CVS
PHYSIOLOGY

Modified NO: 16

كتابة: ميس قشّوع و فرح ظاهر

تدقيق: خديجة ناصر

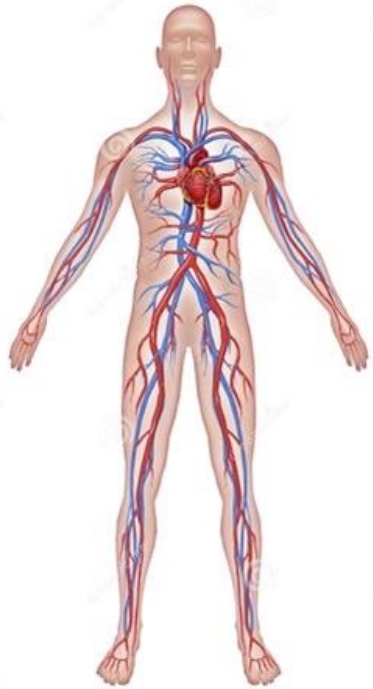
الدكتور: فاطمة ريالات

Cardiovascular Physiology

Fatima Ryalat, MD, PhD

Assistant Professor, Physiology and Biochemistry Department

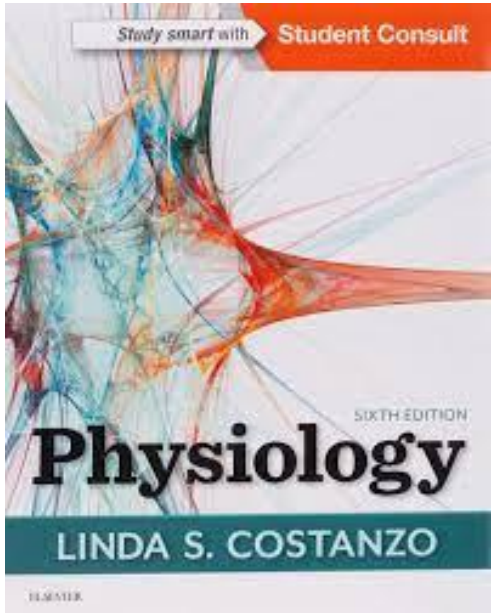
School of Medicine, University of Jordan

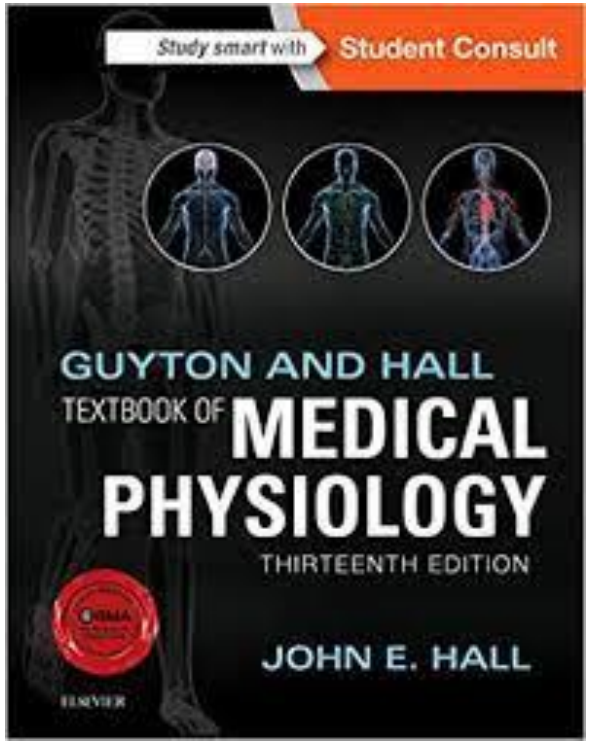


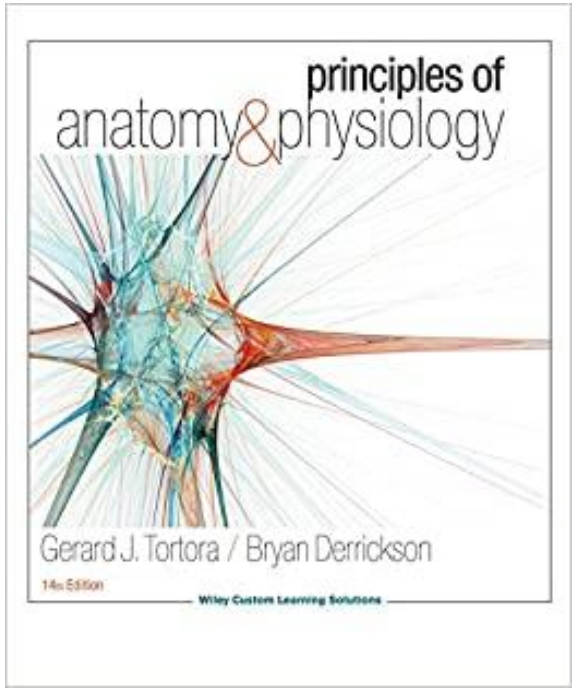
Color code

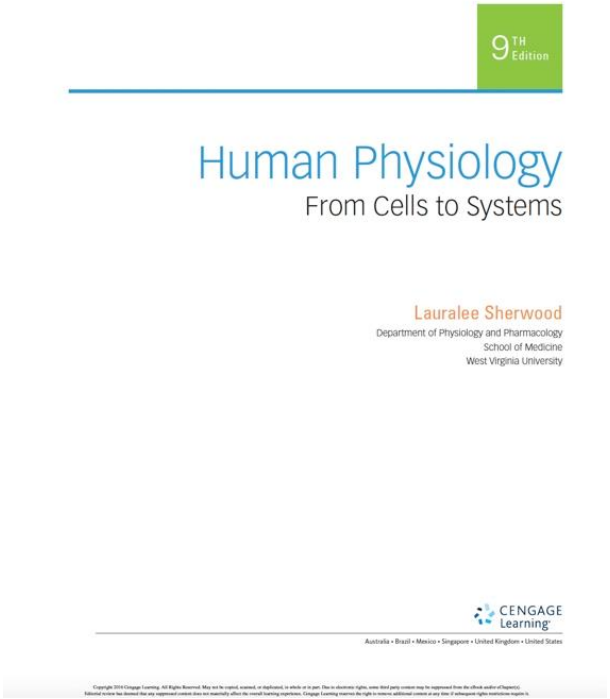
- Slides
- Doctor
- Additional info
- Important

References


Study smart with
Student Consult
SIXTH EDITION
Physiology
LINDA S. COSTANZO
ELSEVIER


Study smart with
Student Consult
GUYTON AND HALL
TEXTBOOK OF MEDICAL
PHYSIOLOGY
THIRTEENTH EDITION
JOHN E. HALL
ELSEVIER


principles of
anatomy & physiology
Gerard J. Tortora / Bryan Derrickson
14th Edition
Wiley Custom Learning Solutions


9TH Edition
Human Physiology
From Cells to Systems
Lauralee Sherwood
Department of Physiology and Pharmacology
School of Medicine
West Virginia University
CENGAGE Learning
Australia • Brazil • Mexico • Singapore • United Kingdom • United States

Blood flow and blood pressure regulation

- Remember, in the previous lecture we discussed that arterioles are the main vessels for resistance. They can change their diameter, which allows them to control resistance. Thus, in turn, affects both blood pressure and blood flow. Therefore, when talking about the control of local blood flow, we are primarily referring to the effect of arterioles, especially their acute effects.

