Chapter 4: Autonomic Drugs

Autonomic Drugs

- Haveles (p. 34)
- Certain autonomic nervous system (ANS) drugs are used in dentistry
  - Vasoconstrictors added to local anesthetic and drugs used to increase salivary flow
- Some ANS drugs produce oral adverse reactions
  - Anticholinergics produce xerostomia
- Members of other drug groups have effects similar to ANS drugs
  - Antidepressants and antipsychotics have anticholinergic effects

Autonomic Nervous System

- Haveles (p. 34)
- The ANS functions as an automatic modulating system for many body functions
  - Regulation of blood pressure (BP), heart rate, gastrointestinal (GI) tract motility, salivary gland secretions, and bronchial smooth muscle
- The ANS relies on specific neurotransmitters and a variety of receptors to initiate functional responses in target tissues

Chapter 4 Outline

- Autonomic drugs
  - Autonomic nervous system
  - Parasympathetic autonomic nervous system
  - Sympathetic autonomic nervous system

Autonomic Nervous System

- Haveles (pp. 34-38)
- Anatomy
- Parasympathetic autonomic nervous system (PANS)
- Sympathetic autonomic nervous system (SANS)
- Functional organization
- Neurotransmitters
- Drug groups

Anatomy

- Haveles (pp. 34-35)
- Two divisions of the ANS
  - SANS
  - PANS
- Each division has afferent (sensory) fibers, central integrating areas, and efferent motor preganglionic and postganglionic fibers
Anatomy

Haveles (p. 35) (Fig. 4-1)
- The preganglionic neuron originates in the central nervous system (CNS) and passes out to form the ganglia at the synapse with the postganglionic neuron
- The space between the preganglionic and postganglionic fibers is the synapse
- The postganglionic neuron originates in the ganglia and innervates the effector organ or tissue

Parasympathetic Autonomic Nervous System

Haveles (p. 35)
- Cell bodies in the CNS give rise to preganglionic fibers of the parasympathetic division
- Originate in the nuclei of cranial nerves (III, VII, IX, and X) and sacral (S2-S4) segments of the spinal cord
- Preganglionic fibers of the PANS are relatively long and extend near to or into the innervated organ, which leads to a discrete response
- Postganglionic fibers, originating in ganglia, are usually short and terminate on the innervated tissue

Sympathetic Autonomic Nervous System

Haveles (p. 35)
- Cell bodies that give origin to the preganglionic fibers of the SANS span from the thoracic (T1) to the lumbar (L2) portion of the spinal cord
- Preganglionic fibers exit the spinal cord to enter the sympathetic chain on each side of the vertebral column
- In the sympathetic chain, preganglionic fibers form multiple synaptic connections with postganglionic cell bodies located up and down the sympathetic chain
  * This arrangement produces a diffuse response

Sympathetic Autonomic Nervous System

- The adrenal medulla is also innervated by sympathetic preganglionic fibers
  * It functions much the same as a large sympathetic ganglion
  * When the SANS is stimulated, the adrenal medulla releases primarily epinephrine and a small amount of norepinephrine (NE) into systemic circulation

Functional Organization

Haveles (pp. 35-36) (Fig. 4-2)
- The PANS and SANS divisions of the ANS tend to act in opposite directions
  * PANS: concerned with conservation of body processes
    * Both digestion and intestinal tract motility are greatly influenced by the PANS
  * SANS: designed for emergencies—the fight-or-flight response

Functional Organization

- In most, but not all, instances, the actions produced by each system are opposite
  * The SANS stimulates the radial smooth muscles, producing an increase in pupil size
    * Dilated pupils are termed mydriasis
  * The PANS stimulates the circular smooth muscles, producing a decrease in pupil size
    * Constricted pupils are termed myosis
**Functional Organization**

- Haveles (pp. 35, 37) (Table 4-1)
  - Almost all body tissues are innervated by the ANS
    - Many, but not all, organs receive both parasympathetic and sympathetic innervation
    - The response will be equal to the sum of excitatory and inhibitory influences of the two divisions of the ANS (if a tissue receives both innervations)
    - Sensory fiber in one division can influence motor fibers in the other

**Neurotransmitters**

- Haveles (pp. 36-37) (Table 4-2)
  - Communication between nerves or between nerves and effector tissue takes place by the release of chemical neurotransmitters across the synaptic cleft
    - Neurotransmitters are released in response to the nerve action potential so as to interact with the receptor
    - Receptors are usually found on the postsynaptic fiber and the effector organ but may be located on the presynaptic membrane as well

