The Cardio-VASCULAR System

- ○ Anatomy
- ○ Histology
- ○ Pathology
- ○ Pharmacology
- ● Physiology
- ○ Microbiology

Lec #: **16**

Dr. Name: **Faisal Mohammad**

Done By: **Ala'a Shaban**

- ○ Handout
- ● Sheet
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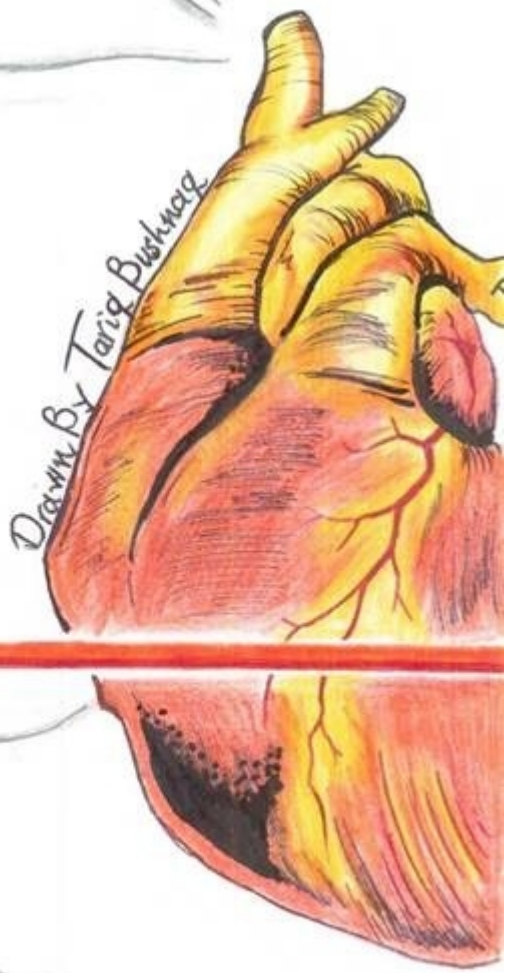
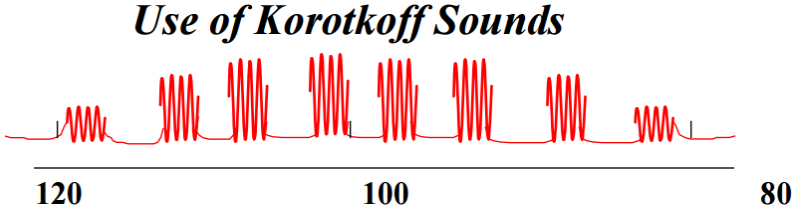


BLOOD PRESSURE REGULATION

Last time we started talking about blood pressure regulation, our objectives are to:

- Outline the short term and long term regulators of BP.
- Know how baroreceptors and chemoreceptors work.
- Know function of the atrial reflex.
- Know function of CNS ischemic reflex.
- Know the role of Epinephrine, Antidiuretic hormone (ADH), Renin-Angiotensin-Aldosterone and Atrial Natriuretic Peptide (ANP) in BP regulation.
- Know the role of Kidney-body fluid system in long term regulation of BP.

The first thing we talked about is how to measure blood pressure, we have two methods; the **auscultatory** method and the **palpatory** method. In the auscultatory method, we use stethoscope with sphygmomanometer; brachial artery is comprised by inflating a cuff around the upper arm generating a pressure above the systolic pressure to the degree that the brachial artery closes so no sound can be heard at this moment by the stethoscope that is placed over the antecubital artery (this artery is distal to the brachial artery), pressure in the cuff is then gradually reduced, when it reaches the systolic pressure, certain sounds start to appear, these sounds result from the **turbulent flow** that comes from constricting the vessel, these sounds are called **Kotrkoff sounds** (in textbook they start from 120 mmHg and disappears at 80 mmHg; these numbers are just for education; normally, the systolic pressure is between 90 mmHg and 140 mmHg, and the diastolic is between 60 mmHg and 90



