Hyponatremia

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Outline

- Background / Overview of hyponatremia
- Epidemiology
- Pathogenesis
- Clinical significance
- Evaluation and diagnosis
- Treatment

Background / Overview

- Hyponatremia is define as serum Na <135 mEq/L
- The most common electrolyte disorder
- Typically a water problem not a sodium deficit problem
  - Retention of water that dilutes serum sodium level and osmolality

$$[Na^+] = \frac{Na_e + K_e}{TBW}$$

Edelman IS et al. J Clin Invest. 1958; 37(9):1236-56.

Background / Overview

Mild	130-135 mEq/L
Moderate	120-129 mEq/L
Severe	<120 mEq/L

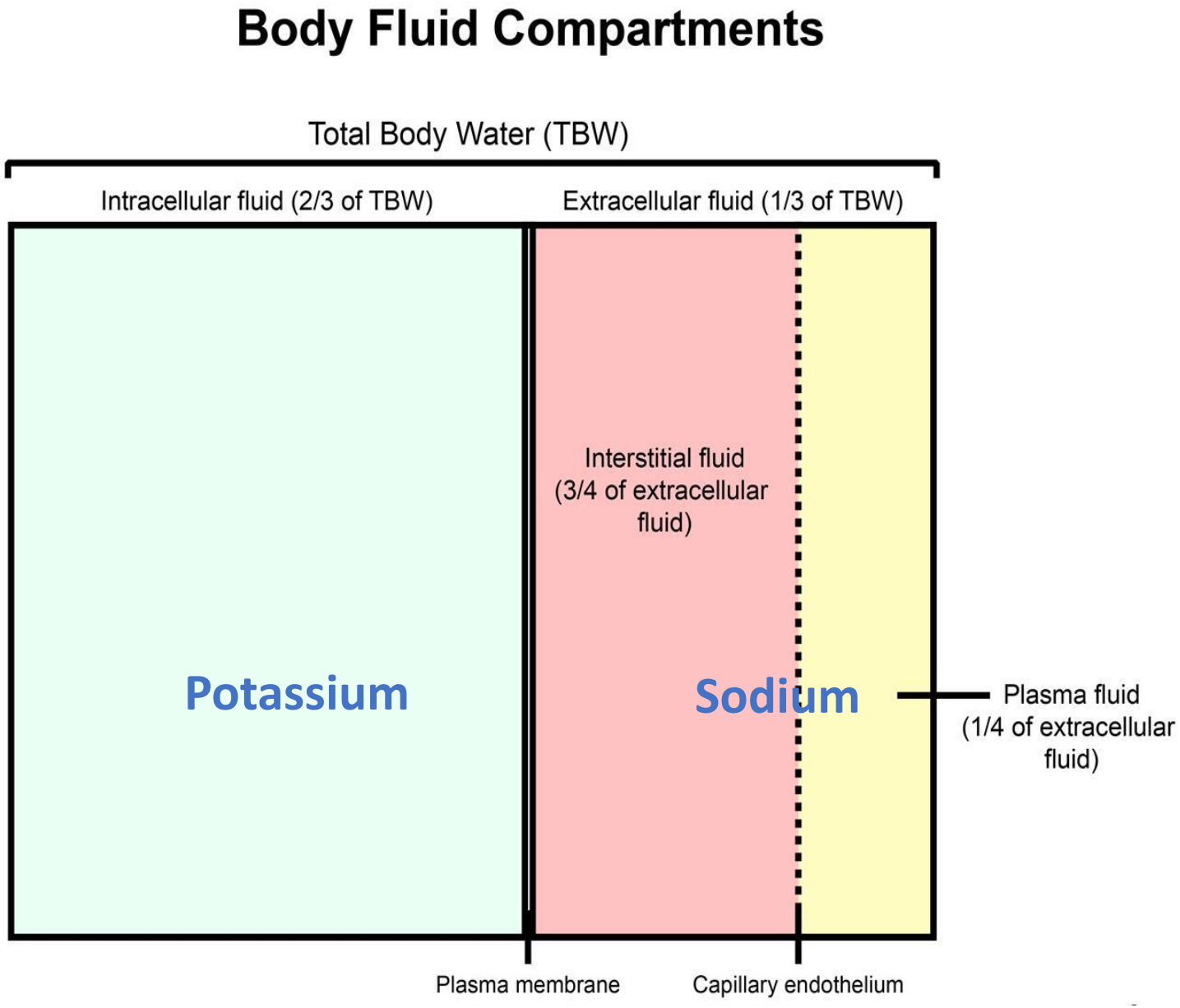
Acute	<48hrs
Chronic	>48hrs

Epidemiology

Patients	Prevalence
Adults	5%
Elderly (>65 years of age)	20%
Hospitalized patients	35%
Heart Failure	30%
Cancer or Cirrhosis	50%

Pathogenesis

- Complex, heterogenous and symptoms vary widely
- Imbalance between TBW and body solutes



Total Osmolality vs Effective Osmolality (Tonicity)

Total Osmolality

- Total number of particles in an aqueous solution
  - Normal serum osmolality 275-290 mOsm/kg

Effective Osmolality (Tonicity)

- Solutes which have the capacity to exert an osmotic force across a membrane

$$\text{Total osmolality (mOsm)} \cong 2 \cdot [Na^+] + \frac{\text{Glucose (mg/dL)}}{18} + \frac{\text{BUN (mg/dL)}}{2.8}$$

$$\text{Tonicity or effective osmolality (mOsm)} \cong 2 \cdot [Na^+] + \frac{\text{Glucose (mg/dL)}}{18}$$

Osmolality vs Effective Osmolality (Tonicity)

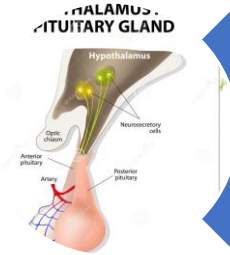
- Osmoles that do not cross the cell membrane freely are considered effective osmoles:
  - Chloride, sodium, proteins, bicarbonate, and glucose.

