MED439
KING SAUD UNIVERSITY

Physiology Team 439

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PHYSIOLOGY

RENAL FILTRATION OF BODY FLUIDS

Objectives

- Identify and describe the role of the sensors and effectors in the renal regulation of body fluid volume.
- Describe the role of the kidney in regulation of body fluid volume & osmolality.
- Identify the site and describe the influence of aldosterone on reabsorption of Na+ in the late distal tubules.
- Understand the role of ADH in the reabsorption of water and urea

Black: in male AND female slides
Red : important
Pink: in female slides only
Blue: in male slides only
Green: Notes
Gray: extra information

Editing file

Introduction

Regulation of ECF

Control of ECF volume

Why is it important to regulate ECF volume

Determines:
blood pressure → tissue perfusion

ECF volume has an effect on blood volume, blood pressure, & perfusion of organs.
Normal plasma means normal blood volume, hence blood pressure is good.
Good blood pressure is important as it perfuses organs.

Regulated by:
Adjusting total body Na+ content (Na Excretion)

Modulates Na body content by modulating Na excretion. So if there is a high amount of Na in the body, ECF volume increases. Na is then excreted from the body through the kidney.

The 2 systems use different:
Sensors
Hormonal transducers
Effectors

Control of ECF Osmolarity

Determines:
Cell volume → cell function

The cell lives in an isotonic solution. So if the osmolarity increases cell shrinks and if it decreases cell swells.
The cells present in the CNS are the most cells affected by change in osmolarity. Once this happens , the cell, no longer functions properly.

Regulated by:
Adjusting total body H_2O content (H_2O Excretion)

When the body wants to adjust the total water content, it asks the kidney to adjust water excretion. However, when osmolarity of ECF becomes hypertonic; ADH is released. This decreases water excretion & osmolarity returns to normal.

Q / Why does the body regulate ECF volume by adjusting body Na^+ content?

Na^+ is the most abundant solutes in the ECF & when we move Na from one compartment to another, water moves with it. This is due to the osmotic gradient created by the movement of Na.