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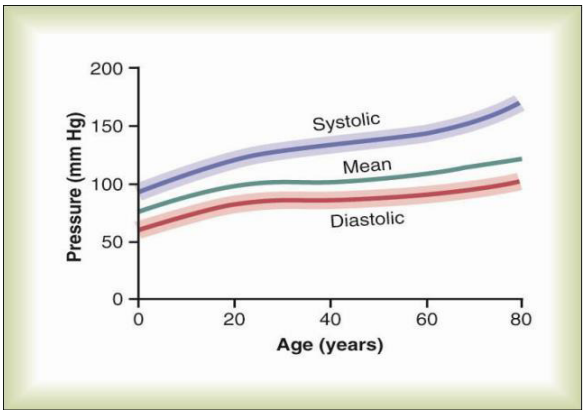
mmHg); afterward, when the pressure around the arm reaches the diastolic pressure, the blood flow becomes **laminar**; laminar flow usually does not produce sounds, so when the sounds disappear, we mark this level as the diastolic pressure.

Nowadays, sphygmomanometers are electrical, we just put them around the cuff without the need to use the stethoscope then press a button to turn the machine on and give us the systolic pressure over the diastolic pressure, these machines are usually calibrated using the mercury sphygmomanometer. In the **palpatory method**, we palpate the pulsation but here the systolic pressure is only measured, diastolic pressure can not be measured by using this method.

Speaking about the arterial pressure, we usually refer to the mean **arterial pressure**, it is closer to the diastolic pressure; the reason behind this comes from the fact that the diastole phase of the heart takes longer time than the systole, so to calculate mean arterial blood pressure (**MAP**) we use this equation:

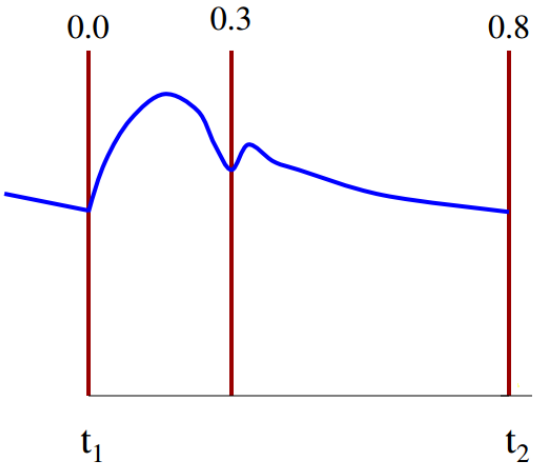


MAP= 2/3 * diastolic pressure + 1/3 * systolic pressure

= diastolic pressure + 1/3 * pulse pressure

This equation is derived to some extent from this equation (the area under the curve) that related the changes in the pressure to the time:

$$MAP = \int_{t2}^{t1} dp.dt/(t_2 - t_1)$$



We talked also about **Owm's law**, from this law we derive the cardiac output law:

Cardiac Output (CO) = Flow = MAP/ TPR

TPR: total peripheral resistance

as a **result; MAP = CO * TPR**

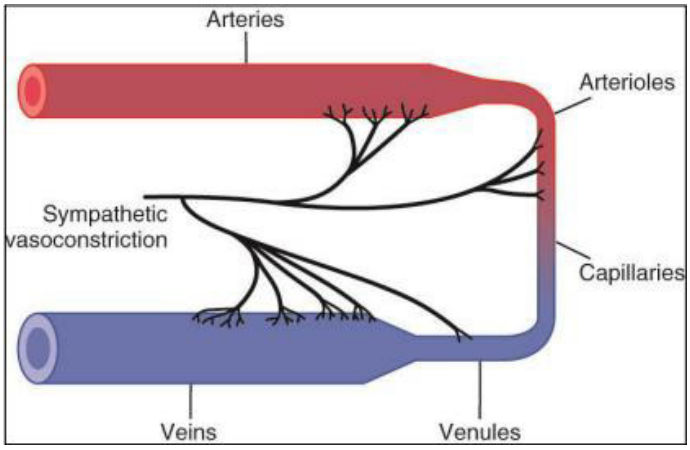
So to change the **mean arterial pressure**, we either change the **cardiac output** or change the **total peripheral resistance**, or we could change **both**. Cardiac output could be changed by changing the heart rate, the stroke volume, or both. Total peripheral resistance is **increased** by vasoconstriction and **reduced** by vasodilatation.

