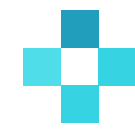


INTERNAL MEDICINE

Na⁺ IMBALANCE PRESENTATION



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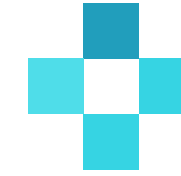
♥ Physiology of Na regulation

♥ Hyponatremia

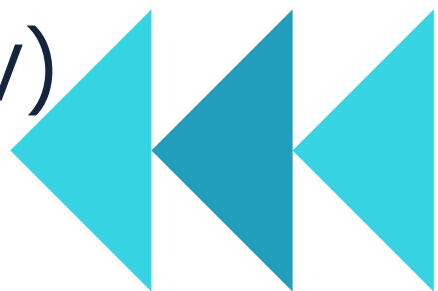
♥ Hypernatremia

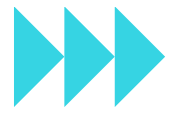


physiology of Na regulation

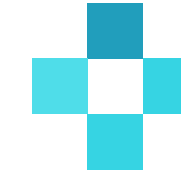


- primary cation in ECF which determines ECF osmolarity
- **NA BALANCE REGULATION**
 1. Na balance (Na excretion = Na intake)
 2. Positive Na balance: increase Na retention → Na in ECF → ECF expansion → increase blood volume and blood pressure
 3. Negative Na balance: increase excretion of Na – decrease Na in ECF → ECF contraction → decrease blood volume and blood pressure
 4. Na is filtered freely from the glomerulus and reabsorbed from the tubular system
 5. Some of Na is excreted in urine
- **Effective arterial blood volume (EABV)**
 1. Any change in EC will cause a parallel change in EABV
 2. Edema: fluid filtered into interstitial space → increase ECF → increase EABV (increase BP) → Na excretion altered by kidneys (attempts to restore normal EABV)