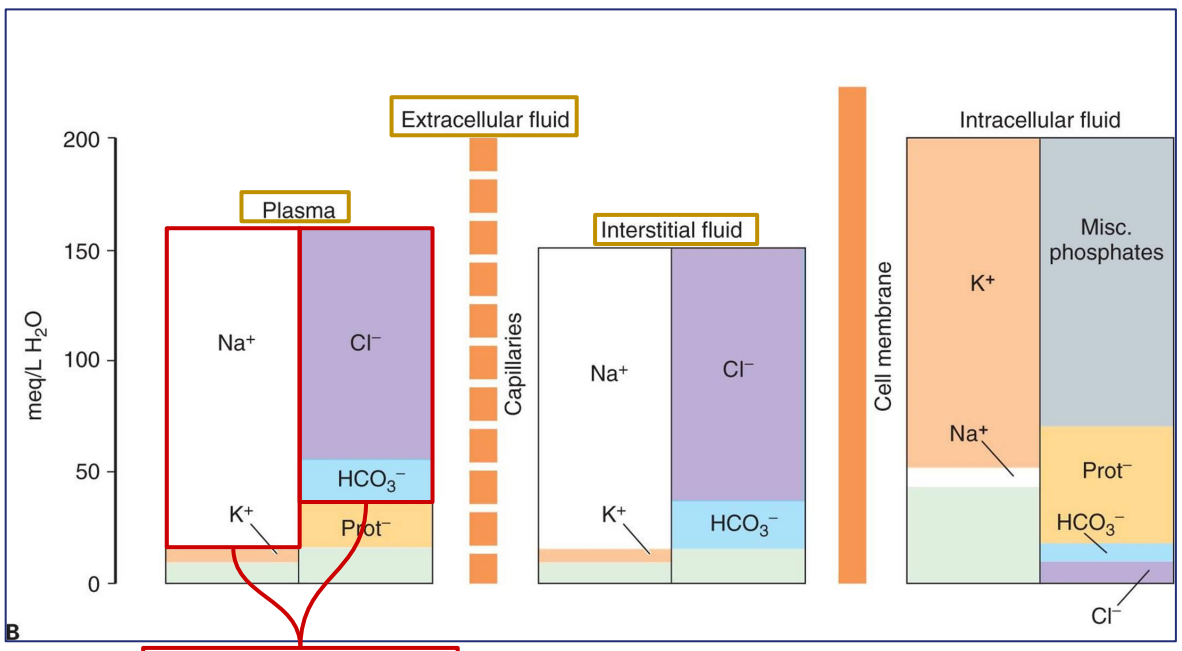
Electrolyte composition of body fluids

01 The most abundant cation in ECF is Na

02 The most abundant anions in ECF are Cl^- and HCO_3-

03 The body regulates ECF volume by monitoring and adjusting total body content of Na^+

04 ECF volume is closely linked to Na^+ balance



The main osmotic constituents of ECF

So any changes in these ions will cause changes in ECF volume.

Why is Na^+ Content the Main Determinant of ECF Volume?

Because Na^+ and its associated anions are the main osmotic constituents of ECF volume,when Na^+ salts moves,water most follow.

01 ↑↑Na in ECF

02 ↑↑ECF osmolarity

03 ↑↑H_2O reabsorption by kidney and stimulate thirst

04 Increase ECF volume

Sodium Balance	
Input	**Output**
Dietary intake	Kidney most important
RDA=1.5-2.3 g/day (RDA= Recommended Dietary Allowance)	**GI loss** (minor pathway under normal condition)
Actual content in western diet = 7g/day	**Sweat** (minor pathway under normal condition) They are a major exit route for Na during pathological conditions.

Body sodium distribution

- ECF (65%) **Exchangeable**
- ICF (5-10%) **Exchangeable**
- Bones (25-30%) **As Na apatite salts** Non-Exchangeable

ECF volume regulation

1.What does the body sense ?

01 The body does not sense ECF volume But it senses Effective circulating volume (ECV).

02 ECV: a functional blood volume that reflects the extent of tissue perfusion in specific regions,as evidenced by the pressure in their blood vessels.

03 ECV reflects adequacy of circulation.Fullness & pressure in the vessels.
Fullness is the amount of blood & pressure of the blood.

04 Usually changes in ECV parallel those of ECF volume.

What is the goal of effective circulation?
To maintain constant perfusion so that the organs receives enough nutrients and O_2

Effective circulating Volume

Increase in ECF volume	Normal ECF volume	Decrease in ECF volume
Increase in ECV	Normal ECV	Decrease in ECV
Increase in ABP & tissue perfusion	Normal ABP and adequate tissue perfusion	Decrease in tissue perfusion

2.What are the Sensors?

Changes in ECV
All down to Na+ balance i.e. absorption & excretion

Sensed by

Baroreceptors

They detect changes in pressure caused by stretch.
They get stretched when BP increases and they will not stretch when BP decreases

in

- **CNS**
- **Vascular "Central"**
  - **Low pressure sensors**
    "Very important ":
    (cardiac atria - pulmonary vasculature)
  - **High pressure sensors**:
    1- carotid sinus 2- aortic arch
    3- juxtaglomerular apparatus (Renal afferent arteriole).
- **Liver**

3.What are the Effectors?

