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**Long Term Regulation Of Mean Arterial Pressure**

Blood pressure is a measure of how well our cardiovascular system is functioning. We all require a blood pressure high enough to give our organs the blood and nutrients they need, but not so high our blood vessels become damaged.

As such, our bodies must maintain control over our blood pressure to keep it at a normal level. In this article, we will consider the short term and long term control of blood pressure, as well as some of the problems when control of blood pressure is lost.

**Blood Pressure**

The body’s blood pressure is a measure of the **pressures** within the cardiovascular system during the pumping cycle of the heart. It is influenced by a vast number of variables, and can alter in either direction for various reasons. Everyone’s blood pressure is slightly different and can change throughout the day depending on activity.

There is a range of normal blood pressures that we consider as acceptable. When blood pressure is outside of this normal range of values, people can start to have problems in both the long and short term. Our body tries to maintain a stable blood pressure in the process of **homeostasis**.

Blood pressure is measured using an automated blood pressure monitor, or manually using a stethoscope and sphygmomanometer. It is given as two values (e.g, **120/80 mmHg),** measured in “millimeters of mercury (mmHg)”:

* **Systolic pressure** – the first number (120 mmHg in the example) is the pressure of the blood during the heart contraction.
* **Diastolic** **pressure** – the second number (80 mmHg in the example) is the pressure of the blood after one contraction but before the next contraction.
* Blood pressure can be calculated as:
* Flow  x  Resistance
* Mean arterial blood pressure  = cardiac output  x  total peripheral resistance

## ****Long-Term Regulation of Blood Pressure****

There are several physiological mechanisms that regulate blood pressure in the long-term, the first of which is the renin-angiotensin-aldosterone system **(RAAS)**.

### **Renin Renin-Angiotensin-Aldosterone System (RAAS)**

Renin is a peptide hormone released by the granular cells of the **juxtaglomerular apparatus** in the kidney. It is released in response to:

* Sympathetic stimulation
* Reduced sodium-chloride delivery to the distal convoluted tubule
* Decreased blood flow to the kidney

Renin facilitates the conversion of angiotensinogen to angiotensin I which is then converted to angiotensin II using angiotensin-converting enzyme **(ACE)**.

Angiotensin II is a potent vasoconstrictor. It acts directly on the kidney to increase sodium reabsorption in the proximal convoluted tubule. Sodium is reabsorbed via the sodium-hydrogen exchanger. Angiotensin II also promotes release of **aldosterone**.

ACE also breaks down a substance called **bradykinin** which is a potent vasodilator. Therefore, the breakdown of bradykinin potentiates the overall constricting effect.

Aldosterone promotes salt and water retention by acting at the distal convoluted tubule to increase expression of **epithelial** sodium channels. Furthermore, aldosterone increases the activity of the basolateral sodium-potassium ATP-ase, thus **i**ncreasing the electrochemical gradien**t** for movement of sodium ions.

More sodium collects in the kidney tissue and water then follows by osmosis. This results in decreased water excretion and therefore increased blood volume and thus blood pressure.

### Anti-Diuretic Hormone (ADH)

The second mechanism by which blood pressure is regulated is release of Anti Diuretic Hormone (ADH) from the OVLT of the hypothalamus in response to **thirst** or an increased plasma osmolarity.

ADH acts to increase the permeability of the collecting duct to water by inserting **aquaporin channels** (AQP2) into the apical membrane.

It also stimulates sodium reabsorption from the thick ascending limb of the loop of Henle. This increases water reabsorption thus increasing plasma volume and decreasing osmolarity.

Further Control of blood pressure.

Other factors that can affect long-term regulation of blood pressure are natriuretic peptides. These include:

* Atrial natriuretic peptide **(ANP)** is synthesised and stored in cardiac myocytes. It is released when the atria are stretched, indicating of high blood pressure.
* ANP acts to promote sodium excretion. It dilates the **afferent arteriole** of the glomerulus, increasing blood flow (GFR). Moreover, ANP inhibits sodium reabsorption along the nephron. Conversely, ANP secretion is low when blood pressure is low.
* **Prostaglandins** act as local vasodilators to increase GFR and reduce sodium reabsorption. They also act to prevent excessive vasoconstriction triggered by the sympathetic nervous and renin-angiotensin-aldosterone systems.

