Chapter 13
Principles of Pharmacology and Emergency Medications

Lesson 13.1
Drug Information and Historical Trends
Learning Objectives

• Explain what a drug is.
• Identify the four types of drug names.

Learning Objectives

• Explain the meaning of drug terms that are necessary to interpret information in drug references safely.
• Outline drug standards and legislation and the enforcement agencies pertinent to the paramedic profession.

Historical Trends

• Pharmacology science may date back to 10,000 to 7,000 BC
  – Medicinal herbs thought to be grown by humans in Neolithic period
    • Unknown if they had healing properties
  – Medicines mentioned in the bible
    • Gums
    • Spices
    • Oils
    • Maybe narcotics
Historical Trends

• Plant-derived drugs used heavily throughout the Middle Ages
  – Digestives
  – Laxatives
  – Diuretics

• “Chemical medicine” concept born in 17th century
  – Some still used today
    • Opium (morphine)
  – 19th century, accurate drug dosage studies led to manufacturing plants to produce drugs
    • Knowledge of expected drug actions became more exact
Historical Trends

• 20th and 21st centuries, important drug discoveries
  – Insulin
  – Antibiotics
  – Fibrinolytics
  – Had major effects on common illnesses
    • Diabetes
    • Bacterial infections
    • Cardiovascular disease

Historical Trends

• Modern health care, pharmaceutics going through many changes
  – Consumer awareness
    • Responsibility for their health, wellness
  – Disease prevention
    • Actively seek to develop new drugs, treatments, cures to prevent diseases

Historical Trends

• Orphan drugs
  – Federal government provides incentives to research, develop less profitable drugs
  – Treat rare, chronic diseases
    • Hemophilia
    • Leprosy
    • Cushing’s syndrome
    • Tourette’s syndrome
Historical Trends

• Investigational drugs
  – Under study
  – Not yet approved for sale by FDA
  – Clinical trials

Drug Names

• Drug defined as “any substance taken by mouth, injected into muscle, blood vessel, body cavity, applied topically, to treat or prevent disease or condition”
• Drugs identified or derived from five major sources
  – Plants (alkaloids, glycosides, gums, oils)
  – Animals and human beings
  – Minerals, mineral products
  – Microorganisms
  – Chemical substances made in laboratory

Drug Names

• Identified by four name types
  – Chemical name
    • Exact description
    • Describes drug chemical composition, molecular structure
  – Generic name (nonproprietary name)
    • Often abbreviated form of chemical name
    • More commonly used than chemical name
    • Usually have same therapeutic efficacy as nongeneric drugs, generally less expensive
    • Official name approved by FDA
Drug Names

- Identified by four name types
  - Trade name (brand or proprietary name)
    - Trademark name designated by drug company
    - Proper nouns, first letter capitalized
    - This text shows name in parentheses after generic name
    - Usually suggested by first drug manufacturer
  - Official name
    - Followed by USP (United States Pharmacopeia), NF (National Formulary), denotes drug listing in one official publication
    - Most cases, name is the same as generic name

Example
- Chemical name: (−)-17-allyl-4α,5α-epoxy-3,14-dihydroxymorphinan-6-one-hydrochloride
- Generic name: naloxone hydrochloride
- Trade name: Narcan
- Official name: naloxone hydrochloride USP

Drug Information Sources

- Publications offer information on various drugs, preparation, recommended administration
  - American Medical Association Drug Evaluation
  - American Hospital Formulary Service Drug Information
  - Medication package inserts
  - Physician’s Desk Reference
  - Nursing Drug Reference
  - Elsevier’s Gold Standard
Drug Information Sources

- Crucial, particularly regarding drugs administered in prehospital setting
- Reliable Internet sources, computer application software (Epocrates®) for handheld devices (PDAs, Smartphones), good information sources

