

**MINISTRY OF HEALTH SERVICE OF UKRAINE**

Zaporozhye State Medical University

The Department of Normal Physiology

# **The autonomic (visceral motor) nervous system**

A electronic manual for independent work at home and in class  
for student for licensing examination “KROK 1”  
on semantic modules 4 of module 1

for students of International Faculty  
(the second year of study)

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and it is recommended for the use in educational process for foreign students.*

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Methodical recommendations compiled in accordance with the program of "normal physiology". Guidelines are intended to help students prepare for practical classes and learn the material. Can be used for training of 2<sup>th</sup>-years students of international faculty, discipline "normal physiology".

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**Theme actuality.** The autonomic nervous system can play a key role in processes regulation of visceral organs. The autonomic nervous system (ANS) is considered to execute its actions subconsciously in contrast to the voluntary nature of the somatic motor system. It provides *visceral reflexes*—reflexes that regulate such primitive functions as blood pressure, heart rate, body temperature, digestion, energy metabolism, respiratory airflow, pupillary diameter, defecation, and urination. In short, the ANS quietly manages a myriad of unconscious processes responsible for the body’s homeostasis. During the course of each disease our visceral functions are altered more or less in some extent. Understanding the regulation of the functions of internal organs with the help of sympathetic and parasympathetic system is necessary in the practice of every physician. Not surprisingly, many drug therapies are based on alteration of autonomic function.

**Study purposes:** to know the principles regulating the functions of internal organs via the autonomic nervous system.

**Concrete purposes of the module:**

**A student must know:**

- Anatomical peculiarities of the ANS divisions;
- Neurotransmitter substances operating in the sympathetic and parasympathetic nervous system;
- Appropriate receptors for the main autonomic neurotransmitters;
- Principles of dual innervation and autonomic “tone”;
- Features of the “fight or flight” reaction and “resting and digesting” state;
- Effects of stimulation on the target organs in case of sympathetic or parasympathetic excitation.

## **General principles of anatomical organization of the autonomic nervous system**

The portion of the nervous system that controls most visceral functions of the body is called the *autonomic nervous system*. This system helps to control arterial pressure, gastrointestinal motility, gastrointestinal secretion, urinary bladder emptying, sweating, body temperature, and many other activities, some of which are controlled almost entirely and some only partially by the autonomic nervous system.

The autonomic nervous system is activated mainly by centers located in the *spinal cord, brain stem, and hypothalamus*. Also, portions of the cerebral cortex, especially of the limbic cortex, can transmit signals to the lower centers and in this way influence autonomic control.

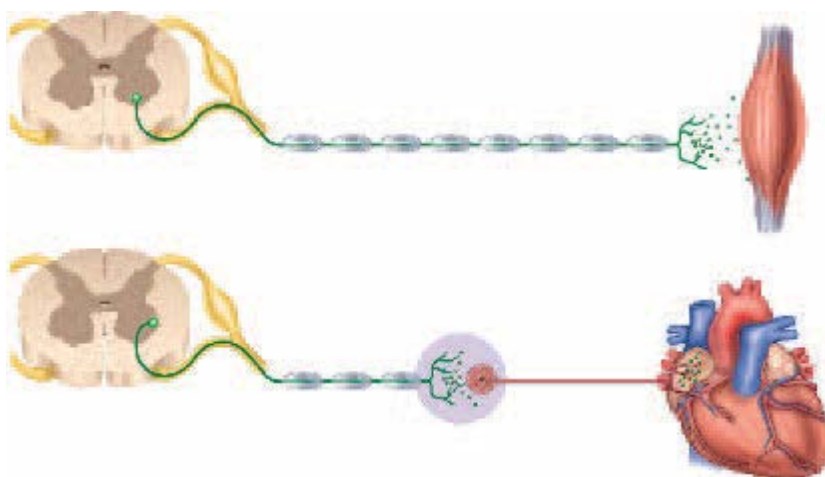
The autonomic nervous system also often operates by means of *visceral reflexes*. That is, subconscious sensory signals from a visceral organ can enter the autonomic ganglia, the brain stem, or the hypothalamus and then return *subconscious reflex responses* directly back to the visceral organ to control its activities.

The efferent autonomic signals are transmitted to the various organs of the body through two major subdivisions called the *sympathetic nervous system* and the *parasympathetic nervous system*, the characteristics and functions of which follow.

These divisions differ in anatomy and function, but they often innervate the same target organs and may have cooperative or contrasting effects on them. The **sympathetic division** prepares the body in many ways for physical activity—it increases alertness, heart rate, blood pressure, pulmonary airflow, blood glucose concentration, and blood flow to cardiac and skeletal muscle, but at the same time, it reduces blood flow to the skin and digestive tract. Cannon referred to extreme sympathetic responses as the “fight or flight” reaction because they come into play when an animal must attack, defend itself, or flee from danger. In our own lives,

this reaction occurs in many situations involving arousal, competition, stress, danger, anger, or fear. Ordinarily, however, the sympathetic division has more subtle effects that we notice barely, if at all. The **parasympathetic division**, by comparison, has a calming effect on many body functions. It is associated with reduced energy expenditure and normal bodily maintenance, including such functions as digestion and waste elimination. This can be thought of as the “resting and digesting” state.

The autonomic motor pathway to a target organ differs significantly from somatic motor pathways. In somatic pathways, a motor neuron in the brainstem or spinal cord issues a myelinated axon that reaches all the way to a skeletal muscle. In autonomic pathways, the signal must travel across two neurons to get to the target organ, and it must cross a synapse where these two neurons meet in an autonomic ganglion. The first neuron, called the **preganglionic neuron**, has a soma in the brainstem or spinal cord whose axon terminates in the ganglion. It synapses there with a **postganglionic neuron** whose axon extends the rest of the way to the target cells, (fig. 1). (Some call this cell the *ganglionic neuron* since its soma is in the ganglion and only its axon is truly postganglionic.) The axons of these neurons are called the *pre-* and *postganglionic fibers*.



**Fig. 1. Somatic and autonomic efferent innervations**

In summary, the autonomic nervous system is a division of the nervous system responsible for homeostasis, acting through the mostly unconscious and involuntary control of glands, smooth muscle, and cardiac muscle. Its target organs are mostly the thoracic and abdominal viscera, but also include some cutaneous and other effectors. It acts through motor pathways that involve two neurons, preganglionic and postganglionic, reaching from CNS to effector. The ANS has two divisions, sympathetic and parasympathetic, that often have cooperative or contrasting effects on the same target organ. Both divisions have excitatory effects on some target cells and inhibitory effects on others. These and other differences between the somatic and autonomic nervous systems are summarized in table 1.

**Table 1. Comparison of the somatic and autonomic nervous systems**

<b>Feature</b>	<b>Somatic</b>	<b>Autonomic</b>
Effectors	Skeletal muscle	Glands, smooth muscle, cardiac muscle
Efferent pathways	One nerve fiber from CNS to effector; no ganglia	Two nerve fibers from CNS to effector; synapse at a ganglion
Neurotransmitters	Acetylcholine (ACh)	ACh and norepinephrine (NE)
Effect on target cells	Always excitatory	Excitatory or inhibitory
Effect of denervation	Flaccid paralysis	Denervation hypersensitivity
Control	Usually voluntary	Usually involuntary

### **The sympathetic division**

The sympathetic division is also called the *thoracolumbar division* because it arises from the thoracic and lumbar regions of the spinal cord. It has relatively short preganglionic and long postganglionic fibers. The preganglionic somas are in the lateral horns and nearby regions of the gray matter of the spinal cord. Their

fibers exit by way of spinal nerves T1 to L2 and lead to the nearby **sympathetic chain** of ganglia (**paravertebral ganglia**) along each side of the vertebral column, (fig. 2). Although these chains receive input from only the thoracolumbar region of the cord, they extend into the cervical and sacral to coccygeal regions as well. Some nerve fibers entering the chain at levels T1 to L2 travel up or down the chain to reach these cervical and sacral ganglia. The number of ganglia varies from person to person, but usually there are 3 cervical (*superior, middle, and inferior*), 11 thoracic, 4 lumbar, 4 sacral, and 1 coccygeal ganglion in each chain.

In the thoracolumbar region, each paravertebral ganglion is connected to a spinal nerve by two branches called *communicating rami*. The preganglionic fibers are small myelinated fibers that travel from the spinal nerve to the ganglion by way of the **white communicating ramus**, which gets its color and name from the myelin. Unmyelinated postganglionic fibers leave the ganglion by way of the **gray communicating ramus**, named for its lack of myelin and duller color, and by other routes. These long fibers extend the rest of the way to the target organ.

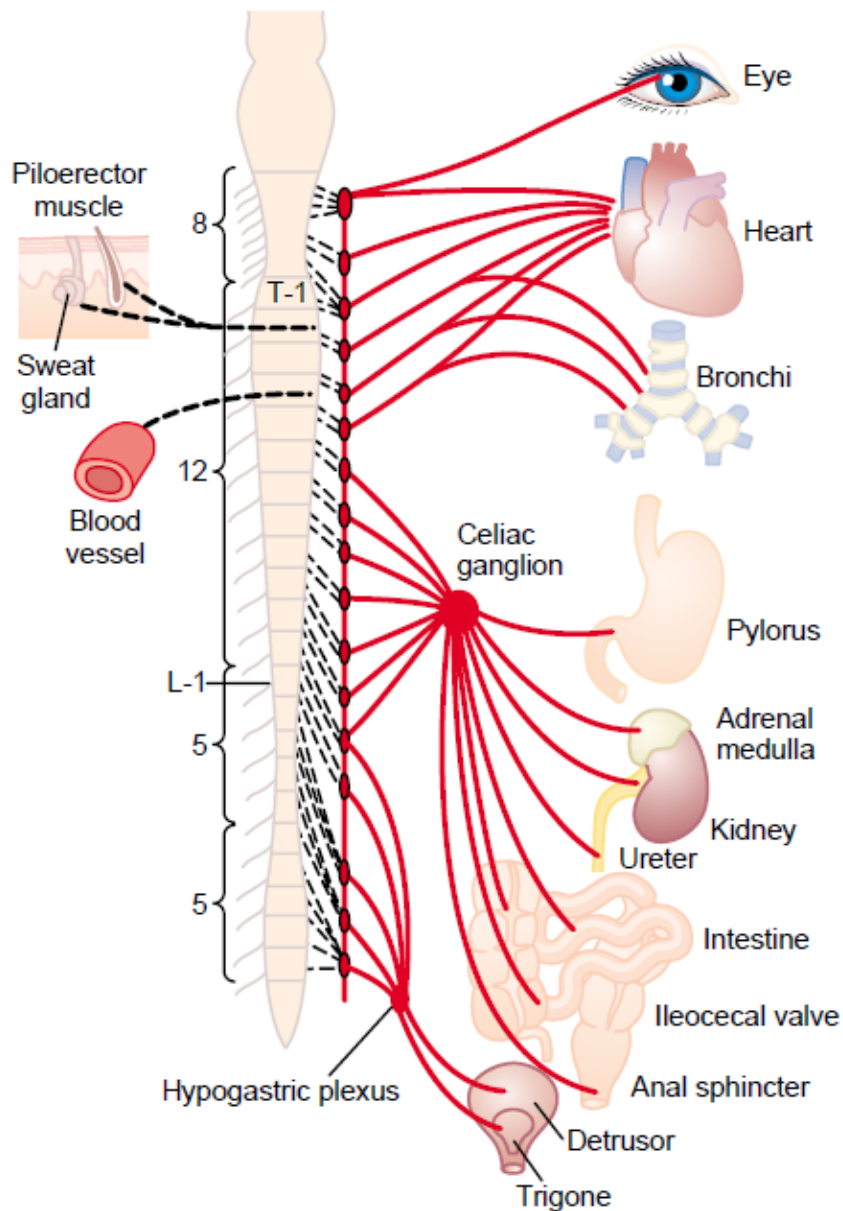
After entering the sympathetic chain, preganglionic fibers may follow any of three courses:

- Some end in the ganglion that they enter and synapse immediately with a postganglionic neuron.
- Some travel up or down the chain and synapse in ganglia at other levels. It is these fibers that link the paravertebral ganglia into a chain. They are the only route by which ganglia at the cervical, sacral, and coccygeal levels receive input.
- Some pass through the chain without synapsing and continue as *splanchnic nerves*, to be considered shortly.

There is no simple one-to-one relationship between preganglionic and postganglionic neurons in the sympathetic division. For one thing, each postganglionic cell may receive synapses from multiple preganglionic cells, thus exhibiting the principle of *neuronal convergence*. Furthermore, each preganglionic fiber branches and synapses with multiple postganglionic fibers, thus showing *neuronal divergence*. There are about 17 postganglionic neurons for every



preganglionic neuron in the sympathetic division. This means that when one preganglionic neuron fires, it can excite multiple postganglionic fibers leading to different target organs. The sympathetic division thus tends to have relatively widespread effects—as suggested by the name *sympathetic*.

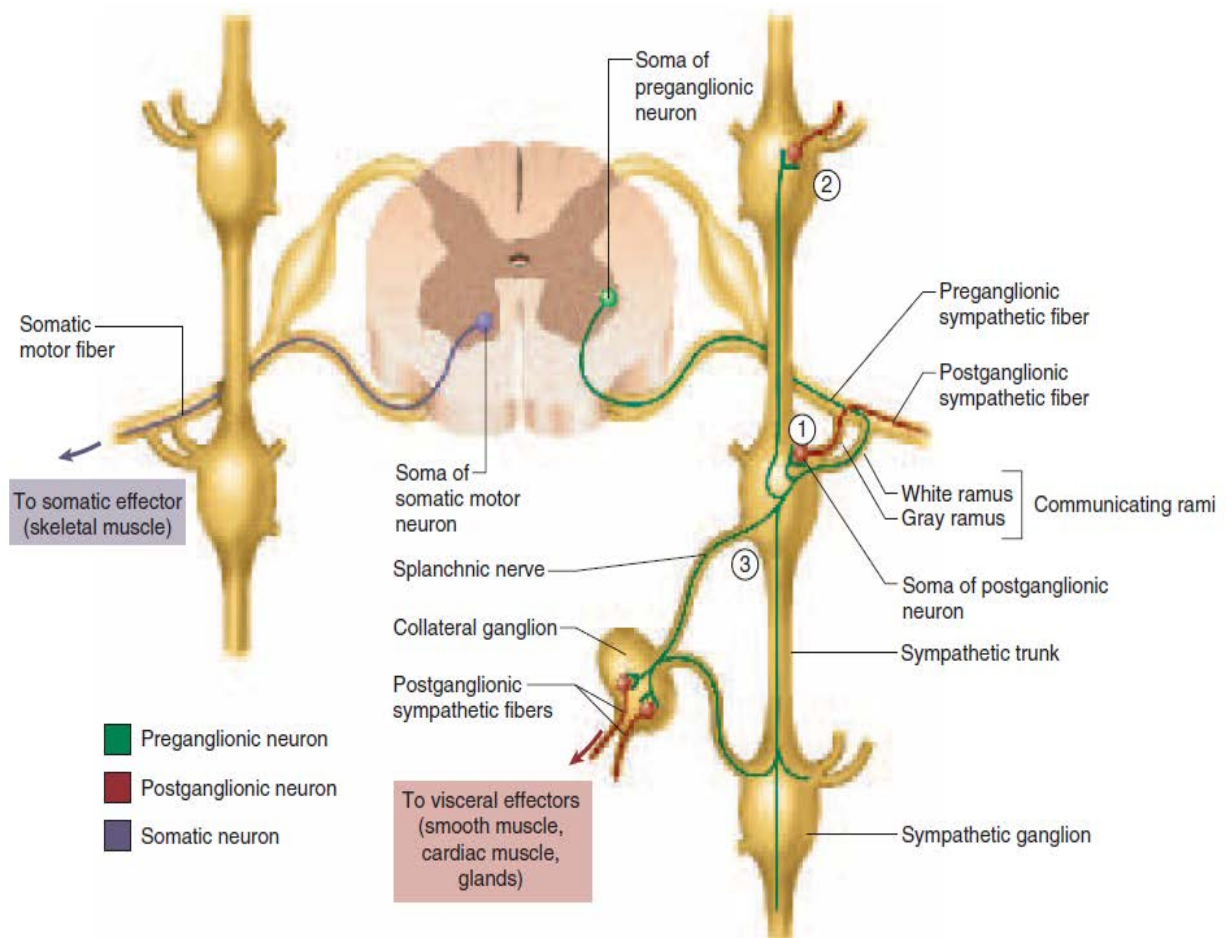


**Fig. 2. Sympathetic nervous system**

Nerve fibers leave the paravertebral ganglia by three routes: spinal, sympathetic, and splanchnic nerves. These are numbered in **figure 3** to correspond to the following descriptions:

1. **The spinal nerve route.** Some postganglionic fibers exit by way of the gray ramus, return to the spinal nerve or its subdivisions, and travel the rest of the way to the target organ. This is the route to most sweat glands, piloerector muscles, and blood vessels of the skin and skeletal muscles.

