



# ELECTROLYTES

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# Topics

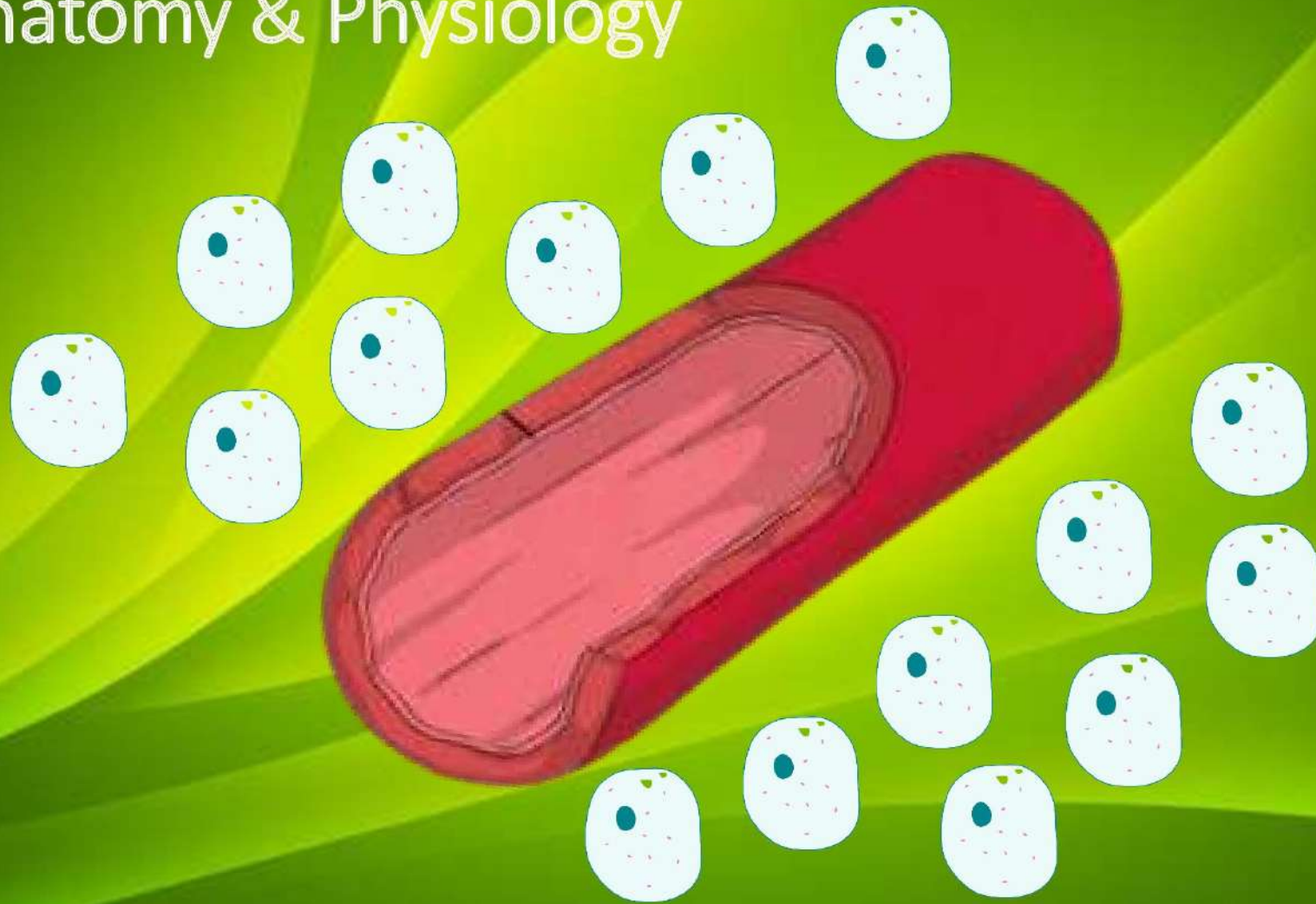
- Basic essentials
- Sodium
- Potassium
- Calcium
- Magnesium
- Phosphate

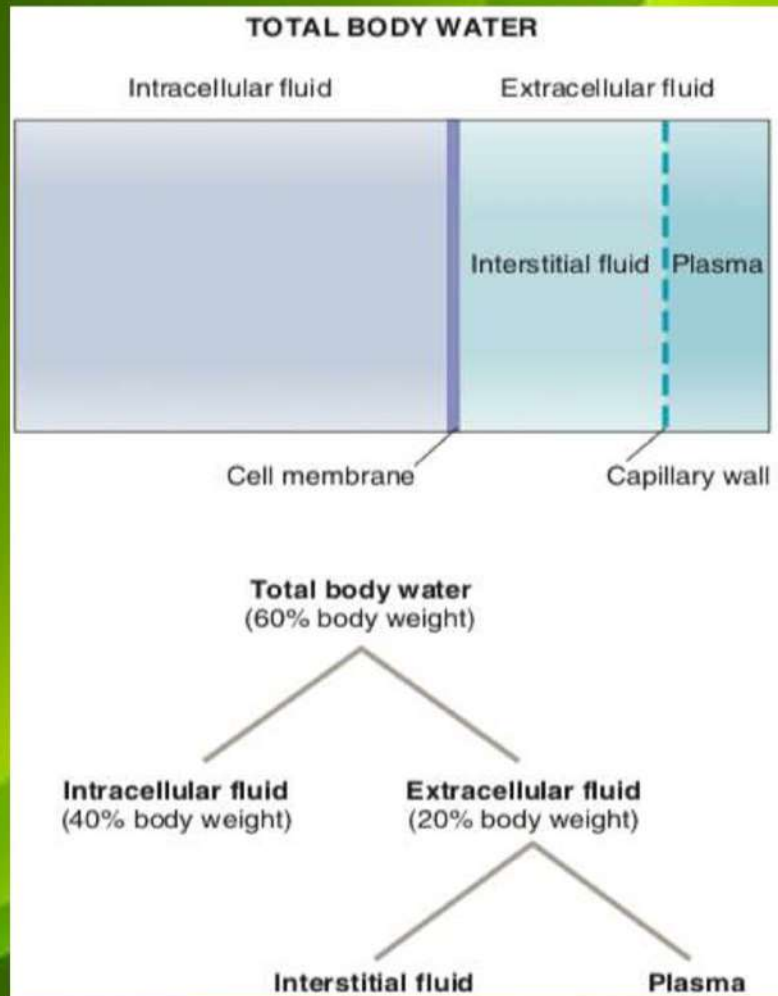
# Electrolytes constituents

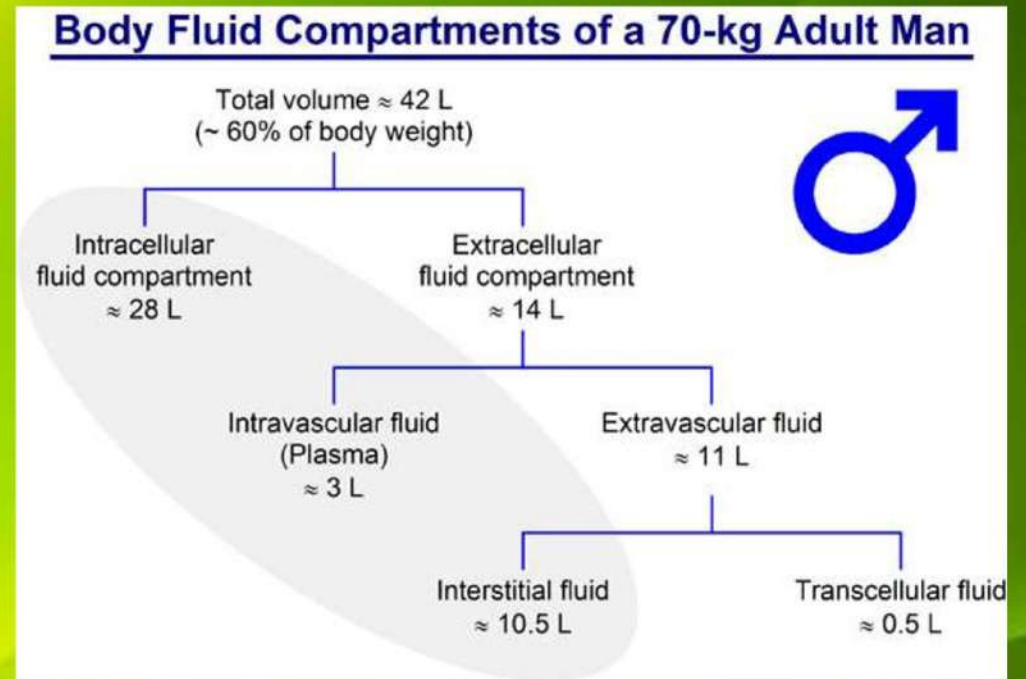
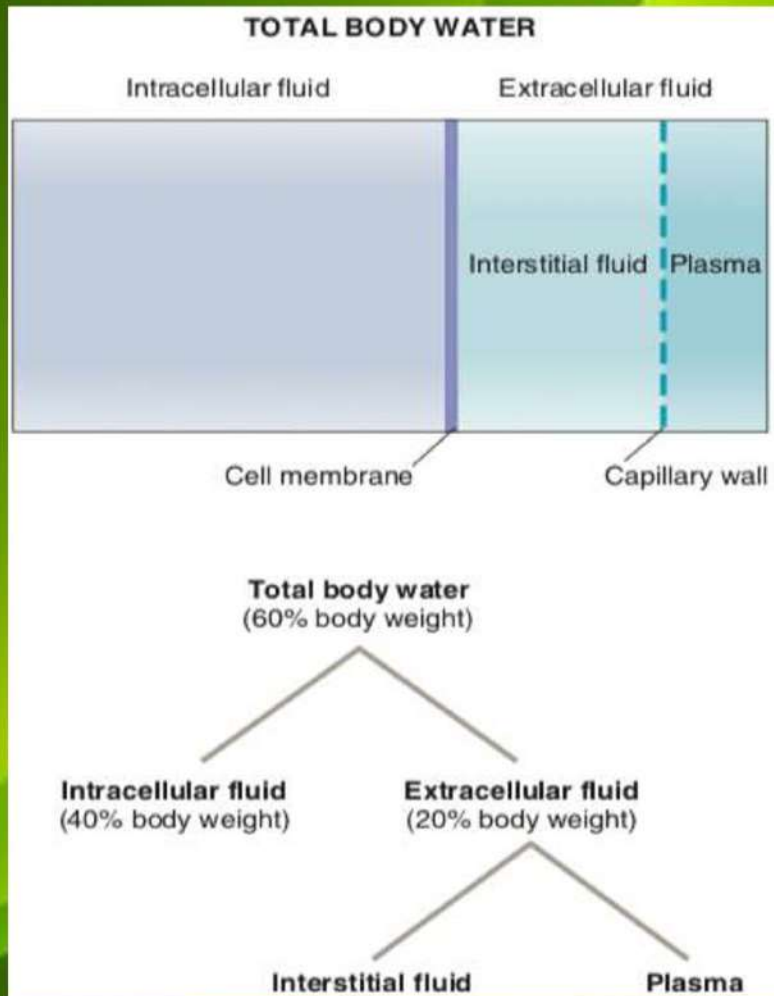


