

Blood pressure regulators:

1- Short term regulation:nervous system

♦Occurs Within secondsof the change in BP (they are short term because after a while (2-3 days) they adapt/reset the new blood pressure which becomes the setting point pressure that's why we need the other regulators).

A. Baroreceptors or pressoreceptos

B. Carotid and Aortic Baroreceptors (low pressure)

2- intermediate / long-term regulation :

A- adrenal medulla system (hormonal / chemicals: can go anywhere in the body and cause vasoconstriction unlike the sympathetic which affects only what it supplies, that's why we need these hormones)

♦Needs 10 minutes to work (to form these chemicals)

♦Epinephrine and norepinephrine- adrenal medulla system

Synthesized from Tyrosine → 80%epinephrine + 20% NE

♦ Mechanism : vasoconstriction

Remember : capillaries don't have smooth muscles

B- ADH (vasopressin) system:

♦Needs 30 minutes to work

♦Mechanism: 1- **water**retention from the last part of the nephron which increases blood volume, venous return EDV, stroke volume and cardiac output.

2-Vasoconstriction which increases the total peripheral resistance to maintain the MAP

If the previous system didn't work and MAP is still dropping, another system starts working which is:

C- Renin-Angiotensin-Aldosterone system:

♦Needs 1 hour to work

♦Intermediate / long term regulator

♦The most important long term regulator

Mechanism: vasoconstriction and water retention

♦Important in maintaining a normal AP during changes in Na intake

ACE: angiotensin
converting enzyme ♦found
mainly in the lungs

↓MAP → ↓ afferent arteriolar pressure of the nephron → **renin** secretion from the afferent arteriolar cells → renin converts **Angiotensinogen** (14 a.a) → **Angiotensin I** (10 a.a peptide) circulates mainly in the endothelial cells of the lung → ACE → **Angiotensin II** (8 a.a peptide)

angiotensin II functions :

1-Most potent vasoconstrictor in the body (increases TPR to maintain MAP)

2-Positive inotropic agent (increases contractility)

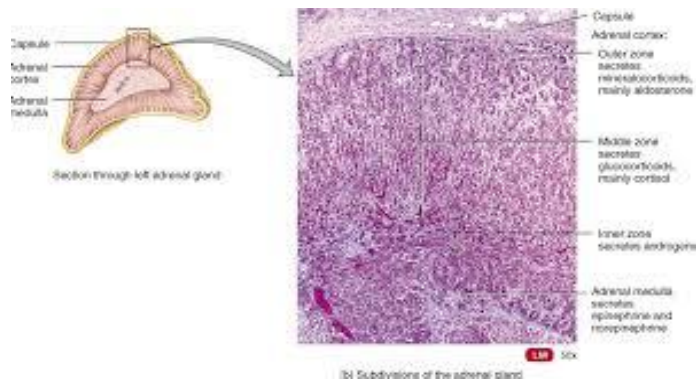
3-Affects the thirst center

Note : The thirst center is affected by : 1) renin-angiotensin system

2) ADH

3) Changes in the osmolarity (due to increased Na intake for example) causes thirst by ADH secretion

4-Stimulates zona glomerulosa of the adrenal cortex to synthesize and secrete Aldosterone (Stimulates kidneys to reabsorb sodium from the distal parts of nephron - Water follows the sodium osmotically → ↑ extracellular fluid volume → ↑ blood volume → ↑ MSFP → ↑ venous return → ↑ EDV → ↑ SV → ↑ CO → ↑ MAP)



Adrenal cortex (from outside to inside):

- Zona glomerulosa
- Zona fasciculata
- Zona reticularis

Summary :

- ♦ **Renin** : Renin is synthesized and stored in modified smooth muscle cells (juxtaglomerular cells) in afferent arterioles of the kidney (in juxtaglomerular apparatus in juxtaglomerular nephrons)
- ♦ **Angiotensin** : circulates in the endothelial cells of the lungs
- ♦ **Aldosterone** : Zona glomerulosa

