Vascular Physiology 3

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Extrinsic control of arterioles

Extrinsic control of arteriolar radius includes both neural and hormonal influences, the effects of the sympathetic nervous system being the most important.

Increased sympathetic activity produces generalized arteriolar vasoconstriction, whereas decreased sympathetic activity leads to generalized arteriolar vasodilation.

These widespread changes in arteriolar resistance bring about changes in mean arterial pressure because of their influence on total peripheral resistance.

Blood flow, blood pressure, and resistance

F = P gradient/ R

For the whole systemic circulation:

CO = MAP/ TPR

So:

MAP = CO x TPR

MAP

- MAP is the main driving force for propelling blood to the tissues.
- This pressure must be closely regulated for two reasons.
- First, it must be high enough to ensure sufficient driving pressure; without this pressure, the brain and other organs do not receive adequate flow, no matter what local adjustments are made in the resistance of the arterioles supplying them.
- Second, the pressure must not be so high that it creates extra work for the heart and increases the risk of vascular damage and possible rupture of small blood vessels.

MAP

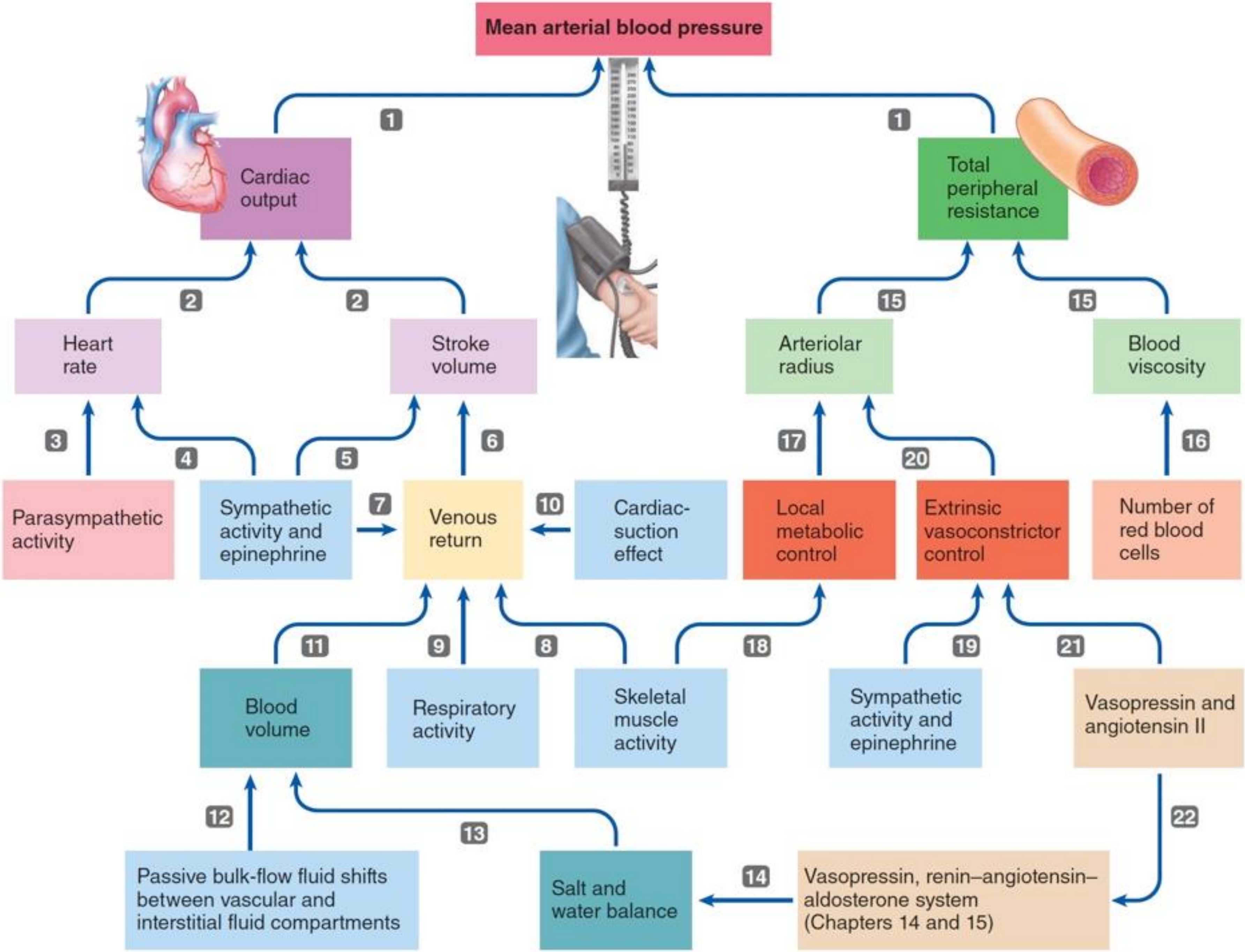
The sympathetically induced arteriolar responses help maintain the appropriate driving pressure (MAP) to all organs.