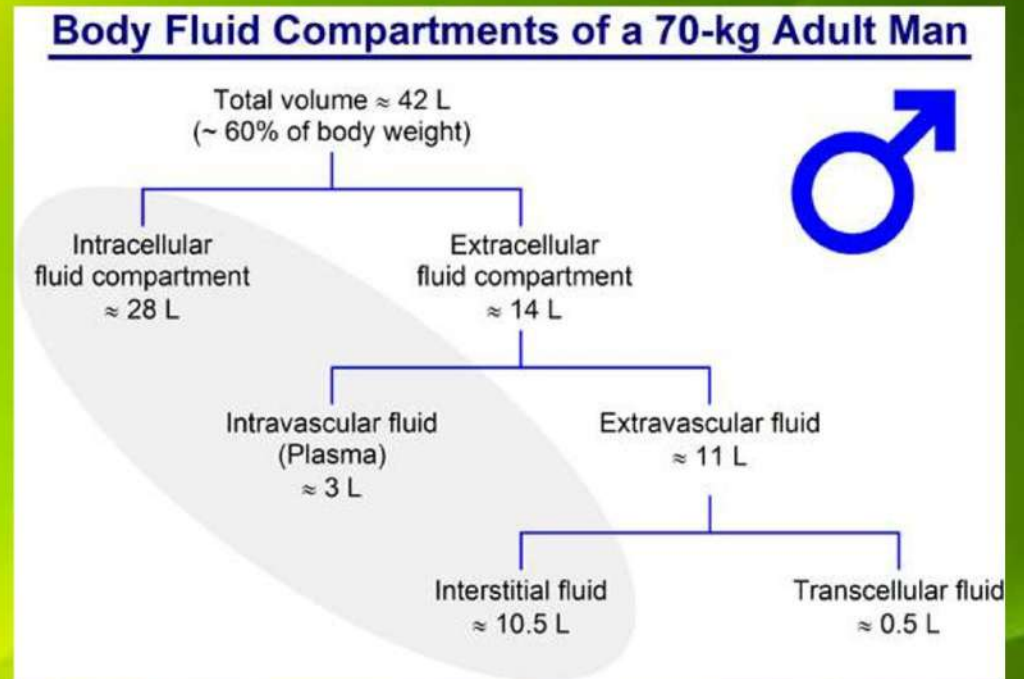
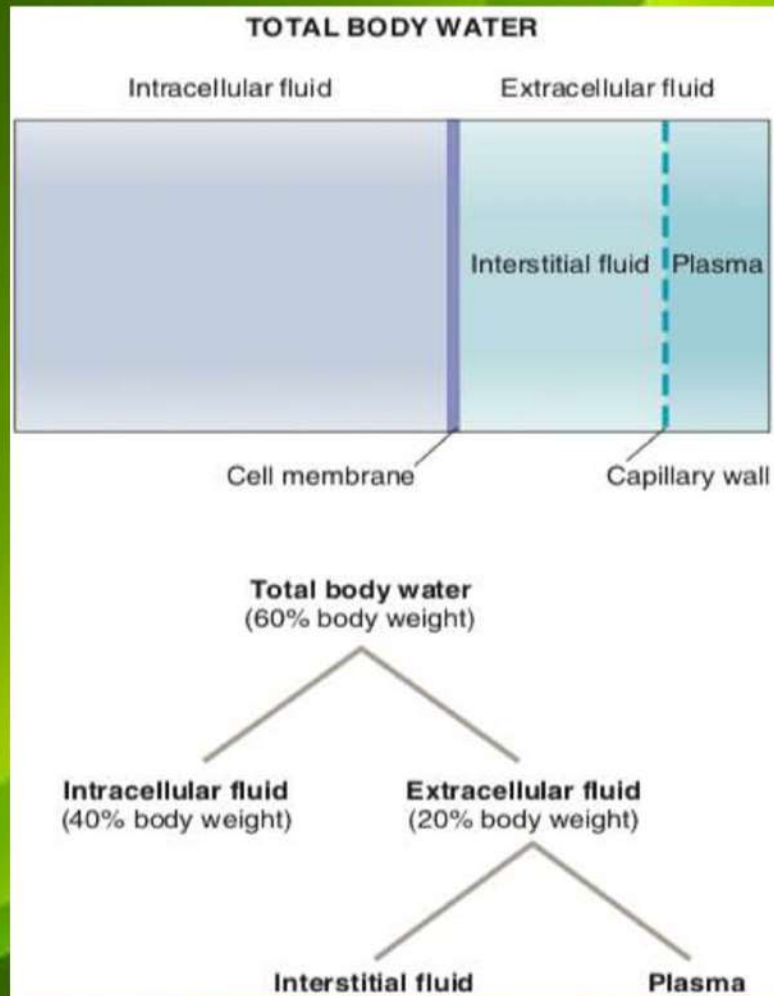


# Anatomy & Physiology



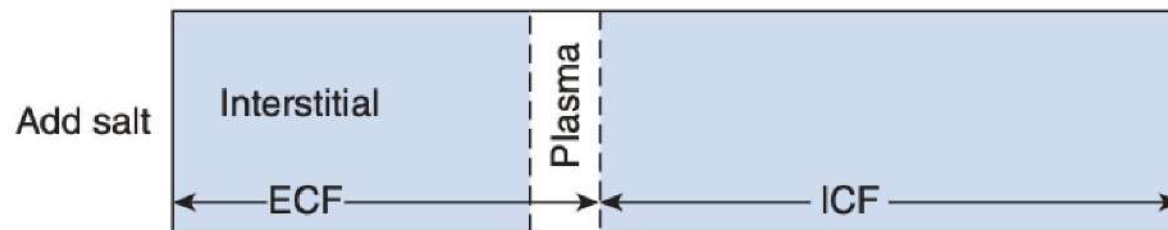
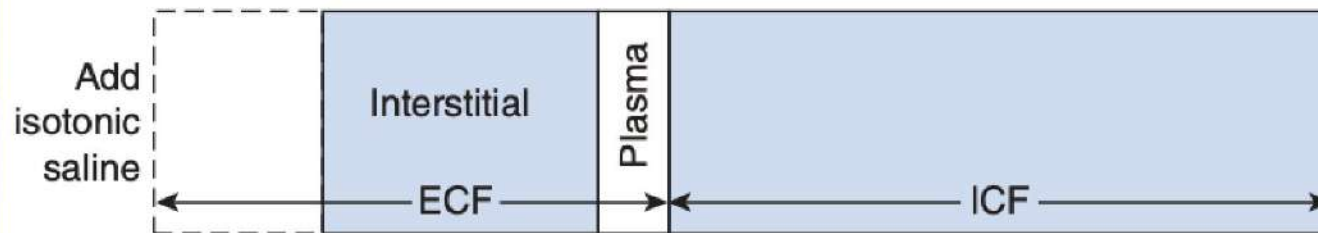
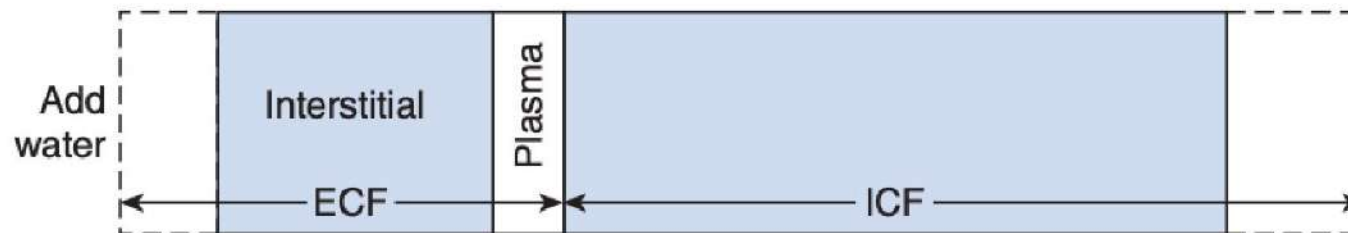
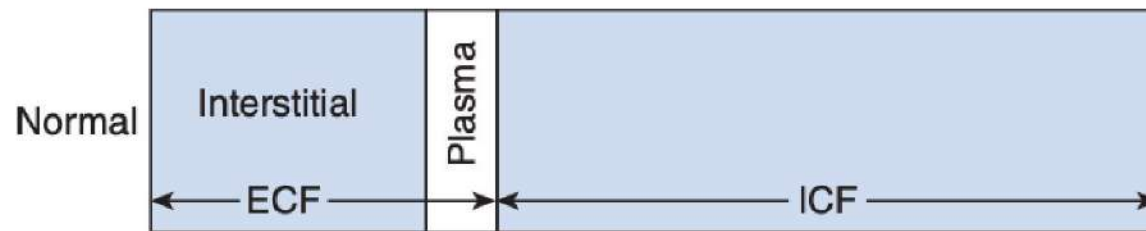






- $TBW = 0.6 \times BW$   
(60% of body weight)