Local control

- Most tissues have the ability to control their own local blood flow in proportion to their specific metabolic needs.
  - Blood flow needs can vary from moment to moment, depending on the activity of the cells [For example, if cell activity increases, more blood flow will be required]. These changes, which represent adaptation, mainly depend on the function of the arterioles. This is because arterioles have the ability to change their diameter through vasoconstriction and vasodilation.
- Local controls override sympathetic vasoconstriction.
  - (To be discussed in details in the "ABP regulation" lecture ⏳).
- Skeletal and cardiac local controls are the most effective.

Local blood flow control

- Local blood flow control can be divided into two phases:

1. Acute control is achieved by rapid changes in local **vasodilation** or **vasoconstriction** [in the diameter] of the arterioles, metarterioles, and precapillary sphincters that occur within seconds to minutes to provide rapid maintenance of appropriate local tissue blood flow.

2. Long-term control means slow, controlled changes in flow over a period of days, weeks, or even months. In general, these long-term changes provide even better control of the flow in proportion to the needs of the tissues.

- These changes come about as a result of an increase or decrease in the physical sizes and numbers of blood vessels supplying the tissues.

Acute control of local blood flow: metabolic control

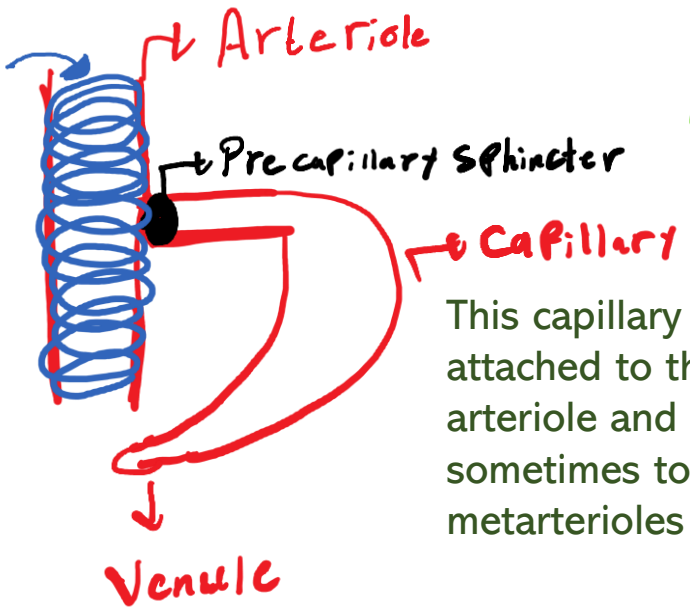
- Increases in Tissue Metabolism Increase Tissue Blood Flow:

- Whenever the availability of oxygen to the tissues decreases, the blood flow through the tissues increases markedly.

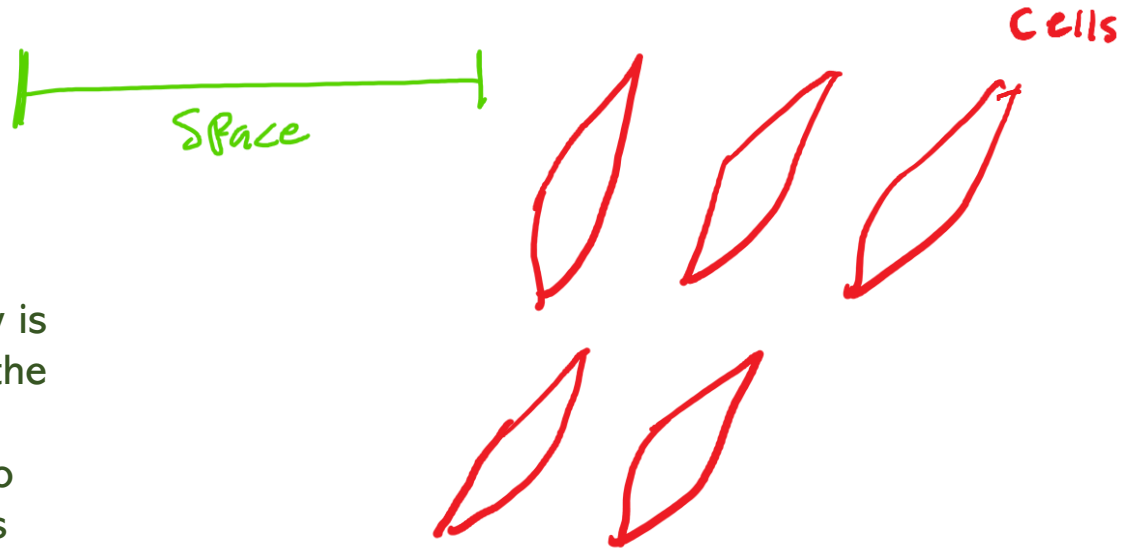
- two main theories have been proposed, the vasodilator theory and the oxygen demand theory.

- What causes the arterioles in a tissue to recognize whether it needs more or less blood flow, leading to vasodilation or vasoconstriction? The answer lies in the metabolic activity of this tissue and the most important factor influencing metabolic activity is oxygen availability.

Around the arterioles there is a thick layer of smooth muscle cells which allows them to constrict or to dilate.



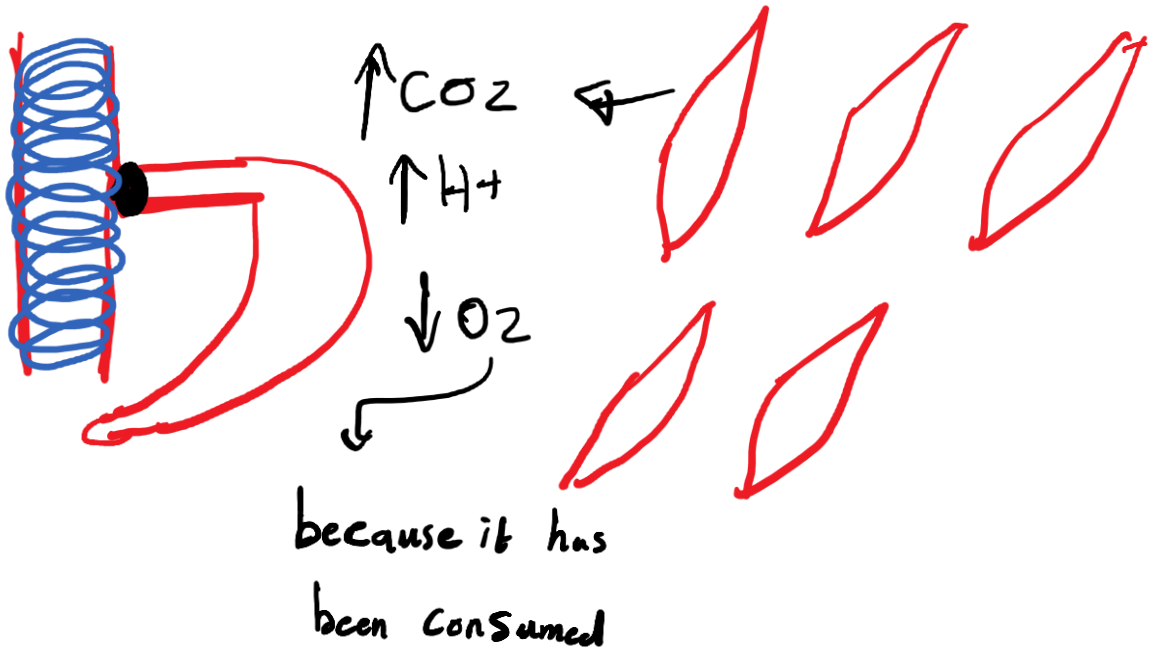
This capillary is attached to the arteriole and sometimes to metarterioles