The mean arterial pressure can be increased by constricting almost all arterioles increasing the total peripheral resistance; they are called the major resistance vessels. Constricting large vessels mainly affects the cardiac output and the venous return; specially, when constricting veins; sympathetic stimulation leads to **venoconsctricion increasing** the mean systemic filling pressure (MSFP) increasing venous return, this **increases** end diastolic volume (EDV) and cardiac output, while sympathetic inhibition leads to venodilation **decreasing** MSFP decreasing venous return, this **decreases** EDV and CO.

Autonomic nervous supply of the circulation:

- Sympathetic nervous system supplies all the vessels except the capillaries, precapillary sphincters and some metarterioles, it supplies also the heart.

- Parasympathetic nervous system supplies only the heart, it does not supply the vessels.



So the capillaries have no nervous supply. There is a continuous sympathetic outflow to the vessels that generates a partial vasoconstriction called **basal tone**.

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Referring to Guyton:

> Under normal conditions, the vasoconstrictor area of the vasomotor center transmits signals continuously to the sympathetic vasoconstrictor nerve fibers over the entire body, causing slow firing of these fibers at a rate of about one half to two impulses per second. This continual firing is called *sympathetic vasoconstrictor tone*. These impulses normally maintain a partial state of contraction in the blood vessels, called *vasomotor tone*.

This tone increases by increasing sympathetic stimulation and decreases by sympathetic inhibition. So increasing or decreasing the resistance happens by altering the sympathetic activity; parasympathetic nervous system does not affect the vessels.

Short term regulation of blood pressure:

Our bodies have receptors to sense if there is a change in the blood pressure, these receptors are called **Baroreceptors** or **Pressor receptors,** baroreceptors are stretch receptors; like any other receptor that responds to a certain change they respond to the change of the blood pressure not to the level of the pressure itself. (Short term regulation means that it works through the nervous system, because nervous response is relatively fast).

1. Aterial baroreceptors (or high pressure receptors as they work at high blood pressure): They are located in two critical places; the aortic arch and the carotid sinus, so they are called the *aortic arch baroreceptores* and the *carotid sinus baroreceptors*.

Signal from carotid sinus baroreceptors run through afferent fibers of **Hering's nerve** *(in honor of Hering; 1866–*

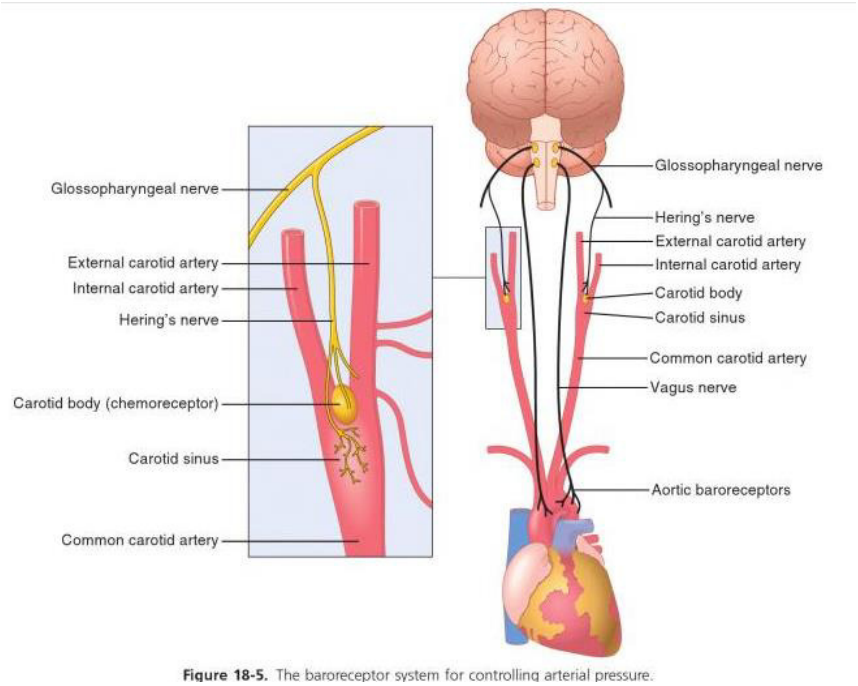


Figure 18-5. The baroreceptor system for controlling arterial pressure.