2. **The sympathetic nerve route.** Other postganglionic fibers leave by way of **sympathetic nerves** that extend to the heart, lungs, esophagus, and thoracic blood vessels. These nerves form a plexus around each carotid artery and issue fibers from there to effectors in the head—including sweat, salivary, and nasal glands; piloerector muscles; blood vessels; and dilators of the iris. Some fibers from the superior cervical ganglion form the *cardiac nerves* to the heart.



**Fig. 3. Sympathetic Pathways (right) Compared to Somatic Efferent 3.**

**The splanchnic nerve route.** This route is formed by fibers that originate predominantly from spinal nerves T5 to T12 and pass through the ganglia without synapsing. Beyond the ganglia, they form greater, lesser, and lumbar **splanchnic nerves**. These lead to the **collateral (prevertebral) ganglia**, which contribute to a network called the **abdominal aortic plexus** wrapped around the aorta. There are three major collateral ganglia in this plexus—the **celiac ganglion, superior mesenteric ganglion, and inferior mesenteric ganglion**—located at points where arteries of the same names branch off the aorta. The postganglionic fibers accompany these arteries and their branches to the target organs. (The term *solar plexus* is regarded by some authorities as a collective designation for the celiac and superior mesenteric ganglia, and by others as a synonym for the celiac ganglion only. The term comes from the nerves radiating from the ganglion like rays of the sun.) Innervation to and from the three major collateral ganglia is summarized in table 2.

**Pathways (left).** Sympathetic fibers can follow any of the three numbered routes: (1) the spinal nerve route, (2) the sympathetic nerve route, or (3) the splanchnic nerve route.

**Table 2. Innervation To and From the Collateral Ganglia**

<b>Sympathetic Ganglia and Splanchnic Nerve→</b>	<b>Collateral Ganglion→</b>	<b>Postganglionic Target Organs</b>
From thoracic ganglia 5 to 9 or 10 via greater splanchnic nerve	Celiac ganglion	Stomach, spleen, liver, small intestine, and kidneys
From thoracic ganglia 9 and 10 via lesser splanchnic nerve	Celiac and superior mesenteric ganglia	Small intestine and colon
From lumbar ganglia via lumbar splanchnic nerve	Celiac and inferior mesenteric ganglia	Distal colon, rectum, urinary bladder, and reproductive organs

**Segmental distribution of the sympathetic nerve fibers.** The sympathetic pathways that originate in the different segments of the spinal cord are not necessarily distributed to the same part of the body as the somatic spinal nerve fibers from the same segments. Instead, the sympathetic fibers from cord segment T-1 generally pass up the sympathetic chain to terminate in the head; from T-2 to terminate in the neck; from T-3, T-4, T-5, and T-6 into the thorax; from T-7, T-8, T-9, T-10, and T-11 into the abdomen; and from T-12, L-1, and L-2 into the legs. This distribution is only approximate and overlaps greatly.

Preganglionic sympathetic nerve fibers pass, without synapsing, all the way from the intermediolateral horn cells of the spinal cord, through the sympathetic chains, then through the splanchnic nerves, and finally into the two adrenal medullae. There they end directly on modified neuronal cells that secrete epinephrine and norepinephrine into the blood stream. These secretory cells embryologically are derived from nervous tissue and are actually themselves postganglionic neurons; indeed, they even have rudimentary nerve fibers, and it is the endings of these fibers that secrete the adrenal hormones epinephrine and norepinephrine.

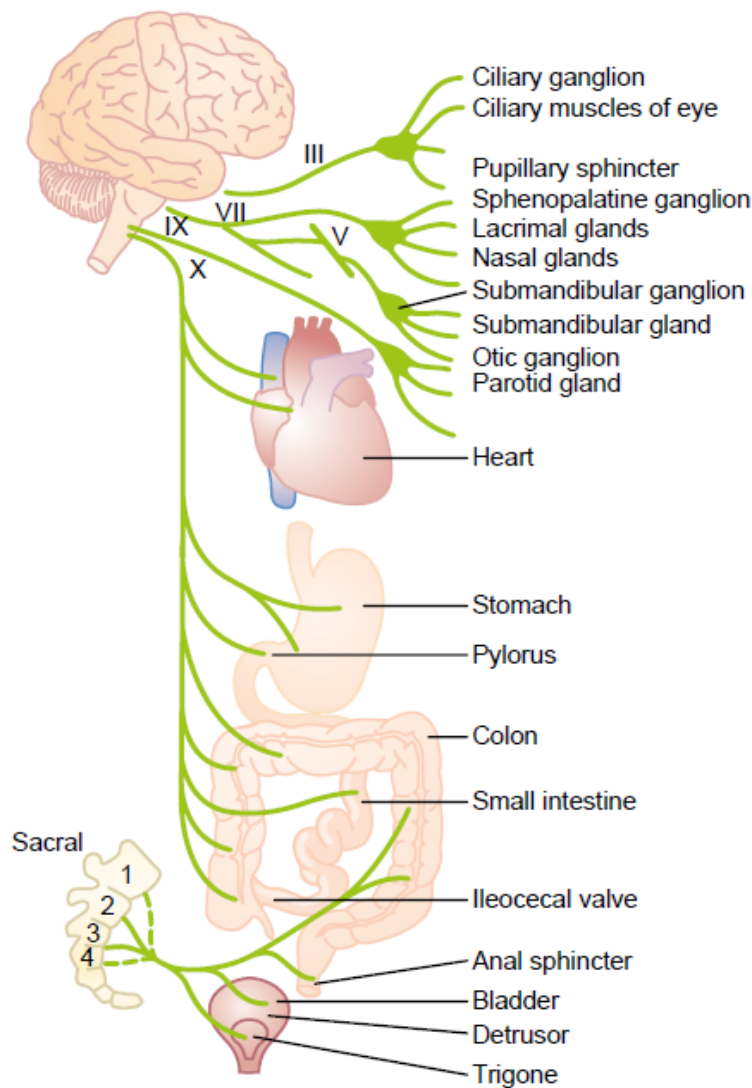
### **The parasympathetic division**

The parasympathetic division is also called the craniosacral division because it arises from the brain and sacral region of the spinal cord; its fibers travel in certain cranial and sacral nerves. The preganglionic neurons are located in the pons, medulla oblongata, and segments S2 to S4 of the spinal cord. They issue long preganglionic fibers which end in terminal ganglia in or near the target organ, (fig. 4). (If a terminal ganglion is embedded within the wall of a target organ, it is also called an intramural ganglion.) Thus, the parasympathetic division has long preganglionic fibers, reaching almost all the way to the target cells, and short postganglionic fibers that cover the rest of the distance.

Parasympathetic fibers leave the brainstem by way of the following four cranial nerves. The first three supply all parasympathetic innervation to the head and the last one supplies viscera of the thoracic and abdominal cavities.

**1. Oculomotor nerve (III).** The oculomotor nerve carries parasympathetic fibers that control the lens and pupil of the eye. The preganglionic fibers enter the orbit and terminate in the ciliary ganglion. Postganglionic fibers enter the eyeball and innervate the ciliary muscle, which thickens the lens, and the pupillary constrictor, which narrows the pupil.

**2. Facial nerve (VII).** The facial nerve carries parasympathetic fibers that regulate the tear glands, salivary glands, and nasal glands. Soon after the facial nerve emerges from the pons, its parasympathetic fibers split away and form two smaller branches. The upper branch ends at **the sphenopalatine ganglion** near the junction of the maxilla and palatine bones. Postganglionic fibers then continue to the tear glands and glands of the nasal cavity, palate, and other areas of the oral cavity. The lower branch crosses the middle-ear cavity and ends at **the submandibular ganglion** near the angle of the mandible. Postganglionic fibers from here supply salivary glands in the floor of the mouth.



**Fig. 4. Parasympathetic nervous system**

**3. Glossopharyngeal nerve (IX).** The glossopharyngeal nerve carries parasympathetic fibers concerned with salivation. The preganglionic fibers leave this nerve soon after its origin and form the tympanic nerve, which crosses the eardrum and ends in **the otic ganglion** near the foramen ovale. The postganglionic fibers then follow the trigeminal nerve to the parotid salivary gland just in front of the earlobe.

**4. Vagus nerve (X).** The vagus nerve carries about 90% of all parasympathetic preganglionic fibers. It travels down the neck and forms three networks in the mediastinum—the cardiac plexus, which supplies fibers to the heart; the pulmonary plexus, whose fibers accompany the bronchi and blood

vessels into the lungs; and the esophageal plexus, whose fibers regulate swallowing.

At the lower end of the esophagus, these plexuses give off anterior and posterior **vagal trunks**, each of which contains fibers from both the right and left vagus. These penetrate the diaphragm, enter the abdominal cavity, and contribute to the extensive abdominal aortic plexus mentioned earlier. As we have seen, sympathetic fibers synapse here. The parasympathetic fibers, however, pass through the plexus without synapsing and lead to the liver, pancreas, stomach, small intestine, kidney, ureter, and proximal half of the colon.

The remaining parasympathetic fibers arise from **levels S2 to S4 of the spinal cord**. They travel a short distance in the ventral rami of the spinal nerves and then form **pelvic splanchnic nerves** that lead to the **inferior hypogastric (pelvic) plexus**. Some parasympathetic fibers synapse here, but most pass through this plexus and travel by way of pelvic nerves to the terminal ganglia in their target organs: the distal half of the large intestine, the rectum, urinary bladder, and reproductive organs. The parasympathetic system does not innervate body wall structures (sweat glands, piloerector muscles, or cutaneous blood vessels). The sympathetic and parasympathetic divisions of the ANS are compared in table 3.

**Table 3. Comparison of the sympathetic and parasympathetic divisions**

<b>Feature</b>	<b>Sympathetic</b>	<b>Parasympathetic</b>
Origin in CNS	Thoracolumbar	Craniosacral
Location of ganglia	Paravertebral ganglia adjacent to spinal column and prevertebral ganglia anterior to it	Terminal ganglia near or within target organs
Fiber lengths	Short preganglionic Long postganglionic	Long preganglionic Short postganglionic
Neuronal divergence	Extensive (about 1:17)	Minimal (about 1:2)

Effects of system	Often widespread and general	More specific and local
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## Neurotransmitters

The sympathetic and parasympathetic nerve fibers secrete mainly one or the other of two synaptic transmitter substances, *acetylcholine (ACh)* or *norepinephrine (NE)*. Those fibers that secrete acetylcholine are said to be *cholinergic*. Those that secrete norepinephrine are said to be *adrenergic*, a term derived from *adrenalin*, which is an alternate name for epinephrine.

**Acetylcholine synthesis.** ACh is synthesized in the cytoplasm of nerve terminals, and acetyl coenzyme A (acetyl-CoA) is synthesized in mitochondria. The reaction acetyl-CoA + choline is catalyzed by *cholineacetyltransferase*, which is synthesized in the soma and reaches the nerve terminals by axoplasmic transport. Since choline must be taken up from extracellular fluid by way of a carrier, this is the ratelimiting step of ACh synthesis.

**Acetylcholine release.** Vesicles on presynaptic nerve terminals empty their contents into the synaptic cleft when the cytosolic  $Ca^{2+}$  concentration rises in response to incoming action potentials. Epinephrine and norepinephrine can *inhibit ACh release* by stimulating presynaptic  $\alpha_2$ -adrenoceptors. In postganglionic parasympathetic fibers, ACh blocks its own release by binding to presynaptic autoreceptors (M-receptors).

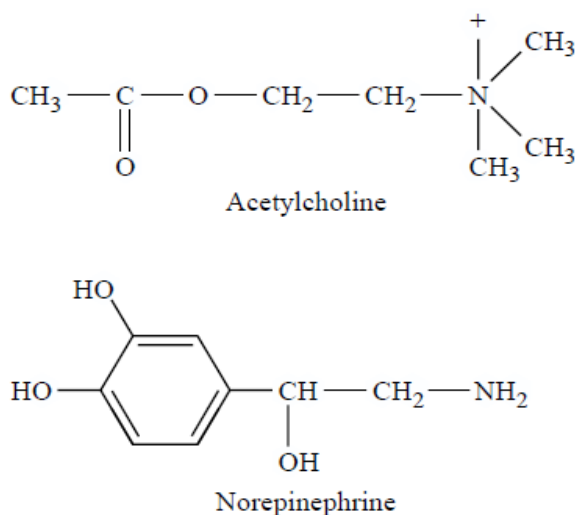
After ACh is secreted by the parasympathetic fibers, it is quickly broken down by acetylcholinesterase (AChE) in the synapse and its effect lasts only a few seconds.

Certain neurons can enzymatically produce *L-dopa* (L-dihydroxyphenylalanine) from the amino acid L-tyrosine. L-dopa is the parent substance of dopamine, norepinephrine, and epinephrine—the three natural **catecholamines**, which are enzymatically synthesized in this order. Dopamine



(DA) is the final step of synthesis in neurons containing only the enzyme required for the first step (the *aromatic L-amino acid decarboxylase*). Dopamine is used as a transmitter by the dopaminergic neurons in the *CNS* and by autonomic neurons that innervate the *kidney*.

**Norepinephrine (NE)** is produced when a second enzyme (*dopamine- $\beta$ -hydroxylase*) is also present. In most *sympathetic postganglionic nerve endings* and noradrenergic central neurons, NE serves as the neurotransmitter along with the *co-transmitters* adenosine triphosphate (ATP), somatostatin (SIH), or neuropeptide Y (NPY). Within the adrenal medulla (see below) and adrenergic neurons of the medulla oblongata, *phenylethanolamine N-methyltransferase* transforms norepinephrine (NE) into **epinephrine (E)**. The molecular structures of acetylcholine and norepinephrine are the following (fig.5):



**Fig. 5. The molecular structures of acetylcholine and norepinephrine**

The endings of unmyelinated sympathetic postganglionic neurons are knobby or *varicose*. These knobs establish synaptic contact, albeit not always very close, with the effector organ. They also serve as sites of **NE synthesis** and **storage**. The adrenergic transmission is described in fig. 6. L-tyrosine (A1) is actively taken up by the nerve endings and transformed into dopamine. In adrenergic stimulation, this step is accelerated by protein kinase A-mediated (PKA- A2) phosphorylation of the responsible enzyme. This yields a larger dopamine supply. Dopamine is transferred to chromaffin vesicles, where it is

transformed into NE (A3). Norepinephrine, the end product, inhibits further dopamine synthesis (negative feedback).

**NE release.** NE is exocytosed into the synaptic cleft after the arrival of action potentials at the nerve terminal and the initiation of  $Ca^{2+}$  influx (A4). Epinephrine also enhances NE release in noradrenergic fibers by way of presynaptic  $\beta_2$ -adrenoceptors (A2, A5).