- The blood supply flows from arterioles to capillaries and then to venules. Surrounding these vessels there are cells (that are supplied by this adjacent blood vessel), but they are not directly connected to the capillaries. Instead, there is a space called the interstitial space, which is filled with interstitial fluid, where the exchange of materials between the blood and surrounding cells occurs.

- Precapillary sphincters are smooth muscles that contract or relax based on the needs of the tissues they supply.

At exercise



ملاحظة: بالنسبة لهاد الموضوع رح اكتب شرح الدكتورة بطريقة تسهل عليكم فهم الموضوع لهيك اسمعوا شرح الدكتورة بعدين اقرأوا المكتوب عشان تفهموا الموضوع منيح 🤗

• When a person transitions from rest to regular exercise, the skeletal muscle cells experience an increased demand for metabolic resources. During exercise, these cells consume more oxygen and release higher amounts of carbon dioxide (CO_2) and hydrogen ions (H^+) as byproducts. This leads to an increase in the concentrations of CO_2 and H^+, along with a decrease in oxygen levels in the interstitial fluid surrounding these cells.

• These changes in the interstitial fluid trigger diffusion of CO_2 and H^+ into nearby blood vessels due to the concentration gradient. **CO_2 and H^+ act as vasodilators**, signalling the smooth muscles of arterioles, metarterioles, and precapillary sphincters to relax. As these smooth muscles relax, the blood vessels dilate, resulting in increased blood flow to the area. This mechanism ensures that the active skeletal muscle tissue receives sufficient blood flow to meet its heightened metabolic demands.

• This process is part of a theory **(first theory)** explaining how arteriolar diameter adjusts in response to the metabolic needs of tissues. Oxygen plays a critical role in regulating vasodilation and vasoconstriction. For example, when oxygen levels decrease, it indicates that the tissue requires more blood flow, triggering vasodilation to supply the needed nutrients.

• Conversely, when metabolic activity decreases, the production of vasodilatory byproducts such as carbon dioxide (CO_2) and hydrogen ions (H^+) declines, while oxygen levels in the tissue increase. The decrease in vasodilator signals, along with the higher oxygen availability, reduces the stimulus for smooth muscle relaxation. This causes the smooth muscles in arterioles, metarterioles, and precapillary sphincters to contract, leading to vasoconstriction and reduced blood flow.

• **Another theory** suggests that oxygen is essential for the contraction of the smooth muscle cells in the blood vessels themselves. To induce contraction in these smooth muscles, a higher oxygen supply is required. (O2 is needed for ATP production, and ATP is needed for the contraction of the muscle fibers -actin and myosin- inside the cells surrounding blood vessels)

•In this context, the metabolic needs of the tissue play a crucial role in regulating the resistance of the arterioles or the radius of these vessels. This regulation directly influences the amount of blood flow that reaches the tissue, ensuring that the supply aligns with the tissue's metabolic demands.

Another example:

Imagine a pipe filled with water, connected to multiple water taps, each with a different diameter.

Completely opened → High diameter → Lower resistance → More blood flow

Partially opened

Completely closed → Lower diameter → Higher resistance → Less blood flow

- So, again the arterioles, metarterioles, and precapillary sphincters regulate the amount of blood flow reaching a tissue based on its specific needs.

• Additional slide (you can skip it) [مع اني ما بنصحك تعمل سكيب 🙄]:

• Summary of the theories of acute control of local blood flow:

1. Metabolic Vasodilation Theory: During increased metabolic activity, such as exercise, skeletal muscle cells consume more oxygen and produce higher levels of carbon dioxide (CO_2) and hydrogen ions (H^+). These byproducts act as vasodilators, triggering the relaxation of smooth muscles in arterioles, metarterioles, and precapillary sphincters. The resulting vessel dilation increases blood flow to match the tissue's elevated metabolic demands. Conversely, when metabolic activity decreases, the production of vasodilatory byproducts such as carbon dioxide (CO_2) and hydrogen ions (H^+) declines, while oxygen levels in the tissue increase. The decrease in vasodilator signals, along with the higher oxygen availability, reduces the stimulus for smooth muscle relaxation. This causes the smooth muscles in arterioles, metarterioles, and precapillary sphincters to contract, leading to vasoconstriction and reduced blood flow.

2. Oxygen-Dependent Smooth Muscle Contraction Theory: Oxygen is critical for smooth muscle contraction in blood vessels. When oxygen levels are adequate, the smooth muscles can contract, increasing vascular resistance and reducing blood flow. In contrast, low oxygen levels limit smooth muscle contraction, promoting vasodilation and enhancing blood flow.

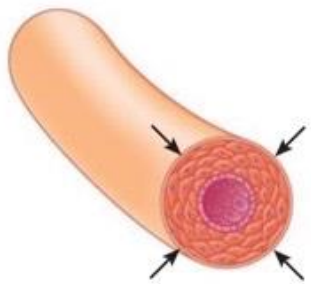
Acute control of local blood flow

- The vasodilator substances are then believed to diffuse through the tissues to the precapillary sphincters, metarterioles, and arterioles to cause dilation.
- Some of the different vasodilator substances that have been suggested are adenosine, carbon dioxide, adenosine phosphate compounds, potassium ions, and hydrogen ions.

•Adenosine and adenosine phosphate compounds (like ADP for example) indicate a low energy state of the cells, meaning they need more oxygen to convert these adenosine compounds into ATP —> hence are considered vasodilators to induce blood flow

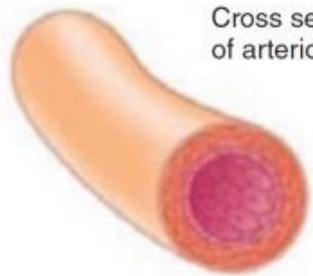
Acute control of local blood flow

- Oxygen demand theory:
- when the oxygen concentration in the tissue rises above a certain level, the precapillary and metarteriole sphincters presumably would close until the tissue cells consume the excess oxygen.
- However, when the excess oxygen is gone and the oxygen concentration falls low enough, the sphincters open once more to begin the cycle again.