- Whereas those that do cross freely are termed ineffective osmoles.
  - Ex: Urea and alcohol

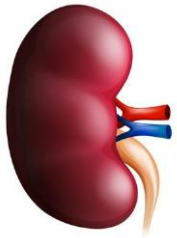
- Water is pulled from areas of low osmolality to high osmolality

What maintains serum sodium and osmolality?

Thirst stimulation



ADH Secretion



Handling of Na by kidneys

Clinical Significance

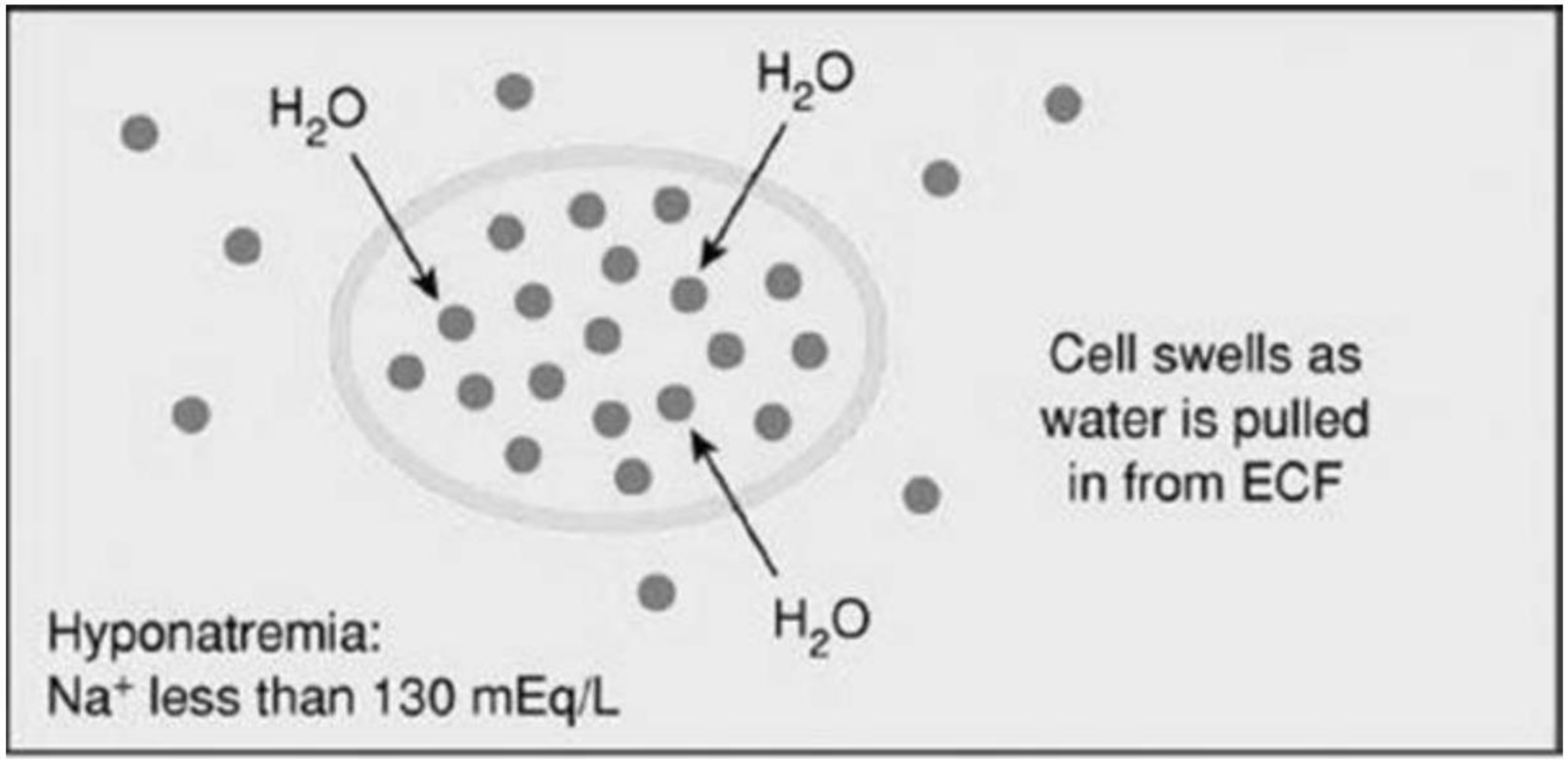
- Increased mortality
- Predictor of hepatorenal syndrome (HRS), hepatic encephalopathy, and death in patients with liver disease
- Increased risks of osteoporosis, gait instability, falls, and fractures
- Associated with marked bone loss and myocardial fibrosis
- Impaired attention, slow mentation even with mild hyponatremia