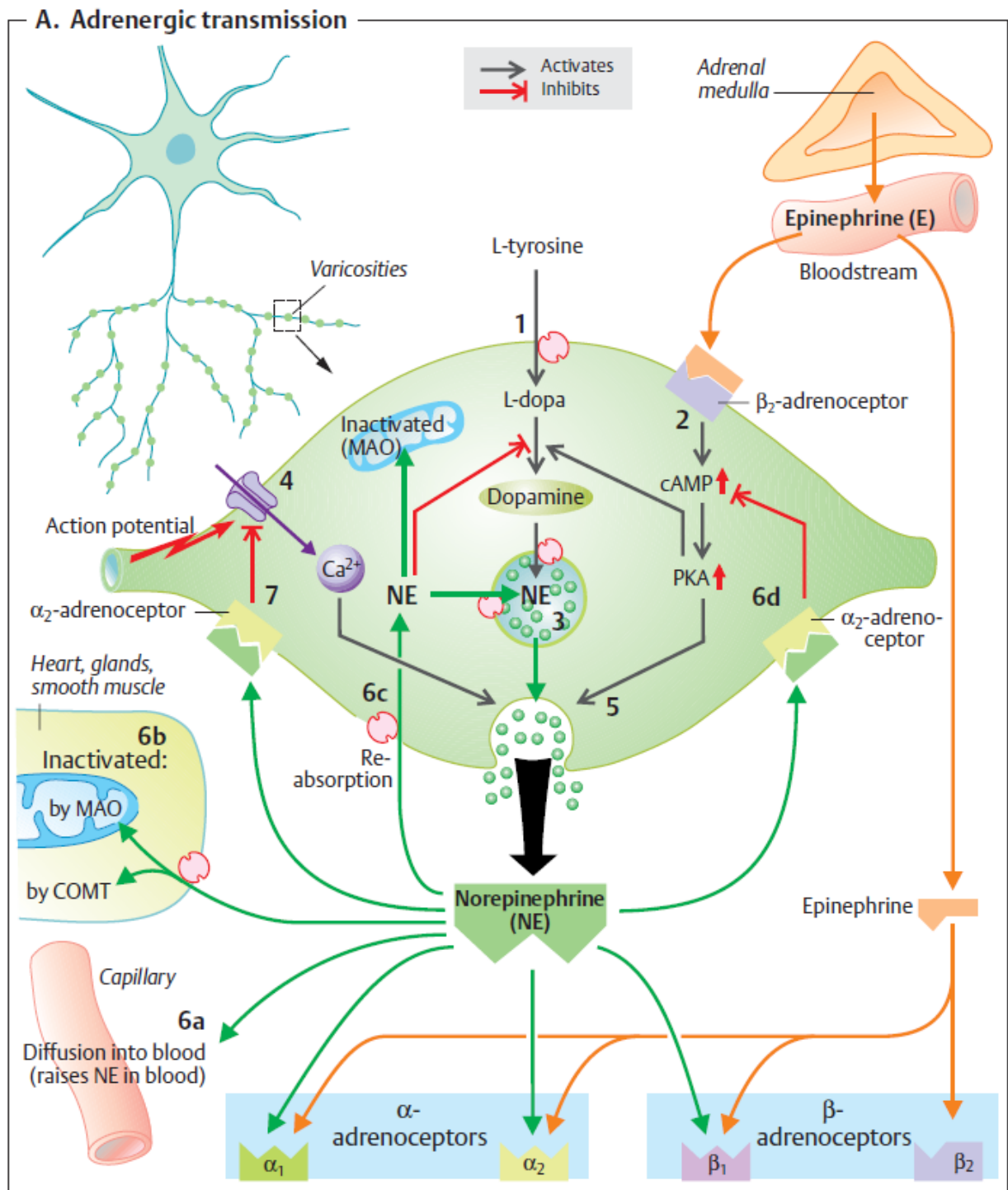
NE in the synaptic cleft is deactivated by (A6 a – d):

- diffusion of NE from the synaptic cleft into the blood;
- extraneuronal NE uptake (in the heart, glands, smooth muscles, glia, and liver), and subsequent intracellular degradation of NE by catecholamine-O-methyltransferase (COMT) and monoamine oxidase (MAO);
- active re-uptake of NE (70%) by the presynaptic nerve terminal. Some of the absorbed NE enters intracellular vesicles (A3) and is reused, and some is inactivated by MAO;

stimulation of presynaptic  $\alpha_2$ -adrenoceptors (autoreceptors; A 6d, 7) by NE in the synaptic cleft, which inhibits the further release of NE.

**Table 4. Locations of cholinergic and adrenergic fibers in the ANS**

<b>Division</b>	<b>Preganglionic Fibers</b>	<b>Postganglionic Fibers</b>
Sympathetic	Always cholinergic	Mostly adrenergic; a few cholinergic
Parasympathetic	Always cholinergic	Always cholinergic

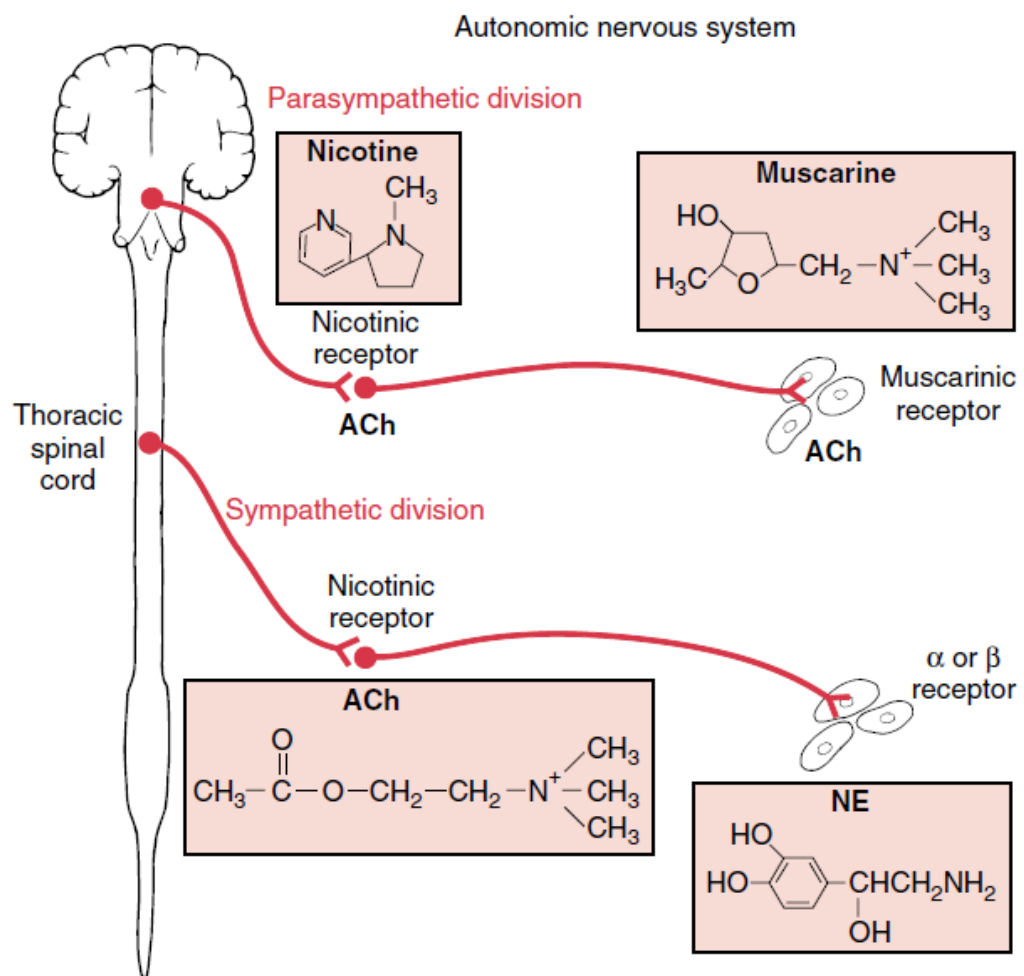


**Fig. 6. The adrenergic transmission.**

ACh and NE are not the only neurotransmitters employed by the ANS. All *preganglionic neurons* are *cholinergic* in both the sympathetic and the parasympathetic nervous systems. Acetylcholine or acetylcholine-like substances, when applied to the ganglia, will excite both sympathetic and parasympathetic postganglionic neurons. Either *all or almost all of the postganglionic neurons* of

*the parasympathetic system are also cholinergic. Conversely, most of the postganglionic sympathetic neurons are adrenergic.* However, the postganglionic sympathetic nerve fibers to the sweat glands, to the piloerector muscles of the hairs, and to a very few blood vessels are cholinergic (fig. 7). Table 4 summarizes locations of cholinergic and adrenergic fibers in the ANS.

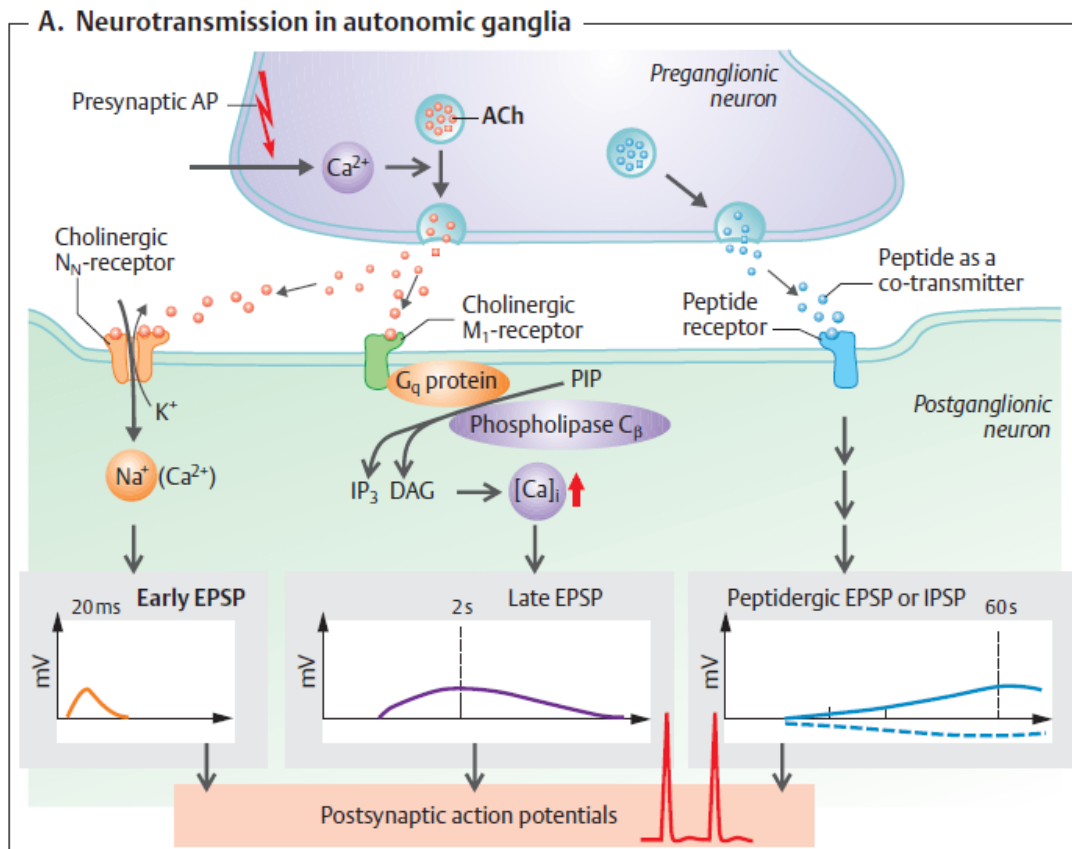
Although all autonomic fibers secrete one of these, many of them also secrete neuropeptides that modulate ACh or NE function. Sympathetic fibers may also secrete enkephalin, substance P, neuropeptide Y, somatostatin, neurotensin, or gonadotropin-releasing hormone. Some parasympathetic fibers relax blood vessels and increase blood flow by stimulating the endothelial cells that line the vessel to release the gas nitric oxide (NO). NO inhibits smooth muscle tone in the vessel wall.



**Fig. 7. Neurotransmitters and Receptors of the Autonomic Nervous System.**

**Receptors on the Effector Organs**

**Cholinergic Receptors.** Acetylcholine binds to two classes of cholinergic receptors—**nicotinic (N)** and **muscarinic (M) receptors**—named for plant toxins that were used to identify and distinguish them. Nicotine binds only to the former type, while muscarine, a mushroom poison, binds only to the latter. Other drugs also selectively bind to one type or the other—atropine binds only to muscarinic receptors and curare only to nicotinic receptors, for example. **Nicotinic receptors** occur on the postsynaptic cells in all ganglia of the ANS, in the adrenal medulla, and in neuromuscular junctions. Nerve-specific  $N_N$ -cholinoceptors on autonomic ganglia differ from muscle specific  $N_M$ -cholinoceptors on motor end plates in that they are formed by different subunits. They are similar in that they are both *ionotropic receptors*, i.e., they act as cholinoceptors and cation channels at the same time. ACh binding leads to rapid  $Na^+$  and  $Ca^{2+}$  influx and in early (rapid) excitatory postsynaptic potentials (EPSP), which trigger postsynaptic action potentials (AP) once they rise above threshold (fig. 8).



**Fig. 8. Neurotransmission in autonomic ganglia.**

**Muscarinic receptors** are found on all effector cells that are stimulated by the postganglionic cholinergic neurons of either the parasympathetic nervous system or the sympathetic system. **M-cholinoceptors** (M1–M5) indirectly affect synaptic transmission through G-proteins (*metabotropic receptors*). **M1-cholinoceptors** occur mainly on *autonomic ganglia*, *CNS*, and *exocrine gland cells*. They activate phospholipase C<sub>β</sub> (PLC<sub>β</sub>) via G<sub>q</sub> protein in the postganglionic neuron and inositol *tris*-phosphate (IP<sub>3</sub>) and diacylglycerol (DAG) are released as second messengers that stimulate Ca<sup>2+</sup> influx and a *late EPSP* (fig.8, middle panel). Synaptic signal transmission is modulated by the late EPSP as well as by co-transmitting peptides that trigger *peptidergic EPSP or IPSP* (fig.8, right panel).

**M2-cholinoceptors** occur in the *heart* and function mainly via a G<sub>i</sub> protein. The G<sub>i</sub> protein *opens specific K<sup>+</sup> channels* located mainly in the sinoatrial node, atrioventricular (AV) node, and atrial cells, thereby exerting negative chronotropic and dromotropic effects on the heart. The G<sub>i</sub> protein also *inhibits adenylate cyclase*, thereby reducing Ca<sup>2+</sup> influx.

**M3-cholinoceptors** occur mainly in *smooth muscles*. Similar to M1-holinoceptors (fig 8. middle panel), M3-cholinoceptors trigger contractions by stimulating  $\text{Ca}^{2+}$  influx. However, they can also induce relaxation by activating  $\text{Ca}^{2+}$ -dependent NO synthase, e.g., in *endothelial cells*.

**Adrenergic Receptors.** There are likewise different classes of adrenergic receptors that account for the effects of norepinephrine (NE) on different target cells. NE receptors fall into two broad classes called **alpha-( $\alpha$ )adrenergic** and **beta-( $\beta$ )adrenergic receptors**. Four main types of adrenoceptors  $\alpha_1$ ,  $\alpha_2$ ,  $\beta_1$  and  $\beta_2$  can be distinguished according to their affinity to E and NE and to numerous agonists and antagonists. All adrenoceptors respond to E, but NE has little effect on  $\beta_2$ - adrenoceptors. Isoproterenol (isoprenaline) activates only  $\beta$ -adrenoceptors, and phentolamine only blocks  $\alpha$ -adrenoceptors. The activities of all adrenoceptors are mediated by G proteins.

Different subtypes ( $\alpha_{1A}$ ,  $\alpha_{1B}$ ,  $\alpha_{1D}$ ) of  **$\alpha_1$ -adrenoceptors** can be distinguished. Their location and function are as follows: CNS (sympathetic activity  $\uparrow$ ), salivary glands, liver (glycogenolysis  $\uparrow$ ), kidneys (alters threshold for renin release), and smooth muscles (trigger contractions in the arterioles, uterus, deferent duct, bronchioles, urinary bladder, gastrointestinal sphincters, and dilator pupillae).