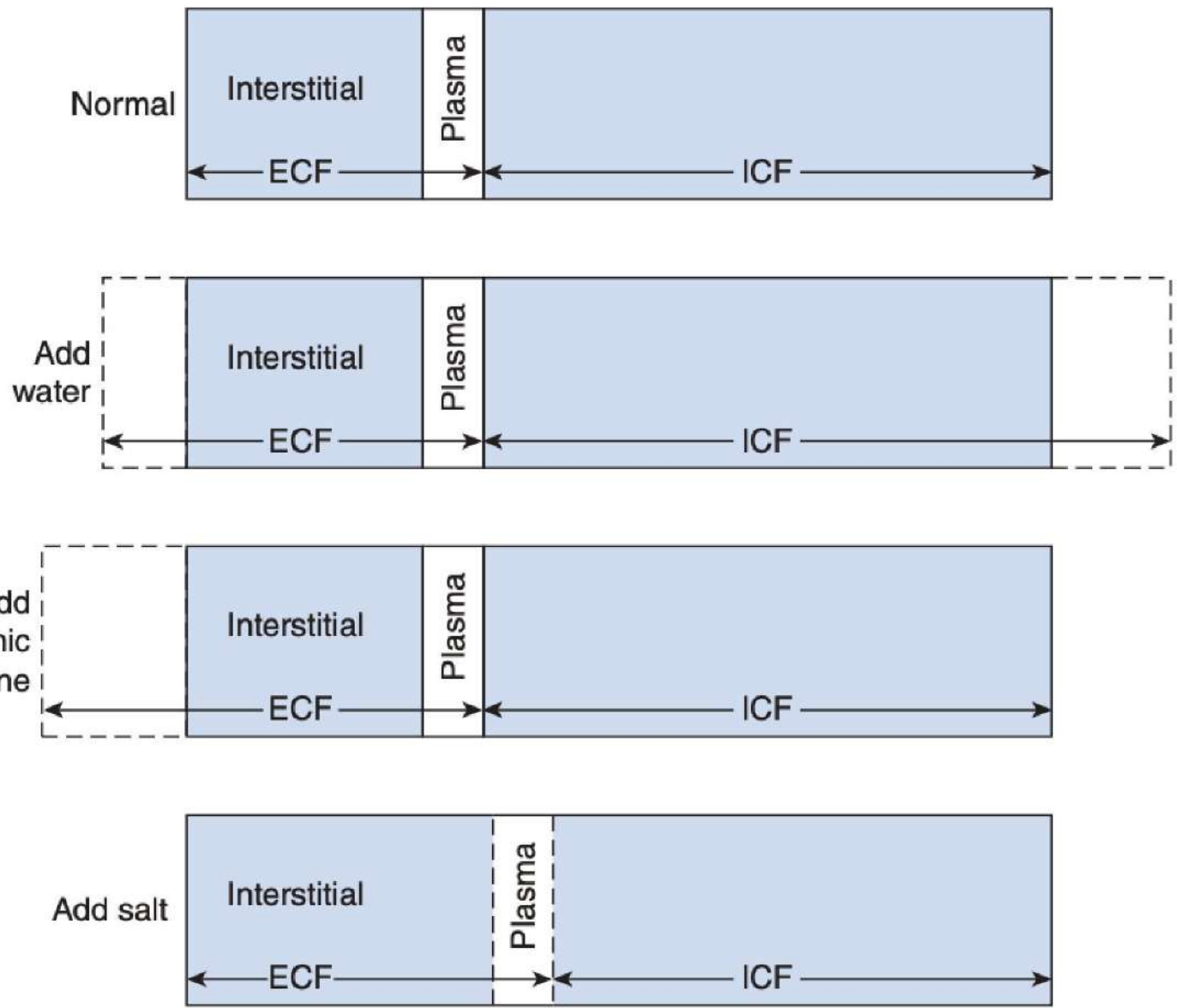




Hypotonic

Isotonic

Hypertonic



# Comparisons...

- **Molarity vs. Molality [concentration]**
- **Osmolarity vs. Osmolality [osmotic pressure]**
- **Tonicity**

# Comparisons...

TONICITY	OSMOLARITY		
	Hyposmotic	Isosmotic	Hyperosmotic
Hypotonic	✓	✓	✓
Isotonic		✓	✓
Hypertonic			✓

# Comparisons...

*Slide 5.* Let's look at the osmolarity and tonicity of two of the most commonly used iv solutions: normal saline (or 0.9% NaCl) and D-5-W [or 5% dextrose (glucose)] in water. If we measure their concentrations on an osmometer, we find that they are both 278 mOsmol/l, so they are isosmotic.

But if we administer them to a person by an iv infusion, we find that normal saline is isotonic because NaCl does not enter cells, whereas D-5-W is hypotonic because glucose goes into cells. Here is an important example of when isosmotic is not isotonic.

Is the tonicity of a solution always the same? No, it depends what cell you are comparing with the solution. An isosmotic solution of sucrose will be isotonic to a mammalian cell because mammals do not have transporters for sucrose, and sucrose cannot enter the cell. On the other hand, plant cells do have sucrose transporters, so an isosmotic sucrose solution will be hypotonic to the plant cell.



# Examples

- **Hypertonic:**

- D5 NaCl
- D5 in Lactated ringers
- D5 0.45% NaCl

- **Isotonic:**

- 0.9% NaCl (Normal Saline)
- Lactated Ringers
- D5W (In the bag)

- **Hypotonic:**

- D5W (in the body)
- 0.25% NaCl
- 0.45% NaCl (half normal saline)
- 2.5% Dextrose

The background of the slide is an abstract composition of flowing, wavy lines in various shades of green and yellow, creating a sense of movement and depth. The colors transition from darker greens on the left to lighter yellows and greens on the right.

**Sodium**

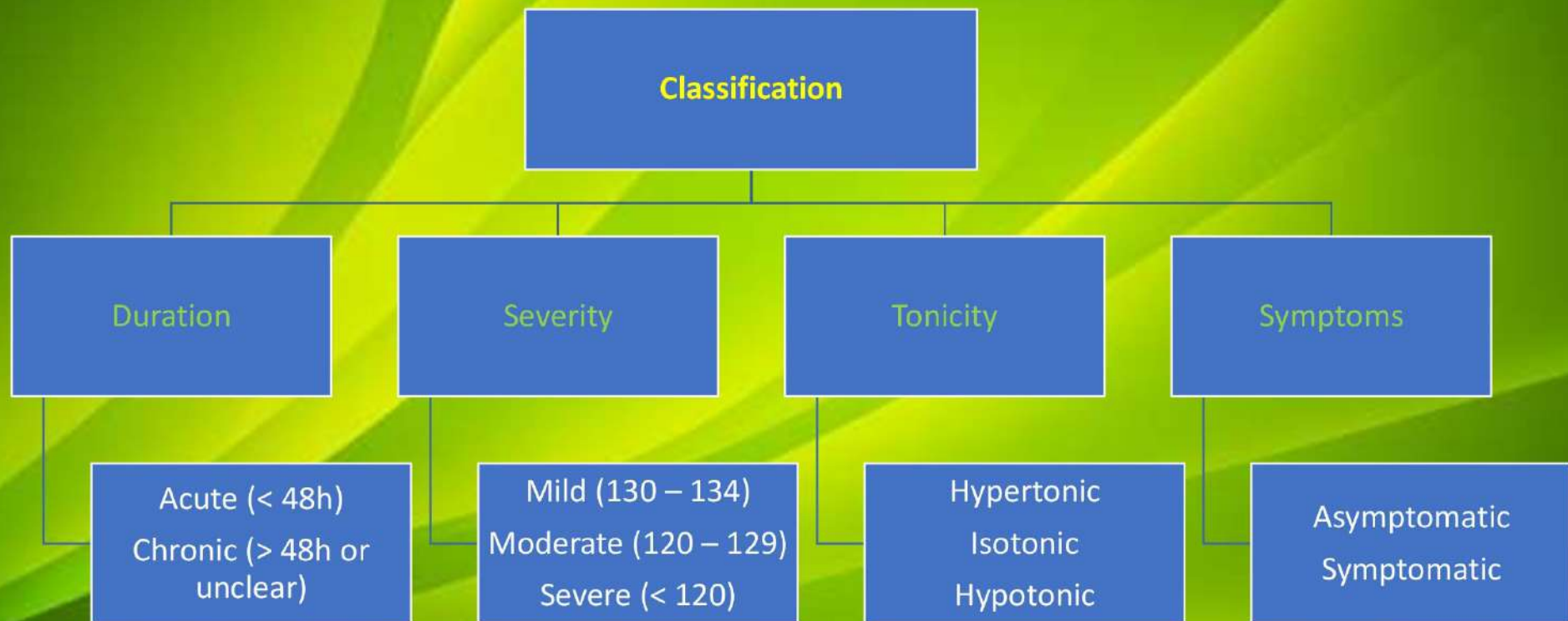
# Hyponatremia

# Intro

- Human body tightly maintains serum  $[\text{Na}^+]$  between 138 and 142 mEq/L despite what may be marked changes in daily intake depending on the person's diet
- Hyponatremia is a condition of excess water relative to  $\text{Na}^+$  and is defined as a **serum  $[\text{Na}^+] < 138 \text{ mEq/L}$**



# Classification



# Causes

**TABLE 17-3** Classification of Hyponatremia According to Serum Osmolality

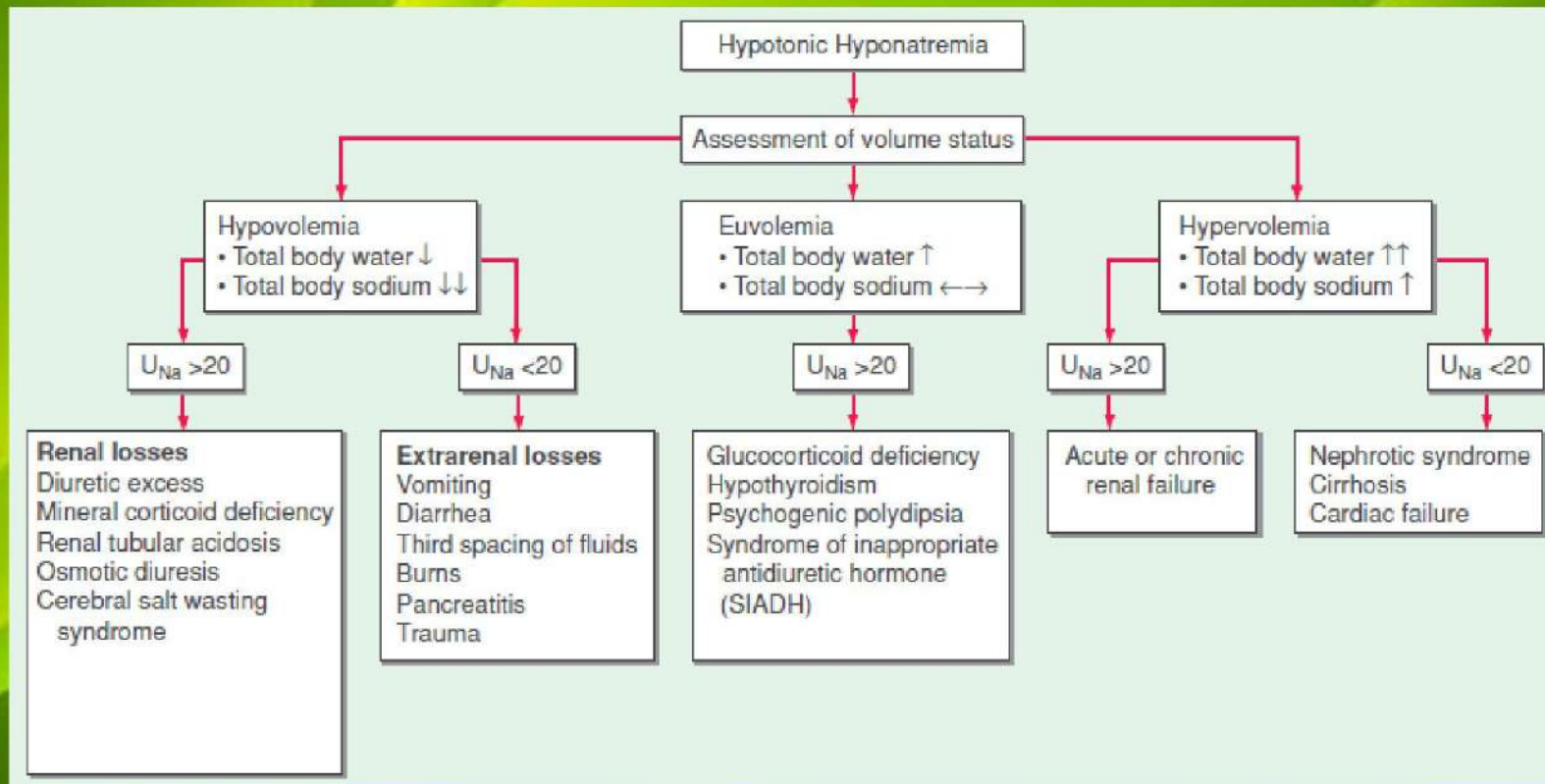
Serum Osmolality	Clinical Conditions	Mechanisms
Hyperosmolality (Hypertonic hyponatremia)	Hyperglycemia Mannitol administration Glycerol administration Maltose administration	Hyponatremia due to osmotic diuresis
Iso-osmolality (Pseudohyponatremia)	Hyperproteinemia Hyperlipidemia	Displacement of serum water by elevated concentration of lipids or protein creating laboratory misinterpretation of normal $[\text{Na}^+]$
Hypo-osmolality (Hypotonic hyponatremia)	See Table 17-4	Hypervolemic Normovolemic Hypovolemic

