DRUG CLASSIFICATIONS

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Topics

- Anatomy & Physiology Related to Pharmacology
- Drugs That Affect the Central Nervous System
- Drugs That Affect the Autonomic Nervous System
- Drugs That Affect the Cardiovascular System
- Drugs That Affect the Respiratory System
- Drugs That Affect the Gastrointestinal System
- Drugs That Affect the Eyes and Ears
- Drugs That Affect the Endocrine System
- Drugs That Affect the Reproductive System
- Drugs Used to Treat Cancer
- Drugs Used to Treat Poisonings
Classifying Drugs

- Drugs can be classified many ways:
  - Body system they affect
  - Mechanism of action
  - Indications
  - Source or by chemical class

- A prototype best demonstrates the class’s common properties and illustrates its particular characteristics.
Drugs Used to Affect the Nervous System
Two major groups of medications used to affect the nervous system are those that affect the central nervous system and those that affect the autonomic nervous system.
The Nervous System

- **Nervous system**
  - CNS
    - Brain
    - Spinal cord
  - PNS
    - Somatic
      - Voluntary
    - Autonomic
      - Involuntary
      - Sympathetic and parasympathetic divisions
Central Nervous System Medications

- Analgesics & Antagonists
- Anesthetics
- Anti-anxiety & Sedative-Hypnotic Drugs
- Antiseizure or Anti-epileptic Drugs
- Central Nervous System Stimulants
- Psychotherapeutic Medications
- Parkinson’s Medications
Central Nervous System Medications

- Analgesics and antagonists
  - Analgesics are medications that relieve the sensation of pain
  - Two subclasses of analgesics
    - Opioid agonists and their derivatives
    - Nonopioioid
DRUGS USED TO CONTROL PAIN

- Two divisions
  - Narcotic and non-narcotics
- Non-narcotic analgesics and antiinflammatory agents
  - Salicilates
  - Acetaminophen
  - Ibuprofen
  - Used for mild to moderate pain
- Narcotic analgesics
  - Opium derivatives
  - Used for visceral pain and discomfort
Central Nervous System Medications

- **Opioids**
  - An opioid is chemically similar to opium
  - Opium is extracted from poppy plant and has been used for centuries for its analgesic and hallucinogenic effects
  - Opium and its derivatives treat pain because of their similarity to natural pain reducing peptides (endorphins)
  - Opioids function by decreasing the sensory neurons ability to propagate pain impulses to the spinal cord and brain
  - Prototype opioid drug is morphine
    - Uses and function of morphine
Central Nervous System Medications

● Nonopioid analgesics
  - Salicylates
  - Nonsteriodial anti-inflammatory drugs
  - Para-aminophenol derivatives
  - This class affect the production of prostaglandins (bradykinins) and cyclooxxygenase which are neurotransmitters involved in pain response
Central Nervous System Medications

- Opioid antagonists
  - Reverse the effects of opioid drugs
  - Naloxone (Narcan) is the prototype

- Adjunct medications
  - Administered to enhance the effects of other drugs
  - Prolong or intensify effects
  - Examples
    - Benzodiazepines and antihistamines
Central Nervous System Medications

- Opioid agonist-antagonists
  - Medication that displays both agonist and antagonist properties
  - Pentazocine (talwin) is the prototype
  - Other examples
    - Nalbuphine (Nubain)
    - Butorphanol (Stadol)
Anesthetics

- Induce a state of anesthesia, or a loss of sensation to touch or pain
- Anesthetics are useful during unpleasant procedures such as surgery or electrical therapy
- Low levels anesthetics produce a decreased sensation of pain, but the patient remains conscious
- Neuroleptanesthesia combines decreased sensation to pain with amnesia while the patient remains conscious
Anesthetics

- As a group anesthetics cause respiratory, CNS, and cardiovascular depression
- Anesthetic agents are rarely used individually
  - Used with other agents to produce desirable effects
    - Example RSI
- Types of anesthetics
  - Inhalation anesthetics
  - Intravenous anesthetics
  - Ultra-short acting barbiturates
Anesthetics

- Gaseous anesthetics are administered by inhalation and include halothane, enflurane, and nitrous oxide
- The first clinically useful anesthetic was ether
- Anesthetics hyperpolarize neural membranes making depolarization more difficult
  - Decreases firing rates of neural impulses slowing the propagation of action potentials through nervous system reducing sensation
Anesthetics

- Most anesthetics used outside the OR are administered intravenously
- Faster onset and shorter duration of action
- Example
  - Facilitate rapid sequence induction and intubation (RSI)
  - Ultra short acting barbiturates (thiopental), (methohexital) or Brevital
  - Benzodiazepines (Valium), (Versed)
  - Opioids (fentanyl)
Anesthetics

- Administered locally to block sensation for medical procedures
- Agent is administered into skin around the nerves that innervate the area of the procedure
- Decreases nerve ability to depolarize and propagate impulse to the brain
- Example
  - Xylocaine
Antianxiety and Sedative-Hypnotic Drugs

- **Reticular Formation**
  - Group of nuclei scattered throughout brainstem and cerebrum
  - Determines level of awareness to environment and governs actions and responses to it
  - Composed of excitatory and inhibitory fibers
  - RF sensitive to depressants and stimulants
    - Antianxiety, sedative-hypnotic agents depress RF
Antianxiety and Sedative-Hypnotic Drugs

- Drugs used to decrease anxiety, induce amnesia, assist sleeping and as part of a balanced approach to anesthesia
- Sedation: state of decreased anxiety and inhibitions
- Hypnosis: instigation of sleep
- Sleep
  - Categorized as REM or non REM
  - REM sleep is characterized as rapid eye movements and lack of motor control
  - Most dreaming occurs during REM sleep
Antianxiety and Sedative-Hypnotic Drugs

- Two main pharmacological classes
  - Benzodiazepines and barbiturates
    - Benzodiazepines are commonly prescribed and are relatively safe and effective for anxiety and insomnia
  - Barbiturates have a broader depressant range and a higher potential for abuse
    - Oldest and largest group
    - 2000 types, but only about a dozen used clinically
Antianxiety and Sedative-Hypnotic Drugs

- **Mechanism of action**
  - Benzodiazepines and barbiturates hyperpolarize the membrane of the CNS neurons decreasing the response to pain
  - Gammaaminobutyric acid (GABA) is chief inhibitory neurotransmitter in CNS
  - GABA receptors are widely dispersed throughout the CNS on proteins that make up chloride ion channels in the cell membrane
  - When GABA combines with receptors, the channel opens and chloride diffuses inside cell membrane
Antianxiety and Sedative-Hypnotic

- Chloride’s intracellular diffusion changes the internal charge of the cell to become electrically negative
  - This change hyperpolarizes the membrane and makes it more difficult to depolarize
  - Depolarization requires a larger stimulus to cause the cell to fire
  - Both benzodiazepines and barbiturates increase the GABA receptor chloride ion channel

- Low dose benzodiazepines and barbiturate decrease anxiety and causes sedation

- As dose increases sleep is induced and higher doses produces anesthesia
Benzodiazepine Receptors

GABA A receptor

Gamma subunit

Benzodiazapine (BDZ) binding site

Benzodiazapine

Postsynaptic membrane

Alpha

Synaptic cleft

GABA

Cl–

Alpha

Alpha

Cytoplasm

Cl–
BENZODIAZEPINES (ANTIANXIETY AGENTS)

- Among the most widely prescribed drugs in clinical medicine
- Calm individual and reduce unpleasant aspects of anxiety
- Site and mechanism of action
  - Bind to specific receptors in cerebral cortex and limbic system
  - Four actions:
    - anxiety reducing
    - sedative-hypnotics
    - muscle relaxing
    - anticonvulsant
  - All are schedule IV drugs because of their potential for abuse
COMMONLY PRESCRIBED BENZODIAZEPINES

- Chlordiazepoxide (Librium)
- Clorazepate (Tranxene)
- Diazepam (Valium)
- Flurazepam (Dalmane)
- Prazepam (Centrax)
- Midazolam (Versed)
- Lorazepam (Ativan)
BARBITURATES

- Once the most commonly prescribed class of medications for sedative-hypnotic effects
- Have been greatly replaced by benzodiazepines
- Divided into four classes according to duration of action
  - Ultra short acting
  - Short acting
  - Intermediate acting
  - Long acting
ULTRA SHORT AND SHORT ACTING BARBITURATES

● Ultra Short Acting
  - Commonly used as IV anesthetics
  - Take effect within a few seconds
  - Example: thiopental sodium (Pentothal)

● Short Acting
  - Produce effects in 10-15 minutes (peak over 3-4 hours)
  - Sometimes used for preanesthesia sedation and in combination with other drugs for psychosomatic disorders
  - Examples: pentobarbital (Nembutal) and secobarbital (Seconal)
INTERMEDIATE AND LONG ACTING BARBITURATES

- **Intermediate**
  - Onset of 45-60 minutes (peak in 6-8 hours)
  - Similar in response to short acting barbiturates
  - Examples: amobarbital (Amytal) and butabarbital (Butisol)

- **Long Acting**
  - Require over 60 minutes for onset (peak over 10-12 hours)
  - Used to treat epilepsy and other chronic neurological disorders and to sedate patients with severe anxiety
  - Examples: phenobarbital (Luminal) and mephobarbital (Gemonil)
Antianxiety and Sedative-Hypnotic Drugs

- Antagonistic drugs
  - Flumazenil (Romazicon)
    - Competitively binds with the benzodiazepine receptors in the GABA receptor chloride ion channel without causing the effects of benzodiazepines
    - Reverses the sedation of benzodiazepines
  - Caution should be exercised with patients who have a history of seizures or are taking tricyclic antidepressants
ANTICONVULSANTS

- Used to treat seizure disorders (most notably epilepsy)
- Exact mode and site of action of anticonvulsants is not understood
  - Depress excitability of neurons that fire to initiate seizure, or suppress the focal depolarization that occurs
    • Prevents the spread of seizure discharge
  - Presumed to modify the ionic movements of Na, K, or calcium across cell membrane
    • Reduces response to incoming electrical or chemical stimulation
  - Many patients require drug therapy throughout their lives to control seizures
Anticonvulsants

- Seizures are a state of hyperactivity of either a section of the brain or all of the brain
- May or may not be accompanied with convulsions
- Goal of seizure management is to balance eliminating the seizures against the side effects of the medications used to treat them
- Controlling seizures is a life-long process for most and medication compliance is essential
Anticonvulsants

- **Treatment of seizures**
  - Several general mechanisms are considered for seizure control
  - Most common is direct action on the sodium and calcium channels in the neural membrane
  - Phenytoin (Dilantin) and carbamazepine (tegretol) inhibit the influx of sodium into cell decreasing the cell’s ability to depolarize and propagate seizures
  - Other pharmacological treatments include barbiturates, benzodiazepines, and valproic acid (Depakote)
Central Nervous System Stimulants