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**Splanchnic Circulati**on: The term ‘splanchnic circulation’ describes the blood flow to the abdominal gastrointestinal organs including the stomach, liver, spleen, pancreas, small intestine, and large intestine. It comprises three major branches of the abdominal aorta; the coeliac artery; superior mesenteric artery (SMA); and inferior mesenteric artery.

**Pulmonary Circulation:** Pulmonary circulation is the system of transportation that shunts de-oxygenated blood from the heart to the lungs to be re-saturated with oxygen before being dispersed into systemic circulation. Deoxygenated blood from the lower half of the body enters the heart from the inferior vena cava while deoxygenated blood from the upper body is delivered to the heart via the superior vena cava. Both the superior vena cava and inferior vena cava empty blood into the right atrium. Blood flows through the tricuspid valve into the right ventricle. It then flows through the pulmonic valve into the pulmonary artery before being delivered to the lungs. While in the lungs, blood diverges into the numerous pulmonary capillaries where it releases carbon dioxide and is replenished with oxygen. Once fully saturated with oxygen, the blood is transported via the pulmonary vein into the left atrium which pumps blood through the mitral valve and into the left ventricle. With a powerful contraction, the left ventricle expels oxygen-rich blood through the aortic valve and into the aorta: This is the beginning of systemic circulation

**Circle of Willis:** The **circle of Willis** is a ring of interconnecting arteries located at the base of the brain around the optic chiasm or chiasma (partial crossing of the optic nerve – CNII; this crossing is important for binocular vision), infundibulum of the pituitary stalk and the hypothalamus

This arterial ring provides blood to the brain and neighbouring structures. Polygonal anastomotic shape offers the possibility of alternate pathways for the blood flow, which is essential for the brain functioning, since it is the structure that is mostly sensitive to hypoxia. Hypoxia of the brain tissue that lasts longer than 6 minutes results with the irreversible changes in the brain parenchyma, and depending on the location of the lesion, the functional damages vary widely.

**Coronary Circulation:** Part of the systemic circulatory system that supplies blood to and provides drainage from the tissues of the heart. In the human heart, two coronary arteries arise from the aorta just beyond the semilunar valves; during diastole, the increased aortic pressure above the valves forces blood into the coronary arteries and thence into the musculature of the heart. Deoxygenated blood is returned to the chambers of the heart via coronary veins; most of these converge to form the coronary venous sinus, which drains into the right atrium**.**

**Cutaneous Circulation:** The cutaneous circulation is the circulation and blood supply of the skin. The skin is not a very metabolically active tissue and has relatively small energy requirements, so its blood supply is different to that of other tissues.

Some of the circulating blood volume in the skin will flow through will flow through **arteriovenous anastomoses (AVAs)** instead of capillaries. AVAs serve a role in temperature regulation. In this article we shall consider the different adaptations of the cutaneous circulation, and its role in body temperature control.

## Arteriovenous Anastomoses

AVAs are low-resistance connections between the small arteries and small veins that supply and drain the skin. These allow the shunt of blood directly into the **venous plexus** of the skin, without it passing through capillaries. Since AVAs contain no capillary section, they are not involved in transport of nutrients to/from the tissues, but instead play a major role in temperature regulation.

## Temperature Regulation

The skin is the body’s main heat dissipating surface: the amount of blood flow to the skin determines the degree of heat loss and therefore the core body temperature. The blood flow through AVAs is heavily influenced by the **sympathetic nervous system.**  At rest, the sympathetic nervous system dominates and acts to constrict AVAs.

Any changes in core temperature are detected by the thermoregulatory centre in the **hypothalamus**. It regulates temperature by altering the level of sympathetic outflow to the cutaneous vessels, to return temperature to its normal range:

In high core temperatures:

* Sympathetic innervation is decreased, reducing the vasomotor tone in the AVAs.
* More blood flows through the AVAs and reaches the venous plexus (close to the surface of the skin), increasing heat loss to reduce core temperature.