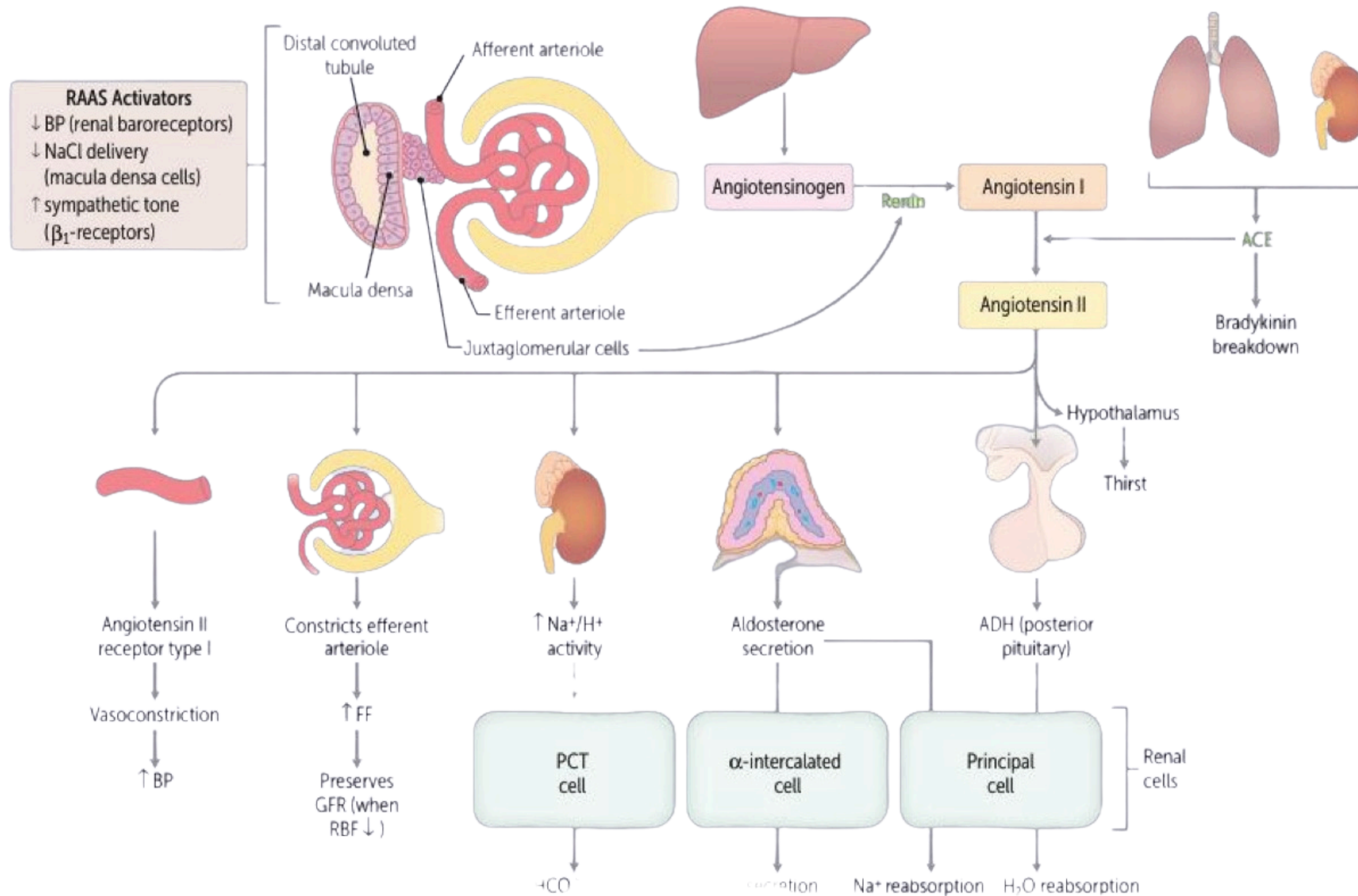




physiology of Na regulation

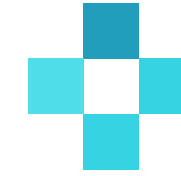


Renin-angiotensin-aldosterone system





physiology of Na regulation



- **Atrial Natriuretic peptide (ANP)**

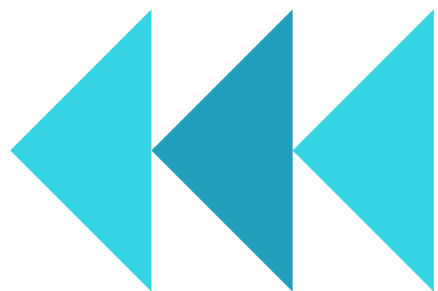
- Released from atrial myocytes in response to high blood volume and atrial pressure

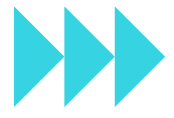
- **ANP causes:**

1. vasodilation and inhibition of Na^+ reabsorption at the renal collecting tubule
2. Dilates afferent renal arterioles and constricts efferent arterioles, promoting diuresis and contributing to the "aldosterone escape" mechanism.
3. Acts opposite to angiotensin 2

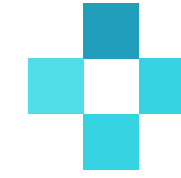
- **Brain Natriuretic peptide (BNP)**

1. Released from ventricular myocytes in response to increased tension.
2. Similar physiologic action to ANP
3. Useful for diagnosing heart failure

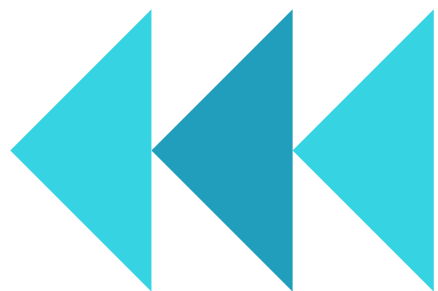
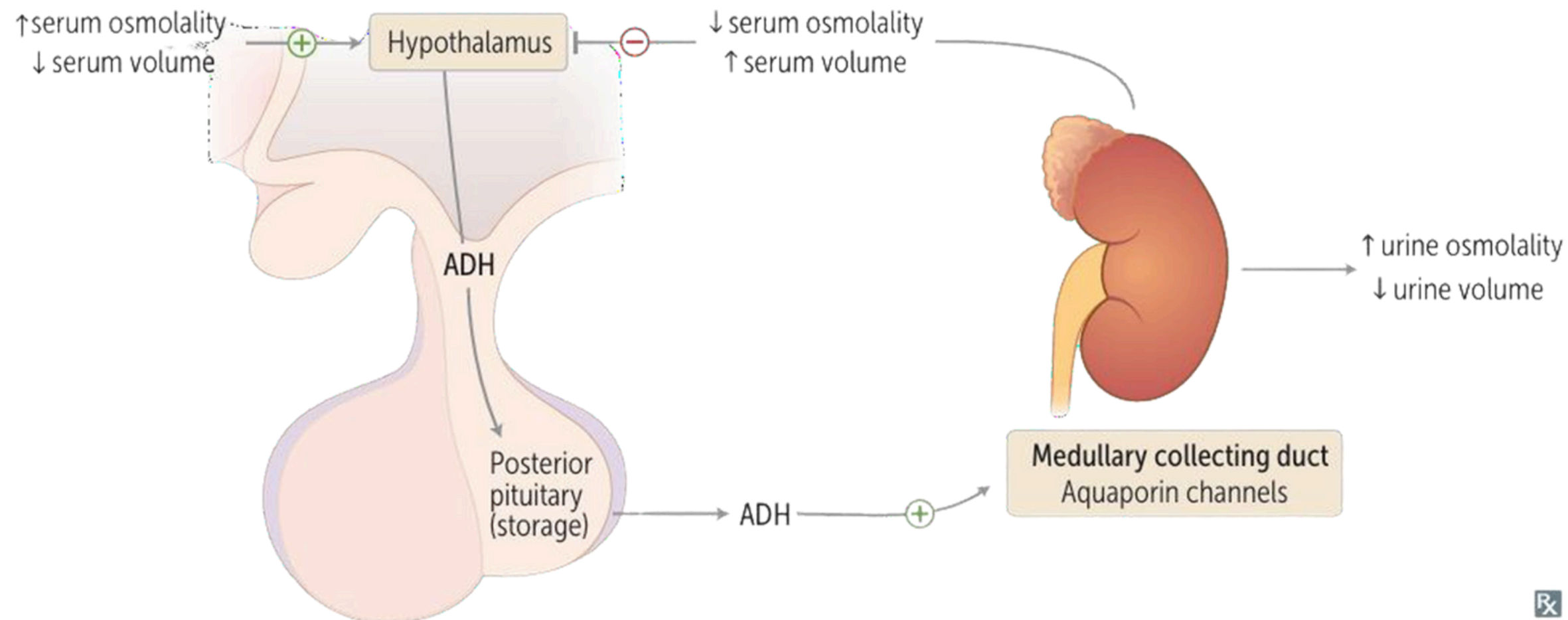




