2.6.3

2.6.3 - Long-Term Regulation

This section will introduce five long-term blood pressure regulation mechanisms: the renin-angiotensin-aldosterone mechanism, the vasopressin/antidiuretic hormone (ADH) mechanism, the fluid shift mechanism, stress-relaxation response, and the atrial natriuretic mechanism. Each of these works to change blood pressure by altering blood volume, or vascular smooth muscle tone (dilation or constriction). Unlike short-term blood pressure regulation that occurs in seconds, long-term regulation can take several minutes, hours or days.

Renin-Angiotensin-Aldosterone Mechanism

The renin-angiotensin-aldosterone mechanism plays a very important and active role in blood pressure regulation on a day-to-day basis. It uses a variety of means, such as water reabsorption in the kidney tubules and vasoconstriction, to regulate blood pressure.

The Renin-Angiotensin-Aldosterone mechanism centers at the level of the enzyme renin in the blood. **Renin** is produced in the kidney in specialized structures known as the **juxtaglomerular apparatus.** When in the blood, renin cleaves a liver-produced inactive protein known as **angiotensinogen.** The cleaved portion is a protein known as **angiotensin I.** Angiotensin I is then cleaved again by an **angiotensin converting enzyme** (largely found in the small vessels of the lung) into **angiotensin II,** the final, active form of the original angiotensinogen. Angiotensin II then initiates several simultaneous responses as it diffuses throughout the body.

The first of these responses results when angiotensin II binds to specific receptors on smooth muscle cells in arterioles and veins. The resultant signal cascade results in widespread vasoconstriction. This in turn increases the amount of venous blood which returns to the heart as well as increasing peripheral resistance. These two factors combine to increase blood pressure. The second response occurs when angiotensin II binds to cells in the adrenal cortex prompting the production and release of the hormone **aldosterone.** Aldosterone acts on kidney structures called nephrons where it increases the reabsorption of sodium and chloride ions (reabsorption means moving from the nephron filtrate back to circulating blood). The increase of Na^+ and Cl^- results in reabsorption of water as well (because the water will follow the net movement of solutes). This prevention of solute and water loss in the urine translates into prevention of blood volume loss. Therefore, blood pressure decreases are minimized because of the manipulation of blood volume. The third and fourth responses initiated by angiotensin II are increased salt appetite and an increased sense of thirst. Increased salt intake means increased water as well, because water follows the net gain of solutes. Increased thirst will raise blood volume directly by virtue of increased water intake.

