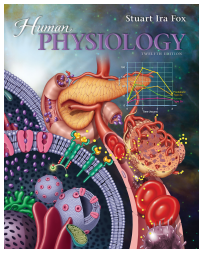
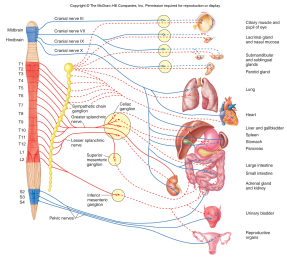


Chapter 9

The Autonomic Nervous System

Lecture PowerPoint

I. Neural Control of Involuntary Effectors



Autonomic Motor Nerves

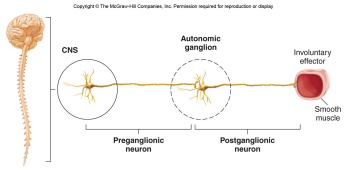
- Innervate organs not under voluntary control
- Effectors include:
  - Cardiac muscle
  - Smooth muscle of visceral organs and blood vessels
  - Glands

Autonomic Neurons

- Somatic motor neurons have cell bodies in the spinal cord and just one neuron traveling from spinal cord to effector.
- The autonomic motor system has two sets of neurons in the PNS.
  - The first has cell bodies in the brain or spinal cord and synapses in an autonomic ganglion.
  - The second has cell bodies in the ganglion and synapses on the effector.

Autonomic Neurons

- Preganglionic neurons: originate in the midbrain or hindbrain or from the thoracic, lumbar, or sacral spinal cord
- Postganglionic neurons: originate in ganglion



Autonomic Ganglia

- Located in the head, neck, and abdomen as well as in chains along either side of the spinal cord

Visceral Effector Organs

- Somewhat independent of innervation and will not atrophy if a nerve is cut (unlike skeletal muscle)
  - Cardiac muscle and some smooth muscle contract rhythmically without nerve stimulation. Autonomic innervation can speed up or slow down intrinsic contractions.
- Unlike somatic motor neurons (which are always stimulatory), autonomic motor neurons can stimulate or inhibit.

Somatic vs. Autonomic System

Table 9.1 | Comparison of the Somatic Motor System and the Autonomic Motor System

Feature	Somatic Motor	Autonomic Motor
Effector organs	Skeletal muscles	Cardiac muscle, smooth muscle, and glands
Presence of ganglia	No ganglia	Cell bodies of postganglionic autonomic fibers located in paravertebral, prevertebral (collateral), and terminal ganglia
Number of neurons from CNS to effector	One	Two
Type of neuromuscular junction	Specialized motor end plate	No specialization of postsynaptic membrane; all areas of smooth muscle cells contain receptor proteins for neurotransmitters
Effect of nerve impulse on muscle	Excitatory only	Either excitatory or inhibitory
Type of nerve fibers	Fast-conducting, thick (9–13 μm), and myelinated	Slow-conducting; preganglionic fibers lightly myelinated but thin (3 μm); postganglionic fibers unmyelinated and very thin (about 1.0 μm)
Effect of denervation	Flaccid paralysis and atrophy	Muscle tone and function persist; target cells show denervation hypersensitivity

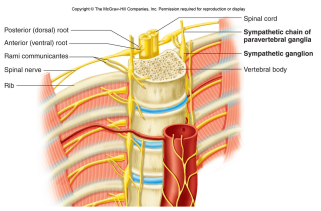
II. Divisions of the Autonomic Nervous System

Sympathetic Division

- Preganglionic neurons come from the thoracic and lumbar regions of the spinal cord.
  - Also called the thoracolumbar division
- They synapse in sympathetic ganglia that run parallel to the spinal cord.
  - These are called the paravertebral ganglia.
  - These ganglia are connected, forming a sympathetic chain of ganglia.

Sympathetic Preganglionic Neurons

- Myelinated axons exit the spinal cord at ventral roots and diverge into white rami communicantes and then into autonomic ganglia at multiple levels.



