



Pathophysiology-Hypertension

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Blood Pressure (BP) Regulation

(Hypertension HTN)

زيادة

hypo → نقصان

Hypertension

❖ What do Blood Pressure Numbers Mean?

→ contraction, depolarization

→ relaxation, repolarization

- **Top** number (Systolic) while the **bottom** number (Diastolic).

- **Normal Blood Pressure:** Blood Pressure of $< 140/90$.

- Blood Pressure of 130 to 139/ 85 to 89 should be closely watched.

- **High Blood Pressure:** Blood Pressure $> 140/90$. Usually **NO SYMPTOMS!** “The **Silent Killer**”. **May have headache, blurry vision, chest pain, and frequent urination at night.**

← القاتل الصامت

↳ symptom?!

↳ increase excretion the urine

↳ Why?! because it is chronic disease with no symptom or maybe mixing with another disease

Hypertension

-
- Hypertension is an ^{intermittent} or ^{sustained} elevation of diastolic or systolic blood pressure. Generally, a sustained systolic blood pressure of 139 mm Hg or higher or a diastolic blood pressure of 89 mm Hg or higher indicates hypertension.
 - Increased blood pressure is the most common health problem in adults and the leading risk factor in CVD.
 - It affects about 1 billion people worldwide.
 - Hypertension increases with age.
 - Males more than females until menopause. More in blacks compared to whites.

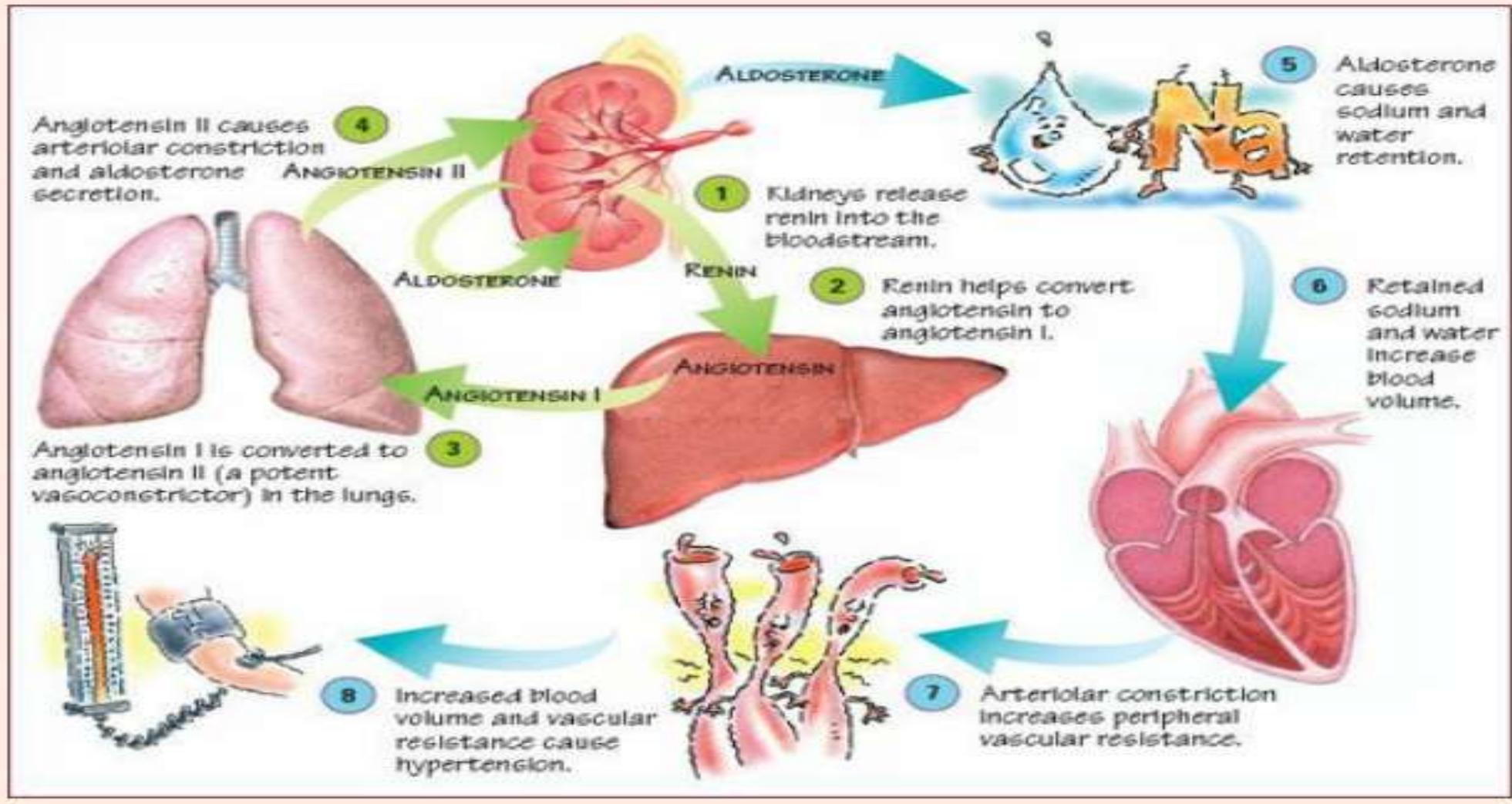
American Heart Association Recommended Blood Pressure Levels

BP Category	Systolic (mmHg)		Diastolic (mmHg)	Follow-up
Optimal <i>120/80 → adult</i>	< 120	and	< 80	Recheck 2 years
Normal <i>140/90 → الكبار بالبحر → optimal</i>	< 130	and	< 85	Recheck 2 years
High Normal	130-139	or	85-89	Recheck 1 year

American Heart Association Recommended Blood Pressure Levels

BP Category	Systolic (mmHg)		Diastolic (mmHg)	Follow-up
Stage 1 (mild HTN)	140-159	or	90-99	Confirm within months
Stage 2 (moderate HTN)	160-179	or	100-109	Evaluate within 1 month
Stage 3 (severe HTN)	180 or >	or	110 or >	Evaluate immediately

④ hypertensive crisis



Angiotensin II causes arteriolar constriction and aldosterone secretion.

4

ANGIOTENSIN II

1 Kidneys release renin into the bloodstream.

1

RENIN

2 Renin helps convert angiotensin to angiotensin I.

2

ANGIOTENSIN

6 Retained sodium and water increase blood volume.

6

Angiotensin I is converted to angiotensin II (a potent vasoconstrictor) in the lungs.

3

ANGIOTENSIN I

8 Increased blood volume and vascular resistance cause hypertension.

8

7 Arteriolar constriction increases peripheral vascular resistance.

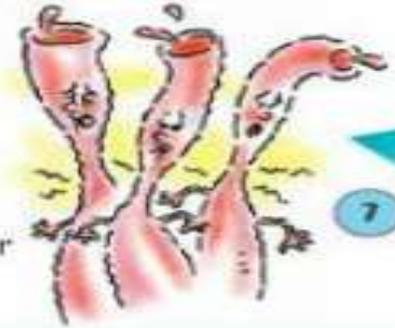
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5 Aldosterone causes sodium and water retention.

5

ALDOSTERONE

ALDOSTERONE



Hypertension

↳ cause dysfunctional endothelial cell ⇒ clotting ⇒ complication:-
① angina ② stroke in brain ③ atherosclerosis ④ ischemic heart disease
⑤ myocardial infarction ⑥ shock ⑦ arrhythmia

- **Divided into two categories:**

- **Primary or idiopathic hypertension:**

- Chronic elevation of blood pressure **without evidence of other diseases.**
- Affect **90-95%** of hypertensive patients.

- **Secondary hypertension:** **caused by other diseases like kidney disease** (if it's **related to a systemic disease that raises peripheral vascular resistance or cardiac output.**)

Secondary hypertension

Secondary hypertension may be caused by:

- Renal hypertension.
- Adrenocortical hormone as:
 - Primary hyperaldosteronism. → excessive produce aldosterone from adrenal gland
 - Excess corticosteroids (Cushing's syndrome). → moon face
- Adrenal gland abnormalities: **Pheochromocytoma** (rare catecholamine-secreting tumor of adrenal chromaffin cells it produces adrenaline & noradrenaline, and they cause hypertension), **characterized by episodes** of **headache**, **excessive sweating**, and **palpitation**.
↳ ضغطان القلب
↳ عرق ←

Secondary hypertension

Secondary hypertension may be caused by:

- Coarctation of the aorta (narrowing or constriction of the aorta).
- Oral contraceptive ^{صنع الحمل} drugs.
- Drugs as cocaine, amphetamine, and erythropoietin.
- Obstructive sleep apnea. → انقطاع النفس
- Diabetes mellitus.
- Dysfunction of the ^{metabolism} thyroid, pituitary, or parathyroid gland. → hypercalcemia
↳ metabolism
- Pregnancy (gestational hypertension. which is part of the preeclamptic toxemia that is **characterized by** edema, hypertension, and proteinuria (protein in urine).
← تسم الحمل
- Neurologic disorders.

