# CV 4. CENTRAL REGULATION

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## LEARNING OBJECTIVES

1. Describe the reflex control of blood pressure (BP).
2. Explain how baroreceptors (pressure sensors) control BP.
3. Explain how other sensors such as the cardio-pulmonary receptors and blood volume receptors can control BP.
4. Describe central control of blood pressure in response to hypertension, hypotension and strenuous exercise.

## CENTRAL CONTROL OF BP

The reflex arc that controls blood pressure on a minute to minute basis involves the central nervous system (Fig 1). The main integrating center is located in the brain stem (medulla oblongata) in an area known as the **medullary cardiovascular control center (MCCC)**. The primary function of the MCCC is to maintain a constant mean arterial pressure (MAP) for adequate perfusion of the organs, in particular brain and heart. Sensory input comes from peripheral sensory receptors sensitive to **stretch (baro-receptors)** and to **volume (cardio-pulmonary) sensors**. The output from the MCCC alters the sympathetic and parasympathetic tone of the body to regulate cardiac output and total peripheral resistance. [Recall that MAP = CO x TPR]

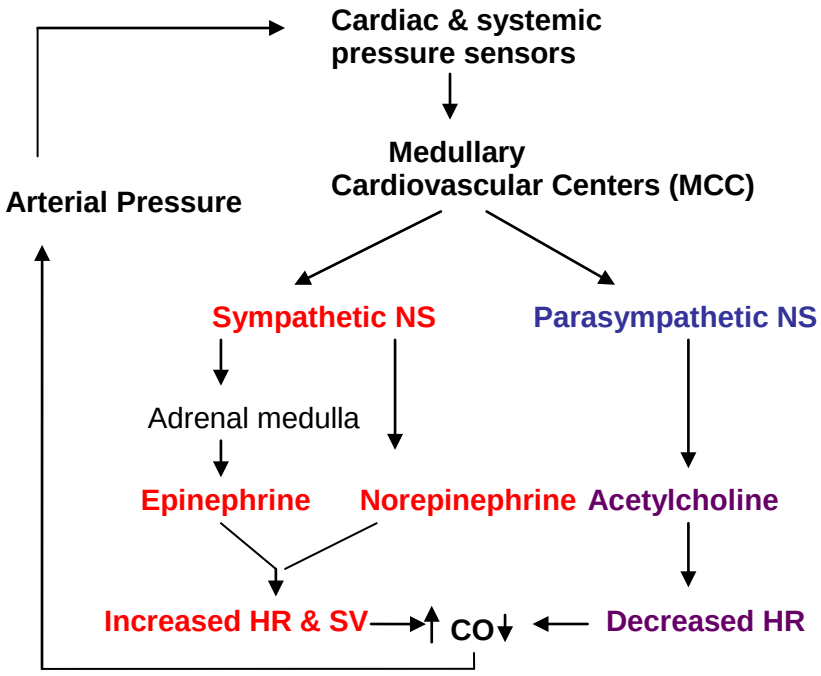


Figure 1. Reflex loop regulates cardiac output.

## BARORECEPTORS REFLEX

Baroreceptors are mechanoreceptors located in the walls of the **carotid artery and aorta**. When *blood pressure increases*, these sensors are stretched and action potentials are sent to the MCCC. Efferent output from the MCCC is relayed by the *parasympathetic nervous system* resulting in slowed heart rate and lower cardiac output thereby lowering blood pressure. Concurrently there is a decrease in MCCC output to the sympathetic nervous system which innervates blood vessels and the heart. Lowered sympathetic tone causes vasodilation and decreased contractility of the ventricular myocardium. Again blood pressure is reduced.

Conversely, if *blood pressure falls*, then the firing from the baroreceptors decreases. This leads to increased output of the MCCC to the *sympathetic nervous system* and decreased output to the parasympathetic system. Consequently heart rate, contractility and TPR increase thereby increasing MAP.

The baroreceptors are not the only mechanism for modulating blood pressure. Inputs from other peripheral receptors include:

(1) **arterial chemoreceptors** which are activated by low blood oxygen levels. These receptors integrate the cardiovascular system with the respiratory system. Integration occurs in the medulla oblongata by the MCCC and the center that controls breathing. This integration is dynamic such that if more oxygen is needed by the tissues, then both cardiac output and breathing is increased.

(2) **hypothalamus** (brain region) which controls body temperature by regulating the sympathetic tone of the vascular beds in the skin.