Convergence and Divergence

- Because preganglionic neurons can branch and synapse in ganglia at any level, there is:
  - Divergence: One preganglonic neuron synapses on postganglionic neurons at different levels.
  - Convergence: Several preganglionic neurons at different levels synapse on one postganglionic neuron.
- Allows the sympathetic division to act as a single unit through mass activation

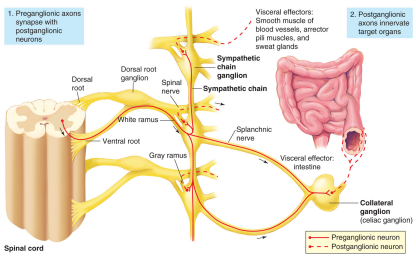
Sympathetic Postganglionic Neurons

- Unmyelinated axons of the postganglionic neurons form the gray rami communicantes, which return to the spinal nerve and travel with other spinal neurons to their effectors.

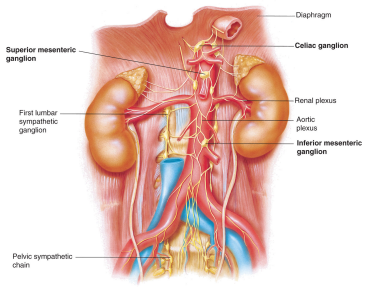
Collateral Ganglia

- Many of the sympathetic neurons that exit the spinal cord below the diaphragm do not synapse in the sympathetic chain of ganglia.
- Instead, they form splanchnic nerves, which synapse in collateral ganglia.
  - Collateral ganglia include celiac, superior mesenteric, and inferior mesenteric ganglia.
  - Postganglionic neurons innervate organs of the digestive, urinary, and reproductive systems.

Sympathetic Neuron Pathways



Collateral Sympathetic Ganglia



Adrenal Glands

- The adrenal medulla secretes epinephrine and norepinephrine when stimulated by the sympathetic nervous system.
- Embryologically, the adrenal medulla is a modified ganglion and is innervated directly by preganglionic sympathetic neurons.

Summary of the Sympathetic Division

Table 9.2 | The Sympathetic Division

Parts of Body Innervated	Spinal Origin of Preganglionic Fibers	Origin of Postganglionic Fibers
Eye	C8 and T1	Cervical ganglia
Head and neck	T1 to T4	Cervical ganglia
Heart and lungs	T1 to T5	Upper thoracic (paravertebral) ganglia
Upper extremities	T2 to T9	Lower cervical and upper thoracic (paravertebral) ganglia
Upper abdominal viscera	T4 to T9	Celiac and superior mesenteric (collateral) ganglia
Adrenal	T10 and T11	Not applicable
Urinary and reproductive systems	T12 to L2	Celiac and interior mesenteric (collateral) ganglia
Lower extremities	T9 to L2	Lumbar and upper sacral (paravertebral) ganglia

Parasympathetic Division

- Preganglionic neurons come from the brain or sacral region of the spinal cord.
  - Also called the craniosacral division
- They synapse on ganglia located near or in effector organs.
  - Called terminal ganglia

Parasympathetic Division

- Preganglionic neurons do not travel with somatic neurons (as sympathetic postganglionic neurons do).
  - Effectors in the skin and skeletal muscles (sweat glands, blood vessels) receive sympathetic but not parasympathetic innervation.

Cranial Nerves and the Parasympathetic Division

- The occulomotor, facial, glosso-pharyngeal, and vagus nerves carry parasympathetic preganglionic neurons.
  - Occulomotor: Preganglionic fibers exit midbrain and synapse on the ciliary ganglion.
  - Postganglionic fibers innervate the ciliary muscle of the eye.

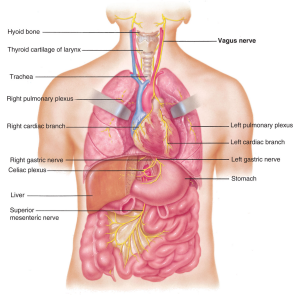
Cranial Nerves and the Parasympathetic Division

- Facial nerve: Preganglionic fibers exit the pons and synapse in:
  - Pterygopalatine ganglion: Postganglionic fibers synapse on nasal mucosa, pharynx, palate, and lacrimal glands.
  - Submandibular ganglion: Postganglionic fibers synapse on salivary glands.
  - Glossopharyngeal: Preganglionic fibers synapse on otic ganglion. Postganglionic fibers innervate salivary gland.