- Stimulation of the CNS is desirable in certain circumstances
  - Fatigue, drowsiness, narcolepsy, obesity, and attention deficit hyperactivity disorder
- Two techniques accomplish this
  - Increasing the release of excitatory neurotransmitters
  - Decreasing the release of inhibitory neurotransmitters
- Three pharmacological classes of CNS stimulants
  - Amphetamines
  - Methylphenidates
  - Methylxanthines
Central Nervous System Stimulants

- Amphetamines increase the release of excitatory neurotransmitters including norepinephrine and dopamine
  - Norepinephrine is primary cause of drug effects which include wakefulness, increased awareness, and decreased appetite
  - Example: Dexedrine

- Methylphenidate (Ritalin)
  - Most commonly prescribed drug for attention deficit hyperactivity disorder
  - Similar mechanism of action as amphetamines
  - Increases the ability to focus
Central Nervous System Stimulants

- Methylxanthines include caffeine, aminophylline, and theophylline
  - Mechanism of action
    - Blocks adenosine receptors
    - Adenosine is an endogenous neurotransmitter
  - Have much lower potential for abuse
Psychotherapeutic Medications

- Drugs used to treat mental dysfunction
- Neurotransmitters control and regulate emotions
- Imbalances of the neurotransmitters (especially dopamine) appear to be most responsible for mental disease
- Regulating these and other excitatory and inhibitory neurotransmitters forms basis for psychopharmaceutical therapy
ANTIPSYCHOTIC DRUGS

- Selective action on thalamus and limbic system
- Do not cure mental illness but calm the predisposed patient
  - Relieve despondency of severely depressed
  - Activate the immobile and withdrawn
  - *Have antiemetic effects
- Mechanism of action
  - Neurotransmitter blockade
  - Dopaminergic inhibition
Psychotherapeutic Medications

- Schizophrenia is due to increased release of dopamine so therapy is aimed at blocking dopamine receptors
- Depression is due to inadequate amounts of neurotransmitters so treatment is aimed at increasing their release or duration
Psychotherapeutic Medications

- Major diseases treated with psychotherapeutic medications
  - Schizophrenia
  - Depression
  - Bipolar disorder
Psychotherapeutic Medications

- Schizophrenia chief characteristics
  - Lack of contact with reality and disorganized thinking
  - Manifestations include
    - Delusions
    - Hallucinations
    - Disorganized and incoherent speech
    - Disorganized or catatonic behavior
  - Treatment
    - Antipsychotic drugs alone
    - Antipsychotic drugs with antianxiety agents or antidepressants
    - Extrapyramidal symptoms are common side effect of antipsychotic medications
Two chief pharmaceutical classes of antipsychotics and neuroleptics are phenothiazines and butyrophenones.

Medications in this group block:
- Dopamine, muscarinic acetylcholine, histamine, alpha 1 adrenergic receptors
- Therapeutic effects come from blocking dopamine receptors

Chlorpromazine (Thorazine) is prototype phenothiazine.

Haloperidol (Haldol) is the prototype butyrophenones.
ANTIPSYCHOTIC AGENTS

- Thorazine
- Compazine
- Trilafon
- Haldol
- Lithium

**Major adverse effects**
- Extrapyramidal symptoms
  - Tremors, muscular rigidity
  - Treatment: benadryl, cogentin (anticholinergic)
Psychotherapeutic Medications

- Antidepressants
  - Depression characterized
  - Depressed mood
  - Loss of interest in things that normally give a patient pleasure
  - Weight loss or gain
  - Sleeping disturbances
  - Suicide attempts
  - Feelings of hopelessness
  - Loss of energy, agitation, withdrawal
Psychotherapeutic Medications

- Depression thought to be due to an insufficiency of monoamine neurotransmitters (norepinephrine and serotonin)
- Pharmaceutical interventions for this disease is to increase the number of neurotransmitters released in the brain
- Three ways to increase neurotransmitters
  - Increase the amount of neurotransmitter produced from presynaptic terminal
  - Increase the amount of neurotransmitter released from presynaptic terminal
  - Blocking the neurotransmitter reuptake
Psychotherapeutic Medications

- Three pharmacologic classes of antidepressants
  - Tricyclic antidepressants
  - Selective serotonin reuptake inhibitors
  - Monoamine oxidase inhibitors
Psychotherapeutic Medications

- Tricyclic antidepressants are frequently used in treating depression because they are effective, relatively safe, and have few significant side effects.
- TCA function by blocking the reuptake of norepinephrine and serotonin.
- Have anticholinergic properties that cause many side effects:
  - Blurred vision
  - Dry mouth
  - Urinary retention
  - Tachycardia
  - Convulsions (TCA lowers seizure threshold)
Psychotherapeutic Medications

- TCA’s adverse effects
  - Cardiotoxic
  - Myocardial infarctions
  - Dysrhythmias
  - Hypotension
- Treatment
  - Sodium bicarbonate
  - Alkalanizing the urine to increase excretion
  - Tofranil is prototype TCA
  - Other: Elavil, Norpramin, Pamelor
Tricyclic Antidepressants

<table>
<thead>
<tr>
<th>Norepinephrine Synapse</th>
<th>Serotonin Synapse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transmitting (Presynaptic) Neuron</td>
<td>Transmitting (Presynaptic) Neuron</td>
</tr>
</tbody>
</table>

Norepinephrine and serotonin are normally removed from the synapse by reuptake sites. Tricyclic antidepressants block norepinephrine and serotonin reuptake sites, allowing these neurotransmitters to remain active in the synapse longer.

Reuptake Sites (or Transporters)
Psychotherapeutic Medications

- Selective serotonin reuptake inhibitors
  - Recent addition to the antidepressants
  - Prototype fluoxetine (Prozac) is the most widely prescribed antidepressant in US
  - Antidepressant effects similar to TCAs, but do not effect dopamine or norepinephrine
  - Adverse reactions
    - Sexual dysfunction
    - Headache and nausea
  - Other examples
    - Zoloft
    - Paxil
SSRI Antidepressants

Serotonin is normally removed from the synapse by reuptake sites on the presynaptic neuron. SSRIs block the serotonin reuptake sites, allowing serotonin to remain active in the synapse longer.
Psychotherapeutic Medications

- Monoamine oxidase inhibitors
  - Monoaminde oxidase is an enzyme that metabolizes monoamines into active metabolites
    - MAOI inhibit monoamine oxidase and blocks monamines breakdown, thus increasing their availability
      - Increase the amount of norepinephrine
      - MAO are no longer commonly used
**Monoamine Oxidase Inhibitors**

Norepinephrine or Serotonin Synapse
Transmitting (Presynaptic) Neuron

Norepinephrine and serotonin are normally destroyed by the enzyme monoamine oxidase (MAO).
MAO inhibitors block this enzyme, inhibiting the destruction of norepinephrine and serotonin, allowing the neurotransmitters to remain active longer.

- Neurotransmitter Transporter (or Reuptake Site)
- Neurotransmitter Receptor

Synapse

Receiving (Postsynaptic) Neuron
Psychotherapeutic Medications

- Bipolar disorder (manic depression)
  - Cyclic swings from mania to depression with periods of normalcy in between
    - Characterized by hyperactivity, thoughts of grandeur, decreased need for sleep, increased goal oriented behavior, increased productivity, distractibility, increased risk taking
  - Lithium is the drug of choice for the management of bipolar disease
Drugs Used to Treat Parkinson’s Disease

- Parkinson’s disease is a nervous disorder caused by the destruction of dopamine releasing neurons in the basal ganglia.
- Basal ganglia is a specialized area in brain involved in controlling fine movements.
- Parkinson’s disease is characterized by:
  - dyskinesia or involuntary tremors
  - unsteady gait
  - postural akinesia
  - Later stages presents with dementia, depression and impaired memory.
Drugs Used to Treat Parkinson’s Disease

- Parkinson’s is a progressive disease that usually begins in middle age and progressive to a state of incapacitation.
- Goal in treating patients is to restore their ability to function without causing unacceptable side effects.
- Medications used to treat Parkinson’s Disease are also effective in treating extrapyramidal reactions:
  - Fine motor control is based on a balance of inhibitory and excitatory neurotransmitters.
  - Dopamine is inhibitory and acetylcholine is excitatory.
Drugs Used to Treat Parkinson’s Disease

- Pharmacologic therapy for Parkinson’s Disease seeks to restore the balance of dopamine and acetylcholine.
  - Done by increasing the stimulation of dopamine receptors or decreasing the stimulation of acetylcholine receptors
  - Drugs can do this by dopaminergic effects or anticholinergic effects
  - Levodopa is drug of choice for Parkinson’s disease
    - Inactive drug that crosses blood brain barrier and increases amount of dopamine available for release
    - Other drug therapy: Sinemet, Symmetrel, Benztropine (Cogentin) and Benadryl (anticholinergic agents)
- Amantadine
  - Promotes the release of dopamine from those dopamine-releasing neurons that remain unaffected by the disease
Autonomic Nervous System

- Two functional divisions of the autonomic nervous system
  - Sympathetic
    - Fight or flight
    - Responds to stress
  - Parasympathetic
    - Controls vegetative functions such as digestion of food

- Work in constant opposition to control organ responses
Autonomic Nervous System

- Nerves of the autonomic nervous system exit the central nervous system.
- Autonomic Ganglia
  - Preganglionic nerves
  - Postganglionic nerves

Sympathetic Branch of the Autonomic Nervous System
Autonomic Nervous System

- Synapse
  - No physical connection
- Neurotransmitters
  - Acetylcholine
  - Norepinephrine
Autonomic Nervous System Medications

- Drugs Affecting the Parasympathetic System:
  - Cholinergics
  - Anticholinergics
  - Ganglionic Blocking Agents
  - Neuromuscular Blocking Agents
  - Ganglionic Stimulating Agents
Autonomic Nervous System Medications

- Drugs Affecting the Sympathetic System:
  - Adrenergic Receptors
  - Adrenergic Agonists
  - Adrenergic Antagonists
  - Skeletal Muscle Relaxants
Distribution of Sympathetic Post-Ganglionic Fibers
Sympathetic Division of Autonomic Nervous System

- Sympathetic Division of ANS
  - Preganglionic (first-order) neurons in spinal segments T1–L2
    - Ganglionic (second-order) neurons
    - Sympathetic chain ganglia (paired)
      - Via post-ganglionic fibers
        - Visceral effectors in thoracic cavity, body wall, and limbs
    - Collateral ganglia (unpaired)
      - Visceral effectors in abdominopelvic cavity
    - Adrenal medulla (paired)
      - Organs and systems throughout body
        - Via release of neurotransmitters into circulation
Drugs Affecting the Parasympathetic Nervous System