Hypertension

❖ Controllable Risk Factors:

- Increased salt intake.
- Obesity (**Lectin** works fine in non-obese people, but when an adipose tissue (fat) increases in the body, the sensor gets damaged).
- Alcohol.
- Stress.
- Lack of exercise.

smoking

❖ Uncontrollable Risk Factors:

- Heredity. وراثته
- Age.
 - ✓ Men between age 35 and 50.
 - ✓ Women after menopause.
- Race: العرق
 - ✓ 1 out of every 3 African Americans.
 - ✓ Higher incidence in non-Hispanic blacks and Mexican Americans.

Hypertension

❖ Women and High Blood Pressure:

- Birth Control Pill. حبوب منع الحمل
- Pregnancy. الحمل
- Overweight. obesity
- After Menopause.
- African Americans.

Hypertension

❖ What does High Blood Pressure do to my body?:

- Stroke.
 - Congestive heart failure.
 - Kidney failure.
 - Heart attack.
 - Heart rhythm problems.
 - Aneurysm. *تحد الأوعية الدموية*
- High blood pressure adds to the workload of the heart.
 - The heart must pump harder.
 - If high blood pressure continues for a long time, the heart and arteries may not function appropriately. *بشكل صحيح*
 - The heart may at first thicken and then dilate and weaken causing heart failure.
 - Other body organs may also be affected.

Arterial Blood Pressure Regulation

● Short term regulation of blood pressure:

- ❖ A regulation of blood pressure due to a change in position.
- ❖ Baroreceptor reflex (Immediate rapid mechanism). This is done/regulated by baroreceptors, which are responsible for regulating blood pressure from moment to moment. Baroreceptors prevent fluctuating BP.
تقلبات
- ❖ Baroreceptors are neurons (collection of nuclei) located in the arch of the aorta and large blood vessels of the chest.
- ❖ These baroreceptors are sensitive to either increase or decrease in blood flow. *(change in BP)*

Arterial Blood Pressure Regulation

● Short term regulation of blood pressure:

- ❖ In the case of decreasing blood flow (hypotension), these receptors will send an impulse through the glossopharyngeal nerve to the vasomotor center, which is located in the medulla oblongata (have a collection of nuclei which are called tractus solitarius).
- ❖ The vasomotor center (tractus solitarius) will stimulate the sympathetic nervous system, increasing contractility, and cardiac output. It also enhances the release of epinephrine & norepinephrine from the medulla of the adrenal gland which leads to central vasodilation and peripheral vasoconstriction; so, BP will return to normal.

Arterial Blood Pressure Regulation

● Short term regulation of blood pressure:

- ❖ In the case of an increase in blood flow, the impulse will be sent to the vasomotor center (tractus solitaries). It will block the sympathetic nervous system rather than stimulate the parasympathetic nervous system. Thus, contractility and cardiac output will be decreased, vasodilation peripherally will occur, and BP will return to normal.

Nervous Regulation of the Circulation

Nervous control of the circulation mainly affects more ^{الوظائف الكافية} global functions (e.g., redistribution of blood flow, cardiac contractility, and rapid control of arterial blood pressure).
← إعادة توزيع

Autonomic Nervous System

- **Sympathetic Nervous System** (Norepinephrine is the neurotransmitter substance): It stimulates vasoconstriction by activation of alpha adrenoceptors on vascular smooth muscle.

Nervous Regulation of the Circulation

Autonomic Nervous System

- **Sympathetic Nervous System:**

- ② • Vasoconstriction of arterioles results in ① increased vascular resistance and redistribution of blood flow.

- ② • Vasoconstriction of veins results in ① increased circulating blood volume, increased venous return, which subsequently leads to ② increased ventricular filling and ③ stroke volume.

- Increase in the activity of the heart (heart rate and contractility ↑).

Nervous Regulation of the Circulation

Autonomic Nervous System

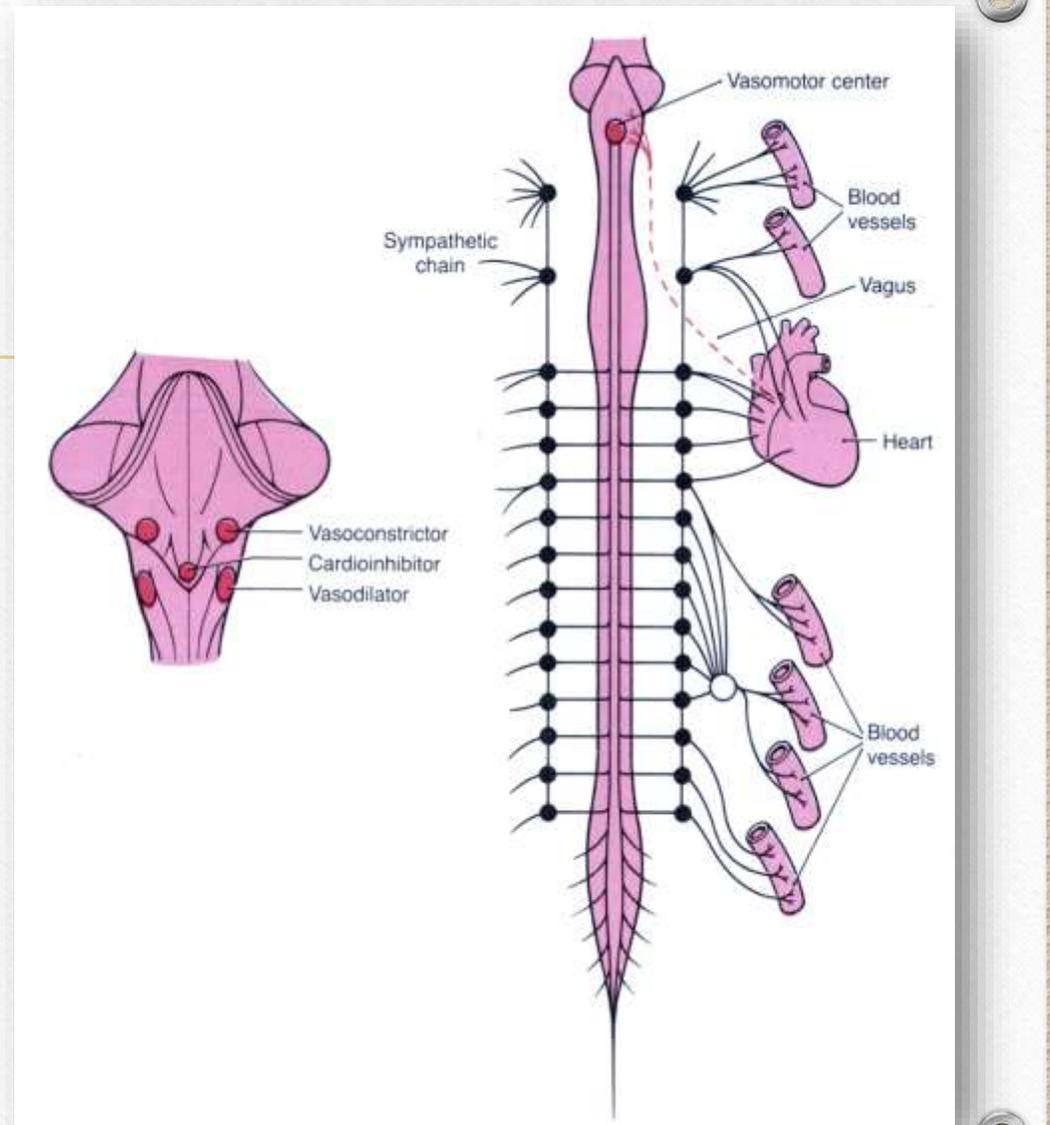
- **Parasympathetic system:**

Plays a minor role in the regulation of circulation. Its important function relates to its control of the heart rate (stimulation of *vagus nerves* results in a decrease in heart rate and contractility).

Anatomy of the Sympathetic Nervous Control of the Circulation

Nerves leave the spinal cord **through thoracic and lumbar spinal nerves, pass into the sympathetic chain, and then into the circulation through:**

- Specific sympathetic nerves innervate the vasculature of the internal viscera and the heart.
- The spinal nerves innervate mainly the vasculature of the peripheral metarterioles.



The Sympathetic Vasoconstrictor System and its Control by the Central Nervous System

❖ The distribution of vasoconstrictor fibers varies:

- Greater distribution in the kidneys, gut, spleen, and the skin.

