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▲ TABLE 7-2 Sites of Release for Acetylcholine and Norepinephrine

Acetylcholine	Norepinephrine
All preganglionic terminals of the autonomic nervous system	Most sympathetic postganglionic terminals
All parasympathetic postganglionic terminals	Adrenal medulla
Sympathetic postganglionic terminals at sweat glands and some blood vessels in skeletal muscle	Central nervous system
Terminals of efferent neurons supplying skeletal muscle (motor neurons)	
Central nervous system	

monly known as **norepinephrine.**[1] Both acetylcholine and norepinephrine also serve as chemical messengers elsewhere in the body (▲ Table 7-2).

Postganglionic autonomic fibers do not end in a single terminal swelling like a synaptic knob. Instead, the terminal branches of autonomic fibers have numerous swellings, or **varicosities,** that simultaneously release neurotransmitter over a large area of the innervated organ rather than on single cells (see ● Figures 7-1 and 8-32, p. 297). This diffuse release of neurotransmitter, coupled with the fact that any resulting change in electrical activity is spread throughout a smooth or cardiac muscle mass via gap junctions (see p. 59), means that autonomic activity typically influences whole organs instead of discrete cells.

The sympathetic and parasympathetic nervous systems dually innervate most visceral organs.

Afferent information coming from the viscera (internal organs) usually does not reach conscious level (see p. 187). Examples of visceral afferent information include input from the baroreceptors that monitor blood pressure and input from the chemoreceptors that monitor the protein or fat content of ingested food. This input is used to direct the activity of the autonomic efferent neurons. Autonomic efferent output regulates visceral activities such as circulation, digestion, sweating, and pupillary size. Like visceral afferent input, autonomic efferent output operates outside the realm of consciousness and voluntary control.

Most visceral organs are innervated by both sympathetic and parasympathetic nerve fibers (● Figure 7-3). Innervation of a single organ by both branches of the autonomic nervous system is known as **dual innervation** (*dual* means "pertaining to two"). ▲ Table 7-3 summarizes the major effects of these autonomic branches. Although the details of this wide array of autonomic responses are described more fully in later chapters that discuss the individual organs involved, you can consider several general concepts now. As you can see from the table, the sympathetic and parasympathetic nervous systems generally exert opposite effects in a particular organ. Sympathetic stimulation increases the heart rate, whereas parasympathetic stimulation decreases it; sympathetic stimulation slows down movement within the digestive tract, whereas parasympathetic stimulation enhances digestive motility. Note that both systems increase the activity of some organs and reduce the activity of others.

Rather than memorize a list such as in ▲ Table 7-3, it is better to logically deduce the actions of the two systems by first understanding the circumstances under which each system dominates. Usually both systems are partially active; that is, normally some level of action potential activity exists in both the sympathetic and the parasympathetic fibers supplying a particular organ. This ongoing activity is called **sympathetic** or **parasympathetic tone** or **tonic activity.** Under given circumstances, activity of one division can dominate the other. *Sympathetic dominance* to a particular organ exists when the sympathetic fibers' rate of firing to that organ increases above tonic level, coupled with a simultaneous decrease below tonic level in the parasympathetic fibers' frequency of action potentials to the same organ. The reverse situation is true for *parasympathetic dominance.* The balance between sympathetic and parasympathetic activity can be shifted separately for individual organs to meet specific demands (for example, sympathetically induced dilation of the pupil in dim light; see p. 197), or a more generalized, widespread discharge of one autonomic system in favor of the other can be elicited to control bodywide functions. Massive widespread discharges take place more frequently in the sympathetic system. The value of massive sympathetic discharge is clear, considering the circumstances during which this system usually dominates.