- **Cholinergic drugs**
  - Act either directly or indirectly
    - Direct acting cholinergics stimulate the effects of acetylcholine by directly binding to cholinergic receptors
    - Prototype: Bethanechol (Urecholine)
  - Indirect acting cholinergic drugs affect acetylcholinesterase
    - Inhibit action of degrading acetylcholine prolonging the cholinergic response
    - Neostigmine is prototype reversible cholinesterase inhibitor
    - Physostigmine is a reversible cholinesterase inhibitor
Drugs Affecting the Parasympathetic Nervous System

- **Anticholinergics**
  - Oppose the parasympathetic nervous system
  - Muscarinic Cholinergic Antagonists
    - Block the effects of acetylcholine almost exclusively at the muscarinic receptors
    - Often called anticholinergics or parasympatholytics
    - Atropine is prototype
    - Scopolamine is anticholinergic used to prevent motion sickness
Nicotinic Cholinergic Antagonists

- Block acetylcholine only at nicotinic sites
- Include:
  - Ganglionic blocking agents
    - Block the nicotine receptors in the autonomic ganglia
  - Neuromuscular blocking agents
    - Block nicotine at the neuromuscular junction
Ganglionic Blocking Agents

- Ganglionic blockade is produced by competitive antagonism with acetylcholine at the nicotine receptors in the autonomic ganglia
- Two drugs in this class are trimethaphan (Arfonad) and mecamylamine (Inversine)
- Both agents are used to treat hypertension
Neuromuscular Blockade

- Neuromuscular blockade produces a state of paralysis without affecting consciousness.
- Neuromuscular blockade is caused by competitive antagonism of nicotine receptors at the neuromuscular junction.
- Useful during surgery and to facilitate emergency intubation.
- Neuromuscular blockade agents are either depolarizing or nondepolarizing.
  - Most are nondepolarizing.
  - Depolarizing agent is succinylcholine (rapid acting with short half life).
Drugs Used to Affect the Sympathetic Nervous System

- Stimulation of sympathetic chain ganglia
  - Stimulation of secretion by sweat glands
  - Constriction of blood vessels in skin
  - Increase in blood flow to skeletal muscles
  - Increase in heart rate and force of cardiac contraction
  - Bronchodilation
  - Stimulation of energy production
Drugs Used to Affect the Sympathetic Nervous System

- Stimulation of collateral ganglia
  - Reduction of blood flow to abdominal organs
  - Decreased digestive activity
  - Relaxation of smooth muscle in the wall of the urinary bladder
  - Release of glucose stores from the liver
Drugs Used to Affect the Sympathetic Nervous System

- Adrenergic receptors
  - Alpha 1
  - Alpha 2
  - Beta 1
  - Beta 2
- Adrenergic agonists
- Adrenergic antagonists

<table>
<thead>
<tr>
<th>Table 9-5</th>
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<tbody>
<tr>
<td>Receptor</td>
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<tr>
<td>-----------</td>
</tr>
<tr>
<td>Alpha 1 (α₁)</td>
</tr>
<tr>
<td>Alpha 2 (α₂)</td>
</tr>
<tr>
<td>Beta 1 (β₁)</td>
</tr>
<tr>
<td>Beta 2 (β₂)</td>
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<tr>
<td>Dopaminergic</td>
</tr>
</tbody>
</table>

*Stimulation of α₂ adrenergic receptors inhibits the continued release of norepinephrine from the pre-synaptic terminal. It is a feedback mechanism that limits the adrenergic response at that synapse. These receptors have no other identified peripheral effects.
**Table 9-6: Adrenergic Receptor Specificity**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Alpha₁</th>
<th>Alpha₂</th>
<th>Beta₁</th>
<th>Beta₂</th>
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<td>Phenylephrine</td>
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<td>Norepinephrine</td>
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<tr>
<td>Ephedrine</td>
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<tr>
<td>Terbutaline</td>
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</table>

*Receptor specificity is dose-dependent. The higher the dose, the less dopaminergic effects are seen.*
Skeletal Muscle Relaxants

- Skeletal muscle relaxants are used to treat muscle spasm from injury and muscle spasticity from CNS injuries or diseases

- Types
  - Central acting muscle relaxants
    - Functions via general sedation
    - Prototype: Baclofen
    - Other agents: Flexeril, soma, skelaxin, robaxin
  - Direct acting
    - Decrease the release of calcium from the sarcoplasmic reticulum
    - Calcium is necessary for the cross-bridging of actin and myosin filaments
    - Prototype: dantrolene (Dantrium)
Drugs Used to Affect the Cardiovascular System
Location, Size, and Shape of the Heart

- Located in Mediastinum
  - Lying in front of spinal column, behind sternum, and between lungs
  - 2/3 lies to left of midline sternum
  - Apex lies just above diaphragm
  - Base lies at level of the second-third rib
  - Size of owner’s closed fist
  - PMI
Anatomy of the Heart

The Heart is muscle

- **Myocardium** - heart muscle
- “Two-sided pump”
  - **Atrium** [atria]
    - Small upper chambers
    - Separated by interatrial septum
    - Receiving chambers
    - Fill ventricles
  - **Ventricles**
    - Lower chambers
    - Separated by interventricular septum
Cardiovascular Anatomy

- Tissue Layers
  - Endocardium
  - Myocardium
  - Pericardium
    - Visceral Pericardium
    - Parietal Pericardium
Myocardial Cell Types

- Electrical Cells
  - Properties
    - Automaticity
    - Excitability
    - Conductivity

- Mechanical (working cells)
  - Properties
    - Excitability
    - Contracion
Cardiac Conduction System

- Components
  - Sinoatrial Node
  - Internodal Atrial Pathways
  - Bachman’s Bundle
  - Atrioventricular Node
  - Atrioventricular Junction
  - Bundle of His
  - Left and Right Bundle Branches
  - Purkinje Fibers
Action potential of cardiac pacing cells slows influx of Ca$$^{++}$$ (leaking) and, to a lesser extent, Na$$^{+}$$ is responsible for automaticity or spontaneous depolarization. Class IV antidysrhythmics inhibit these calcium channels and decrease heart rate.
Action Potential
Cardiac Contractile Tissue

- Outlined into five phases
  - 4: resting membrane potential
  - 0: depolarization
  - 1: plateau
  - 2: beginning of repolarization
  - 3: repolarization
Introduction to Dysrhythmias

- **Dysrhythmia**
  - Any deviation from normal sinus rhythm
  - A disturbance in the normal heart rate or rhythm

- **Arrhythmia**
  - Absence of cardiac electrical activity
  - Term used interchangeably with dysrhythmia

- **Golden rule of management**
  - Treat the patient, not the monitor
Causes of Dysrhythmias

- Myocardial Ischemia, Necrosis, or Infarction
- Autonomic Nervous System Imbalance
- Distention of the Chambers of the Heart
- Blood Gas Abnormalities
- Electrolyte Imbalances
- Trauma to the Myocardium
- Drug Effects and Drug Toxicity
- Electrocution
- Hypothermia
- CNS Damage
- Idiopathic Events
- Normal Occurrences
Dysrhythmias

- Mechanism of impulse formation
  - Disturbance in automaticity
  - Disturbance in conductivity
  - Combination of altered automaticity and conductivity
  - Ectopic foci
    - Ectopic beats
- Reentry
- Antegrade conduction
- Retrograde conduction
Mechanism of Reentrant Pathways

- Normal pathway
- Right branch
- Left branch
- Purkinje fiber
- Ventricular muscle

(a) Right branch
(b) Unilateral block
(c) Bidirectional block
(d) Abolishment of unidirectional block
**Dysrhythmias**

- Classification by Site of Origin
  - Dysrhythmias Originating in the SA Node
  - Dysrhythmias Originating in the Atria
  - Dysrhythmias Originating Within the AV Junction (AV Blocks) and Bundle Branches
  - Dysrhythmias Sustained in or Originating in the AV Junction
  - Dysrhythmias Originating in the Ventricles
  - Dysrhythmias Resulting from Disorders of Conduction
DRUGS THAT EFFECT THE HEART

- Cardiac muscle
  - Composed of many interconnected branching fibers or cells that form the walls of the two atria and ventricles
  - Some cells are specialized to generate and conduct electrical impulses (pacemaker or electrical cells)
    - Conduction system
    - Some have contraction as their primary function (working cells)
  - Cardiac drugs are classified by their effects on these tissues
PHARMACOLOGICAL TERMS TO DESCRIBE ACTIONS OF CARDIOVASCULAR DRUGS

- **Chronotropic drugs**
  - Affect heart rate
  - A drug that accelerates heart rate is said to have a positive chronotropic effect (epinephrine)
  - A drug that decreases heart rate is said to have a negative chronotropic effect (verapamil)

- **Dromotropic drugs**
  - Affect conduction velocity through the conduction tissues of the heart
  - Speeds conduction: positive dromotropic effect (isoproterenol)
  - Slows conduction: negative dromotropic effect (adenosine)
Inotropic Agents
- Affects force of contraction
- Strengthens or increases the force of contraction: positive inotropic effect (epinephrine)
- Weakens or decreases the force of contraction: negative inotropic effect (propranolol)
Classifications of Cardiovascular Drugs

- **Antidysrhythmics:**
  - Used to treat and prevent abnormal cardiac rhythms.

- **Antihypertensives:**
  - Drugs used to treat hypertension.
Classifications of Cardiovascular Drugs

- Hemostatic Agents:
  - Drugs used to stop bleeding.