The extent to which each organ actually receives blood flow is determined by local arteriolar adjustments that override the sympathetic constrictor effect.

If all arterioles were dilated, blood pressure would fall substantially, so there would not be an adequate driving force for blood flow.

MAP

- The two determinants of MAP are CO and TPR.
- CO and TPR are not independent variables. Changes in TPR can alter CO and changes in CO can indirectly alter TPR. Therefore it cannot be stated that if TPR doubles, MAP also doubles.
- CO and TPR are affected by many factors.



Mean arterial blood pressure
1
1
Cardiac output
Total peripheral resistance
2
2
15
15
Heart rate
Stroke volume
Arteriolar radius
Blood viscosity
3
4
5
6
17
20
16
Parasympathetic activity
Sympathetic activity and epinephrine
7
Venous return
10
Cardiac-suction effect
Local metabolic control
Extrinsic vasoconstrictor control
Number of red blood cells
11
9
8
18
19
21
Blood volume
Respiratory activity
Skeletal muscle activity
Sympathetic activity and epinephrine
Vasopressin and angiotensin II
12
13
22
14
Passive bulk-flow fluid shifts between vascular and interstitial fluid compartments
Salt and water balance
Vasopressin, renin–angiotensin–aldosterone system (Chapters 14 and 15)

Neural control of the circulation

- The nervous system controls the circulation almost entirely through the autonomic nervous system.

- In most tissues, all the vessels except the capillaries are innervated by sympathetic neurons.

Neural control of BP

- One of the most important functions of nervous control of the circulation is its capability to cause rapid increases in arterial pressure.
- For this purpose, the entire vasoconstrictor and cardioaccelerator functions of the sympathetic nervous system are stimulated together.
- At the same time, there is reciprocal inhibition of parasympathetic vagal inhibitory signals to the heart.

Sympathetic NS

- The sympathetic nerves carry large numbers of vasoconstrictor nerve fibers and only a few vasodilator fibers.
- The vasoconstrictor fibers are distributed to essentially all segments of the circulation, but more to some tissues than to others.

- This sympathetic vasoconstrictor effect is especially powerful in the kidneys, intestines, spleen, and skin but is much less potent in skeletal muscle, heart.

Parasympathetic NS

Arterioles have no significant parasympathetic innervation, with the exception of the abundant parasympathetic vasodilator supply to the arterioles of the penis and clitoris.

The rapid, profuse vasodilation induced by parasympathetic stimulation in these organs (by means of promoting release of NO) is largely responsible for accomplishing erection.

Vasodilation elsewhere is produced primarily by decreasing sympathetic vasoconstrictor activity below its normal tone level.