- Less/potent in the skeletal muscle and brain.

❖ Vasomotor center:

- Located in the brain (reticular substance of the medulla and lower pons).

- ^①transmits impulses through the spinal cord and hence ^②sympathetic vasoconstrictor fibers to almost all blood vessels of the body for ^③blood pressure control. ^④

Areas of the Vasomotor Center:

1. Vasoconstrictor Area:

Neurons secrete norepinephrine which stimulates the vasoconstrictor neurons of the sympathetic nervous system.

2. Vasodilator Area:

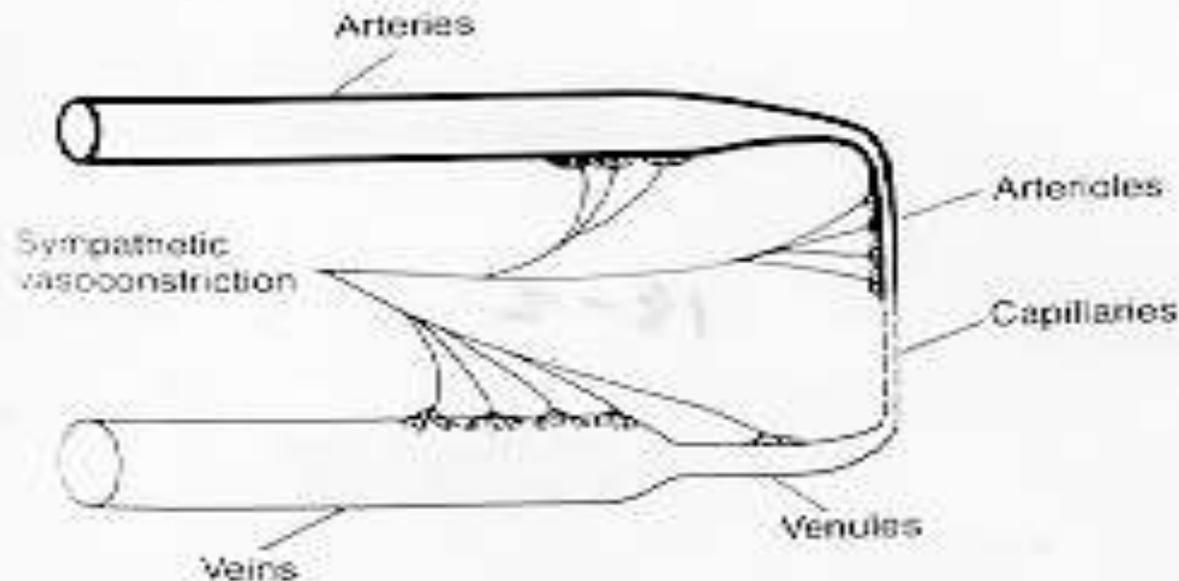
Fibers from neurons in this area project upward to the vasoconstrictor area and inhibit vasoconstrictor activity.

تحت الأعلى

3. Sensory Area:

Receives sensory nerve signals from the vagus and glossopharyngeal nerves and the output signals from this sensory area then help to control the activities of both the vasoconstrictor and vasodilator areas, thus providing "reflex" control of many circulatory functions (e.g., baroreceptor reflex for blood pressure control).

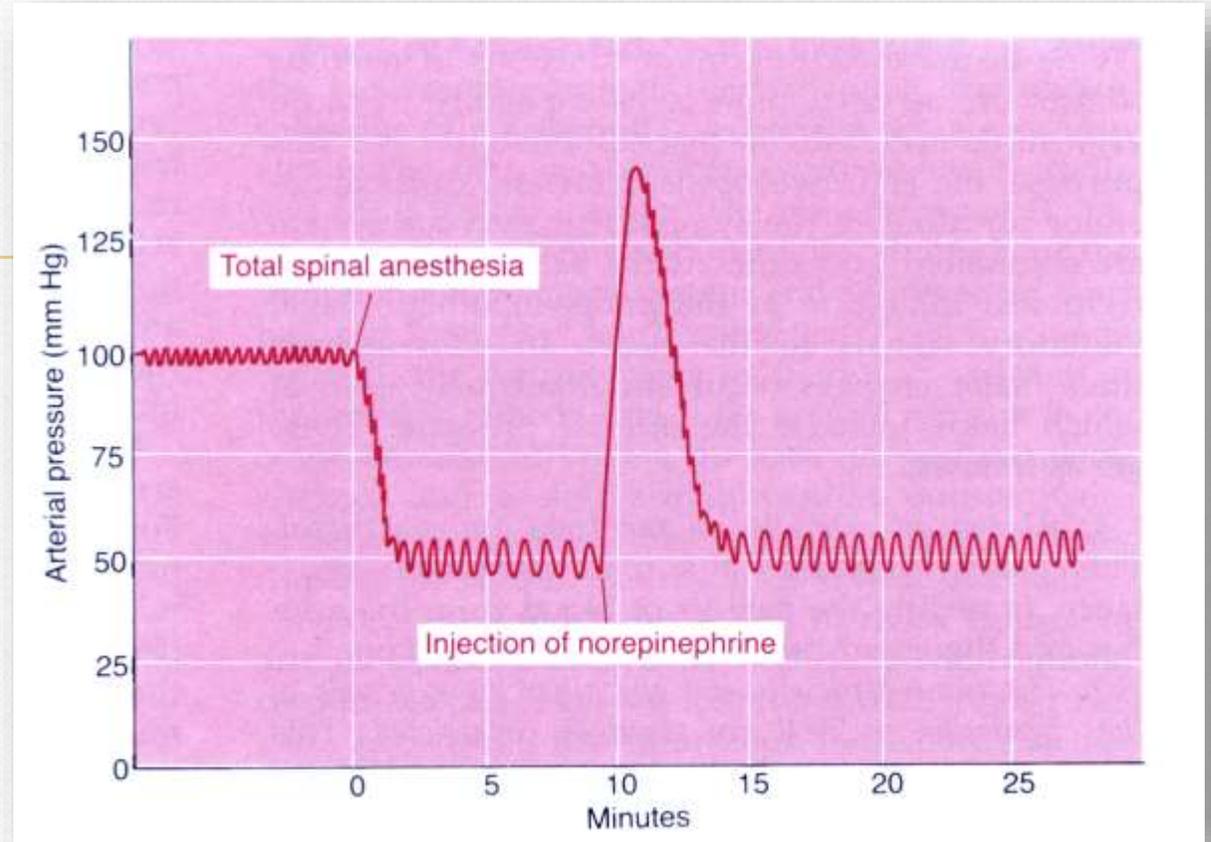
All vessels ^① except capillaries, ^② pre-capillary sphincters, and ^③ most metarterioles are innervated. Small arteries and arterioles when stimulated will increase resistance to flow and decrease the flow of blood to the tissues. Innervation of large vessels (e.g., veins) decreases the volume of the veins and alters the volume of the venous side of the circulation, so the volume is transferred to the arterial side. (Again, “reservoir function”)



Sympathetic carry mostly vasoconstrictor fibers and a lot are present in the kidney, gut, spleen, skin, and *less are in* the skeletal muscle and brain.

- **Sympathetic Vasoconstrictor Tone**

Under normal conditions, the vasoconstrictor area transmits signals continuously (0.5-2 impulses/sec). These impulses maintain a partial state of contraction in vascular smooth muscle (vasomotor tone).



Effect of total spinal anesthesia on arterial blood pressure decrease
کدیر

- **Control of Heart Activity by the Vasomotor Center:**

Sympathetic nerve fibers to the heart increase heart rate and contractility when stimulated, whereas impulses from the vagus nerve (parasympathetic nerve fibers) decrease heart rate.

- **Control of Heart Activity by Higher Nervous Centers:**

Reticular substance in medullae

Hypothalamus can either excite or inhibit the vasomotor center

Cerebral Cortex

- **The Adrenal Medullae:**

Excitation of sympathetic fibers to the adrenal medullae cause the secretion of epinephrine and norepinephrine into the circulation.

Role of the Nervous System for Rapid Control of Arterial Pressure

The entire vasoconstrictor and cardioaccelerator functions of the SNS are stimulated as a unit. At the same time, there is reciprocal inhibition of the normal parasympathetic vagal inhibitory signals. As a result, 3 changes occur, each of which contributes to increasing arterial blood pressure: ① arteriolar constriction and large vessel constriction (especially veins) increases circulating blood volume and venous return, ② increased cardiac contractility and stroke volume, and ③ increase in arterial pressure. Direct stimulation of the heart (HR increases up to 3-fold and contractility is increased).

These effects can double arterial pressure within 10-15 sec. Sudden inhibition can decrease pressure by half within 10-40 sec.

