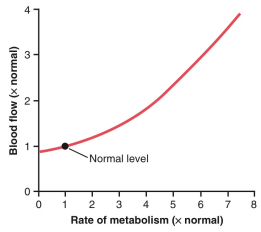
CONTROL OF BLOOD FLOW TO THE TISSUES

** Local control :

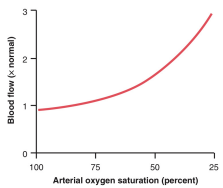
1) Acute control : rapid control

- Increases in Tissue Metabolism Increase Tissue Blood Flow



- Reduced Oxygen Availability Increases Tissue Blood Flow

~ reduction of oxygen …. Vasodilation … increase blood flow



adenosine, carbon dioxide, adenosine phosphate compounds, potassium, histamine and hydrogen ions

* Mechanisms of acute control :

1)VASODILATOR THEORY

Increase in metabolic rate/ decrease in oxygen availability….. increase formation of vasodilators

2)Oxygen (or nutrient) demand theory

Decrease in oxygen …. Relaxation of blood vessels (VASODILATION)

Increase utilization of oxygen….. increase metabolic rate ….. decrease availability of oxygen….. VASODILATION

- Vasomotion

The oxygen concentration is higher than normal level ….. precapillary sphincters would close …. Tissue consume the excess oxygens …. Decrease oxygen concentration … percapillary sphincters would open .

** Nutrients

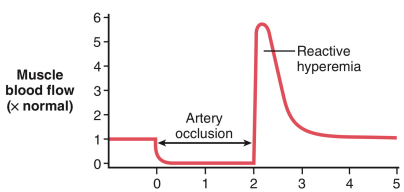
Lack of glucose/ Fatty acid/ amino acids …. VASODILATION

Vitamin deficiency [Vitamin B] …. VASODILATION

3) REACTIVE HYPEREMIA.

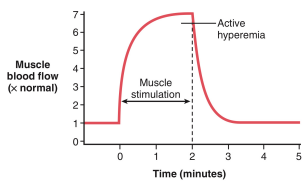
Blood supply is blocked…. Increase formation of vasodilators ….

Blood supply become unblocked …. Increase blood flow



4) ACTIVE HYPEREMIA

Increased metabolic activity…… increase production of vasodilators…. Increase blood flow



2) long- term control

*** Mechanisms of acute control :**

1) VASCULARITY OF TISSUE

Overactive of tissue ….. increase demand of oxygen and Nutrients….. increase in size and number of blood vessels…… ANGIOGENESIS

***Vascular growth factors**

VEGF (vascular endothelial growth factor) , PDGF(platelet derivative growth factor) , FGF(fibroblasts growth factor) and angiogenin

***Antiangiogenic peptides :** block the growth of new blood vessels. For example, angiostatin, and endostatin.

2) COLLATERAL CIRCULATION :

block of blood supply… formation channel around the blockage .. resupply to the tissue

ACUTE + LONG TERM CONTROL

Acute : vascular dilation

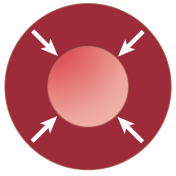
Long term control : formation of new blood vessels

3) REMODELING : change of blood vessels to adapt the new condition

4 forms:

I) inward eutrophic remodeling. (in small blood vessels) …. AUTOREGULATION

زيادة الضغط بتزيد تدفق الدم، عشان أمنع زيادة تدفق الدم بالرغم من زيادة الضغط فـ



The endothelial cells rearrange around the lumen Causing a decrease in diameter

Diameter: Decrease

Cross sectional area : No change ….

T= r* P

الضغط زاد، و نصف قطر تجويف الوعاء قل فـ قوة الشد ثابتة . عشان هيك مساحة سطح الوعاء ما تغير

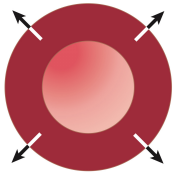
II) hypertrophic remodeling. (in large arteries)

Increase in pressure in large arteries …. Cause expansion of the wall vessel

Increase in pressure… increase in Tension…. Hypertrophy in vascular smooth cells ….formation in extracellular matrix proteins (collagen) … weak vessel (non elastic vessel)

T= r * P

الضغط زاد، نصف القطر ثابت، قوة الشد زادت فـ

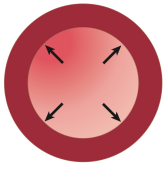


Cross sectional area : increase

Diameter: no change

In renal dialysis: A-V fistula

III) outward remodeling



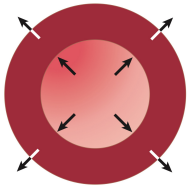
In artery:

Decrease resistance ….. increase the blood flow …. Increase shear stress … increase Diameter

Diameter: increase

Cross sectional area: increase

IV) outward hypertrophic remodeling



In vein :

Diameter : increase

Cross sectional area : increase

3) AUTOREGULATION

Mechanisms :

A) metabolic theory :

Increase arterial pressure… increase blood flow … increase oxygen and nutrients to the tissue….. decline the vasodilators …. VASOCONSTRICTION…. Increases resistance …. return blood flow to normal level * nearly* .