Factors that increase blood volume:

- 1) Na/water intake (major factor)
- 2) shifting of fluid from the extravascular compartment

D- Atrial Natriuretic peptide (ANP) – works in contrast with the previous systems:-

♦28 a.a peptide released mainly from the right atrium(can be secreted from the left) in response to stretch/ increased volume of the rt. atrium (The last 5 amino acids are the most active ones (penta-peptide)

Mechanism: secreted when the RAP increases It causes increase in GFR(glomerular filtration rate) so increase Na⁺ and water excretion

ANP → ↑GFR → ↑Na/water excretion → ↓blood volume → ↓MSFP → ↓venous return → ↓EDV → ↓CO → ↓MAP

Factors Which Decrease Renal Excretory Function and Increase Blood Pressure:

- Angiotensin II (vasoconstrictor)
- Aldosterone (Na/water retention)
- Sympathetic nervous activity (short term regulation)
- Endothelin (local vasoconstrictor secreted from endothelial cells)
- NO (Local vasodilator-has important function in the kidney)
- Dopamine (vasodilator)
- Atrial natriuretic peptide

The long term regulation pathways are mainly affected by the extracellular fluid volume mainly, because even though an increase in the resistance can increase MAP, after a while the C.O. will decrease (compensation) bringing MAP to its previous level, that's why changes in resistance are not important for long term regulation, so, the main factor here is the ECF volume.

♦That's why we use vasodilators for acute treatment because after a while the body will adapt and it won't be effective anymore (if someone comes to the emergency room with 220/120 pressure the first thing we do would be giving him vasodilators, but this is not enough to send home because after a week he will come back with high pressure again so, we have to use a long term treatment).

♦for long term treatment we need to work on body fluids and renal system :

1-Diuretics

2-Angiotensin converting enzyme inhibitor (captopril)

3-AngiotensinII receptorblocker (sartans)

Example on how the body regulates blood pressure :

If a patient received an infusion of normal saline → ↑blood volume → ↑MSFP → ↑venous return → ↑EDV → ↑CO → ↑MAP.

↑MAP → ↑Renal output (BP regulators) → ↓blood volume → ↓MAP

Atrial and Pulmonary Artery Reflexes:

Low pressure receptors in atria and pulmonary arteries minimize arterial pressure changes in response to changes in blood volume.

Increase in blood volume activates low pressure receptors which in turn lower arterial pressure.

1) Atrio-hypothalamic reflex : decreases Anti Diuretic Hormone (ADH) -Vasopressin-in case of high BP.

2) Atrio-renal reflex : increases the Glomerular Filtration Rate (GFR) and decreases Na reabsorption in case of high BP.

↑blood volume → ↑atrial stretch → ↓renal sympathetic activity and ↑ ANP → ↑Na / water excretion

Activation of low pressure receptors enhances excretion of Na⁺ and water by:

- Decreasing rate of antidiuretic hormone (by atrio-hypothalamic reflex)
- Increasing glomerular filtration rate (by atrio-renal reflex)
- Decreasing Na⁺ reabsorption (by atrio-renal reflex)

Bainbridge reflex:

Prevents damming of blood in veins, atria and pulmonary circulation.

Atrial stretch → stimulates vasomotor centre → increase in heart rate and contractility

Pressure Natriuresis and Diuresis:

Any acute increase in the body fluid volume (IV fluid for example) → ↑MAP → but there is also an ↑ in urine formation by kidneys, bringing MAP back to its normal values.

But chronic increase in blood volume will keep the MAP high.

pressure diuresis : The effect of pressure to increase water excretion

pressure natriuresis: The effect of pressure to increase Na excretion

Pressure diuresis curve (renal output curve):

Any increase in the MAP will increase the urinary output (which normally equals salt and water intake) to get ECF volume back to normal thus bringing MAP back to normal.