Cranial Nerves and the Parasympathetic Division

Vagus: Preganglionic fibers exit medulla, branch into several plexi and nerves, and travel to ganglia within effector organs (heart, lungs, esophagus, stomach, pancreas, liver, intestines).

Cranial Nerves and the Parasympathetic Division



Sacral Nerves

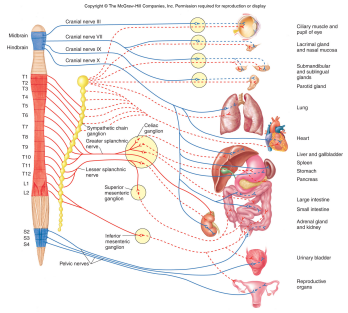
- Preganglionic nerves from the sacral region of the spinal cord provide innervation to the lower part of the large intestine, rectum, urinary and reproductive organs.
- Terminal ganglia are located within these organs.

Summary of Parasympathetic Division

Table 9.3 | The Parasympathetic Division

Nerve	Origin of Preganglionic Fibers	Location of Terminal Ganglia	Effector Organs
Oculomotor (third cranial) nerve	Midbrain (cranial)	Ciliary ganglion	Eye (smooth muscle in iris and ciliary body)
Facial (seventh cranial)	Pons (cranial)	Pterygopalatine and submandibular ganglia	Lacrimal, mucous, and salivary glands
Glossopharyngeal (ninth cranial) nerve	Medulla oblongata (cranial)	Otic ganglion	Parotid gland
Vagus (tenth cranial) nerve	Medulla oblongata (cranial)	Terminal ganglia in or near organ	Heart, lungs, gastrointestinal tract, liver, pancreas
Pelvic spinal nerves	S2 to S4 (sacral)	Terminal ganglia near organs	Lower half of large intestine, rectum, urinary bladder, and reproductive organs

Comparison of the Sympathetic and Parasympathetic Divisions



III. Functions of the Autonomic Nervous System

Sympathetic Functions

- The sympathetic division activates the body for “fight or flight” through the release of norepinephrine from postganglionic neurons and the secretion of epinephrine from the adrenal medulla.
  - Prepares the body for intense physical activity in emergencies by increasing heart rate and blood glucose levels and by diverting blood to skeletal muscles

Parasympathetic Functions

- The parasympathetic division is antagonistic to the sympathetic division.
- Allows the body to “rest and digest” through the release of ACh from postganglionic neurons
  - Slows heart rate, dilates visceral blood vessels, increases digestive activities

Summary of Autonomic Functions

Table 9.4 | Effects of Autonomic Nerve Stimulation on Various Effector Organs

Effector Organ	Sympathetic Effect	Parasympathetic Effect
Eye		
Iris (radial muscle)	Dilation of pupil	–
Iris (sphincter muscle)	–	Constriction of pupil
Ciliary muscle	Relaxation (for far vision)	Contraction (for near vision)
Glands		
Lacrimal (tear)	–	Stimulation of secretion
Sweat	Stimulation of secretion	–
Salivary	Saliva becomes thick	Increased secretion; saliva becomes thin
Stomach	–	Stimulation of secretion
Intestine	–	Stimulation of secretion
Adrenal medulla	Stimulation of hormone secretion	–
Heart		
Rate	Increased	Decreased
Conduction	Increased rate	Decreased rate
Strength	Increased	–
Blood Vessels	Mostly constriction; affects all organs	Dilation in a few organs (e.g., penis)
Lungs		
Bronchioles (tubes)	Dilation	Constriction
Mucous glands	Inhibition of secretion	Stimulation of secretion
Gastrointestinal Tract		
Motility	Inhibition of movement	Stimulation of movement
Sphincters	Closing stimulated	Closing inhibited
Liver	Stimulation of glycogen hydrolysis	–
Adipose (Fat) Cells	Stimulation of fat hydrolysis	–
Pancreas	Inhibition of exocrine secretions	Stimulation of exocrine secretions
Spleen	Contraction	–
Urinary Bladder	Muscle tone aided	Contraction
Arrector Pili Muscles	Erection of hair and goose bumps	–
Uterus	If pregnant: contraction; if not pregnant: relaxation	–
Penis	Ejaculation	Erection (due to vasodilation)