(3) **kidney** which regulates fluid volume by responding to hormones such as **atrial natriuretic factor (ANF)** which increases fluid loss in urine and **vasopressin** which reduces fluid loss in urine (see discussion below).

## ORTHOSTATIC HYPOTENSION

The baroreceptor reflex functions whenever you rise from a prone position. When you are lying down, blood is evenly distributed throughout the circulation and gravitational pull is equally applied along the body axis. However, on standing, gravity causes a shift in the blood volume such that it pools in your legs. Consequently there is less blood returning to the heart at the beginning of the next contraction. This decrease in venous return reduces cardiac output and MAP. This reflex is known as **orthostatic hypotension.** In the normal person, **orthostatic hypotension decreases baroreceptor firing leading to an increase in sympathetic tone.** Concurrently, parasympathetic activity decreases. The baroreceptor reflex causes a rapid increase in TPR and CO returning MAP to normal.

## HYPOTENSION DUE TO HEMORRHAGE

With loss of fluid volume due to hemorrhage (volume depletion), the baroreceptors decrease their activity (Fig 2). The end result is to increase TPR, CO and MAP.

There are two hormones that act during hemorrhage to correct for the loss of blood volume, vasopressin from the pituitary (brain) and renin from the kidney which leads to the production of angiotensin II. Both vasopressin and angiotensin II are potent vasoconstrictors. These two hormones will act to increase TPR (hence venous return). Vasopressin acts directly on the kidney to increase the reabsorption of water from the urine thereby increasing blood volume.

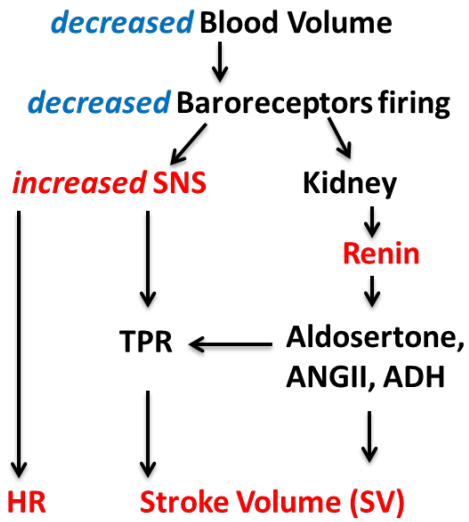


Figure 2. Response to volume depletion activates multiple effectors including the sympathetic nervous system (SNS) and hormones (aldosterone, antidiuretic hormone (ADH) and angiotensin II (ANGII)].

## EFFECT OF EXERCISE

Baroreceptors will reset during strenuous **aerobic exercise** such as running and swimming. Under these conditions, **baroreceptors act as if MAP decreased.** They decrease their firing which increases sympathetic drive to **increase CO and HR**. **TPR also decrease**s due to local signals that cause vasodilation of the capillaries in the working skeletal muscle and skin. Consequently, MAP increases slightly because the rise in CO is offset by the drop in TPR.

| **Pre-exercise level** | **Aerobic exercise level** |
|---|---|
| **CO = 5 L/min** | **CO = 20 L/min** |
| **HR = 70 bpm** | **150 bpm** |
| **20% flow to muscle** | **increased flow to muscle (vasodilation)** |
| **TPR = basal** | **Decreased due to vasodilation in skeletal muscle** |
| **MAP = basal** | **Slightly increased** |

## CARDIOVASCULAR DISEASE

**Sustained hypertension** (>140/90) will cause the **baroreceptors to reset their set point higher** with subsequent down regulation of their activity. Without input from the baroreceptors, the MCCC interprets the high blood pressure as normal.

Is this a problem? Yes. Hypertension is a risk factor for cardiovascular disease. Afterload increases and with increased pressures the endothelium lining the blood vessels may be damaged.

This condition leads to atherosclerotic plaques. In addition, MAP must increase to maintain CO constant at a higher TPR. The heart muscle responds to increased afterload by hypertrophy (growth) which thickens the ventricular wall. With time, this response in the left ventricle fails to meet demand and the CO of the two ventricles is no longer matched, pulmonary edema ensues. Why? What happens to SV with high afterload and lower contractility? Fluid in the interstitial space of the lung interferes with oxygen exchange resulting in less oxygen in the arterial blood perfusing the heart. This damages the myocardium and the contractility of the left ventricle is compromised further (Fig 3). This leads to **heart failure**.

