Vascular Physiology

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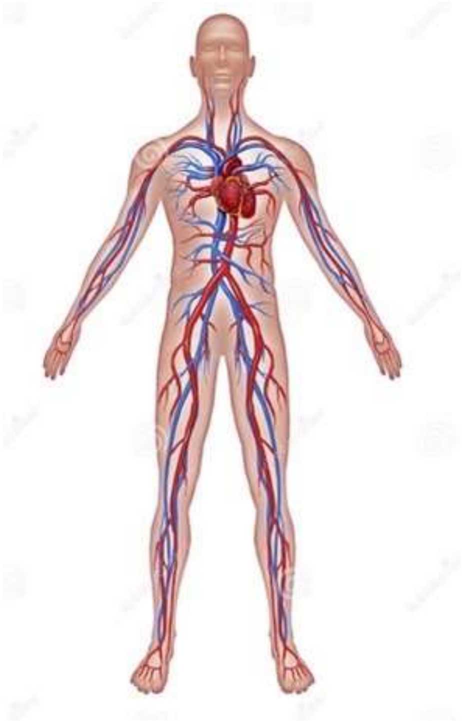
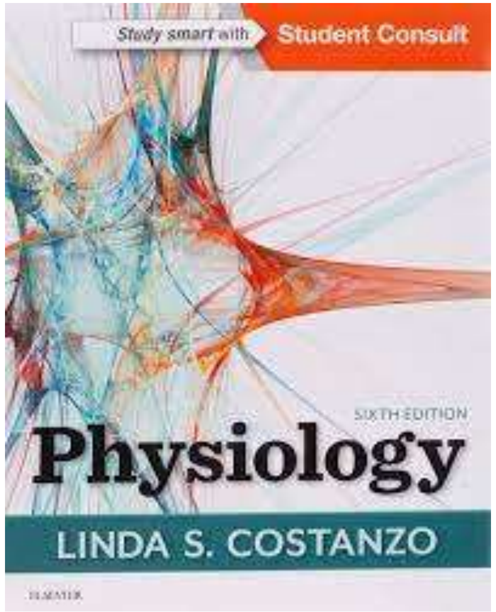