Drug Standards and Legislation

- Before 1906, little control exercised over medication use
  - Drugs often sold, distributed by traveling medicine men, drugstores, mail order companies, legitimate and self-proclaimed physicians
  - Drug ingredients not required to be listed
    - Many contained opium, heroin, alcohol, potentially harmful to user

- 1906, Congress passed Pure Food and Drug Act
  - Protected public from mislabeled, adulterated drugs
  - Prohibited use of false, misleading claims for drugs
  - Restricted sale of drugs with potential for abuse
  - Designated United States Pharmacopeia, National Formulary as official standards
  - Empowered federal government to enforce standards
  - 1980, United States Pharmacopeial Convention purchased National Formulary
  - Made it the only official book of drug standards in United States
Drug Standards and Legislation

- Drugs made by different manufacturers may vary significantly in strength, activity
- Strength, purity, or effectiveness measured through chemical laboratory analysis; assay

Bioassay (biological assay)
- Used to measure bioequivalence or relative therapeutic effectiveness of two chemically equivalent drugs

Drug Regulatory Agencies

- July 1973, Drug Enforcement Agency became sole legal drug enforcement body in United States
- Other regulatory bodies or services
  - FDA
    - Responsible for enforcing federal Food, Drug, Cosmetic Act, 1937
    - May seize offending goods
    - Criminally prosecute individuals involved
News stories often feature “miracle” drugs that are used in other countries but that are not yet available in the United States because they lack FDA approval. Why wouldn’t the FDA automatically approve drugs already known to be helpful in the international market?

Drug Regulatory Agencies

- Other regulatory bodies or services
  - Public Health Service
    - Agency of U.S. Department of Health and Human Services
    - Regulates biological products
  - Federal Trade Commission
    - Agency directly responsible to president
    - Suppresses false, misleading advertising

- Canadian Drug Control
  - Canada’s Health Protection Branch of Department of National Health and Welfare
  - Responsible for administering and enforcing
    - Food and Drugs Act
    - Proprietary or Patent Medicine Act
    - Narcotics Control Act
Drug Regulatory Agencies

- International Drug Control
  - Began in 1912 when first "Opium Conference" was held in The Hague
  - Various international treaties adopted, obligating governments to control narcotic substances
  - 1961, treaties consolidated into one document called the Single Convention on Narcotic Drugs (effective 1964)
  - International Narcotics Control Board later established to enforce law

Your patient is acutely ill. She reports taking only an herbal medicine, which is not found in standard drug reference materials. Where can you or the medical staff find information about these alternative therapies?

Drug Terminology

- Antagonism
  - Opposition of effects between two or more medications that occurs when combined (conjoint) effect of two drugs is less than sum of drugs acting separately
- Contraindications
  - Medical or physiological factors that make it harmful to administer medication that would otherwise have therapeutic value
Drug Terminology

• Cumulative action
  – Tendency for repeated doses of a drug to accumulate in blood and organs, causing increased and sometimes toxic effects
  – Occurs when several doses are administered or when absorption occurs more quickly than removal by excretion or metabolism

• Depressant
  – Substance that decreases body function or activity

Drug Terminology

• Drug allergy
  – Systemic reaction to drug resulting from previous sensitizing exposure and development of immunological mechanism

• Drug dependence
  – State in which withdrawal of drug produces intense physical or emotional disturbance; previously known as habituation

Drug Terminology

• Drug interaction
  – Beneficial or detrimental modification of effects of one drug by prior or concurrent administration of another drug that increases or decreases the pharmacological or physiological action of one or both drugs
Drug Terminology

• Idiosyncrasy
  – Abnormal or peculiar responses to drug
  (accounting for 25% to 30% of all drug reactions)
  thought to result from genetic enzymatic
  deficiencies or other unique physiological
  variables and leading to abnormal mechanisms of
  drug metabolism or altered physiological effects
  of drug

Drug Terminology

• Potentiation
  – Enhancement of effect caused by concurrent
    administration of two drugs in which one drug increases
    the effect of the other drug