**Neurotransmitters**

- Haveles (p. 36)
  - The specificity of the neurotransmitter and receptors dictates the tissue response
    - Between the preganglionic and postganglionic nerves
      - Acetylcholine is the neurotransmitter
      - Nerves that release acetylcholine are cholinergic
      - Because this synapse is stimulated by nicotine, it is termed nicotinic in response

**Neurotransmitters**

- Haveles (pp. 36, 38-39) (Figs. 4-3, 4-4, 4-5, 4-6)
  - Between postganglionic nerves and effector tissues
    - PANS: the neurotransmitter released from the postganglionic nerve is acetylcholine
      - It is also termed cholinergic
      - Because the postsynaptic tissue responds to muscarine, it is called muscarinic
    - SANS: NE is the transmitter substance released by the postganglionic nerves
      - It is called adrenergic

**Neurotransmitters**

- Haveles (pp. 36-38)
  - Neuromuscular junction
    - Although not within the ANS, the neuromuscular junction of skeletal muscle releases acetylcholine and is termed cholinergic
    - It is part of the somatic system

**Drug Groups**

- Haveles (pp. 36-38)
  - The four drug groups in the ANS exert their effects primarily on the organs or tissues innervated by the ANS
    - The action of each of the divisions of the ANS can be increased or decreased
Drug Groups
- These four functions divide the ANS drugs into four groups:
  - A drug that stimulates the PANS is called P⁺ (cholinergic or parasympathomimetic)
  - A drug that blocks the PANS is called P⁻ (anticholinergic, parasympatholytic, or cholinergic blockers)
  - A drug that stimulates the SANS is called S⁺ (sympathomimetic or adrenergic)
  - A drug that blocks the SANS is called S⁻ (adrenergic blockers, sympathetic blockers, or sympatholytic)

Parasympathetic Autonomic Nervous System
- Haveles (pp. 38-43)
- Cholinergic (parasympathomimetic) agents
- Anticholinergic (parasympatholytic) agents
- Nicotinic agonists and antagonists

Parasympathetic Autonomic Nervous System
- Haveles (pp. 38-39) (Fig. 4-7)
- Acetylcholine is the principal mediator in the PANS
- An action potential causes release of acetylcholine
- In postganglionic parasympathetic fibers, the postsynaptic tissue is an effector organ
- The action of released acetylcholine is terminated by hydrolysis by acetylcholinesterase to yield inactive metabolites—choline and acetic acid

Cholinergic (Parasympathomimetic) Agents
- Haveles (pp. 38-40) (Fig. 4-8; Table 4-3)
- Cholinergic agents are classified as direct acting (acts on receptor) or indirect acting (causes release of neurotransmitter)
- Direct-acting agents include choline derivatives and pilocarpine
- Indirect-acting parasympathomimetic agents or cholinesterase inhibitors act by inhibiting the enzyme cholinesterase

Pharmacologic Effects (Cholinergic)
- Haveles (pp. 39-40)
- Cardiovascular effects
  - Direct effect on the heart produces a negative chronotropic and inotropic action
  - A decrease in cardiac output is associated with these agents
  - The effect on smooth muscle results in relaxation and vasodilation, producing a decrease in total peripheral resistance
  - The indirect effect is an increase in heart rate and cardiac output
- Because direct and indirect effects are opposite, the effect will depend on the concentration of the drug present
  - Generally causes bradycardia and a decrease in BP and cardiac output

Pharmacologic Effects (Cholinergic)
- GI effects
  - Cholinergic agents excite smooth muscle of the GI tract
  - Produces an increase in activity, motility, and secretion
Pharmacologic Effects
(Cholinergic)

- Effects on the eye
  - Cholinergic agents produce miosis (contraction) and cycloplegia (loss of accommodation)
  - Intraocular pressure is decreased
  - These agents are useful for treatment of glaucoma

Adverse Reactions (Cholinergic)

- Adverse reactions are extensions of the pharmacologic effects
  - Large doses produce toxic effects described by the acronym SLUD (salivation, lacrimation, urination, and defecation)
  - With even larger doses, neuromuscular paralysis can occur
  - Treatment of an overdose of cholinesterase inhibitors such as insecticides or organophosphates (parathion) includes a combination of pralidoxime and atropine

Contraindications (Cholinergic)