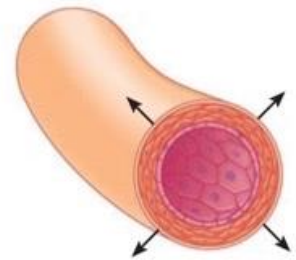
Caused by:
- ↑ Myogenic activity
- ↑ Oxygen (O_2)
- ↓ Carbon dioxide (CO_2) and other metabolites
- ↑ Endothelin
- ↑ Sympathetic stimulation
- Vasopressin; angiotensin II
- Cold

(c) Vasoconstriction (increased contraction of circular smooth muscle in the arteriolar wall, which leads to increased resistance and decreased flow through the vessel)



Cross section of arteriole

(b) Normal arteriolar tone



Caused by:
- ↓ Myogenic activity
- ↓ O_2
- ↑ CO_2 and other metabolites
- ↑ Nitric oxide
- ↓ Sympathetic stimulation
- Histamine release
- Heat

(d) Vasodilation (decreased contraction of circular smooth muscle in the arteriolar wall, which leads to decreased resistance and increased flow through the vessel)

Acute control of local blood flow

Examples of acute control:

- Active hyperemia: [hyper: increased , Emia: blood flow]: so, it is an increased blood flow due to the need of the tissue (it becomes more active).
- When a tissue becomes highly active, such as an exercising muscle or the brain during increased mental activity, so more use of oxygen and more vasodilation so the rate of blood flow through the tissue increases.
- The increase in local metabolism causes the cells to devour tissue fluid nutrients rapidly and release large quantities of vasodilator substances.
- The result is dilation of local blood vessels and increased local blood flow.
- In this way, the active tissue receives the additional nutrients required to sustain its new level of function.

Acute control of local blood flow

- Reactive hyperemia:
- When the blood supply to a tissue is blocked for a few seconds to as long as 1 hour or more and then is unblocked, blood flow through the tissue usually increases immediately to four to seven times normal.

- In reactive hyperaemia, there is a temporary blockage of blood flow to an organ. For example, when we use a tourniquet to drain blood from a patient, we tighten the tourniquet, blocking blood flow downstream. After finishing the blood drainage and removing the tourniquet, blood flow to the area increases. However, this increase in blood flow is much higher than normal, typically 3-5 (in slides is 4-7) times the usual flow. This happens because, while the tourniquet was in place, blood supply to the organ was blocked. **Despite this**, the organ continued to consume oxygen, and release carbon dioxide (CO_2) and hydrogen ions (H^+) , leading to vasodilation. Since blood flow was restricted during this process, once the blockage is removed, a large amount of blood comes to the area (we have already accumulated large amounts of vasodilators produced during the time of blockage).
- The greater the duration of the blockage, the more pronounced the reactive hyperaemic response will be.

Blood flow autoregulation

- Another example of local control of blood flow is called autoregulation.

- It is the ability of each tissue to adjust its vascular resistance and to maintain normal blood flow during changes in arterial pressure between approximately 70 and 175 mm Hg is called blood flow autoregulation.

- Blood flow changes rarely last for more than a few hours in most tissues, even when increases in arterial pressure or increased levels of vasoconstrictors are sustained.

- The reason for the relative constancy of blood flow is that each tissue's local autoregulatory mechanisms eventually override most of the effects of vasoconstrictors to provide a blood flow that is appropriate for the needs of the tissue.

• When blood pressure (BP) increases in a tissue, we might expect blood flow to also increase. However, this relationship is not directly proportional. While both BP and blood flow may rise, what matters more is the local demand of the tissue. For example, even if **systemic BP** is high, the tissue may not require much blood supply. In this case, the blood vessels will adjust their resistance based on the tissue's needs, regardless of the BP values. If the tissue requires more blood, the vessels will dilate (vasodilation), and if it doesn't need more blood, the vessels will constrict (vasoconstriction).

• Therefore, the relationship between BP and blood flow is not linear. The blood flow to a tissue is usually maintained within a certain range of BP, typically between 70 and 175 mmHg.
• To sum up, autoregulation is the process by which blood vessels adjust their resistance to maintain a stable blood flow to the tissue based on its needs, regardless of changes in systemic BP.

بالمختصر

- Autoregulation is the process by which blood vessels adjust their resistance to maintain consistent blood flow to a tissue based on its local needs, independent of changes in systemic blood pressure. When blood pressure rises, the vessels either dilate or constrict to ensure that the tissue receives the right amount of blood supply. This process helps maintain stable blood flow within a specific range of blood pressure, typically between 70 and 175 mmHg.

Blood flow autoregulation

- Autoregulation Attenuates the Effect of Arterial Pressure on Tissue Blood Flow:
- One might expect an increase in arterial pressure to cause a proportionate increase in blood flow through the body's tissues.
- However, the effect of arterial pressure on blood flow in many tissues is usually far less than one might expect.
- This is because an increase in arterial pressure not only increases the force that pushes blood through the vessels, but also initiates compensatory increases in vascular resistance within a few seconds through activation of the local control mechanisms,

Acute control of blood flow in the kidney

- Different organs have different autoregulatory mechanisms tailored to their specific needs.

- In the kidneys, blood flow control is significantly vested in a mechanism called tubuloglomerular feedback, in which the composition of the fluid in the early distal tubule is detected by an epithelial structure of the distal tubule, called the macula densa.

- This structure is located where the distal tubule lies adjacent to the afferent and efferent arterioles at the nephron juxtaglomerular apparatus. When too much fluid filters from the blood through the glomerulus into the tubular system, feedback signals from the macula densa cause constriction of the afferent arterioles, thereby reducing renal blood flow and glomerular filtration rate back to nearly normal.

Acute control of blood flow in the brain

- In the brain, in addition to control of blood flow by tissue oxygen concentration, the concentrations of carbon dioxide and hydrogen ions play prominent roles.

- An increase of either or both of these substances dilates the cerebral vessels and allows rapid washout of the excess carbon dioxide or hydrogen ions from the brain tissues.

- This mechanism is important because the level of excitability of the brain is highly dependent on exact control of both carbon dioxide concentration and hydrogen ion concentration.

- In the brain, central chemoreceptors are responsible for detecting changes in carbon dioxide (CO_2) and hydrogen ion (H^+) concentrations. This is crucial because the excitability of neural cells is influenced by these two factors. As part of the brain's autoregulatory mechanisms, these chemoreceptors are highly sensitive to the levels of CO_2 and H^+, ensuring that neural activity remains stable.

- When there is an increase in carbon dioxide (CO_2) or hydrogen ions (H^+) in the brain, the central chemoreceptors detect these changes and trigger a response to restore balance. Specifically, an increase in either or both of these substances causes vasodilation of the cerebral blood vessels. This vasodilation allows for an increase in blood flow to the brain.

- The previous factors are related to the tissues surrounding these vessels, which regulate their own blood flow. Additionally, there are other factors specific to the vessels themselves.