MAP is maintained by two things: 1- the intake 2-output

♦This curve is Normal MAP: normal level of angiotensin II

1- high levels of angiotensin II (due to a kidney disease) → the curve will be shifted to the right

→MAP is high

Treatment: 1) angiotensin converting enzyme inhibitor and angiotensin II receptor blocker

2) Diuretics and decrease Na intake

2-low levels of angiotensin II → The curve will be shifted to the left

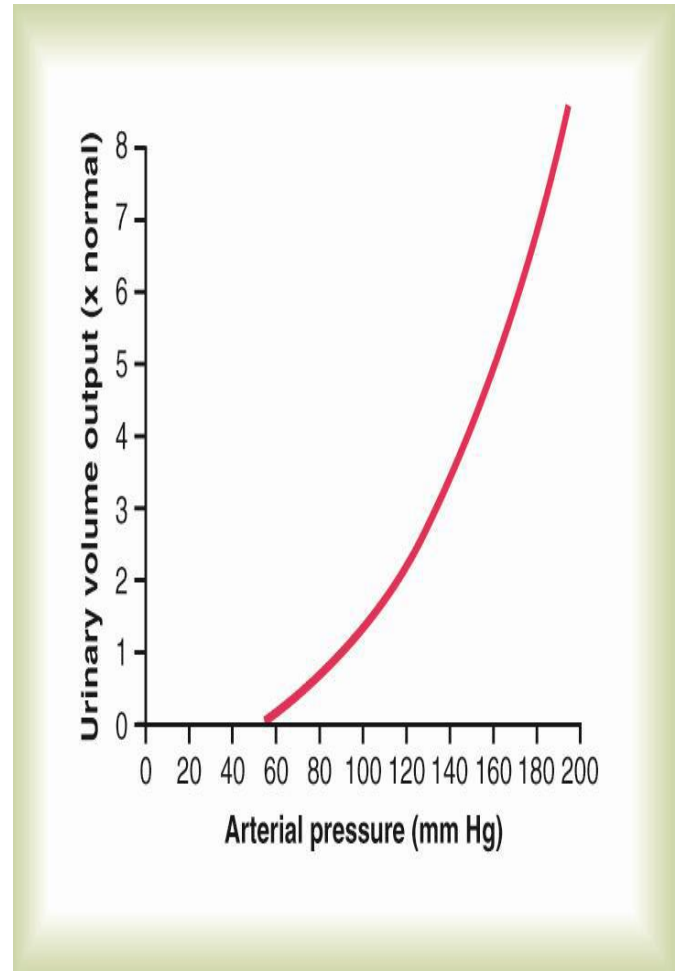
→MAP is low

So, the curve can be shifted to the left or right by increasing or decreasing angiotensin II even though the intake is constant.

Renal body fluid feedback system has an infinite gain

Gain = correction/error

Note: The curve is not affected by vasodilators because they work in acute manner neither it is affected by eating a salty meal.



The blue line represents the normal MAP (100 mmHg): normal renal function and normal intake.

Elevated pressure (150 mmHg) causes:

*1st figure: renal disease + normal intake

Note: **Renal diseases** are the most common cause of secondary hypertension

*2nd figure: Normal kidney + increased fluid intake on long term.

