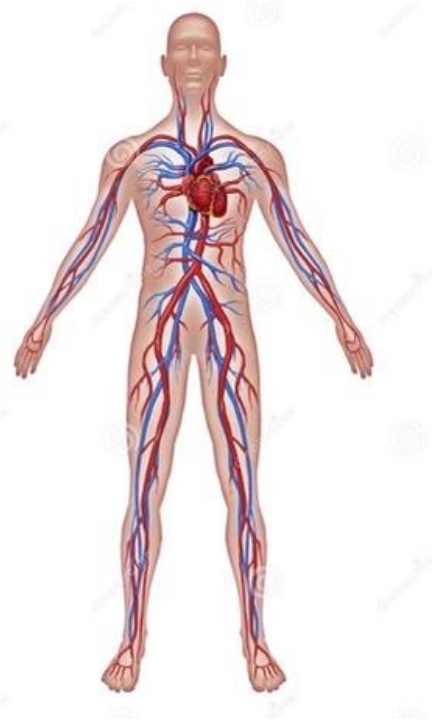
# Cardiovascular Physiology

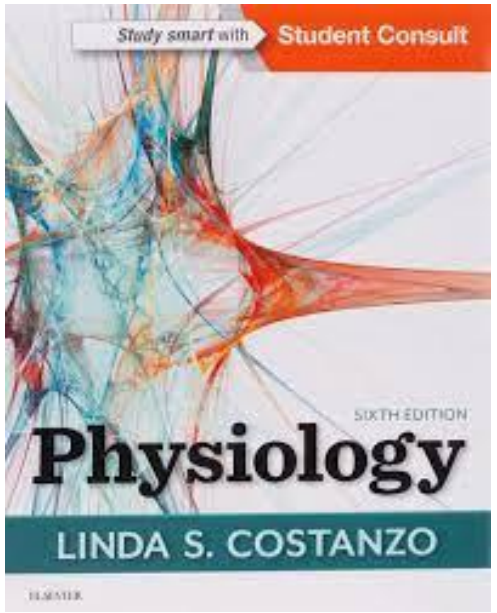
Fatima Ryalat, MD, PhD

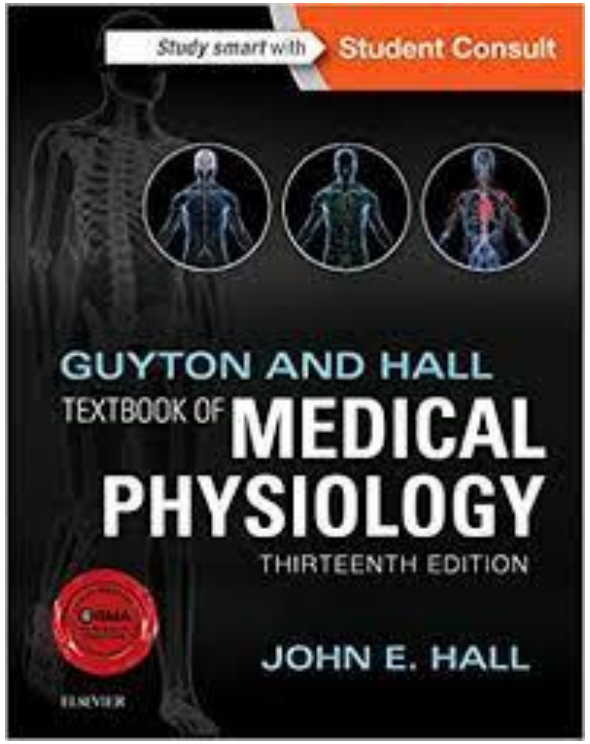
Assistant Professor, Physiology and Biochemistry Department

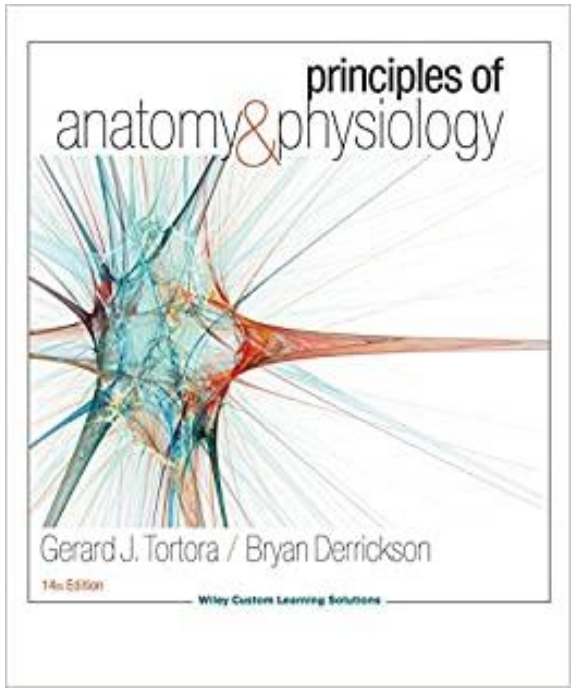
School of Medicine, University of Jordan