1948, an Austrian physician; who first described it), a branch of the ninth cranial nerve the **glossopharangreal nerve**. Signals from aortic arch baroreceptors are transmitted through afferent fibers of the tenth cranial nerve the **vagus nerve**.

Referring to Guyton:

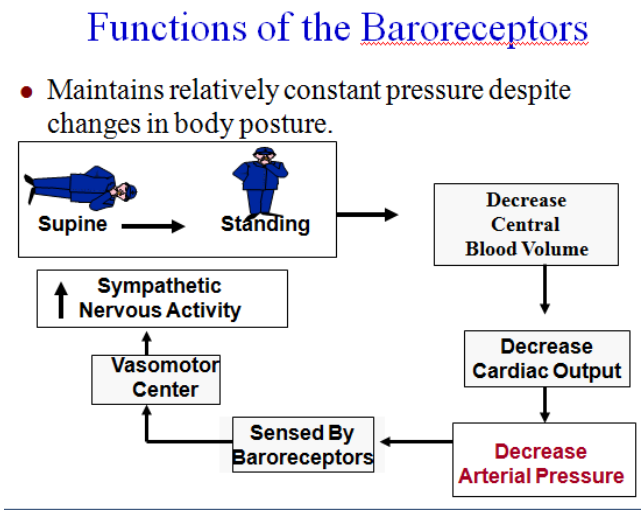
> Figure 18-5 shows that signals from the "carotid baroreceptors" are transmitted through small *Hering's nerves* to the *glossopharyngeal nerves* in the high neck, and then to the *tractus solitarius* in the medullary area of the brain stem. Signals from the "aortic baroreceptors" in the arch of the aorta are transmitted through the *vagus nerves* also to the same tractus solitarius of the medulla.

Baroreceptors as mentioned are stretch receptors; when the blood pressure increases, the stretch increases; they're stimulated increasing the firing (discharge) rate of the action potential from the neurons supplying those receptors. When the blood pressure decreases, the stretch decreases, decreasing the basal discharge rate. Impulses transmitted from baroreceptors run through the afferent fibers to reach the brain stem, most importantly the **Medulla Oblongata**. Medulla Oblongata has **cardiovascular centers**; these contains two entities; **cardiac centers (CC)** and **vasomotor centers (VMC);** cardiac centers are cardio-acceleratory centers and cardio-inhibitory centers, cardio-acceleratory centers function to increase the heart rate through the sympathetic neurons, cardio-inhibitory centers function to decrease the heart rate through the parasympathetic neurons; Vasomotor centers are located bilaterally in the reticular substance of the medulla and the lower third of the pons; Vasomotor centers have three areas: sensory area, vasoconstrictor area, and vasodilator area; the sensory area receives the sensation, vasoconstrictor area sends its impulses to the vessels through the sympathetic nervous system, vasodilator area does not send impulses down through the parasympathetic nervous system; vasoconstricor areas and vasodilator areas have **reciprocal innervations** in the medulla oblongata; when