# Causes

**TABLE 17-4** Classification, Differential Diagnosis, and Features of Hyponatremia According to Volume Status

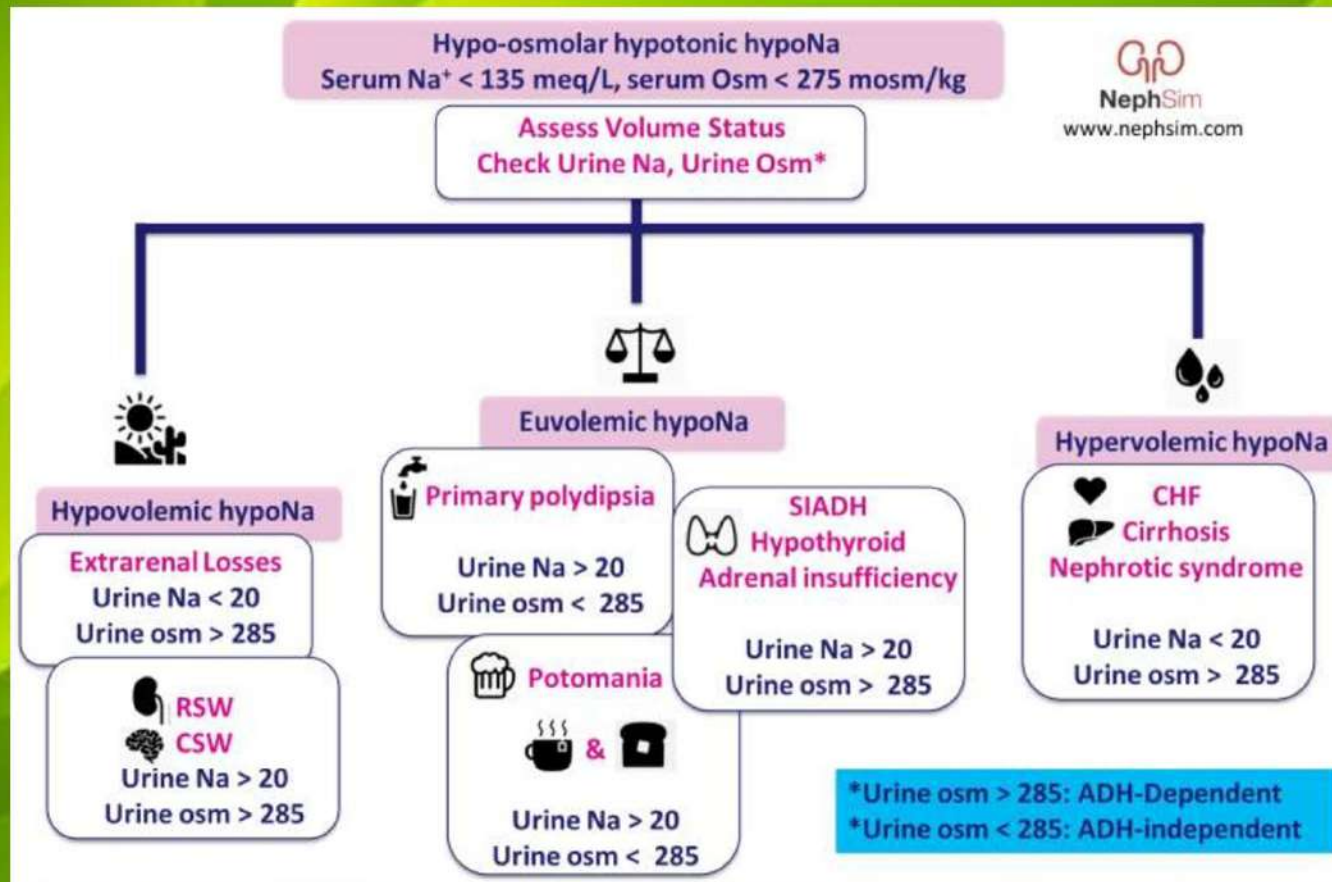
	Clinical Conditions	Orthostatic Hypotension	Edema	$U_{(Na^+)_r}$ mEq/L*	$U_{osm}$ mOsm/L*
Hypervolemic hyponatremia	CHF Cirrhosis Nephrotic syndrome Acute and chronic kidney disease	Absent	Yes	Compensated: >20 Decompensated: <10	Compensated: <100 Decompensated: >100
Normovolemic hyponatremia	Psychogenic polydipsia Glucocorticoid deficit Hypokalemia Drugs SIADH	Absent	No	>20	>100
Renal hypovolemic hyponatremia	Diuretics Mineralocorticoid deficit Salt-losing nephropathy	Normally present	No	>20	>100
Extrarenal hypovolemic hyponatremia	Vomiting Diarrhea	Normally present	No	<10	>100

# Causes





# Causes



# Treatment

- Acute & Chronic

# ACUTE HYPONATREMIA: INITIAL THERAPY (FIRST SIX HOURS)

## Asymptomatic

- In acutely hyponatremic patients with a serum sodium  $< 130 \text{ mEq/L}$  who are asymptomatic, treat with a **50 mL bolus of 3% saline** (ie, hypertonic saline) to prevent the serum sodium from falling further, except in autocorrection condition

# ACUTE HYPONATREMIA: INITIAL THERAPY (FIRST SIX HOURS)

## Symptomatic (even mild symptoms)

- Might be due to **increased intracranial pressure** (seizures, obtundation, coma, respiratory arrest, headache, nausea, vomiting, tremors, gait or movement disturbances, or confusion)
- Treat with a **100 mL bolus of 3% saline**, followed, if symptoms persist, with up to **two additional 100 mL doses (to a total dose of 300 mL); each bolus is infused over 10 minutes**
- An alternative approach, recommended in by European organizations, is to treat with **two 150 mL bolus infusions of 3% saline, each given over 20 minutes**, measuring the serum sodium between infusions



## ACUTE HYPONATREMIA: INITIAL TREATMENT (FIRST SIX HOURS)

### Symptomatic (even mild symptoms)

- Might be due to **increased intracranial pressure**, leading to obtundation, coma, respiratory arrest, headache, nausea, vomiting, tremors, gait or movement disturbances, or convulsions.
- Treat with a **100 mL bolus of 3% saline**, followed, if symptoms persist, with up to **two additional 100 mL doses (to a total dose of 300 mL); each bolus is infused over 10 minutes**
- An alternative approach, recommended in by European organizations, is to treat with **two 150 mL bolus infusions of 3% saline, each given over 20 minutes**, measuring the serum sodium between infusions



# CHRONIC HYPONATREMIA: INITIAL THERAPY (FIRST SIX HOURS)

## Severe symptoms / known intracranial pathology

- In all patients with severe symptoms of hyponatremia (eg, seizures, obtundation, coma, respiratory arrest), treat with a **100 mL bolus of 3% saline** followed, if symptoms persist, by up to **two additional 100 mL doses** (to a total dose of 300 mL); each bolus is **infused over 10 – 30 minutes**
- An alternative approach, recommended by European organizations, is to infuse **150 mL of 3% saline followed 20 minutes later by a second 150 mL bolus** (if the serum sodium does not increase by 4 to 6 mEq/L after the initial dose)



# CHRONIC HYPONATREMIA: INITIAL THERAPY (FIRST SIX HOURS)

## Severe symptoms / known hyponatremia

- In all patients with severe hyponatremia (eg, seizures, obtundation, coma, respiratory depression) with a 100 mL bolus of 3% saline followed, if symptoms persist, by two additional 100 mL doses (to a total dose of 300 mL) which is infused over 10 – 30 minutes
- An alternative approach, recommended by European organizations, is to infuse 150 mL of 3% saline followed 20 minutes later by a second 150 mL bolus (if the serum sodium does not increase by 4 to 6 mEq/L after the initial dose)



**300cc  
in total**

# CHRONIC HYPONATREMIA: INITIAL THERAPY (FIRST SIX HOURS)

## Severe hyponatremia

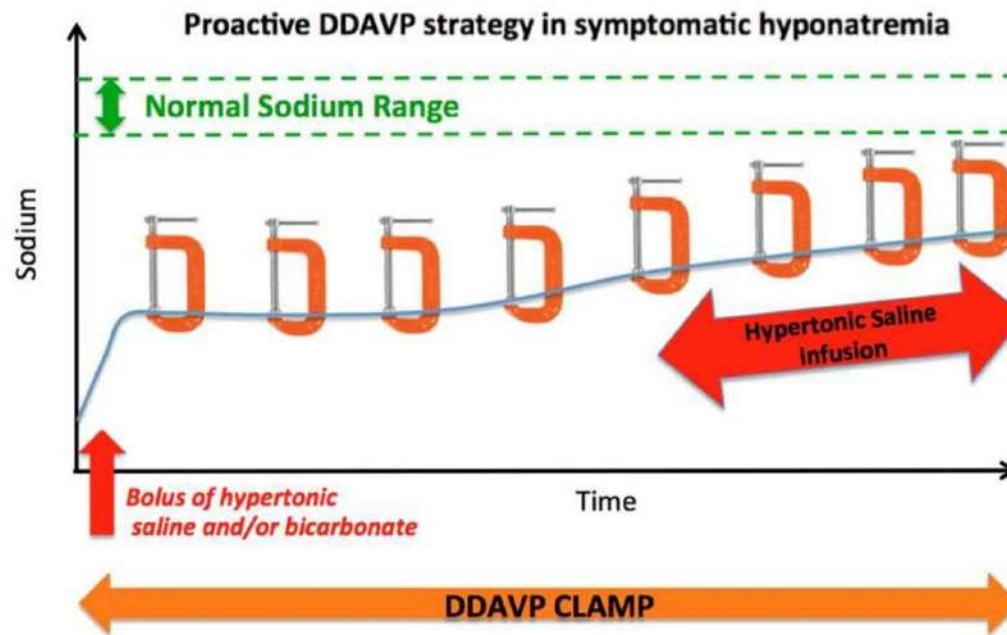
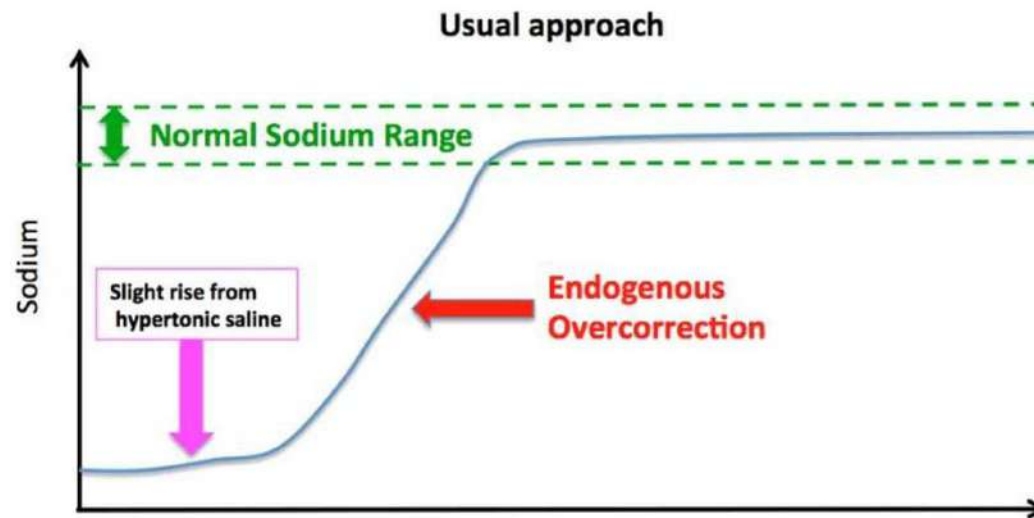
- Initiate intravenous **3% saline beginning at a rate of 15 to 30 mL/hour**, administered via a peripheral vein
- Use 3% saline (rather than normal saline) in patients **with and without** suspected hypovolemia
- Patients with severe hyponatremia are at risk of worsening symptoms if the serum sodium falls further and, conversely, at risk of ODS if the serum sodium rises too quickly
- The lower the serum sodium concentration, the greater the risk
- Isotonic saline can be given concurrently (with 3% saline), if needed, to correct symptomatic hypovolemia or prerenal azotemia