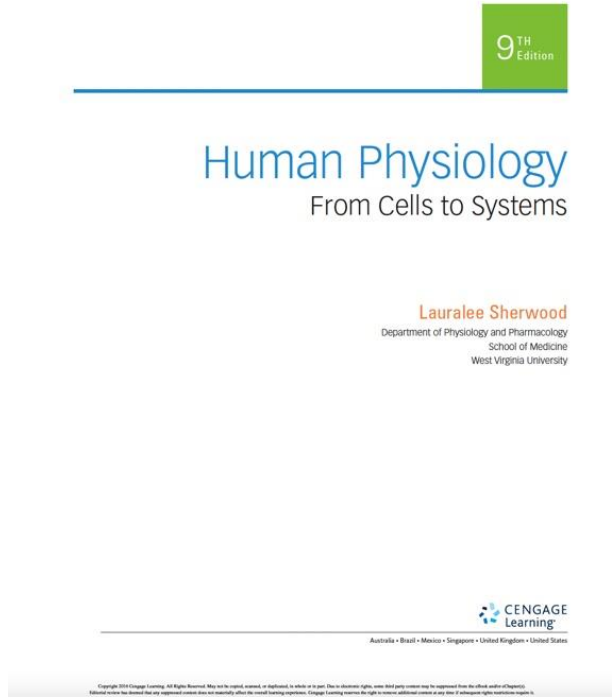


# References


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

# Local control

- most tissues have the ability to control their own local blood flow in proportion to their specific metabolic needs.
- Local controls override sympathetic vasoconstriction.
- Skeletal and cardiac local controls are the most effective.

# Local blood flow control

- Local blood flow control can be divided into two phases, acute control and long-term control.
- Acute control is achieved by rapid changes in local vasodilation or vasoconstriction of the arterioles, metarterioles, and precapillary sphincters that occur within seconds to minutes to provide rapid maintenance of appropriate local tissue blood flow.
- 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.

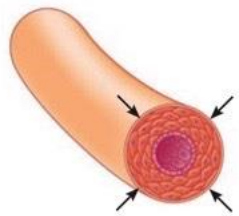
- two main theories have been proposed, the vasodilator theory and the oxygen demand theory.

# 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.

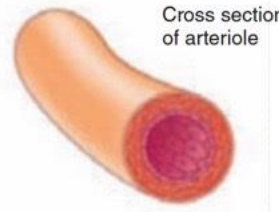
# Acute control of local blood flow

- 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.

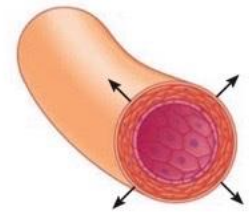


**Caused by:**
- ↑ Myogenic activity
- ↑ Oxygen ($O_2$)
- ↓ Carbon dioxide ($CO_2$) and other metabolites
- ↑ Endothelin
- ↑ Sympathetic stimulation
- Vasopressin; angiotensin II
- Cold

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




**(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

- Active hyperemia:
- When a tissue becomes highly active, such as an exercising muscle or the brain during increased mental activity, 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.

# 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,

# Blood flow autoregulation

- 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.

# Acute control of blood flow in the kidney

- 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.

# 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.

# Long term blood flow regulation

- long-term regulation gives far more complete control of blood flow.
- 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 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.

- 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.

# Long term blood flow regulation: changes in tissue vascularity

- In premature babies who are put into oxygen tents 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.

# Long term blood flow regulation: changes in tissue vascularity

- Vascular growth factors
- Steroid hormones
- Antiangiogenic factors

- Vascularity Determined by Maximum Blood Flow Need, Not by Average Need.