physiology of Na regulation

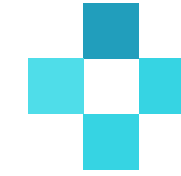


- **Anti diuretic hormone (ADH)**
- Source: supraoptic and paraventricular nuclei in posterior pituitary
- Regulates blood pressure (V1-receptors) and serum osmolality (V2-receptors)
- ADH induces reabsorption of water causing:
 1. increase in urine osmolality
 2. Decrease in serum osmolality



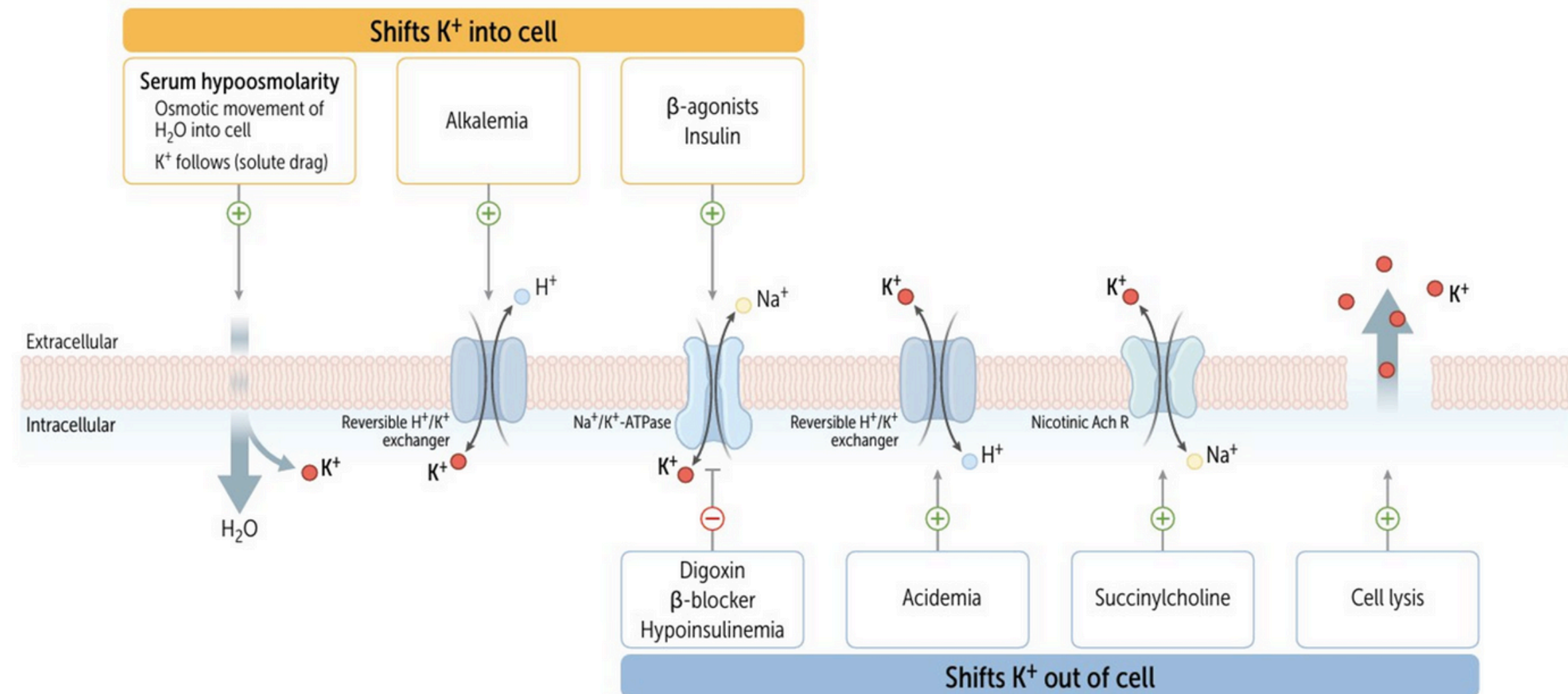


physiology of K⁺ regulation



- Potassium (K⁺): primary intracellular cation (98%)
- Regulates intracellular osmolarity
- Concentration gradient across cell membrane establishes resting membrane potential, essential for excitable cell function (e.g. myocardium)
- Potassium (K⁺) is regulated mainly via Na⁺/K⁺ ATPase pump
- K⁺ is filtered freely from the glomerulus and reabsorbed from the tubular system
- Some of K⁺ is excreted in urine

Potassium shifts

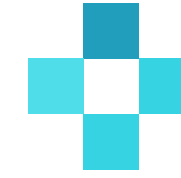


DEFINITION

- **Hyponatremia:** decreased $[Na^+]$ level in the blood
 - That happen by :
 - Losing Na^+ more than water
 - Gaining water more than Na^+
- **Normal level of $[Na^+]$** is between (135-145mosm/L)
- **Hyponatremia** is when the $[Na^+](<135\text{mosm/L})$