References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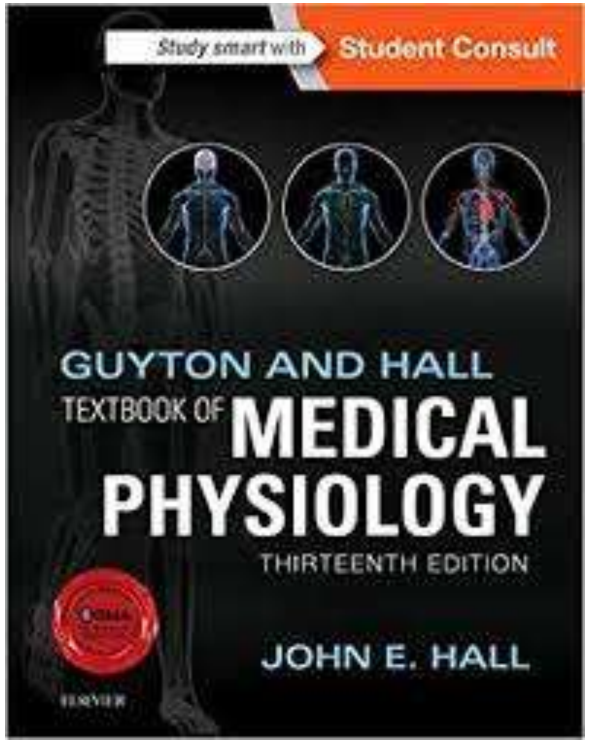
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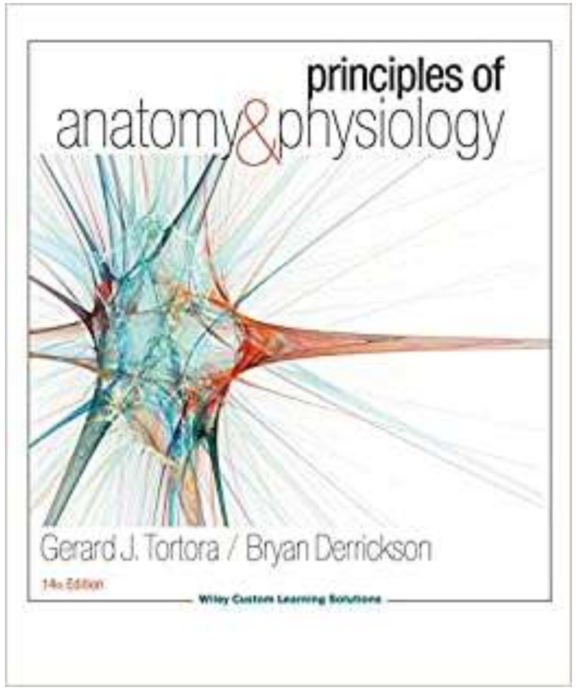
