Lecture 4

Water and Na Metabolism
Physiology of hormones
2007
Outline

- Review of pituitary, hypothalamus and adrenal hormones.
- Internal homeostasis.
- Water metabolism.
- Major Mediators of Sodium and Water Balance.
The Hypothalamus Gland

- Located in the lower brain, it is the sole link between the endocrine and nervous systems, wrapped around the third ventricle and containing two sets of neurosecretory cells.

- Neurosecretory neurons secrete hormones that control the pituitary gland, located directly below it; together they control multiple hormones.
Hypothalamic Coordination

- Autonomic centers that exert direct influence over the endocrine cells of the adrenal medullae
- Release of ADH and Oxytocin
- Secretion of Regulating Factors
  - Releasing Hormones
  - Inhibiting Hormones
Hypothalamus continued...

- After receiving information from nerves in the body and in other parts of the brain, the hypothalamus gland issues a response.
1. Control of sympathetic output to adrenal medullae

2. Production of ADH and oxytocin

3. Secretion of regulatory hormones to control activity of anterior pituitary

Hypothalamus

Anterior pituitary

Posterior pituitary

Adrenal medulla

Preganglionic motor fibers

Adrenal gland

Hormones secreted by anterior pituitary control other endocrine organs

Release of ADH and oxytocin

Secretion of epinephrine and norepinephrine
Neurohormones: secreted into the Blood by Neurons

Figure 7-12: Synthesis, storage, and release of posterior pituitary hormones
Endocrine Control: Three Levels of Integration

- Hypothalamic stimulation—from CNS
- Pituitary stimulation—from hypothalamic trophic Hs
- Endocrine gland stimulation—from pituitary trophic Hs
Endocrine Control: Three Levels of Integration

Figure 7-13: Hormones of the hypothalamic-anterior pituitary pathway
(b) The anterior pituitary
(a) The posterior pituitary

Hormone: ADH, Oxytocin

Target: Kidney tubules, Mammary glands, uterine muscles
**Hypothalamic Hormones:**

- Produces ADH and oxytocin.
- Secretes:
  - Thyrotropin-releasing hormone (TRH)
  - Gonadotropin-releasing hormone (GnRH)
  - Growth hormone-releasing hormone (GHRH)
  - Corticotropic-releasing hormone (CRH)
  - Somatostatin
  - Dopamine
Adrenal Physiology

Adrenal cortex - outer layer

- zona glomerulosa - produces mineralocorticoids (aldosterone)
- zona fasciculata - produces glucocorticoids (cortisol)
- zona reticularis - produces androgens (dihydroepiandrosterone and androstenedione)
Figure 21. Schematic showing the cellular zonation of the adrenal cortex and blood flow through the cortex to the collecting veins in the medulla.
Body fluids

- All biological reactions occur in body fluids.
- Any abnormal reduction in the body fluids caused physiological imbalance.
Total body fluids

Extra cellular fluid

ECF

1. Interstitial fluids
2. Blood Plasma
3. Cerebrospinal fluid
4. Amniotic fluid

intra cellular fluid

ICF

All the fluids inside the cell
Functions of body fluids

- **Transport and exchange**
  - nutrients.
  - Hormones
  - Gases
  - Waste
- **regulate**
  - heat
  - Acidity
- **Biological reaction media**
Internal environment and homeostasis

- The internal environment of each cell is the extra cellular fluids.
- The aim of all biological processes is to maintain the internal environment (extracellular fluids).
Homeostasis: The dynamic constancy of the internal environment, the maintenance of which is the principal function of physiological regulatory mechanisms. The concept of homeostasis provides a framework for understanding most physiological process.
WATER METABOLISM

- Water is important to our health and makes up approximately two-thirds of our body by weight.
About two thirds of the body is water.

- Two thirds of the water is intracellular and
- one third is extracellular.
- Two thirds of the extracellular water is interstitial and
- one third is intravascular.

What determines the volume of the different fluid compartments? (Hint – it is NOT water)
What are the major solutes?

Fluid compartment volume is determined by the content of the major solute in each compartment.

- Potassium and magnesium are the major intracellular solutes.
- Sodium is the major extracellular solutes.
- Serum protein is the additional "solute" of the intravascular component.

The body controls the content of each fluid compartment by regulating the amount of each major solute.
For all practical purposes, *water* is in equilibrium among all of the fluid compartments.

If the *osmolality* changes in any of the compartments, water will redistribute among compartments until osmolality equilibrates.