B) Myogenic theory :

I- High pressure:

Increase in pressure….. stretch smooth muscle cells in tunica media … open calcium gated channel …. Influx calcium ions to smooth muscles cause depolarisation… activation sensitive calcium channels.. more influx …. CONTRACTION… decrease diameter… decrease blood flow.

II- Low pressure:

Decrease in pressure…. Less stretch …. Less contraction…. Smooth muscle relaxation… decrease resistance…. Return blood flow to normal

F= P/ R

قل الضغط ، قلت المقاومة … التدفق ثابت

Endothelium derived constricting or relaxing factors:

* relaxing factor:

Nitric oxide (NO)

Activates soluble guanylate cyclases in vascular smooth muscle cells, resulting in relaxation the blood vessels.

Release stimulated by angiotensin II

* constricting factor:

Endothelin

Found in injured blood vessels.

Humoral control of the circulation:

Vasoconstrictors :

1)Epinephrine & Norepinephrine

2)Angiotensin II

Increase TPR …. decrease water & sodium excretion… increase arterial pressure

3) Vasopressin (ADH)

Vasodilators:

1) Bradykinin: increase capillaries permeability (Edema)

2) Histamine: release almost in allergic reaction. Induce edema .

Vascular effects of ions and other chemical factors

1)Potassium: Vasodilator
2) Magnesium : Powerful vasodilator
Magnesium & potassium inhibit smooth muscle contraction
3) Hydrogen ion : Vasodilator (low pH)
4) Carbon dioxide : Vasodilator especially in brain
5) Anion (acetate & citrat) : Vasodilators

** Blood pressure regulation

MAP = CO * TPR

CO and TPR are not independent variables(when TPR doubles, cardiac output simultaneously is almost halved, and Pa will increase only modestly.if cardiac output is halved, there is a compensatory increase in TPR, and Pa will decrease but it will not be halved)

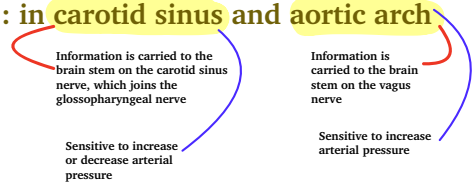
Mechanisms of BP regulation:

1) Neural regulation
- Baroreceptor reflex : rapid , Baroreceptor = Mechanoreceptor

بخلي Pa ثابت، كيف ؟؟

Chang the output of sympathetic & parasympathetic nervous systems to the heart and blood vessels

* location of baroreceptors : in carotid sinus and aortic arch



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

Baroreceptor reflex response to increase in arterial pressure

Increase Pa …. Baroreceptor activation….. increase firing rate in carotid sinus & vagus afferent nerves …. Join vagus with glossopharyngeal nerve in nucleus tractus … goooo to cardiovascular centers to return Pa to the normal level…… increase output of parasympathetic and decrease output of sympathetic system to the heart & vessels
Increase output parasympathetic system …. Decrease heart rate
Decrease output sympathetic system …. Decrease contraction of arteries…. Vasodilation…. Decrease resistance… decrease Pa
Decrease concentration of veins …. Vasodilation…. Decrease Pa
Decrease contractility ….. decrease cardiac output.

Baroreceptor reflex response to decrease in arterial pressure

Decrease Pa … Decrease stretch in Baroreceptor…. Decrease firing rate of Carotid sinus nerve… go to nucleus tractus …. Decrease output of parasympathetic & increase output of sympathetic system
Increase output of sympathetic system…. Increase Heart rate & contractility
Increase contraction of arteries…. Increase TPR
Increase contraction of veins ….. increase venous return…. Increase cardiac output.

- Peripheral chemoreceptors

Location : in carotid & aortic bodies

sensitive to decreases in (PO2) also are sensitive to increases in (PCO2) and decreases in pH, particularly when PO2 is simultaneously decreased.

Decrease arterial PO2 ….. increase firing rate of nerves from carotid and aortic bodies … activation vasoconstrictor centers… increase sympathetic output …. ARTERIOLAR VASOCONSTRICTION

- Central chemoreceptors

most sensitive to CO2 and pH and less sensitive to O2.

Increase PCO2 and decrease pH ….. medullary chemoreceptors …..increase sympathetic output…. Arteriolar vasoconstriction… increase TPR .