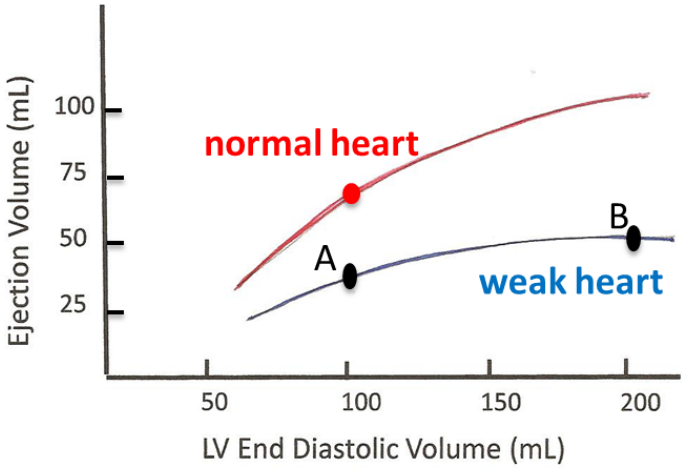


Figure 3. Normal and weak hearts exhibit increased ejection volume (stroke volume) with increased end diastolic volume (filling) of the left ventricle.

Heart failure can also occur in the right ventricle due to hypertension within the lung vasculature. Failure of the right heart to maintain normal CO leads to an accumulation of blood in the systemic veins, increased capillary filtration, and edema.

There are two common treatments for heart failure.
(1) Reduce afterload by administering a diuretic which cause more fluid loss from the kidney and thus lower blood volume.

(2) Administer a Ca++ blocker. Why? Blood vessels will dilate when Ca++ is unable to enter the vascular smooth muscle which reduces TPR and hence MAP. If needed, a beta adrenergic agonist is given to sustain adequate CO.

One other target is angiotensin II, a homeostatic response triggered by the kidney. Drugs called **ACE inhibitors** are given because they inhibit the enzyme that converts angiotensin I to the active vasoconstrictor, angiotensin II, in the blood stream. The end result is a decrease in TPR. What will happen to CO when resistance is decreased?

## KEY CONCEPTS

- Cardiac output is matched with tissue blood flow by maintaining constant mean arterial blood pressure (MAP).
- Baroreceptors act as short term regulators of arterial blood pressure by providing sensory information to the cardiovascular center in the medulla (MCCC). Autonomic outflow from the MCCC maintains blood pressure constant.

- Hemorrhage leads to reduced CO (hypotension) as a result of reduced ventricular EDV. The normal compensatory response to hemorrhage is vasoconstriction of arteries and capacitance veins and increased cardiac contractility and heart rate.
- Hypotension can also result from a sudden postural change or prolonged quiet standing (orthostatic hypotension). The compensatory response is stated above for hemorrhage.
- Failure of the left heart to maintain normal CO leads to an accumulation of blood in the lungs which inhibits gas exchange.
- Failure of the right heart to maintain normal CO leads to an accumulation of blood in the systemic veins, increased capillary filtration, and edema.
- Compensation for decreased arterial pressure caused by heart failure includes increases in HR and TPR, vasoconstriction of veins, and retention water by the kidneys.

## QUESTIONS

1. Fred has newly diagnosed hypertension. His doctor prescribed an angiotensin converting enzyme inhibitor (ACE inhibitor) and instructed him to return for a follow up in three months.
   A. What are two effects of angiotensin II?
   B. What does the ACE inhibitor do?

2. When a baroreceptor activity decreases due to a decrease in blood pressure _____.
   A. sympathetic activity increases.
   B. cardiac output increases.
   C. peripheral resistance decreases.
   D. **A** and **B**
   E. **B** and **C**

3. John donated 1 liter of blood to the Red Cross. In response, the baroreceptors ____ their firing.
   A. increased
   B. decreased
   C. no effect

4. Predict the effect of aging on baroreceptor activity.
   A. resets to higher set point
   B. resets to lower set point
   C. activated chronically
   D. inhibited chronically
   E. remains unchanged

## ANSWERS

1. A. Vasoconstriction as well as the release of aldosterone (from the adrenal) leading to water reabsorption by the kidney (i.e., concentrated urine).
   B. Prevents conversion of angiotensin I to angiotensin II by the angiotensin converting enzyme (ACE).
2. D. is correct.
3. B. resulting in an increase in sympathetic activity
4. A. baroreceptors will reset to a higher set point.