▶▶ Causes & classifications of hyponatremia

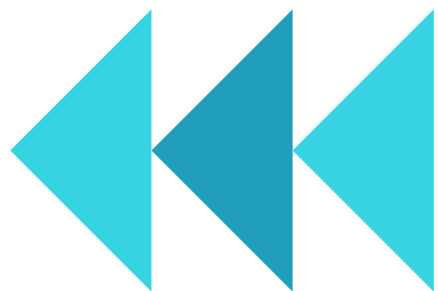


❑ Hypotonic hyponatremia [Serum osmolality <280 mOsm/kg]

- According to ECF volume status :
 - hypervolemic hypotonic hyponatremia
 - Euvolemic hypotonic hyponatremia
 - Hypovolemic hypotonic hyponatremia

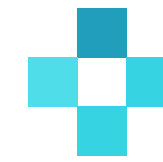
❑ Isotonic hyponatremia [Serum osmolality (280-295)mOsm/kg]

❑ Hypertonic hyponatremia [Serum osmolality >295 mOsm/kg]





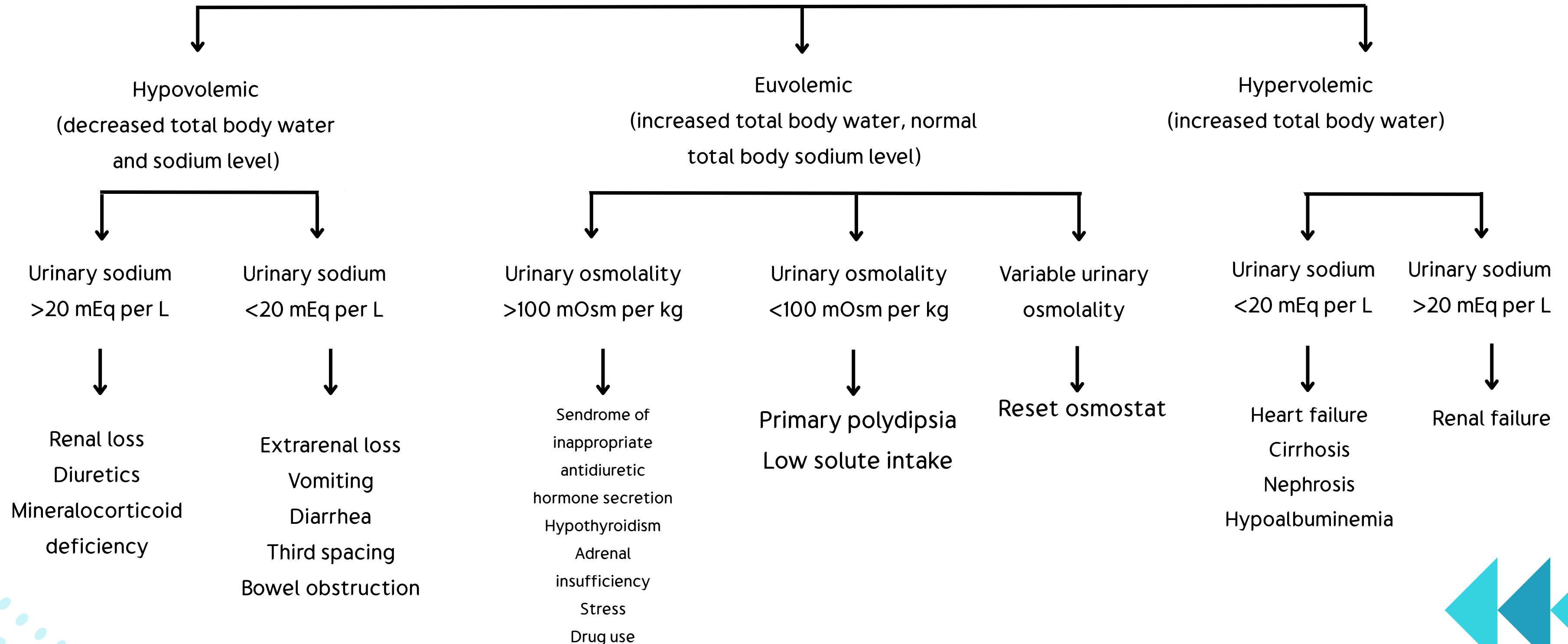
Hypotonic hyponatremia



Serum osmolality < 280 mOsm/kg

Hypotonic hyponatremia

(Serum osmolality < 280 mOsm per kg)



A-Hypervolemic hypotonic hyponatremia

❖ Overview:

large increase of Total body water( ECF) & small increase of Na+

❖ Causes:

- CHF
- Liver Cirrhosis
- Nephrotic syndrome
- Chronic kidney disease



A-Hypervolemic hypotonic hyponatremia



Mechanism :

- fluid leaks out blood vessels to the Interstitial space and lead to performing edema,ascitis,JVD
- decreased effective arterial blood volume → Stimulate Renine angiotensin aldosterone system:
 - 1 ↑ ADH → Increase water retention
 - 2 ↑ Aldosterone → Increased Na+retain → that lead to increase H2O retention (water follow Na+)
- Low urine sodium due to water retaining states.



