4.2.5

Hormonal Regulation of Urine Production

We have just discussed how the kidneys can generate gradients to reabsorb or secrete water, but the question still remains: how do the kidneys know when to reabsorb or secrete the water? This question will be answered in this section.

As previously mentioned, the principle cells of the collecting duct have aquaporin channels in the membranes of vesicles, essentially waiting for the signal for insertion into the plasma membrane. The hormone that induces insertion of the channels is called antidiuretic hormone (ADH; or arginine vasopressin). This hormone is produced by hypothalamic neurons and released from the posterior pituitary gland. There are three regulatory pathways to induce the release of ADH: Osmoreceptors, baroreceptors, and the renin-angiotensin-aldosterone system.

Osmoreceptors

The primary regulator of ADH secretion is blood osmolarity. Specialized nerve cells called osmoreceptors are located in the hypothalamus. These receptors are very sensitive to changes in blood ion concentrations. The area of the brain where they are located lacks the typical blood brain barrier and allows for easier access to ions. As a result, if the concentration of ions in the blood and interstitial fluids increases (conditions of dehydration), water moves out the osmoreceptors by osmosis to re-establish equilibrium. As the cells lose water they shrink and this shrinking induces action potentials. The action potentials are conducted to the posterior pituitary gland and stimulate the release of ADH.

Baroreceptors

Located within the walls of the aortic arch and carotid sinuses are specialized receptors called baroreceptors. These baroreceptors respond to stretch of the blood vessels which elicits action potentials in neurons to travel to the hypothalamus and synapse with hypothalamic neurons. Consequently, decreased blood pressure and lack of stretch of the baroreceptors in these vessels stimulate ADH secretion, while increased blood pressure (and subsequent increased strectch) decreases ADH secretion.