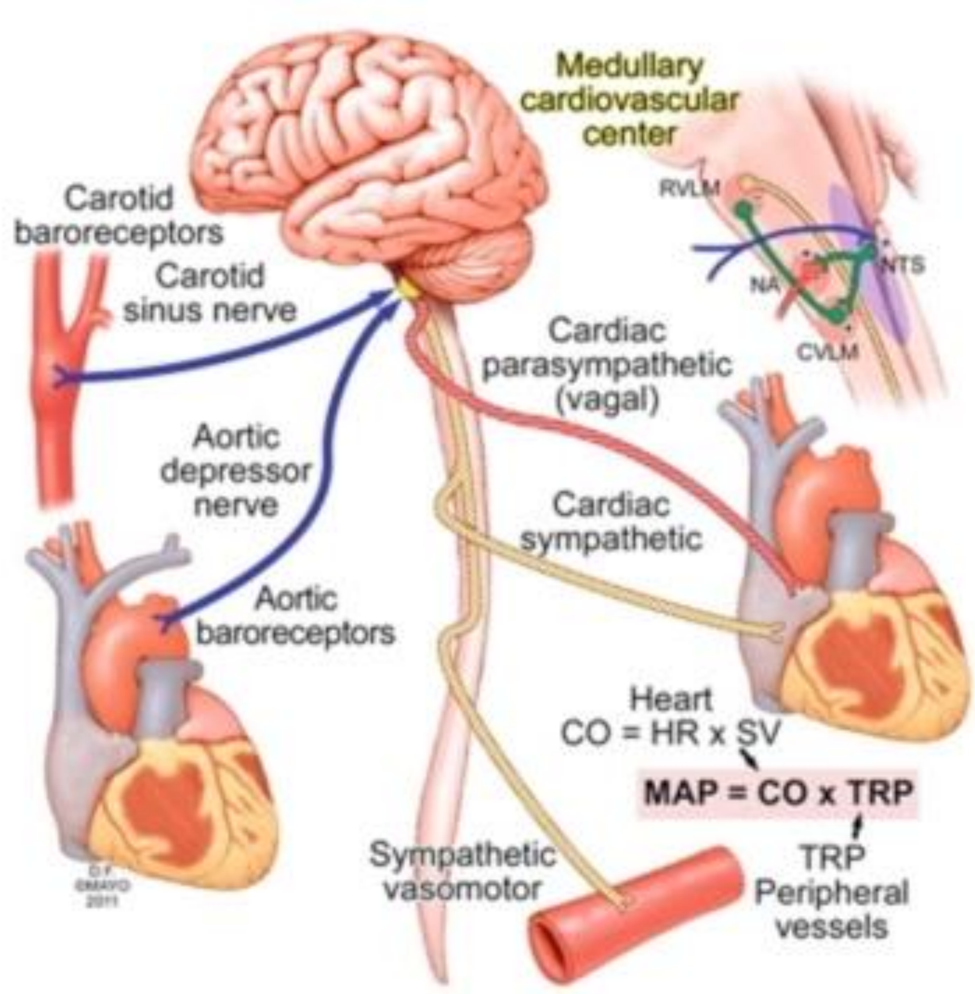
When MAP rises above normal, reflex reduction in sympathetic vasoconstrictor activity accomplishes generalized arteriolar vasodilation to help bring the driving pressure down toward normal.

Also, the hormone epinephrine causes vasodilation in arteriolar smooth muscle specifically in the skeletal muscles and heart.

Cardiovascular center in the brain

- The main region of the brain that adjusts sympathetic output to the arterioles is the cardiovascular control center in the medulla of the brain stem. This is the integrating center for blood pressure regulation. Several other brain regions also influence blood distribution, the most notable being the hypothalamus, which, as part of its temperature-regulating function, controls blood flow to the skin to adjust heat loss to the environment.

Cardiovascular center in the brain



Baroreflex

Any change in MAP triggers an autonomically mediated baroreceptor reflex that influences the heart and blood vessels to adjust CO and TPR in an attempt to restore blood pressure toward normal.