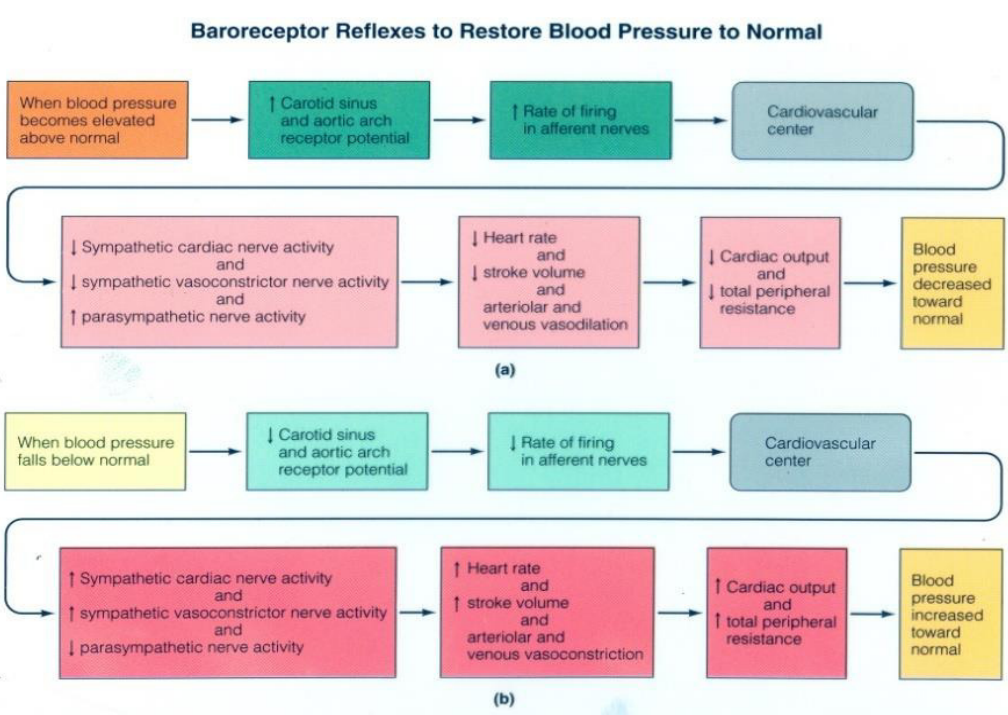
the vasoconstrictor area is stimulated, it inhibits the vasodilator; when the vasodilator area is stimulated, it inhibits the vasoconstrictor area.

Arterial Baroreceptor Reflex:

Arterial baroreceptor reflex is important in short term regulation of blood pressure; e.g. it maintains constant blood pressure despite changes of posture. Standing suddenly after sleeping decreases central volume because of gravity; this decreases cardiac output and blood pressure; baroreceptor reflex functions very fast (in terms of milliseconds) to increase blood pressure toward normal values. When lying down suddenly after being standing, the opposite thing happens.



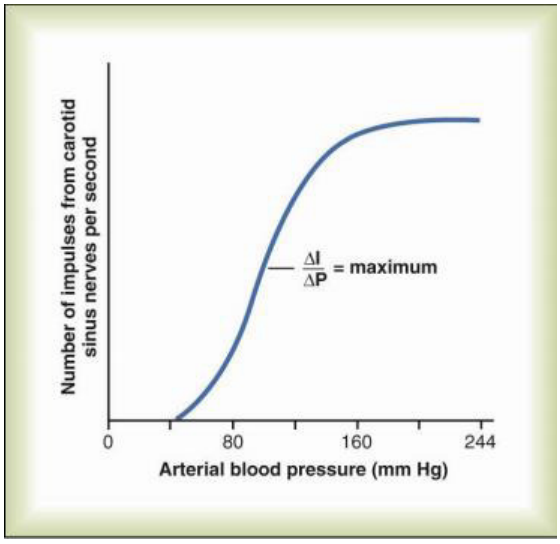
When arterial blood pressure **increases**, baroreceptors are stretched so the **firing rate is increased** and the number of impulses transmitted through the afferent neurons is increased. These impulses reach the cardiovascular center to **inhibit** the cardio-acceleratory center and **stimulate** the cardio-inhibitory center, resulting in less sympathetic impulses sent to the heart so the heart rate decreases and heart contractility decreases, decreasing stroke volume, also more