الضغط ليهتف
عنا

↳ for sympathetic nervous system

Increased Arterial Pressure during Exercise:

During exercise, active muscles require greatly increased blood flow. by 2-

- ① • Local vasodilatory mechanisms.
- ② • Elevation of arterial blood pressure (an increase of 30-40% can increase blood flow by 2-fold).

* Exercise is initiated by activation of the motor areas of nervous system. At the same time these areas are activated to initiate exercise, the reticular activating system of the brain stem is also activated (incl. stimulation of the vasoconstrictor and cardioaccelerator areas of the vasomotor center). These raise arterial pressure instantaneously to keep pace with the increase in muscle activity. This occurs with many other types of stress (e.g., fight or flight reaction).

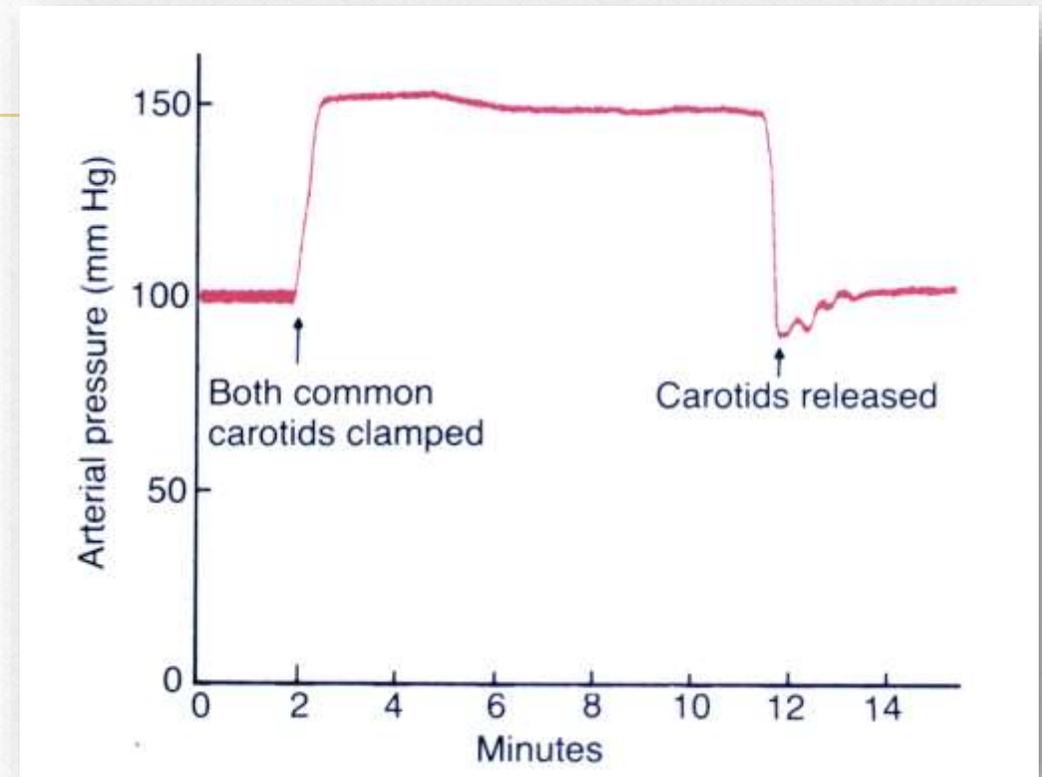
The Baroreceptor Reflex

Once signals have entered the medulla secondary signals **inhibit the vasoconstrictor center** and **excite the vagal center**. **This results** in ① vasodilation of the veins and arterioles throughout the systemic circulation and ② decreased heart rate and contractility.

Therefore, **stimulation of the baroreceptor reflex** reduces blood pressure through a decrease in peripheral resistance and a decrease in cardiac output.

opposite effect.

Low pressure has the
↳ vasodilation



Typical Carotid Sinus Reflex on Arterial Pressure Caused by Clamping Both Common Carotids

change in AP

The Baroreceptor Reflex

Function during changes in body posture:

تغیر و متغیرتگی جسم

When going from **laying down to standing up** there is a **decrease in a stretch of the baroreceptors** which **respond immediately to increase pressure by** ^①removal of inhibition on the vasoconstrictor center.

↳ constriction peripherally

Mechanisms for Maintaining Normal Arterial Pressure

- **Arterial Baroreceptor Control System:**

Receptor: Spray-type nerve endings

Location: ① in the wall of large arterial vessels (internal carotid artery and the wall of aortic arch; (baroreceptor, pressoreceptors) ②

Stimulus: Stretch

Normally, the **carotid baroreceptors** are not stimulated by pressures between 0-60 mmHg. **Above 60 mmHg they respond progressively more** and more rapidly and **reach a maximum at about 180 mmHg.** The **aortic baroreceptors behave similarly but operate at pressures 30 mmHg higher than the carotid.** Respond very rapidly to changes in pressure, with the **rate of impulse firing increasing during systole** and **decreasing during diastole.**

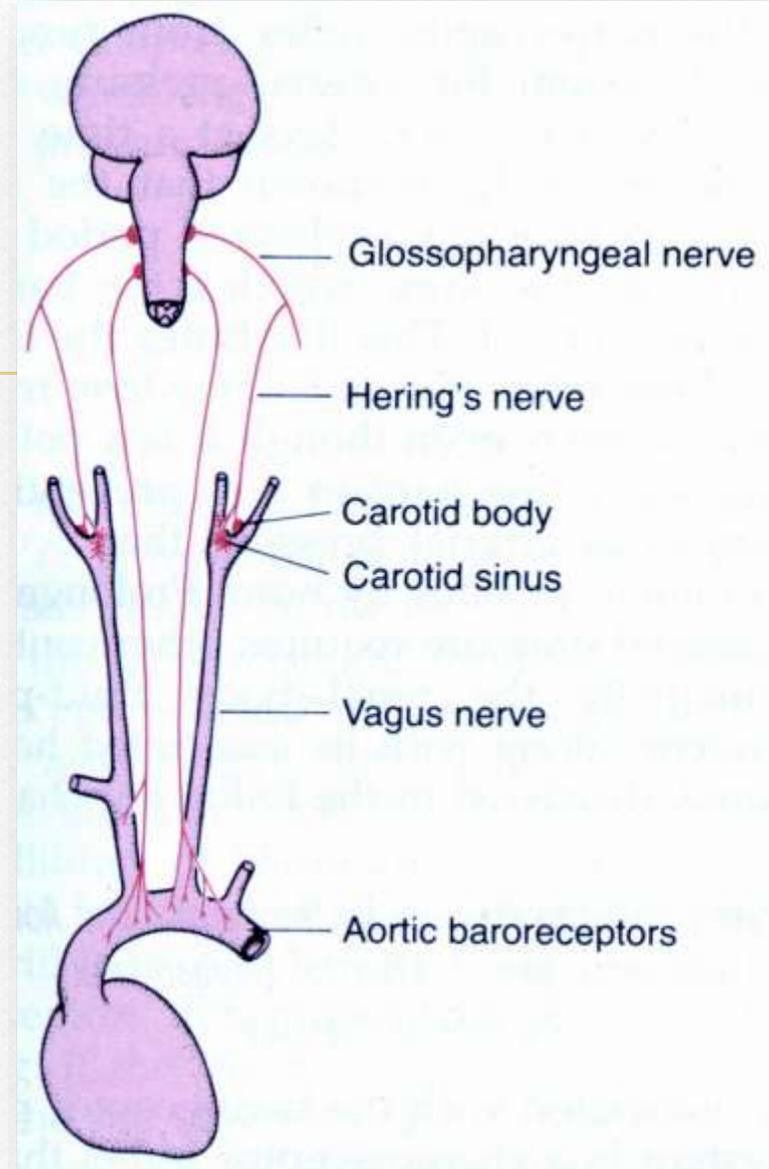
90 mmHg

Arterial Baroreceptor Control System:

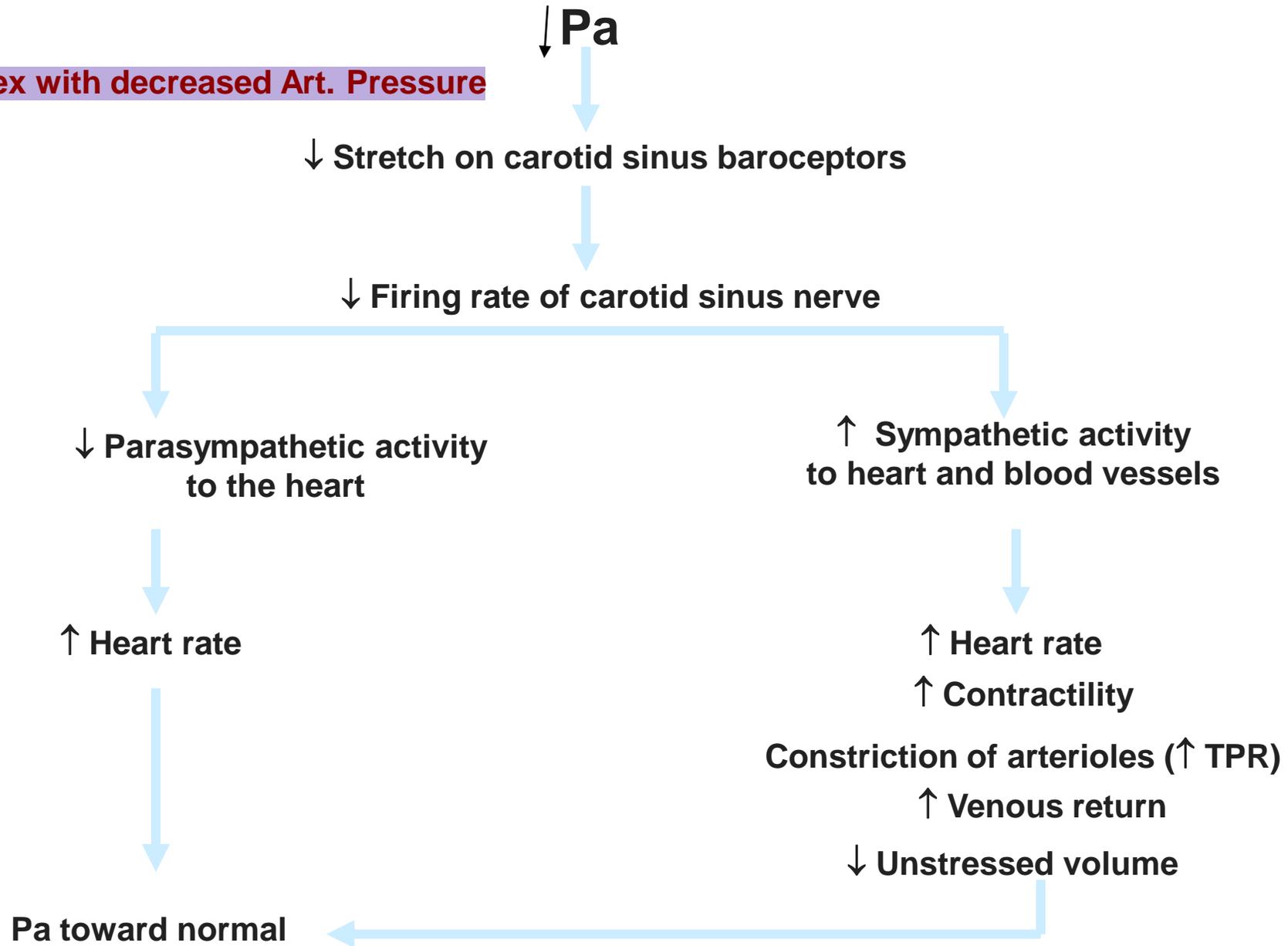
□ Pathway: Internal carotid transmits impulses through Herring's nerve to the glossopharyngeal nerve and hence to the tractus solitarius in the medulla.

□ Signals from the aortic arch are transmitted through the vagus nerves also into this area of the medulla.

↳ tractus solitarius



Baroreceptor Reflex with decreased Art. Pressure



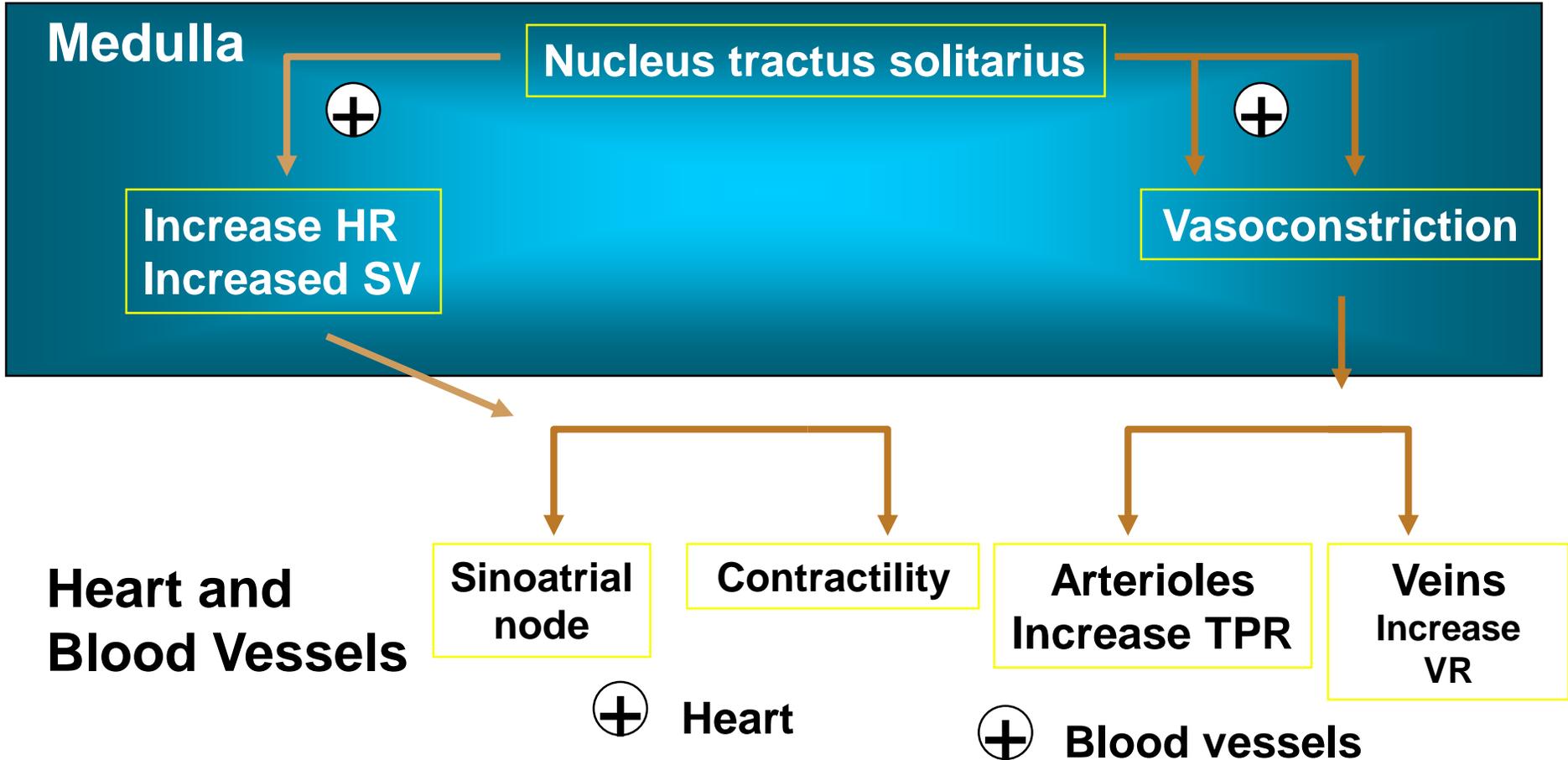
**Baroreceptors
w/ increased P**

Carotid sinus baroreceptors

Aortic arch baroreceptors

Carotid sinus nerve (+)
glossopharyngeal nerve

(+) Vagus nerve



• Carotid and Aortic Chemoreceptors:

- Closely associated with the baroreceptors.
 - **Stimulus:** lack of O_2 , excess of CO_2 , or excess of H^+ \rightarrow decrease or increase to pH
 - **Receptor:** located in several small organs (1-2 mm in size), carotid, and aortic bodies.
- Each body has close contact with the arterial blood. Low pressure stimulates the chemoreceptors because diminished blood flow reduces oxygen and increases carbon dioxide and hydrogen ions. These receptors are not strongly stimulated until systolic pressure falls below 80 mmHg.
- **Pathway:** same as Baroreceptor.
 - carotid via glossopharyngeal nerve
 - aortic via Vagus nerve
 - **The Reflex:** The ^① signals transmitted from the chemoreceptors into the vasomotor center ^② EXCITE the vasomotor center and increase arterial pressure. ^③