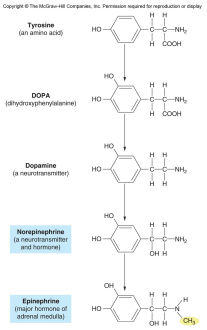
Cholinergic Synaptic Transmission

- Acetylcholine (ACh) is the neurotransmitter used by all preganglionic neurons.
  - It is also the neurotransmitter released from *most* parasympathetic postganglionic neurons.
  - Some sympathetic postganglionic neurons (those that innervate sweat glands and skeletal muscle blood vessels) release ACh.
  - These synapses are called cholinergic.

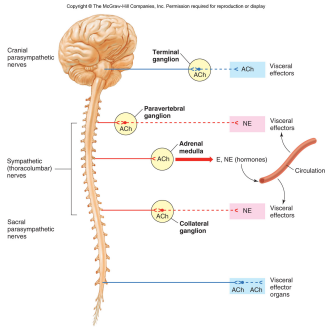
Adrenergic Synaptic Transmission

- Norepinephrine is the neurotransmitter released by *most* sympathetic postganglionic neurons.
  - These synapses are called adrenergic.

Adrenergic Synaptic Transmission



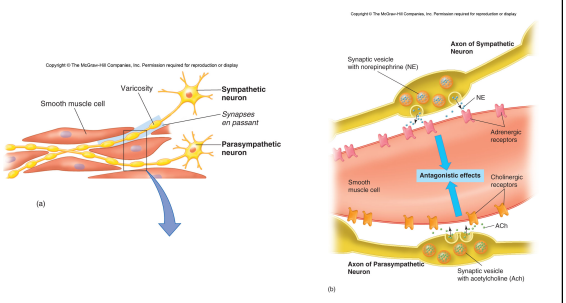
Neurotransmitters of the Autonomic Nervous System



Varicosities

- Axons of postganglionic neurons have various swellings called varicosities that release neurotransmitter along the length of the axon.
- They form “synapses en passant” in passing.
- Sympathetic and parasympathetic neurons innervate the same tissues.

Varicosities



Response to Adrenergic Stimulation

- Can stimulate or inhibit, depending on receptors
  - Stimulation: heart, dilatory muscles of the iris, smooth muscles of some blood vessels (causes vessel constriction)
  - Inhibition: Bronchioles in lungs, other blood vessels; inhibits contraction and causes dilation of these structures

α and β Adrenergic Receptors

- Two types of α (α_1 and α_2)
- Two types of β (β_1 and β_2)
- All act using G-proteins and second messenger systems.
  - β receptors use cAMP.
  - α receptors use a Ca^{2+} second messenger system.

α and β Adrenergic Receptors

- Adrenergic effects in different organs

Table 9.5 | Selected Adrenergic Effects in Different Organs

Organ	Adrenergic Effects of Sympathoadrenal System	Adrenergic Receptor
Eye	Contraction of radial fibers of the iris dilates the pupils	α_1
Heart	Increase in heart rate and contraction strength	β_1 primarily
Skin and visceral vessels	Arterioles constrict due to smooth muscle contraction	α_1
Skeletal muscle vessels	Arterioles constrict due to sympathetic nerve activity	α_1
	Arterioles dilate due to hormone epinephrine	β_2
Lungs	Bronchioles (airways) dilate due to smooth muscle relaxation	β_2
Stomach and intestine	Contraction of sphincters slows passage of food	α_1
Liver	Glycogenolysis and secretion of glucose	α_1, β_2

Source: Simplified from table 6-1, pp. 110–111, of Goodman and Gilman's *The Pharmacological Basis of Therapeutics.* Ninth edition. J.E. Hardman et al., eds. 1996. McGraw-Hill.