- Antihyperlipidemic Agents:
  - Drugs used to treat high cholesterol.
## Antidysrhythmic Classification

### Table 9-7: Antidysrhythmic Classifications and Examples

<table>
<thead>
<tr>
<th>General Action</th>
<th>Class</th>
<th>Prototype</th>
<th>ECG Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium Channel Blockers</td>
<td>IA</td>
<td>Quinidine, procainamide*,</td>
<td>Widened QRS, prolonged QT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>disopyramide</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IB</td>
<td>Lidocaine*, phenytoin,</td>
<td>Widened QRS, prolonged QT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>tocainide, mexiletine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IC</td>
<td>Flecaïnide*, propafenone</td>
<td>Prolonged PR, widened QRS</td>
</tr>
<tr>
<td>(Miscellaneous)</td>
<td>I</td>
<td>Moricizine*</td>
<td>Prolonged PR, widened QRS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta Blockers</td>
<td>II</td>
<td>Propranolol*, acebutolol,</td>
<td>Prolonged PR, bradycardias</td>
</tr>
<tr>
<td></td>
<td></td>
<td>esmolol</td>
<td></td>
</tr>
<tr>
<td>Potassium Channel Blockers</td>
<td>III</td>
<td>Bretylum*, amiodarone</td>
<td>Prolonged QT</td>
</tr>
<tr>
<td>Calcium Channel Blockers</td>
<td>IV</td>
<td>Verapamil*, diltiazem</td>
<td>Prolonged PR, bradycardias</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td></td>
<td>Adenosine, digoxin</td>
<td>Prolonged PR, bradycardias</td>
</tr>
</tbody>
</table>

* prototype
Antidysrhythmics

- Sodium channel blockers (Class I)
  - Medications affect the sodium influx in phases 0 and 4 of fast potentials
  - Slows the propagation of impulses down the conduction system of the atria and ventricles
  - Class IA drugs include quinidine, procainamide, and disopyramide (Norpace)
  - Drugs decrease the repolarization rate
  - Widens QRS and prolongs QT interval
Antidysrhythmics

- Class IB drugs
  - Include lidocaine, dilantin, tocainide
  - Increase rate of depolarization
  - Reduce automaticity in ventricular cells
  - Primary use is to terminate ventricular dysrhythmia
Antidysrhythmics

- Class IC
  - Include flecainide (Tambocor) and propafenone (Rythmol)
  - Drugs decrease conduction velocity through atria and ventricles
  - Delay ventricular repolarization
  - Depress myocardial contractility
  - Have prodysrhythmic effects
  - Administered to prevent recurrence of ventricular dysrhythmias
Antidysrhythmics

- Beta Blockers (Class II)
  - Include propranolol, acebutolol (Sectral), and esmolol (Brevibloc)
  - Beta adrenergic antagonists
  - Inderal is nonselective, acebutolol and esmolol are Beta 1 specific
  - Indicated for the treatment of tachycardias due to excessive sympathetic stimulation
  - Beta 1 receptor is attached to calcium channel
  - Blocking the Beta 1 receptor prevents the influx of calcium in phase 0 of action potential
Antidysrhythmics

- Potassium Channel Blockers (Class III)
  - Drugs are known as antiadrenergic medications because of their action on sympathetic terminals
  - Include bretylium and amiodarone
  - Blocking influx of potassium drugs prolong repolarization and the effective refractory period
  - Indicated for ventricular fibrillation and refractory ventricular tachycardia
Antidysrhythmics

- Calcium Channel Blockers (Class IV)
  - Decrease SA and AV node automaticity
  - Decreases conduction velocity through the AV node
  - Indicated for the treatment of atrial fibrillation, flutter, and to terminate supraventricular tachycardias
  - Include verapamil (Calan) and diltiazem (Cardizem)
  - Adverse effect is hypotension
Miscellaneous Antidysrhythmics

- Adenosine
  - Endogenous nucleoside with a very short half life
  - Acts on both potassium and calcium channels, increasing potassium efflux and inhibiting calcium influx
    - Results in hyperpolarization that effectively slows conduction
    - Agent of first choice for the treatment of PSVT
Miscellaneous Antidysrhythmics

- **Digoxin (Lanoxin)**
  - Decreases intrinsic firing rate of SA node and slows conduction velocity through AV node
  - Increases cardiac contractility

- **Magnesium**
  - Drug of choice for torsade de pointes
  - Thought to act on the sodium or potassium channels or on sodium-potassium ATPase
CARDIAC GLYCOSIDES

- Naturally occurring plant substances that have characteristic actions on the heart
- Contain a carbohydrate molecule (sugar)
- Mechanism of action
  - Blocks certain ionic pumps (membrane ATPase) in the cellular membrane
  - Increases calcium concentration to the contractile proteins
- Affect the heart in two ways:
  - Increase force of contraction (positive inotropic effect)
  - Dual electrophysiological effect
    - Modest negative chronotropic effect causing slight slowing
    - Profound dromotropic effect, decreasing conduction velocity
CLINICAL USES FOR CARDIAC GLYCOSIDES

- Congestive heart failure
  - Increase myocardial contractility.

- Tachydyssrhythmias
  - Slows AV nodal conduction
  - Slows ventricular rate

- Commonly prescribed agents
  - Digitalis
  - Digoxin
  - Lanoxin
SIDE EFFECTS OF CARDIAC GLYCOSIDES

- Cardiac glycosides have a small therapeutic index
- Side effects are common
- Symptoms may be neurological, visual, gastrointestinal, cardiac or psychiatric
- Common side effects
  - Anorexia
  - Nausea and vomiting
  - Altered color vision, flashing lights
  - Cardiac rhythm disturbances
    - Usually slowing with varying degrees of blocked conduction
    - Ventricular dysrhythmias
Antihypertensives

- Hypertension affects more than 50 million people in the United States
- Silent killer
- Two types
  - Essential: unknown cause
  - Secondary: known cause
- Major contributor to:
  - Coronary artery disease
  - Stroke
  - Renal failure
  - Blindness
Antihypertensives

- Medication classes
  - Diuretics
  - Adrenergic inhibiting agents
    - Beta blockers
  - Angiotensin converting enzyme (ACE) inhibitors
  - Angiotensin II receptor antagonists
  - Calcium channel blockers
  - Direct vasodilators
Antihypertensives (Diuretics)

- Drugs used to increase urine flow
  - Chief medical application
    - Removal of excess extracellular (edema) fluid in disease
    - Drug of choice in treating patients with hypertension and CHF

- Action:
  - Increase amount of Na ion in the urine
  - Result in a loss of excess salt and water from the body by renal excretion
    - Decrease in plasma and extracellular fluid volume (which decreases preload and stroke volume), plus a direct effect on arterioles results in lowered BP
    - Causes an initial decline in cardiac output, followed by a decrease in peripheral vascular resistance and a lowering of BP
Antihypertensives

- Diuretics
  - Reduce circulating blood volume by increasing the amount of urine
  - Reduces preload which in turn lessens cardiac output
  - Main categories of diuretics include: loop diuretics, Thiazides, and potassium sparing agents
  - All effect the reabsorption of sodium and chloride and create an osmotic gradient that decreases the reabsorption of water
  - Classes differ according to which area of the nephron they effect
    - Earlier in the nephron the drug works, the more sodium and water will be affected.
    - Drug that decreases sodium reabsorption in the proximal convoluted tubule will cause the kidneys to excrete more water than a drug that works on the distal convoluted tubule
Loop diuretics
- Profoundly affect circulating blood volume
- Decrease blood volume so well that they are typically considered excessive for treating moderate hypertension
- Primary medication used to treat left ventricular failure and cardiogenic pulmonary edema
Loop Diuretics

- Furosemide (Lasix) is the prototype loop diuretic
  - Blocks sodium reabsorption in the ascending loop of Henle
  - Decreases the pull of water from the tubule and into the capillary bed
  - Side effects: hyponatremia, hypovolema, hypokalemia, and dehydration
Antihypertensives

- Thiazides
  - Have a mechanism similar to loop diuretics
  - Mechanism affects the early part of the distal convoluted tubules and therefore cannot block as much sodium from reabsorption
  - Often drugs of choice for hypertension treatment because they decrease fluid volume sufficiently to prevent hypertension, but do not promote hypotension
  - Hydrochlorothiazide is prototype
Antihypertensives

- Potassium-sparing agents
  - Inhibit either the effects of aldosterone on the distal tubules or the specific sodium-potassium exchange mechanism
  - Not very potent diuretics because they act so late in the nephritic loop
  - Typically administered with other diuretics
  - Spironolactone (Aldactone) is prototype
Antihypertensive

- Adrenergic Inhibiting Agents
  - Inhibiting the effects of adrenergic stimulation can also control hypertension
  - Agents include
    - Beta adrenergic antagonism
    - Centrally acting alpha adrenergic antagonism
    - Adrenergic neuron blockade
    - Alpha 1 blockade
    - Alpha-beta blockade
SYMPATHETIC BLOCKING AGENTS

- Beta Blocking Agents
  - Used to treat cardiovascular disorders including hypertension
  - Work by decreasing cardiac output and inhibiting renin secretion from the kidneys
  - Compete with epinephrine for available beta receptor sites
    - Inhibit tissue and organ response to beta stimulation
  - Beta 1 blocking agents (cardioselective)
    - Acebutolol (Sectral)
    - Atenolol (Tenormin)
    - Metoprolol (Lopressor)
  - Beta 1 and 2 blocking agents (nonselective)
    - Labetalol (Normodyne)
    - Nadolol (Corgard)
    - Propranolol (Inderal)
Antihypertensives

● Beta Adrenergic Antagonists
  – Selective beta 1 blockade is useful in treating hypertension for several reasons
  – Decreases contractility reducing cardiac output
  – Reduces reflex tachycardia
  – Represses renin release from the kidneys
  – Prototype drug is lopressor
Antihypertensives

- Centrally acting adrenergic inhibitors
  - Reduce hypertension by inhibiting CNS stimulation of adrenergic receptors
  - In effect, they are CNS alpha 2 agonists
  - Alpha 2 receptors inhibit the release of norepinephrine to counterbalance sympathetic stimulation
  - By increasing the stimulation of alpha 2 receptors in the section of the CNS responsible for cardiovascular regulation, centrally acting adrenergic inhibitors decrease sympathetic stimulation of both alpha 1 and beta 2 receptors
  - Net result is to decrease heart rate and contractility by decreasing the release of norepinephrine at beta 1 receptors and to promote vasodilation by decreasing release of norepinephrine at alpha 1 receptors
  - Catapres is prototype drug
Antihypertensives

- Peripheral Adrenergic Neuron Blocking Agents
  - Function indirectly to decrease stimulation of adrenergic receptors
  - Decrease the amount of norepinephrine released from sympathetic presynaptic terminals
  - Prototype drug is reserpine
    - Decreases synthesis of norepinephrine
    - Exposes norepinephrine in the terminal vesicles to monoamine oxidase
    - Inhibition of norepinephrine decreases stimulation of alpha 1 receptors resulting in vasodilation
  - No longer commonly prescribed
Antihypertensives

- **Alpha 1 antagonists**
  - Prototype alpha 1 antagonist is Minipress
  - Decreases blood pressure by competitively blocking the alpha 1 receptors
  - By causing the arterioles to dilate afterload is reduced
  - Venous dilation occurs reducing preload
  - Decreased afterload and preload help lower the blood pressure
Antihypertensives

- Combined Alpha/Beta Antagonists
  - Labetalol (Normodyne) and carvedilol (Coreg) competitively bind with alpha 1 and beta 1 receptors increasing their antihypertensive action
  - Hypertension is treated by decreasing alpha 1 mediated constriction and beta 1 mediated contractility and heart rate
  - Preload, afterload and cardiac workload are reduced
VASODILATOR DRUGS