Arterial Blood Pressure Regulation

● Long-Term Control

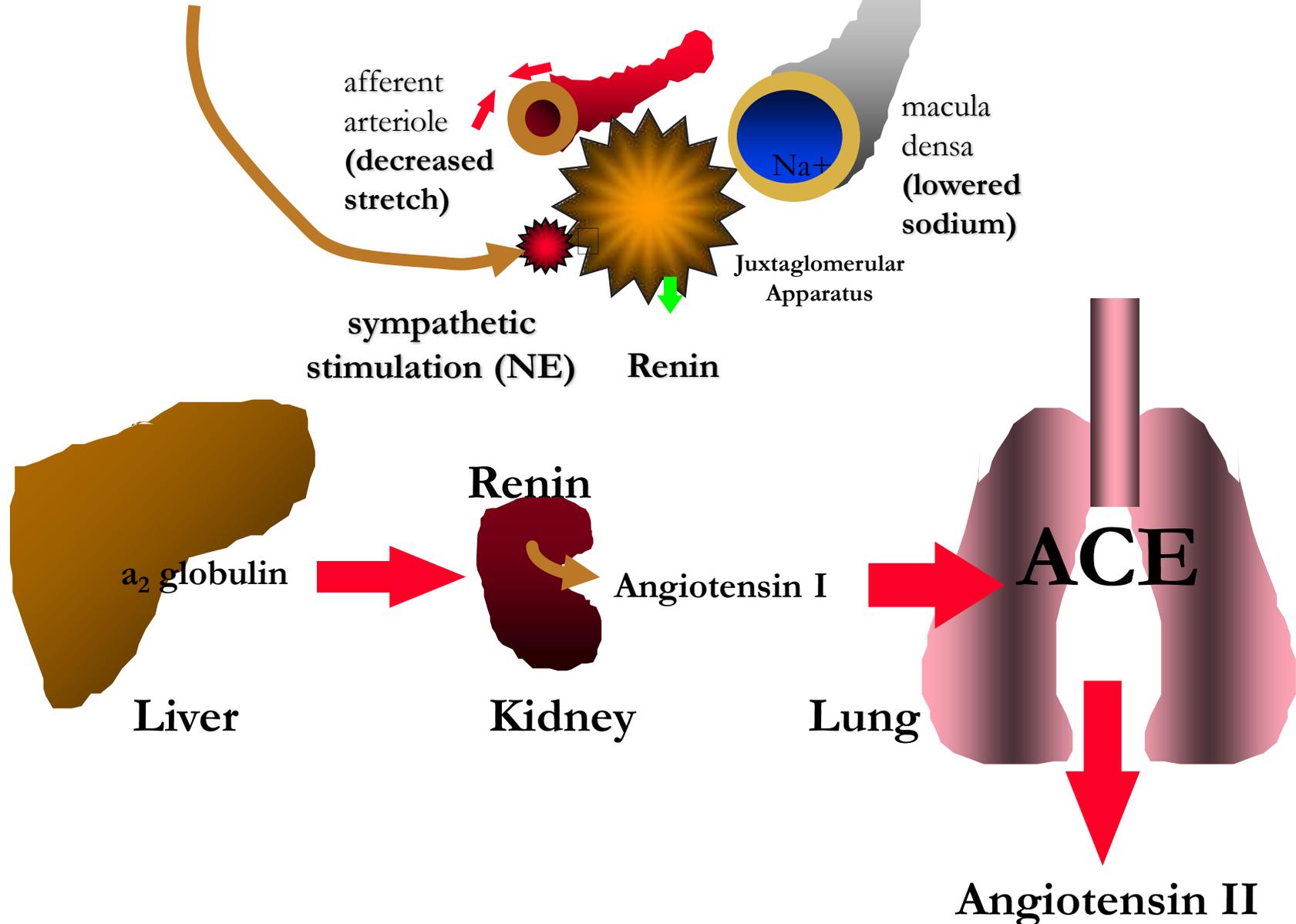
- It is done through the Renin-Angiotensin-Aldosterone System [RAS].
- When cardiac output decreases, it decreases CO in all the body including the kidneys.
- When the globular filtration rate or the renal perfusion decreases, the kidneys will respond to this by increasing renin production.

Baroreceptors in long term AP regulation

However, if BP is maintained for 1 to 2 days, **the baroreceptors will reset at this 'new' level of 160 mmHg.** Therefore, **baroreceptors are not as important, in long-term regulation.**

← يعني تتكيف مع الضغط الجديد لو زاد الارتفاع عن يومين

Sympathetic



Renin

- Renin is a protease that cleaves **angiotensinogen to angiotensin I**. Then **angiotensin 1 is converted to angiotensin 2** by the **angiotensin-converting enzymes (ACE)** in the lungs. → by renin
- Renin is secreted by the juxtaglomerular apparatus in response to a ^① reflexive sympathetic activity or ^② beta receptor stimulation, ^③ decreased central volume of blood or ^④ decreased plasma Na⁺.

Angiotensin II

- **One of the most potent vasoconstrictors known.**
- Octapeptide (8 amino acids).
- Constricts principally arteriolar smooth muscle to increase resistance. → constriction peripherally
- Stimulates the vasomotor center of the brain.
- **Stimulates the release of Aldosterone (steroid hormone) by the adrenal medulla.**
- Inactivated by angiotensinase enzyme.

Effect of Angiotensin to Cause Retention of Salt and Water

● **Direct Renal Effect** (can decrease urinary output 4-6 fold):

- ✓ Enhances the reabsorption of Na ions from the proximal tubule (Na reabsorption = water retention = increase in volume... vasoconstriction). → afferent and efferent arteriols in kidney

● **Stimulation of Aldosterone Secretion** from the adrenal glands

- ✓ ^① Increase in salt reabsorption by the kidney tubules, ^② increase in extracellular fluid sodium, ^③ and water retention.

● **Blocks bradykinin**, which is a local mediator of vasodilation:

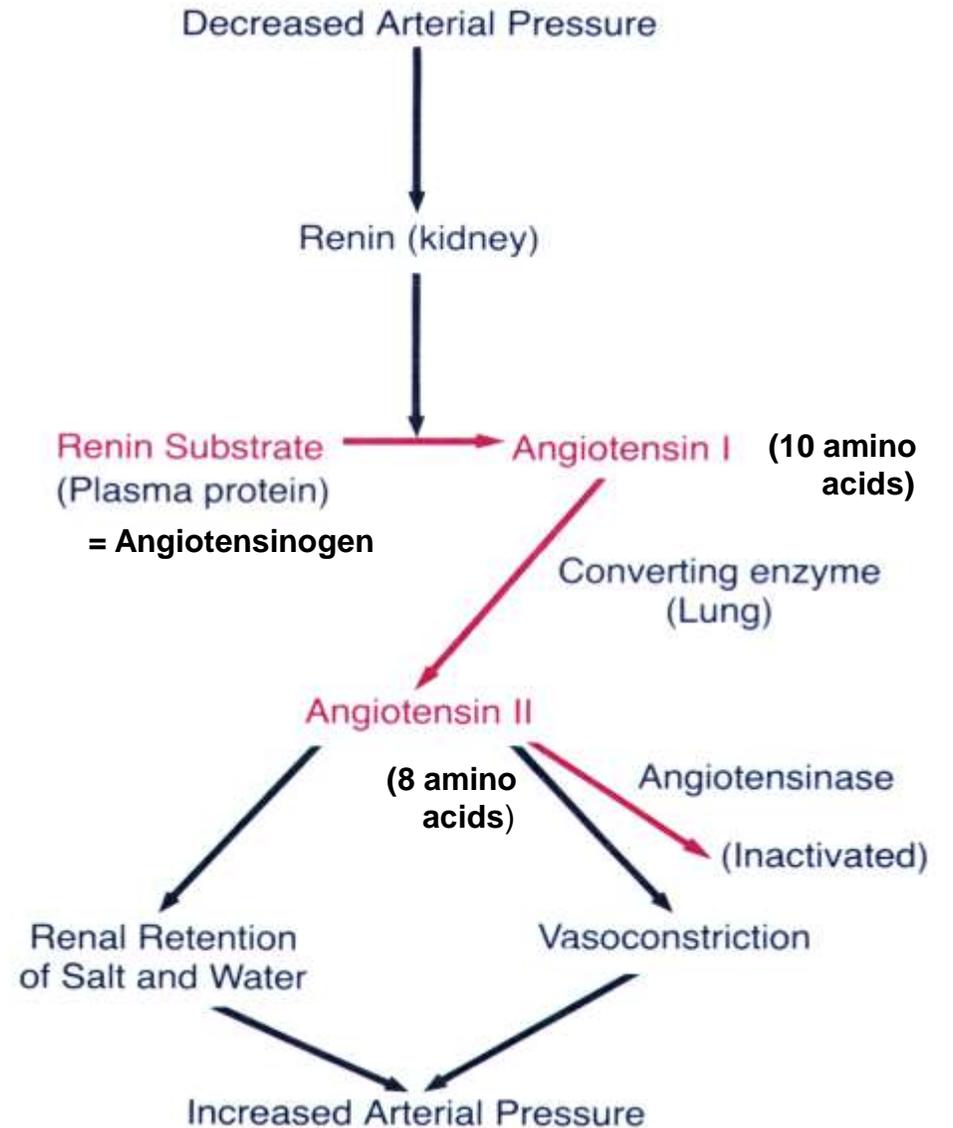
- ✓ So, blocking it causes vasoconstriction.