Activation of  $\alpha_1$ -adrenoceptors, mediated by *Gq proteins* and *phospholipase C $\beta$*  (PLC $\beta$ ), leads to formation of the second messengers *inositol tris-phosphate* (IP3), which increases the cytosolic  $\text{Ca}^{2+}$  concentration, and *diacylglycerol* (DAG), which activates protein kinase C (PKC). Gq protein-mediated  $\alpha_1$ -adrenoceptor activity also activates  $\text{Ca}^{2+}$ -dependent *K<sup>+</sup> channels*. The resulting  $\text{K}^+$  outflow hyperpolarizes and relaxes target smooth muscles, e.g., in the gastrointestinal tract.

Three subtypes ( $\alpha_{2A}$ ,  $\alpha_{2B}$ ,  $\alpha_{2C}$ ) of  **$\alpha_2$ -adrenoceptors** can be distinguished. Their location and action are as follows: CNS (sympathetic activity  $\downarrow$ , e.g., use of the  $\alpha_2$  agonist clonidine to lower blood pressure), salivary glands (salivation  $\downarrow$ ), pancreatic islets (insulin secretion  $\downarrow$ ), lipocytes (lipolysis  $\downarrow$ ), platelets (aggregation  $\uparrow$ ), and neurons (presynaptic autoreceptors, see below). Activated  $\alpha_2$ -adrenoceptors

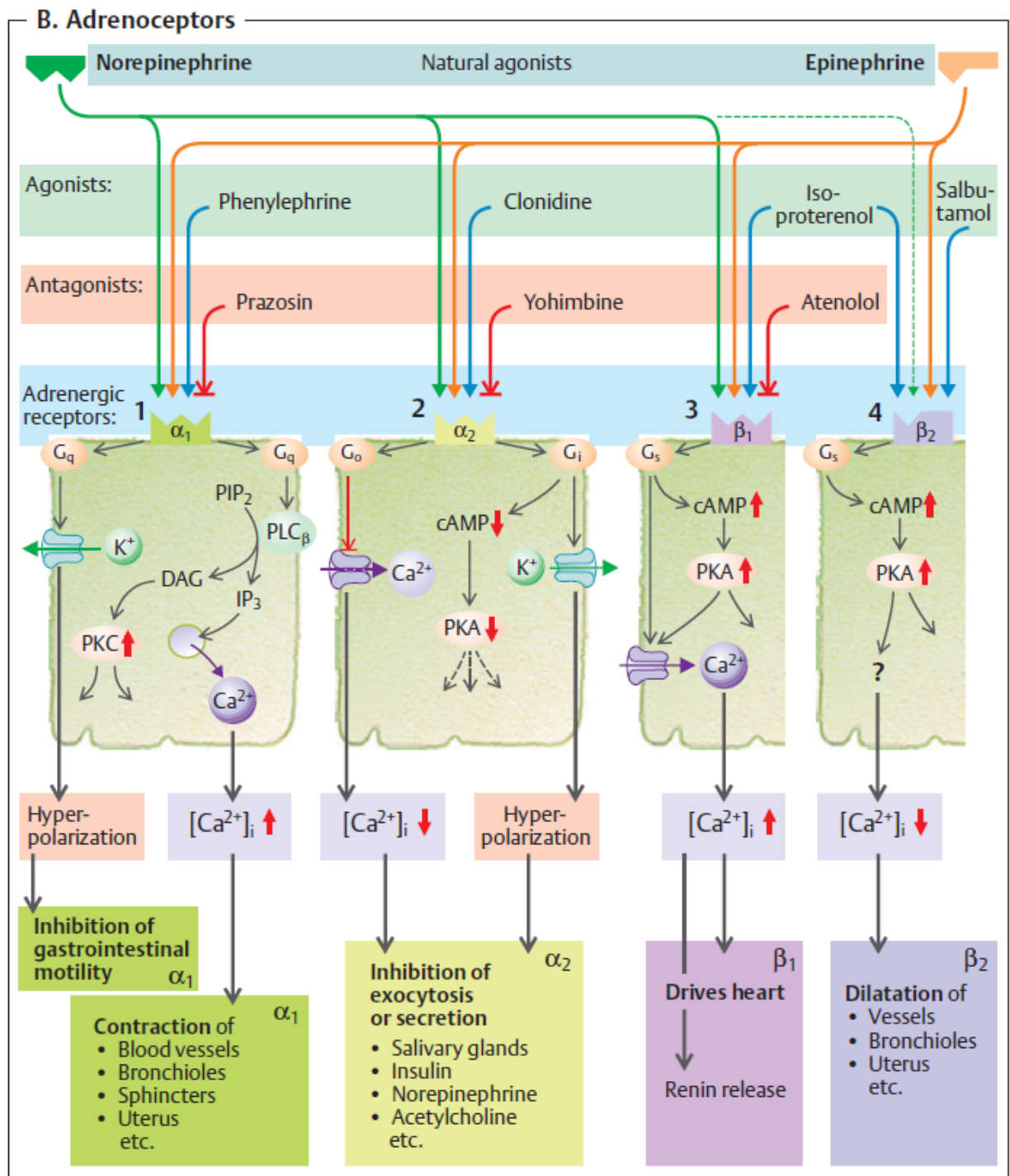
link with *Gi protein* and inhibit (via  $\alpha_i$  subunit of  $G_i$ ) adenylate cyclase (*cAMP synthesis* ↓) and, at the same time, increase (via the  $\beta\gamma$  subunit of  $G_i$ ) the open probability of voltage-gated  $K^+$  channels (*hyperpolarization*). When coupled with  $G_0$  proteins, activated  $\alpha_2$ -adrenoceptors also inhibit voltage-gated  $Ca^{2+}$  channels.

All  **$\beta$ -adrenoceptors** are coupled with a  $G_s$  protein, and its  $\beta_s$  subunit releases cAMP as a second messenger. cAMP then activates protein kinase A (PKA), which phosphorylates different proteins, depending on the target cell type.

NE and E work via  **$\beta_1$ -adrenoceptors** to open L-type  $Ca^{2+}$  channels in *cardiac cell* membranes. This increases the  $[Ca^{2+}]_i$  and therefore produces *positive chronotropic, dromotropic, and inotropic effects*. Activated  $G_s$  protein can also directly increase the open probability of voltage-gated  $Ca^{2+}$  channels in the heart. In the *kidney*, the basal renin secretion is increased via  $\beta_1$ -adrenoceptors.

Activation of  **$\beta_2$ -adrenoceptors** by epinephrine increases cAMP levels, thereby lowering the  $[Ca^{2+}]_i$  (by a still unclear mechanism). This *dilates* the bronchioles and blood vessels of skeletal muscles and *relaxes* the muscles of the uterus, deferent duct, and gastrointestinal tract. Further effects of  $\beta_2$ -adrenoceptor activation are *increased insulin secretion* and *glycogenolysis* in liver and muscle and *decreased platelet aggregation*.





**Fig 9.** summarizes the locations of these receptors and neurotransmitters in different divisions of ANS.

Heat production is increased via  **$\beta_3$ -adrenoceptors** on brown lipocytes.

The binding of NE to  $\alpha$ -adrenergic receptors is usually excitatory, and its binding to  $\beta$ -adrenergic receptors is usually inhibitory, but there are exceptions to

both. For example, NE binds to  $\beta$ -receptors in cardiac muscle but has an excitatory effect. The  $\beta$ -receptors in turn are divided into  $\beta_1$  and  $\beta_2$  receptors because certain chemicals affect only certain beta receptors. Also, there is a division of  $\alpha$ -receptors into  $\alpha_1$  and  $\alpha_2$  receptors. Norepinephrine and epinephrine, both of which are secreted into the blood by the adrenal medulla, have slightly different effects in exciting the alpha and beta receptors. Norepinephrine excites mainly  $\alpha$ -receptors. Conversely, epinephrine excites both types of receptors approximately equally.

### **Adrenal Medulla**

After stimulation of preganglionic sympathetic nerve fibers (cholinergic transmission), 95% of all cells in the adrenal medulla secrete the endocrine hormone **epinephrine (E)** into the blood by exocytosis, and another 5% release **norepinephrine (NE)**. Compared to noradrenergic neurons, *NE synthesis* in the adrenal medulla is similar, but most of the NE leaves the vesicle and is enzymatically metabolized into E in the cytoplasm. Special vesicles called *chromaffin bodies* then actively store E and get ready to release it and co-transmitters (enkephalin, neuropeptide Y) by exocytosis.

In **alarm reactions**, secretion of E (and some NE) from the adrenal medulla increases substantially in response to physical and mental or emotional stress. Epinephrine secretion from the adrenal medulla (mediated by increased sympathetic activity) is stimulated by certain **triggers**, e.g., *physical work*, cold, heat, anxiety, anger (stress), *pain*, *oxygen deficiency*, or a *drop in blood pressure*. In severe hypoglycemia, for example, the plasma epinephrine concentration can increase by as much as 20-fold, while the norepinephrine concentration increases by a factor of only 2.5, resulting in a corresponding rise in the E/NE ratio.

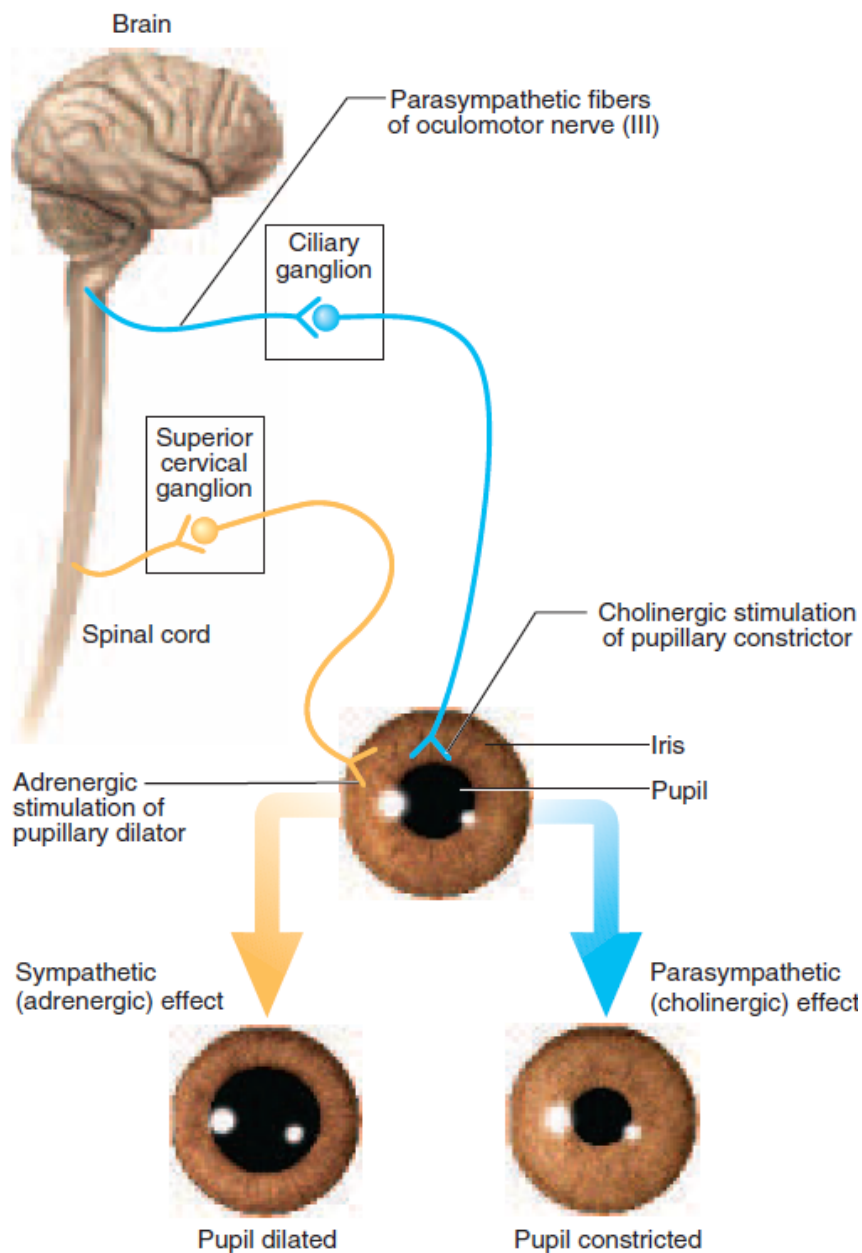
The **main task of epinephrine** is to mobilize stored chemical energy, e.g., through *lipolysis* and *glycogenolysis*. Epinephrine enhances the uptake of glucose into skeletal muscle and activates enzymes that accelerate glycolysis and lactate formation. To enhance the blood flow in the muscles involved, the body increases

the cardiac output while curbing gastrointestinal blood flow and activity. Adrenal epinephrine and neuronal NE begin to stimulate the secretion of hormones responsible for replenishing the depleted energy reserves while the alarm reaction is still in process.

### **Dual Innervation**

Most of the viscera receive nerve fibers from both the sympathetic and parasympathetic divisions and thus are said to have **dual innervation**. In such cases, the two divisions may have either *antagonistic* or *cooperative* effects on the same organ. **Antagonistic effects** oppose each other. For example, the sympathetic division speeds up the heart and the parasympathetic division slows it down; the sympathetic division inhibits digestion and the parasympathetic division stimulates it; the sympathetic division dilates the pupil and the parasympathetic division constricts it. In some cases, these effects are exerted through dual innervation of the same effector cells, as in the heart, where nerve fibers of both divisions terminate on the same muscle cells. In other cases, antagonistic effects arise because each division innervates different effector cells with opposite effects on organ function. In the iris of the eye, for example, sympathetic fibers innervate the pupillary dilator and parasympathetic fibers innervate the constrictor (fig. 10).

**Cooperative effects** are seen when the two divisions act on different effectors to produce a unified overall effect. Salivation is a good example. The parasympathetic division stimulates serous cells of the salivary glands to secrete a watery, enzyme-rich secretion, while the sympathetic division stimulates mucous cells of the same glands to secrete mucus. The enzymes and mucus are both necessary components of the saliva. Even when both divisions innervate a single organ, they do not always innervate it equally or exert equal influence. For example, the parasympathetic division forms an extensive plexus in the wall of the digestive tract and exerts much more influence over it than the sympathetic division does. In the ventricles of the heart, by contrast, there is much less parasympathetic than sympathetic innervation.

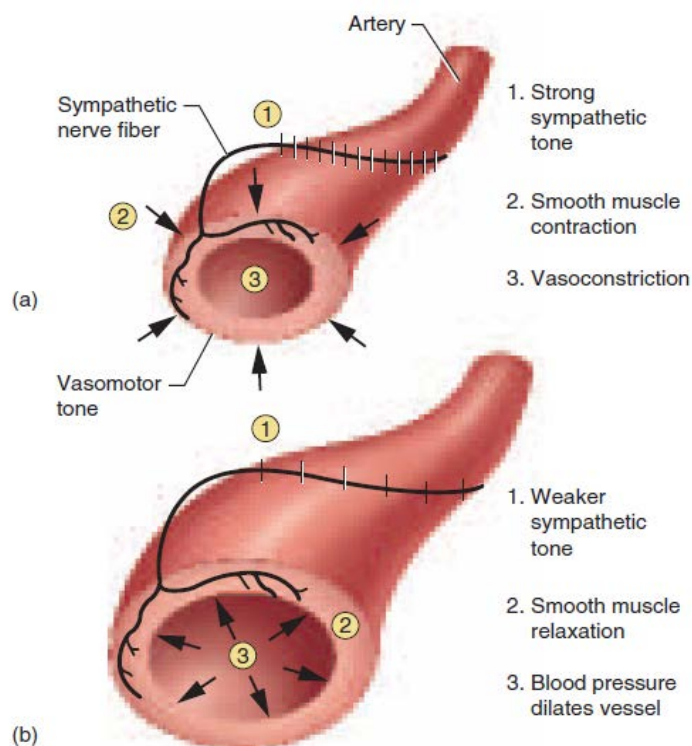


**Fig 10. Dual innervations of the iris. Shows antagonistic effects of the sympathetic and parasympathetic divisions.**

### **Control Without Dual Innervation**

Dual innervation is not always necessary for the ANS to produce opposite effects on an organ. The adrenal medulla, piloerector muscles, sweat glands, and

many blood vessels receive only sympathetic fibers. The most significant example of control without dual innervations is regulation of blood pressure and routes of blood flow. The sympathetic fibers to a blood vessel have a baseline sympathetic tone which keeps the vessels in a state of partial constriction called **vasomotor tone** (fig. 11). An increase in firing rate causes vasoconstriction by increasing smooth muscle contraction. A drop in firing frequency causes vasodilation by allowing the smooth muscle to relax. The blood pressure in the vessel, pushing outward on its wall, then dilates the vessel. Thus, the sympathetic division alone exerts opposite effects on the vessels.