*The Cushing reaction : head injury… increase intracranial pressure… decrease perfusion of the brain … increase PCO2 & decrease pH …. Chemoreceptors activation

Brain stem cardiovascular centers

1) Vasoconstrictor center (C1)

Location : anterolateral portion of the upper medulla

2) Vasodilator center

Location : anterolateral portion of the lower medulla

3) Cardiac accelerator center : part of sympathetic system… increase heart rate … increase contraction… increase velocity of conduction

4) Cardiac decelerator center : part of parasympathetic system…. Decrease heart rate

-Atrial reflexes

low-pressure baroreceptors

Location: in veins, arteries …. (blood vessels)

Decrease BP by change the blood volume

Increase blood volume… increase atrial natriuretic peptide (ANP) … Relaxation of vascular smooth muscle…. Vasodilation… decrease TPR …. In kidney, increase excretion of sodium and water.. decrease ECF … decrease blood volume

Increase blood volume… decrease Renal sympathetic activity… vasodilation.. increase excretion of sodium and water

Increase blood volume… increase atria pressure… decrease ADH … decrease reabsorption of water … increase water excretion

Increase blood volume… increase heart rate … increase CO … increase perfusion of the kidney …. increase water & sodium excretion

2) Hormonal regulation

Renin- angiotensin- aldosterone system: slower than neural regulation

* regulation of BP by change blood volume.

*activated in response to a decrease in the BP.

*renin catalyzes the conversion of angiotensinogen to angiotensin I.

*Angiotensin II activates type 1 G protein–coupled angiotensin II receptors (AT1 receptors). ARBs inhibit the AT1 receptor.

Mechanism:

decrease in BP … decrease in renal perfusion pressure … sensed by mechanoreceptors in afferent arterioles of the kidney

decrease in BP causes prorenin to be converted to renin in the. juxtaglomerular cells.

Renin secretion by the juxtaglomerular cells is also increased by stimulation of renal sympathetic nerves.

In the lungs and kidneys, angiotensin I is converted to angiotensin II, catalyzed by angiotensin-converting enzyme (ACE). ACE inhibitors inhibit formation of angiotensin II.

Angiotensin II acts on the zona glomerulosa cells of the adrenal cortex to stimulate the synthesis and secretion of aldosterone.

Aldosterone tacts on the principal cells of the renal distal tubule and collecting duct … increase Na+ reabsorption …. increase ECF volume and blood volume.

Angiotensin II also has its own direct action on the kidney, independent of its actions through aldosterone.

Angiotensin II stimulates Na+/H+ exchange in the renal proximal tubule and increases the reabsorption of Na+ and HCO3-

Angiotensin II acts directly on the arterioles by binding to G protein–coupled AT1 receptors …vasoconstriction..increase TPR..increase BP

Angiotensin II acts on the hypothalamus to increase thirst and water intake. It stimulates secretion of antidiuretic hormone (ADH), which increases water reabsorption in collecting ducts…increase total body water …. increases in Na+ reabsorption (caused by aldosterone and Na+ -H+ exchange)… increase ECF volume…. Increase blood volume … increase blood pressure.

MICROCIRCULATION :

The exchange of solutes and gases across the capillary wall occurs by simple diffusion

* Depending on whether the solute or gas is lipid soluble, the diffusion occurs through:

I) endothelial cells II) Between the cells

A) O2 & CO2 , highly lipid soluble

Diffusion through the endothelial cells

Rate of diffusion depends on:

1) the driving force (the partial pressure difference for the gas)
2) the surface area available for diffusion.

The greater the number of open capillaries, the greater the surface area for diffusion.

B)Water-soluble substances : water, ions, glucose, and amino acids

Diffusion through the aqueous clefts between endothelial cells

C) Proteins

- Too large, don't leave capillaries through the space between endothelial cells.
- in tissue (brain) , little amount of protein can leave
- in kidney, fenestrated capillaries , Large amount of proteins can cross it .

**Starling Equation:

$$J_v = K_f\,[(P_c - P_i) - (\pi_c - \pi_i)]$$

where

J_v = Fluid movement (mL/min)

K_f = Hydraulic conductance (mL/min • mm Hg)

P_c = Capillary hydrostatic pressure (mm Hg)

P_i = Interstitial hydrostatic pressure (mm Hg)

π_c = Capillary oncotic pressure (mm Hg)

π_i = Interstitial oncotic pressure (mm Hg)

Filtration: net fluid movement is out of the capillary into the interstitial fluid
Absorption: net fluid movement is from the interstitium into the capillary

**Kf, hydraulic conductance, is the water permeability of the capillary wall.
*depend on the size of the clefts between endothelial cells.
Kf is increased in capillary injury (e.g., toxins or in burns).

**Pc, capillary hydrostatic pressure
*determined by both arterial and venous pressures, closer to arterial more than venous pressure.
* Pc is more affected by changes in venous pressure than by changes in arterial pressure.

**Pi, interstitial hydrostatic pressure: zero or slightly negative

**πc , capillary oncotic pressure:
it is determined by the protein concentration of capillary blood. Therefore, increases in protein concentration of blood cause increases in πc and decrease filtration, and decreases in protein concentration of blood cause decreases in πc and increase filtration.

**πi, interstitial oncotic pressure

— LYMPH
*The lymphatic capillaries possess one-way flap valves, which permit interstitial fluid and protein to enter, but not leave, the capillaries.
* The wall of lymphatics : smooth muscle .
*factors that determine lymph flow are
- the interstitial fluid pressure
- the activity of the lymphatic pump