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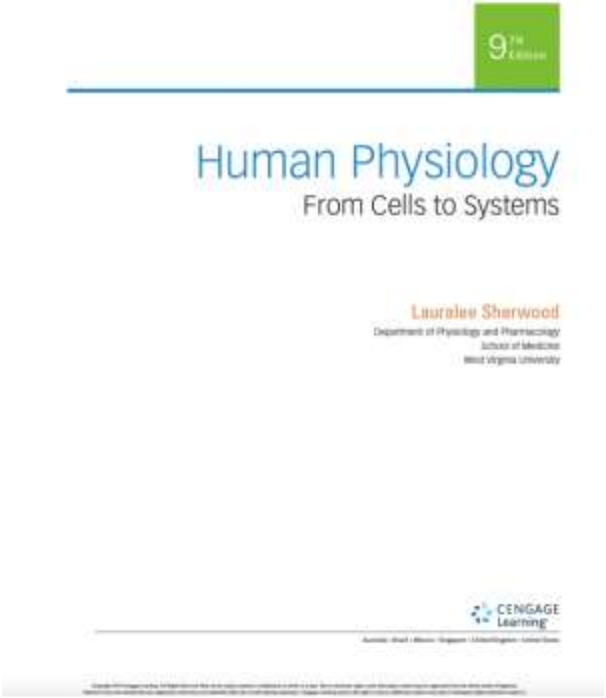
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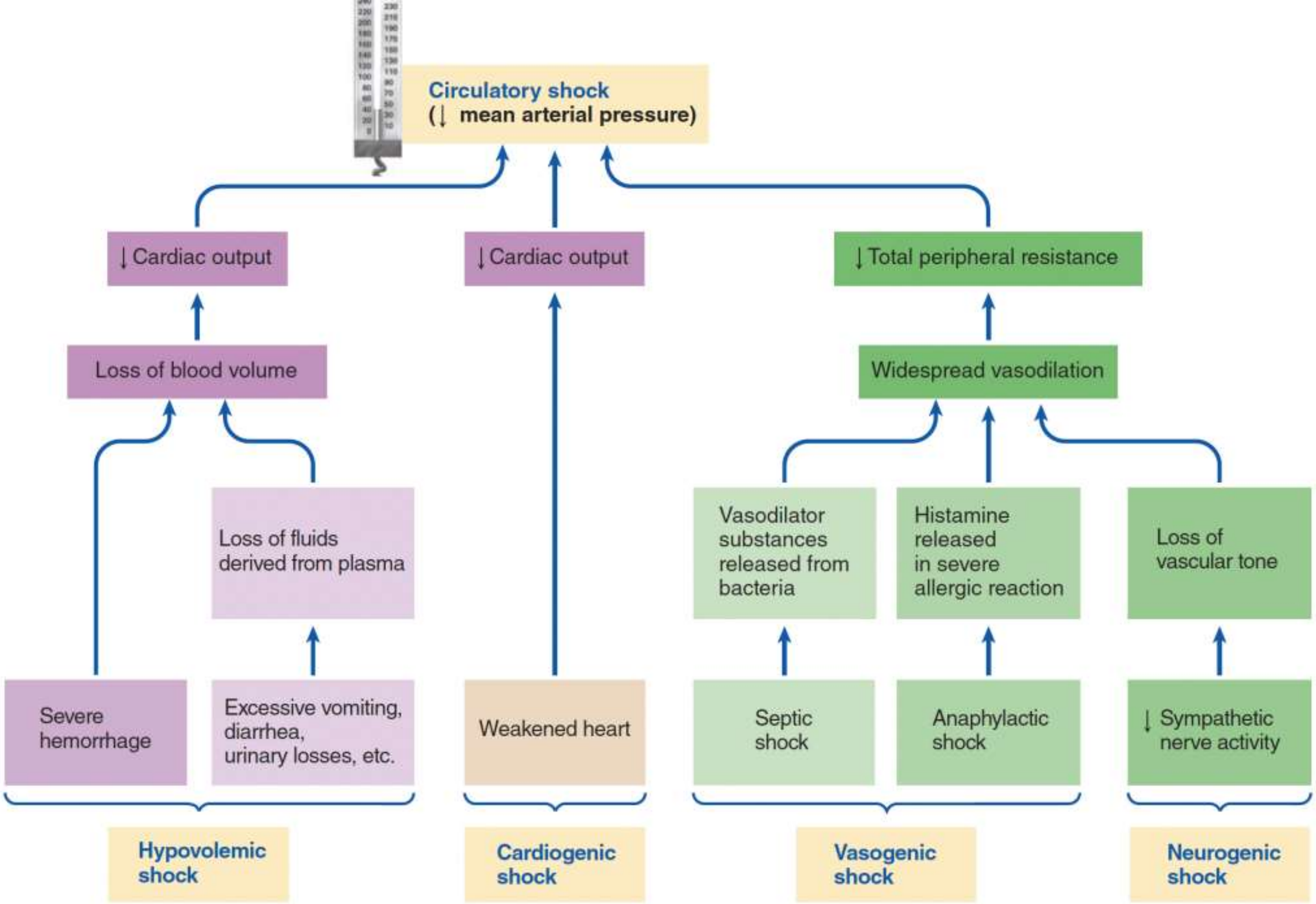
Special circulations