Clinical presentation

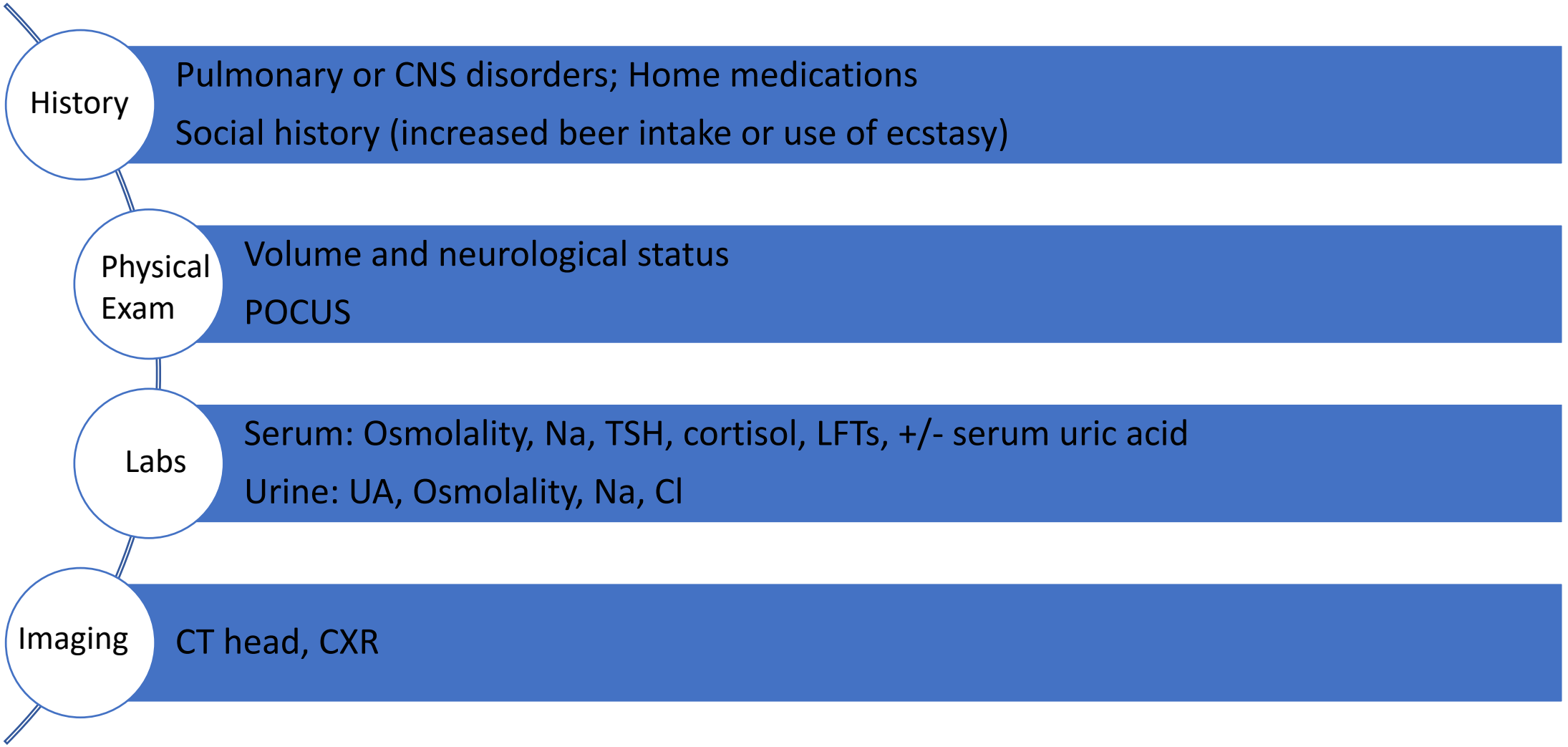
- Depends on the degree and rate of change of serum sodium level.
- Mild (Na >125): usually asymptomatic to minimally symptomatic
- Moderate: Lethargy, headache, Nausea/vomiting, disorientation, muscle cramps, reduced reflexes
- Severe: encephalopathy, seizures, coma, respiratory arrest, brainstem herniation and death