• Side effect
  – Undesirable and often unavoidable effect of using
    therapeutic doses of a drug; action or effect other than
    those for which the drug was originally given

• Stimulant
  – Drug that enhances or increases body function or activity

Drug Terminology

• Summation
  – Combined effect of two drugs such that the total effect
    equals the sum of the individual effects of each agent
    \((1 + 1 = 2)\)

• Synergism
  – Combined action of two drugs such that the total effect
    exceeds the sum of the individual effects of each agent
    \((1 + 1 = 3 \text{ or more})\)

• Therapeutic action
  – Desired, intended action of a drug
Drug Terminology

• Tolerance
  – Decreased physiological response to repeated administration of a drug or chemically related substance, possibly necessitating an increase in dosage to maintain therapeutic effect (tachyphylaxis)
• Untoward effect
  – Side effect that proves harmful to patient

Mechanisms of Drug Action

• Drugs act many ways
  – Desirable, therapeutic effect
  – Undesirable or harmful, side effect
• May interact with other drugs
  – May produce uncommon, frequently unpredictable effects

Mechanisms of Drug Action

• Exert several effects rather than a single one
• Do not confer any new functions on tissue or organ; only modify existing functions
Mechanisms of Drug Action

- Actions achieved by biochemical interaction between drug and body tissue components, usually receptors
  - Agonist
    - Interacts with receptor to stimulate response
  - Antagonist
    - Attaches to receptor but does not stimulate response

Mechanisms of Drug Action

- To produce desired effect, drug must first enter body
  - Then must reach appropriate concentrations at action site
  - Process influenced by three drug activity phases
    - Pharmaceutical phase
    - Pharmacokinetic phase
    - Pharmacodynamic phase

Pharmaceutical Phase

- Pharmaceutics
  - Science of dispensing drugs
  - Study of ways in which forms of drugs (solid, liquid) influence pharmacokinetic, pharmacodynamic activities
  - All drugs must be in solution to cross cell membranes to achieve absorption
Pharmaceutical Phase

- Dissolution
  - Rate at which solid drug goes into solution after ingestion
    - The faster the dissolution rate, the more quickly the drug is absorbed

Pharmacokinetic Phase

- Study of how the body handles a drug over period of time
- Includes processes of
  - Absorption
  - Distribution
  - Biotransformation
  - Excretion
    - These factors affect patient’s drug therapy response

Pharmacokinetic Phase

- Drug absorption
  - Movement of drug molecules from entry site to general circulation
  - Degree to which drugs attain pharmacological activity depends on rate, extent they are absorbed
    - Depend on drug’s ability to cross the cell membrane
    - Through passive diffusion and active transport
    - Most enter by passive diffusion
    - Some require carrier-mediated mechanism to assist across membrane
Pharmacokinetic Phase

• Drug absorption
  – Begins at administration site
  – Nature of absorbing surface (cell membrane) drug must traverse
    • If drug must pass through single layer of cells (intestinal epithelium), transport is faster than passing through several layers of cells (skin)
    • The greater the surface area of the absorbing site, the greater the absorption, drug effect is quicker
    • Small intestine has large absorption area
    • Stomach has small absorption area

Pharmacokinetic Phase

• Blood flow to administration site
  – Rich blood supply enhances absorption
  – Poor blood supply delays absorption
    • May not respond to intramuscular drug administration
    • IV administration immediately places drug in circulatory system where it is absorbed completely, delivered to target tissue

Pharmacokinetic Phase

• Drug solubility
  – More soluble, more rapidly absorbed
  – Drugs prepared in oily solutions absorbed more slowly than drugs dissolved in water or isotonic sodium chloride
Pharmacokinetic Phase

- Drug environment pH
  - Nonionized drug
    - Lipid (fat) soluble
    - Readily diffuses across cell membrane
    - Uncharged
  - Ionized drug
    - Lipid insoluble
    - Generally does not cross cell membrane
    - Charged

Why would a nonionized drug readily diffuse across the cell membrane?