- The lining of blood vessels is made up of endothelial cells (ECs). These cells are not merely passive barriers that form the vessel wall and allow blood to flow through; instead, they play an active role in regulating vascular function. In response to various stimuli, such as increased pressure or stress on the vessel walls, endothelial cells can produce molecules that help adapt to these changes. For example, they release nitric oxide (NO), a potent vasodilator, which helps relax and widen the blood vessels.

- Clinically, nitric oxide (NO) plays a significant role in treating certain conditions. For example, in coronary artery disease, we use nitroglycerin, a drug that increases NO levels, causing vasodilation and improving blood flow to the heart. Similarly, NO is involved in treating erectile dysfunction. Medications like sildenafil (commonly known as Viagra) work by enhancing NO-mediated vasodilation. Sildenafil specifically inhibits phosphodiesterase type 5 (PDE5), an enzyme that breaks down cyclic GMP, thereby promoting prolonged blood vessel relaxation and improving erectile function.

- Endothelial cells (ECs) can also release endothelin, a potent vasoconstrictor. This molecule is typically released during pathological states such as injury, trauma, or bleeding, where its vasoconstrictive action helps minimize blood loss.

- In **chronic hypertension**, injured endothelial cells produce high levels of endothelin, which is considered a hallmark of the disease. Hypertension also induces changes in the extracellular matrix (ECM), leading to fibrosis and increased stiffness of the blood vessels. Additionally, smooth muscle cells in the vessel walls undergo hypertrophy, further contributing to vascular remodelling and impaired function.

Local control :endothelial derived factors: **NO**

- Clinicians used nitroglycerin and other nitrate derivatives to treat patients who had angina pectoris—that is, severe chest pain caused by ischemia of the heart muscle. These drugs cause dilation of blood vessels throughout the body, including the coronary blood vessels.

- Other important applications of NO is the clinical use of drugs (e.g., sildenafil) that inhibit cGMP-specific phosphodiesterase- 5 (PDE-5), an enzyme that degrades cGMP. By preventing the degradation of cGMP, the PDE-5 inhibitors effectively prolong the actions of NO to cause vasodilation.

- The primary clinical use of the PDE-5 inhibitors is to treat erectile dysfunction.

Local control :endothelial derived factors: **endothelin**

- Endothelial cells also release vasoconstrictor substances.
- The most important of these is endothelin that requires only minute amounts (nanograms) to cause powerful vasoconstriction.
- This substance is present in the endothelial cells of all or most blood vessels but greatly increases when the vessels are injured.
- After severe blood vessel damage, local release of endothelin and subsequent vasoconstriction helps prevent extensive bleeding from arteries.
- Increased endothelin release is also believed to contribute to vasoconstriction when the endothelium is damaged by hypertension.

- Sometimes, changes in tissue status and needs stay for a long time (chronically), like when someone starts to go to the gym every day.

- Now vasoconstriction and dilation are not practical because muscles mass and activity increase, we need another robust way to regulate the blood flow.

- When we talk about long term regulation, we mean structural changes in vascular system. For example: increasing metabolic activity will increase capillaries' number and density to increase the blood flow.

Long term blood flow regulation

- long-term regulation gives far more complete, robust and almost 100% control of blood flow to make adaptation.
- Long-term regulation of blood flow is especially important when the metabolic demands of a tissue change. Thus, if a tissue becomes chronically overactive and requires increased quantities of oxygen and other nutrients, the arterioles and capillary vessels usually increase both in number (angiogenesis) and size within a few weeks to match the needs of the tissue, unless the circulatory system has become pathological or too old to respond.

Long term blood flow regulation: changes in tissue vascularity

- A key mechanism for long-term local blood flow regulation is to change the amount of vascularity of the tissues, these changes need time, and the result differs between tissues, younger tissues give better vascularity than older (old tissues lose their functioning cells) .

- For example, if the metabolism in a tissue is increased for a prolonged period, vascularity increases, a process generally called angiogenesis; if the metabolism is decreased, vascularity decreases.

Long term blood flow regulation: changes in tissue vascularity

- the time required for long-term regulation to take place may be only a few days in the neonate or as long as months in older adults.
- Furthermore, the final degree of response is much better in younger than in older tissues; thus, in the neonate, the vascularity will adjust to match almost exactly the needs of the tissue for blood flow, whereas in older tissues, vascularity frequently lags far behind the needs of the tissues.

- Usually, we put premature babies in an incubator, to provide optimal circumstances for them, including oxygen concentration and other factors, but this oxygen concentration should be studied carefully.

- If the doctor increases the oxygen concentration more than the therapeutic dose, the baby will not grow well later!

- At one point we will take the child out of the incubator and put him/her in the room atmosphere which has less oxygen than the incubator, and this is a problem! The child will sensitize this as hypoxia (since he adapted to the high O2 pressure at the incubator & his blood vessels were formed according to those conditions, and now he's facing totally different conditions where the otherwise normal pressure, to normal people, is seen to be low with those babies), leading to overgrowth and increase in angiogenesis, especially in the retina causing blindness.

- The oxygen concentration is very important especially in children because they have high response.

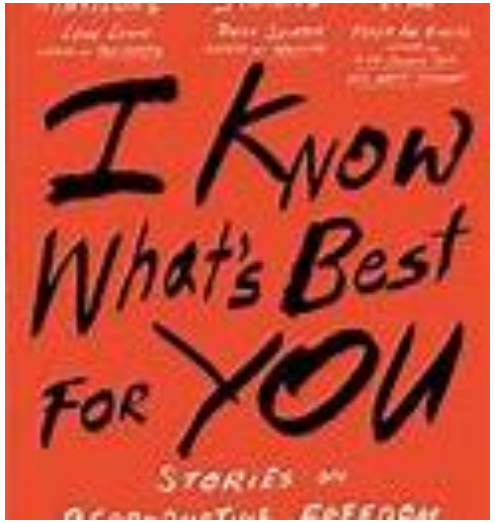
لأنه الدكتور حب يعمل خير زيادة راح عمى الطفل(:

Long term blood flow regulation: changes in tissue vascularity

- In premature babies who are put into oxygen tents (incubator) for therapeutic purposes, the excess oxygen causes almost immediate cessation of new vascular growth in the retina of the premature baby's eyes and even causes degeneration of some of the small vessels that already have formed.
- When the infant is taken out of the oxygen tent, explosive overgrowth of new vessels then occurs to make up for the sudden decrease in available oxygen.
- Often, so much overgrowth occurs that the retinal vessels grow out from the retina into the eye's vitreous humor, eventually causing blindness, a condition called retrolental fibroplasia.