# CHRONIC HYPONATREMIA: INITIAL THERAPY (FIRST SIX HOURS)

## Mild to moderate hyponatremia

- Associated with absent or mild or moderate symptoms are often not admitted to the hospital
- Do not treat with hypertonic saline
- Identify and discontinue drugs that could be contributing to hyponatremia
- Identify and, if possible, reverse the cause of hyponatremia
- Limit further intake of water [eg, fluid restriction, discontinue hypotonic intravenous infusions])



## CHRONIC HYPONATREMIA: INITIAL THERAPY (FIRST SIX HOURS)

- In patients with reversible causes of hyponatremia who are likely to develop a water diuresis during the course of therapy, or who are at high risk of developing ODS, desmopressin can be given proactively at the beginning of therapy with 3% saline (ie, before any treatment is given to correct the hyponatremia)
- Use 1 to 2 mcg of desmopressin, intravenously or subcutaneously, every 6 – 8 hours for a period of 24 to 48 hours
- Although we prefer 3% saline to treat severe hyponatremia in hypovolemic patients, some clinicians use normal saline instead; in such cases, desmopressin should only be given after the serum sodium has been increased by 4 to 6 mEq/L

**Table 2.** Comparison of the United States and European guidelines

Subject	United States Guideline	European Guideline
Acute or symptomatic hyponatremia	Severe symptoms: Bolus 3% NaCl (100 ml over 10 min × 3 as needed)  Moderate symptoms: Continuous infusion 3% NaCl (0.5–2 ml/kg per h)	Severe symptoms: Bolus 3% NaCl (150 ml over 20 min 2–3 times as needed) Moderate symptoms: Bolus 3% NaCl (150 ml 3% over 20 min once)
Chronic hyponatremia SIAD	Fluid restriction (first line) Demeclocycline, urea, or vaptan (second line)	Fluid restriction (first line) Urea or loop diuretics + oral NaCl (second line) Do not recommend or recommend against vaptan <sup>a</sup> Recommend against lithium or demeclocycline
Hypovolemic hyponatremia	Isotonic saline	Isotonic saline or balanced crystalloid solution
Hypervolemic hyponatremia	Fluid restriction Vaptans <sup>b</sup>	Fluid restriction Recommend against vaptan
Correction rates	Minimum: 4–8 mmol/L per d, 4–6 mmol/L per d (high risk of ODS) Limits: 10–12 mmol/L per d, 8 mmol/L per d (high risk of ODS)	No minimum  Limit: 10 mmol/L per d
Management of overcorrection	Baseline $S_{Na} \geq 120$ mmol/L: probably unnecessary Baseline $S_{Na} < 120$ mmol/L: start relowering with electrolyte-free water or desmopressin after correction exceeds 6–8 mmol/L per d	Start once limit is exceeded  Consult an expert to discuss infusion containing electrolyte-free water (10 ml/kg) with or without 2 µg desmopressin iv

<sup>a</sup>“Do not recommend” when  $S_{Na} < 130$  mmol/L, “recommend against” when  $S_{Na} < 125$  mmol/L.<sup>b</sup>In liver cirrhosis, restrict to patients where potential benefit outweighs risk of worsened liver function.<sup>9</sup>

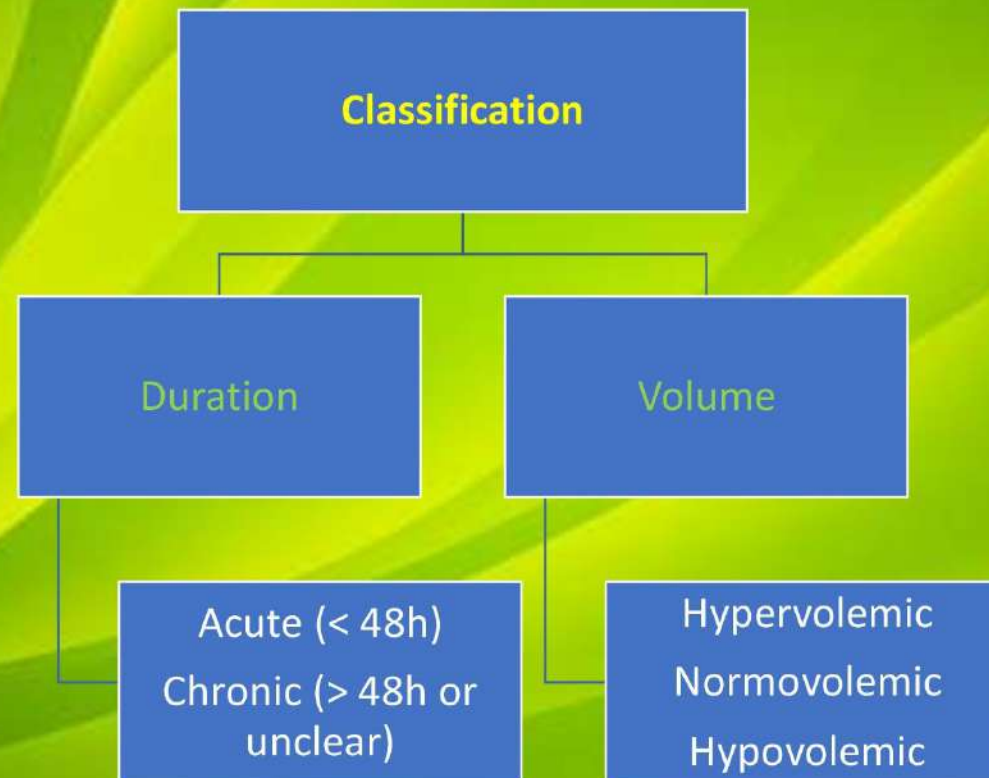


# Hypernatremia

# Intro

- **[Na<sup>+</sup>] >145 mEq/L and hyperosmolality** (serum osmolality >295 mOsm/L)

# Classification



# Causes

**TABLE 17-9** Hyponatremia Classification and Features According to Volume Status

Volume Status	Clinical Conditions	Diagnosis	$U_{OSM}$ , mOsm/kg $H_2O$	$U_{[Na^+]}$ , mEq/L
Hypervolemic hyponatremia	Cushing's syndrome Primary hyperaldosteronism Salt water intake Iatrogenic Hemodialysis	Cortisol test History of hypertension and hypokalemia Psychiatric disorder Hypertonic saline, enteral feeding, bicarbonate infusion Clinical history	>100	>20
Normovolemic hyponatremia	Central DI Partial DI  Nephrogenic DI  Hypodipsia Medications	History of CNS lesion, urinary concentration after desmopressin  History of nephrotoxic drugs, no response to desmopressin History of poor oral intake Amphotericin, aminoglycosides, lithium, phenytoin	Central DI <300 Partial DI >300 but <800 <200  >100 <200	>20
Renal hypovolemic hyponatremia	Osmotic diuretics Loop diuretics Postobstructive diuresis	Hyperglycemia. High sodium level after correction Clinical history Clinical history	>100	>20
Extrarenal hypovolemic hyponatremia	Vomiting Diarrhea GI fistulas Sweating Burns	Clinical history	>800	<10

Abbreviations: DI = diabetes insipidus;  $U_{[Na^+]}$  = urine sodium;  $U_{OSM}$  = urine osmolality.



# Treatment

- First, shock, hypoperfusion, or volume deficits should be treated with isotonic (0.9%) saline
- Second, treat any existing underlying cause → diabetes insipidus, vomiting, diarrhea, or fever
- Third, correct the patient's free water deficit

have salt poisoning.

Acute

Chronic

**Goal:**

- Replace entire water deficit within 24 hours.

**Initial fluid regimen:**

- IV D5W at 3 to 6 mL/kg/hour.
- Add ongoing hourly water losses, if known.

Monitor serum sodium and blood glucose every one to two hours. Once the serum sodium is  $<145$  mEq/L, reduce infusion rate to 1 mL/kg/hour and monitor serum sodium every two to four hours until a serum sodium of 140 mEq/L is restored.

Modify the infusion rate if the pace of correction is too fast or too slow. Also, the infusion rate may need to be decreased if hyperglycemia develops.

Electrolyte replacement (either sodium replacement in a patient with hypovolemia or potassium replacement in a patient with hypokalemia) can be given as a separate infusion or combined with the water replacement (eg, if the appropriate infusion rate of D5W is 100 mL/hour, then one-half isotonic saline can be given at 200 mL/hour).