Aldosterone

- *Steroid hormone* secreted by the adrenal medulla in response to angiotensin II formation.
- Increases blood volume by promoting the reabsorption of sodium and water.
- Takes hours to be effective in raising blood pressure and volume because it requires protein synthesis.

← why? ←

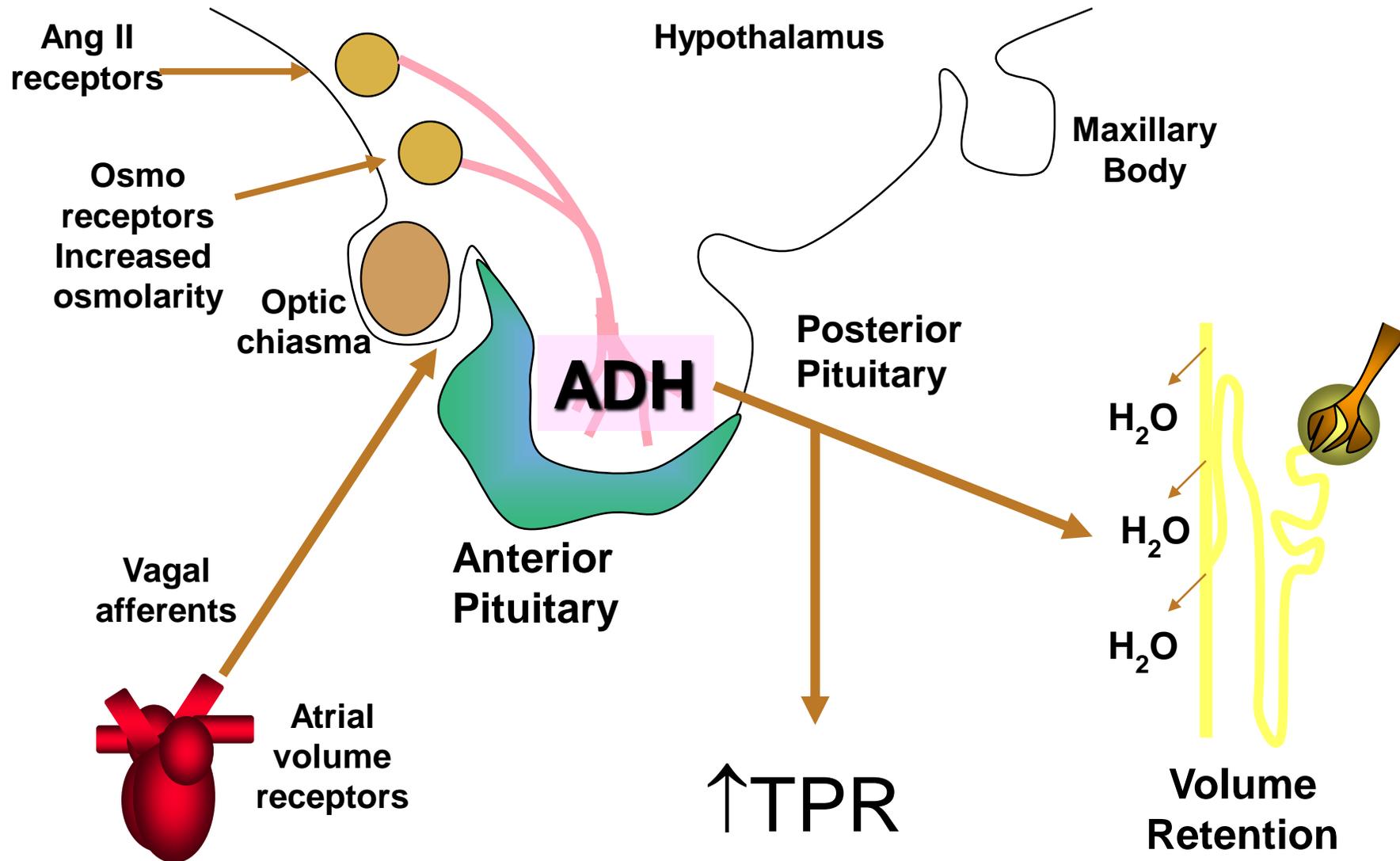
The Role of the Renin-Angiotensin System in Regulating Arterial Pressure



Antidiuretic Hormone (ADH, Vasopressin)

1. ADH is an **oligopeptide** that is synthesized in the hypothalamus and stored in the posterior pituitary before it is released into the bloodstream.
2. ADH release is **stimulated by osmoreceptors** in the anterior pituitary, triggers ADH and thirst (**2% osmolarity**) change is enough.
3. These hormones ^{Function?} prevent diuresis (**loss of water in urine**) in case of dehydration and hypovolemia.

ADH (Vasopressin) and Blood Volume



ADH (Vasopressin) receptors

- **V₁ receptors** are in vascular smooth muscle.
- **V₂ receptors** are in the principal cells of the renal collecting duct.
- **V₂ receptors** are involved in water reabsorption in the collecting duct and in the maintenance of body osmolarity.

The Renal-Body Fluid System for Long Term Control of Arterial Pressure:

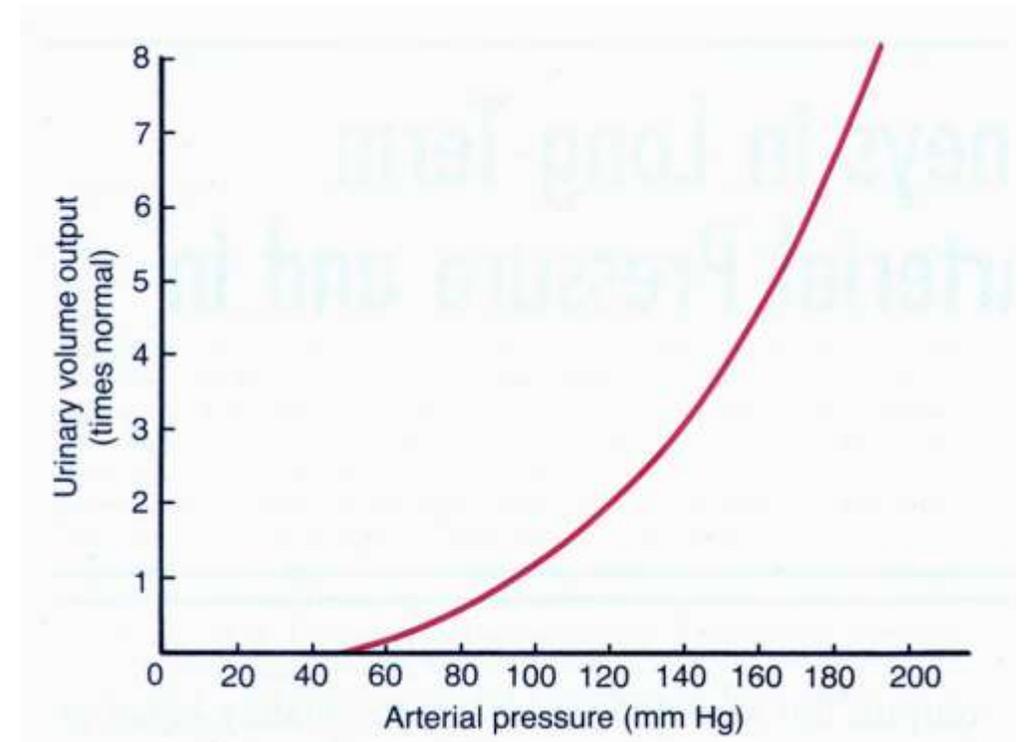
When the body contains too much extracellular fluid, arterial pressure rises. This increase in pressure causes the kidneys to excrete the excess fluid until pressure returns to normal (pressure diuresis).