**Fig 11. The sympathetic vasomotor tone in blood vessels**

Sympathetic control of vasomotor tone can shift blood flow from one organ to another according to the changing needs of the body. In times of emergency, stress, or exercise, the skeletal muscles and heart receive a high priority and the sympathetic division dilates the arteries that supply them. Such processes as digestion, nutrient absorption, and urine formation can wait; thus the sympathetic division constricts arteries to the gastrointestinal tract and kidneys. It also reduces blood flow through the skin, which may help to minimize bleeding in the event that the stress-producing situation leads to injury. Furthermore, since there is not

enough blood in the body to abundantly supply all the organ systems at once, it is necessary to temporarily divert blood away from some organs in order to supply an adequate amount to the muscular system.

### **Effects of Sympathetic and Parasympathetic Stimulation on Specific Organs**

**Eyes.** Two functions of the eyes are controlled by the autonomic nervous system. They are (1) the pupillary opening and (2) the focus of the lens. Sympathetic stimulation contracts the meridional fibers of the iris that dilate the pupil, whereas parasympathetic stimulation contracts the circular muscle of the iris to constrict the pupil.

The parasympathetics that control the pupil are reflexly stimulated when excess light enters the eyes; this reflex reduces the pupillary opening and decreases the amount of light that strikes the retina. Conversely, the sympathetics become stimulated during periods of excitement and increase pupillary opening at these times.

Focusing of the lens is controlled almost entirely by the parasympathetic nervous system. The lens is normally held in a flattened state by intrinsic elastic tension of its radial ligaments. Parasympathetic excitation contracts the ciliary muscle, which is a ringlike body of smooth muscle fibers that encircles the outside ends of the lens radial ligaments. This contraction releases the tension on the ligaments and allows the lens to become more convex, causing the eye to focus on objects near at hand.

**Glands of the Body.** The nasal, lacrimal, salivary, and many gastrointestinal glands are strongly stimulated by the parasympathetic nervous system, usually resulting in copious quantities of watery secretion. The glands of the alimentary tract most strongly stimulated by the parasympathetics are those of the upper tract, especially those of the mouth and stomach. On the other hand, the glands of the

small and large intestines are controlled principally by local factors in the intestinal tract itself and by the intestinal enteric nervous system and much less by the autonomic nerves.

Sympathetic stimulation has a direct effect on most alimentary gland cells to cause formation of a concentrated secretion that contains high percentages of enzymes and mucus. But it also causes vasoconstriction of the blood vessels that supply the glands and in this way sometimes reduces their rates of secretion.

*The sweat glands* secrete large quantities of sweat when the sympathetic nerves are stimulated, but no effect is caused by stimulating the parasympathetic nerves. However, the sympathetic fibers to most sweat glands are cholinergic (except for a few adrenergic fibers to the palms and soles), in contrast to almost all other sympathetic fibers, which are adrenergic. Furthermore, the sweat glands are stimulated primarily by centers in the hypothalamus that are usually considered to be parasympathetic centers. Therefore, sweating could be called a parasympathetic function, even though it is controlled by nerve fibers that anatomically are distributed through the sympathetic nervous system.

*The apocrine glands* in the axillae secrete a thick, odoriferous secretion as a result of sympathetic stimulation, but they do not respond to parasympathetic stimulation. This secretion actually functions as a lubricant to allow easy sliding motion of the inside surfaces under the shoulder joint. The apocrine glands, despite their close embryological relation to sweat glands, are activated by adrenergic fibers rather than by cholinergic fibers and are also controlled by the sympathetic centers of the central nervous system rather than by the parasympathetic centers.

**Intramural Nerve Plexus of the Gastrointestinal System.** The gastrointestinal system has its own intrinsic set of nerves known as the intramural plexus or the intestinal enteric nervous system, located in the walls of the gut. Also, both parasympathetic and sympathetic stimulation originating in the brain can affect gastrointestinal activity mainly by increasing or decreasing specific actions in the gastrointestinal intramural plexus. Parasympathetic stimulation, in

general, increases overall degree of activity of the gastrointestinal tract by promoting peristalsis and relaxing the sphincters, thus allowing rapid propulsion of contents along the tract. This propulsive effect is associated with simultaneous increases in rates of secretion by many of the gastrointestinal glands, described earlier.

Normal function of the gastrointestinal tract is not very dependent on sympathetic stimulation. However, strong sympathetic stimulation inhibits peristalsis and increases the tone of the sphincters. The net result is greatly slowed propulsion of food through the tract and sometimes decreased secretion as well—even to the extent of sometimes causing constipation.

**Heart.** In general, sympathetic stimulation increases the overall activity of the heart. This is accomplished by increasing both the rate and force of heart contraction. Parasympathetic stimulation causes mainly opposite effects—decreased heart rate and strength of contraction. To express these effects in another way, sympathetic stimulation increases the effectiveness of the heart as a pump, as required during heavy exercise, whereas parasympathetic stimulation decreases heart pumping, allowing the heart to rest between bouts of strenuous activity.

**Systemic Blood Vessels.** Most systemic blood vessels, especially those of the abdominal viscera and skin of the limbs, are constricted by sympathetic stimulation. Parasympathetic stimulation has almost no effects on most blood vessels except to dilate vessels in certain restricted areas, such as in the blush area of the face. Under some conditions, the beta function of the sympathetics causes vascular dilation instead of the usual sympathetic vascular constriction, but this occurs rarely except after drugs have paralyzed the sympathetic alpha vasoconstrictor effects, which, in blood vessels, are usually far dominant over the beta effects.



**Effect of Sympathetic and Parasympathetic Stimulation on Arterial Pressure.** The arterial pressure is determined by two factors: propulsion of blood by the heart and resistance to flow of blood through the peripheral blood vessels. Sympathetic stimulation increases both propulsion by the heart and resistance to flow, which usually causes a marked acute increase in arterial pressure but often very little change in long-term pressure unless the sympathetics stimulate the kidneys to retain salt and water at the same time.

Conversely, moderate parasympathetic stimulation via the vagal nerves decreases pumping by the heart but has virtually no effect on vascular peripheral resistance. Therefore, the usual effect is a slight decrease in arterial pressure. But very strong vagal parasympathetic stimulation can almost stop or occasionally actually stop the heart entirely for a few seconds and cause temporary loss of all or most arterial pressure.

**Effects of Sympathetic and Parasympathetic Stimulation on Other Functions of the Body.** Because of the great importance of the sympathetic and parasympathetic control systems, they are discussed many times in this text in relation to multiple body functions. In general, most of the entodermal structures, such as the ducts of the liver, gallbladder, ureter, urinary bladder, and bronchi, are inhibited by sympathetic stimulation but excited by parasympathetic stimulation. Sympathetic stimulation also has multiple metabolic effects such as release of glucose from the liver, increase in blood glucose concentration, increase in glycogenolysis in both liver and muscle, increase in skeletal muscle strength, increase in basal metabolic rate, and increase in mental activity. Finally, the sympathetics and parasympathetics are involved in execution of the male and female sexual acts.

Autonomic effects of sympathetic and parasympathetic divisions on various organs of the body are summarized in the table 5.

**Table 5. ANS effects on various organs of the body**

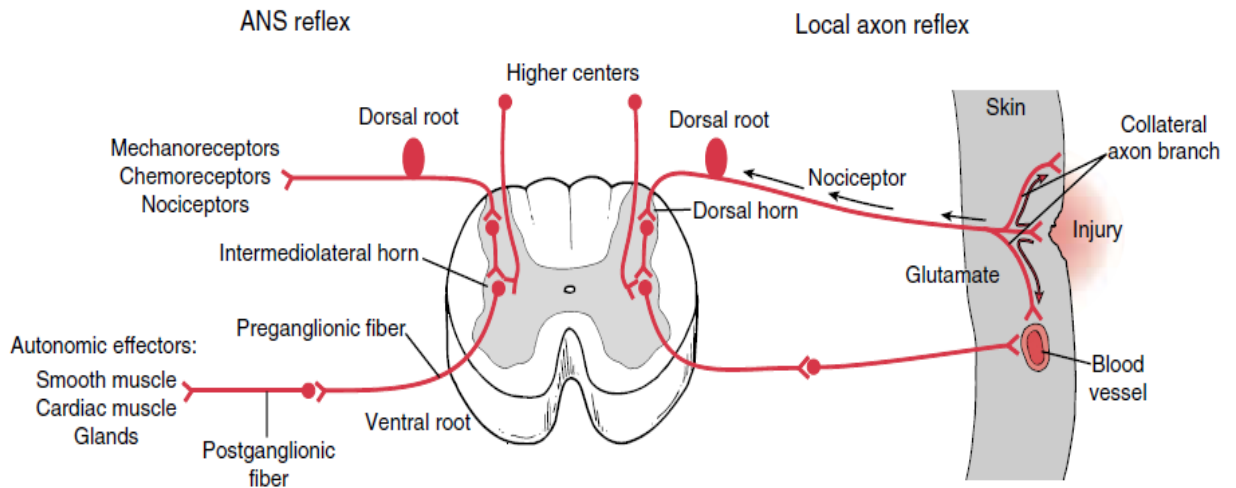
<b>Target</b>	<b>Sympathetic Effect and Receptor Type</b>	<b>Parasympathetic Effect (all muscarinic)</b>
<b>Eye</b>		
Dilator of pupil	Pupillary dilation ( $\alpha_1$ )	No effect
<i>Constrictor of pupil</i>	No effect	Pupillary constriction
<i>Ciliary muscle and lens</i>	Relaxation for far vision ( $\beta_2$ )	Contraction for near vision
<i>Lacrimal (tear) gland</i>	None	Secretion
<b>Integumentary System</b>		
<i>Merocrine sweat glands (cooling)</i>	Secretion (muscarinic)	No effect
<i>Apocrine sweat glands (scent)</i>	Secretion ( $\alpha_1$ )	No effect
<i>Piloerector muscles</i>	Hair erection ( $\alpha_1$ )	No effect
<b>Adipose Tissue</b>	Decreased fat breakdown ( $\alpha_2$ )	No effect
	Increased fat breakdown ( $\alpha_1, \beta_1$ )	
<b>Adrenal Medulla</b>	Hormone secretion (nicotinic)	No effect
<b>Circulatory System</b>		
<i>Heart rate and force</i>	Increased ( $\beta_1, \beta_2$ )	Decreased
<i>Deep coronary arteries</i>	<i>Vasodilation (<math>\beta_2</math>)</i>	<i>Slight vasodilation</i>
	Vasoconstriction ( $\alpha_1, \alpha_2$ )	
<i>Blood vessels of most viscera</i>	Vasoconstriction ( $\alpha_1$ )	Vasodilation
<i>Blood vessels of skeletal muscles</i>	Vasodilation ( $\beta_2$ )	No effect
<i>Blood vessels of skin</i>	Vasoconstriction ( $\alpha_1, \alpha_2$ )	Vasodilation, blushing
<i>Platelets (blood clotting)</i>	Increased clotting ( $\alpha_2$ )	No effect
<b>Respiratory System</b>		
<i>Bronchi and bronchioles</i>	Bronchodilation ( $\beta_2$ )	Bronchoconstriction
<i>Mucous glands</i>	Decreased secretion ( $\alpha_1$ )	No effect
	Increased secretion ( $\beta_2$ )	
<b>Urinary System</b>		
<i>Kidneys</i>	Reduced urine output ( $\alpha_1, \alpha_2$ )	No effect
<i>Bladder wall</i>	No effect	Contraction
<i>Internal urethral sphincter</i>	Contraction, urine retention ( $\alpha_1$ )	Relaxation, urine release

<b>Digestive System</b>		
<i>Salivary glands</i>	Thick mucous secretion ( $\alpha 1$ )	Thin serous secretion
<i>Gastrointestinal motility</i>	Decreased ( $\alpha 1$ , $\alpha 2$ , $\beta 1$ , $\beta 2$ )	Increased
<i>Gastrointestinal secretion</i>	Decreased ( $\alpha 2$ )	Increased
<i>Liver</i>	Glycogen breakdown ( $\alpha 1$ , $\beta 2$ )	Glycogen synthesis
<i>Pancreatic enzyme secretion</i>	Decreased ( $\alpha 1$ )	Increased
<i>Pancreatic insulin secretion</i>	Decreased ( $\alpha 2$ ) Increased ( $\beta 2$ )	No effect
<b>Reproductive System</b>		
<i>Penile or clitoral erection</i>	No effect	Stimulation
<i>Glandular secretion</i>	No effect	Stimulation
<i>Orgasm, smooth muscle roles</i>	Stimulation ( $\alpha 1$ )	No effect
<i>Uterus</i>	Relaxation ( $\beta 2$ )	No effect
	Labor contractions ( $\alpha 1$ )	

### Sensory Input Contributes to Autonomic Function

The ANS is traditionally regarded as an efferent system, and the sensory neurons innervating the involuntary organs are not considered part of the ANS. Sensory input, however, is important for autonomic functioning. The sensory innervation to the visceral organs, blood vessels, and skin forms the afferent limb of autonomic reflexes (Fig. 12). Most of the sensory axons from ANS-innervated structures are unmyelinated C fibers.

Sensory information from these pathways may not reach the level of consciousness. Sensations that are perceived may be vaguely localized or may be felt in a somatic structure rather than the organ from which the afferent action potentials originated. The perception of pain in the left arm during a myocardial infarction is an example of pain being referred from a visceral organ.



**Fig. 12. Sensory components of autonomic function.**

Left, sensory action potentials from mechanical, chemical, and nociceptive receptors that propagate to the spinal cord can trigger ANS reflexes. Right, local axon reflexes occur when an orthodromic action potential from a sensory nerve ending propagates antidromically into collateral branches of the same neuron. The antidromic action potentials may provoke release of the same neurotransmitters, like substance P or glutamate, from the nerve endings as would be released at the synapse in the spinal cord. Local axon reflexes may perpetuate pain, activate sweat glands, or cause vasomotor actions.

### **Local axon reflexes are paths for autonomic activation**

A sensory neuron may have several terminal branches peripherally that enlarge the receptive area and innervate multiple receptors. As a sensory action potential which originated in one of the terminal branches propagates afferently, or **orthodromically**, it may also enter some other branches of that same axon and then conduct efferently, or **antidromically**, for short distances. The distal ends of the sensory axons may release neurotransmitters in response to the antidromic action potentials. The process of action potential spread can result in a more wide-ranging reaction than that produced by the initial stimulus. If the sensory neuron innervates blood vessels or sweat glands, the response can produce reddening of

the skin as a result of vasodilation, local sweating as a result of sweat gland activation, or pain as a result of the action of the released neurotransmitter. This process is called a **local axon reflex** (see Fig. 12). It differs from the usual reflex pathway in that a synapse with an efferent neuron in the spinal cord or peripheral ganglion is not required to produce a response. The neurotransmitter producing this local reflex is likely the same as that released at the synapse in the spinal cord—substance P or glutamate for sensory neurons or ACh and NE at the target tissues for autonomic neurons. Local axon reflexes in nociceptive nerve endings that become persistently activated after local trauma can produce dramatic clinical manifestations.