- Relative contraindications or cautions
  - Bronchial asthma: cholinergic agents may cause bronchospasms or precipitate an asthmatic attack
  - Hyperthyroidism: may cause an increased risk of atrial fibrillation
  - GI or urinary tract obstruction: an increase in secretions and motility could cause pressure
  - Severe cardiac disease: reflex tachycardia may exacerbate a severe cardiac condition
  - Myasthenia gravis treated with neostigmine: these patients should not be given irreversible cholinesterase inhibitors, neostigmine occupies the enzyme, and the irreversible agent would not function
  - Peptic ulcer: anticholinergic agents stimulate gastric acid secretion and increase gastric motility

Uses (Cholinergic)

- Direct-acting agents are used primarily in the treatment of glaucoma
  - Occasionally, they are used to treat myasthenia gravis, a disease that reduces the effect of acetylcholine on voluntary muscles
  - Pilocarpine (Salagen), a naturally occurring cholinergic agent, is used to treat xerostomia
  - Success may be limited because of potential side effects, including perspiration, nausea, rhinitis, chills, and flushing

Uses (Cholinergic)

- Indirect-acting cholinergic agents (cholinesterase inhibitors) are divided into groups based on the degree of reversibility with which they are bound to the enzyme
  - Physostigmine (Antilirium) has been used to treat acute toxicity from anticholinergic agents (e.g. atropine) and other agents with anticholinergic action (e.g. phenothiazines, tricyclic antidepressants, and antihistamines)
  - Cholinesterase inhibitors used as insecticides and chemical warfare agents are essentially irreversible and are called the irreversible cholinesterase inhibitors

Anticholinergic (Parasympatholytic) Agents

- Prevent the action of acetylcholine at postganglionic parasympathetic nerve endings
  - The release of acetylcholine is not blocked, but the receptor site is competitively blocked by the anticholinergics
  - These agents are called antimuscarinic agents because they block muscarinic but not nicotinic receptors
Pharmacologic Effects (Anticholinergic)

- Haveles (p. 41) (Fig. 4-10)
  - CNS effects
    - Anticholinergics may produce stimulation or depression, depending on dose
      - Usual doses of scopolamine more often cause sedation, whereas atropine in high doses can cause stimulation
    - Atropine and scopolamine are tertiary agents
      - Tertiary agents are lipid soluble and can easily penetrate the brain
  - cont'd...

Pharmacologic Effects (Anticholinergic)

- propantheline (Pro-Banthine) and glycopyrrolate (Robinul) are quaternary agents
  - Quaternary agents are water soluble and do not penetrate the CNS well
  - Quaternary agents have fewer CNS effects because they are less likely to enter the brain
  - cont'd...

Pharmacologic Effects (Anticholinergic)

- Effects on exocrine glands
  - Anticholinergics reduce the flow and volume of exocrine secretions
  - This effect is used therapeutically in dentistry to decrease salivation and create a dry field
  - cont'd...

Pharmacologic Effects (Anticholinergic)

- Effects on smooth muscle
  - Anticholinergics relax the smooth muscle in the respiratory and GI tracts
    - Ipratropium is an anticholinergic inhaler used to treat asthma
    - Spasmolytic agents are anticholinergics used to reduce GI motility
  - cont'd...

Pharmacologic Effects (Anticholinergic)

- Effects on the eye
  - Parasympatholytics cause mydriasis (dilation of the pupil) and cycloplegia (paralysis of accommodation) of the eye
  - These are useful to prepare the eye for ophthalmologic examination
  - cont'd...

Pharmacologic Effects (Anticholinergic)

- Cardiovascular effects
  - With large doses, anticholinergic agents can produce vagal blockade, resulting in tachycardia
    - This effect has been used to prevent cardiac slowing during general anesthesia
  - With small doses, bradycardia predominates
  - cont'd...
Adverse Reactions (Anticholinergic)

Haveles (p. 42)

Adverse reactions associated with the anticholinergics are extensions of their pharmacologic effects

- Xerostomia, blurred vision, photophobia, tachycardia, fever, urinary and gastrointestinal stasis
- Hyperpyrexia and hot, dry, flushed skin caused by lack of sweating are also seen
- Toxicity can cause signs of CNS excitation

Contraindications (Anticholinergic)

Haveles (p. 42)

Contraindications or cautions to the use of anticholinergics

- Glaucoma: can cause an acute rise in intraocular pressure in patients with narrow-angle glaucoma
- Prostatic hypertrophy: can exacerbate urinary retention; men with prostatic hypertrophy should be given these agents with caution
- Intestinal or urinary obstruction or retention: constipation or acute urinary retention can be precipitated by use of these agents in susceptible patients
- Cardiovascular disease: anticholinergic agents have the ability to block the vagus nerve