Information from the carotid sinus baroreceptors is carried to the brain stem on the carotid sinus nerve, which joins the glossopharyngeal nerve. Information from the aortic arch baroreceptors is carried to the brain stem on the vagus nerve.

Baroreflex

- Baroreceptors closely monitor P and compare it with the set-point value. If P increases above the set point or decreases below the set point, the cardiovascular system makes adjustments in CO, in TPR, or in both, attempting to return P to the set-point value.

- Increases in arterial pressure cause increased stretch on the baroreceptors and increased firing rate in the afferent nerves. Decreases in arterial pressure cause decreased stretch on the baroreceptors and decreased firing rate in the afferent nerves.

Baroreflex

- Although the baroreceptors are sensitive to the absolute level of pressure, they are even more sensitive to changes in pressure and the rate of change of pressure. The strongest stimulus for the baroreceptors is a rapid change in arterial pressure.

Baroreflex: as a buffering system

- Because the baroreceptor system opposes increases or decreases in arterial pressure, it is called a pressure buffer system, and the nerves from the baroreceptors are called buffer nerves.

- A primary purpose of the arterial baroreceptor system is therefore to reduce the minute by minute variation in arterial pressure to about one-third that which would occur if the baroreceptor system were not present.

Baroreflex in Hypertension (Chronic High BP)

- The sensitivity of the baroreceptors can be altered by disease.
- The baroreceptors do not respond to bring blood pressure back to normal during hypertension because they adapt, or are “reset,” to operate at a higher level.
- In the presence of chronically elevated blood pressure, the baroreceptors still function to regulate blood pressure, but they maintain it at a higher mean pressure.

Hypertension

- Whatever the underlying defect, once initiated, hypertension appears to be self-perpetuating.
- Constant exposure to elevated blood pressure damages vessel walls and predisposes them to development of atherosclerosis.
- The resultant narrowing of vessel lumens by atherosclerotic plaques increases TPR, which further elevates blood pressure.
- Thus a detrimental positive-feedback cycle ensues where hypertension and atherosclerosis each promote development of the other.