The Renin-Angiotensin-Aldosterone System

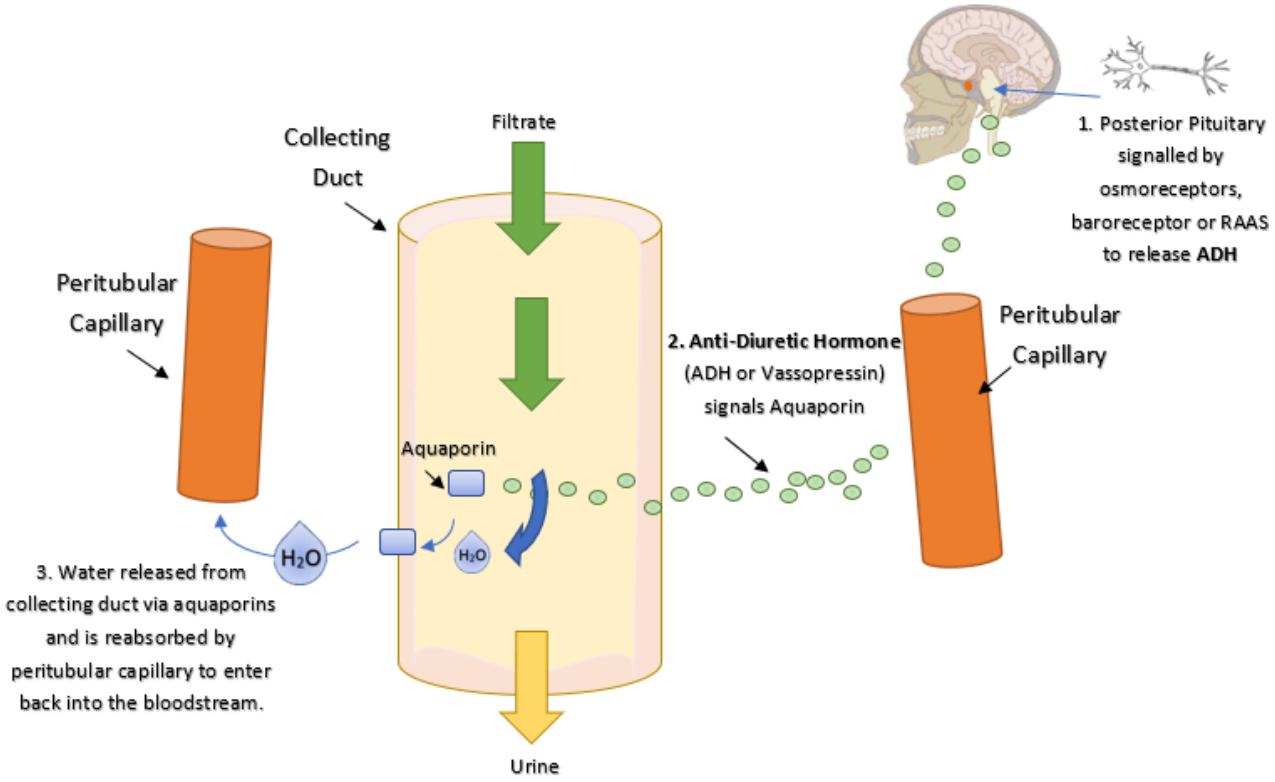
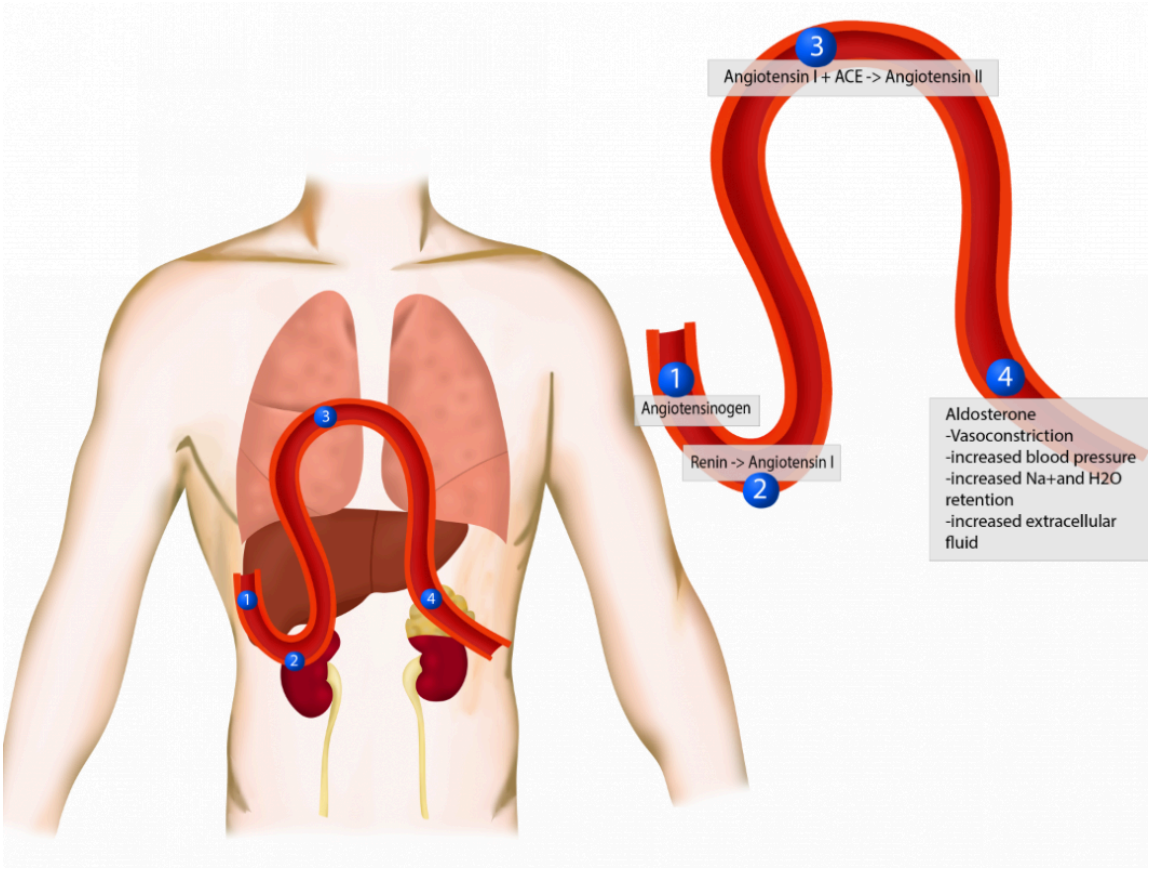


Image by BYU-I Becky T F18



Conversion of Angiotensin I to Angiotensin II increasing water reabsorption in kidney

https://cnx.org/resources/e20e7d6b1033f92c7ec59e78633956192c772da6/2626_Renin_Aldosterone_Angiotensin.jpg Author: OpenStax College License: Creative Commons Attribution 3.0 Unported license.