● Act directly on smooth muscle walls of arterioles, veins or both
  – Lower peripheral resistance and BP

● Stimulate sympathetic nervous system and activate baroreceptor reflexes
  – Leads to an increased heart rate, cardiac output and renin release

● Combined therapy is usually prescribed to inhibit sympathetic response

● Also useful in treating angina pectoris (i.e., nitrates)
VASODILATOR DRUGS

- ACE Inhibitor Drugs
  - Renin-angiotension-aldosterone system plays an important role in maintaining BP
    - Disturbance in this system can result in hypertension
    - Kidney damage can result in an inability to regulate release of renin, causing an elevated BP
  - Mechanism
    - Angiotension II is a powerful vasoconstrictor
    - Raises BP and causes release of aldosterone
      - Contributes to sodium and H2O retention
    - By inhibiting conversion of angiotension I to the active molecule angiotension II (brought about by ACE)
    - Renin-angiotension-aldosterone system is depressed lowering BP
  - Examples:
    - Captopril (Capoten), Enalapril (Vasotec), Lisinopril (Prinivil)
Antihypertensives

- Angiotensin Converting Enzyme (ACE) Inhibitors
  - Agents in this class interrupt the renin-angiotension-aldosterone system by preventing the conversion of angiotensin I to angiotension II
  - Angiotensin II is a potent vasoconstrictor
  - Decreasing the amount of circulating angiotensin II peripheral vascular resistance is decreased and the blood pressure lowered
Antihypertensives

- Angiotensin Converting Enzyme Inhibitors
  - The glomerular apparatus in the kidneys releases renin in response to decreases in blood volume, sodium, and blood pressure.
  - Renin acts as an enzyme to convert the inactive protein angiotensinogen into angiotension I.
  - Angiotensin converting enzyme immediately converts angiotension I into angiotensin II.
  - Angiotensin II causes both systemic and local vasoconstriction.
  - Angiotensin II also increases the release of aldosterone.
    - Aldosterone contributes to the retention of Na and H2O.
Renin-Angiotensin-Aldosterone System

- Renin
- Angiotensin I
- Angiotensin II
- Angiotensinogen
- Liver
- Lung
- Kidney

Legend:
- Secretion from an organ
- Stimulatory signal
- Inhibitory signal
- Reaction
- Active transport
- Passive transport

Water and salt retention. Effective circulating volume increases. Perfusion of the juxtaglomerular apparatus increases.
Antihypertensives

- Angiotensin converting enzyme inhibitors
  - Prototype ACE inhibitor is captopril (capoten)
    other is Vasotec
  - Main advantage is the absence of side effects common to other antihypertensives
    - Does not interfere with beta receptors
    - Does not cause potassium depletion
  - Most dangerous side effect is pronounced hypotension after the first dose
Antihypertensives

- Calcium channel blocking agents
  - Block the influx of calcium in cardiac and vascular smooth muscles
  - Subclass of calcium blockers are dihydropyridine I
    - Prototype is Nifedipine (Procardia, Adalat)
    - Differ from verapamil and cardizem in that they do not effect the calcium channels in the heart at therapeutic doses
    - Act only on vascular smooth muscle by blocking calcium channels in the arterioles
    - Vasodilation results
Antihypertensives

- Direct vasodilators
  - Selective dilation of arterioles causes decrease in peripheral vascular resistance
  - Decreasing peripheral vascular resistance lowers the BP, decreased CO, and reduces cardiac workload
  - Dilating veins increases capacitance and decreases preload
  - Decreases blood pressure and CO
Antihypertensives

- Direct vasodilators
  - Prototype is Hydralazine (Apresoline)
  - Selective arteriole dilator decreasing peripheral vascular resistance and afterload
  - Side effects include reflex tachycardia
  - Other agent - Sodium Nitroprusside
    - Fast acting antihypertensive used in emergent situations
Antihypertensives

- **Ganglionic blocking agents**
  - Nicotine antagonists
  - Prototype is Trimethaphan (Arfonad)
  - Competitive antagonism results in a blocking of the autonomic nervous system
  - Drugs reduce preload, afterload and the BP lowers
  - Dangerous and not commonly used medications for hypertension
Antihypertensives

- **Cardiac glycosides**
  - Cardiac glycosides occur naturally in the foxglove plant
  - Two drugs in this class
    - Digoxin (Lanoxin)
    - Digitoxin (Crystodigin)
  - Digoxin is one of the ten most commonly prescribed medications in US
  - Indicated for heart failure and some dysrhythmias
  - Complex mechanism of action, but digoxin interferes with the sodium-potassium pump increasing the amount of intracellular calcium
    - Muscle contraction occurs longer and harder
    - Increases myocardial contractility and cardiac output
    - Very small therapeutic index
Other Vasodilators and Antianginals

- Pathophysiology of angina
  - Imbalance between myocardial oxygen supply and demand
- Three types of angina pectoris (chest pain)
  - Stable
  - Unstable
  - Prinzmetal
- Stable angina
  - Predictable
- Unstable angina
  - Changes in frequency, severity and duration of pain
  - Need for more nitrates to terminate event
- Prinzmetal angina
  - Vasospastic
  - Occurs in patients with relatively clean CA
- Treatment
  - Nitrates/Calcium and beta blockade
ANTIANGINAL AGENTS

- Three categories
  - Nitrates
  - Beta adrenergic blocking agents
  - Calcium channel blockers
- Nitrates
  - Relax vascular smooth muscle promoting vasodilation
  - Dilate coronary arteries improving myocardial perfusion
  - Decrease venous return by venous dilation and pooling
  - Reduce left ventricular end diastolic volume and pressure
  - Decreases myocardial O2 demand and relief of chest discomfort associated with ischemia
Knowledge of the drugs that affect blood coagulation and the use of thrombolytic agents is important in prehospital care.

Blood coagulation

- Process that results in formation of a stable fibrin clot that entraps platelets, blood cells and plasma
  - Results in a blood clot or thrombus
  - Abnormal thrombus formation (intravascular clotting) is a major cause of MI and CVA

Arterial thrombi are commonly associated with

- Atherosclerotic plaques
- Hypertension
- Turbulant blood flow that damages endothelial lining of blood vessels
Hemostatic Agents

- **Antiplatelets:**
  - Drugs that decrease the formation of platelet plugs.

- **Anticoagulants:**
  - Drugs that disrupt the clotting cascade.

- **Thrombolytics:**
  - Drugs that act directly on thrombi to break them down.
Hemostatic Agents

- Antiplatelet medications
  - Antiplatelet drugs decrease the formation of platelet plugs
  - Prototype drug is aspirin
    - Aspirin inhibits cyclooxygenase, an enzyme needed for the synthesis of thromboxane A2
    - Aspirin decreases the formation of platelet plugs and potential thrombi
    - Aspirin has no effect on existing thrombi
    - Aspirin is indicated for an acute MI and often for post MI or stroke patients
    - Side effect - bleeding
Hemostatic Agents

- **Anticoagulants**
  - Interrupt the clotting cascade
  - Two main types of anticoagulants are parenteral and oral
  - Prototype parenteral drug is heparin
    - Heparin enhances antithrombin III’s ability to interrupt the clotting cascade
  - Low-molecular-weight heparin
    - Has greater bioavailability, is easier to dose, and has fewer effects on platelet function
      - Heparin is indicated for treating and preventing DVT, pulmonary emboli, strokes, and used in conjunction with thrombolytics to treat AMI
  - Prototype oral anticoagulant is warfarin (Coumadin)
    - Functions by antagonizing the effects of vitamin K
Fibrinolytics Therapy

- Fibrinolytic agents
  - Dissolve blood clots after their formation by promoting the digestion of fibrin
  - Treatment of choice for AMI in certain groups of patients
    - Goal is to reestablish blood flow and prevent myocardial ischemia and tissue death
  - Also used to treat acute pulmonary embolism, DVT, and peripheral arterial occlusion
  - Examples
    - Streptokinase
    - Anisoylated plaminogen streptokinase activator anistreplase (Eminase)
    - Tissue plasminogen activator/ Alteplase (tPA), reteplase (Retavase))
    - Urokinase
Hemostatic Agents

- Thrombolytics
  - Clot dissolving enzyme
  - Agents
    - Streptokinase
    - Eminase
    - tPA
  - All function by converting plasminogen to plasmin (active agent that lysis clots)
  - Indicated for the treatment of AMI and strokes
Antihyperlipidemics

- Drugs used to treat high blood cholesterol
  - These agents are also known as statins
- Examples
  - Lovastatin (Mevacor)
  - Simvastatin (Zocor)
- Bile acid-binding resins can also reduce LDL levels
  - Cholestyramine (Questran) is the prototype
Antihyperlipidemic Agents

- Elevated levels of low-density lipoproteins (LDLs) have been clearly indicated as a causative factor in coronary artery disease.
- Lipoproteins are transport mechanisms for lipids (triglycerides and cholesterol).
- LDLs contain most of the cholesterol in the blood.
- LDLs are known as bad cholesterol because they increase blood cholesterol levels and risk for CAD.
- Goal of lowering LDL levels is to prevent atherosclerosis and subsequent CAD.
Antihyperlipidemic Agents

- Several classes of antihyperlipidemic agents are used
  - Most common are drugs that inhibit hydroxymethylglutaryl coenzyme A reductase
  - HMGCoA is necessary to synthesize cholesterol
  - Inhibiting this enzyme HMGCoA agents lower LDL levels
  - Agents include Mevacor, Zocor
  - Bile acid binding resins can also reduce LDL levels
Drugs Used to Affect the Respiratory System
DRUGS THAT AFFECT THE RESPIRATORY SYSTEM

- **Review of Anatomy and Physiology**
  - Respiratory system includes all structures involved in exchange of oxygen and carbon dioxide
  - Serious narrowing of any portion of respiratory tract may be an indication for pharmacological therapy
  - Emergencies involving the respiratory system are usually caused by reversible conditions
    - Asthma
    - Emphysema with infection
    - Foreign body obstruction
ANATOMY AND PHYSIOLOGY

- Smooth muscle fibers
  - Smooth muscle fibers of the tracheobronchial tree directly influence diameter of the airways
    - Muscle tone is maintained by impulses from the ANS
    - Parasympathetic fibers from vagus nerve innervate bronchial smooth muscle through the release of acetylcholine
      - Interacts with muscarinic receptors on the cell membranes producing bronchoconstriction (CGMP)
    - Sympathetic fibers affect beta 2 receptors through the release of catecholamines (CAMP)
      - Produce smooth muscle relaxation and promote bronchodilation
Antiasthmatic Medications