Stimulate Baroreceptors will generate:

- **neural pathway**
  - **Sympathetic NS**
- **hormonal pathways**
  - **RAAS**
  - **ANP**
  - **ADH**

Sympathetic Nervous System (SNS)

- Its role is thought to be especially important during stressful conditions, e.g. hemorrhage.
- ↓ ECV → ↓Blood pressure → Stimulate SNS through baroreceptors:

direct effect in the kidney

- ↑ Na+ reabsorption by PCT
- ↑ Renal vascular resistance
  vasoconstriction of afferent
  → ↓GFR
  → ↓ Na excretion

Indirect Effect

Stimulate renin release from JGA:

- ↑ aldosterone
- ↑ angiotensin II

The end result will be Decrease of Na+ excretion (more Na+ return into circulation) —> increase ECV

The Renin-Angiotensin-Aldosterone System (RAAS)

Occurs during:
Hemorrhage
Dehydration
Shock
Hypotension

↓ ECV

↓stretch of baroreceptors in the afferent due to low BP

Causes granular cells in JGA to release Renin

Renin

Angiotensinogen

Angiotensin-I

ACE

Renin secreted by:
1-↓perfusion pressure
2- Sympathetic stimulation via B1
3-↓Na+ reaching macula densa

Angiotensin-II
Long Term Regulation of Arterial Pressure
negative feedback

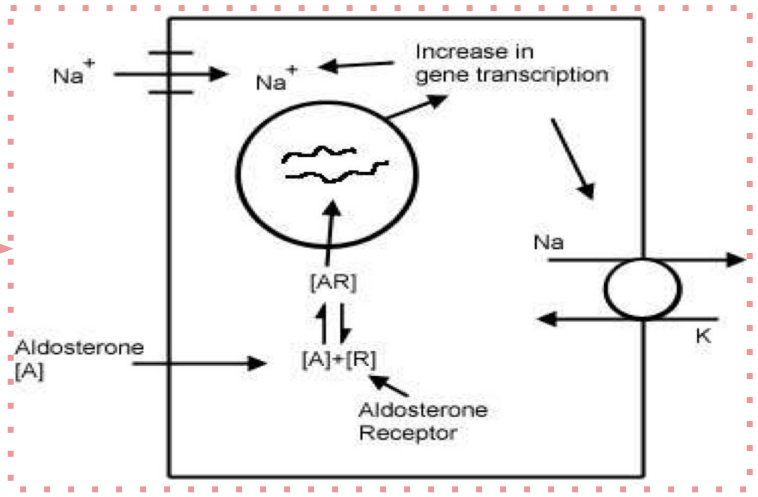
Actions of angiotensin II via AT1:

- **↑reabsorption of Na+** at PCT direct Stimulation of Na-K ATPase and Na-H counter transport
- **↑thirst** In hypothalamus
- **↑Aldosterone** (Mineralocorticoids)
- **Vasoconstriction** lead to↑ BP
- **↑ ADH** ↑water absorption Released from posterior pituitary gland

↓↓Na+ Excretion

- Angiotensin II increase aldosterone secretion from adrenal cortex via AT1 receptors.
- Aldosterone↑ Na water reabsorption in exchange with K or H excretion at the P cells of DCT & CD by:

1. ↑Number of Na+ channels at the apical membrane.
2. Stimulate Na-K pump at basolateral membrane.



Atrial Natriuretic Peptide (ANP)

- ANP promotes **natriuresis** (Na+ excretion)
- Secreted by atrial myocytes in response to stretch

ANP is Antagonist of renin-angiotensin:

01 relaxation of mesangial cells, vasodilation of afferent arteriole and vasoconstriction of efferent →↑GFR

02 ↓ADH release

03 ↓renin release

04 ↓Na+ reabsorption at CD by inhibiting:
-Na+ channels at apical membrane.
-Na+-K+ ATPase at basolateral membrane.

05 ↓direct aldosterone release

↓ECV
↓ANP release
atria is not stretch
↓Na+ and water excretion

↑ECV
↑ANP release
atria is stretch
↑Na+ and water excretion

Male slides only

Antidiuretic hormone (ADH)/Vasopressin

Main functions of ADH:

1 water reabsorption

2 stimulate thirst center

1

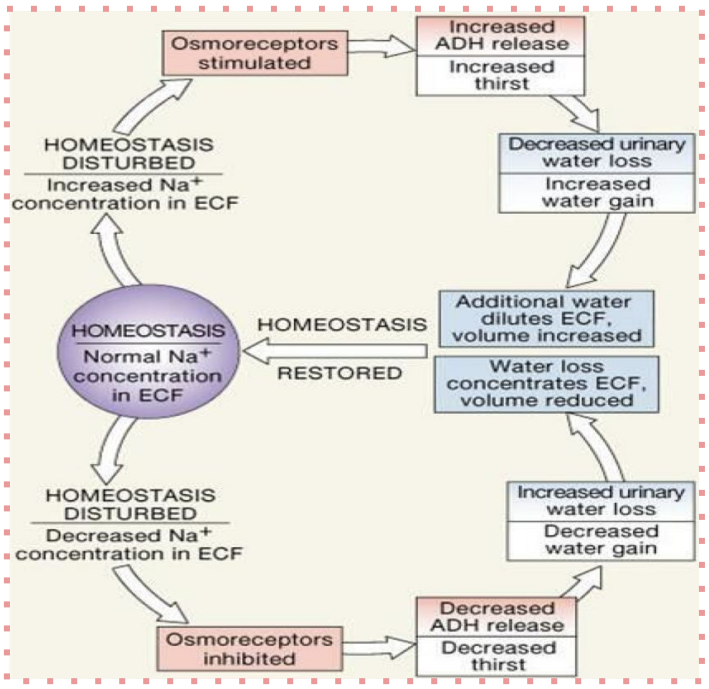
↑Osmolarity and ↓ECV

Stimulate Osmoreceptors in the anterior Hypothalamus

posterior pituitary gland release ADH

V2 receptors Antidiuretic action Water retention Via Aquaporin II channels

V1 receptors Vasopressor action



2

- Drinking is by habit. So when we drink enough water, we doesn't get thirsty. Thirst is an emergency mechanism when there is a lack of water.
- Stimuli for thirst is similar to osmoreceptors which produce and release ADH.
- Major mechanism for causing sensation of thirst is an "intracellular dehydration" mainly due to ↑Osmolality of extracellular fluid

H_2O permeability & control of intake

The permeability of the distal tubule to H_2O is regulated by ADH for example:

H_2O diuresis and ↑H_2O intake	Cause	↓permeability in distal tubule and produce dilute urine
Dehydration	Cause	↑H_2O reabsorption resulting in concentrated urine (max of 1200 mOsm)

Other hormones that control of Na reabsorption

1 Glucocorticoids

- Have weak mineralocorticoid activity

2 Sex hormones

- Estrogen↑ Na^+ reabsorption

3 PGE 2

↑ Na^+ excretion through:

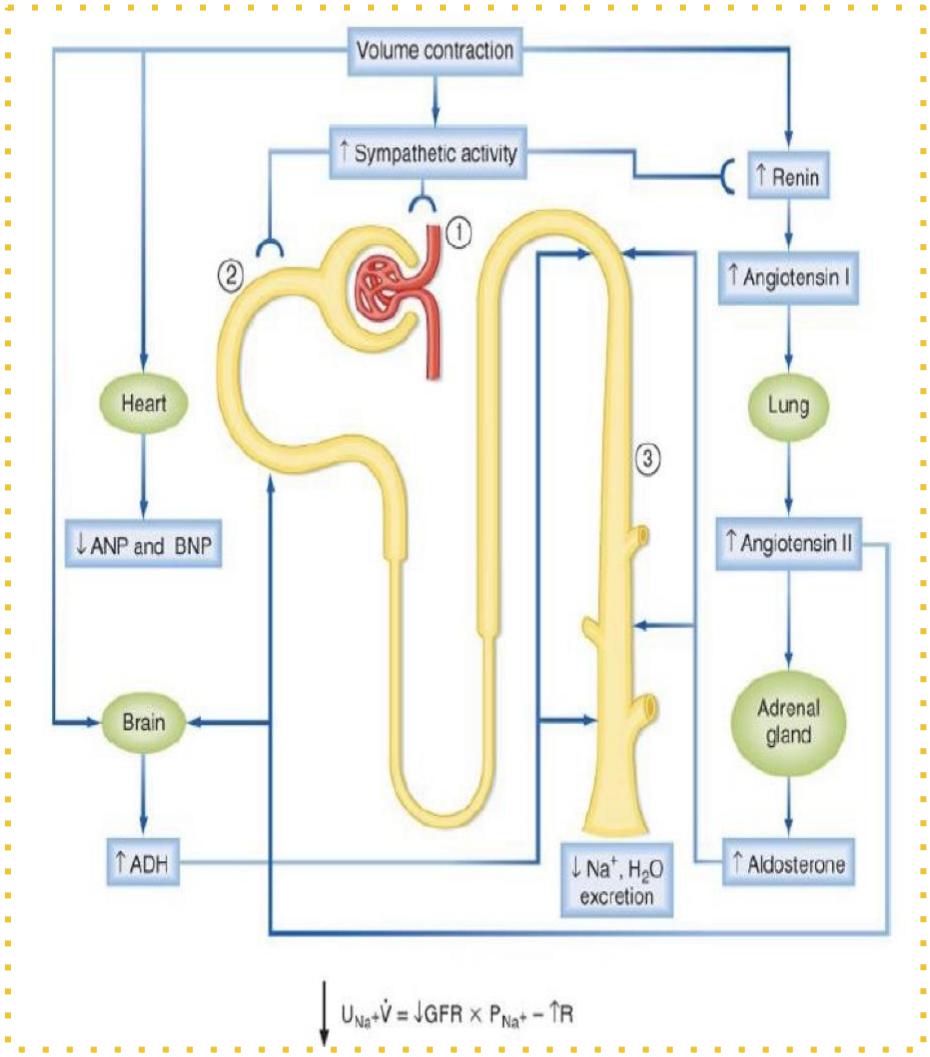
- Inhibit apical Na^+ channels
- Inhibit Na^+-K^+ ATPase