B- Euvolemic **hypotonic hyponatremia**

❖ Overview

Elevated total body fluids (but without evidence of expanding of ECF)& normal level of Na⁺

❖ Classifications according urine osmolality

1-High concentrated urine

Caused by :SIADH (Small cell lung cancer and carbamazepine)

Mechanism: Inappropriate ADH release lead to water retention & dilution of sodium, while ECF volume remains normal due to sodium excretion by urination (Aldosterone escape mechanism)

2- Diluted urine

Caused by :

1. Adrenal insufficiency
2. Hypothyroidism
3. Primary polydipsia (Drinking too much of water)
4. Potomania(Drinking too much of alcohol)



C- Hypovolemic **hypotonic hyponatremia**

❖ Overview

Small decrease of total body fluids( ECF) & large decrease of Na+
Low urine sodium

❖ Causes

▪ 1-Extra renal losses:

A-Diarrhea & Vomiting

B-diaphoresis

C-burns



C- Hypovolemic **hypotonic hyponatremia**

- 2-Renal causes :

- A. Diuretics (eg:Thiazides)

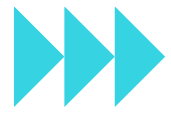
- B. Mineralocorticoid deficiency (eg:Addison's disease)

- 3-Cerebral salt wasting:

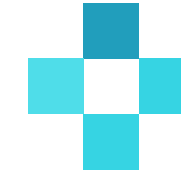
disruption in the hypothalamic pituitary axis **or** brain injury like(SAH,Brain tumors)

Increased natriuretic peptide → that decreased renal sodium reabsorption & enhanced renal sodium excretion

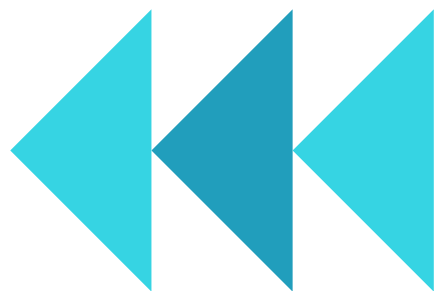




Diagnosis & Treatment:

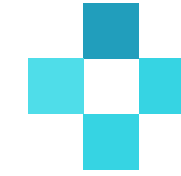


Subtype	Diagnosis	Treatment
Hypovolemic Hypotonic Hyponatremia	- Signs of dehydration: hypotension, tachycardia.- - Urine sodium: <20 mmol/L in non-renal loss, >20 mmol/L in renal loss.	- Volume resuscitation: Normal saline 0.9%.- - Treat underlying cause (discontinue diuretics, treat Addison's disease).
Euvolemic Hypotonic Hyponatremia	- No signs of dehydration or overload.- - Urine sodium: >20 mmol/L, high urine osmolality in SIADH.	- Fluid restriction: 1–1.5 L/day.- - Treat underlying cause (e.g., SIADH, adrenal insufficiency, hypothyroidism).
Hypervolemic Hypotonic Hyponatremia	- Signs of fluid overload: edema, ascites, JVD.- - Urine sodium: <20 mmol/L in heart failure, cirrhosis, nephrotic syndrome.	- Fluid and sodium restriction.- - Diuretics (e.g., furosemide).- - Treat underlying condition (e.g., heart failure, cirrhosis).





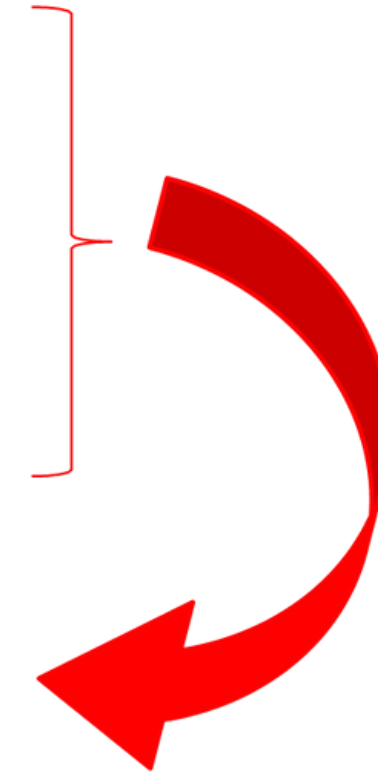
Isotonic hyponatremia (pseudo hyponatremia)



Overview:

Normal level of Na^+ & Normal H_2O volume

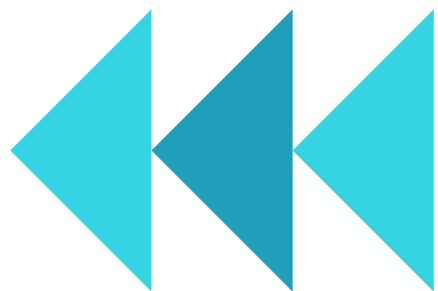
Increased level of: Triglycerides (Hyperlipidemia)
Protein (Multiple myeloma)