### **Control of the autonomic nervous system**

The autonomic nervous system utilizes a hierarchy of reflexes to control the function of autonomic target organs. These reflexes range from local, involving only a part of one neuron, to regional, requiring mediation by the spinal cord and associated autonomic ganglia, to the most complex, requiring action by the brainstem and cerebral centers. In general, the higher the level of complexity, the more likely the reflex will require coordination of both sympathetic and parasympathetic responses. Somatic motor neurons and the endocrine system may also be involved.

### **The Autonomic Ganglia Can Modify Reflexes**

Although the paravertebral ganglia may serve merely as relay stations for synapse of preganglionic and postganglionic sympathetic neurons, evidence suggests that synaptic activity in these ganglia may modify efferent activity. Input from other preganglionic neurons provides the modifying influence. Prevertebral ganglia also serve as integrative centers for reflexes in the gastrointestinal tract. Chemoreceptors and mechanoreceptors located in the gut produce afferent action potentials that pass to the spinal cord and then to the celiac or mesenteric ganglia where changes in motility and secretion may be instituted during digestion. The

integrative actions of these ganglia are also responsible for halting motility and secretion in the gastrointestinal tract during a generalized stress reaction (the fight-or-flight response).

The intrinsic plexuses of the gastrointestinal visceral wall are reflex integrative centers where input from presynaptic parasympathetic axons, postganglionic sympathetic axons, and the action of intrinsic neurons may all participate in reflexes that influence motility and secretion. The intrinsic plexuses also participate in centrally mediated gastrointestinal reflexes.

### **The spinal cord coordinates many autonomic reflexes**

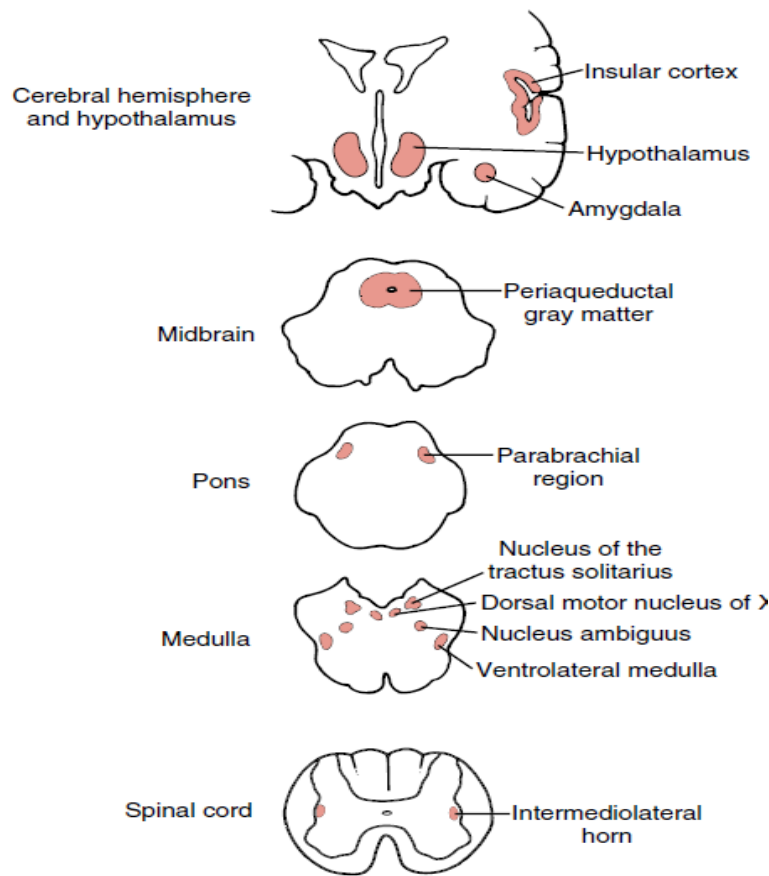
Reflexes coordinated by centers in the lumbar and sacral spinal cord include micturition (emptying the urinary bladder), defecation (emptying the rectum), and sexual response (engorgement of erectile tissue, vaginal lubrication, and ejaculation of semen). Sensory action potentials from receptors in the wall of the bladder or bowel report about degrees of distention. Sympathetic, parasympathetic, and somatic efferent actions require coordination to produce many of these responses.

Higher centers provide facilitating or inhibiting influences to the spinal cord reflex centers. The ability to voluntarily suppress the urge to urinate when the sensation of bladder fullness is perceived is an example of higher CNS centers inhibiting a spinal cord reflex. Following injury to the cervical or upper thoracic spinal cord, micturition may occur involuntarily or be provoked at much lower than normal bladder volumes. Episodes of hypertension and piloerection in spinal cord injury patients are another example of uninhibited autonomic reflexes arising from the spinal cord.

### **The brainstem is a major control center for autonomic reflexes**

Areas within all three levels of the brainstem are important in autonomic function (Fig. 13). The **periaqueductal gray matter** of the midbrain coordinates

autonomic responses to painful stimuli and can modulate the activity of the sensory tracts that transmit pain.



**Fig. 13. The central autonomic network.**

The **parabrachial nucleus** of the pons participates in respiratory and cardiovascular control. The **locus ceruleus** may have a role in micturition reflexes. The medulla contains several key autonomic areas. The **nucleus of the tractus solitarius** receives afferent input from cardiac, respiratory, and gastrointestinal receptors. The **ventrolateral medullary area** is the major center for control of the preganglionic sympathetic neurons in the spinal cord. Vagal efferents arise from this area also. Neurons that control specific functions like blood pressure and heart rate are clustered within this general region. The descending paths for regulation of the preganglionic sympathetic and spinal parasympathetic neurons are not yet fully delineated. The reticulospinal tracts may carry some of these axons. Autonomic

reflexes coordinated in the brainstem include pupillary reaction to light, lens accommodation, salivation, tearing, swallowing, vomiting, blood pressure regulation, and cardiac rhythm modulation.

### **The hypothalamus and cerebral hemispheres provide the highest levels of autonomic control**

The **periventricular, medial, and lateral areas** of the **hypothalamus** in the diencephalon control circadian rhythms, and homeostatic functions such as thermoregulation, appetite, and thirst. Because of the major role of the hypothalamus in autonomic function, it has at times been labeled the “head ganglion of the ANS.” The **insular and medial prefrontal areas** of the cerebral cortex are the respective sensory and motor areas involved with the regulation of autonomic function. The **amygdala** in the temporal lobe coordinates the autonomic components of emotional responses. The areas of the cerebral hemispheres, diencephalon, brainstem, and central path to the spinal cord that are involved with the control of autonomic functions are collectively termed the **central autonomic network** (see fig. 13).

## **Lecture Autonomic Nervous System**

### *I. Overview of the Autonomic Nervous System (ANS)*

A. Major Functions: maintain optimal performance of visceral organs, glands, smooth muscle, and cardiac muscle in order to maintain homeostatic state within body

1. involuntary nervous system - not under conscious control: regulates heart rate, blood pressure, respiratory rate, body temperature, smooth muscle contraction, glandular function, and secretions

2. General visceral motor system - most “effectors” (organs & tissues regulated) are visceral (as opposed to somatic - skeletal muscle & joints)



- B. Somatic vs. Autonomic Nervous Systems
  - 1. Effectors (Target of Motor Neuron)
    - a. SOMATIC - skeletal muscle
    - b. AUTONOMIC - organs, glands, smooth & cardiac muscle
  
  - 2. Efferent (Motor Neuron) Pathway
    - a. SOMATIC - one motor neuron from CNS to skeletal muscle
    - b. AUTONOMIC - two neurons in the motor pathway
      - i. preganglionic neuron - located in the CNS, sends its axon to an autonomic ganglion located outside the CNS; lightly myelinated, thin axons
      - ii. postganglionic neuron - located in the autonomic ganglion, sends its axon to the effector (tissue to be effected); unmyelinated, very thin axons
  
  - 3. Action of Neurotransmitters
    - a. SOMATIC - acetylcholine (ACh); stimulatory
  
    - b. AUTONOMIC - post ganglionic neurons may release either ACh or Norepinephrine (NE); whether response is stimulatory or inhibitory depends on the effector
  
  - 4. Coordination of Somatic and Autonomic Systems
    - a. Both systems send their motor neurons to effectors via the 31 pairs of spinal nerves and 12 pairs of cranial nerves
    - b. When skeletal muscle is active, autonomic must regulate other body activities for sufficient blood, oxygen, waste removal
  
- C. Divisions of the Autonomic Nervous System - the sympathetic and parasympathetic divisions work in contrasting fashion to stimulate and inhibit effectors

1. Sympathetic Division - classic "flight-or-fight" response in scary situations
  - a. increased heart rate
  - b. rapid, deep breathing pattern
  - c. cold, sweaty skin
  - d. dilated eye pupils
  - e. large burst of energy available (glucose)
  - f. constriction of blood vessels
  - g. increased blood pressure
  - h. dilation of bronchioles (more air)
  
2. Parasympathetic Division - the "resting and digesting" system, keeps body calm, stimulates digestion, urination, and defecation

## II. Physiology of Autonomic Nervous System

### A. Autonomic Neurotransmitters and Their Receptors

1. Acetylcholine (ACh) - the same neurotransmitter at the neuromuscular junction is used by autonomic fibers in two places (cholinergic fibers):
  - a. secreted by ALL preganglionic neurons of the ANS
  - b. secreted by MOST postganglionic neurons of PARASYMPATHETIC onto target cells
2. Acetylcholine (cholinergic) receptors
  - a. nicotinic receptors - ACh receptors that can also be activated by nicotine - STIMULATE
    - i. at neuromuscular junction of skeletal muscle
    - ii. located on ALL postganglionic nerve cell bodies of ANS
    - iii. hormone-producing cells of adrenal medulla

b. muscarinic receptors - ACh receptors which are activated by mushroom toxin muscarine STIMULATE or INHIBIT depending of target cell

i. located on the target cells of the body receiving ACh from the parasympathetic division

cardiac muscle -> INHIBITORY

smooth muscle of GI tract -> STIMULATORY

3. Norepinephrine (noradrenaline) - released by most postganglionic neurons of the SYMPATHETIC system (adrenergic fibers)

exceptions: postganglionic sympathetic fibers to some sweat glands of skin, some blood vessels to skeletal muscle and external genitalia

4. norepinephrine (noradrenergic) receptors

a. alpha adrenergic receptors - generally STIMULATE the effector organ/tissue

b. beta adrenergic receptors - generally INHIBIT the effector organ/tissue

B. Drug Effects on the Autonomic NS

1. synaptic cleft enzyme inhibitors

a. neostigmine - blocks acetylcholinesterase for accumulation of ACh (myasthenia gravis)

2. tricyclic antidepressants - prolong the binding of norepinephrine to postsynaptic receptors

3. beta-blockers - block binding of norepinephrine to beta-I receptors; reduce heart rate

C. Antagonistic Control with Sympathetics & Parasympathetics

Target	Parasympathetic	Sympathetic
eye pupil	constricts	dilates
heart	decreases heart rate	increases heart rate
lung	constricts bronchioles	dilates bronchioles

GI Tract	increases digestion	decreases digestion
urinary	promotes urination	inhibits urination
most glands	stimulate secretion	inhibits secretion

#### D. Sympathetic Tone and Parasympathetic Tone

1. Sympathetic Tone - constriction of blood vessels almost exclusively controlled by sympathetic

a. blood pressure - sympathetic stimulation causes vasoconstriction of blood vessels and increase in blood pressure; when stimulation decreases, blood pressure likewise decreases

b. phentolamine - blocks NE, used to treat with high blood pressure

2. Parasympathetic Tone - primary control of heart rate (decrease), GI tract (stimulate), and urinary function (stimulate)

a. anticholinergic drugs - block ACh causing increased heart rate, decreased defecation and urination

b. anticholinergic side effects - drugs that partially block ACh causing problems of symptoms of anticholinergic drugs (many psychotropic drugs like anti-depressants)

#### E. Other Roles of the Autonomic Nervous System

1. Cooperative Effects - parasympathetic causes vasodilation of penis and clitoris; sympathetic causes ejaculation and peristalsis of vagina

2. Sympathetic ONLY -

a. stimulation of adrenal medulla to secrete hormones norepinephrine and epinephrine

b. stimulates sweat glands to secrete

c. arrector pili hair to stand up on arm/neck

d. blood vessels - causes to constrict

e. thermoregulation - vasodilation of capillaries in skin and sweat gland stimulation

f. release of renin from kidney - release of hormone causes increased blood pressure

g. metabolic effects - increases general alertness

i. increased metabolic rate

ii. increased glucose release to blood

iii. mobilization of fat for fuel use

iv. activate reticular formation of brain

### III. Central Nervous System Regulation of the Autonomic NS

#### A. Control by Brain Stem and Spinal Cord

1. medulla - can regulate heart rate (cardiac center), blood vessel constriction (vasomotor center), respiration, and some gastrointestinal activity

2. pons - can regulate respiration (respiratory center), and the pupils (oculomotor nuclei)

3. spinal cord - can regulate defecation/urination

#### B. Hypothalamus - Overall Integration of Autonomics

1. hypothalamus - can coordinate the regulation of heart rate, blood pressure, body temperature, water/electrolyte balance, hormonal activity, pleasure, rage, thirst, hunger, and sex drive

a. sympathetic - lateral & posterior hypothalamus

b. parasympathetic - medial & anterior hypothalamus

hypothalamus ----> reticular formation ----> preganglionic autonomics

C. Cerebral Cortex and Biofeedback - making patient aware of autonomically controlled functions (heart rate, blood pressure) can allow them to learn how to better control them

### IV. Abnormalities of Autonomic Control Mechanisms

A. hypertension - increased blood pressure due to overstimulation of sympathetics that results from stress; NE blockers to treat

B. Raynaud's disease - abnormal vasoconstriction of vessels in the extremities; surgery to sever sympathetic fibers used to treat this problem

C. autonomic hyperflexia - massive reflex activation of all autonomies that occurs in response to spinal injury; can cause death due to loss of control of visceral function

## Task for independent training

1. Structurally, the autonomic nervous system consists of following subdivisions:
  - A. somatic and visceral
  - B. somatic and autonomic
  - C. sympathetic and parasympathetic
  - D. sensory and motor
  - E. sensory and autonomic
  
2. Clusters of neuron cell bodies located outside the CNS are called
  - A. centers
  - B. ganglia
  - C. nuclei
  - D. nerves
  - E. all answers are incorrect
  
3. All of the following are effectors innervated by the ANS *except*
  - A. smooth muscle fibers
  - B. cardiac muscle fibers
  - C. skeletal muscle fibers
  - D. salivary glands
  - E. sweat glands
  
4. Which of the following *does not* describe the sympathetic division of the ANS?
  - A. preganglionic axons leave the thoracic and upper lumbar spinal segments
  - B. preganglionic axons synapse in ganglia near the spinal cord
  - C. also called the "fight-or-flight" division
  - D. A and B
  - E. nicknamed the "rest-and-digest" division

5. Because of the location of its preganglionic neuron cell bodies, the sympathetic division is also called the \_\_\_\_\_ division
- A. prevertebral
  - B. paravertebral
  - C. craniosacral
  - D. cervical
  - E. thoracolumbar
6. The \_\_\_\_\_ division innervates visceral organs and tissues throughout the body, while the \_\_\_\_\_ division innervates only visceral structures served by cranial nerves or lying in the abdominal cavity or pelvic region.
- A. parasympathetic, sympathetic
  - B. sympathetic, parasympathetic
  - C. visceral sensory, visceral motor
  - D. preganglionic, postganglionic
  - E. preganglionic , parasympathetic
7. The cell bodies of postganglionic neurons are located in the:
- A. autonomic ganglia
  - B. posterior root ganglia
  - C. autonomic plexuses
  - D. visceral motor nuclei
  - E. A and C
8. What are the two types of sympathetic ganglia?
- A. terminal and intramural
  - B. prevertebral and collateral
  - C. paravertebral and terminal
  - D. sympathetic trunk and prevertebral
  - E. B and C