α_2 Receptors

- Located on presynaptic axons
- When stimulated, result in inhibition of norepinephrine release in the synapse
  - May be a negative-feedback system
  - Some drugs to lower blood pressure act on these α_2 receptors to inhibit presynaptic neurons in the brain, inhibiting the whole sympathetic nervous system.

Response to Cholinergic Stimulation

- ACh released from preganglionic neurons of both the sympathetic and parasympathetic division is stimulatory.
- ACh from postganglionic neurons of the parasympathetic division can be stimulatory or inhibitory, depending on receptors.

Cholinergic Receptors

- Nicotinic: found in autonomic ganglia
  - Stimulated by ACh
  - Serve as ion channels
- Muscarinic: found in visceral organs
  - Five types identified; can be stimulatory or inhibitory (opening K^+ or Ca^{2+} channels)
  - Use G-proteins and second messenger system

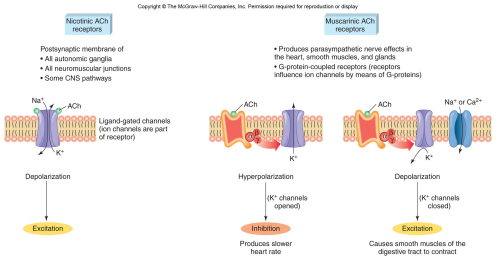
ACh Receptor Function

Table 9.6 | Cholinergic Receptors and Responses to Acetylcholine

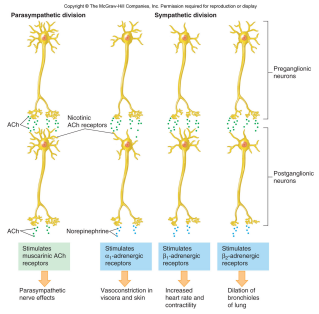
Receptor	Tissue	Response	Mechanisms
Nicotinic	Skeletal muscle	Depolarization, producing action potentials and muscle contraction	ACh opens cation channel in receptor
Nicotinic	Autonomic ganglia	Depolarization, causing activation of postganglionic neurons	ACh opens cation channel in receptor
Muscarinic (M_1, M_3)	Smooth muscle, glands	Depolarization and contraction of smooth muscle, secretion of glands	ACh activates G-protein coupled receptor, opening Ca^{2+} channels and increasing cytosolic Ca^{2+}
Muscarinic (M_2)	Heart	Hyperpolarization, slowing rate of spontaneous depolarization	ACh activates G-protein coupled receptor, opening channels for K^+

Source: Simplified from table 6-2, p. 119 of Goodman and Gilman's *The Pharmacological Basis of Therapeutics.* Ninth edition. J.E. Hardman et al., eds. 1996 and table 6-3, p. 156 of the Eleventh edition, 2006. McGraw-Hill.

ACh Receptor Structure



Summary of Receptor Activity in the Autonomic Nervous System



Other Autonomic Neurotransmitters

- Some postganglionic autonomic neurons are not inactivated by drugs that block ACh or norepinephrine activity.
- Called "nonadrenergic, noncholinergic fibers"
- Proposed neurotransmitters include ATP, vasoactive intestinal peptide, and nitric oxide.

Nonadrenergic, Noncholinergic Fibers

- Important for erection of the penis.
- Parasympathetic neurons innervate blood vessels, causing relaxation and vasodilation using NO.
- NO can also produce smooth muscle relaxation in the stomach, intestines, and urinary bladder.

Organs with Dual Innervation

- Most visceral organs are innervated by both sympathetic and parasympathetic neurons.
- Most of the time these systems are antagonists:
  - Heart rate
  - Digestive functions
  - Pupil diameter

Cooperative Effects

- Occur when both divisions produce different effects that work together to promote a single action:
  - Erection and ejaculation: Parasympathetic division causes vasodilation and erection; sympathetic causes ejaculation
  - Urination: Parasympathetic division aids in urinary bladder contraction; sympathetic helps with bladder muscle tone to control urination.