TIMES OF SYMPATHETIC DOMINANCE The sympathetic system promotes responses that prepare the body for strenuous physical activity in emergency or stressful situations, such as a physical threat from the outside. This response is typically referred to as a **fight-or-flight response** (some physiologists even throw in **fright,** too), because the sympathetic system readies the body to fight against or flee from (and be frightened by) the threat. Think about the body resources needed in such circumstances. The heart beats more rapidly and more forcefully, blood pressure is elevated by generalized constriction (narrowing) of the blood vessels, respiratory airways open wide to permit maximal airflow, glycogen

[1] *Noradrenaline (norepinephrine)* is chemically very similar to *adrenaline (epinephrine),* the primary hormone product secreted by the adrenal medulla gland. Because a U.S. pharmaceutical company marketed this product for use as a drug under the trade name Adrenalin, the scientific community in this country prefers the alternative name "epinephrine" as a generic term for this chemical messenger, and accordingly, "noradrenaline" is known as "norepinephrine." In most other English-speaking countries, however, "adrenaline" and "noradrenaline" are the terms of choice.

TABLE 7-3 Effects of Autonomic Nervous System on Various Organs

Organ	Effect of Sympathetic Stimulation (and Types of Adrenergic Receptors)	Effect of Parasympathetic Stimulation
Heart	Increased rate, increased force of contraction (of whole heart) (β_1)	Decreased rate, decreased force of contraction (of atria only)
Most Innervated Blood Vessels	Constriction (α_1)	Dilation of vessels supplying the penis and clitoris only
Lungs	Dilation of bronchioles (airways) (β_2)	Constriction of bronchioles
	Inhibition of mucus secretion (α)	Stimulation of mucus secretion
Digestive Tract	Decreased motility (movement) (α_2, β_2)	Increased motility
	Contraction of sphincters (to prevent forward movement of contents) (α_1)	Relaxation of sphincters (to permit forward movement of contents)
	Inhibition of digestive secretions (α_2)	Stimulation of digestive secretions
Urinary Bladder	Relaxation (β_2)	Contraction (emptying)
Eye	Dilation of pupil (contraction of radial muscle) (α_1)	Constriction of pupil (contraction of circular muscle)
	Adjustment of eye for far vision (β_2)	Adjustment of eye for near vision
Liver (glycogen stores)	Glycogenolysis (glucose released) (β_2)	None
Adipose Cells (fat stores)	Lipolysis (fatty acids released) (β_2)	None
Exocrine Glands		
Exocrine pancreas	Inhibition of pancreatic exocrine secretion (α_2)	Stimulation of pancreatic exocrine secretion (important for digestion)
Sweat glands	Stimulation of secretion by most sweat glands (α_1; most are cholinergic)	Stimulation of secretion by some sweat glands
Salivary glands	Stimulation of small volume of thick saliva rich in mucus (α_1)	Stimulation of large volume of watery saliva rich in enzymes
Endocrine Glands		
Adrenal medulla	Stimulation of epinephrine and norepinephrine secretion (cholinergic)	None
Endocrine pancreas	Inhibition of insulin secretion; stimulation of glucagon secretion (α_2)	Stimulation of insulin and glucagon secretion
Genitals	Ejaculation and orgasmic contractions (males); orgasmic contractions (females) (α_1)	Erection (caused by dilation of blood vessels in penis [male] and clitoris [female])
Brain Activity	Increased alertness (receptors unknown)	None

(stored sugar) and fat stores are broken down to release extra fuel into the blood, and blood vessels supplying skeletal muscles dilate (open more widely). All these responses are aimed at providing increased flow of oxygenated, nutrient-rich blood to the skeletal muscles in anticipation of strenuous physical activity. Furthermore, the pupils dilate and the eyes adjust for far vision, letting the person visually assess the entire threatening scene. Sweating is promoted in anticipation of excess heat production by the physical exertion. Because digestive and urinary activities are not essential in

TABLE 7-5 Distinguishing Features of Sympathetic Nervous System and Parasympathetic Nervous System