• Most drugs do not ionize fully following administration
  • Reach equilibrium between ionized, nonionized forms allowing nonionized form to be absorbed
Pharmacokinetic Phase

- Ionization depends on whether drug is acid or base
  - Acidic drug (aspirin)
    - Relatively nonionized
    - Does not dissociate well in acidic environment
    - Easily absorbed in stomach
  - Basic drug
    - Tends to ionize, not easily absorbed through gastric membrane
    - Reverse occurs when drug is in alkaline medium

Pharmacokinetic Phase

- Drug concentration
  - Administered in high concentrations, absorbed more rapidly than low concentrations
  - Loading dose (large dose)
    - Temporarily exceeds capacity for drug excretion
    - Rapidly establishes therapeutic drug level at receptor site
  - Maintenance dose (smaller dose)
    - Administered to replace drug amount excreted
    - Based more on excretion, less on distribution volume

Pharmacokinetic Phase

- Drug dosage form
  - Drug absorption manipulated by pharmaceutical processing
Lesson 13.2  
Drug Administration Routes and Distribution

Learning Objectives

• Distinguish between characteristics of routes of drug administration.
• Discuss factors that influence drug absorption, distribution, and elimination.

Drug Administration Routes

• Mode affects rate onset of action occurs, therapeutic response
• Administration routes categorized; greatly influences drug absorption
Enteral Route

- Orally, rectally, through gastric tube
- Safest, most convenient, most economical
- Least reliable

Enteral Route

- Slowest of common routes
  - Frequent changes in GI environment
- Allows four absorption types
  - Oral
  - Gastric
  - Absorption from small intestine
  - Rectal

Enteral Route

- Oral absorption
  - Oral cavity has rich blood supply
  - Little absorption normally occurs in mouth
  - Absorbed in upper GI tract, enters systemic circulation
    - Initially bypasses gastrointestinal fluids, liver
**Enteral Route**

- Drugs absorbed in stomach, intestines absorbed into liver's portal vein system
  - Subject to first-pass metabolism in liver (concentration of drug being reduced before it reaches systemic circulation)
- Sublingual drugs placed under tongue dissolve in salivary secretions
  - Effects usually clear within few minutes
- Buccal drugs, placed between teeth and cheek's mucous membrane, rapid absorption

**Enteral Route**

- Gastric absorption
  - Not considered important drug absorption site
  - Time medication remains in stomach varies, depending on environment pH and gastric motility
    - Many administered on empty stomach with sufficient water, ensures rapid passage into small intestine
    - Others cause gastric irritation and are usually given with food

**Enteral Route**

- Absorption from small intestine
  - Rich blood supply, larger absorption area
  - Most occurs in upper part
  - Intestinal fluid pH is alkaline, increases rate of basic drugs
  - Prolonged exposure allows more absorption time
  - Increased intestinal motility (diarrhea) diminishes absorption
Enteral Route

- Rectal absorption
  - Surface area not large
  - Vascular, capable of drug absorption
  - Subject to erratic absorption
    - Rectal contents
    - Local drug irritation
    - Drug retention uncertainty
  - 50% estimated to bypass liver after absorption
    - Makes first-pass metabolism by liver less than oral dose

The drugs given rectally in emergencies usually are anticonvulsants. Why do you think this route would be chosen over the oral or intravenous route?