Please, please, please watch this video NOW
It is very helpful

https://youtu.be/WncY79XPIC0?si=W5Bb4_xy57-OxFfw



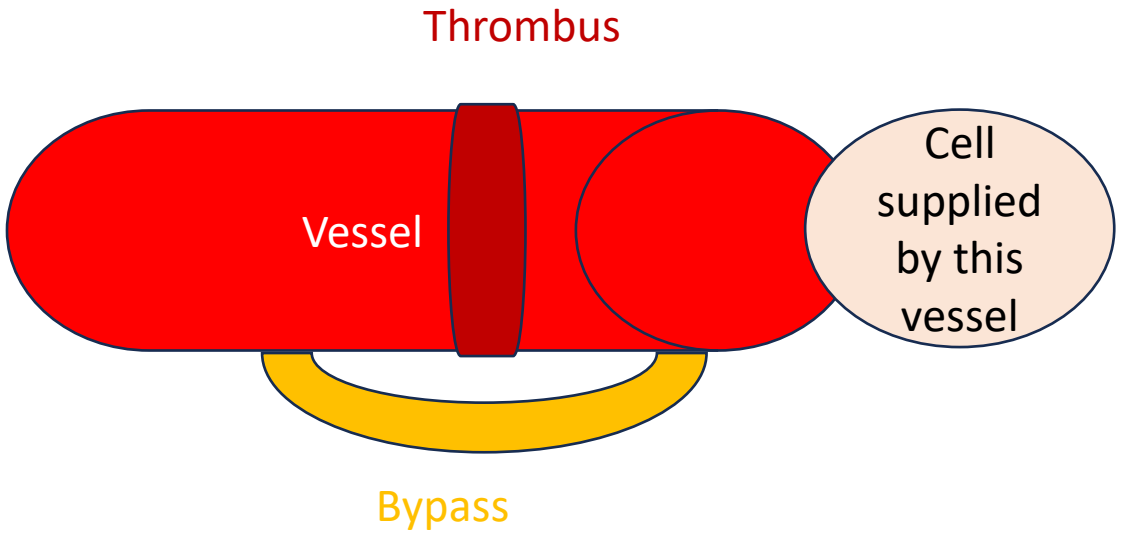
Long term blood flow regulation: changes in tissue vascularity

Long term blood regulation can be affected by:

- Vascular growth factors
- Steroid hormones
- Antiangiogenic factors
- Vascularity Determined by Maximum Blood Flow Need, Not by Average Need.

- If someone goes to the gym, there will be days filled with intense exercise, leading to the highest level of metabolic activity and vascularity. However, this same person will also go through periods where they won't engage in strenuous exercise in their daily life.
- So, We form blood vessels based on the highest level of metabolic processes.
- If we need them, we use them, and if not, we close them with the precapillary sphincter (by the short-term regulatory mechanisms).

Collateral circulation



- If we have a blockage in one of the blood vessels supplying a cell, the body - as part of long term adaptation - builds collateral circulation. In other words, it creates a new blood vessel that bypasses the blockage.
- The speed and efficiency of collateral circulation will determine the outcome.
- Low speed and efficiency lead to ischemic heart disease (MI) .

Long term blood flow regulation: changes in tissue vascularity

- A clinical example of vascularity changes is Collateral circulation

- An important example of the development of collateral blood vessels occurs after thrombosis of one of the coronary arteries. By the age of 60 years, many people have experienced closure or at least partial occlusion of at least one of the smaller branch coronary vessels, but they are not aware of it because collateral blood vessels have developed rapidly enough to prevent myocardial damage.

- When collateral blood vessels are unable to develop quickly enough to maintain blood flow because of the rapidity or severity of the coronary insufficiency, serious heart attacks can occur.

Long term blood flow regulation: vascular remodeling

Regulating blood flow does not always mean increasing it. For a person with paralysis in the lower limb, there is no need to supply blood to this low metabolic activity area.
In this case, we reduce the number and diameter of the blood vessels.

- In addition to changes in capillary density, there may also be changes in the structure of large blood vessels in response to long-term changes in blood pressure and blood flow.
- When blood pressure is chronically elevated above normal, for example, the large and small arteries and arterioles remodel to accommodate the increased mechanical wall stress of the higher blood pressure.

- In most tissues, the small arteries and arterioles rapidly respond (within seconds) to increased arterial pressure with vasoconstriction, which helps autoregulate tissue blood flow if the pressure stays high, this vasoconstriction becomes structural and remodeling changes.
- The vasoconstriction decreases lumen diameter, which in turn tends to normalize the vascular wall tension (T), which, according to Laplace's equation, is the product of the radius (r) of the blood vessel and its pressure (P): $T = r \times P$

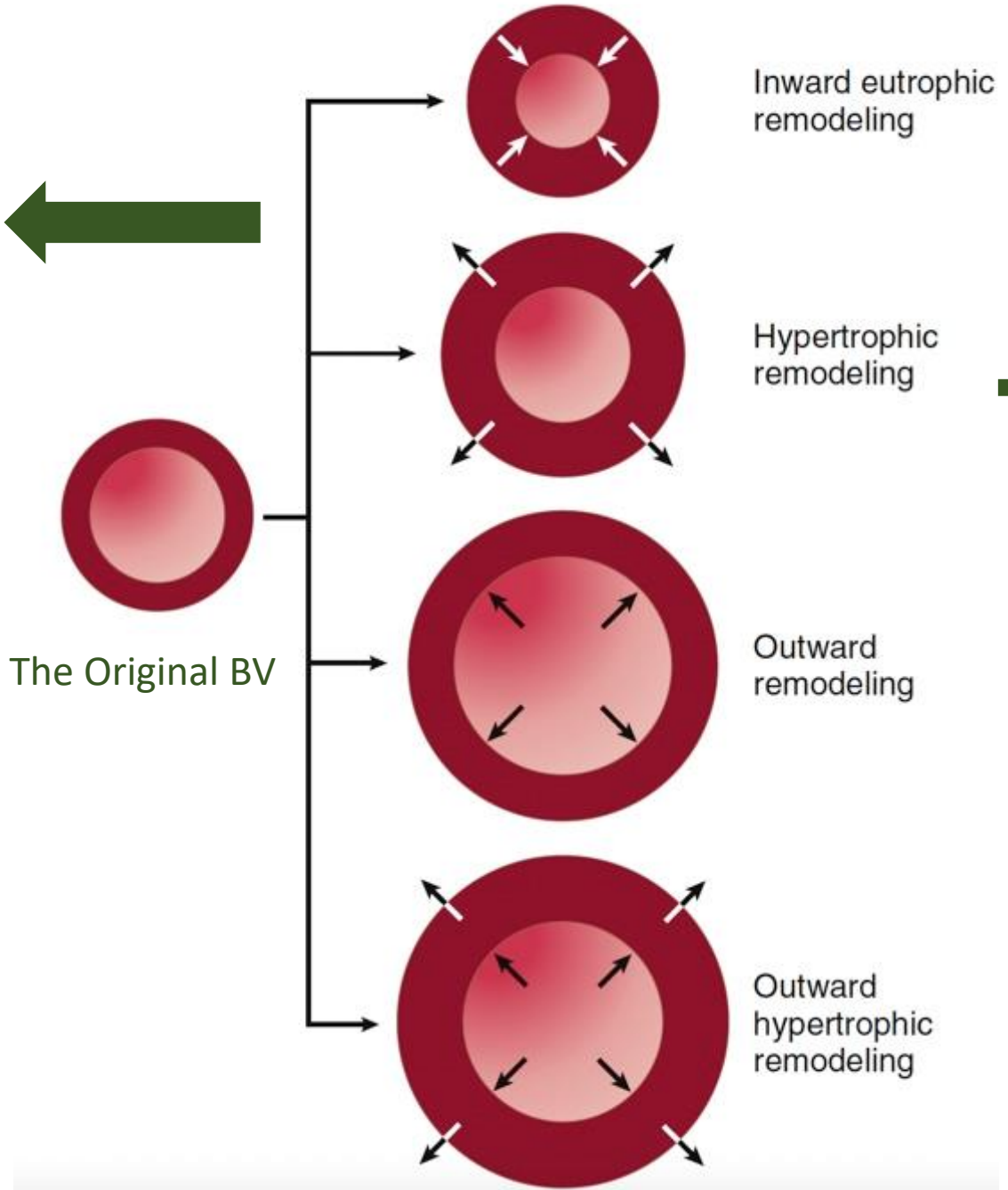
By vasoconstriction we decrease the radius and so decrease the tension.