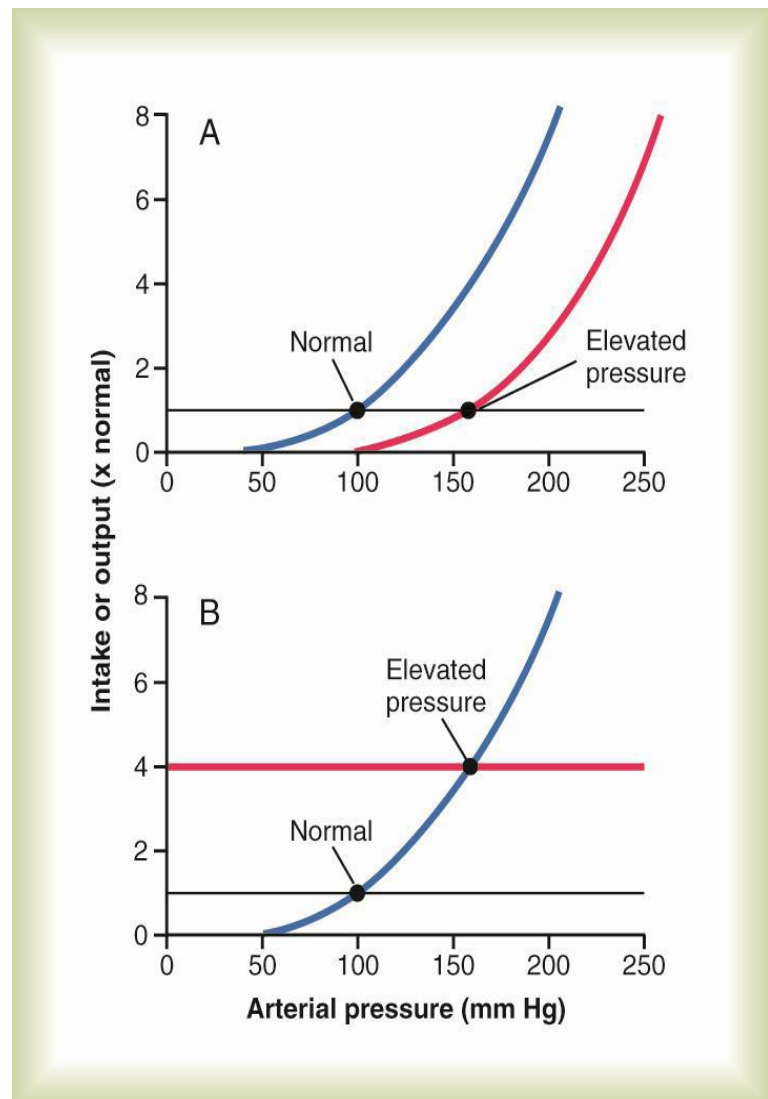
Those are the two factors (kidney and intake) that affect MAP on the long term.

Equilibrium point is where intake and output curves intersect.

Remember: angiotensin II increases blood volume by increasing ADH.

*ECF volume is mainly controlled by Na intake because it is the main ECF cation and it is responsible for increasing osmolarity which increases ADH, increasing ECF volume.

*the intake of water alone will have an acute effect only, so the intake should include Na.



This curve is just to tell you that changing the TPR for a long period of time does not change the MAP, because this period of time will allow C.O to compensate.

→ Because the change in the TPR will be modified by changing the cardiac output so the MAP stays constant