Parenteral Route

- Administered by injection
- Subcutaneous route
  - Given beneath skin into connective tissue or fat, immediately beneath dermis
  - Used for small volumes (<0.5 mL) that do not irritate tissue
  - Absorption rate slow, can provide sustained effect
Parenteral Route

- Intramuscular route
  - Given into skeletal muscle
  - Absorption more rapid
  - Greater tissue blood flow

- Intravenous route
  - Directly into bloodstream, bypassing absorption process
  - Produces almost immediate pharmacological effect
  - Most drugs administered slowly, helps prevent adverse reactions

- Intradermal route
  - Injection below epidermis
  - Primarily for allergy testing and to administer local anesthetics
  - Drugs not absorbed into general circulation

- Intraosseous route
  - Injection directly into bone marrow cavity through established intraosseous infusion system
  - Circulates via medullary cavity of bone
  - Through numerous long bone venous channels, drugs rapidly enter central circulation
  - Time to disperse equals IV route
Parenteral Route

- Intraosseous route
  - Known effective emergency medications for this route
    - Amiodarone (Cordarone)
    - Epinephrine (Adrenaline)
    - Atropine
    - Sodium bicarbonate
    - Dopamine (Intropin),
    - Dobutamine (Dobutrex)
    - Lidocaine (Xylocaine)

Parenteral Route

- Endotracheal route
  - Allows drug delivery into alveoli and systemic absorption via lung capillaries
  - Reserved for situations in which IV or intraosseous line cannot be established

Parenteral Route

- Endotracheal route
  - Medications
    - Naloxone (Narcan)
    - Atropine
    - Vasopressin (Pitressin)
    - Epinephrine (Adrenaline)
    - Lidocaine (Xylocaine)
  - 2 to 2½ times recommended IV dose (diluted 10 mL normal saline) recommended
Can you recall any other patient situations where administration of vasopressin might be indicated?

**Parenteral Route**

- Pulmonary route
  - Administered by inhalation in gas form or fine mist (aerosol)
  - Bronchodilators
  - Can absorb many other medications if necessary
  - Because of large surface area, rich alveoli capillary network, rapid drug absorption
  - Bronchodilators are steroids given by inhalation devices
    - Nebulizers propel drug into alveolar sacs, produce mainly local effects
    - Occasionally produce unwanted systemic effects (elevated heart rate, tachycardia)

- Topical route—skin
  - Drugs absorbed rapidly
  - Only lipid-soluble compounds
    - Skin acts as barrier to most water-soluble compounds
    - Use intact skin surfaces for administration sites to prevent adverse systemic effects
Parenteral Route

- Topical route—nasal
  - Nasal mucosa is highly vascular
  - Rapid absorption into bloodstream and cerebral spinal fluid
  - Effective in management of
    - Seizures
    - Pain
    - Hypoglycemia
    - Opiate overdose
    - Other medical conditions

Parenteral Route

- Topical route—nasal
  - Greatly reduces risk of needle-stick injury
  - Some vaccines administered by intranasal route in select patient groups
    - Live attenuated influenza vaccine (LAIV)
    - Influenza virus vaccine live (Intranasal FluMist)

Drug Distribution

- Transport through bloodstream
  - To various tissues, ultimately to site of action
  - After drug enters circulatory system, distributed rapidly throughout body
  - Distribution rate depends on capillary permeability to drug molecules
Drug Distribution

• Lipid-soluble drugs
  – Readily cross capillary membranes
  – Enter most tissue
  – Fluid compartments
  – Require more time to arrive at action point
  – Cardiac output, regional blood flow affect distribution rate, extent into tissues
  – Generally distributed first to organs with rich blood supply
    • Heart, liver, kidneys, brain
  – Drug next enters tissue, lesser blood supply, muscle, fat

• Drug reservoirs
  – Formed by drugs binding to specific tissues
  – Serum levels decline, tissue-bound drug released from storage site into bloodstream
  – Released drug maintains serum drug levels, may permit sustained drug release over time
    • Allows continued pharmacological effect at receptor site

• Drug reservoirs
  – General processes that create reservoirs
    • Plasma protein binding
    • Tissue binding
  – As drugs enter circulatory system, may attach to plasma proteins (mainly albumin), forming drug–protein complex
    • Binding extent affects intensity, duration of effect
Drug Distribution