Testing the *osmolality* in plasma estimates *osmolality* of all body fluid compartments.
EXTRACELLULAR FLUID COMPARTMENT CONTROL

- The normal human is beautifully designed for regulating extracellular fluid volume by regulating body sodium.
- Your body has two major systems for balancing sodium content
  - the "affector" and "effector" systems. The affector (or sensing) system monitors whether there is too much, too little, or just the right content of sodium
Controlling .......... It does this through the baroreceptors in the aortic arch, carotid arteries, atria, brain, and liver.

- If the sodium content is incorrect, the effector systems go to work. The renin-angiotensin-aldosterone, catecholamine, and vasopressin systems increase blood pressure and sodium retention.

- The atrial natriuretic peptide (ANP) system causes renal sodium loss.
Now let’s turn our attention to how the body normally handles water.

Most cells and biological systems seem to work best within a narrow range of Posm. Normal Posm is 286 - 294 mOsm/kg.
Three major systems are required to work properly:

- a) normal vasopressin (VP) production and release,
- b) a kidney that responds normally to VP, and
- c) normal thirst and water intake.
Let’s review each of these three systems
Thirst is one of the most poorly understood parts of water balance. Normally, it stimulates the sensation of thirst when

- Posm increases.
- Habit,
- medications,
- emotions,
- and culture also affects thirst.
FUNCTIONS OF THE KIDNEY

- Water balance
- Electrolyte balance
- Plasma volume
- Acid-base balance
- Osmolarity balance
- Excretion
- Hormone secretion
Role of ADH (antidiuretic hormone)

Synthesized in the hypothalamus and stored in the posterior pituitary

Released in response to plasma hyperosmolality and decreased effective circulating volume

Actions of ADH → 1. Increases the water permeability of the collecting tubule
                           2. Mildly increases vascular resistance
INTEGRATION OF NORMAL WATER BALANCE MECHANISMS

- Now let’s summarize by describing what happens when a normal individual drinks a water load and then takes in no water for several hours.

- The individual starts with a normal state of hydration, electrolytes, and Posm, then drinks 2 liters of water in 30 minutes. The water is absorbed, reduces serum sodium and Posm, and suppresses VP release. The low VP causes the renal collecting ducts to become relatively impermeable to water and a large output of maximally diluted urine ensues. If the individual drinks nothing for several hours, water is lost in the urine, breath and sweat causing the Posm to increase.
VP levels increase when the threshold for VP release is reached. Increasing VP causes the collecting ducts become more permeable to water, until maximal urinary concentration is reached. Water continues to be lost in breath, sweat and urine raising Posm further until the threshold for thirst is reached. When drinking again satisfies thirst, water is absorbed from the gut, reducing Posm, thirst drive, VP levels and urine concentration. (I’ve just described the normal physiological response to a water load and water deprivation test.) Most of the time, our Posm remains in a tight range between the threshold for VP release and thirst, and urine is moderately concentrated, finely balanced without us having to think about it.
Major Mediators of Sodium and Water Balance

- Angiotensin II
- Aldosterone
- Antidiuretic hormone (ADH)
Mineralocorticoid regulation and function

- **Aldosterone** secretion is under tonic control of ACTH, but is also regulated by renin-angiotensin system and K+

- **Renin-angiotensin system**
  - Decrease in blood volume → decrease renal perfusion → renin secretion → conversion of angiotensinogen to angiotensin I, which in turn is converted to angiotensin II by ACE (angiotensin converting enzyme)
Mineralocorticoid regulation and function

- **Angiotensin II** causes increased conversion of corticosterone to aldosterone in the zona glomerulosa.

- **Aldosterone** increases renal Na+ reabsorption, restoring extracellular fluid volume and blood volume.

- **Aldosterone** also increases renal K+ secretion in the face of hyperkalemia.
Renin-Angiotensin-Aldosterone Axis

Angiotensinogen → Renin → Angiotensin I → Angiotensin II

Angiotensin II → 1. Stimulates production of aldosterone
2. Acts directly on arterioles to cause vasoconstriction
3. Stimulates Na⁺/H⁺ exchange in the proximal tubule

Aldosterone → 1. Stimulates reabsorption of Na⁺ and excretion of K⁺ in the late distal tubule
2. Stimulates activity of H⁺ ATPase pumps in the late distal tubule
Renin-angiotensin-aldosterone system

**Legend**
- **Blue** secretory organ
- **Blue dashed** stimuliatory signal
- **Orange dashed** inhibitory signal
- **Red** reaction
- **Black** active transport
- **Gray** passive transport

**Water and salt retention. Effective circulating volume increases. Perfusion of the juxtaglomerular apparatus increases.**
Questions?
Thank you