Complementary Effects

- Occur when both divisions produce similar effects on the same target
  - Salivary gland secretion: Parasympathetic division stimulates secretion of watery saliva; sympathetic constricts blood vessels so the secretion is thicker.

Organs Without Dual Innervation

- The following organs are innervated by the sympathetic division only:
  - Adrenal medulla
  - Arrector pili muscles in skin
  - Sweat glands in skin
  - Most blood vessels
- Regulated by increase and decrease in sympathetic nerve activity
- Important for body temperature regulation

Control of ANS by the Brain

- Many visceral functions are regulated by autonomic reflexes.
  - Sensory input is sent to brain centers (usually by the vagus nerve), which integrate the information and modify the activity of preganglionic neurons.
  - Medulla oblongata controls many cardiovascular, pulmonary, urinary, reproductive, and digestive functions.

Regulation of the Medulla

- Higher brain regions regulate the medulla.
  - Hypothalamus: major regulatory center of the ANS
  - Limbic system: responsible for autonomic responses during emotional states (blushing, pallor, fainting, sweating, racing heart rate)

Autonomic Reflexes

Table 9.8 | Effects Resulting from Sensory Input from Afferent Fibers in the Vagus, Which Transmit This Input to Centers in the Medulla Oblongata

Organs	Type of Receptors	Reflex Effects
Lungs	Stretch receptors	Further inhalation inhibited; increase in cardiac rate and vasodilation stimulated
	Type J receptors	Stimulated by pulmonary congestion—produces feelings of breathlessness and causes a reflex fall in cardiac rate and blood pressure
Aorta	Chemoreceptors	Stimulated by rise in CO_2 and fall in O_2—produces increased rate of breathing, rise in heart rate, and vasoconstriction
	Baroreceptors	Stimulated by increased blood pressure—produces a reflex decrease in heart rate
Heart	Atrial stretch receptors	Antidiuretic hormone secretion inhibited, thus increasing the volume of urine excreted
	Stretch receptors in ventricles	Produces a reflex decrease in heart rate and vasodilation
Gastrointestinal tract	Stretch receptors	Feelings of satiety, discomfort, and pain

Summary of Autonomic Functions

Table 9.7 | Adrenergic and Cholinergic Effects of Sympathetic and Parasympathetic Nerves

	Effect of			
	Sympathetic		Parasympathetic	
Organ	Action	Receptor[a]	Action	Receptor[a]
Eye				
Iris				
Radial muscle	Contracts	α_1	–	–
Circular muscle	–	–	Contracts	M
Heart				
Sinoatrial node	Accelerates	β_1	Decelerates	M
Contractility	Increases	β_1	Decreases (chb)	M
Vascular Smooth Muscle				
Skin, splanchnic vessels	Contracts	$\alpha_1\beta$	–	–
Skeletal muscle vessels	Relaxes	β_2	–	–
	Relaxes	M[b]	–	–
Bronchiolar Smooth Muscle	Relaxes	β_2	Contracts	M
Gastrointestinal Tract				
Smooth muscle				
Walls	Relaxes	β_2	Contracts	M
Sphincters	Constricts	α_1	Relaxes	M
Secretion	Decreases	α_2	Increases	M
Myenteric plexus	Inhibits	α_2	–	–
Genitourinary Smooth Muscle				
Bladder wall	Relaxes	β_2	Contracts	M
Urethral sphincter	Constricts	α_1	Relaxes	M
Uterus, pregnant	Relaxes	β_2	–	–
	Contracts	α_1	–	–
Penis	Ejaculation	α_1	Erection	M
Skin				
Pilomotor smooth muscle	Contracts	α_1	–	–
Sweat glands				
Thermoregulatory	Increases	M	–	–
Apocrine (stress)	Increases	α_1	–	–

[a]Adrenergic receptors are indicated as alpha (α) or beta (β); cholinergic receptors are indicated as muscarinic (M).
[b]Vascular smooth muscle in skeletal muscle has sympathetic cholinergic dilator fibers.
Source: Reproduced and modified, with permission, from Katzung, B.G., *Basic and Clinical Pharmacology*, 6th edition, copyright Appleton & Lange, Norwalk, CT, 1995.