- Drug reservoirs
  - Albumin molecule too large to diffuse through blood vessel membrane
    - Traps bound drug in bloodstream
    - Drug bound to plasma protein is pharmacologically inactive
    - Protein becomes circulating drug reservoir
  - Free drug (non-protein-bound drug) exists in proportion to protein-bound fraction and is only drug portion that is biologically active
    - As it is eliminated from body, drug–protein complex dissociates and more drug is released
  - Free drug + protein → drug–protein complex

Drug Distribution

- Albumin, other plasma proteins provide number of binding sites
  - Two drugs can compete for same site, displace each other
  - Certain drug combinations may be given at the same time
  - Drug competition can have serious consequences
    - Severe hemorrhage

Drug Distribution

- Other factors influence a drug’s binding ability
  - Plasma protein concentration (especially albumin)
  - Number of binding sites on protein
  - Affinity (attraction) of drug for protein
  - Patient’s acid-base balance
Drug Distribution

• Other factors influence a drug’s binding ability
  – Various disease states alter body’s ability to handle many medications
    • Result from decreased serum albumin levels, decreased hepatic metabolism
    • May result in more free drug available for distribution to tissue sites

Drug Distribution

• “Drug pooling” occurs in fat tissue, bone
  – Lipid-soluble drugs have high affinity for adipose tissue, where drugs are stored
  – Fat tissue has low blood flow, serves as stable drug reservoir
  – Some lipid-soluble drugs can remain in body fat three hours after administration
  – Other drugs have unusual affinity for bone
    • Drugs accumulate in bone after being absorbed onto bone crystal surface

Tetracycline typically is not given to pregnant women because of the harmful effects it has on the development of the baby’s teeth. Why would it affect the teeth?
Drug Distribution

• Drug distribution barriers
  – Blood-brain barrier, placental barrier are protective membranes
    • Prevent passage of certain drugs into respective body sites

• Blood-brain barrier has single layer capillary endothelial cells
  • Line of blood vessels entering CNS
  • Tightly joined at common borders by continuous intercellular junctions
  • Special arrangement permits only lipid-soluble drugs to be distributed into brain, cerebrospinal fluid (general anesthetics, barbiturates)
  • Drugs poorly soluble in fat (many antibiotics) have trouble passing barrier, cannot enter brain

• Placental barrier, made up of membrane layers
  • Separate blood vessels of mother, fetus
  • Not permeable to many lipid-insoluble drugs
  • Placenta offers some protection of fetus
  • Placenta allows passage of certain non-lipid-soluble drugs
    • Steroids
    • Narcotics
    • Anesthetics
    • Some antibiotics
Biotransformation (Metabolism)

- Drugs are chemically converted to metabolites (smaller components)
  - Purpose: “detoxify” drug, render it less active
  - Liver is primary drug metabolism site
  - Other tissues can be involved
    - Plasma
    - Kidneys
    - Lungs
    - Intestinal mucosa

Biotransformation (Metabolism)

- Orally administered drugs absorbed through gastrointestinal tract normally travel to liver before entering general circulation
  - Large drug amount may be metabolized before reaching systemic circulation (first-pass metabolism)
    - Reduces drug amount available for distribution
  - Medications affected by initial biotransformation in liver
    - May be given in higher dosages
    - Administered parenterally to bypass liver

Biotransformation (Metabolism)

- Individuals metabolize drugs at various rates
  - Liver, renal, cardiovascular disease
    - Prolonged drug metabolism
  - Infants, older adults
    - Depressed biotransformation
  - If drug metabolism delayed, drug accumulation and cumulative drug effects may occur
  - May need to consider dosage reductions
Excretion

- Elimination of toxic or inactive metabolites
- Kidney, primary organ
  - May also involve
    - Intestine
    - Lungs
    - Mammary, sweat, and salivary glands