Circulatory Shock

- Circulatory shock may result from
- (1) extensive loss of blood volume as through hemorrhage (hypovolemic shock)
- (2) failure of a weakened heart to pump blood adequately (cardiogenic shock)
- (3) widespread arteriolar vasodilation (vasogenic shock) triggered by vasodilator substances (such as extensive histamine release in severe allergic reactions)
- (4) neurally defective vasoconstrictor tone (neurogenic shock)

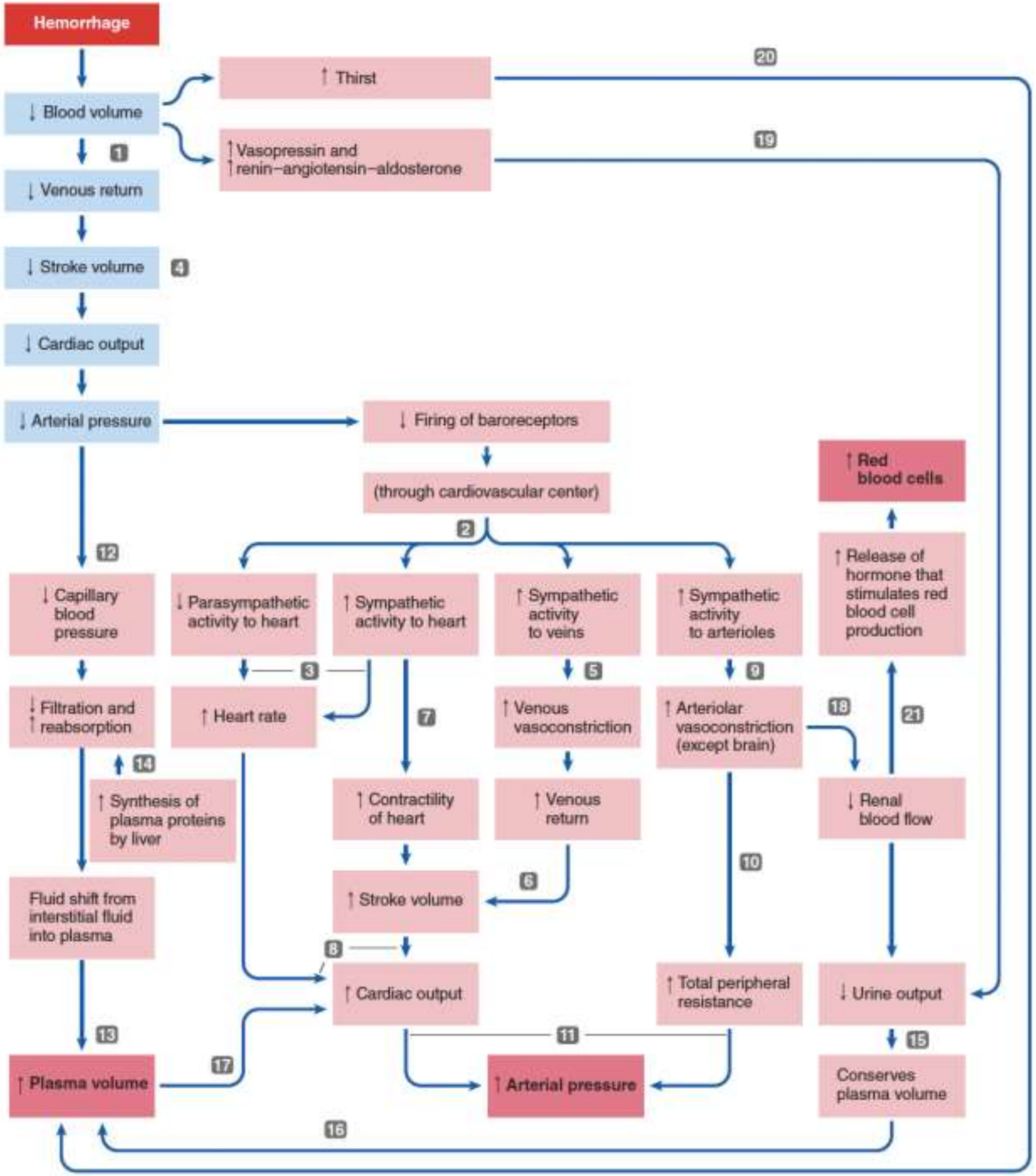

Circulatory shock
(↓ mean arterial pressure)
↓ Cardiac output
↓ Cardiac output
↓ Total peripheral resistance
Loss of blood volume
Widespread vasodilation
Loss of fluids derived from plasma
Vasodilator substances released from bacteria
Histamine released in severe allergic reaction
Loss of vascular tone
Severe hemorrhage
Excessive vomiting, diarrhea, urinary losses, etc.
Weakened heart
Septic shock
Anaphylactic shock
↓ Sympathetic nerve activity
Hypovolemic shock
Cardiogenic shock
Vasogenic shock
Neurogenic shock

Stages of Circulatory Shock

- Compensated

- Progressive

- Irreversible



Hemorrhage
↓ Blood volume
↑ Thirst
↑ Vasopressin and
↑ renin–angiotensin–aldosterone
↓ Venous return
↓ Stroke volume
↓ Cardiac output
↓ Arterial pressure
↓ Firing of baroreceptors
(through cardiovascular center)
↑ Red blood cells
↑ Release of hormone that stimulates red blood cell production
↓ Capillary blood pressure
↓ Parasympathetic activity to heart
↑ Sympathetic activity to heart
↑ Sympathetic activity to veins
↑ Sympathetic activity to arterioles
↓ Filtration and
↑ reabsorption
↑ Heart rate
↑ Venous vasoconstriction
↑ Arteriolar vasoconstriction (except brain)
↓ Renal blood flow
↑ Synthesis of plasma proteins by liver
↑ Contractility of heart
↑ Venous return
↑ Stroke volume
Fluid shift from interstitial fluid into plasma
↑ Cardiac output
↑ Total peripheral resistance
↓ Urine output
↑ Plasma volume
↑ Arterial pressure
Conserves plasma volume
1
2
3
4
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Coronary circulation

- An unusual feature of the coronary circulation is the effect of mechanical compression of the blood vessels during systole in the cardiac cycle.
- This compression causes a brief period of occlusion and reduction of blood flow.
- When the period of occlusion (i.e., systole) is over, reactive hyperemia occurs to increase blood flow and O_2 delivery.