Remember: $MAP = TPR \times CO$

↑TPR → ↓CO

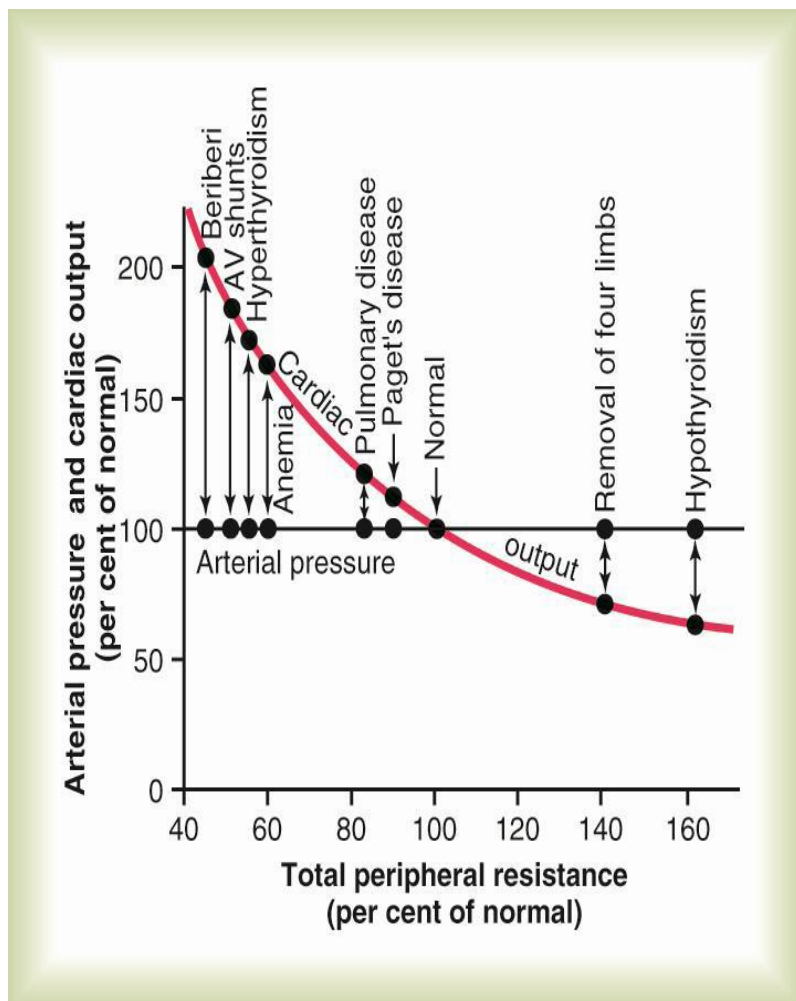
Factors affecting TPR:

- 1-arteriolar radius
- 2-blood viscosity

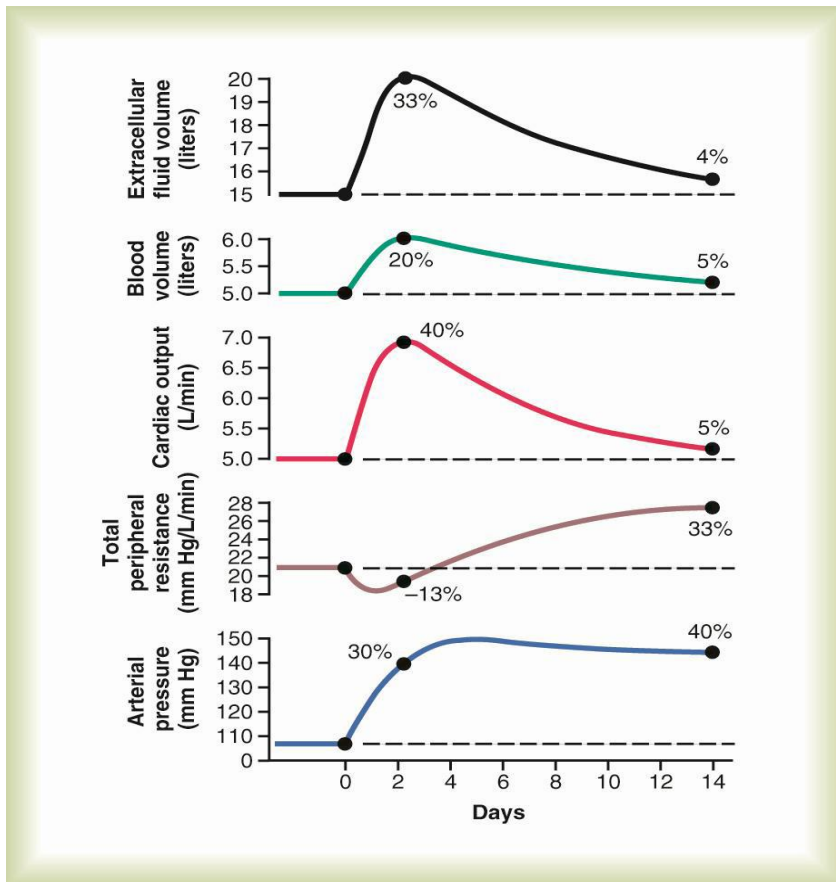
Diseases that decrease TPR:

- 1)hyperthyroidism
- 2)pulmonary disease
- 3)beriberi disease

Vasodilators /vasoconstrictors work In acute manner



Volume loading hypertension:



↑Extracellular volume → ↑blood volume → ↑MSFP → ↑VR → ↑EDV → ↑CO → ↓TPR → ↑MAP

Then it gets back to normal because of the increase in urine formation

Types of shock:

1) hypovolemic shock

Causes :

1- Hemorrhage

2- Dehydration

3- Diarrhea

A- First stage (non-progressive/ reversible shock)

B- Second stage (progressive) → tissue damage

C- Third stage (irreversible shock) MAP drops below 60 mmHg → damage to the vital organs (heart and brain) → Death

2)Anaphylactic shock : hypersensitivity /Allergy

↑histamine → ↑permeability of capillaries → ↓blood volume → ↓MAP

3)septic shock :

The most common cause of sepsis is **gram -ve bacteria** (E-coli)

→Because it secretes edotoxins → vasodilation → ↓TPR → hypotension

In spite of the increase in CO (due to increased heart rate), the cytokines produced due to the inflammatory reaction will cause a massive vasodilation leading to a decreased TPR, as a result, MAP will decrease (hypotension), leading to a shock.

→That’s why it’s called **high CO shock**(C.O may reach 10L/min but still not enough to supply the need of the tissues).

*note: shock: the tissue doesn’t receive its need of blood. (The need can be high or low, if high and didn’t get its need → shock)

CNS Ischemic Response:

♦systemic response due to cerebral ischemia when MAP falls below 60mmHg
greatest activation occurs at pressures of **15-20mmHg**.

MAP below 60 → brain ischemia → extensive sympathetic stimulation to raise the pressure

If it is raised → the patient might survive with some damage to the brain tissue

If it isn't raised → death (irreversible shock)

That’s why we call it the **last chance response**

- One of the most powerful activators of the sympathetic vasoconstrictor system.
- Reduced cerebral blood flow → CO2 buildup → stimulates vasomotor center → increase arterial pressure.
- Prolonged CNS ischemia has a depressant effect on the vasomotor center.
- Cushing reaction is a special type of CNS ischemic response.

↑co2

**Cerebral
Ischemia**

**Vasomotor
Center**

**↑Sympathetic
Activity**

**↑Arterial
Pressure**

Control of blood tissue blood flow

Local control of blood flow:

Each tissue controls its own blood flow in proportion to its needs by vasoconstriction or vasodilation and not by changing MAP because the flow is proportional to the r^4 so it will be affected by it more than MAP, also MAP has a lot of factors that will maintain it, but we can change the radius easily.

If the tissue increases its metabolic rate, this will lead to vasodilation, increase flow to the tissue, increased C.O (because it is the sum of the flow to the tissues).

Tissue needs include:

- 1) delivery of oxygen to tissues
- 2) delivery of nutrients such as glucose, amino acids, etc.
- 3) removal of carbon dioxide, hydrogen and other metabolites from the tissues
- 4) transport various hormones and other substances to different tissues

A) Acute control of local blood flow (autoregulation):

Two major theories for local control of blood flow are:

- 1) The vasodilator theory
- 2) Oxygen demand theory

\uparrow metabolites \rightarrow \downarrow Po₂/ \uparrow Pco₂ \rightarrow vasodilation

B) Long term regulation (as in cases of hyperthyroidism \rightarrow increased metabolic rate)

Angiogenesis: growth of new blood vessels.

Angiogenesis occurs in response to angiogenic factors released from ischemic tissue

so ischemia to the heart will stimulate formation of a collateral circulation

\rightarrow That's why mortality rate for MI is lower for elderly patients because of **preexisting collateral circulation** due to previous ischemia.

Done by: Farah Kittaneh.

Sorry for any mistake.