Excretion by kidneys
- Drug can be excreted in urine unchanged
- Excreted as chemical metabolite of its previous form
- Renal excretion has three mechanisms
  - Passive glomerular filtration
  - Active tubular secretion
  - Partial reabsorption
Excretion by Kidneys

- Passive glomerular filtration
  - Simple filtration process
  - Measured as glomerular filtration rate (GFR)
    - Total quantity of glomerular filtrate formed each minute in all nephrons of both kidneys
    - Expressed in milliliters
    - Drug availability depends on its free concentration in plasma
    - Unbound drugs and water-soluble metabolites, filtered by glomeruli
    - Drugs highly bound to protein do not pass glomeruli

Excretion by Kidneys

- Passive glomerular filtration
  - After filtration, lipid-soluble compounds reabsorbed by renal tubules
    - Reenter systemic circulation
    - Water-soluble compounds not reabsorbed, are eliminated from body
    - As free drug is filtered from blood, bound drug is released from binding sites into plasma
    - Drug excretion rate and biological half-life depend on how quickly bound drug is released
You pick up your patient at the renal dialysis center. How will you know which medicines you can safely administer?

Excretion by Kidneys

• Active tubular secretion
  – Occurs in renal tubules
  – Free drug transported or secreted from blood across proximal tubule, deposited in urine
  – Drugs can compete with other drugs for same active transport process

Excretion by Kidneys

• Partial reabsorption
  – Passive diffusion
    • Influenced by pH of tubular urine
  – Weak acids
    • Excreted more readily in alkaline urine
    • Secreted more slowly in acidic urine
    • Ionized in alkaline urine
    • Nonionized in acidic urine
Excretion by Kidneys

- Partial reabsorption
  - Weak bases
    - Increased urinary pH decreases reabsorption
    - Increases clearance of weak acids
    - Decreased urinary pH increases clearance of weak bases (e.g., amphetamine, tricyclic antidepressants)

Excretion by Kidneys

- Hemodialysis
  - Substances completely excreted by normal kidney removed by artificial process
  - Resembles glomerular filtration
  - Used to remove wide variety of substances
    - Not effective for drugs that are highly tissue or protein bound
    - Limited benefit for removal of rapidly acting toxins

Excretion by Intestine

- Drugs eliminated by biliary excretion
  - After liver metabolism, metabolites are carried in bile, passed into duodenum
    - Metabolites then eliminated with feces
  - Some drugs reabsorbed by bloodstream
    - Returned to liver
    - Later excreted by kidneys
Excretion by Lungs

- Some drugs eliminated
  - General anesthetics
  - Volatile alcohols
  - Inhaled bronchodilators
- Certain factors alter drug elimination
  - Respiration rate, depth
  - Cardiac output

Excretion by Lungs

- Deep breathing and increased cardiac output promote excretion
  - Respiratory compromise and decreased cardiac output may occur during illness or injury
  - Can prolong time required to eliminate drugs

Excretion by Sweat and Salivary Glands

- Sweat is unimportant means of drug excretion
  - Method can cause various skin reactions and discolor sweat
- Drugs excreted in saliva usually are swallowed
  - Eliminated in same manner as other orally administered medicines
Excretion by Sweat and Salivary Glands

• Certain substances given by IV can be excreted into saliva
  – May cause person to complain about “taste of drug,” even though given intravenously
    • Adenosine (Adenocard)
    • Calcium chloride

Excretion by Mammary Glands

• Many drugs/their metabolites excreted through breast milk
• Nursing mothers advised not to take medicine except under doctor’s supervision
• Mothers usually advised to take prescribed medicines right after breast-feeding
  – Diminishes any risk to infant

Factors that Influence Drug Actions

• Age
  – Pediatric, geriatric, highly sensitive
  – Reduce efficiency of excretory, metabolic mechanism
Factors that Influence Drug Actions

• Body mass
  – Larger the patient, the lower the concentration for any given drug dose
  – Average adult drug dose
    • Calculated on drug quantity needed to produce particular effect when administered to 50% of population
    • Includes only people between 18 and 65 years who weigh about 68 kg (150 lbs)
  – Child drug doses always based on body mass