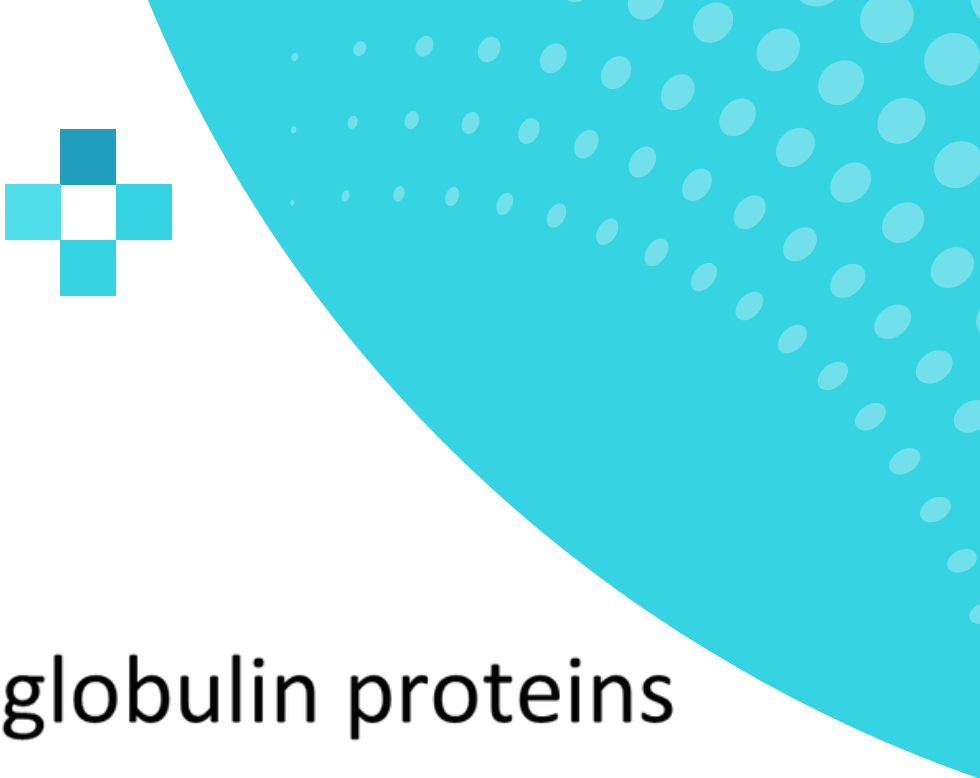


- These factors lead to false lab results

decreased Na^+ result

Mechanism: Traditional sodium measurement methods : These assume plasma is composed of 93% water and 7% non-water components. When lipids or proteins are excessively elevated, they dilute the plasma water portion, resulting in falsely low sodium readings.

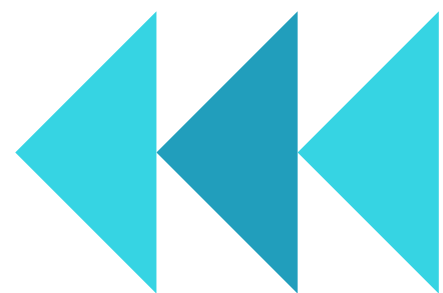




▶▶▶ Diagnosis:

1. Serum osmolality: normal osmolality (280-295mOsm/kg)
2. plasma lipid & protein levels: elevated triglycerides & immunoglobulin proteins

▶▶▶ Treatment:

1. **Hyperlipidemia**: lifestyle modification or lipid lowering medications (eg: statins)
 2. **Hyperproteinemia** : Treat the underlying disease (eg: chemotherapy for multiple myeloma)
 3. **Avoid unnecessary sodium correction** : because plasma water sodium concentration is normal
- 

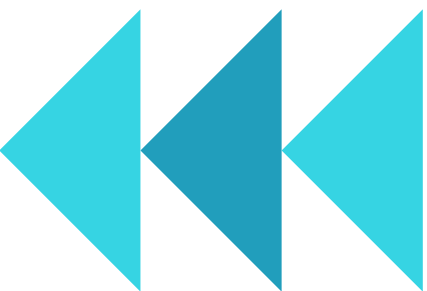
▶▶▶ **Hypertonic hyponatremia**



Caused by the presence of osmotic substances that increase plasma osmolality then cause an osmotic shift of water out of cells. The dilution of plasma sodium leads to hyponatremia

These substances include:

- Glucose-Hyperglycemia
- Mannitol, sorbitol, glycerol, maltose
- Radiocontrast agents





Hypertonic hyponatremia

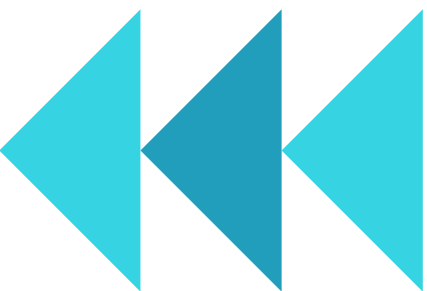


❖ Diagnosis:

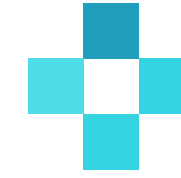
- Elevated serum osmolality
- Elevated serum glucose

❖ Treatment

- 1-Treat the underlying causes :
 - **Hyperglycemia:** Use insulin therapy
 - **Mannitol or contrast agent exposure:** stop or adjust the use of the osmotic agent
- 2-sodium correction:
 - Gradually to avoid osmotic demyelination syndrome
- 3- monitoring for neurological symptoms



▶▶ Clinical features



❖ Symptoms usually begin when the Na^+ level falls to $<120\text{mEq/L}$

❖ Symptoms:-

1- **Neurological symptoms:** caused by osmotic water shifts which lead to increased ICF volume —————> Brain edema