Feature	Sympathetic System	Parasympathetic System
Origin of Preganglionic Fiber	Thoracic and lumbar regions of spinal cord	Brain and sacral region of spinal cord
Origin of Postganglionic Fiber (location of ganglion)	Sympathetic ganglion chain (near spinal cord) or collateral ganglia (about halfway between spinal cord and effector organs)	Terminal ganglia (in or near effector organs)
Length and Type of Fiber	Short cholinergic preganglionic fibers	Long cholinergic preganglionic fibers
	Long adrenergic postganglionic fibers	Short cholinergic postganglionic fibers
Effector Organs Innervated	Cardiac muscle, almost all smooth muscle, most exocrine glands, and some endocrine glands	Cardiac muscle, most smooth muscle, most exocrine glands, and some endocrine glands
Types of Receptors for Neurotransmitters	For preganglionic neurotransmitter: nicotinic	For preganglionic neurotransmitter: nicotinic
	For postganglionic neurotransmitter: α_1, α_2, β_1, β_2	For postganglionic neurotransmitter: muscarinic
Dominance	Dominates in emergency "fight-or-flight" situations; prepares body for strenuous physical activity	Dominates in quiet, relaxed situations; promotes "general housekeeping" activities such as digestion

mol selectively activates β_2 adrenergic receptors at low doses, making it possible to dilate the bronchioles in the treatment of asthma without undesirably stimulating the heart (the heart has mostly β_1 receptors). By contrast, *metoprolol* selectively blocks β_1 adrenergic receptors and is prescribed to treat high blood pressure because it decreases the amount of blood the heart pumps into the blood vessels. Metoprolol does not affect β_2 receptors and so has no effect on the bronchioles. The less specific drug *propanolol* also lowers blood pressure by blocking β_1 receptors, but it also blocks β_2 receptors located in the bronchioles, leading to narrowing of these airways and asthma as an undesirable side effect in susceptible people.

Many regions of the central nervous system are involved in the control of autonomic activities.

Messages from the CNS are delivered to cardiac muscle, smooth muscle, and glands via the autonomic nerves, but which regions of the CNS regulate autonomic output? Autonomic control of these effectors is mediated by reflexes and through centrally located control centers. Going back one step further, ultimately information carried to the CNS via the visceral afferents is used to determine the appropriate output via the autonomic efferents to the effectors to maintain homeostasis. Indeed, some physiologists regard the visceral afferents as part of the autonomic nervous system, while others consider the sympathetic and parasympathetic efferents as being the only components of the autonomic nervous system. Whatever way you classify these parts of the nervous system, the point remains that visceral afferent input is critical for determining sympathetic and parasympathetic output.

- Some autonomic reflexes, such as urination, defecation, and erection, are integrated at the spinal-cord level, but all these spinal reflexes are subject to control by higher levels of consciousness.
- The medulla within the brain stem is the region most directly responsible for autonomic output. Centers for controlling cardiovascular, respiratory, and digestive activity via the autonomic system are located there.
- The hypothalamus plays an important role in integrating the autonomic, somatic, and endocrine responses that automatically accompany various emotional and behavioral states. For example, the increased heart rate, blood pressure, and respiratory activity associated with anger or fear are brought about by the hypothalamus acting through the medulla.
- Autonomic activity can also be influenced by the prefrontal association cortex through its involvement with emotional expression characteristic of the individual's personality. An example is blushing when embarrassed, which is caused by dilation of blood vessels supplying the skin of the cheeks. Such responses are mediated through hypothalamic-medullary pathways.

▲ Table 7-5 summarizes the main distinguishing features of the sympathetic and parasympathetic nervous systems.