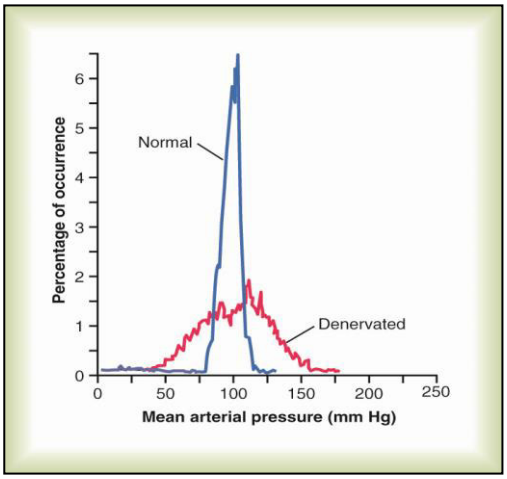
parasympathetic impulses are sent to the heart to **decrease** the heart rate, so the net effect is decreased cardiac output; this decreases the mean arterial blood pressure. At the other side, the relatively high number of impulses sent from baroreceptors to the Medulla Oblongata **stimulates** the vasodilator area and **inhibits** the **vasoconstrictor area**, so less number of sympathetic impulses is sent to the vessels resulting in vasodilatation; this **decreases** the total peripheral resistance in order to **decrease** the mean arterial blood pressure. Therefore, by these two mechanisms MAP goes down to the normal levels.

When blood pressure **decreases**, stretch exerted on baroreceptors **decreases**; so the firing rate and the impulses transmitted through the afferent neurons **decrease**. The less number of impulses that reach the Medulla Oblongata **stimulates** the cardio-acceleratory center and inhibits the cardio-inhibitory center, so more sympathetic impulses are sent to the heart to **increase** the heart rate and increase the stroke volume by increasing contractility; at the same time, less parasympathetic impulses sent to the heart will also **increase** the heart rate; so the net effect is **increased** cardiac output and **increased** MAP. At other side, the relatively low number of impulses reaching the Medulla Oblongata **inhibits** the vasodilator area and **stimulates** the vasoconstrictor area; this increases the number of sympathetic impulses transmitted to the vessels causing vasoconstriction **increasing** TPR; this **increases** MAP. Therefore, by these two mechanisms MAP is elevated to the normal levels.

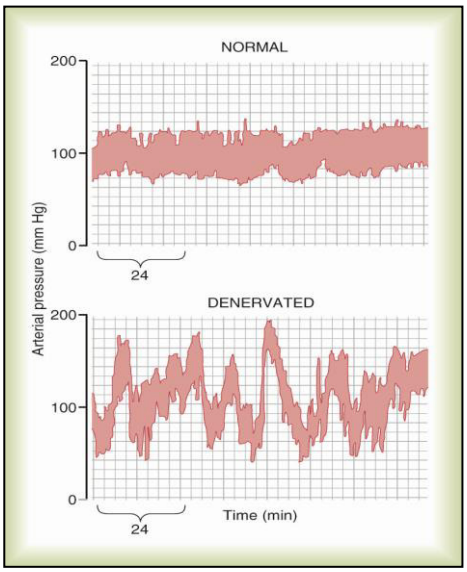
Carotid sinus baroreceptors respond to pressures between 60 mmHg and 180 mmHg. They are not stimulated at all by pressures below 60 mmHg; these low pressures might result in ischemia to the brain. At pressures above 180 mmHg an increase in blood pressure might stimulate these baroreceptors more but



this stimulation will be very little and sluggish. Looking at the adjacent curve, we can realize that the **maximum** change in the number of impulses per change in pressure (highest value of the slope) is around the level of one hundred mmHg arterial blood pressure; i.e. any increase or decrease in blood pressure around this level results in too much increase or decrease respectively in the impulses rate. This level of arterial blood pressure is the level of the normal MAP, so most of the change in impulses rate occurs around this level to keep the arterial blood pressure at its normal levels. This curve looks like biochemistry buffer curves, so the function of the baroreceptor system led it to be called *pressure buffer system* and the nerves from baroreceptors to be called *buffer nerves*.



If baroreceptors were denervated, they would not be able to send impulses to the brain stem, then by measuring the arterial blood pressures frequencies, we can get this adjacent red curve. We realize that most of the readings of the blood pressure in the normally innervated baroreceptors curve are around 100 mmHg which is the normal level of MAP, while in the denervated baroreceptors curve even though most of the readings are around the normal MAP, there are much more readings than the normal curve readings below or above the normal levels (more variation).