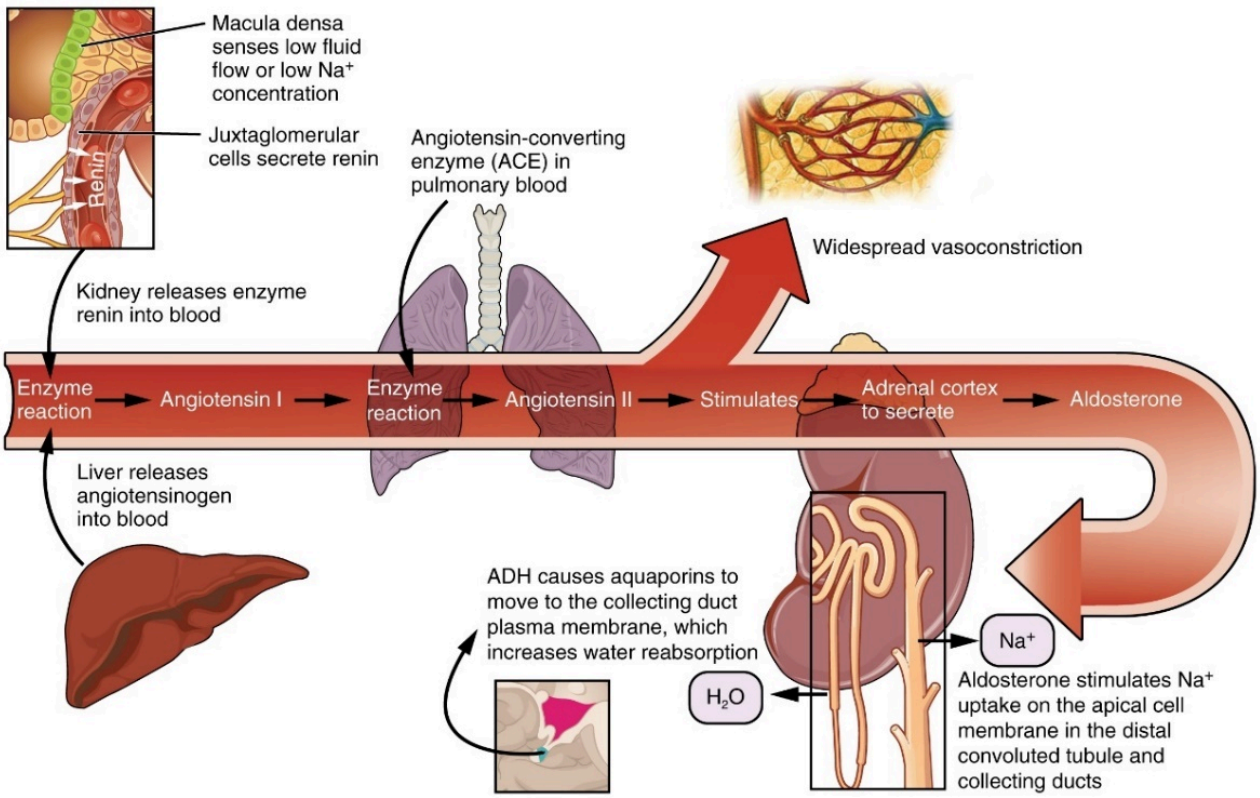
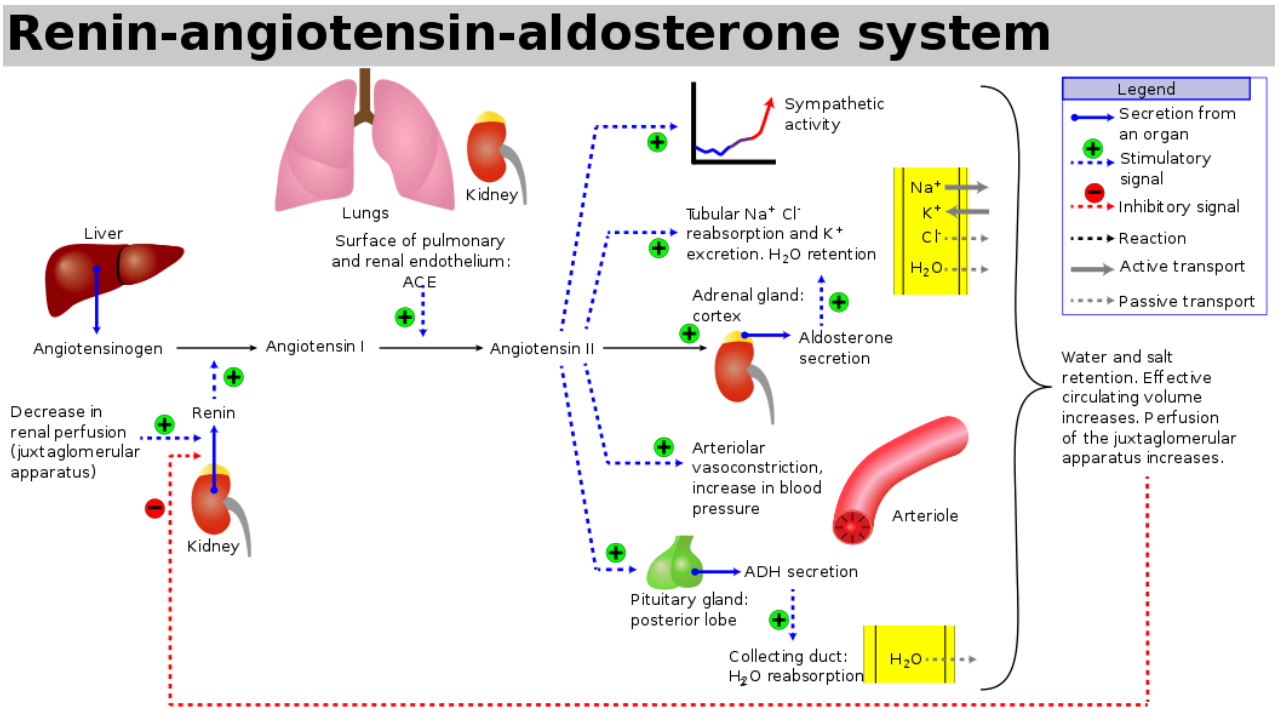