- Asthma is a common disease that decreases pulmonary function and may limit daily activities.
- Typically presents with shortness of breath, wheezing, and coughing.
- Basic pathophysiology has two components:
  - Bronchoconstriction
  - Inflammation
- Drug treatment of asthma is aimed at relieving bronchospasm and swelling of mucus membranes.
# Antiasthmatic Medications

## Table 9-8  Drugs Used in the Treatment of Asthma

<table>
<thead>
<tr>
<th>Mechanism of Action</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bronchodilators</strong></td>
<td></td>
</tr>
<tr>
<td>Nonspecific agonists</td>
<td>Epinephrine</td>
</tr>
<tr>
<td></td>
<td>Ephedrine</td>
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<tr>
<td><strong>Beta$_2$ specific agonists</strong></td>
<td></td>
</tr>
<tr>
<td>Inhaled (short acting)</td>
<td>Albuterol (Ventolin, Proventil)</td>
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<tr>
<td></td>
<td>Metaproterenol (Alupent)</td>
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<td></td>
<td>Terbutaline (Brethine)</td>
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<tr>
<td></td>
<td>Bitolterol (Tornalate)</td>
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<tr>
<td>Inhaled (long-acting)</td>
<td>Salmeterol (Serevent)</td>
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<tr>
<td><strong>Methyloxanthines</strong></td>
<td>Theophylline (Theo-Dur, Slo-Bid)</td>
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<td>Aminophylline</td>
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<tr>
<td><strong>Anticholinergics</strong></td>
<td>Atropine</td>
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<td>Ipratropium (Atrovent)</td>
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<td><strong>Anti-inflammatory agents</strong></td>
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<td><strong>Glucocorticoids</strong></td>
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<tr>
<td>Inhaled</td>
<td>Beclomethasone (Beclovent)</td>
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<td>Triamcinolone (Azmacort)</td>
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<td>Methyprednisolone (Solu-Medrol)</td>
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<td></td>
<td>Dexamethasone (Decadron)</td>
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<tr>
<td><strong>Leukotriene Antagonists</strong></td>
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<tr>
<td></td>
<td>Zafirlukast (Accolate)</td>
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<td></td>
<td>Zileuton (Zyflo)</td>
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<tr>
<td><strong>Mast-Cell Membrane Stabilizer</strong></td>
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<tr>
<td></td>
<td>Cromolyn (Intal)</td>
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</tbody>
</table>
BRONCHODILATOR DRUGS

- Primary treatment for COPD
- Drugs are grouped according to their receptor action
  - Nonselective adrenergic drugs have alpha and beta 1 (cardiac) and beta 2 (respiratory) actions
    - Alpha activity mediates vasoconstriction to reduce mucosal edema
    - Beta 2 activity produces bronchodilation and vasodilation
    - Undesirable beta 2 effects include muscle tremors and CNS stimulation
  - Nonselective beta adrenergic drugs have both beta 1 and 2 effects
    - Cardiac side effects (HR increase)
  - Selective beta 2 receptor drugs act primarily on beta 2 receptors in lungs (bronchial smooth muscle)
    - Lessens the incidence of unwanted cardiac effects
    - Better tolerated by patients with hypertension, cardiac disease and diabetes
Antiesthastmatic Medications

- Beta 2 specific agents
  - Drugs that are selective for beta 2 receptors are the mainstay for the treatment of asthma induced shortness of breath
  - Albuterol is prototype of this class
  - Agents relax bronchial smooth muscle promoting bronchodilation and relief from bronchospasm
  - First line therapy for acute shortness of breath and prophylaxis
Antiasthmatic Medications

- Nonselective sympathomimetics
  - Medications that stimulate both beta 1 and beta 2 receptors
  - Rarely used to treat asthma because they have undesirable side effects
  - Agents include: epinephrine, ephedrine, and isoproterenol
BRONCHODILATOR DRUGS

• Xanthine Derivatives
  – Phosphodiesterase inhibitors
  – Includes caffeine, theophylline and theobromine
  – Relax bronchial smooth muscle
  – Stimulate cardiac muscle and CNS
  – Increase diaphragmatic contractility
  – Promote diuresis through increased renal perfusion
  – Theophylline products vary in their rate of absorption and therapeutic effects
    • No longer a first line medication for the treatment of reactive airway disease
Methylxanthines

- Methylxanthines are CNS stimulants that have additional bronchodilatory properties
- Used when beta 2 specific agents are ineffective
- Agents block adenosine receptors
- Prototype: Aminophylline
Antiasthmatic Medications

● Anticholinergics
  – Ipratropium (Atrovent) is an atropine derivative administered by nebulizer
  – Atrovent is a muscarinic antagonist resulting in bronchodilation
  – Atrovent is inhaled and therefore has no systemic effects
  – Atrovent and beta 2 agonists are often administered concurrently
Antiasthmatic Medications

- **Glucocorticoids**
  - Have anti-inflammatory properties
  - Lower the production and release of inflammatory substances such as histamine, prostaglandins, and leukotrienes
  - Reduce mucus and edema secondary to decreasing vascular permeability
  - Medications can be inhaled, taken orally, or intravenously
  - Prototype inhaled drug is beclomethasone
  - Prototype oral agent is prednisone
  - Prototype injectable agent is methylprednisolone
  - Other agent - Cromolyn Sodium (Intal)
    - Prophylactic agent inhibiting the release of histamine from the mast (basophil) cell
Antiasthmatic Medications

- **Leukotriene Antagonists**
  - Leukotrienes are mediators released from mast cells upon contact with allergens
    - Contribute to both inflammation and bronchoconstriction
  - Leukotrine antagonists are agents that block the synthesis of leukotrienes or block their receptors
  - Agents
    - Zileuton (Zyflo) is prototype that blocks synthesis
    - Zarfirlukast (Accolate) is prototype that block receptors
OTHER RESPIRATORY DRUGS

- Antihistamines
  - Histamine is a chemical mediator found in high concentrations in skin, lungs and GI tract
  - Body releases histamine when exposed to an antigen
    - Results in increased capillary permeability and swelling of tissues
    - Produces contractile action on bronchial smooth muscle
    - Systemic effects may result in anaphylaxis
  - Antihistamines compete with histamine for receptor sites preventing physiological action of histamine
    - H1 receptors act primarily on blood vessels and bronchioles
    - H2 receptors act mainly on GI tract
  - Antihistamines also have anticholinergic effects (nicotine antagonists)
Drugs Used for Rhinitis and Cough

- Nasal Decongestants
- Antihistamines
- Antitussives
- Expectorants
- Mucolytic
Drugs Used for Rhinitis and Cough

- Rhinitis is inflammation of the nasal lining
  - Comprises a group of symptoms including nasal congestion, itching, redness, sneezing, and rhinorrhea
- Medications that treat symptoms of rhinitis are commonly found over the counter
- Nasal decongestants, antihistamines, and cough suppressants are available in prescription medications
Drugs Used for Rhinitis and Cough

- Nasal decongestants
  - Nasal congestion is caused by dilated and engorged nasal capillaries
  - Drugs that constrict these capillaries are effective nasal decongestants
  - Main pharmacological classification for treatment are alpha 1 agonists
  - Examples: phenylephrine, pseudoephedrine, and phenylpropanolamine
    - Administered as mist or drops
  - Rebound congestion from continued use
Drugs Used for Rhinitis and Cough

● Antihistamines
  – Arrest the effects of histamine by blocking its receptors
  – Histamine is an endogenous substance that affects a wide variety of organ systems
  – Histamine receptors
    • H1 receptors located in vasculature and lungs
      – Stimulation causes vasodilation and increased capillary permeability
      – Brochoconstriction
    • H2 receptors is gastrointestinal system
      – Stimulation causes an increase in gastric acid release
Drugs Used for Rhinitis and Cough

- **Antihistamines**
  - Histamine is synthesized and stored in two types of granulocytes
    - Tissue bound mast cells
    - Plasma bound basophils
  - When these cells are exposed to allergens they develop antibodies
  - On subsequent exposure the antibodies bind with their specific allergen and cells release their contents
  - Antihistamines function by antagonizing the histamine receptors
Drugs Used for Rhinitis and Cough

- **First generation of antihistamines**
  - Alkylamines and ethanolamines (Benadryl), and phenothiazines (Promethazine)
  - Different classes of agents have same effect they differ in their degree of sedation
  - Medications also have anticholinergic effects

- **Second generation of antihistamines**
  - Terfenadine (Seldane), loratadine (Claritin), and fexofenadine (Allegra), cetirizine (Zyrtec).
  - Actions are similar to first generation except they do not cross the blood brain barrier
  - Do not cause sedation
Drugs Used for Rhinitis and Cough

- Cough suppressants
  - Coughing is a reflex that depends on functions in the CNS, PNS, and respiratory muscles
  - Protective mechanism
  - Productive and nonproductive coughs
  - Antitussives
    - Suppress the stimulus to cough in the CNS
    - Two pharmacological types: opioid and nonopioid
      - Opioid: codeine and hydrocodone
      - Both inhibit cough stimulus in brain, but also produce a degree of euphoria
Drugs Used for Rhinitis and Cough

- **Cough suppressants**
  - Nonopioid antitussives
    - No potential for abuse
    - Dextromethorphan is leading drug in this class
    - Most common drug used over the counter usually in combination with other products
    - Benadryl is also used as a nonopioid antitussive
    - Expectorant: medication intended to increase the productivity of cough
    - Mucolytic: medication that makes mucus more watery
Drugs Used to Affect the Gastrointestinal System

- Main indications for gastrointestinal drug therapy
  - Peptic ulcers
  - Constipation
  - Diarrhea and emesis
  - Digestion
Drugs Used to Treat Peptic Ulcer Disease

- Peptic ulcer disease is characterized by an imbalance between factors in the gastrointestinal system that increase acidity and those that protect against acidity.
- PUD manifests itself as indigestion, heartburn, or more seriously as perforated ulcers.
- Portion of GI system lining may be eaten away exposing the tissue underneath to the acidic environment of the stomach or duodenum.
- Most common cause of PUD is the Helicobacter pylori bacterium.
  - Thought to decrease the body’s ability to produce protective mucus lining.
Drugs Used to Treat Peptic Ulcer Disease

- Approaches to treat PUD include antibiotics and drugs that block or decrease the secretion of gastric acid
- Antibiotics are most effective
  - Flagyl, amoxicillin, and tetracycline
- H2 receptor antagonists
- Proton pump inhibitors
- Antacids
- Anticholinergics
Drugs Used to Treat Peptic Ulcer Disease

- **H2 receptor antagonists**
  - Block the H2 receptors in the gut
  - Inhibits gastric acid secretion and helps return the balance between protective and aggressive factors