This type of remodeling is called inward eutrophic remodeling

Long term blood flow regulation: vascular remodeling

- In small blood vessels that constrict in response to increased blood pressure, the vascular smooth muscle cells and endothelial cells gradually—over a period of several days or weeks, long term—rearrange themselves around the smaller lumen diameter, a process called inward eutrophic remodeling, with no change in the total cross-sectional area of the vascular wall.
- In larger arteries that do not constrict in response to the increased pressure, the vessel wall is exposed to increased wall tension that stimulates a hypertrophic remodeling response and an increase in the cross-sectional area of the vascular wall.
- The hypertrophic response increases the size of vascular smooth muscle cells and stimulates formation of additional extracellular matrix proteins, such as collagen and fibronectin, that reinforce the strength of the vascular wall to withstand the higher blood pressures.
- However, this hypertrophic response also makes the large blood vessels stiffer, which is a hallmark of chronic hypertension.

Both are under high pressure



- Happens in small BVs
- Inward = constriction
- Eutrophic = no change in the cross sectional area
- Only decreased lumen diameter

- Happens in large BVs
- Increase in cross sectional area
- Hypertrophy
- Increase in wall thickness

Long term blood flow regulation: vascular remodeling

- Another example of vascular remodeling is the change that occurs when a large vein (often the saphenous vein) is implanted in a patient for a coronary artery bypass graft procedure.
- Veins are normally exposed to much lower pressures than arteries and have much thinner walls, but when a vein is sewn onto the aorta and connected to a coronary artery, it is exposed to increases in intraluminal pressure and wall tension.
- The increased wall tension initiates hypertrophy of vascular smooth muscle cells and increased extracellular matrix formation, which thicken and strengthen the wall of the vein; as a result, several months after implantation into the arterial system, the vein will typically have a wall thickness similar to that of an artery.

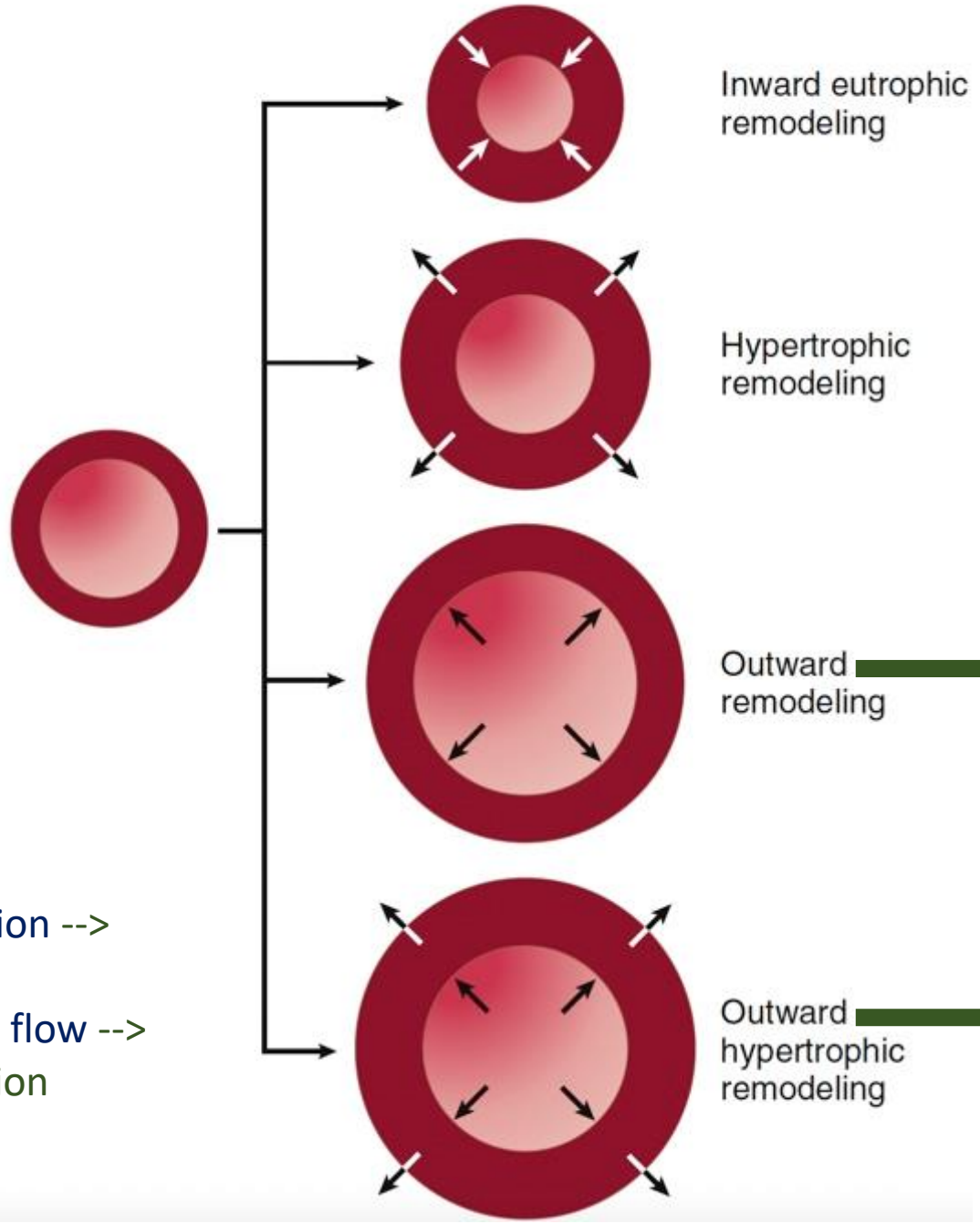
- This condition leads to arterialization of the vein.
- From low pressure to high pressure causing hypertrophy.