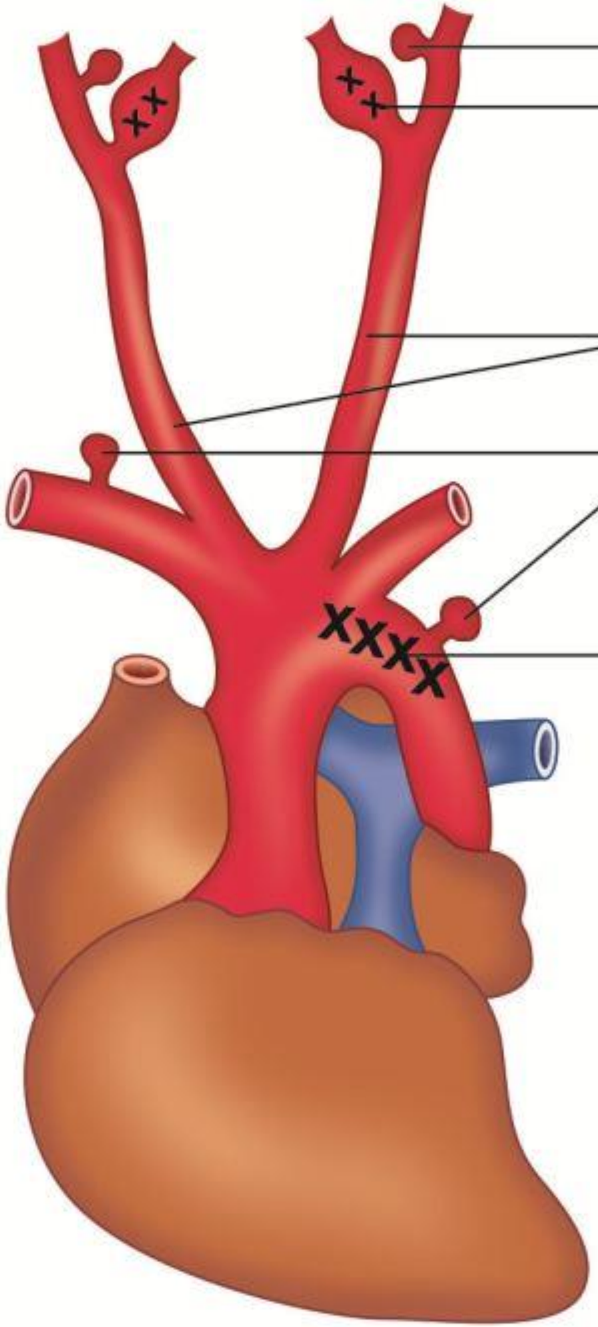
Complications of hypertension

- Hypertension imposes stresses on both the heart and the blood vessels.

- The heart has an increased workload because it is pumping blood out against an increased TPR, and the high internal pressure may damage blood vessels, particularly when the vessel wall is weakened by the degenerative process of atherosclerosis.

Complications of hypertension

- (1) left ventricular hypertrophy maybe followed by systolic heart failure.
- (2) stroke.
- (3) heart attack.
- (4) renal failure.
- (5) retinal damage.



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Peripheral Chemoreceptors

- Peripheral chemoreceptors for O_2 are located in the carotid bodies near the bifurcation of the common carotid arteries and in the aortic bodies along the aortic arch.

- Their chemoreceptors are primarily sensitive to decreases in (PO_2). The chemoreceptors also are sensitive to increases in (PCO_2) and decreases in pH, particularly when PO_2 is simultaneously decreased.

- The response of the peripheral chemoreceptors to decreased arterial PO_2 is greater when the PCO_2 is increased or the pH is decreased.

Peripheral Chemoreceptors

- When arterial PO_2 decreases, there is an increased firing rate of afferent nerves from the carotid and aortic bodies that activates sympathetic vasoconstrictor centers. As a result, there is arteriolar vasoconstriction in skeletal muscle, renal, and splanchnic vascular beds.

- The chemoreceptors excite nerve fibers that along with the baroreceptor fibers, pass through Hering’s nerves and the vagus nerves into the vasomotor center of the brain stem.

Peripheral chemoreceptors

- It is at the lower pressures that this reflex becomes important to help prevent further decreases in arterial pressure.
- It is related to respiratory control.

Central Chemoreceptors

- The brain is intolerant of decreases in blood flow, and therefore it is not surprising that chemoreceptors are located in the medulla itself.
- These chemoreceptors are most sensitive to CO_2 and pH and less sensitive to O_2.

- Changes in PCO_2 or pH stimulate the medullary chemoreceptors, which then direct changes in outflow of the medullary cardiovascular centers.

Central Chemoreceptors

- If the brain becomes ischemic (i.e., there is decreased cerebral blood flow), cerebral PCO2 immediately increases and pH decreases.
- The medullary chemoreceptors detect these changes and direct an increase in sympathetic outflow that causes intense arteriolar vasoconstriction in many vascular beds and an increase in TPR.
- Blood flow is thereby redirected to the brain to maintain its perfusion. As a result of this vasoconstriction, BP increases dramatically, even to life-threatening levels.

Central Chemoreceptors

- **The Cushing reaction:**
- When intracranial pressure increases (e.g., tumors, head injury), there is compression of cerebral arteries, which results in decreased perfusion of the brain.
- There is an immediate increase in PCO2 and a decrease in PH.
- The medullary chemoreceptors respond to these changes in PCO2 and pH by directing an increase in sympathetic outflow to the blood vessels to increase TPR and dramatically increase BP.

Atrial and pulmonary artery reflexes

- The atria and pulmonary arteries have stretch receptors in their walls called low-pressure receptors.
- Low-pressure receptors are similar to the baroreceptor stretch receptors of the large systemic arteries.
- These low-pressure receptors play an important role, especially in minimizing arterial pressure changes in response to changes in blood volume.