**Goal:**

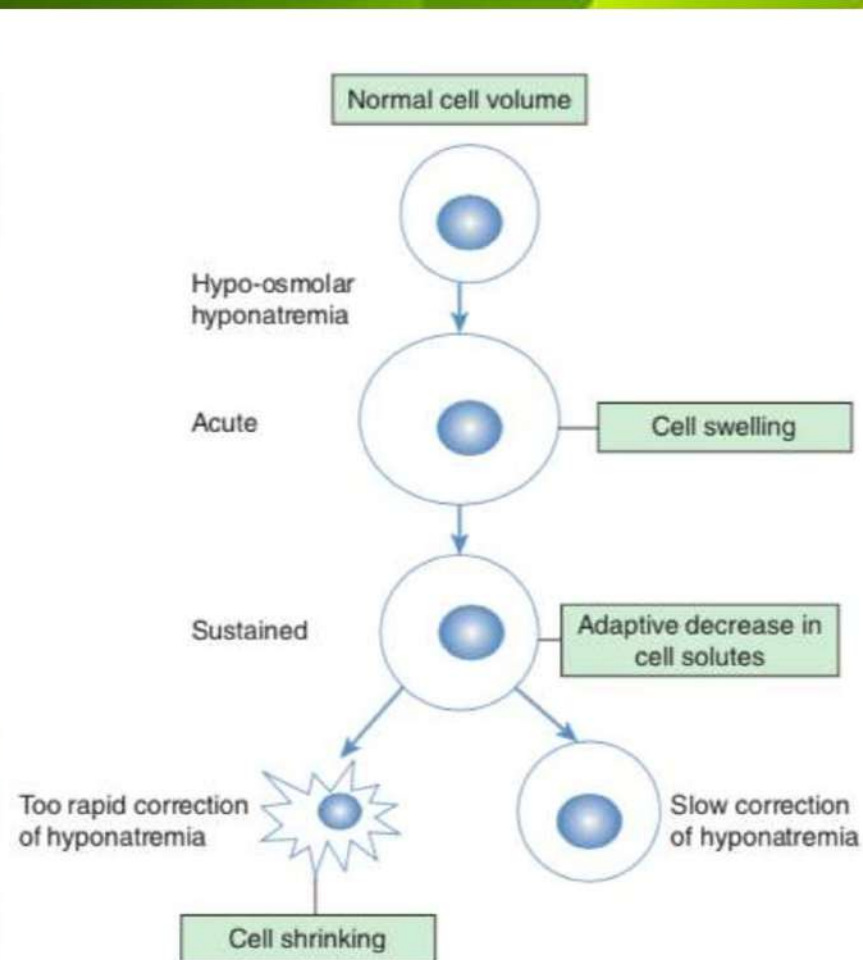
- Lower the serum sodium by 10 mEq/L in 24 hours.

**Initial fluid regimen:**

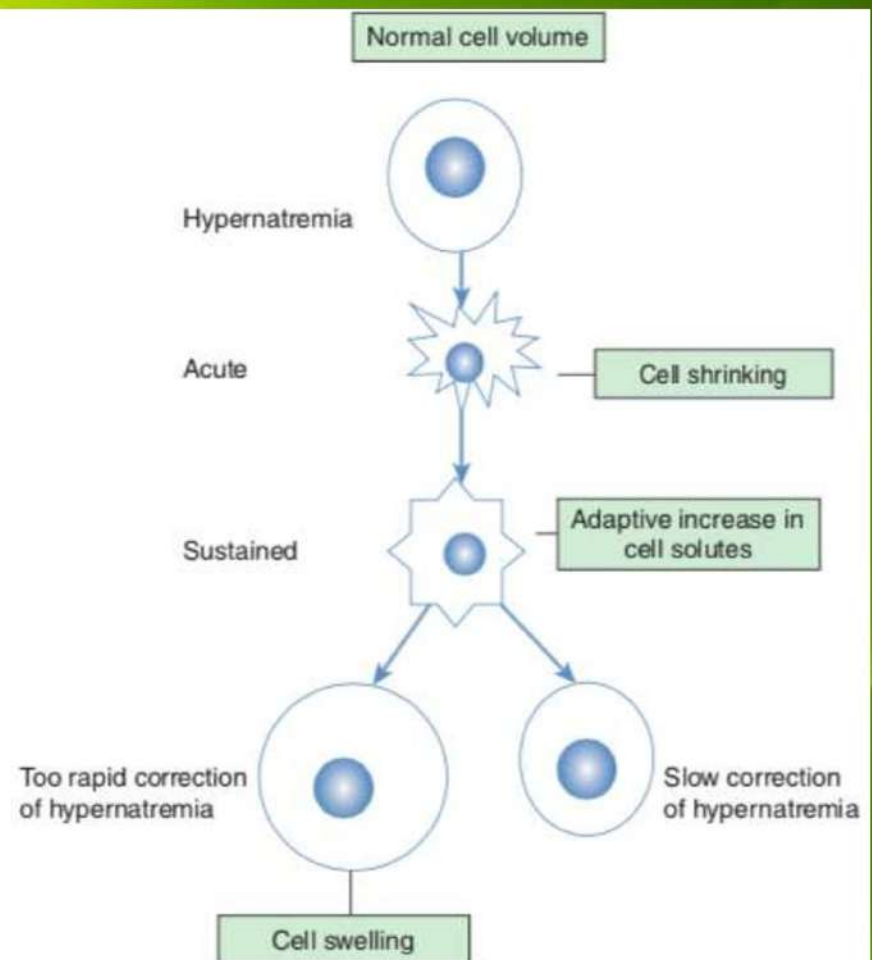
- IV D5W at 1.35 mL/kg/hour.
- Add ongoing hourly water losses, if known.

Monitor serum sodium four to six hours after initiation of the replacement regimen. If the target rate of correction is attained, monitor serum sodium every 12 to 24 hours until normonatremia is attained. If the desired rate of correction is not attained, modify the infusion rate and measure serum sodium after four to six hours.

Electrolyte replacement (either sodium replacement in a patient with hypovolemia or potassium replacement in a patient with hypokalemia) can be given as a separate infusion or combined with the water replacement (eg, if the appropriate infusion rate of D5W is 100 mL/hour, then one-half isotonic saline can be given at 200 mL/hour).



**FIGURE 17-2.** Adaptation of brain volume to hyponatremia and effect of correction.



**FIGURE 17-3.** Adaptation of brain volume to hypernatremia and effect of correction.

The background of the slide is an abstract composition of flowing, wavy lines in various shades of green and yellow, creating a sense of movement and depth. The colors transition from a bright yellow-green in the center to a darker, more saturated green towards the edges.

# Potassium



# Intro

- Major intracellular cation of body
- 98% of total body  $K^+$  in healthy subjects is intracellular; 70% to 75% of total  $K^+$  is in muscle tissues
- Normal intracellular concentration  $\sim 150 \text{ mEq/L}$ ; normal extracellular concentration is 3.5 to 5.0 mEq/L
- $K^+$  is excreted predominantly by kidneys (80% to 90%)
- $[K^+]$  rising about  $0.6 \text{ mEq/L}$  for every  $0.1$  decrease in pH and vice versa, through an exchange between  $H^+$  and  $K^+$

The background of the slide is an abstract composition of flowing, wavy lines in various shades of green and yellow, creating a sense of movement and depth. The colors range from a deep forest green to a bright, almost white yellow, with smooth gradients between them.

# Hypokalemia

# Intro

- $< 3.5 \text{ mEq/L}$
- Makes the resting potential more electronegative, thus enhancing depolarization
- Reduction in  $[\text{K}^+]$  conduction delays repolarization, causing some changes in ECG



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**What are the  
ECG changes?**



# Intro

- $< 3.5 \text{ mEq/L}$
- Makes the resting potential more electronegative, thus enhancing depolarization
- Reduction in  $[\text{K}^+]$  conduction delays repolarization, causing some changes in ECG
- **Prolonged PR, prolonged QTc, flattened T waves, appearance of U waves in the ECG**

# Causes

TABLE 17-13 Causes of Hypokalemia	
Transcellular shifts	Alkalosis* Increased plasma insulin (treatment of diabetic ketoacidosis) $\beta$ -Adrenergic agonists Hypokalemic periodic paralysis (congenital) Thyrotoxic hypokalemic periodic paralysis
Decreased intake	Fasting Alcoholism (worsened by hypomagnesemia) Eating disorders
GI loss	Vomiting*, nasogastric suction Diarrhea* (including laxative, enema abuse) Malabsorption Ureterosigmoidostomy Enteric fistula Villous adenoma
Renal loss	Diuretics (carbonic anhydrase inhibitors, loop diuretics, and thiazide-like diuretics)* Primary hyperaldosteronism Secondary hyperaldosteronism Licorice ingestion Excessive use of chewing tobacco Renal tubular acidosis Postobstructive diuresis Osmotic diuresis Bartter's syndrome (mimics loop diuretic use) Gitelman's syndrome (mimics thiazide diuretic use) Apparent mineralocorticoid excess and related syndromes (Conn's, Liddle's) Drugs and toxins (aminoglycosides, echinocandins, carbenicillin, penicillins, amphotericin B, levodopa, lithium, thallium, cesium, barium, toluene, theophylline, chloroquine, steroids, etc.)
Sweat loss	Heavy exercise Heatstroke Fever
Other	Hypomagnesemia Acute leukemia and lymphomas IV hyperalimentation Recovery from megaloblastic anemia Hypothermia (accidental or induced)

\*Frequently encountered etiologies in the ED.

# Symptoms

- Usually start when serum concentrations reach 2.5 mEq/L
- Attention must be paid to cardiac arrhythmias, usually tachyarrhythmias (atrial fibrillation torsades de pointes, ventricular tachycardia, and ventricular fibrillation), which can be life threatening



# Symptoms

**TABLE 17-14** Symptoms and Signs of Hypokalemia

Cardiovascular	Hypertension Orthostatic hypotension Potentiation of digitalis toxicity Dysrhythmias (usually tachyarrhythmias) T-wave flattening, QT prolongation, U waves, ST depression
Neuromuscular	Malaise, weakness, fatigue Hyporeflexia Cramps Paresthesias Paralysis Rhabdomyolysis
GI	Nausea, vomiting Abdominal distention Ileus
Renal	Increased ammonia production Urinary concentrating defects Metabolic alkalemia, paradoxical aciduria Nephrogenic diabetes insipidus
Endocrine	Glucose intolerance



# Investigations

- Renal profile & electrolytes
- Spot urinary electrolytes

# Investigations

- Renal profile & electrolytes
- Spot urinary electrolytes
- $\text{UNa}^+$ ,  $\text{UOSM}$ , and  $\text{POSM}$  should be measured, because a  $\text{UNa}^+$  value  $<30$  mEq/L and a  $\text{UOSM}$  value  $< \text{POSM}$   $\rightarrow$  suggest polyuria
- This can increase  $\text{K}^+$  excretion even if total body  $\text{K}^+$  is depleted  $\rightarrow$  urinary  $\text{K}^+$  may be misleading
- **Transtubular  $\text{K}^+$  gradient** =  $(\text{Urinary } \text{K}^+ \times \text{POSM}) / (\text{UOSM} \times \text{Plasma } \text{K}^+)$ , with normal values of 8 to 9 mEq/L
  - Values  $<5$  mEq/L  $\rightarrow$  suggest hyperaldosteronism; if paralysis is present
  - values  $<3$  mEq/L  $\rightarrow$  suggest hypokalemic periodic paralysis
- Calcium/phosphate ratio  $>1.7$  is 100% sensitive and 96% specific for thyrotoxic hypokalemic periodic paralysis