Headache, muscle twitching, hyperactive deep tendon reflex

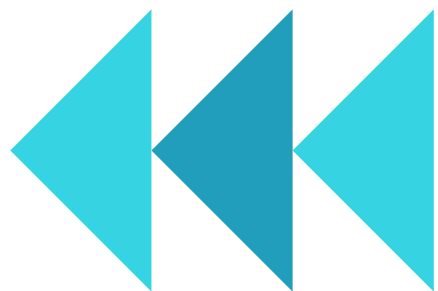
Increased ICP, Coma, Seizure

2- **GI symptoms:** vomiting, watery diarrhea

3- **Cardio Vascular symptoms:** HTN due to increased ICP

4- **Increased salivation & lacrimation**

5 **Oliguria progressing to anuria** (maybe reversible)

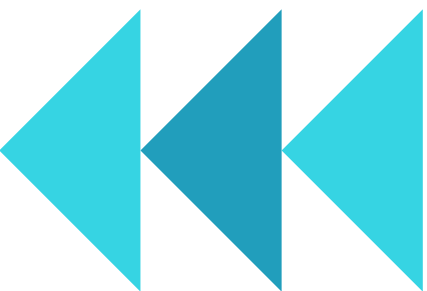


Hypernatremia



- **General Features of hypernatremia**

- Defined as $\text{Na} > 145 \text{ mEq/L}$
- Hypernatremia is much less common than hyponatremia and nearly always indicates a water deficit.
- Hypernatremia is always associated with high osmolarity which stimulate thirst center in the brain making the patient thirsty so hypernatremia doesn't occur unless the patient experiences one of the following:
 1. The thirst center doesn't stimulate water intake or there is limited access to water
 2. The patient lost a lot of fluids (Febrile illness, burns, diarrhea, diuretics)



Hypernatremia

- **Clinical features**
- Symptoms of hypernatremia are non-specific
 1. Irritability, confusion, stupor, and coma
 2. Convulsions occur in severe hypernatremia.
- **Causes of hypernatremia**
- Most important ones are:
 1. Central diabetes insipidus
 2. Nephrogenic diabetes insipidus
 3. Impaired thirst in elderly

? Box 9.16 Causes of hypernatraemia

Antidiuretic hormone (ADH) deficiency

- Pituitary diabetes insipidus (see p. 641)

Iatrogenic

- Administration of hypertonic sodium solutions
- Administration of drugs with a high sodium content (e.g. piperacillin)
- Use of 8.4% sodium bicarbonate after cardiac arrest

Insensitivity to ADH (nephrogenic diabetes insipidus)

- Lithium
- Tetracyclines

- Amphotericin B
- Acute tubular necrosis
- Osmotic diuresis
- Total parenteral nutrition
- Hyperosmolar hyperglycaemic state (see p. 725)

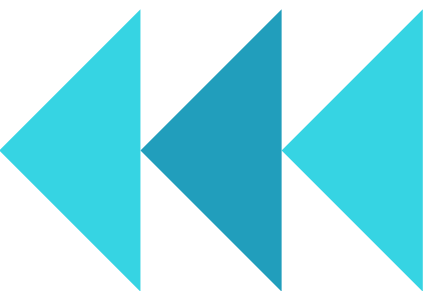
Plus

- Deficient water intake: impaired thirst or consciousness
- Excessive water loss through skin or lungs

Hypernatremia



- Diabetes insipidus means loss of ADH effects causing:
 1. Polyuria
 2. Polydipsia
- Central Diabetes insipidus:
 1. There is little or Low ADH
 2. It's usually due to trauma, Surgery or tumor in the brain but there are many other causes
- Nephrogenic Diabetes insipidus:
 1. ADH is normal but the kidneys don't response to ADH
 2. Resistance to ADH
 3. Causes:
 - Electrolyte disturbances: Hypercalcemia, Hypokalemia (severe: < 3.0 meq/L)
 - Drugs: Lithium, Amphotericin B, and demeclocycline
 - Hereditary: ADH Receptor mutation



▶▶▶ Hypernatremia +

- **Diagnosis**

- Serum Osmolarity: Hypernatremia or normal sodium
- Urine Osmolarity is low (50-200 mOsm/L)
- Diluted urine: Specific gravity < 1.006

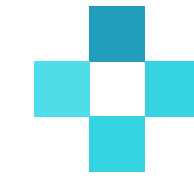
- **Water deprivation test**

1. After 8 hours of no fluid, urine should be concentrated
2. No increase in urine osmolarity (Urine remains diluted) which excludes primary polydipsia

- **Desmopressin test**

1. Desmopressin is ADH analogue which stimulates ADH V2 receptor triggering water reabsorption and urine concentration
2. Urine osmolarity increase significantly (Concentrated urine) : Central DI
3. Diluted urine : Nephrogenic DI

▶▶▶ Hypernatremia



- **Treatment**

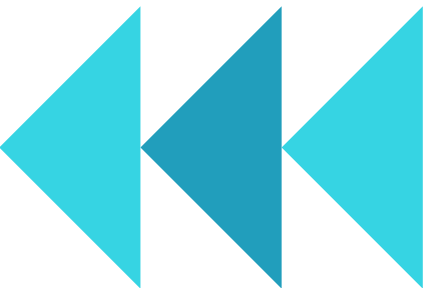
- Water (ideally PO)
- IV Fluids (D5W)