Atrial and pulmonary artery reflexes

- Even though the low-pressure receptors in the pulmonary artery and in the atria cannot detect the systemic arterial pressure, they do detect simultaneous increases in pressure in the low-pressure areas of the circulation caused by increase in volume.

Atrial volume reflex

- Stretch of the atria and activation of low-pressure atrial receptors also causes reflex reductions in renal sympathetic nerve activity, decreased tubular reabsorption, and dilation of afferent arterioles in the kidneys.
- Signals are also transmitted simultaneously from the atria to the hypothalamus to decrease secretion of antidiuretic hormone (ADH).

Atrial volume reflex

- All these mechanisms that tend to return blood volume back toward normal after a volume overload act indirectly as pressure controllers, as well as blood volume controllers, because excess volume drives the heart to greater cardiac output and higher arterial pressure.

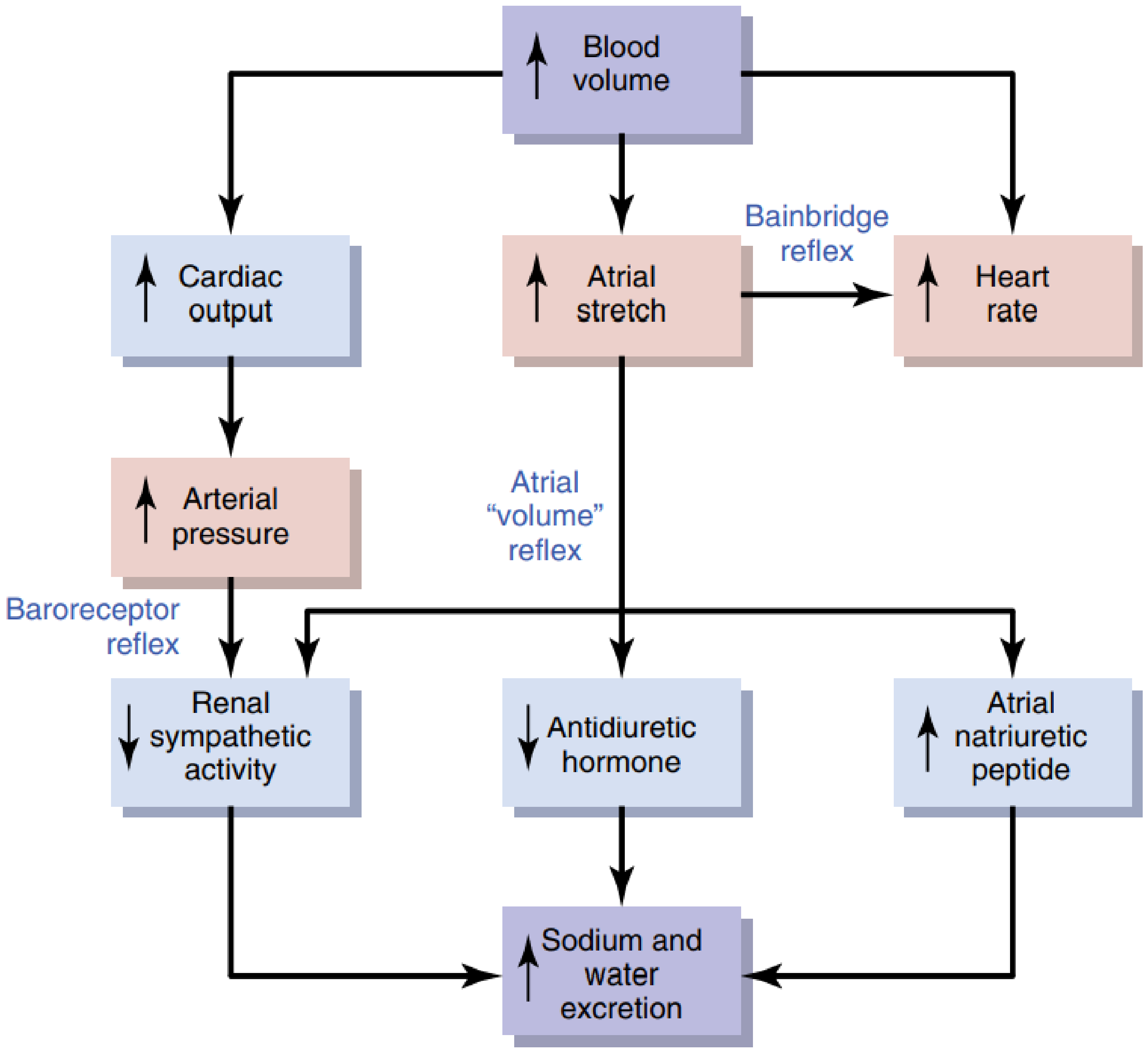
Bainbridge reflex

- Information from the low pressure atrial receptors travels in the vagus nerve to the nucleus tractus solitarius (as does information from the high-pressure arterial receptors involved in the baroreceptor reflex).

- The difference lies in the response of the medullary cardiovascular centers to the low- and high-pressure receptors. Whereas an increase in pressure at the arterial high-pressure receptors produces a decrease in heart rate (trying to lower arterial pressure back to normal), an increase in pressure at the venous low-pressure receptors produces an increase in heart rate (Bainbridge reflex).

Bainbridge reflex

- The low-pressure atrial receptors, sensing that blood volume is too high, direct an increase in heart rate and thus an increase in cardiac output; the increase in cardiac output leads to increased renal perfusion and increased Na^+ and water excretion.



Blood volume
Cardiac output
Atrial stretch
Bainbridge reflex
Heart rate
Arterial pressure
Atrial "volume" reflex
Baroreceptor reflex
