…etc).

Hypernatremia



Questions

Case 1

a 48-year-old man, is a heavy cigarette smoker who presents with increasing cough, hemoptysis, and drowsiness. He is taking no medications. During the last year, he lost approximately 10 kg, and his current weight is 65 kgs. His mucous membranes are moist, skin turgor is normal, and he does not have an orthostatic fall in blood pressure. Other than nicotine stains on his right index and middle fingers, his physical examination is normal.

Chest radiograph reveals a 4-cm right lung mass. His serum sodium is 123 mEq/L, potassium is 4.3 mEq/L, and creatinine is 80 umol/l.

Which of the following is your initial investigation?

(A) Serum osmolality

(B) Serum uric acid

(C) Urine osmolality

(D) Urine sodium

Is this a “true” hyponatremia?

Measured osmolality is 270 mOsm/kg H2O, What is the next step in this patient’s work up?

(A) Serum Glucose

(B) Serum uric acid

(C) Urine osmolality

(D) Urine sodium

Diagnosis?

- Urine osmolality is 600 mOsm/kg, uric acid level is 250 mmol/l (Low), and urine sodium is 45 mEq/L. Thyroid stimulating hormone and cortisol level are normal.
- The most likely diagnosis?
  - Diabetes insipidus
  - SIADH
  - Primary Polydipsia
  - Pseudohyponatremia

Diagnosis?

- SIAHD with bronchogenic carcinoma (small cell lung cancer)
  - Ectopic ADH secretion by malignant cells

Case 2. A 44-year-old man comes to the emergency department with polyuria and polydipsia. Over the past 3 days, he has noted increased urination with nearly constant thirst. Physical examination is normal.

Admission laboratory results included serum sodium of 155 mmol/L, plasma glucose of 8.3 mmol/L, and urine osmolality of 117 mosm/kg .

What is the most likely cause of the hypernatremia?

(A)Diabetes insipidus
(B)Diabetes mellitus
(C)Vomiting
(D)Primary polydipsia

Questions