In low core temperatures:

* Sympathetic innervation is increased, increasing the vasomotor tone in the AVAs.
* Less blood flows to the apical skin (of nose, lips, ears, hands and feet), reducing heat loss to increase the core temperature

**Cardiovascular adjustments during exercising**

During exercise, the heart is subjected to intermittent hemodynamic stresses of pressure overload, volume overload, or both. To normalize such stress and to meet the systemic demand for an increased blood supply, the heart undergoes morphological adaptation to recurrent exercise by increasing its mass, primarily through an increase in ventricular chamber wall thickness. This augmentation of heart size is primarily the result of an increase in the size of individual terminally differentiated cardiac myocytes. Adaptive remodeling of the heart in response to exercise typically occurs with preservation or enhancement of contractile function. This contrasts with pathologic remodeling due to chronic sustained pressure overload (e.g., during hypertension or aortic stenosis), which can proceed to a loss of contractile function and heart failure.

Recent work in experimental animal exercise models has identified several cellular and molecular alterations involved in the physiologic growth program of the heart that accompanies exercise conditioning. Whereas pathologic remodeling of the heart is associated with a reduction in oxidative energy production via fatty acid oxidation and more reliance on glucose utilization, mitochondrial biogenesis and capacity for fatty acid oxidation are enhanced following exercise. A recent study suggests that changes in myocardial glycolytic activity during acute exercise and the subsequent recovery period can also play an important role in regulating the expression of metabolic genes and cardiac remodeling. Possibly upstream of these metabolic changes, studies have also revealed a dominant role for IGF-1 and insulin receptor signaling, via the PI3K/Akt1 pathway leading to the activation of transcriptional pathways associated with protein synthesis and hypertrophy. Untargeted approaches have identified other major determinants of transcriptional programs that drive the exercise-induced hypertrophic response. For instance, it has been reported that exercise-induced reduction in the expression of CCAAT-enhancer binding protein β (C/EBPβ) relieves its negative regulation by CBP/p300-interactive transactivator with ED-rich carboxy-terminal domain-4 (Cited4). Activation of Cited4 has been found to be necessary for exercise-induced cardiac hypertrophy, and cardiac-specific overexpression of the gene is sufficient to increase heart mass and protect against ischemia/reperfusion injury. Other transcriptional pathways known to be activated by pathologic stimuli and cardiac hypertrophy, such as NFATc2, are decreased in exercise models, suggesting that some signaling pathways activated during exercise-induced growth program may directly antagonize specific factors that promote pathological remodeling.

In addition to metabolic and molecular remodeling, exercise can also promote functional adaptation of the heart, which may ultimately increase cardiac output and reduce the risk of arrhythmia. Clinical studies have shown that exercise-trained individuals have improved systolic and diastolic function ([85](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6172294/#B85), [86](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6172294/#B86)), while results of studies using animal models of exercise show that endurance exercise promotes enhanced cardiomyocyte contraction-relaxation velocities and force generation ([87](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6172294/#B87)–[90](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6172294/#B90)). This effect of exercise on cardiomyocyte contractile function may be related to alterations in the rise and decay rates of intracellular Ca2+ transients, possibly due to enhanced coupling efficiency between L-type Ca2+ channel-mediated Ca2+ entry and activation of subsarcolemmal ryanodine receptors (RyR; i.e., calcium-induced calcium release), and increased expression and activity of the sarcoendoplasmic reticulum Ca2+ ATPase (SERCA2a) and sodium-calcium exchanger (NCX) ([88](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6172294/#B88), [91](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6172294/#B91), [92](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6172294/#B92)). In addition, the sensitivity of the cardiomyocyte contractile apparatus may also become more sensitive to Ca2+, thus producing a greater force of contraction at a given [Ca2+]i, following exercise, ([93](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6172294/#B93)). These changes may at least partially depend on upregulation of the Na+/H+ antiporter and altered regulation of intracellular pH.

During pathologic remodeling of the heart, electrical instability can result from a lack of upregulation of key cardiac ion channel subunits associated with action potential repolarization relative to an increase in myocyte size ([94](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6172294/#B94)). In contrast, increased myocyte size in physiological hypertrophy is associated with the upregulation of depolarizing and repolarizing currents, which may be protective against abnormal electrical signaling in the adapted heart . For example, cardiac myocytes isolated from mice after 4 weeks of swim training were found to have elevated outward K+ current densities (i.e., Ito,f, IK,slow, Iss, and IK1) and increased expression of underlying molecular component Kv and Kir subunits in parallel with increases in total protein levels. Interestingly, a follow up study found that while increases in K+ channel subunit expression following exercise training requires PI3K, these changes occur independently of Akt1 and hypertrophy.