- **Four approved H₂ receptor antagonists**
  - Cimetidine (Tagamet), ranitidine (Zantac), Famotidine (Pepcid), Nizatidine (Axid Pulvules)
  - Primary therapeutic use is for ulcers, gastrointestinal reflux, acid indigestion
Drugs Used to Treat Peptic Ulcer Disease

- Proton pump inhibitors
  - Act directly on the potassium, hydrogen, ATPase enzyme that secretes gastric acid
  - Omeprazole (Prilosec), Lansoprazole (Prevacid)
- Antacids
  - Alkalotic compounds used to increase the gastric environment’s pH
- Anticholinergics
  - Seldom used but can block the Ach receptors in the gut
Drugs Used to Treat Constipation

- Laxatives
  - Decrease the firmness of stool and increase the water content
  - Laxatives are traditionally grouped into four categories
    - Bulk forming
    - Surfactant
    - Stimulant
    - Osmotic
Drugs Used to Treat Constipation

- **Bulk forming**
  - Produce a response almost identical to normal dietary fiber
  - Absorb water and makes stool softer and more bulky
  - (methylcellulose or Citrucel)

- **Sufactant laxatives**
  - Decrease surface tension, which increases water absorption into the feces
  - (Colace)

- **Stimulant laxatives increase motility**
  - Increase water secretion and decrease its absorption
  - (phenolphthalein or Ex-Lax)

- **Osmotic laxatives**
  - Salts that increase the feces osmotic pull, thereby increasing water content
  - (Milk of Magnesia)
Drugs Used to Treat Diarrhea

- Diarrhea is the abnormally frequent passage of soft, liquid stool
- Symptom of an underlying disease, usually a bacterial infection
- Caused by
  - Increased gastric motility
  - Increased water secretion
  - Decreased water absorption
- Often a helpful process because it increases the expulsion of the offending agent
- Antibiotic therapy
Drugs Used to Treat Emesis

- Emesis is a complex process involving different parts of the brain, receptors, and muscles in the stomach
- Brain components
  - Vomiting center in medulla
  - Chemoreceptor trigger zone
- Vomiting center stimulated by H1 and Ach receptors in pathways between itself and inner ear and by sensory input from eyes and nose
- CTZ stimulates vomiting center in response to stimuli from serotonin receptors in stomach and blood borne substances (opioids, ipecac)
Drugs Used to Treat Emesis

- **Antiemetics**
  - Medications used to prevent vomiting
  - Indicated in conjunction with chemotherapy and prophylactic treatment of motion sickness
  - Multiple transmitters are involved in the vomiting reflex
    - Serotonin, dopamine, acetylcholine, and histamine
Drugs Used to Treat Emesis

- **Serotonin Antagonists**
  - Prototype is Zofran
  - Blocks serotonin in the CTZ, stomach, and small intestines

- **Dopamine antagonists**
  - Phenothiazines and butyrophenones block dopamine receptors in CTZ
    - Phenothiazines include prochlorperazine (Compazine) and promethazine (Phenergan)
    - Butyrophenones include haloperidol (Haldol) and droperidol (Inapsine)
  - Side effects: extrapyramidal effects

- **Reglan**: Blocks dopamine and serotonin in the CTZ
Drugs Used to Treat Emesis

- Cannabinoids
  - Derivatives of tetrahydrocannabinol (THC)
  - Effective antiemetics used to treat chemotherapy-induced nausea and vomiting
  - Available agents are dronabinol (Marinol) and nabilone (Cesamet)
Several drugs are available to aid digestion of carbohydrates and fats.

Two such drugs are pancreatin (Entozyme) and pancrelipase (Viokase).
Drugs Used to Affect the Eyes
Drugs Used to Affect the Eyes

- Ophthalmic drugs are used to treat conditions involving the eyes
  - Glaucoma
    - Degenerative disease that affects the optic nerve
    - Medications used to treat glaucoma are aimed to reduce intraocular pressure
    - Beta blockers and cholinergic drugs are most common
    - Timolol and betaxolol (beta blockers) and Pilocarpine cholinergic
  - Trauma
    - Tetracaine (Pontocaine) local anesthetic used to decrease pain and sensation
Drugs Used to Affect the Ears
Drugs Used to Affect the Ears

- Most drugs used to treat conditions involving the ear are aimed at eliminating underlying bacterial or fungal infections or at breaking up impacted ear wax.
  - Chlorampenicol (Chloromycetin otic).
  - Gentamicin sulfate (Garamycin).
Drugs Used
to
Affect the Endocrine System
<table>
<thead>
<tr>
<th>Gland</th>
<th>Hormone</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posterior pituitary</td>
<td>Oxytocin</td>
<td>Uterine contraction, milk ejection</td>
</tr>
<tr>
<td></td>
<td>Vasopression (ADH)</td>
<td>Retains salt and water, increases ECF volume</td>
</tr>
<tr>
<td>Anterior pituitary</td>
<td>Thyroid-stimulating hormone (TSH)</td>
<td>Increases metabolic rate</td>
</tr>
<tr>
<td></td>
<td>Growth hormone (GH)</td>
<td>Increases use of stored fats, decreases glucose use</td>
</tr>
<tr>
<td></td>
<td>Adrenocorticotropic hormone (ACTH)</td>
<td>Stimulates adrenal cortex to release hormones</td>
</tr>
<tr>
<td></td>
<td>Follicle-stimulating hormone (FSH)</td>
<td>Males: sperm production; females: stimulates growth and development of ovarian follicles</td>
</tr>
<tr>
<td></td>
<td>Luteinizing hormone (LH)</td>
<td>Males: responsible for secretion of testosterone by testes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Females: ovulation, secretion of estrogen and progesterone</td>
</tr>
<tr>
<td></td>
<td>Prolactin (PRL)</td>
<td>Enhances breast development and milk production</td>
</tr>
<tr>
<td>Thyroid</td>
<td>Thyroid hormone</td>
<td>Increases metabolic rate</td>
</tr>
<tr>
<td>Parathyroid</td>
<td>Parathyroid hormone</td>
<td>Increases calcium in ECF</td>
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<tr>
<td>Pancreas</td>
<td>Insulin</td>
<td>Decreases blood glucose</td>
</tr>
<tr>
<td></td>
<td>Glucagon</td>
<td>Increases blood glucose</td>
</tr>
<tr>
<td>Adrenal</td>
<td>Glucocorticoids</td>
<td>Increases blood glucose, prevents inflammation</td>
</tr>
</tbody>
</table>
Drugs Used to Affect the Endocrine System

- Anterior pituitary drugs
  - Conditions treated with pituitary like drugs are those associated with abnormal growth
    - Dwarfism
      - Caused by a deficiency in growth hormone
      - Therapy is aimed at hormone replacement
      - Somatrem (Protropin) and somotropin (Humatrope) increase skeletal growth
    - Acromegaly and Gigantism
      - Caused by excessive growth hormone usually from a tumor
      - Treatment: surgical or medication to inhibit hormones
Drugs Used to Affect the Endocrine System

- **Posterior pituitary drugs**
  - Two posterior pituitary drugs are oxytocin and antidiuretic hormone
  - ADH is key to regulating blood volume, blood pressure, and electrolyte balance
  - Drugs are used to reverse ADH deficiency
    - Vasopressin
    - Desmopressin
    - Lypressin
Drugs Affecting the Parathyroid and Thyroid Glands

- Parathyroid glands are responsible for regulating calcium levels
  - Therapy is for replacement of calcium and vitamin D
  - Surgical removal of the parathyroids

- Thyroid
  - Produce thyroid hormones that regulate growth, maturation, and metabolism
  - Hypothyroidism
    - Juvenile onset - Dwarfism and mental retardation
    - Adult onset - decreased metabolic rate, fatigue, and bradycardia
  - Treatment - thyroid replacement
    - Levothyroxine (Synthroid)
  - Hyperthyroidism (Grave’s disease)
    Treatment - Radioactive iodine or surgical removal of thyroid gland
Drugs Affecting the Adrenal Cortex

- Adrenal cortex synthesizes and secretes three classes of hormones
- Glucocorticoids
  - Increase the production of glucose by enhancing carbohydrate metabolism, promoting gluconeogenesis, and reducing peripheral glucose utilization
- Mineralocorticoids
  - Regulate salt and water balance
- Androgens
  - Regulating sexual maturation and development
Drugs Affecting the Adrenal Cortex

- **Pathologies**
  - Cushing’s disease
    - Hypersecretion of adrenocorticotropic hormone
    - Increases synthesis of corticoids leading to excessive glucocorticoid secretion
    - Treatment usually surgical
  - Addison’s disease
    - Hyposecretion of corticoids due to damage of the adrenal gland
    - Treatment: replacement therapy, cortisone and hydrocortisone are drugs of choice
Drugs Affecting the Pancreas

- Diabetes mellitus is the most important disease involving the pancreas
- Pathophysiology of diabetes
  - Diabetes Type I and Type II
- Insulin: substance that decreases blood glucose levels
- Glucagon: substance that increases blood glucose levels
Drugs Affecting the Pancreas

- Insulin preparations
  - Insulin comes from three sources
    - Beef or pork intestines
    - Recombinant DNA technology
  - Insulin preparations differ in their onset and duration of action and in their incidence of allergic reactions
    - Short acting
    - Intermediate acting
    - Long acting
Drugs Affecting the Pancreas

- **Insulin preparations**
  - Classified as natural or modified
    - Natural insulins are used as they occur in nature
    - Modified insulins have been altered to increase their duration of action and thus decrease the frequency of administration
      - Examples: NPH, lente series, have a protein or zinc molecule attached respectively to last longer
  - Insulin is administered subcutaneously
<table>
<thead>
<tr>
<th>Classification</th>
<th>Trade Name</th>
<th>Source</th>
<th>Onset (Hrs)</th>
<th>Peak (Hrs)</th>
<th>Duration (Hrs)</th>
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</table>
Drugs Affecting the Pancreas

● Oral hypoglycemic agents
  – Used to stimulate insulin secretion from the pancreas in patients with NIDDM
  – Four pharmacological classes
    • Sulfonylureas (Orinase, Diabinese, Glucotrol, Micronase)
    • Biguanides (Glucophage)
    • Alpha-glucosidase inhibitors (Precose, Glyset)
    • Thiazolidinediones (Rezulin)
Hyperglycemic Agents

- D50W is a sugar solution given intravenously for acute hypoglycemia.
- Glucagon is indicated for emergency treatment when an IV is unobtainable.
Drugs Affecting the Female and Male Reproductive Systems
Drugs Affecting the Female Reproductive System

- Four main groups of drugs affecting the female reproductive system
  - Estrogen and progestins
  - Oral contraceptives
  - Drugs affecting uterine contraction
  - Drugs used to treat infertility
Drugs Affecting the Female Reproductive System