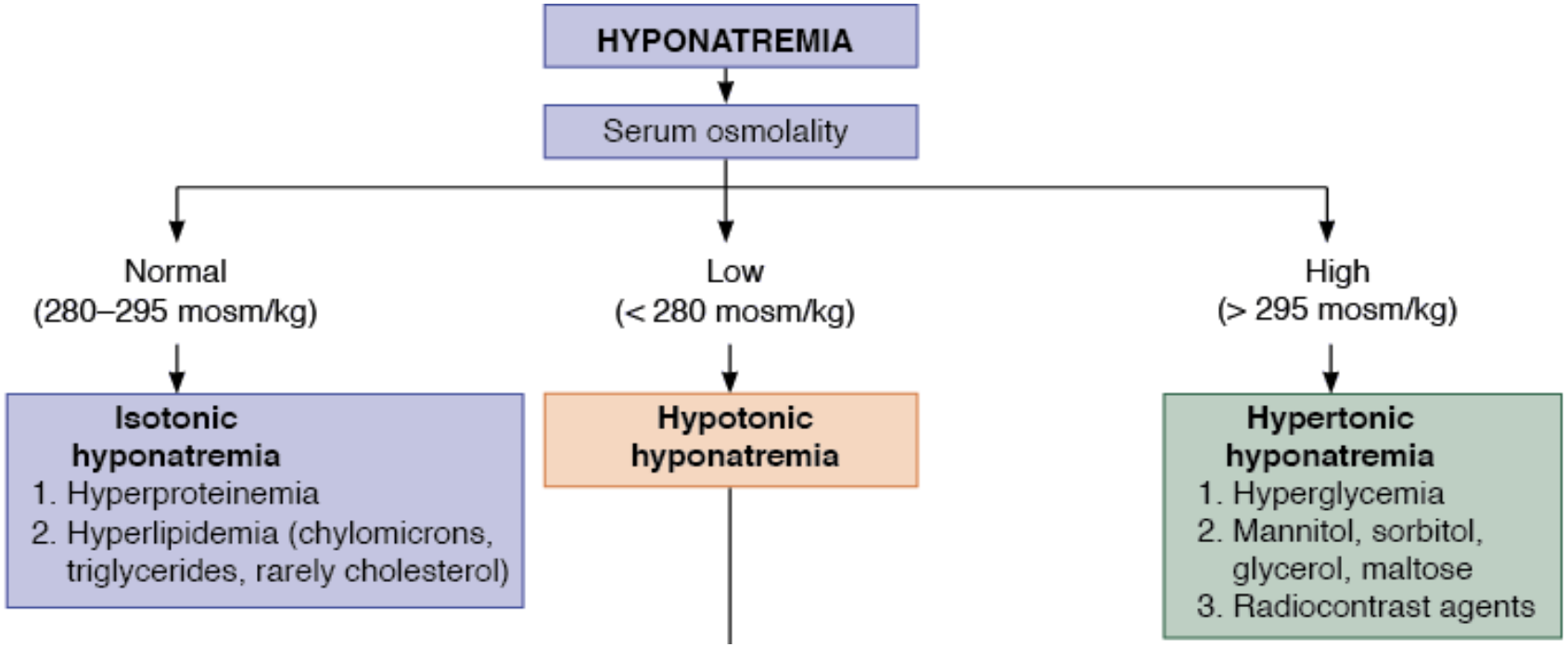
Osmotic adaptation

- Drop in Na → drop in osmolality → water shift intracellularly → cerebral edema
- Rapid adaptation → loss of Na/K/Cl-
- Slow adaptation → loss of organic osmolytes



Evaluation of Hyponatremia




HYPONATREMIA
Serum osmolality
Normal
(280–295 mosm/kg)
Low
(< 280 mosm/kg)
High
(> 295 mosm/kg)
Isotonic hyponatremia
1. Hyperproteinemia
2. Hyperlipidemia (chylomicrons, triglycerides, rarely cholesterol)
Hypotonic hyponatremia
Hypertonic hyponatremia
1. Hyperglycemia
2. Mannitol, sorbitol, glycerol, maltose
3. Radiocontrast agents

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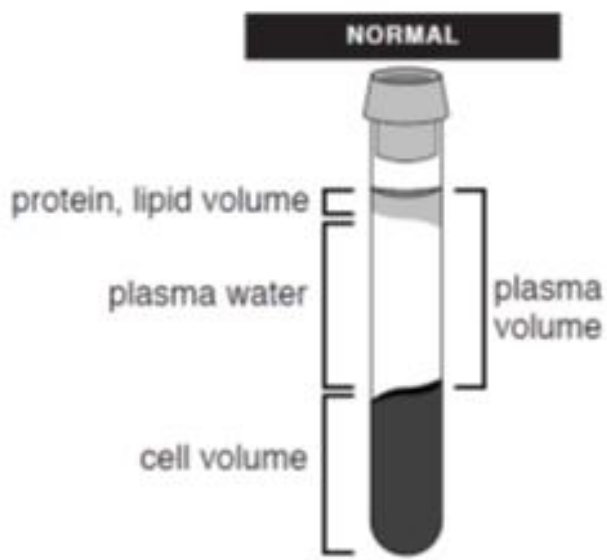
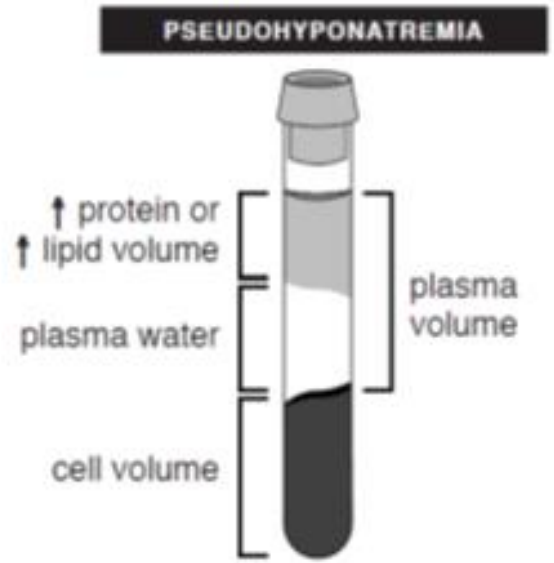




The lab reports [Na^+] as this…

$$\frac{Na^+}{\text{plasma water}}$$

but the lab actually measures this:

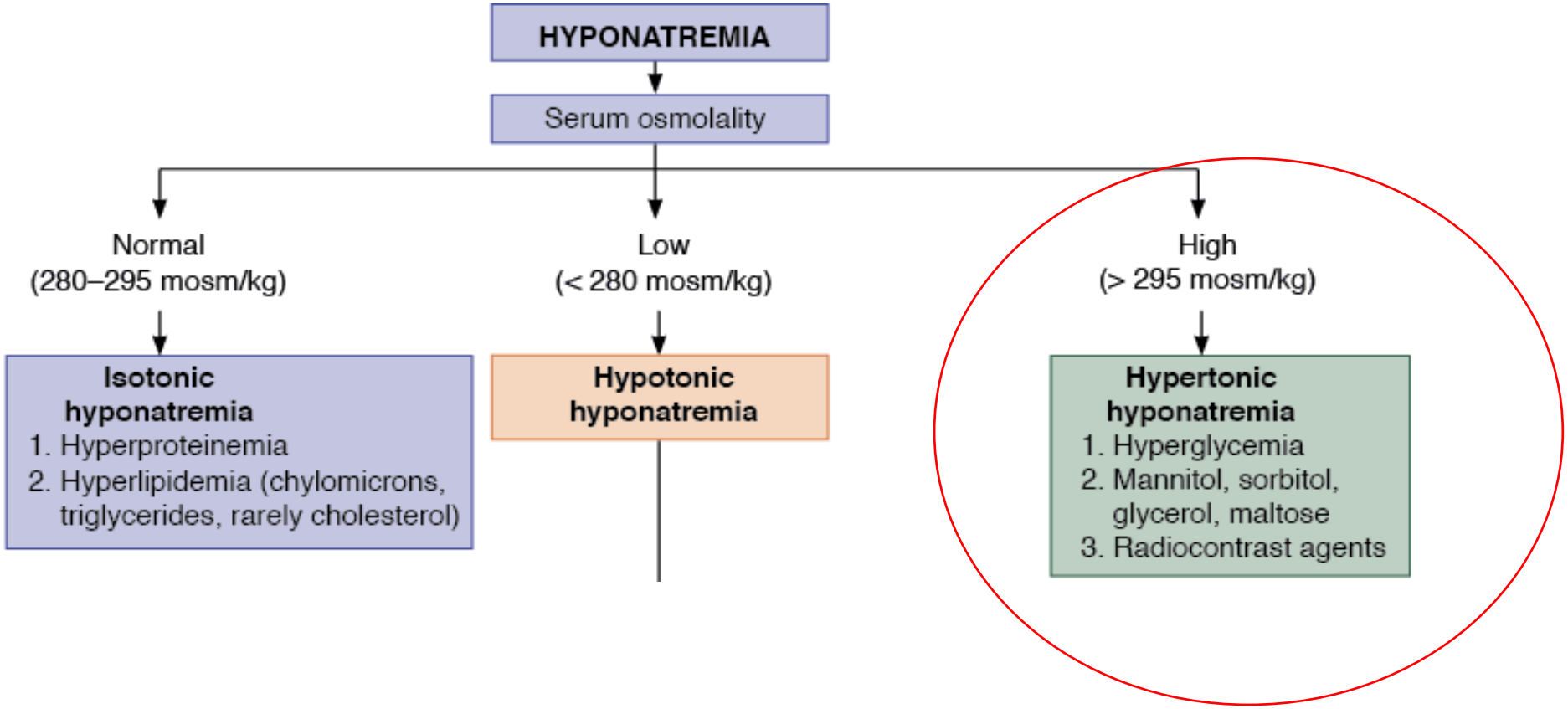
$$\frac{Na^+}{\text{plasma volume}}$$

With ↑ solute, this is normal:

$$\frac{Na^+}{\text{plasma water}}$$

but this is low:

$$\frac{Na^+}{\text{plasma volume}}$$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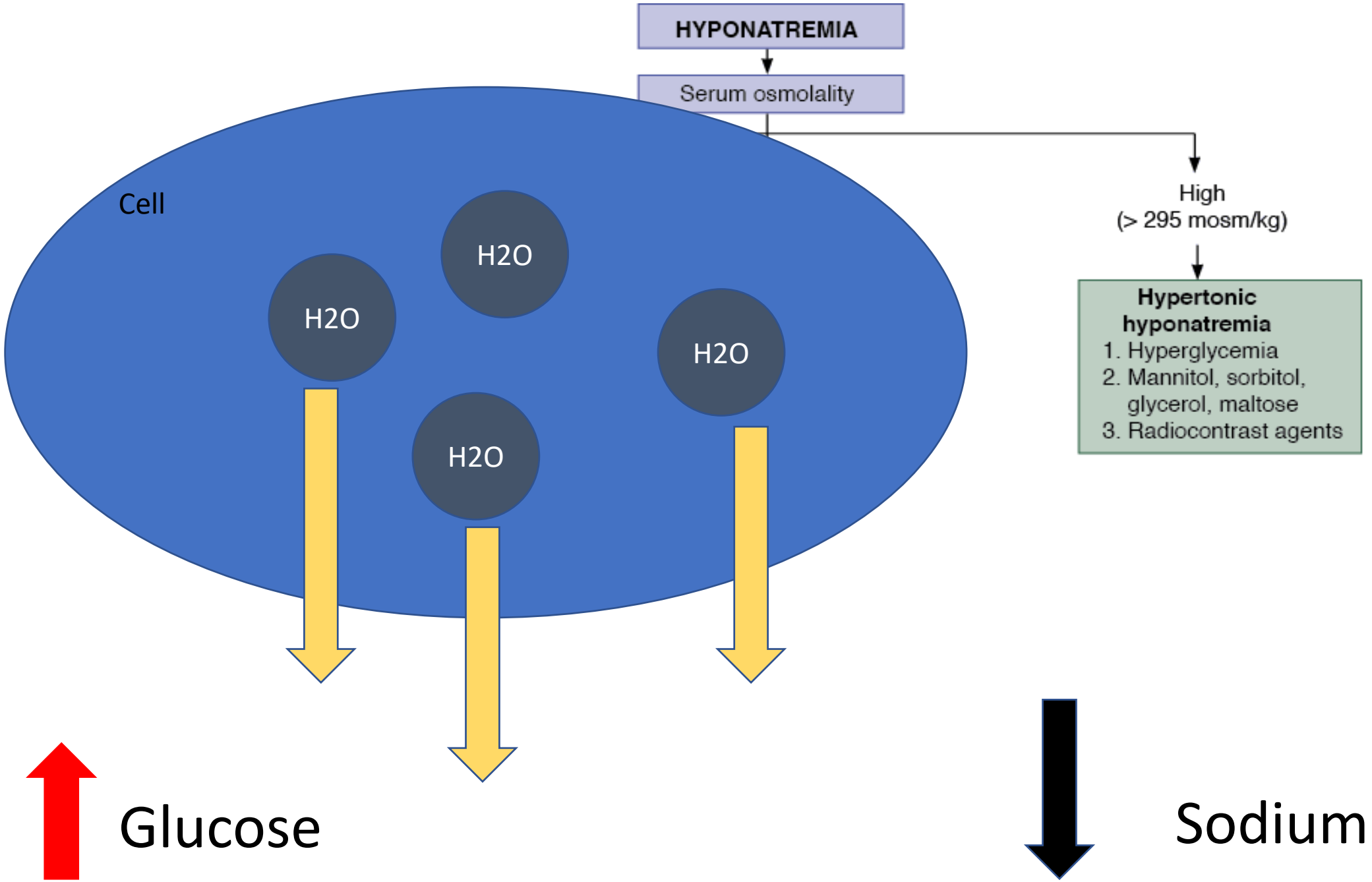
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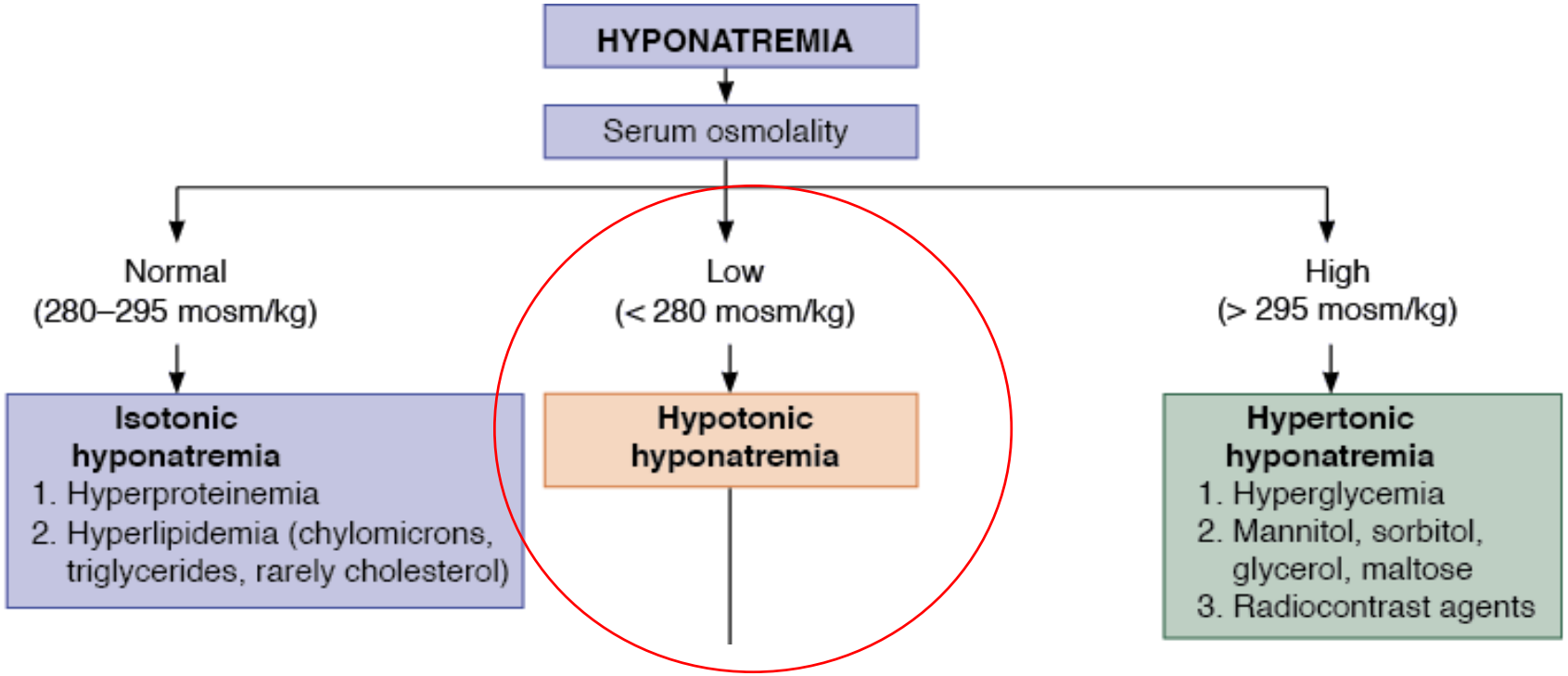
Cell
H2O
H2O
H2O
H2O
Glucose
Sodium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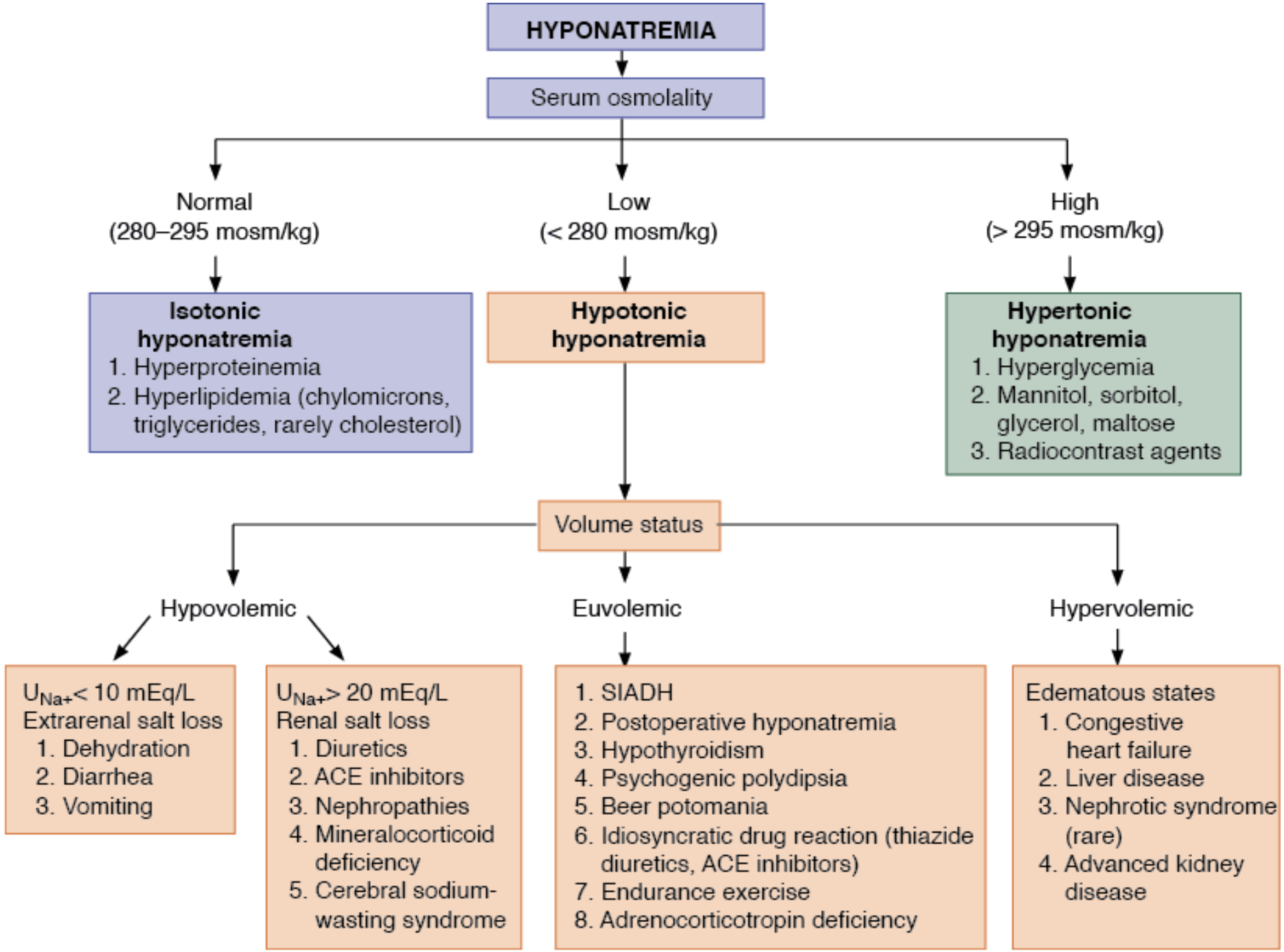
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Volume status
Hypovolemic
Euvolemic
Hypervolemic
U_{Na+} < 10 mEq/L
Extrarenal salt loss
1. Dehydration
2. Diarrhea
3. Vomiting
U_{Na+} > 20 mEq/L
Renal salt loss
1. Diuretics
2. ACE inhibitors
3. Nephropathies
4. Mineralocorticoid deficiency
5. Cerebral sodium-wasting syndrome
1. SIADH
2. Postoperative hyponatremia
3. Hypothyroidism
4. Psychogenic polydipsia
5. Beer potomania
6. Idiosyncratic drug reaction (thiazide diuretics, ACE inhibitors)
7. Endurance exercise
8. Adrenocorticotropin deficiency
Edematous states
1. Congestive heart failure
2. Liver disease
3. Nephrotic syndrome (rare)
4. Advanced kidney disease