Image drawn by BYU-Idaho student Fall 2013



Renin-angiotensin-aldosterone system schematic.

The three images above illustrate the renin-angiotensin-aldosterone system which promotes the direct retention of Na+, and thus, the indirect retention of water. The system starts with the release of **renin**, an enzyme produced by specialized

cells of the afferent arteriole. Renin is released in response to a decrease in GFR (paracrine signaling) or a decrease in blood pressure (**baroreceptors**). In response to these stimuli, renin is released into the circulation. Renin is an enzyme that acts on a plasma protein called **angiotensinogen**. Angiotensinogen is produced by the liver and released into the circulation. As a result of the enzymatic cleavage by renin, **angiotensin I** is produced from angiotensinogen. Subsequently, angiotensin I is converted to **angiotensin II** by an enzyme called **angiotensin-converting enzyme (ACE)**. Although ACE can be found in many tissues it is in especially high concentrations in the blood capillaries of the lungs. Angiotensin II has four major effects:

1. It stimulates the release of aldosterone from the adrenal gland (*note: aldosterone release can also be directly stimulated by increased extracellular K+ levels)*
2. It preferentially constricts the efferent arteriole
3. It is a potent vasoconstrictor of the systemic arterioles
4. It induces the release of ADH from the posterior pituitary gland

These actions enhance Na+ reabsorption and water retention by the following mechanisms: Aldosterone is a hormone from the adrenal cortex that directly influences Na+/K+ ATPase by inducing the synthesis of new pumps and increasing the activity of existing pumps. Increasing the number and activity of this pump will greatly enhance the reabsorption of Na+ and the secretion of K+. Because of this effect on K+, aldosterone release is also tied to extracellular K+. If extracellular K+ levels increase, aldosterone is also released. If aldosterone levels are increased, the extracellular K+ concentrations will decrease. In some cases of excessive aldosterone the K+ levels can become dangerously low.

Constriction of the efferent arteriole will increase the pressure in the glomerular capillaries and thus increase the GFR. Increasing GFR will then promote increased filtration of Na+ thereby increasing the rate of reabsorption. Systemic vasoconstriction increases the mean arterial blood pressure. Because of the potent vasoconstricting effects of angiotensin II, a useful therapeutic tool to help reduce blood pressure is a family of drugs known as ACE inhibitors. By inhibiting the enzyme ACE, the production of angiotensin II is decreased, as its effect on blood pressure. Finally, inducing the release of ADH allows for the insertion of aquaporins and thus the increased reabsorption of water as it follows the increased sodium reabsorption. Based on these actions we can think of aldosterone as being primarily involved in regulating extracellular fluid volume due to its effects on Na+ reabsorption. Likewise, the primary role of ADH is regulating plasma osmolarity. These hormones can work in concert or they can function independently, depending on the needs of the body.

What if there is too much blood volume? **Atrial natriuretic hormone** (ANH) is a hormone produced by the atrial cells of the right atrium of the heart in response to stretch (high blood pressure).

In addition, **brain natriuretic peptide** (BNP) is produced by the ventricular cells of the heart and certain brain neurons, also in response to stretch. Once released these hormones act to decrease renin, aldosterone and vasopressin secretion. This results in an increase in both water and Na+ excretion by the kidney. These peptides also dilate the afferent arteriole enhancing the filtration rate.