9. Preganglionic axons enter the nearby sympathetic trunk ganglia by way of
- A. autonomic nerves
  - B. posterior roots
  - C. white rami
  - D. gray rami
  - E. gray rami and posterior roots
10. Every spinal nerve receives a \_\_\_\_\_ ramus which carries postganglionic axons towards the blood vessels, sweat glands and piloerector muscles of the hairs.
- A. gray
  - B. white
  - C. posterior
  - D. anterior
  - E. white and posterior
11. The integration and command center for autonomic functions is the:
- A. cerebral cortex
  - B. hypothalamus
  - C. brainstem
  - D. spinal cord
  - E. medulla
12. Describe the number of neurons and their location in the autonomic reflex arc:
- A. Two neurons – one within the CNS and second within the ganglia
  - B. Three neurons – one within the paravertebral ganglia, others within prevertebral ganglia
  - C. One neuron – in the anterior horn of the spinal cord
  - D. Two neurons – both inside the brainstem

E. There is no correct answer

13. What cranial nerves contain the preganglionic neurons of the parasympathetic division?

- A. Oculomotor nerve, glossopharyngeal and facial nerve
- B. Olfactory nerve, glossopharyngeal and facial nerve
- C. Vagus nerve, glossopharyngeal and facial nerve
- D. Optic nerve, vagus nerve, glossopharyngeal nerve
- E. Oculomotor nerve, glossopharyngeal, facial and vagus nerve

14. Sympathetic nerve fibers which supply visceral organs of the thorax arise from:

- A. Th3-Th9 segments of spinal cord
- B. C1-C3 segments of spinal cord
- C. L1-L2 segments of spinal cord
- D. Th3-Th6 segments of spinal cord
- E. Th1-L2 segments of spinal cord

15. Because of the location of its preganglionic neuron cell bodies, the parasympathetic division is also called the \_\_\_\_\_ division

- A. prevertebral
- B. paravertebral
- C. craniosacral
- D. cervical
- E. thoracolumbar

16. What type of neurotransmitter is released from the preganglionic sympathetic fibers?

- A. norepinephrine
- B. epinephrine
- C. dopamine

D. acetylcholine

E. GABA

17. What type of neurotransmitter is released from the preganglionic parasympathetic fibers?

A. norepinephrine

B. epinephrine

C. dopamine

D. GABA

E. acetylcholine

18. What type of receptors is present in the celiac ganglion of the sympathetic division?

A. M-cholinoreceptors

B. N-cholinoreceptors

C. Alpha-adrenoreceptors

D. Beta-adrenoreceptors

E. H<sub>2</sub>-receptors

19. What type of receptors is present in the intramural ganglion of the parasympathetic division?

A. N-cholinoreceptors

B. M-cholinoreceptors

C. Alpha-adrenoreceptors

D. Beta-adrenoreceptors

E. H<sub>2</sub>-receptors

20. What type of receptors is excited in the smooth muscles of the stomach in case of acetylcholine presence?

A. H-cholinoreceptors

- B. M-cholinoreceptors
- C. Alpha-adrenoreceptors
- D. Beta-adrenoreceptors
- E. H<sub>2</sub>-receptors

21. Drugs which block nicotinic receptors are called:

- A. Anticholinesterase drugs
- B. Antimuscarinic drugs
- C. Nicotinic drugs
- D. Ganglionic blocking drugs
- E. Sympathomimetic drugs

22. What drug can stimulate postganglionic neurons in the same manner as acetylcholine of both the parasympathetic and the sympathetic nervous systems?

- A. Nicotine
- B. Muscarine
- C. Atropine
- D. Reserpine
- E. Isoproterenol

23. Drugs that block cholinergic activity at effector organs are called antimuscarinic drugs. Which one is the antimuscarinic drug:

- A. Nicotine
- B. Muscarine
- C. Atropine
- D. Reserpine
- E. Isoproterenol

24. Some drugs are able to inhibit enzyme, thus preventing rapid destruction of the acetylcholine liberated at parasympathetic nerve endings. What are these drugs?

- A. Nicotinic drugs
- B. Anticholinesterase drugs
- C. Antimuscarinic drugs
- D. Ganglionic blocking drugs
- E. Sympathomimetic drugs

25. What are the main prevertebral ganglia of the sympathetic division:

- A. Celiac, geniculate ganglion
- B. Superior and inferior mesenteric ganglia
- C. Petrosal, nodose and celiac ganglion
- D. Pelvic, superior and inferior mesenteric ganglia
- E. Celiac, superior and inferior mesenteric ganglia

26. Axons which release norepinephrine onto their effectors are called:

- A. excitatory
- B. inhibitory
- C. cholinergic
- D. adrenergic
- E. inhibitory, cholinergic

27. What neurotransmitter is released by most sympathetic postganglionic axons?

- A. epinephrine
- B. norepinephrine
- C. acetylcholine
- D. dopamine
- E. GABA

28. The arterial pressure of 40-year-old man have been increased after mental stress. What is the reason of this effect?

- A. Increase of the sympathetic tone
- B. Dilation of the arterioles

- C. Stimulation of the muscarinic receptors
- D. Hyperpolarization of the cardiomyocytes
- E. Increase of the parasympathetic tone

29. What type of neurotransmitter is released by all preganglionic axons?

- A. norepinephrine
- B. epinephrine
- C. acetylcholine
- D. dopamine
- E. GABA

30. What type of receptors is stimulated on the radial muscle of the iris by the meaning of noradrenergic fibers?

- A.  $\beta_1$
- B.  $\beta_2$
- C.  $\alpha_2$
- D.  $\alpha_1$
- E.  $\beta_1, \beta_2$

31. For the better examination of the eye-ground the doctor dropped the solution of the atropine in the patient's conjunctiva. It resulted in dilation of the pupil through the blockage of such membrane receptors:

- A. M-cholinoreceptors
- B. H-cholinoreceptors
- C. Alpha-adrenoreceptors
- D. Beta-adrenoreceptors
- E. H<sub>2</sub>-receptors

32. Nicotinic receptors are found in:

- A. the autonomic ganglia of the sympathetic division

- B. the autonomic ganglia of the parasympathetic division
- C. on all effector cells that are stimulated by the postganglionic cholinergic neurons
- D. on all effector cells that are stimulated by the postganglionic adrenergic neurons
- E. the autonomic ganglia of both the sympathetic and parasympathetic systems

33. Muscarinic receptors are found on:

- A. the autonomic ganglia of the sympathetic division
- B. the autonomic ganglia of the parasympathetic division
- C. on all effector cells that are stimulated by the postganglionic cholinergic neurons
- D. on all effector cells that are stimulated by the postganglionic adrenergic neurons
- E. the autonomic ganglia of both the sympathetic and parasympathetic systems

34. What type of receptors is stimulated on the smooth muscle of bronchi by the meaning of noradrenergic fibers?

- A.  $\beta_1$
- B.  $\beta_2$
- C.  $\alpha_2$
- D.  $\alpha_1$
- E.  $\beta_1, \beta_2$

35. What neurotransmitter is released from the postganglionic parasympathetic fibers?

- A. epinephrine
- B. norepinephrine
- C. GABA
- D. dopamine

E. acetylcholine

36. The motility of the intestine increased after stimulation of the following receptors:

- A. muscarinic
- B. nicotinic
- C. adrenergic
- D.  $\beta$ - adrenergic
- E.  $\alpha$ - adrenergic

37. What type of neurotransmitter increases secretion of digestive juices?

- A. epinephrine
- B. norepinephrine
- C. GABA
- D. dopamine
- E. acetylcholine

38. Describe changes in the motility of the digestive tract during stimulation of sympathetic fibers:

- A. Contraction of the wall muscles and relaxation of sphincters
- B. Relaxation of the wall muscles and contraction of sphincters
- C. Contraction of the wall muscles and contraction of sphincters
- D. Relaxation of the wall muscles and relaxation of sphincters
- E. All answers are incorrect.

39. What happens with blood vessels of most viscera after stimulation of parasympathetic fibers?

- A. Constriction because of the muscarinic receptors excitation
- B. Relaxation because of the nicotinic receptors excitation
- C. Constriction because of the adrenergic receptors excitation
- D. Relaxation because of the muscarinic receptors excitation



E. Constriction because of the  $\alpha$ -receptors excitation

40. During stress conditions adrenal medulla release large amount of adrenaline, which causes vasoconstriction due to:

- A. Stimulation of the  $\alpha$ -adrenoreceptors
- B. Stimulation of the  $\beta$ -adrenoreceptors
- C. Stimulation of the nicotinic receptors
- D. Stimulation of the muscarinic receptors
- E. Stimulation of the  $\beta_1$ -adrenoreceptors

41. The rate and force of heart contraction is facilitated due to the stimulation of the following receptors:

- A.  $\alpha_1$ -adrenoreceptors
- B.  $\beta_1, \beta_2$  –adrenoreceptors
- C.  $\alpha_2$ - adrenoreceptors
- D. M-cholinoreceptors
- E. N –cholinoreceptors

42. Which of these is not a neurotransmitter in the autonomic nervous system?

- A. Acetylcholine
- B. Norepinephrine
- C. Epinephrine
- D. Muscarine
- E. Neuropeptide Y

43. What kind of autonomic nerve and what kind of neurotransmitter causes contraction of the sphincter muscle of the iris and the ciliary muscle?

- A. oculomotor nerve, acetylcholine
- B. facial nerve, acetylcholine
- C. oculomotor nerve, norepinephrine
- D. facial nerve, norepinephrine

E. optic nerve, adrenaline

44. Smooth muscles of bronchi are relaxed whenever there is stimulation of:

A.  $\alpha$ 1-adrenoreceptors

B.  $\beta$ 2 –adrenoreceptors

C.  $\alpha$ 2- adrenoreceptors

D. M-cholinoreceptors

E. N –cholinoreceptors

45. Compared to the ANS, receptors of the somatic nervous system include

A. nicotinic cholinergic receptors only

B. muscarinic cholinergic receptors only

C. nicotinic and muscarinic cholinergic receptors

D. cholinergic and nicotinic receptors

E. all answers are correct

46. In which of the following cranial nerves the parasympathetic preganglionic nerve fibers for organs of the thorax and upper abdomen are present?

A. Facial

B. Glossopharyngeal

C. Oculomotor

D. Opticus

E. Vagus

47. Which of the following ganglia are associated with the parasympathetic division of the autonomic nervous system?

A. Collateral

B. Paravertebral

C. Sympathetic

D. Terminal

E. All are incorrect

48. Parasympathetic preganglionic axons in pathways leading to the visceral effectors in the head occur in each of the following cranial nerves except the:

- A. Facial nerves
- B. Glossopharyngeal nerves
- C. Vagus nerves
- D. Oculomotor nerves
- E. All are incorrect

49. The parasympathetic fibers that control the secretion of saliva, tears and nasal secretions are conveyed in the:

- A. Facial nerves
- B. Glossopharyngeal nerves
- C. Oculomotor nerves
- D. vagus nerves
- E. All are incorrect

50. Parasympathetic fibers of the vagus nerves form each of the following autonomic plexuses except the:

- A. Cardiac
- B. Esophageal
- C. Inferior hypogastric
- D. Pulmonary
- E. All are correct

51. Which of the following is a terminal ganglion of the parasympathetic division?

- A. Ciliary ganglion
- B. Celiac ganglion
- C. Inferior mesenteric ganglion
- D. Superior mesenteric ganglion

E. All are incorrect

52. Parasympathetic centers are present within the following divisions of the CNS:

A. Midbrain

B. Medulla oblongata

C. Midbrain , medulla oblongata , sacral segments of the spinal cord

D. thoracic segments of the spinal cord

E. lumbar segments of the spinal cord

53. In which of the following segments of the spinal cord parasympathetic preganglionic nerve fibers for the organs of the pelvic cavity are present?

A. Brainstem

B. Cervical

C. Lumbar

D. Thoracic

E. Sacral

54. Which of the following are not exclusively cholinergic neurons?

A. Parasympathetic preganglionic

B. Parasympathetic postganglionic

C. Sympathetic preganglionic

D. Sympathetic postganglionic

E. Somatic motor fibers

55. Which of the following are usually adrenergic neurons?

A. Parasympathetic preganglionic

B. Parasympathetic postganglionic

C. Sympathetic preganglionic

D. Sympathetic postganglionic

E. All answers are correct

56. Which of the following is NOT a parasympathetic effect?
- A. Constriction of the pupils of the eyes
  - B. Contraction of the urinary bladder
  - C. Decreased heart rate
  - D. Constriction of the bronchioles in the lungs
  - E. Dilation of the bronchioles in the lungs
57. The parasympathetic fibers that control the muscles involved in constriction of the pupils in response to a bright light shined in eyes are conveyed in the:
- A. Facial nerves
  - B. Glossopharyngeal nerves
  - C. Oculomotor nerves
  - D. Vagus nerves
  - E. Opticus
58. Which of the following receptors occur in the membranes of target cells of parasympathetic postganglionic neurons?
- A. alpha and beta adrenergic
  - B. Muscarinic cholinergic
  - C. Nicotinic cholinergic
  - D. alpha or beta adrenergic or muscarinic cholinergic
  - E. gamma adrenergic
59. Which of the following is a parasympathetic blocking agent used to dilate the pupils during an eye examination?
- A. Albuterol
  - B. Atropine
  - C. Phenylephrine
  - D. Propranolol

E. Thyocetam

60. What function is not controlled by the dual innervation of the autonomic nervous system:

- A. Contraction of the urinary bladder
- B. Heart rate
- C. Diameter of blood vessels in skeletal muscles
- D. Diameter of bronchioles in the lungs
- E. Pulse rate

61. Dilation of pupils is stimulated whenever there is:

- A. Increased parasympathetic tone
- B. Decreased parasympathetic tone
- C. Decreased sympathetic tone
- D. Increased sympathetic tone
- E. All answers are incorrect

62. Pupils are constricted due to the:

- A. Increased parasympathetic tone
- B. Decreased parasympathetic tone
- C. Decreased sympathetic tone
- D. Increased sympathetic tone
- E. All answers are incorrect

63. Which of the following events happens because of the increased parasympathetic activity?

- A. Increased heart rate
- B. Dilation of bronchi
- C. Increased gastric juice secretion
- D. Dilation of pupils
- E. Increased blood pressure

64. What kind of influence is exerted by the sympathetic nerves on the sphincters of the gastrointestinal tract?

- A. Contraction because of the  $\alpha$ -receptors stimulation
- B. Relaxation because of the  $\beta$ -receptors stimulation
- C. Contraction because of the M-receptors stimulation
- D. Relaxation because of the N-receptors stimulation
- E. They have no effect on the sphincters.