Syndrome of Inappropriate Antidiuretic Hormone (SIADH)

- ADH
  - Synthesized in the hypothalamus, stored in the posterior pituitary gland.
  - Increases the reabsorption of water in the kidneys (Vasopressin receptors)
  - ADH should be reduced when serum osmolality is low (Normal)

- ADH secretion
    - Triggered by change in tonicity (enhancement or suppression)
    - Stimulated by Baroreceptors due to reduced effective circulatory volume, nausea, pain, stress and drugs.
- SIADH (ADH is not reduced)
  - Unsuppressed release of ADH from the pituitary gland or nonpituitary sources or its continued action on vasopressin receptors.

SIADH

- Many causes
  - Neoplastic, Pulmonary disorders, CNS disorders, Drugs and others
  - Acute: Pain, stress, nausea, general anesthesia

- Diagnosis
  - H&P
  - Risk factors
  - Low serum Osmolality, high urine Osmolality, high urine sodium
  - Low serum uric acid has been suggested as a marker of SIADH

- Treatment
  - Fluid restriction, salt tabs, urea powder +/- loop diuretics

SIADH vs Cerebral salt wasting (CSW)

	SIADH	CSW
Serum Osmolality	Low	Low
Urine Osmolality	High	High
Urine sodium	High	High
Serum uric Acid	Low	Low
Volume status	Euvolemic	Hypovolemic
Treatment	Fluid restriction, salt tabs, urea	IVF

Treatment Overview

- Depends on:
  - Degree of hyponatremia (Mild, moderate or severe)
  - Duration of hyponatremia (Acute or chronic)
  - Severity of symptoms
  - Volume status (hypovolemia, euvolemia or hypervolemia)

- The severity of symptoms determine intensity of treatment

- Osmolality of the administered fluids MUST be higher than urine Osmolality (Otherwise hyponatremia can worsen)

Osmolality of different fluids

- 1L of isotonic saline
  - Na 154 mEq/L and Cl 154 mEq/L
  - Osmolality = 2 x 154 = 308
- 1L of 3% saline
  - Na 513 mEq/L and Cl 513 mEq/L
  - Osmolality = 2 x 513 = 1026

Normal Solutions	Percent Solution	NaCl Concentration
	5% (50 g/L)	854 mEq/L
	3% (30 g/L)	513 mEq/L
	2% (20 g/L)	342 mEq/L
normal	0.9% (9 g/L)	154 mEq/L
half normal	0.45% (4.5 g/L)	77 mEq/L
quarter normal	0.225% (2.25 g/L)	38 mEq/L
	0.20% (2.0 g/L)	34 mEq/L

Emergency Treatment

- Patients with severe symptoms:
  - Somnolence, seizures, cardiorespiratory distress, vomiting, confusion
  - At high risk of life-threatening complications.

- Immediate treatment may include:
  - Airway protection, supplemental oxygen, ventilatory support, or anticonvulsant therapy.
  - Admission to the ICU may also be required for monitoring of vital signs, central nervous system status, urine output, and fluid administration.

- Hypotonic fluids and hyponatremia inducing drugs must be withheld.

Emergency Treatment

- 3% sodium chloride bolus should be given ASAP
  - 100ml over 10-20 minutes, may repeat 2-3x until desired sodium level is achieved.
  - May be given via peripheral access
- Mild to moderate acute hyponatremia
  - May start with 3% sodium chloride infusion without bolus
- Current guidelines recommend correction of the serum sodium level by 4-6 mEq/L within 1 to 2 hours, which can reverse hyponatremic encephalopathy.
- Monitoring of serum Na level after each bolus is required

Category specific treatments

- Treatment of underlying cause
- Hypovolemia
  - Isotonic fluids administration and holding diuretics.
- Hypervolemia
  - Restrict salt and fluids, and administer loop diuretics.
- Euvolemia
  - Fluid restriction, Salt tabs, Urea powder
  - Loop diuretics

Goal of sodium correction rate

- Acute hyponatremia (<48hrs)
  - Can correct back to baseline with no restrictions or timeframe

- Chronic hyponatremia (>48hrs)
  - Focuses on the risk of Osmotic Demyelination Syndrome (ODS)
  - High risk patients
    - Advanced liver disease, alcoholism, hypokalemia, malnutrition and severe hyponatremia Na<105
      - High risk → no more than 4-6mEq/L over 24hrs
      - Low risk → no more than 4-8mEq/L over 24hrs

Osmotic Demyelination Syndrome (ODS)

- Previously known as Central Pontine Myelinolysis (CPM)
- A condition that can be caused by rapid correction of serum sodium
- Leads to brain cell dysfunction caused by destruction of myelin sheath
- Progressive and sometimes permanent neurologic deficits that can occur one to several days later

Overcorrection (Rescue strategy)

- When to use?
  - Chronic hyponatremia
  - Correction that have exceeded 8mEq/L in any 24-hour period

- What to use?
  - D5W, 6ml/kg lean body weight infused over 2 hours
  - Desmopressin, 2mcg IV or SubQ every 6hrs

Vaptans

- Vasopressin receptor antagonists
- Tolvaptan (oral) and Conivaptan (IV)
- May be useful in resistant euvolemic hyponatremia
- No need for fluid restriction
- Cons:
  - Interacts with medications that are metabolized by CYP3A4
  - Cannot be used in patients with liver disease
  - Not recommended to use more than 30 days
  - Expensive

Conclusion

- Hyponatremia is the most common electrolyte disorder
- Hyponatremia is a marker of mortality and can have devastating consequences if left untreated
- Failure to correct or overcorrect can be harmful
- Identify high risk patients
- Close and frequent monitoring of serum sodium level and urine studies is key

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Thank you

Questions ??

Comments !!