Coronary circulation

- Metabolic factors, especially myocardial oxygen consumption, are the major controllers of myocardial blood flow.

- Whenever the direct effects of nervous stimulation reduce coronary blood flow, the metabolic control of coronary flow usually overrides the direct coronary nervous effects within seconds.

Cerebral circulation

- The cerebral circulation is controlled almost entirely by local metabolites and exhibits autoregulation and active and reactive hyperemia.

- The most important local vasodilator in the cerebral circulation is CO_2 (or H^+). An increase in cerebral PCO_2 (producing an increase in H^+ concentration and a decrease in pH) causes vasodilation of the cerebral arterioles, which results in an increase in blood flow to assist in removal of the excess CO_2.

- It is interesting that many circulating vasoactive substances do not affect the cerebral circulation because their large molecular size prevents them from crossing the blood-brain barrier.

Pulmonary circulation

- The pulmonary circulation is controlled by O_2.
- The effect of O_2 on pulmonary arteriolar resistance is the exact opposite of its effect in other vascular beds:

- In the pulmonary circulation, hypoxia causes vasoconstriction.

- Regions of hypoxia in the lung cause local vasoconstriction, which effectively shunts blood away from poorly ventilated areas where the blood flow would be “wasted” and toward well-ventilated areas where gas exchange can occur.

Renal circulation

- Renal blood flow is tightly autoregulated so that flow remains constant even when renal perfusion pressure changes.

- Renal autoregulation is independent of sympathetic innervation, and it is retained even when the kidney is denervated (e.g., in a transplanted kidney).

Skeletal muscle circulation

- Blood flow to skeletal muscle is controlled both by local metabolites and by sympathetic innervation of its vascular smooth muscle.

- The degree of vasoconstriction of skeletal muscle arterioles is a major determinant of TPR because the mass of skeletal muscle is so large, compared with that of other organs.

Skeletal muscle circulation

- At **rest,** blood flow to skeletal muscle is regulated primarily by its sympathetic innervation.
- Vascular smooth muscle in the arterioles of skeletal muscle is densely innervated by sympathetic nerve fibers that are vasoconstricting ($\alpha 1$ receptors).
- There are also $\beta 2$ receptors on the vascular smooth muscle of skeletal muscle that are activated by epinephrine and cause vasodilation.
- Thus activation of $\alpha 1$ receptors causes vasoconstriction, increased resistance, and decreased blood flow.
- Activation of $\beta 2$ receptors causes vasodilation, decreased resistance, and increased blood flow.
- Usually, vasoconstriction predominates