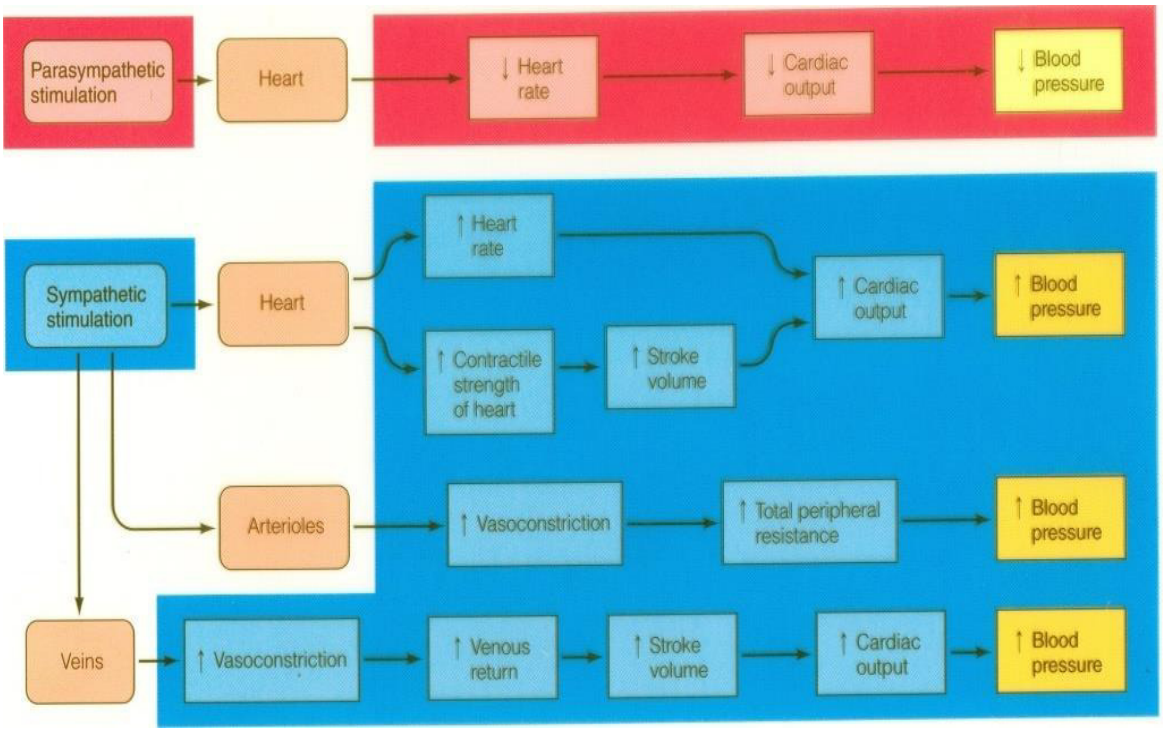
This variety of the readings could also be seen by measuring blood pressure changes through time. In the normally innervated baroreceptors curve, the arterial blood pressures levels stay nearly constant with time; this resembles the buffer function of the baroreceptor as they reduce the change in the normal levels of the blood pressure, while in the denervated baroreceptors curve blood

pressure varies with time; it goes up and down frequently; this resembles the absence of normal homeostasis.

Old people could have some kind of atherosclerosis; atherosclerosis in the carotid artery makes the carotid sinus baroreceptors less sensitive to changes in blood pressure, so baroreceptor response will not be as fast as young people. This explains why some old people could feel like they are fainting when they stand suddenly after lying down. These people should not change their posture suddenly; it is preferred to do it gradually to avoid sudden pressure changes.

This figure summarize the:

Effect of Parasympathetic and Sympathetic Nervous Systems on Factors that Influence the Mean Arterial Pressure



2. Low Pressure Baroreceptors:

The low pressure areas are located in the right atrium and the right ventricle. Right atrial pressure is affected mainly by the volume of blood. If there is an increase in the volume of the blood in the

Reminder: Bainbridge reflex is a sympathetic reflex initiated by increased volume of blood in the right atrium; it increases the heart rate and the strength of contraction; this reflex inhibits damming of blood in the veins, atria, and pulmonary circulation.

right atrium (venous return is increased), right atrial pressure **increases**; at the end, this will lead to **increased** MAP by increased cardiac output due to increase in stroke volume according to *Frank-Starling law*. In order to inhibit this increase in MAP, the low pressure receptors in the right atrium and the right ventricle are **stimulated** when the right atrial pressure is increased.