Uses (Anticholinergic)

Haveles (p. 42) (Table 4-4)

Preoperative medication

- Anticholinergic agents inhibit secretions of saliva and bronchial mucus that can be stimulated by general anesthesia and have the ability to block vagal slowing of the heart that results from general anesthesia

Treatment of GI disorders

- Many types of disorders associated with increased motility or acid secretion have been treated with anticholinergic agents

Ophthalmologic examination

- Mydriasis allows full visualization of the retina
- Cycloplegia relaxes the lens such that proper eyeglass prescriptions may be determined

Drug Interactions (Anticholinergic)

Haveles (pp. 42-43)

May have an added anticholinergic effect with other anticholinergic agents

- Other agents with anticholinergic effect, including phenothiazines, antihistamines, and tricyclic antidepressants, can be additive with parasympatholytics
- Symptoms of toxicity include urinary retention, blurred vision, acute glaucoma, and even paralytic ileus

Nicotinic Agonists and Antagonists

Haveles (p. 43)

Nicotine is so toxic that one drop on skin is rapidly fatal

- Low doses produces stimulation because of depolarization
- High doses produces paralysis of ganglia, resulting in respiratory paralysis
- Peripherally, nicotine increases BP and heart rate and increases GI motility and secretions
- Constricts the blood vessels and reduces blood flow to extremities
Sympathetic Autonomic Nervous System

- Haveles (pp. 43-48)
  - Sympathetic autonomic nervous system receptors
  - Adrenergic (sympathomimetic) agents
  - Adrenergic blocking agents
  - Neuromuscular blocking drugs

Sympathetic Autonomic Nervous System

- Haveles (p. 43)
  - The major neurotransmitters in the SANS include NE and epinephrine
    - NE is the major neurotransmitter released at the terminal nerve endings of the SANS
    - With stimulation, epinephrine is released from the adrenal medulla and distributed throughout the body via the blood
    - Dopamine receptors are important in the brain and splanchnic and renal vasculature

Sympathetic Autonomic Nervous System Receptors

- Haveles (p. 43) (Fig. 4-11)
  - Adrenergic drugs can be classified by their mechanism of action
    - Direct acting
      - Epinephrine, NE, and isoproterenol produce effects directly on the receptor site
    - Indirect acting
      - These agents, such as amphetamine, release endogenous NE, which then produces a response
      - Depletion of NE with reserpine diminishes the response
    - Mixed action
      - These agents, such as ephedrine, can either stimulate the receptor directly or release endogenous NE to cause a response

α-Receptors

- Haveles (p. 43)
  - Stimulation of α-receptors causes smooth-muscle excitation or contraction, which then causes vasoconstriction
  - α-Receptors are located in skin and skeletal muscle, therefore vasoconstriction of skin and skeletal muscle follows stimulation
  - Drugs that block the action of neurotransmitters on the α-receptors are called α-adrenergic blocking agents

β-Receptors

- Haveles (pp. 43-44) (Fig. 4-12; Table 4-1)
  - At least two types of β-receptors (β₁ and β₂) have been developed
    - β₁: excitation stimulates heart muscle and results in positive chronotropic effect (increased rate) and positive inotropic effect (increased strength)
      - Other actions include metabolic effects on glycogen formation (glycogenolysis)
    - β₂: stimulation results in smooth-muscle inhibition or relaxation
      - Stimulation causes vasoconstriction of skeletal muscle
      - Relaxation of smooth muscles of bronchioles results in bronchodilation
Drugs that block β-receptor effects are called β-adrenergic blocking agents. Some are nonspecific, blocking both β₁- and β₂-receptors. Others are more selective, blocking primarily β₂-receptors.

Adrenergic (Sympathomimetic) Agents

- Haveles (pp. 43-46)
- Pharmacologic effects
- Adverse reactions
- Uses
- Specific adrenergic agents

Adrenergic (Sympathomimetic) Agents

- Haveles (pp. 43-46) (Table 4-5)
- Play an important part in treatment of anaphylaxis and asthma
- Added to local anesthetic solutions (vasoconstrictors) to prolong their action

Pharmacologic Effects (Adrenergic)

- The effects of these agents depend on their ability to stimulate various receptors
  - General actions are discussed with specific reference to α-receptor or β-receptor effect

Pharmacologic Effects (Adrenergic)