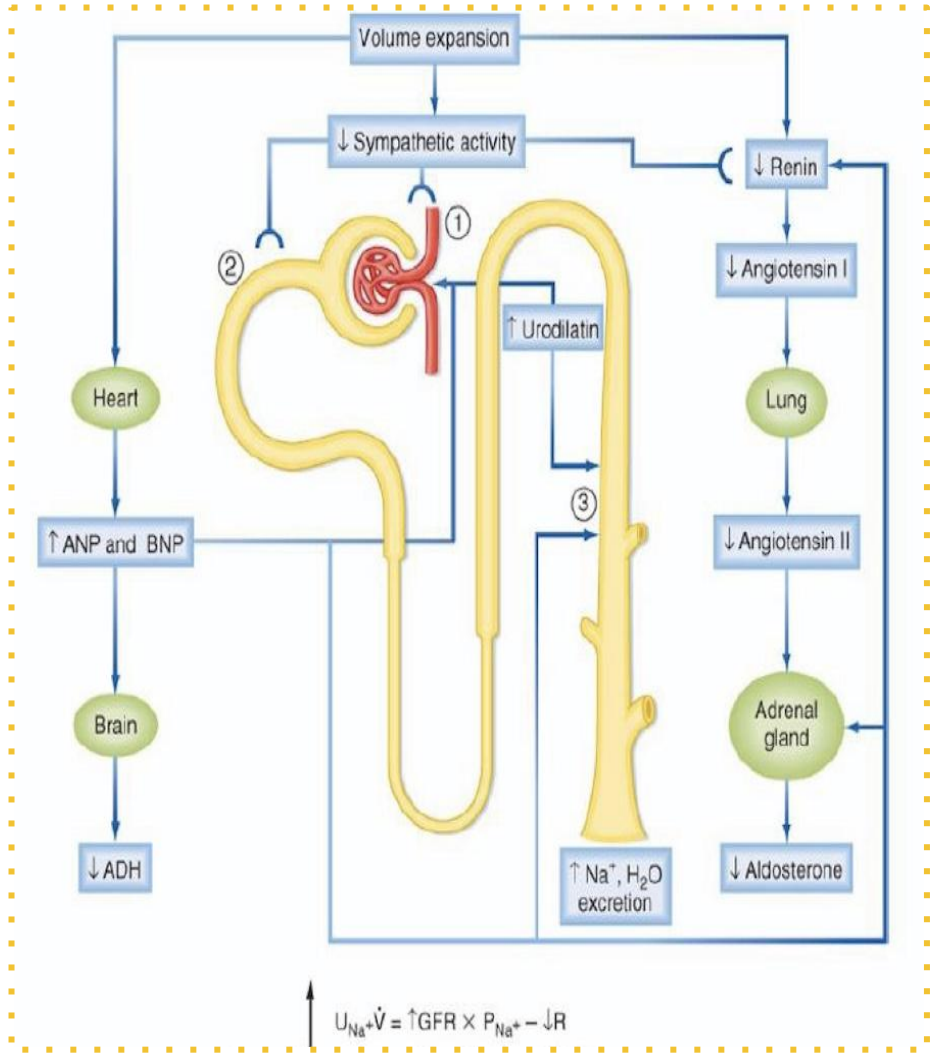
(Action similar to ANP and opposite to aldosterone)