TABLE 7-4 Properties of Autonomic Receptor Types

Receptor Type	Neurotransmitter Affinity	Effector(s) with Receptor Type	Mechanism of Action at Effector	Effect on Effector
Nicotinic	Acetylcholine from autonomic preganglionic fibers	All autonomic postganglionic cell bodies; adrenal medulla	Opens nonspecific cation receptor-channels	Excitatory
	Acetylcholine from motor neurons	Motor end plates of skeletal muscle fibers	Opens nonspecific cation receptor-channels	Excitatory
Muscarinic	Acetylcholine from parasympathetic postganglionic fibers	Cardiac muscle, smooth muscle, most exocrine and some endocrine glands	Activates various G-protein-coupled receptor pathways, depending on effector	Excitatory or inhibitory, depending on effector
α_1	Norepinephrine from sympathetic postganglionic fibers; epinephrine from adrenal medulla: Norepinephrine > epinephrine	Most sympathetic target tissues	Activates IP_3/Ca^{2+} second-messenger pathway	Excitatory
α_2	Norepinephrine > epinephrine	Digestive organs	Inhibits cAMP	Inhibitory
β_1	Norepinephrine = epinephrine	Heart	Activates cAMP	Excitatory
β_2	Epinephrine only	Smooth muscles of arterioles and bronchioles	Activates cAMP	Inhibitory

organs. Receptors of the β_2 type bind almost exclusively with epinephrine, whereas β_1 receptors have about equal affinities for norepinephrine and epinephrine, and α receptors of both subtypes have a greater sensitivity to norepinephrine than to epinephrine (see ● Figure 7-2).

All adrenergic receptors are coupled to G proteins, but the ensuing pathway differs for the various receptor types. Activation of both β_1 and β_2 receptors brings about the target cell response by activating the cAMP second-messenger pathway (see p. 121). Stimulation of α_1 receptors elicits the desired response via the IP_3/Ca^{2+} second-messenger system (see p. 122). By contrast, binding of a neurotransmitter to an α_2 receptor inhibits cAMP production in the target cell.

Activation of α_1 receptors usually brings about an excitatory response in the effector—for example, arteriolar constriction caused by increased contraction of smooth muscle in the walls of these blood vessels. The α_1 receptors are present in most sympathetic target tissues. Activation of α_2 receptors, in contrast, brings about an inhibitory response in the effector, such as decreased smooth muscle contraction in the digestive tract. Stimulation of β_1 receptors, which are found primarily in the heart, causes an excitatory response, namely, increased rate and force of cardiac contraction. The response to β_2 receptor activation is generally inhibitory, such as arteriolar or bronchiolar (respiratory airway) dilation caused by relaxation of the smooth muscle in the walls of these tubular structures. As a quick rule of thumb, activation of the subscript "1" versions of adrenergic receptors lead to excitatory responses and activation of the subscript "2" versions lead to inhibitory responses.

AUTONOMIC AGONISTS AND ANTAGONISTS Drugs are available that selectively alter autonomic responses at each of the receptor types. An **agonist** binds to the neurotransmitter's receptor and causes the same response as the neurotransmitter would. An **antagonist,** by contrast, binds with the receptor, preventing the neurotransmitter from binding and causing a response, yet the antagonist itself produces no response. Thus an agonist mimics the neurotransmitter's response and an antagonist blocks the neurotransmitter's response. Some of these drugs are only of experimental interest, but others are very important therapeutically. For example, *atropine* blocks the effect of acetylcholine at muscarinic receptors but does not affect nicotinic receptors. Because acetylcholine released at both parasympathetic and sympathetic preganglionic fibers combines with nicotinic receptors, blockage at nicotinic synapses would knock out both these autonomic branches. By acting selectively to interfere with acetylcholine action only at muscarinic junctions, which are the sites of parasympathetic postganglionic action, atropine effectively blocks parasympathetic effects but does not influence sympathetic activity at all. Doctors use this principle to suppress salivary and bronchial secretions before surgery, to reduce the risk of a patient inhaling these secretions into the lungs.

Likewise, drugs that act selectively at α and β adrenergic receptor sites to either activate or block specific sympathetic effects are widely used. Following are several examples. *Salbuta-*