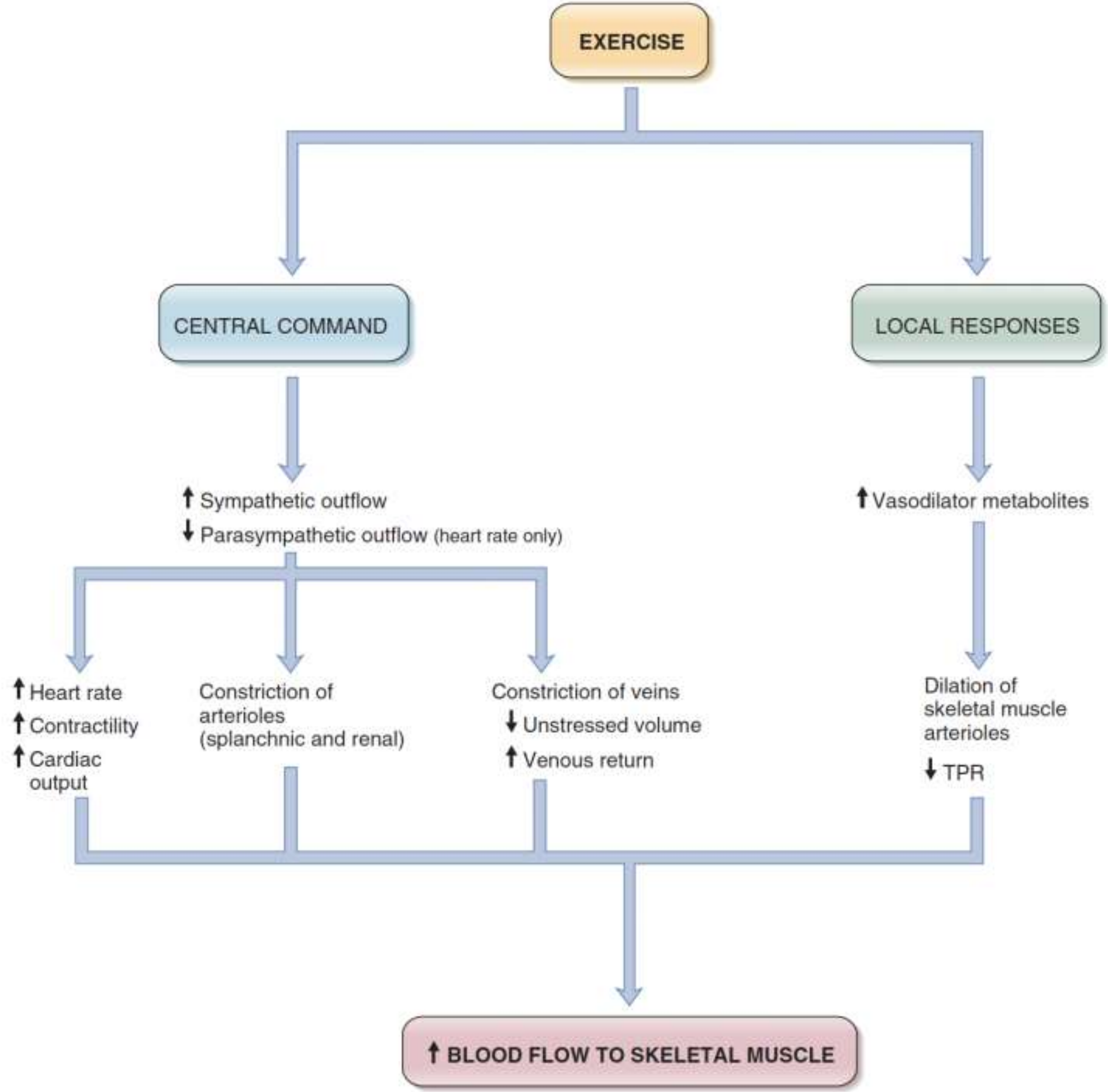
Skeletal muscle circulation

- During **exercise**, blood flow to skeletal muscle is controlled primarily by local metabolites.
- Each of the phenomena of local control is exhibited: **autoregulation and active and reactive hyperemia.**
- During exercise, the demand for O_2 in skeletal muscle varies with the activity level, and, accordingly, blood flow is increased or decreased to deliver sufficient O_2 to meet the demand.
- The local vasodilator substances in skeletal muscle are lactate, adenosine, and K^+.
- Mechanical compression of the blood vessels in skeletal muscle can also occur during exercise and cause brief periods of occlusion.
- When the period of occlusion is over, a period of reactive hyperemia will occur, which increases blood flow and O_2 delivery.

Exercise

- The CNS responses include a central command from the cerebral motor cortex, which directs changes in the autonomic nervous system.

- The local responses include effects of metabolites to increase blood flow and O2 delivery to the exercising skeletal muscle.


EXERCISE
CENTRAL COMMAND
LOCAL RESPONSES
↑ Sympathetic outflow
↓ Parasympathetic outflow (heart rate only)
↑ Vasodilator metabolites
↑ Heart rate
↑ Contractility
↑ Cardiac output
Constriction of arterioles (splanchnic and renal)
Constriction of veins
↓ Unstressed volume
↑ Venous return
Dilation of skeletal muscle arterioles
↓ TPR
↑ BLOOD FLOW TO SKELETAL MUSCLE

Exercise

- The central command refers to a series of responses, directed by the cerebral motor cortex, which are initiated by the anticipation of exercise.