Quantification of pressure diuresis using renal function curves

As pressure increases urinary volume, there is an equal effect on the urinary output of salt (pressure natriuresis),

i.e. the relationship is similar for sodium excretion

Typical Renal Output Curve
Measured in an Isolated
Perfused Kidney

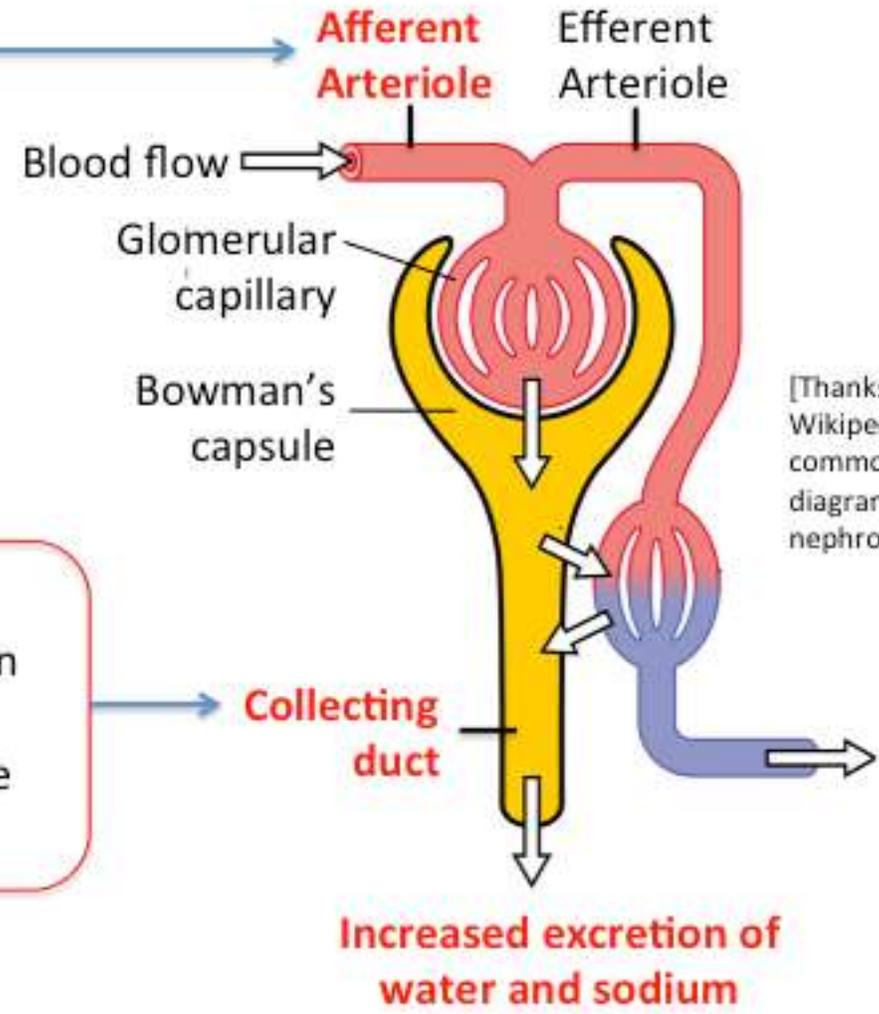


Atrial Natriuretic Peptide (ANP)

يعكس الكلى فوق

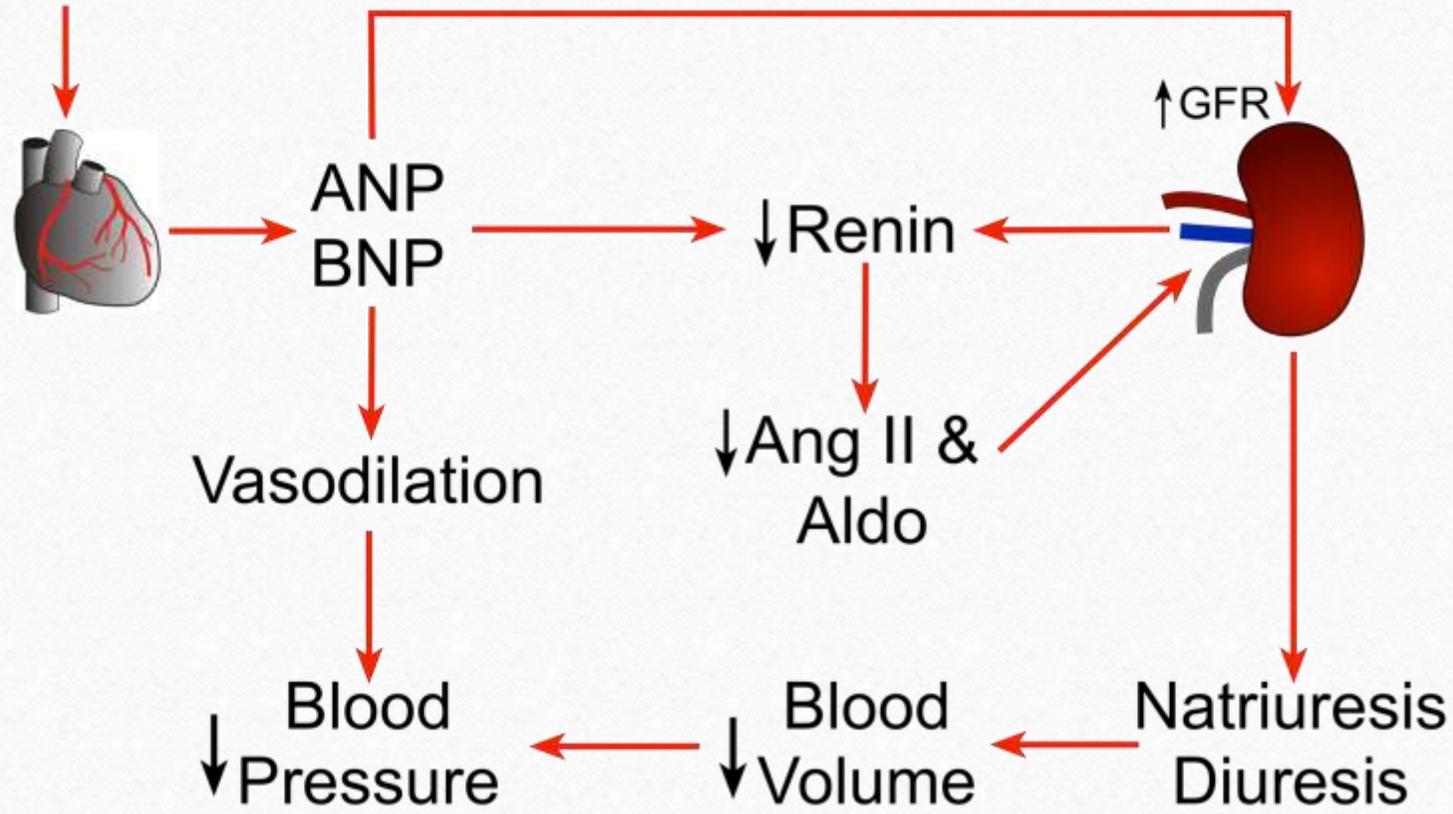
ANP dilates the afferent arteriole leading to increased blood flow and filtration -> diuresis

ANP suppresses reabsorption of Na⁺ in collecting duct and other segments of the nephron -> naturesis



[Thanks to Wikipedia commons for diagram of nephron]

Cardiac distension
Sympathetic stimulation
Angiotensin II



□ What Can I Do?

- High blood pressure is a lifelong disease.
- Blood pressure can be controlled not cured. ^{2x5 ←}
- Controlling blood pressure will reduce the risk of stroke, heart attack, heart failure, and kidney disease.

□ What Can I Do?

- Loose weight if your overweight.
- Get regular physical activity.
- Avoid excessive alcohol.
- Stop smoking.
- Manage your stress.
لعلاج
- Decrease salt intake.
- Eat for heart health.
- Discuss the use of oral contraceptives with your doctor.
ناقش
- Discuss the use of some medications with your doctor.

• ^{بلاغ} Commandments for Blood Pressure Control:

-Know your blood pressure

- Have it checked regularly

-Know what your weight should be

- Keep it at that level or below

-Don't use excessive salt in cooking or at meals

- Avoid salty foods

-Eat a low-fat diet

- According to AHA regulations

-Don't smoke cigarettes

- Or use ^{تباغ} tobacco products

-Take your medicine exactly as ^{موصوف} prescribed

- Don't ^{توقف} run out of pills even for a single day

-Keep your ^{التواعد} appointments with the doctor

-Follow your doctor's advice about exercise

□ Main medication for HTN

➤ Diuretics:

- Rid the body of excess fluids and salt

➤ Beta-blockers: or alpha blocker

- Reduce the heart rate and the work of the heart

➤ Calcium antagonists:

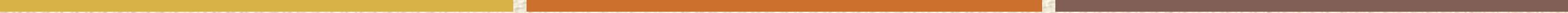
- Reduce heart rate and relax blood vessels

➤ Angiotensin II receptor blockers (ACE):

- Interfere with the bodies production of angiotensin, a chemical that causes the arteries to constrict (narrow)

➤ Vasodilators:

- Cause the muscle in the wall of the blood vessels to relax, allowing the vessel to dilate (widen).



Thank You