- CNS
  - Sympathetic agents such as amphetamine produce CNS excitation, or alertness
  - With higher doses, anxiety, apprehension, restlessness, and even tremors can occur
Pharmacologic Effects (Adrenergic)

- Haveles (p. 44)
- Cardiovascular effects
  - Heart: general effect is increased in force and strength of contraction
  - Final effect on BP is a combination of direct and indirect effects
    - NE, primarily an α-agonist, produces vasoconstriction, increasing peripheral resistance, resulting in an increase in BP
    - With an increase in BP, the vagal reflex decreases heart rate
    - Epinephrine, an α- and β-agonist, constricts α-receptors and dilates β-receptors
      - This widens pulse pressure with an increase in systolic and a decrease in diastolic BP
    - Isoproterenol, primarily a β-agonist, produces vasodilation that triggers an increase in heart rate (vagal reflex)

- Vessels
  - Agents with α-receptor effects will produce vasoconstriction primarily in skin and mucosa
  - Agents with β-receptor effects will produce vasodilation of skeletal muscle
  - The resulting effect on the total peripheral resistance is an increase with an α-receptor agent and a decrease with a β-receptor agent

- The sympathomimetic effect on BP is generally an increase
  - Epinephrine causes a rise in systolic BP and a decrease in diastolic BP
  - NE causes a rise in both systolic BP and diastolic BP
  - Isoproterenol causes little change in systolic BP but a decrease in diastolic BP

 Effects on the eye
- Sympathomimetic agents have at least two effects on the eye
  - Decreased intraocular pressure
  - Mydriasis (dilation of the pupil)

 Effects on the respiratory system
- Sympathomimetic agents cause relaxation of bronchial smooth muscle caused by the β-adrenergic effect
- Useful for treatment of asthma and anaphylaxis

cont’d…
Pharmacologic Effects (Adrenergic)

- Metabolic effects
  - Hyperglycemia resulting from β-receptor stimulation is explained on the basis of increased glycogenolysis and decreased insulin release
  - Fatty acid mobilization, lipolysis, and gluconeogenesis are stimulated

Effects on salivary glands
- The mucus-secreting cells of the submaxillary and sublingual gland are stimulated to release a small amount of thick, viscous saliva
- The parotid gland does not have sympathetic innervation; the sympathomimetics produce vasoconstriction, therefore the flow of saliva is often reduced, resulting in xerostomia

Adverse Reactions (Adrenergic)

- Adverse reactions associated with adrenergic drugs are extensions of their pharmacologic effects
- Anxiety and tremors may occur, the patient may have palpitations
  - Serious arrhythmias can result
- Agents with an α-adrenergic action can cause a dramatic rise in BP
  - Sympathomimetic agents should be used with caution in patients with angina, hypertension, or hyperthyroidism

Contraindications

- These drugs should not be used in persons with uncontrolled hypertension, angina, or hyperthyroidism
- They stimulate α- and β-receptors in the heart and would further increase BP and heart rate

Uses (Adrenergic)

- Vasoconstriction
  - Prolonged action: agents with α effect are added to local anesthetic solutions to prolong their action and reduce the potential for systemic toxicity
  - Hemostasis: epinephrine can be applied topically or infiltrated around the bleeding area to produce hemostasis
  - Decongestion: sympathomimetic agents are often incorporated into nose drops or sprays to treat nasal congestion

Cardiac effects
- Treatment of shock: (controversial) the drug will lower elevated BP, but correcting the cause of shock is more important
- Treatment of cardiac arrest: sympathomimetic agents, especially epinephrine, are used to treat cardiac arrest
Uses (Adrenergic)

- Bronchodilation
  - Sympathomimetic agents are bronchodilators
    - Patients with asthma or emphysema are often treated with adrenergic agents
    - Epinephrine is the drug of choice for anaphylaxis when bronchoconstriction is predominant

- CNS stimulation
  - Amphetamine-like agents have been used as “diet pills”
    - They are indicated for attention-deficit disorder (ADD) and narcolepsy
  - Adrenergic agonists with some specificity for CNS stimulation are used for both legitimate and illegitimate purposes
    - methylphenidate (Ritalin) and dextroamphetamine (Dexedrine) are adrenergic agonists used to treat ADD in both children and adults