Upon stimulation, these receptors send impulses to the **Hypothalamus,** where the production of *antiduretic hormone* (*ADH*; it is also called *vasopressin; it is a vasoconstrictor*) occurs, these impulses decrease the secretion of ADH; so the net effect is vasodilatation that **decreases** the total peripheral resistance. Therefore, MAP is brought back to normal; this mechanism is called **Atrio-Hypothalamic reflex**. ADH also stimulates water reabsorption of the distal part of the *nephrone* (water reabsoption increases extracellular volume; this increases the blood volume which in turn increases MSFP and the venous return); so decreased ADH secretion through the low pressure receptor reflex **decreases** water reabsorption; this decreases extracellular volume decreasing blood volume which in turn decreases MSFP and venous return in order to **decrease** right atrial pressure.

Another reflex occurs from the right atrium to the kidney; this reflex is called **Atrio-Renal reflex**. Stimulated low pressure receptors in the right atrium induce a reflex through neurons to the kidney; causing afferent arteriolar vasodilatation; this increases blood flow to the kidney **increasing** the *glomerular filtration rate (GFR)* which in turn increases urine output and water loss; this decreases extracellular volume decreasing blood volume in order to decrease MSFP and venous return. So when the right atrial pressure is elevated, both of the previous two reflexes decrease the pressure.

In case of hypotention right atrial pressure drops down; this **decreases** stimulation of low pressure receptors, this **increases** ADH secretion leading to vasoconstriction which **increases** total peripheral resistance and MAP; increased ADH also **increases** water reabsorption increasing extracellular volume; this increases blood

volume which in turn increases MSFP and venous return; this **increases** right atrial pressure (resembles increase in end diastolic volume) then according to *Frank-Starling law* cardiac output increases increasing MAP. This is about the *Atrio-Hypothalamic reflex*.

On the other hand, decreased right atrial pressure also through *Atrio-Renal reflex* induces afferent arteriolar vasoconstriction decreasing GFR; this increases blood volume which in turn **increases** venous retrun and CO.

3. Chemoreceptors:

These receptors are not the same as baroreceptors but they are located in the same areas of arterial baroreceptors; *carotid sinus* and *aortic arch*; these are called **peripheral chemoreceptors**. Central chemoreceptors are located in the Medulla Oblongata. These *peripheral chemoreceptors* respond to decrease in PO_2, increase in PCO_2, and increase in hyrdogen ions concentration i.e. decrease in PH.

Normally, these peripheral chemoreceptors are supplied by **too much** blood flow to the extent that O_2 and CO_2 concentrations in the interstitial fluid around them are **equal** to their concentrations in the arterial blood. If there is an **increase** in the arterial pressure, the blood flow to these receptors increases increasing oxygen concentration and decreasing CO_2 and H^+ concentrations around them (increase in washing out hydrogen ions increases PH), this **inhibits** these chemoreceptors **decreasing** the impulses transmitted to the cardiovascular areas; resulting in **inhibition** of the sympathetic activity leading to vasodilation and decrease in heart rate and contractility; at the same time this **stimulates** the parasympathetic activity decreasing the heart rate. The net effect is **decrease** in the cardiac output; this decreases MAP. If there is a **decrease** the arterial pressure, the blood flow to the peripheral chemoreceptors decreases; increasing CO_2 and H^+ concentrations and decreasing O_2 concentration around them; this **stimulates** these receptors **increasing** the impulses transmitted to the cardiovascular centers; this **inhibits** the parasympathetic activity and **increases** the sympathetic activity; increasing blood pressure.

References:

1. Lecture recording.

2. Blood Pressure Regulation slides.

3. Guyton And Hall Textbook of Medical Physiology, twelfth and thirteenth editions; (some paragraphs were cited literally, others were rephrased according to the lecture).

This Sheet Is Dedicated to: Baha'a Al-Shreideh, Omar Al-Qeisi, Abdullah Al-Shurman and Mamoun Soulaiman.