- **Estrogens and progestins**
  - Ovaries, ovarian follicles, and in pregnancy the placenta produce estrogen
  - Principal indication for estrogen is replacement therapy for postmenopausal women
  - Following menopause estrogen levels drop significantly predisposing women to osteoporosis and CAD
  - Hormonal replacement therapy with estrogen has shown to reverse these risk factors
  - Progestin
    - Counteracts the untoward effects of estrogen on the endometrium
    - Used to treat amenorrhea, endometriosis, and dysfunctional uterine bleeding
Drugs Affecting the Female Reproductive System

- Oral contraceptives
  - Effective means of preventing pregnancy
  - Primary mechanism of action is the prevention of ovulation
  - Makes the endometrium less favorable for implantation and
  - Promotes development of a thick mucus plug that blocks access to sperm through the cervix
  - Pills are a combination of estrogen and progestin or progestin only
Drugs Affecting the Female Reproductive System

- Uterine stimulants and relaxants
  - Drugs used to increase uterine contraction are oxytocics
    - Induce labor and treat postpartum bleeding
    - Smooth muscle contraction
  - Drugs used to decrease uterine contraction are tocolytics
    - Smooth muscle relaxation
    - Stimulation of beta 2 receptors
    - Example: terbutaline
Drugs Affecting the Female Reproductive System

- **Infertility Agents**
  - Most infertility drugs are developed for women and promote maturation of ovarian follicles.
  - Clomiphene (Clomid), urofollitropin (Metrodin), and menotropins (Pergonal)
Drugs Affecting the Male Reproductive System

- Agents include those that treat testosterone deficiency and benign prostatic hyperplasia
- Benign prostatic hyperplasia is an enlarged prostate
  - Common and age-related problematic disease
  - Age 70, 75% of men will suffer symptoms
Drugs Affecting Sexual Behavior

- Most notable is Viagra
  - Approved in 1998 for therapy in patients with erectile dysfunction
  - Viagra acts by relaxing vascular smooth muscle which increases blood flow to the corpus cavernosum
  - vardenafil (Levitra), and tadalafil (Cialis)
- Side effects
  - Used in combination with nitrates can dangerously decrease preload
  - BP lowers
  - AMI potential
  - Nitrates contraindicated with recent Viagra use
Drugs Used to Treat Cancer
Drugs Used to Treat Cancer

- Known as antineoplastic agents
- Pathophysiology
  - Cancer involves modification of cellular DNA leading to an abnormal growth of tissues
  - Only a few cancers are treated with chemotherapy
- Chemotherapy
  - Many side effects
  - Drugs kill cancerous cells and normal cells
  - Most chemotherapy drugs are antimetabolites
Drugs Used to Treat Cancer

- Drugs used to treat cancer are called antineoplastic agents
  - Most antineoplastic agents have their greatest effect on cancer cells during mitosis
- Examples include:
  - Fluorouracil (Adrucil)
  - Mechlorethamine (Mustargen)
  - Vinblastine (Velban)
  - Vincristine (Oncovin)
Drugs Used to Treat Infectious Diseases and Inflammation
Drugs Used to Treat Infectious Diseases and Inflammation

- **Antibiotics**
  - An antibiotic agent may either kill the offending bacteria or decrease the bacteria’s growth so that the patient’s immune system can effectively fight the infection.
    - Macrolide, aminoglycoside, and tetracycline antibiotics inhibit protein synthesis.
    - The penicillin, cephalosporin classes, and vancomycin, are bactericidal and act by inhibiting cell wall synthesis.
Drugs Used to Treat Infectious Diseases and Inflammation

- **Antibiotics**
  - Agent that kills or decreases the growth of bacteria
  - Mechanism of action
    - Disrupt cell membrane
    - Inhibit protein synthesis
    - Antimetabolites

- **Antifungal and antiviral agents**
  - Inhibit growth
  - Antiviral agents
    - Zovirax, Retrovir (AZT), and Indinavir
Drugs Used to Treat Inflammation

- Nonsteroidal antiinflammatory drugs
  - Used as analgesics and antipyretics
  - Agents interrupt with the production of prostaglandins thereby interrupting the inflammatory process
  - Indicated for pain, fever, and inflammation
  - Examples
    - Ibuprofen
    - Ketorolac (Toradol), piroxicam (Feldene), and naproxen (Naprosyn)

- Uricosuric Drugs
  - Used to treat and prevent acute episodes of gout
  - Colchicine and allopurinol (Zyloprim)
Serums, Vaccines, and other Immunizing Agents

- Serums and vaccines augment the immune system
- Serum is a solution containing whole antibodies for a specific pathogen
- Vaccine is a solution containing a modified pathogen that does not actually cause disease, but still stimulates the development of antibodies specific to it
  - Best age for vaccination against disease is within the first two years of life
### Table 9-11: Recommended Childhood Immunization Schedule
#### United States, January-December 1999

Vaccines are listed under routinely recommended ages. Bars indicate range of recommended ages for immunizations. Any dose not given at the recommended age should be given as a "catch-up" immunization at any subsequent visit when indicated and feasible. Ovals indicate vaccines to be given if previously recommended doses were missed or given earlier than the recommended minimum age.

<table>
<thead>
<tr>
<th>Age Vaccine</th>
<th>Birth</th>
<th>1 mo</th>
<th>2 mos</th>
<th>4 mos</th>
<th>6 mos</th>
<th>12 mos</th>
<th>15 mos</th>
<th>18 mos</th>
<th>4-6 yrs</th>
<th>11-12 yrs</th>
<th>14-16 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B²</td>
<td>Hep B</td>
<td>Hep B</td>
<td>DTaP</td>
<td>DTaP</td>
<td>Hep B</td>
<td>DTaP</td>
<td>Hep B</td>
<td>DTaP</td>
<td>Hep B</td>
<td>DTaP</td>
<td>Td</td>
</tr>
<tr>
<td>Diphtheria, Tetanus, Pertussis³</td>
<td>Hib</td>
<td>Hib</td>
<td>Hib</td>
<td>Hib</td>
<td>Hib</td>
<td>Hib</td>
<td>Hin</td>
<td>Polio</td>
<td>Polio</td>
<td>MMR</td>
<td>MMR</td>
</tr>
<tr>
<td>H. influenzae type b⁴</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Rotavirus⁸</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measles, Mumps, Rubella⁷</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicella⁸</td>
<td></td>
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</tr>
</tbody>
</table>

Approved by the Advisory Committee on Immunization Practices (ACIP), the American Academy of Pediatrics (AAP), and the American Academy of Family Physicians (AAFP)
Drugs Used to Treat Infectious Diseases and Inflammation

- Immune Suppressing and Enhancing Agents
  - Suppressing the immune system is indicated to prevent the rejection of transplanted organs and grafted skin.
    - Azathioprine (Imuran)
  - Immunomodulating agents enhance the natural immune reaction in immunosuppressed patients.
    - Zidovudine (Retrovir), ritonavir (Norvir) and saquinavir (Invirase)
Drugs Used to Affect the Skin
Drugs Used to Affect the Skin

- Dermatologic drugs are used to treat skin irritations.
- They are common over-the-counter medications.
Drugs Used to Affect the Diet
Many disease processes affect the production, distribution, and utilization of essential dietary nutrients.
Drugs Used to Supplement the Diet

- Dietary supplements can help to maintain needed levels of essential nutrients and fluids
  - Vitamins
  - Minerals
  - Fluids and electrolytes
Drugs Used to Supplement the Diet

- **Vitamins**
  - **Fat Soluble**
    - Stored
  - **Water Soluble**
    - Must be routinely ingested

### Table 9-12: Vitamin Sources and Deficiencies

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Problems Resulting from Deficiency</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat Soluble</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>Night blindness, skin lesions</td>
<td>Butter, yellow fruit, green leafy vegetables, milk</td>
</tr>
<tr>
<td>D</td>
<td>Bone and muscle pain, weakness, softening of bones</td>
<td>Fish, fortified milk, exposure to sunlight</td>
</tr>
<tr>
<td>E</td>
<td>Hyporeflexia, ataxia, anemia</td>
<td>Nuts, green leafy vegetables, wheat</td>
</tr>
<tr>
<td>K</td>
<td>Increased bleeding</td>
<td>Liver, green leafy vegetables</td>
</tr>
<tr>
<td>Water Soluble</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B₁ (thiamin)</td>
<td>Peripheral neuritis, depression, anorexia, poor memory</td>
<td>Whole grain, beef, pork, peas, beans, nuts</td>
</tr>
<tr>
<td>B₂ (riboflavin)</td>
<td>Sore throat, stomatitis, painful or swollen tongue, anemia</td>
<td>Milk, eggs, cheese, green leafy vegetables</td>
</tr>
<tr>
<td>B₃ (niacin)</td>
<td>Skin eruptions, diarrhea, enteritis, headache, dizziness, insomnia</td>
<td>Meat, eggs, milk</td>
</tr>
<tr>
<td>B₆ (pyridoxine)</td>
<td>Skin lesions, seizures, peripheral neuritis</td>
<td>Liver, meats, eggs, vegetables</td>
</tr>
<tr>
<td>B₉ (folic acid)</td>
<td>Megaloblastic anemia</td>
<td>Liver, fresh green vegetables, yeast</td>
</tr>
<tr>
<td>B₁₂ (cyanocobalamin)</td>
<td>Irreversible nervous system damage, pernicious anemia</td>
<td>Fish, egg yolk, milk</td>
</tr>
<tr>
<td>C</td>
<td>Scurvy</td>
<td>Citrus fruits, tomatoes, strawberries</td>
</tr>
</tbody>
</table>
Drugs Used to Treat Poisoning and Overdoses
Drugs Used to Treat Poisoning and Overdoses

- Treatment greatly depends on the substance involved
- Therapy aimed at eliminating the substance
  - Emptying gastric contents
  - Increasing gastric motility in order to decrease the time available for absorption
  - Alkalinizing the urine
  - Filtering the substance for the blood with dialysis
- General mechanism for antidote action include
  - receptor site antagonism
  - blocking enzyme actions involved with metabolism
  - chemical binding
Summary

- Anatomy & Physiology Related to Pharmacology
- Drugs That Affect the Central Nervous System
- Drugs That Affect the Autonomic Nervous System
- Drugs That Affect the Cardiovascular System
- Drugs That Affect the Respiratory System
- Drugs That Affect the Gastrointestinal System
- Drugs That Affect the Eyes and Ears
- Drugs That Affect the Endocrine System
- Drugs That Affect the Reproductive System
- Drugs Used to Treat Cancer
- Drugs Used to Treat Poisonings
Thank you!