- The efferent limb of the reflex produces increased sympathetic outflow to the heart and blood vessels and decreased parasympathetic outflow to the heart.

Exercise

- Cardiac output cannot increase without a concomitant increase in venous return (Frank-Starling relationship).

- In exercise, this concomitant increase in **venous return** is accomplished by two effects on the veins: The contraction of skeletal muscle around the veins has a **mechanical (squeezing) action, and activation of the sympathetic** nervous system produces venoconstriction.

Exercise

- Another consequence of the increased sympathetic outflow in the central command is **selective arteriolar vasoconstriction**.

- In the circulation of the skin, splanchnic regions, kidney, and inactive muscles, vasoconstriction occurs via $\alpha 1$ receptors, which results in increased resistance and decreased blood flow to those organs.

Exercise

- In the exercising skeletal muscle, however, local metabolic effects override any sympathetic vasoconstricting effects, and arteriolar vasodilation occurs.

- Other locations where vasoconstriction does not occur are in the coronary circulation (where blood flow increases to meet the increased level of myocardial O_2 consumption) and the cerebral circulation.

Exercise

- In the **cutaneous circulation, there is a biphasic response.** Initially, vasoconstriction occurs (due to increased sympathetic outflow); later, however, as body temperature increases, there is selective inhibition of sympathetic cutaneous vasoconstriction resulting in vasodilation and dissipation of heat through the skin.

Exercise

- Local control of blood flow in the exercising skeletal muscle is orchestrated by active hyperemia.
- As the metabolic rate of the skeletal muscle increases, production of vasodilator metabolites such as lactate, K^+, and adenosine also increases.
- These metabolites act directly on the arterioles of the exercising muscle to produce local vasodilation.
- Vasodilation of the arterioles results in increased blood flow to meet the increased metabolic demand of the muscle.
- This **vasodilation in the exercising muscle also produces an overall decrease in TPR.**

Skin circulation

- The skin has blood vessels with dense sympathetic innervation, which controls its blood flow.
- The principal function of the sympathetic innervation is to alter blood flow to the skin for **regulation of body temperature.**
- **Local vasodilator metabolites have little effect on cutaneous blood flow.**

Temperature regulation

- Humans maintain a normal body temperature at a set point of 37°C (98.6°F).
- Because environmental temperatures vary greatly, the body has mechanisms, coordinated in the anterior hypothalamus, for both heat generation and heat loss to keep body temperature constant.
- When the environmental temperature decreases, the body generates and conserves heat.
- When the environmental temperature increases, the body reduces heat production and dissipates heat.

Mechanisms for generating heat

- When environmental temperature is less than body temperature, mechanisms are activated that increase heat production and reduce heat loss.
- These mechanisms include **stimulation of thyroid hormone** production, **activation of the sympathetic nervous system, and shivering.**
- **Behavioral** components also may contribute by reducing the exposure of skin to the cold (e.g., wrapping arms around oneself, adding more clothing).

Mechanisms for generating heat

- Thyroid hormones are thermogenic: Their actions on target tissues result in heat production.

- Therefore, it is logical that exposure to cold temperatures activates thyroid hormones.

Mechanisms for generating heat

- Because **thyroid hormones are thermogenic**, it follows that an excess or deficit of thyroid hormones would cause disturbances in the regulation of body temperature.
- In hyperthyroidism, metabolic rate increases, O_2 consumption increases, and heat production increases.
- In hypothyroidism, there is a decreased metabolic rate, decreased O_2 consumption, decreased heat production, and extreme sensitivity to cold.

Mechanisms for generating heat

- Cold environmental temperatures activate the **sympathetic nervous system.**
- One consequence of this activation is **stimulation of β receptors in brown fat,** which increases metabolic rate and heat production.
- This action of the sympathetic nervous system is synergistic with the actions of thyroid hormones:
- For thyroid hormones to produce maximal thermogenesis, the sympathetic nervous system must be simultaneously activated by cold temperatures.
- A second consequence of activation of the sympathetic nervous system is stimulation of $\alpha 1$ receptors in vascular smooth muscle of skin blood vessels, producing vasoconstriction.
- Vasoconstriction **reduces blood flow to the surface of the skin and, consequently, reduces heat loss**.