- **Caution: cerebral edema**

1. Occurs with overly-rapid correct of hypernatremia
 2. Maximum correction: 12 mEq/L/day
- From high to low, your brain will blow (Cerebral edema)

- **Central diabetes insipidus treatment: Desmopressin (DDAVP)**

- Desmopressin (DDAVP) doesn't have any vasoconstrictive effects



Hypernatremia

- **Nephrogenic diabetes insipidus treatment:**

- **Low sodium diet**

- **Thiazide diuretics: HCTZ**

1. Inhibit NaCl cotransporter

2. Loss of a high amount of NaCl

3. Activation of RAAS

4. Reabsorption of Na and water

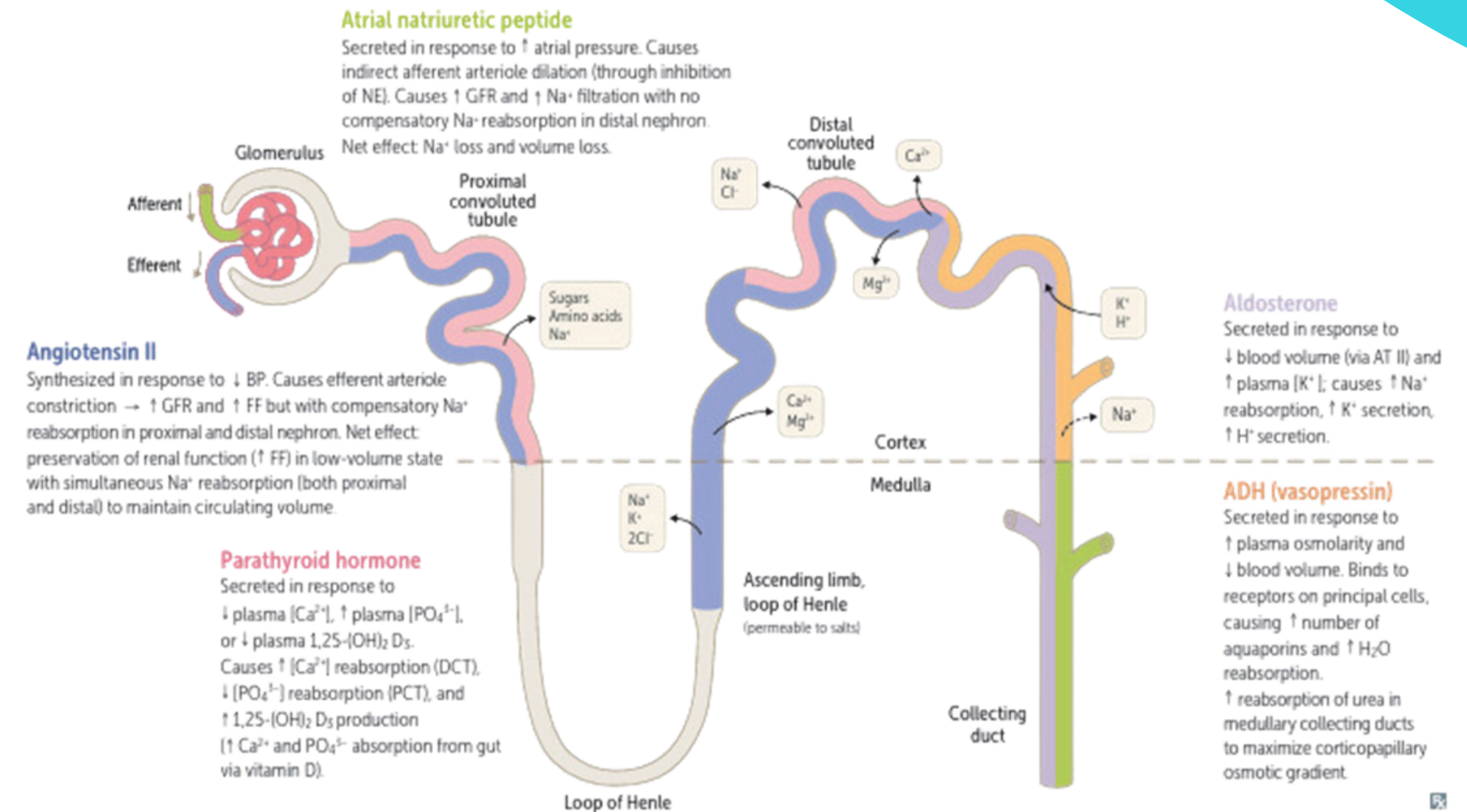
5. **Paradoxical antidiuretic effect**

- **NSAIDs: Indomethacin**

- prostaglandins antagonize the effect of ADH

- NSAIDS inhibit renal synthesis of prostaglandins which improves ADH activity

Hormones acting on kidney



Hypernatremia

- Central vs Nephrogenic diabetes insipidus

	Central DI	Nephrogenic DI
Definition	Low ADH	ADH resistance
ADH Level	LOW	NORMAL
Water deprivation test	Urine remains diluted	Urine remains diluted
Desmopressin test	Concentrated urine	Diluted urine
Treatment	Desmopressin (DDAVP)	HCTZ Indomethacin Low sodium diet



GROUP C6



THANK YOU

FOR YOUR ATTENTION

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