Doctor notes

- under physiologic conditions, the body regulates plasma volume & plasma osmolarity independently because, plasma volume is regulated by: Na+ and the main effector is: RAAS, sympathetic and ANP while the plasma osmolarity is regulated by: water and the main effector is: ADH and thirst.
- under pathological conditions, severe derangements in fluid & electrolyte balance may challenge the system by presenting two **conflicting** changes in osmolarity and volume. For example: someone has hypotension and hypo-osmolarity at the same time, Hypo-osmolarity is corrected by: inhibit ADH → water loss → severe hypotension "so its getting worse".
- In general, if there is two **conflicting** changes the body defends **volume** at the expense of osmolarity. "so volume is more important than osmolarity, because it determines the perfusion".

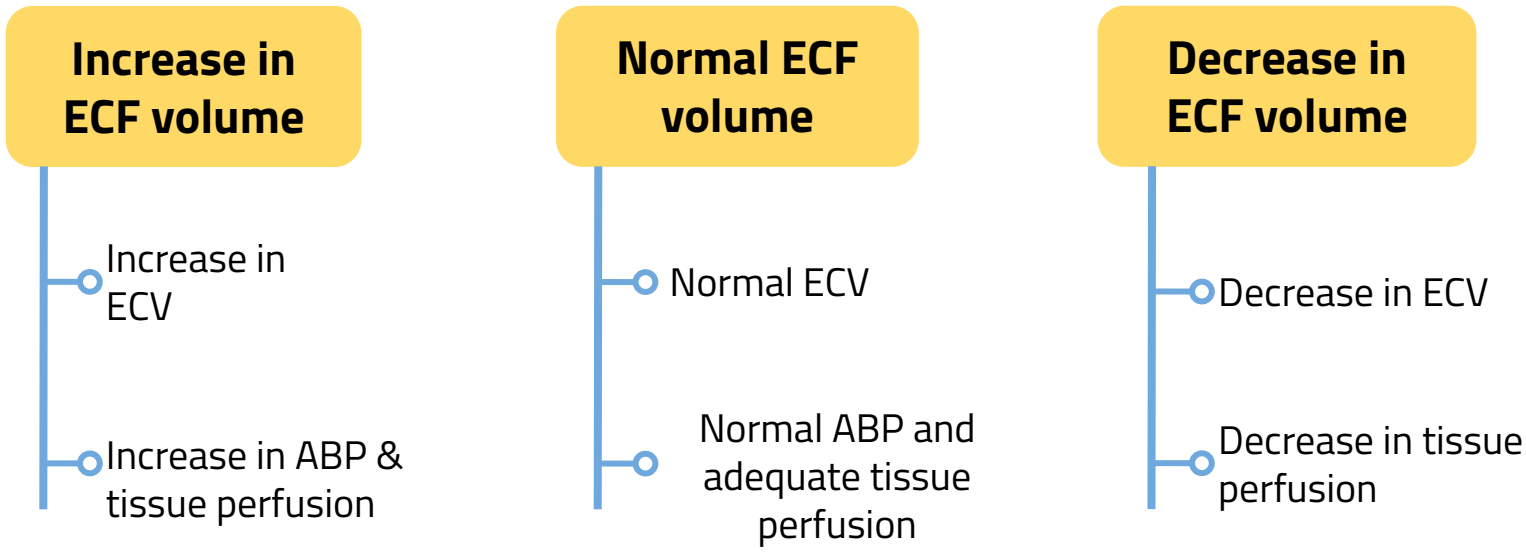
Summary





Summary

- **Identify and describe the role of the sensors and effectors in the renal regulation of body fluid volume.**
- The body sense the Effective circulating volume ECV.
  There are three effectors depend on ECF:



- **Describe the role of the kidney in regulation of body fluid volume & osmolality.**
- The kidney regulates osmolarity by adjusting total body water(water Excretion).
  The kidney regulates volume by adjusting total body Na+ content (Na+ Excretion).

- **Identify the site and describe the influence of aldosterone on reabsorption of Na+ in the late distal tubules.**
- ↑Na+ reabsorption in exchange with K or H excretion at the P cells of DCT & CD.

- **What is the role of ADH in the reabsorption of water and urea?**
- Water deficit→ ↑extracellular osmolarity→ osmoreceptors will fire→↑ADH secretion→ ↑plasma ADH→ ↑H2O permeability in DT and CD→ ↑H2O reabsorption→ ↓H2O excreted

MCQ & SAQ

Q1: The most abundant extracellular cation is

A. Potassium
B. Chloride
C. Sodium
D. Phosphate

Q2: What is the major route for excretion of sodium

A. GI loss
B. Kidney
C. Sweat
D. Lungs

Q3: All of the following are high pressure sensors EXCEPT

A. Carotid sinus
B. Aortic arch
C. Cardiac atria
D. Juxtaglomerular apparatus

Q4: All of the following are actions of angiotensin II EXCEPT

A. ↑Reabsorption of Na^+
B. ↑ Thirst
C. ↑ Aldosterone
D. Vasodilatation

Q5: Which of the following is a low pressure receptor

A. Renal afferent arterioles
B. Pulmonary vasculature
C. Carotid sinus
D. Aortic arch

Q6: Osmoreceptors are located in

A. Supraoptic nuclei
B. Anterior hypothalamus
C. Posterior pituitary
D. Adrenal cortex

answer key:
1: C
2: B
3: C
4: D
5: B
6: B

1- What are the fluid compartments of the body?

2- What happens to a person who has excessive diarrhea and is in dehydrated state?

3- When does edema occur?

4- What happened if a person is take high amount of water in short time?

A1: Intracellular (inside the cells): contain most of the fluid
Extracellular (outside the cell): contain fluid in the: 1. Blood (vascular) 2. Interstitium (between cells)

A2: Increase Sodium concentration → Increase extracellular osmolarity that surrounding the osmoreceptors in the hypothalamus → movement of water from intracellular (osmoreceptors cells) to extracellular → stimulation of osmoreceptors and send signals to posterior pituitary in hypothalamus → release ADH also called (arginine vasopressin)

A3: When there is an inappropriate secretion of ADH that will lead to hypo- osmolar condition of ECF and sodium concentration will be 120 mEq\L and below.

A4: Decreased Sodium concentration → decrease extracellular osmolarity that surrounding the osmoreceptors in the hypothalamus → movement of water from extracellular to intracellular (osmoreceptors cells) → stimulation of osmoreceptors and send signals to posterior pituitary in hypothalamus → decrease ADH

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