# Treatment (Orally)

- Foods rich in  $K^+$
- Chronic hypokalemia induced by loop or thiazide → use spironolactone
- Hypokalemia secondary to respiratory alkalosis → simply correct the acid-base imbalance (through reassurance or anxiolytics) can correct  $[K^+]$



# Treatment (IV)

- Indicated in:
  - Severe ( $<2.5$  mEq/L) hypokalemia
  - In symptomatic with moderate (2.5 to 3 mEq/L) hypokalemia
  - Cardiac arrhythmias or prolonged QTc or when oral replacement is not tolerated or not feasible
- Use potassium chloride and avoid administering  $K^+$  in glucose solutions → reduce insulin-induced  $K^+$  transfer into cells.
- Potassium is irritating to endothelium → painful
- Most hypokalemic are also hypomagnesemic → magnesium may be added to the infusion both to optimize tubular reuptake of potassium and to contrast proarrhythmic effect of hypokalemia



# Hyperkalemia

# Intro

- Serum  $[K^+]$  of  $>5.5$  mEq/L
- Resting potential of excitable myocardium becomes less electronegative, with a consequent partial depolarization that reduces the activation of voltage-dependent sodium channels → results in slower and reduced amplitude of action potential
- Calcium administration does not affect potassium levels, but antagonizes the effects of hyperkalemia & raising the threshold potential, thus restoring the membrane potential and myocyte excitability close to normal

# Causes

**TABLE 17-17** Causes of Hyperkalemia

Pseudohyperkalemia	Tourniquet use Hemolysis (in vitro)* Leukocytosis Thrombocytosis
Intracellular to extracellular potassium shift	Acidosis* Heavy exercise $\beta$ -Blockade Insulin deficiency Digitalis intoxication Hyperkalemic periodic paralysis
Potassium load	Potassium supplements Potassium-rich foods IV potassium Potassium-containing drugs Transfusion of aged blood Hemolysis (in vivo) GI bleeding Cell destruction after chemotherapy Rhabdomyolysis/crush injury* Extensive tissue necrosis
Decreased potassium excretion	Renal failure* Drugs—potassium-sparing diuretics,* $\beta$ -blockade, NSAIDs, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, cyclosporine, tacrolimus Aldosterone deficiency* Selective defect in renal potassium excretion (pseudohypoaldosteronism, systemic lupus erythematosus, sickle cell disease, obstructive uropathy, renal transplantation, type IV renal tubular acidosis)

\*Frequent or important ED diagnostic considerations.



# Symptoms

- Cardiac dysrhythmias → VF, sinoatrial and atrioventricular blocks until complete heart block, and asystole, may occur
- Death from hyperkalemia → usually result of diastolic arrest or VF
- Other common symptoms → neuromuscular dysfunctional weakness, paresthesias, areflexia, ascending paralysis, GI effects (nausea, vomiting, diarrhea)



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# Symptoms

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- **ECG changes → small P wave, prolonged PR, broad QRS, shortened QT, tall T wave, sinusoidal pattern, arrhythmias**



# Investigations

- Renal profile & electrolytes
- Spot urinary electrolytes
  - Elevated spot urine  $K^+$  ( $>20$  mEq/L)  $\rightarrow$  suggests extrarenal cause (and will more likely be responsive to therapy)
  - Low urine  $K^+$  output ( $<10$  mEq/L)  $\rightarrow$  suggests oliguric kidney failure or drug effect (ACEI or ARB)

# Treatment (orally)

- Immediate cessation of further K<sup>+</sup> administration, reduction of dietary intake, and suspension of drugs impairing K<sup>+</sup> renal excretion directly
- **Resonium** → sodium polystyrene sulfonate (associated with intestinal necrosis)
- **Kalimate** → calcium polystyrene sulfonate
- **Patiromer & sodium zirconium cyclosilicate** → too slow to be of benefit in life-threatening hyperkalemia



# Treatment (IV)

- Fluid administration enhances K<sup>+</sup> renal excretion through increasing urine output
- **Lytic cocktail?**

Effect	Agent	Dose	Onset	Duration
Membrane Stabilization	Calcium Gluconate (10%)	10mL IV over 10 min	Immediate	30 – 60 minutes
	Hypertonic (3%) Normal Saline	50mL IV push	Immediate	Unknown
Shifters	Insulin (Short Acting)	10 units IV push with 25 – 40 g dextrose (50% solution)	20 minute	4 – 6 hours
	Albuterol	10 – 20 mg in 4 mL of Normal Saline nebulized over 10 minutes	30 minute	2 hours
Excreters	Furosemide	40 – 80 mg IV x1	15 minute	2 -3 hours
	Sodium Bicarbonate	150mmol/L IV at variable rate	Hours	Duration of Infusion
	Sodium Polystyrene Sulfonate	15 – 30 g in 15 – 30 mL (70% sorbitol orally)	> 2 hours	4 – 6 hours
Definitive	Hemodialysis	-----	Immediate	3 hours

## Initial Fluid & Potassium Replacement

### Restoration of circulating volume is a priority

#### Systolic BP (SBP) <90 mm Hg

Likely to be due to low circulating volume, but consider other causes such as heart failure, sepsis, etc.

- Give 500 mL of 0.9% saline solution over 10–15 minutes. If SBP remains <90 mm Hg, repeat.
- Most patients require between 500–1000 mL given rapidly. Consider colloids e.g. Gelafundin if BP fails to pick up.
- Once SBP >90 mm Hg give 1000 mL of 0.9% saline over the next 60 minutes.

Addition of potassium is likely to be required in the second litre of fluid, especially if baseline potassium <5 mmol/L and to maintain potassium between 4–5 mmol/L.

#### Systolic BP on admission ≥90 mmHg

- Give 1000 mL of 0.9% saline for first 60 minutes

### Potassium replacement:

Potassium level (mmol/L)	Potassium replacement mmol/L of infusion solution
>5.5	Nil
3.5–5.5	40 mmol/L (3 g KCL)
<3.5	Additional potassium required

#### Caution:

Withhold potassium replacement if no urine output.

### Intravenous bicarbonate:

The use of intravenous bicarbonate is not indicated to correct acidosis in DKA due to:

- Rise in  $p\text{CO}_2$  in CSF which may lead to a paradoxical increase in CSF acidosis.
- Delay in the fall of blood lactate and ketone level.
- Risk of cerebral oedema especially in younger age groups.



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**Calcium**



# Intro

- Most abundant mineral in the body
- The total body  $[Ca^{2+}]$  is 15 g/kg of body weight, or about 1 kg in an average-sized adult
- Excretion of  $Ca^{2+}$  is primarily via the stool
- 3 different forms:
  - **Ionized calcium**, 50% of total (4.5 to 5.6 milligrams/dL; 1.1 to 1.4 mmol/L) → the only active fraction
  - **Protein-bound calcium**, 40% of total → inactive and not filtered by glomerulus
  - **Complexed calcium**, 10% of total, → bound to anions (phosphate, carbonate, citrate)

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# Hypocalcemia

# Intro

- $<2.0$  mEq/L ( $<4$  milligrams/dL or  $<1.1$  mmol/L)
- Shock or sepsis, will tend to reduce ionized  $[Ca^{2+}]$  by allowing increased net movement of  $Ca^{2+}$  across the cell membrane into the cytoplasm of the poorly functioning cells



# Causes

**TABLE 17-24** Selected Causes of Hypocalcemia

Cause	Mechanism(s)
Decreased calcium absorption	
Vitamin D deficiency	Malnutrition
Decreased oral intake	Intestinal bypass, gastrectomy
Decreased intestinal absorption	Liver failure
Decreased production of 25(OH)D <sub>3</sub>	Renal failure, hyperphosphatemia
Decreased synthesis of 1,25(OH <sub>2</sub> )D <sub>3</sub>	Malabsorption
Malabsorption syndromes	
Increased calcium excretion/reduced bone resorption	
Alcoholism	Hypomagnesemia causing inhibition of PTH secretion, PTH resistance to bone resorption
Hypoparathyroidism	Genetic, autoimmune, surgical, tumoral
Pseudohypoparathyroidism	Resistance to PTH action
Hypomagnesemia	Inhibition of PTH secretion, PTH resistance to bone resorption
Drugs (Table 17-25)	
Malignancy	Pseudohypocalcemia, hyperphosphatemia, hypomagnesemia, vitamin D or PTH deficiency, osteoblastic metastasis
Sepsis	
Acute pancreatitis	Fatty acids combine with [Ca <sup>2+</sup> ] to form insoluble Ca <sup>2+</sup> soaps and lead to a reduction of serum [Ca <sup>2+</sup> ]
Massive transfusions	
Rhabdomyolysis	

Abbreviations: 25(OH)D<sub>3</sub> = 25-hydroxyvitamin D<sub>3</sub>; 1,25(OH<sub>2</sub>)D<sub>3</sub> = 1,25-dihydroxyvitamin D<sub>3</sub>; PTH = parathyroid hormone.

# Symptoms

- Neuromuscular and cardiovascular signs and symptoms predominate
- ECG finding → prolonged QTc interval, T wave may be of normal width, ST segment prolonged

**TABLE 17-26** Symptoms and Signs of Hypocalcemia

Muscular	Weakness, fatigue Spasms, cramps
Neurologic	Seizures Tetany Chvostek sign, Trousseau sign Circumoral and digital paresthesias Impaired memory, confusion Hallucinations, dementia Extrapyramidal disorders
Dermatologic	Hyperpigmentation Coarse, brittle hair Dry, scaly skin
Cardiovascular	Heart failure Ventricular arrhythmias, QT <sub>c</sub> prolongation leading to torsades de pointes Vasoconstriction
Skeletal	Osteodystrophy Rickets Osteomalacia
Miscellaneous	Dental hypoplasia Cataracts Decreased insulin secretion

# Investigations

- Full electrolyte panel, renal function tests, ionized  $[Ca^{2+}]$ , and magnesium levels, albumin level
- Blood gas analysis, phosphate level, PTH and vitamin D3 levels



# Treatment (orally)

- Food rich in  $\text{Ca}^{2+}$
- Not severe or prolonged for >10 to 14 days → oral  $\text{Ca}^{2+}$  ( $\text{Ca}^{2+}$  lactate, ascorbate, carbonate, gluconate)

# Treatment (IV)

- IV  $\text{Ca}^{2+}$  is recommended only in cases of symptomatic or severe hypocalcemia<sup>2</sup> (ionized  $[\text{Ca}^{2+}] < 1.9 \text{ mEq/L}$  or  $< 0.95 \text{ mmol/L}$ )
- IV  $\text{Ca}^{2+}$  can cause vasoconstriction and possible ischemia
- **IV  $\text{Ca}^{2+}$  gluconate is preferred over IV calcium chloride ( $\text{CaCl}_2$ )** → due to the dangers of extravasation with  $\text{CaCl}_2$  (calcinosis cutis)
- Hypocalcemia is difficult to correct if hypomagnesemia is also present because of reduction of PTH and  $\text{Ca}^{2+}$  releases from bone → magnesium should be replaced before, or in conjunction with,  $\text{Ca}^{2+}$  replacement