Mechanisms for generating heat

- **Shivering**, which involves rhythmic contraction of skeletal muscle, is the most potent mechanism for increasing heat production in the body.
- Cold environmental temperatures activate centers in the posterior hypothalamus, which then activate the **α and γ motoneurons innervating skeletal muscle.**
- The skeletal muscle contracts rhythmically, generating heat and raising body temperature.

Mechanisms for dissipating heat

- When the environmental temperature increases, mechanisms are activated that result in increased heat loss from the body.
- Since heat is a normal byproduct of metabolism, the body must dissipate this heat just to maintain body temperature at the set point.
- Mechanisms for dissipating heat are coordinated in the anterior hypothalamus.
- Increased body temperature **decreases sympathetic activity** in skin blood vessels.

Mechanisms for dissipating heat

- This decrease in sympathetic tone results in increased blood flow through skin arterioles and greater arteriovenous shunting of blood to venous plexuses near the surface of skin.
- In effect, warm blood from the body core is shunted to the body surface.
- Shunting of blood to the surface is evidenced by redness and warmth of the skin.
- There also is increased activity of the **sympathetic cholinergic fibers innervating thermoregulatory sweat glands** to produce increased sweating (cooling).
- The **behavioral** components to dissipate heat include increasing the exposure of skin to the air (e.g., removing clothing, fanning).

Regulation of body temperature

- The temperature-regulating center is located in the anterior hypothalamus. This center receives information about environmental temperature from thermoreceptors in the skin and about core temperature from thermoreceptors in the anterior hypothalamus itself.
- The anterior hypothalamus then orchestrates the appropriate responses, which may involve heat generating or heat-dissipating mechanisms.
- If core temperature is below the set-point temperature, then heat-generating and heat-retaining mechanisms are activated.
- If core temperature is above the set-point temperature, then heat-dissipating mechanisms are activated.
- These mechanisms include vasodilation of blood vessels of the skin (decreased sympathetic tone) and increased activity of sympathetic cholinergic fibers to sweat glands

Fever

- Fever is an abnormal elevation of body temperature.
- **Pyrogens** produce fever by **increasing the hypothalamic set-point temperature**. The result of such a change in set point is that a normal core temperature is “seen” by the hypothalamic center as too low relative to the new set point. The anterior hypothalamus then activates heat-generating mechanisms (e.g., shivering) to raise body temperature to the new set point.

- At the cellular level, the mechanism of pyrogen action is increased production of interleukin-1 (IL-1) in phagocytic cells. IL-1 then acts on the anterior hypothalamus to increase local production of **prostaglandins**, which increase the set-point temperature.

Fever

- When fever is treated, the temperature sensors in the anterior hypothalamus now “see” body temperature as too high relative to the set-point temperature and set in motion the mechanisms for dissipating heat including vasodilation and sweating.

Disturbances of temperature regulation

- Heat exhaustion can occur as a consequence of the body’s responses to elevated environmental temperature.
- Normally, the response to increased temperature includes vasodilation and sweating in order to dissipate heat.
- However, if the sweating is excessive, it can result in decreased ECF volume, decreased blood volume, decreased arterial pressure, and fainting.
- Heat stroke occurs when body temperature increases to the point of tissue damage.
- If the normal response to elevated environmental temperature is impaired (e.g., if sweating does not occur), then heat cannot be appropriately dissipated and core temperature increases to dangerous levels.

Malignant hyperthermia

- Malignant hyperthermia is characterized by a massive increase in metabolic rate, increased O2 consumption, and increased heat production in skeletal muscle.
- The heat-dissipating mechanisms are unable to keep pace with the excessive heat production, and if the hyperthermia is not treated, body temperature may increase to dangerously high, or even fatal, levels.
- In susceptible individuals, malignant hyperthermia can be caused by inhalation anesthetics.

Thank you