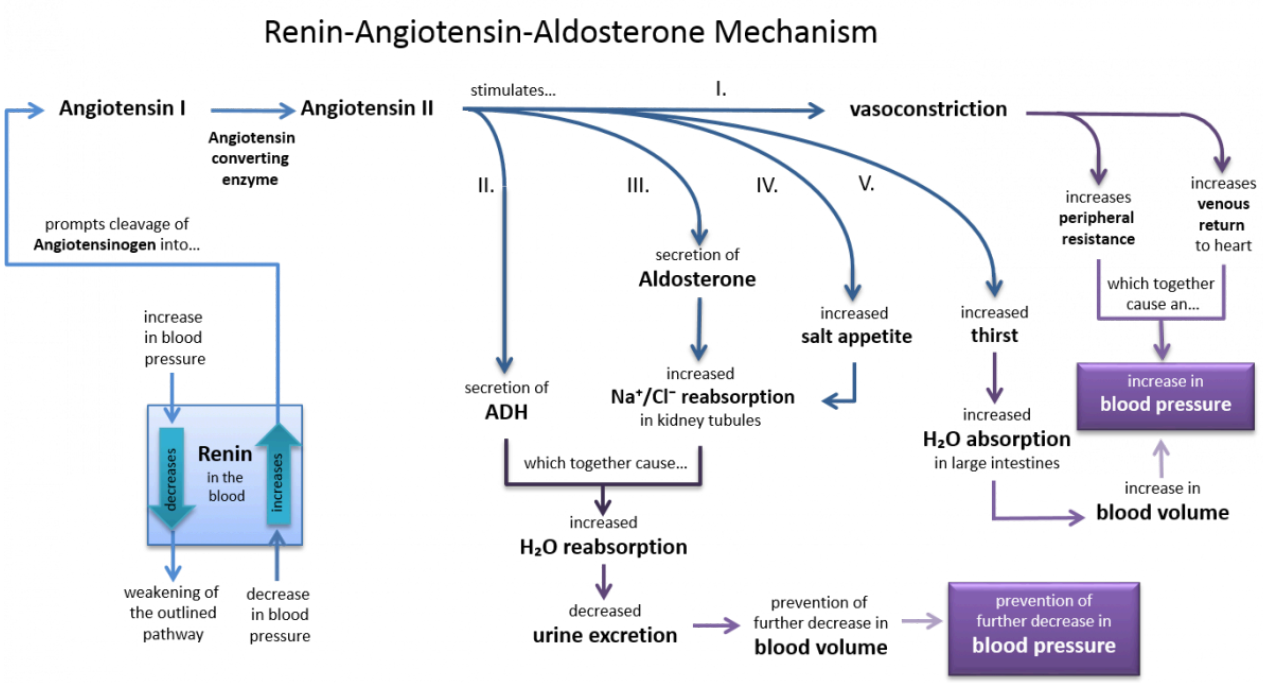

Image drawn by BYUI student Fall 2013

Vasopressin/Anti-Diuretic Hormone (ADH) Mechanism

The **vasopressin/anti-diuretic hormone (ADH) mechanism** works side-by-side with the Renin-Angiotensin-Aldosterone mechanism to raise blood pressure. ADH is able to cause vasoconstriction which will increase peripheral resistance. In fact, another name for ADH is vasopressin because of its ability to constrict vessels of the vascular system. However, its main effect is to increase water reabsorption from the kidney nephrons, thus the other name "ADH" which means Anti-Diuretic Hormone. Diuresis means an increase production and excretion of urine. The ADH reflex is activated by two specific indicators: high blood osmolality and low blood pressure.

Fluid Shift Mechanism

The **fluid shift mechanism** is a simple yet very effective means of long-term blood pressure regulation. When blood pressure is high, the amount of interstitial fluid increases, which lowers blood volume. When blood pressure is low, the amount of interstitial fluid is decreased to raise the blood volume. This occurs mostly through the capillaries when pressure deviations change the equilibrium balance pointed out in the section on capillary exchange. It is functional in as little as minutes and is maximally effective in a matter of hours. It is an especially important means of compensating for changes that occur during dehydration and hyperosmolarity.

Atrial Natriuretic Mechanism

The **atrial natriuretic mechanism** is powered by **atrial natriuretic factor** sometimes called (ANF) which is produced in specialized cells of the right atrium of the heart. When blood volume or vasoconstriction causes more blood to return to the right atrium, the atrium is stretched and there is an increase in release of ANF from the atrial cells. As ANF is distributed throughout the body's vasculature, it causes vasodilation. This decreases peripheral resistance and, as a result, lowers the blood pressure. Simultaneously, the atrial natriuretic factor acts on the kidney tubules to increase the excretion of both sodium and water in the urine. This in turn decreases blood volume.

Stress-Relaxation Response

The final long-term blood pressure regulation mechanism is the **stress-relaxation response.** This response is a simple adjustment of blood vessel smooth muscle tone in the hours following a change in blood pressure. If, for example,

blood volume rose by 400 mL, the blood pressure would rise accordingly. To compensate for this, smooth muscles in the walls of the various types of vessels would gradually relax until the blood pressure drops to a safer level. Oppositely, in the case of a drop in blood volume, vascular smooth muscles would contract gradually in an attempt to raise blood pressure. This change in smooth muscle tone happens automatically even without any nervous system or hormonal regulation. The tendency of smooth muscle to gradually relax under significant tension or gradually contract under very low tension is an intrinsic property of smooth muscle cells.