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# Hypercalcemia



# Intro

- $>10.5$  milligrams/dL or an ionized  $[\text{Ca}^{2+}]$  level  $>2.7$  mEq/L
- Neuromuscular changes  $\rightarrow$  decreased sensitivity, responsiveness, and strength of muscular contraction and nerve conduction
- The conduction of the heart is slowed and automaticity is decreased with a shortening of refractory period
- Loss of concentrating ability  $\rightarrow$  the most frequent renal effect of hypercalcemia
- Increasing microscopic  $\text{Ca}^{2+}$  deposits in kidney can lead to progressive renal insufficiency
- Associated with hyperparathyroidism or malignancy

# Causes

**TABLE 17-27** Causes of Hypercalcemia

Cause	Mechanism
<i>Hypercalcemia due to increased bone <math>\text{Ca}^{2+}</math> resorption</i> Primary hyperparathyroidism Malignancy  Pseudohyperparathyroidism Renal failure  Addison's disease Hyperthyroidism Immobilization	↑ PTH Osteolysis, PTH-related protein (PTHrP) production PTH from non-parathyroid tissue source Secondary and tertiary hyper-PTH due to chronic hypocalcemia ↑ Albumin, bone resorption Increased bone resorption Osteoclast activation
<i>Hypercalcemia due to decreased urinary <math>\text{Ca}^{2+}</math> excretion</i> Familial hypercalcemic hypocalciuria Thiazides	Mutation of CaSR Increased kidney $\text{Ca}^{2+}$ reabsorption in proximal tubule
<i>Hypercalcemia due to increased GI <math>\text{Ca}^{2+}</math> absorption</i> Granulomatous diseases (sarcoidosis, tuberculosis, coccidioidomycosis, histoplasmosis) Milk (calcium)-alkali syndrome  Vitamin D intoxication	1 $\alpha$ -Hydroxylase activity  ↑ $\text{Ca}^{2+}$ intake (calcium carbonate) and absorption Increased calcium absorption and bone resorption

Abbreviations: CaSR =  $\text{Ca}^{2+}$ -sensing receptor; PTH = parathyroid hormone.



# Symptoms

- Associated with depressed ST segments, widened T waves, shortened ST segments and QT intervals
- In severe hypercalcemia, ST-segment elevation mimicking MI
- Bradyarrhythmias may occur, with bundle branch patterns that may progress to second-degree block or complete heart block

**TABLE 17-28** Signs and Symptoms of Hypercalcemia

General	Cardiovascular
Malaise, weakness	Hypertension
Polydipsia, dehydration	Dysrhythmias
Neurologic	Vascular calcifications
Confusion	ECG abnormalities
Apathy, depression, stupor	QT shortening
Decreased memory	Coving of ST-T wave
Irritability	Widening of T wave
Hallucinations	Digitalis sensitivity
Headache	GI
Ataxia	Anorexia, weight loss
Hyporeflexia, hypotonia	Nausea, vomiting
Mental retardation (infants)	Constipation
Metastatic calcification	Abdominal pain
Band keratopathy	Peptic ulcer disease
Conjunctivitis	Pancreatitis
Pruritus	Urologic
Skeletal	Polyuria, nocturia
Fractures	Renal insufficiency
Bone pain	Nephrolithiasis
Deformities	



# Investigations

- Ionized  $[Ca^{2+}]$ ; then electrolytes, CBC, phosphate, magnesium, BUN, creatinine, and alkaline phosphatase
- ECG, chest radiograph

# Treatment

- Symptomatic patients or asymptomatic with  $[Ca^{2+}]$  levels  $>14$  milligrams/dL → should receive treatment starting with volume repletion
- **0.9% normal saline at 500 to 1000 mL/h for 2 to 4 hours**
- 3 to 4 L should be given over the first 24 hours, then 2 to 3 L per 24 hours until a urine output of 2 L/d is achieved
- Furosemide is recommended to promote a diuresis of 150 to 200mL/h → increases calciuric effect, with an initial dose of 20 to 40 milligrams
- IV bisphosphonates can be used → pamidronate or zoledronate (zoledronic acid)

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# Magnesium



# Intro

- Total body content of magnesium ( $\text{Mg}^{2+}$ ) is 24g or 2000 mEq, 50% to 70% of which is fixed in bone
- Most of the remaining  $\text{Mg}^{2+}$  is found in ICF space (~40 mEq/L)
- 2<sup>nd</sup> most abundant intracellular cation
- Normal serum [ $\text{Mg}^{2+}$ ] ranges between 1.5 and 2.5 mEq/L (0.7 to 1.1 mmol/L or 1.7 to 2.7 milligrams/dL)
- Circulating  $\text{Mg}^{2+}$  is 25% to 35% bound to proteins (mainly albumin), 10% to 15% complexed, and 50% to 60% ionized (the active portion)

**What it does???**

# What it does???

- About 300 enzymes have their activities regulated by  $Mg^{2+}$ ; it assists the production of adenosine triphosphate, participates in nucleic acid and protein synthesis, and is involved in coagulation, platelet aggregation, and neuromuscular activity, as well as in cardiac action potential
- $Mg^{2+}$  homeostasis is very complex and finely regulated by many factors, such as parathyroid hormone, calcitonin, ADH, glucose, insulin, glucagon, catecholamines, sodium, potassium, calcium, and phosphorus levels



# Hypomagnesemia

# Causes

**TABLE 17-20** Causes of Hypomagnesemia

Redistribution	IV glucose Correction of diabetic ketoacidosis IV hyperalimentation Refeeding after starvation Acute pancreatitis Postparathyroidectomy (hungry bone syndrome) Osteoblastic metastasis (hungry bone syndrome)
Extrarenal loss	Nasogastric suction (infrequent) Lactation Profuse sweating, burns, sepsis Intestinal or biliary fistula Diarrhea
Decreased intake	Alcoholism (cirrhosis) Malnutrition, poor intake Small bowel resection Malabsorption (steatorrhea)
Renal loss	Ketoacidosis Saline or osmotic diuresis Potassium depletion Phosphorus depletion Familial hypophosphatemia Tubulointerstitial renal disease
Drugs	Loop diuretics Aminoglycosides Amphotericin B Vitamin D intoxication Alcohol Cisplatin Theophylline Proton pump inhibitors Calcineurin inhibitors (cyclosporine, tacrolimus)
Endocrine disorders	Syndrome of inappropriate antidiuretic hormone secretion Hyperthyroidism Hyperparathyroidism Hypercalcemic states Primary or secondary aldosteronism

# Symptoms

**TABLE 17-21** Symptoms and Signs of Hypomagnesemia

Neuromuscular	Tetany Muscle weakness Chvostek and Trousseau signs Cerebellar (ataxia, nystagmus, vertigo) Confusion, obtundation, coma Seizures Apathy, depression Irritability Paresthesias
GI	Dysphagia Anorexia, nausea
Cardiovascular	Heart failure Dysrhythmias Hypotension
Miscellaneous	Hypokalemia Hypocalcemia Anemia



# Treatment

- Hypokalemia, hypocalcemia, and hypophosphatemia are often present with severe hypomagnesemia
- Treat or stop the cause
- For asymptomatic → magnesium supplements; Magnesium lactate, chloride, gluconate, and proteinate
- For severe & symptomatic → urgent IV replacement: magnesium sulfate ( $\text{MgSO}_4$ )
- In life-threatening conditions (torsades de pointes, eclampsia) → 1 to 4 grams or 8 to 32 mEq diluted in at least 100 mL of 5% dextrose or normal saline (0.9%) solution can be administered in 10 to 60 minutes

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# Hypermagnesemia

# Causes

**TABLE 17-22** Causes of Hypermagnesemia

Renal Failure	Acute or Chronic
Increased magnesium load	Magnesium-containing laxatives, antacids, or enemas* Treatment of preeclampsia/eclampsia (mothers and neonates) Diabetic ketoacidosis (untreated)* Tumor lysis Rhabdomyolysis*
Increased renal magnesium absorption	Hyperparathyroidism Familial hypocalciuric hypercalcemia Hypothyroidism Mineralocorticoid deficiency, adrenal insufficiency (Addison's disease)

\*Most likely presentations relevant to the ED.



# Symptoms

**TABLE 17-23** Symptoms and Signs of Hypermagnesemia

Magnesium Level (mEq/L)	Clinical Manifestations
2.0–3.0	Nausea
3.0–4.0	Somnolence
4.0–8.0	Loss of deep tendon reflexes
8.0–12.0	Respiratory depression
12.0–15.0	Hypotension, heart block, cardiac arrest

# Treatment

- Immediate cessation of  $Mg^{2+}$  administration
- Dilution by IV fluids followed by furosemide (40 to 80mg IV) may be indicated (provided no renal failure)
- Calcium directly antagonizes the cardiac effects of magnesium → reverts the calcium channel blockade provoked by elevated  $[Mg^{2+}]$
- Severe symptomatic hypermagnesemia → 10 mL of 10% calcium chloride IV over 2 to 3 minutes. Further infusion of 40 to 60 mL during the next 24 hours can be administered
- Renal failure may benefit from dialysis

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**Phosphate**



# Intro

- Highly reactive mineral
- Involved in oxidative phosphorylation and mitochondrial respiration, the essential component of ATP
- Total body phosphorus store ~ 700 grams (10 to 15 grams/kg)
- Homeostasis of  $\text{PO}_4^{3-}$  is mainly regulated by gut absorption and urine excretion
- Excretion is predominantly in urine by glomerulus, with majority reabsorbed in proximal tubules; regulated by PTH

# Hypophosphatemia

# Causes

**TABLE 17-29** Causes of Hypophosphatemia

Shift from ECF to ICF without depletion of $\text{PO}_4^{3-}$	Glucose Insulin Catecholamines Respiratory alkalosis
Shift from ECF to ICF with depletion of $\text{PO}_4^{3-}$	Hyperalimentation Refeeding syndrome
Decreased intestinal absorption	Low intake Malabsorption Chronic use of calcium acetate or bicarbonate, aluminum hydroxide Vitamin D deficiency
Increased renal loss	Hyperparathyroidism Increased fibroblast growth factor-23 (FGF-23) Genetic hypophosphatemia mutations Tubular acidosis Fanconi's syndrome Hypokalemia Hypomagnesemia Polyuria Acidosis
Miscellaneous causes	Alcoholism (poor intake, vitamin D deficiency) Diabetic ketoacidosis (osmotic diuresis) Toxic shock syndrome
Drugs	See Table 17-30

Abbreviations: ECF = extracellular fluid; ICF = intracellular fluid.



# Symptoms

**TABLE 17-31** Symptoms and Signs of Hypophosphatemia

## Hematologic

- Reduced survival and function of platelets and red and white blood cells
- Impaired macrophage function

## Neuromuscular

- Weakness, tremors, circumoral and fingertip paresthesias, decreased deep tendon reflexes, decreased mental status, anorexia

## Cardiac

- Impaired myocardial function

## Metabolic

- Insulin resistance