Specific Adrenergic Agents

- Haveles (pp. 45-46) (Fig. 4-13)
- Epinephrine: the drug of choice for acute asthmatic attacks and anaphylaxis
- Phenylephrine: used as a mydriatic and in nose sprays to relieve congestion
- Levonordefrin: a vasoconstrictor often added to local anesthetic
- Ephedrine and pseudoephedrine: have both \( \alpha \) - and \( \beta \) -receptor activity
- Dopamine: neurotransmitter in parts of the CNS, both an \( \alpha \) - and \( \beta \)-agonist, used primarily in treatment of shock
- Dipivefrin: sympathomimetic ophthalmics used to treat glaucoma

Adrenergic Blocking Agents

- Haveles (pp. 46-47) (Table 4-6)
- Can block
  - All the adrenergic receptors (\( \alpha \)- and \( \beta \)-blockers)
  - Just the \( \alpha \) -receptors (\( \alpha \)-blockers) or just the \( \beta \) -receptors (\( \beta \)-blockers)
  - Just \( \alpha _1 \)-receptors (\( \alpha _1 \)-blockers), \( \alpha _2 \)-receptors (\( \alpha _2 \)-blockers), \( \beta _1 \)-receptors (\( \beta _1 \)-blockers), or \( \beta _2 \)-receptors (\( \beta _2 \)-blockers)

\( \alpha \)-Adrenergic Blocking Agents

- Haveles (pp. 46-47)
- \( \alpha \)-Adrenergic blocking agents competitively inhibit the vasoconstricting effects of adrenergic agents
  - Reduces sympathetic tone in blood vessels, producing a decrease in total peripheral resistance and reflex tachycardia
- Patients pretreated with alpha blocking agents and then given epinephrine exhibit a predominance of beta effects, which lowers BP
  - This is called epinephrine reversal because BP goes down rather than up

Examples of \( \alpha \)-Adrenergic Blocking Agents (Antagonists)

- Haveles (p. 46) (Table 4-6)
  - \( \alpha \)
    - phentolamine (Regitine)
  - \( \alpha _1 > \alpha _2 \)
    - phenoxybenzamine (Dibenzyline)
  - \( \alpha _1 \gg \alpha _2 \)
    - prazosin (Minipress)
  - \( \alpha _2 \)
    - Yohimbine
  - \( \alpha \) (partial agonist and antagonist)
    - Ergot
β-Adrenergic Blocking Agents

- Competitively block the β-receptors in the adrenergic nervous system (generic drugs end in -olol)
- Nonselective drugs block effects of beta stimulation to produce bradycardia and in asthmatics, possible bronchoconstriction
- Specific β-blockers have more activity on the heart and blood vessels than on the lungs, producing fewer side effects

<table>
<thead>
<tr>
<th>Examples of β-Adrenergic Blocking Agents (Antagonists)</th>
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<tbody>
<tr>
<td>- Nonspecific (nonselective) β</td>
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<td>- propranolol (Inderal)</td>
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<tr>
<td>- Specific (selective) β₁ &gt; β₂</td>
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<tr>
<td>- acebutolol (Sectral)</td>
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<td>- atenolol (Tenormin)</td>
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<td>- α- and β-adrenergic antagonists</td>
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<td>- labetalol (Normodyne, Trandate)</td>
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α- and β-Blocking Agents

- labetalol (Normodyne, Trandate) has both alpha and beta blocking action
  - It is a selective α-blocker and a nonselective β-blocker
  - Indicated for treatment of hypertension

<table>
<thead>
<tr>
<th>Neuromuscular Blocking Drugs</th>
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<tbody>
<tr>
<td>- Haveles (p. 47)</td>
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<tr>
<td>- Agents that affect transmission between motor nerve endings and nicotinic receptors on skeletal muscle</td>
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<tr>
<td>- Act either as antagonists (nondepolarizing) or as agonists (depolarizing)</td>
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<tr>
<th>Nondepolarizing (Competitive) Blockers</th>
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<td>- Haveles (p. 47)</td>
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<tr>
<td>- The poison used in arrows by indigenous people along the Amazon is the neuromuscular blocking drug curare</td>
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<tr>
<td>- This nondepolarizing blocker combines with the nicotinic receptor and blocks the action of acetylcholine</td>
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<td>- These competitive blockers can be overcome by the administration of cholinesterase inhibitors such as neostigmine</td>
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<th>Depolarizing Agents</th>
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<tr>
<td>- Haveles (p. 47)</td>
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<tr>
<td>- Depolarizing agents such as succinylcholine attach to the nicotinic receptor and, similar to acetylcholine, result in depolarization</td>
</tr>
<tr>
<td>- Succinylcholine produces muscle fasciculations followed by paralysis</td>
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<tr>
<td>- Succinylcholine is broken down by plasma cholinesterase</td>
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