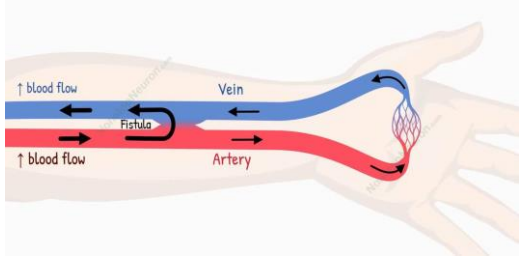
Long term blood flow regulation: vascular remodeling

- Vascular remodeling also occurs when a blood vessel is exposed chronically to increased or decreased blood flow.
- The creation of a fistula connecting a large artery and large vein, thereby completely bypassing high-resistance small vessels and capillaries, provides an especially interesting example of remodeling in the affected artery and vein.
- In patients with renal failure who undergo dialysis, an arteriovenous (A-V) fistula directly from the radial artery to the antecubital vein of the forearm is created to permit vascular access for dialysis. The blood flow rate in the radial artery may increase as much as 10 to 50 times the normal flow rate, depending on the patency of the fistula.

Long term blood flow regulation: vascular remodeling

- As a result of the high flow rate and high shear stress on the vessel wall, the luminal diameter of the radial artery increases progressively (outward remodeling), whereas the thickness of the vessel wall may remain unchanged, resulting in an increase in cross-sectional area of the vascular wall.
- In contrast, wall thickness, lumen diameter, and cross-sectional area of the vascular wall on the venous side of the fistula increase in response to increases in pressure and blood flow (outward hypertrophic remodeling).
- This pattern of remodeling is consistent with the idea that long-term increases in vascular wall tension cause hypertrophy and increased wall thickness in large blood vessels, whereas increased blood flow rate and shear stress cause outward remodeling and increased luminal diameter to accommodate the increased blood flow.





Both have high volume

- Happens in radial artery in hemodialysis
- Increase in lumen diameter
- Increase in cross-sectional area
- No big change in wall thickness
- Dilation due to volume increase

- Happens in antecubital vein in hemodialysis
- Thickness, diameter, cross sectional area, pressure and volume are all increased, so we have both dilation and hypertrophy

To conclude:
Increased pressure/tension --> hypertrophy
Increased volume/blood flow --> Streching, outward dilation

Long term blood flow regulation

- When blood flow is greatly reduced, the diameter of the vascular lumen is also reduced and, when blood pressure is reduced, the thickness of the vascular wall usually decreases. Thus, vascular remodeling is an important adaptive response of the blood vessels to tissue growth and development, as well as to physiological and pathological changes in blood pressure and blood flow to the tissues.

Humoral control of the circulation: vasoconstrictors

Humoral control of the circulation:
Vasoconstrictors
- epinephrine & norepinephrine
- Angiotensin II
- Vasopressin (ADH)

Vasodilators
- Bradykinin
- Histamine

The blood flow may be affected by external factors like hormones.

- Epinephrine and norepinephrine:
- Norepinephrine is an especially powerful vasoconstrictor hormone; epinephrine is less powerful as a vasoconstrictor and, in some tissues, even causes mild vasodilation. (A special example of vasodilation caused by epinephrine is that which occurs to dilate the coronary arteries during increased heart activity.) but the major effect is a mild vasoconstriction.
- When the sympathetic nervous system is stimulated in most parts of the body during stress or exercise, the sympathetic nerve endings in the individual tissues release norepinephrine, which excites the heart and constricts the veins and arterioles. In addition, the sympathetic nerves to the adrenal medullae cause these glands to secrete norepinephrine and epinephrine into the blood.

Humoral control of the circulation: vasoconstrictors

- Angiotensin II
- The effect of angiotensin II is to constrict the small arterioles powerfully.
- It normally acts on many arterioles of the body at the same time to increase the total peripheral resistance and decrease sodium and water excretion by the kidneys, changing the blood volume --> thereby increasing the arterial pressure.
- Thus, this hormone plays an integral role in the regulation of arterial pressure

Humoral control of the circulation: vasoconstrictors

- Vasopressin (ADH):
- Vasopressin, also called antidiuretic hormone, is even more powerful than angiotensin II as a vasoconstrictor, thus making it one of the body's most potent vascular constrictor substances. It is formed in nerve cells in the hypothalamus of the brain but is then transported downward by nerve axons to the posterior pituitary gland, where it is finally secreted into the blood. So, the synthesis happens in hypothalamus, but the posterior pituitary gland releases it.
- It is clear that vasopressin could have enormous effects on circulatory function. Yet, because only minute amounts of vasopressin are secreted in most physiological conditions, most physiologists have thought that vasopressin plays little role in vascular control. However, experiments have shown that the concentration of circulating blood vasopressin after severe hemorrhage can increase enough to attenuate reductions in arterial pressure markedly. In some cases, this action can, by itself, bring the arterial pressure almost back up to normal.
- Vasopressin has the major function of greatly increasing water reabsorption from the renal tubules back into the blood and therefore helps control body fluid volume. That is why this hormone is also called antidiuretic hormone.

Humoral control of the circulation: vasodilators

- Bradykinin causes both powerful arteriolar dilation and increased capillary permeability and causes edema.
- Kinins appear to play special roles in regulating blood flow and capillary leakage of fluids in inflamed tissues.

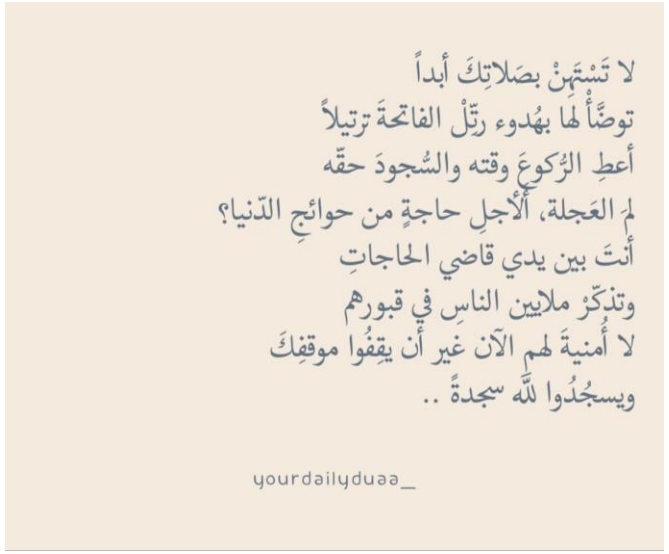
Humoral control of the circulation: vasodilators

- Histamine
- Histamine is released in almost every tissue of the body if the tissue becomes damaged or inflamed or is the subject of an allergic reaction. Most of the histamine is derived from mast cells in the damaged tissues and from basophils in the blood.
- Histamine has a powerful vasodilator effect on the arterioles and, like bradykinin, has the ability to increase capillary porosity greatly, allowing leakage of fluid and plasma protein into the tissues. In many pathological conditions, the intense arteriolar dilation and increased capillary porosity produced by histamine cause large quantities of fluid to leak out of the circulation into the tissues, inducing edema. The local vasodilatory and edema-producing effects of histamine are especially prominent during allergic reactions

Thank you

Additional sources:

1. Rective Hyperemia



VERSIONS	SLIDE #	BEFORE CORRECTION	AFTER CORRECTION
V1→ V2			
V2→V3			

امسح الرمز و شاركنا بأفكارك لتحسين أدائنا!!