65. Stimulation of the posterior thalamic nuclei leads to the:

- A. Contraction of the smooth muscles of bronchi
- B. Increased heart rate
- C. Increased gastric juice secretion
- D. Constriction of the pupils
- E. Dilation of the blood vessels

66. Which of the following is caused by the sympathetic stimulation?

- A. Elevation of the blood pressure
- B. Increased heart rate
- C. Decreased gastric juice secretion
- D. Dilation of pupils
- E. All answers are correct

67. Fibers are called adrenergic whenever they are:

- A. Postganglionic, sympathetic
- B. Postganglionic, parasympathetic
- C. Preganglionic, sympathetic
- D. Preganglionic, parasympathetic
- E. Pre- and postganglionic, sympathetic

68. Sympathetic fibers accelerate the rate of heart contraction due to the:
- A.  $\alpha$ -receptors excitation
  - B.  $\beta$ -receptors excitation
  - C. M-receptors excitation
  - D. N-receptors excitation
  - E.  $\alpha$ -receptors inhibition
69. What are the effects of parasympathetic stimulation?
- A. Contraction of the gastrointestinal sphincters
  - B. Dilation of pupils
  - C. Increased glycogenolysis
  - D. Increased lypolysis
  - E. Decreased heart rate
70. Patient, who is suffering from stress after injury, has dilation of the pupils. What type of neurotransmitter is responsible for this effect?
- A. Glycine
  - B. Serotonin
  - C. ATP
  - D. Acetylcholine
  - E. Norepinephrine
71. According to the legend in ancient India the criminal was asked to swallow handful of rice. If he was guilty, he was not able to do this because of:
- A. Increased parasympathetic tone
  - B. Decreased parasympathetic tone
  - C. Decreased sympathetic tone
  - D. Increased sympathetic tone
  - E. All answers are incorrect



72. Arterial pressure is often increased before the exam. What type of receptors is responsible for this effect?

- A.  $\alpha_1$ -receptors
- B.  $\beta_1$ -receptors
- C. M-receptors
- D. N-receptors
- E.  $\beta_2$ -receptors

73. Stimulation of the posterior thalamic nuclei leads to the:

- A. Dilation of pupils, bradycardia, hyperglycemia
- B. Dilation of pupils, tachycardia, hypoglycemia
- C. Constriction of pupils, tachycardia, hyperglycemia
- D. Constriction of pupils, bradycardia, hypoglycemia
- E. Constriction of pupils, bradycardia, hyperglycemia

74. The ANS has preganglionic and postganglionic fibers. Which organ receives only the preganglionic fibers?

- A. Stomach and salivary glands
- B. Adrenal gland
- C. Sweat glands
- D. Heart and blood vessels
- E. All answers are correct

75. After the vagotomy patient was suffering from severe atony of the stomach. What type of receptors was not activated?

- A.  $\alpha_1$ -adrenergic receptors
- B.  $\beta_1$ -adrenergic receptors
- C. M-cholinergic receptors
- D. N-cholinergic receptors
- E.  $\beta_2$ -adrenergic receptors

76. Reddening of the skin as a result of vasodilation, local sweating as a result of sweat gland activation, or pain as a result of the action of the released neurotransmitter when an orthodromic action potential from a sensory nerve ending propagates antidromically into collateral branches of the same neuron is called:

- A. Local axon reflex
- B. Transverse axon reflex
- C. Baroreceptive reflex
- D. Accommodation reflex
- E. All answers are incorrect

77. During acute experiment it was necessary to abolish the influence of all ANS divisions. What drugs must be introduced?

- A. muscarinic receptor blockers
- B. ganglia blockers
- C.  $\alpha$ -receptor blockers
- D.  $\beta$ -receptor blockers
- E.  $\alpha$ - and  $\beta$ -receptor blockers

78. Patient suffering from an accident has the following symptoms: increased heartbeat, elevated arterial pressure, dilation of pupils, and dryness in the mouth. This is because of activation of:

- A. vagus nerve
- B. parasympathetic system
- C. sympathetic system
- D. hypothalamic-pituitary system
- E. local reflexes

79. The peripheral end of vagus nerve is constantly stimulated with the help of electrical current. Which of the following changes in the activity of visceral organs can be observed?

- A. increased rate of breathing
- B. increased heart rate
- C. dilation of bronchi
- D. decreased heart rate
- E. decreased motility of intestine

80. What happened with the eye of rabbit in which several drops of muscarinic blocker were introduced?

- A. constriction of pupil
- B. dilation of pupil
- C. at first dilation, than constriction of pupil
- D. at first constriction, than dilation of pupil
- E. no change took place

81. The man has eaten poisonous mushrooms, which contained muscarine. After several hours the man was poisoned. What is the main feature of the poison during first hours?

- A. constriction of pupils
- B. dilation of pupils
- C. bronchodilation
- D. elevation of the blood pressure
- E. increased heart rate

82. During sleep some people have increased salivation. This happens because of:

- A. stimulation of the nicotinic receptors via vagus nerve
- B. stimulation of the muscarinic receptors via facial nerve
- C. stimulation of the muscarinic receptors via vagus nerve

- D. blockade of the  $\alpha$ -adrenergic receptors
- E. blockade of the  $\beta$ -adrenergic receptors

83. After surgical treatment the doctor decided to increase the peristalsis with the help of drugs which:

- A. increased acetylcholine concentration
- B. decreased acetylcholine concentration
- C. blocked adrenergic receptors
- D. activated adrenergic receptors
- E. correct answer is absent

84. Patient suffering from tachycardia can be treated in such way:

- A. stimulation of  $\beta$ -receptors in the cardiac muscle
- B. stimulation of  $\alpha$ -receptors in the cardiac muscle
- C. blockade of muscarinic receptors in the cardiac muscle
- D. blockade of nicotinic receptors in the cardiac muscle
- E. blockade of  $\beta$ -receptors in the cardiac muscle

85. The patient is suffering from micturition disorders. During urination autonomic pelvic nerves act on the urinary bladder in the following manner:

- A. detrusor muscle is relaxed, internal sphincter is constricted
- B. detrusor muscle is constricted, internal sphincter is relaxed
- C. both detrusor muscle and internal sphincter are constricted
- D. both detrusor muscle and internal sphincter are relaxed
- E. detrusor muscle is relaxed, external sphincter is constricted

86. During esophagoscopy the doctor found out that there is a gastric ulcer on the big curvature of the stomach. Patient suffering from gastric ulcer must be treated with drugs which are able to:

- A. activate muscarinic receptors

- B. activate  $\beta$ -receptors
- C. block  $\alpha$ -receptors
- D. activate nicotinic receptors
- E. block muscarinic receptors

87. During experiment stimulation of the glossopharyngeal nerve conducted on the dog, secretion of saliva changed in such way:

- A. secretion of submandibular gland has increased
- B. secretion of submandibular gland has decreased
- C. secretion of parotid gland has increased
- D. secretion of parotid gland has decreased
- E. secretion of sublingual gland has increased

88. During exam student forgot the correct answer, amount of sweat secretion increased immediately. What is the reason of this condition?

- A. ACH released from the parasympathetic fibers
- B. ACH released from the sympathetic fibers
- C. norepinephrine released from the parasympathetic fibers
- D. norepinephrine released from the sympathetic fibers
- E. dopamine released from the parasympathetic fibers

89. After meal the bile is released from the gallbladder because of:

- A. stimulation of  $\beta$ -receptors via ACH
- B. stimulation of nicotinic receptors via ACH
- C. stimulation of muscarinic receptors via norepinephrine
- D. stimulation of muscarinic receptors via ACH
- E. stimulation of  $\alpha$ -receptors via norepinephrine

90. Match each numbered phenomenon below to the autonomic receptors that mediate it. Low concentrations of epinephrine released from the adrenal medulla cause vasodilatation...

- A. Adrenergic a receptors (beta 1 and beta 2 receptors)
- B. Adrenergic (beta 1 receptors)
- C. Adrenergic (beta 2 receptors)
- D. Cholinergic muscarinic receptors
- E. Cholinergic nicotinic receptors

91. Match each numbered phenomenon below to the autonomic receptors that mediate it. Bronchodilatation...

- A. Adrenergic a receptors (beta 1 and beta 2 receptors)
- B. Adrenergic (beta 1 receptors)
- C. Adrenergic (beta 2 receptors)
- D. Cholinergic Muscarinic receptors
- E. Cholinergic nicotinic receptors

92. The experiment established that the strength of heart contractions is observed on the irritation of the strengthening Pavlov's nerve. What mediator's action in the result connected with?

- A. Noradrenaline
- B. Acetylcholine
- C. Serotonin
- D. Dofamine
- E. GABA

93. Match each numbered phenomenon below to the autonomic receptors that mediate it. Uterus relaxation...

- A. Adrenergic a receptors (beta 1 and beta 2 receptors)

- B. Adrenergic (beta 1 receptors)
- C. Adrenergic (beta 2 receptors)
- D. Cholinergic Muscarinic receptors
- E. Cholinergic nicotinic receptors

94. Reflex arch of vegetative reflex can lock through:

- A. Centers of spinal cord
- B. Centers of brainstem
- C. Vegetative ganglions
- D. Limbic system
- E. Cortex of cerebral hemisphere

95. Salivation can decrease after:

- A. Activation of sympathetic-adrenal system
- B. Activation of parasympathetic nucleus of nerve facials
- C. Decreasing of blood supply of salivary glands
- D. Activation of parasympathetic nucleus of nerve gloss pharyngeal
- E. Inhibition of sympathetic-adrenal system

96. The part of the brain that has hunger, satiety, and sleep centers; affects activities of the ANS; and plays a role in emotional responses such as rage, pain, and pleasure is the

- A. medulla.
- B. pons
- C. hypothalamus
- D. midbrain
- E. epithalamus

97. Match each numbered phenomenon below to the autonomic receptors that mediate it. Lipolysis...

- A. Adrenergic  $\alpha$  receptors (beta 1 and beta 2 receptors)
- B. Adrenergic (beta 1 receptors)
- C. Adrenergic (beta 2 receptors)
- D. Cholinergic Muscarinic receptors
- E. Cholinergic nicotinic receptors

98. 40-year-old man had elevated arterial pressure after emotional excitement.

Name a possible cause of this effect.

- A. Increase of the tonus of the sympathetic nervous system
- B. Atherosclerosis of the arterioles
- C. Decrease of frequency of cardiac contractions
- D. Hyperpolarization of the cardiomyocytes.
- E. Increase of the tonus of the parasympathetic nervous system

99. Match each numbered phenomenon below to the autonomic receptors that mediate it. Low concentrations of epinephrine released from the adrenal medulla cause vasodilatation...

- A. Adrenergic  $\alpha$  receptors (beta 1 and beta 2 receptors)
- B. Adrenergic (beta 1 receptors)
- C. Cholinergic muscarinic and nicotinic receptors
- D. Cholinergic muscarinic receptors
- E. all is incorrect

100. At the man after retention of the respiration for 40 seconds the frequency of heart contractions and system arterial pressure increased. Which regulatory mechanisms realization provides the change of parameters?

- A. Unconditioned sympathetic reflexes
- B. Unconditioned parasympathetic reflexes
- C. Conditioned sympathetic reflexes
- D. Conditioned parasympathetic reflexes



## E. Reflexes

### Answers:

1	C	21	D	41	A	61	C	81	B
2	B	22	A	42	B	62	D	82	A
3	C	23	C	43	D	63	A	83	B
4	E	24	B	44	A	64	C	84	A
5	E	25	E	45	B	65	A	85	E
6	B	26	A	46	A	66	B	86	B
7	A	27	B	47	E	67	E	87	E
8	D	28	C	48	D	68	A	88	C
9	C	29	C	49	C	69	B	89	B
10	A	30	D	50	A	70	E	90	C
11	B	31	B	51	C	71	E	91	C
12	A	32	A	52	A	72	D	92	A
13	E	33	E	53	C	73	A	93	C
14	D	34	C	54	E	74	D	94	C
15	C	35	B	55	D	75	B	95	A
16	D	36	E	56	D	76	C	96	C
17	E	37	A	57	E	77	A	97	B
18	B	38	E	58	C	78	B	98	A
19	A	39	B	59	B	79	C	99	E
20	B	40	D	60	B	80	D	100	A

### Task for independent training (Krok 1)

1. For better examination of the fundus of eye a doctor began to drip the solution of atropine on the conjunctiva of the patient's eye. It resulted in pupil expansion. The blockade of what membranous cytoceptors stipulated such effect?

- A. H<sub>2</sub>-receptors.
- B. N-Cholinoreceptors.
- C.  $\alpha$ -adrenoreceptors.
- D.  $\beta$ -adrenoreceptors.
- E. M-Cholinoreceptors.

2. The consequence of what process is the persistent dilation of pupil under the conditions of intense illumination?

- A. Paralysis of ciliary muscle.
- B. Normal state of regulatory mechanisms.
- C. Overactivity of the parasympathetic part of the nervous system.
- D. Paralysis of the muscle that expands the pupil.
- E. Overactivity of the sympathetic part of the nervous system.

3. A 60-year-old patient was diagnosed with hypothalamic lateral nuclei stroke.

What changes in patient's behavior may be expected?

- A The rejection of food
- B Aggressive behaviour
- C Depression
- D Thirst
- E Unsatisfied hunger

4. Upper neck node of sympathetic trunk was removed from the rabbit on experiment. Reddening and increased temperature of the skin of head is observed. What disorder of peripheral circulation of the blood has developed?

- A Neuroparalytic arterial hyperemia
- B Neurotonic arterial hyperemia

- C Metabolic arterial hyperemia
- D Venous hyperemia
- E Stasis

5. A peripheral segment of vagus nerve on a dog's neck was being stimulated in course of an experiment. The following changes of cardiac activity could be meanwhile observed:

- A Heart rate fall
- B Heart hurry
- C Enhancement of atrioventricular conduction
- D Heart rate and heart force amplification
- E Increased excitability of myocardium

6. Introduction of a pharmaceutical substance to an experimental animal resulted in reduction of salivation, pupil mydriasis. Next intravenous introduction of acetylcholine didn't lead to any significant changes of heart rate. Name this substance:

- A Atropine
- B Adrenaline
- C Propranolol
- D Proserin
- E Salbutamol

7. Arterial pressure of a surgeon who performed a long operation rised up to 140/110 mm Hg. What changes of humoral regulation could have caused the rise of arterial pressure in this case?

- A Activation of sympathoadrenal system
- B Activation of formation and excretion of aldosterone
- C Activation of renin angiotensive system
- D Activation of kallikrein kinin system
- E Inhibition of sympathoadrenal system

8. An aged man had raise of arterial pressure under a stress. It was caused by activation of:

- A Sympathoadrenal system
- B Parasympathetic nucleus of vagus
- C Functions of thyroid gland
- D Functions of adrenal cortex
- E Hypophysis function

9. An ophthalmologist used a 1% mesaton solution for the diagnostic purpose (pupil dilation for eye-ground examination). What is the cause of mydriasis induced by the drug?

- A. Activation of  $\alpha 1$  adrenoreceptors
- B. Activation of  $\alpha 2$  adrenoreceptors
- C. Block of  $\alpha 1$  adrenoreceptors
- D. Activation of  $\beta 1$  adrenoreceptors
- E. Activation of M-cholinoreceptors

10. Students who are taking examinations often have dry mouth. The mechanism that causes this state is the realization of the following reflexes:

- A Conditioned sympathetic
- B Unconditioned parasympathetic
- C Conditioned parasympathetic
- D Unconditioned sympathetic
- E Unconditioned peripheral

11. A man was intoxicated with mushrooms. They contain muscarine that stimulates muscarinic cholinoreceptors. What symptoms signalize intoxication with inedible mushrooms?

- A Myotic pupils

- B Mydriatic pupils
- C Bronchi dilatation
- D ncreased heart rate
- E Rise of arterial pressure

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12. The minute blood volume in a patient with transplanted heart has increased as a result of physical activity. What regulative mechanism is responsible for these changes?

- A Catecholamines
- B Sympathetic unconditioned reflexes
- C Parasympathetic unconditioned reflexes
- D Sympathetic conditioned reflexes
- E Parasympathetic conditioned reflexes

13. During fighting a man had a cardiac arrest as a result of a hard blow to the upper region of anterior abdominal wall. Which of the described mechanisms might have provoked the cardiac arrest?

- A Parasympathetic unconditioned reflexes
- B Sympathetic unconditioned reflexes
- C Parasympathetic conditioned reflexes
- D Sympathetic conditioned reflexes
- E Peripheral reflexes

14. If a man has an attack of bronchospasm it is necessary to reduce the effect of vagus on smooth muscles of bronchi. What membrane cytoceptors should be blocked for this purpose?

- A M-cholinoreceptors
- B N-cholinoreceptors
- C  $\alpha$ -adrenoreceptors

- D  $\beta$ -adrenoreceptors
- E  $\alpha$ - and  $\beta$ -adrenoreceptors

15. A man got poisoned with mushrooms. They contain muscarine that stimulates muscarinic cholinoreceptors. What symptom is typical for poisoning with inedible mushrooms?

- A Miosis
- B Mydriasis
- C Bronchi dilation
- D Heart rate rise
- E Arterial pressure rise

16. Experimental stimulation of the sympathetic nerve branches that innervate the heart caused an increase in the force of heart contractions because the membrane of typical cardiomyocytes permitted an increase in:

- A Calcium ion entry
- B Calcium ion exit
- C Potassium ion exit
- D Potassium ion entry
- E Calcium and potassium ion exit

**Answers:**

1	E
2	E
3	A
4	A
5	A
6	A
7	A
8	A
9	A
10	A
11	A

12	A
13	A
14	A
15	A
16	A

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