Renal sympathetic activity
Antidiuretic hormone
Atrial natriuretic peptide
Sodium and water excretion

Hormonal control of circulation

Adrenal medulla

- Sympathetic stimulation of the adrenal medulla causes this endocrine gland to release epinephrine and norepinephrine.

- Adrenal medullary norepinephrine combines with the same a1 receptors as sympathetically released norepinephrine to produce generalized vasoconstriction.

- However, epinephrine, the more abundant of the adrenal medullary hormones, combines with both b2 and a1 receptors but has a much greater affinity for the b2 receptors. Activation of b2 receptors produces vasodilation, but not all tissues have b2 receptors; they are most abundant in the arterioles of the skeletal muscles and heart.

Adrenal medulla

- During sympathetic discharge, the released epinephrine combines with the b2 receptors in the skeletal muscles and heart to reinforce local vasodilatory mechanisms in these tissues.

- Arterioles in digestive organs and kidneys, in contrast, are equipped only with a1 receptors. Therefore, the arterioles of these organs undergo more profound vasoconstriction during generalized sympathetic discharge than those in the skeletal muscles and heart do.

Vasopressin

Vasopressin (antidiuretic hormone ADH) is primarily involved in maintaining water balance by regulating the amount of water the kidneys retain for the body during urine formation.

RAAS

- The renin–angiotensin II–aldosterone system (RAAS) regulates P primarily by regulating blood volume.
- This system is much slower than the baroreceptor reflex because it is hormonally mediated.
- The renin–angiotensin II–aldosterone system is activated in response to a decrease in the P.
- Activation of this system, in turn, produces a series of responses that attempt to restore arterial pressure to normal.

RAAS

- **Required self reading**:

- https://www.ncbi.nlm.nih.gov/books/NBK470410/

BP measurement

Learn what is considered normal, as recommended by the American Heart Association.

BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)	and/or	DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 – 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 – 139	or	80 – 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

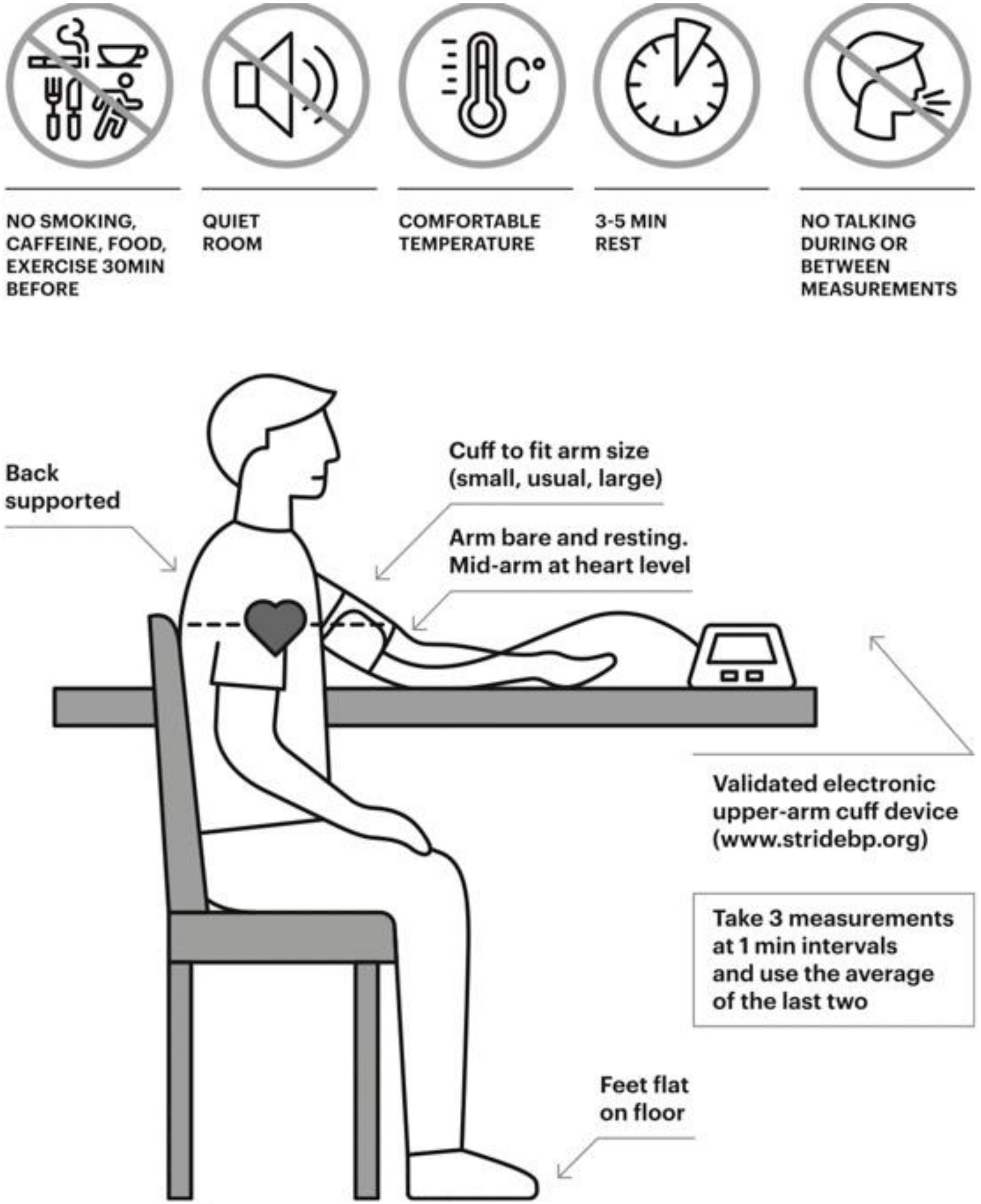


FIGURE 2 Poster of OBP measurement methodology.

BP measurement

Recommended reading

www.ahajournals.org/doi/10.1161/HYP.0000000000000087

Thank you