# Long term blood flow regulation: changes in tissue vascularity

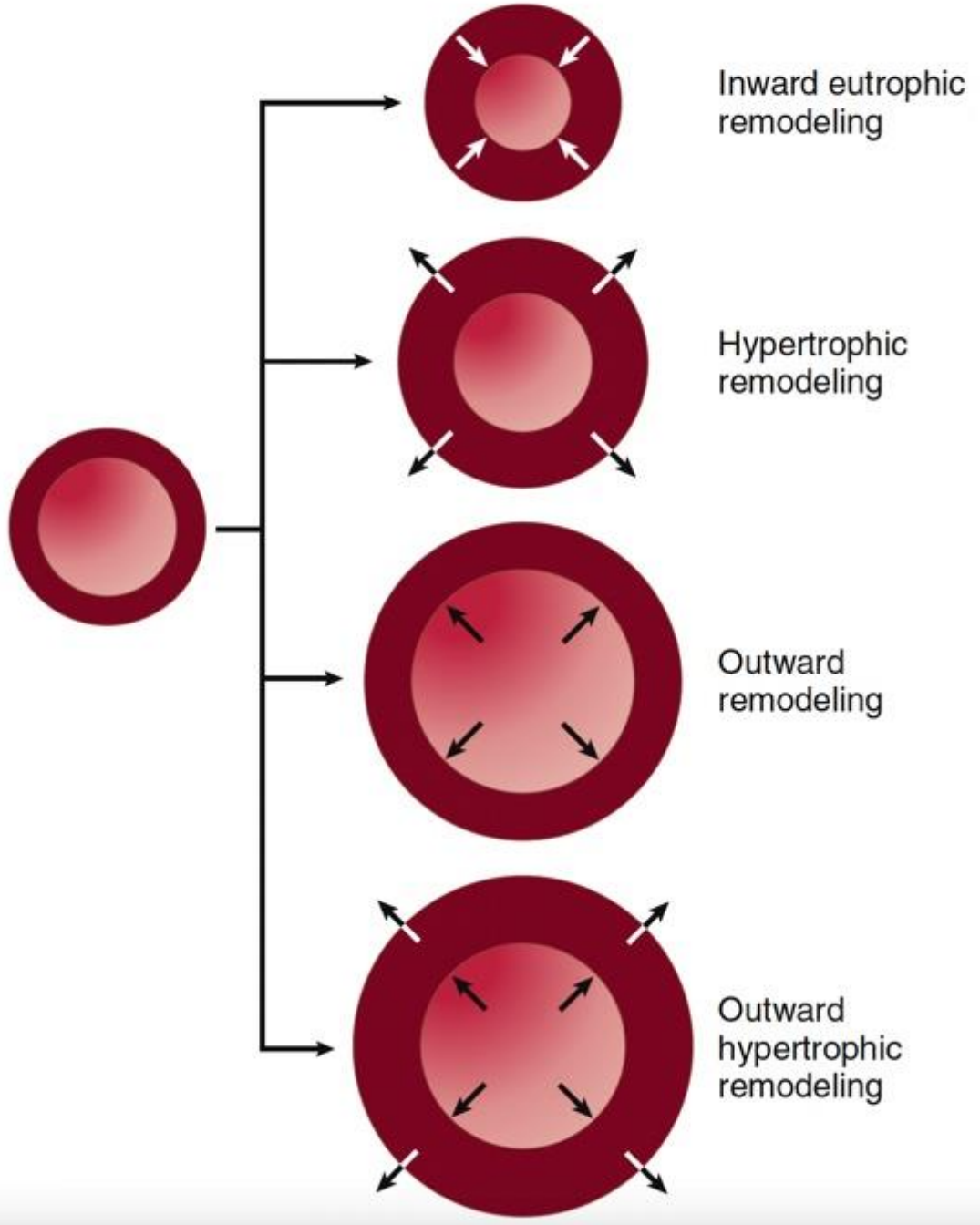
- Collateral circulation
- An important example of the development of collateral blood vessels occurs after thrombosis of one of the coronary arteries. By the age of 60 years, many people have experienced closure or at least partial occlusion of at least one of the smaller branch coronary vessels, but 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

- 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.
- 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): $T = r \times P$

# 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—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.


Inward eutrophic remodeling
Hypertrophic remodeling
Outward remodeling
Outward hypertrophic remodeling

# 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.

# 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.

# 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

- 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.)
- 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, 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:
- 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.
- 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.
- 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