Factors that Influence Drug Actions

• Gender
  – Size differences
  – Fat proportion, body water cause variations in drug distribution

Factors that Influence Drug Actions

• Environment
  – Drugs that affect mood, behavior are susceptible to personality of the user
    • Example: sensory deprivation and sensory overload may affect person’s response to drug
  – Physical environment increases affect
    • Temperature extremes
    • Altitude changes
Factors that Influence Drug Actions

• Time of administration
  – Presence/absence of food in gastrointestinal tract
  – Biological rhythms
    • Sleep-wake cycles
    • Circadian rhythms

Factors that Influence Drug Actions

• Pathological state
  – Illness or injury
  – Severity of symptoms
  – Underlying disease processes
    • Circulatory dysfunction
    • Hepatic dysfunction
    • Renal dysfunction

What effects would nausea, vomiting, anorexia, fever, dehydration, and diarrhea have on drug levels in the body?
Factors that Influence Drug Actions

- Genetic factors
  - Genetics can alter response of some persons to a number of drugs
    - Inherited diseases
    - Enzyme deficiencies
    - Altered receptor site sensitivities
  - Results of genetic abnormalities may manifest as idiosyncrasies (peculiar drug responses) or may be mistaken for drug allergies

Factors that Influence Drug Actions

- Psychological factors
  - Patient’s belief in drug effects may strongly influence, potentiate drug effects
    - Placebo (sugar pill) can have same result as pharmacological agent if patient thinks it will have desired effect
    - Patient hostility, mistrust can lessen perceived drug effects
    - Paramedic can enhance drug action by telling patient that drug is going to work, when it will take effect

Pharmacodynamic Phase

- Study of how drug acts on living organism
  - Pharmacological response observed relative to concentration of drug at active site in organism
  - Drugs do not confer any new function on tissue or organ of body; rather, modify existing functions
  - Most drug actions thought to result from chemical interaction between drug and various receptors throughout the body
  - Most common form of drug action is drug–receptor interaction
Lesson 13.3
Drug Interaction

Learning Objectives

• Describe how drugs react with receptors to produce their desired effects.
• List variables that can influence drug interactions.
• Distinguish among drug forms.

Learning Objectives

• Describe the paramedic’s responsibilities to understand drug profiles.
• Identify special considerations for administering pharmacological agents to pregnant patients, pediatric patients, and older patients.
Drug–Receptor Interaction

• Most drugs bind to drug receptors to produce desired effect
  – Specific portion of drug molecule (active site) selectively combines/interacts with some molecular structure (reactive site on cell surface or within cell)
    • Produces biological effect
    • Reactive cellular sites known as receptors

• Relationship of drug to its receptor may be thought of as key fitting into lock
  • Drug represents key
  • Receptor represents lock
  • Drug molecule with the best fit to receptor produces best response
  • After absorption, gains access to receptor after it leaves bloodstream, distributed to tissues that contain receptor sites
Drug–Receptor Interaction

- Agonist drugs
  - Bind to receptor
  - Cause expected physiological response
- Antagonist drugs
  - Bind to receptor
  - Prevent physiological response
  - Prevent other drugs from binding

Drug-Response Assessment

- Can be assessed by observing drug effect on specific physical findings
  - Monitoring BP after antihypertensive medication administration
  - Pain relief after analgesic administration

Drug-Response Assessment

- Each drug has own characteristic rate of
  - Absorption
  - Distribution
  - Biotransformation
  - Excretion
Drug-Response Assessment

- Tissue concentrations are proportional to drug levels in blood determined by laboratory analysis
- Therapeutic drug levels in blood/serum indicate ranges in tissue drug concentration that produce desired therapeutic response

Drug-Response Assessment

- Plasma-level profiles
  - Demonstrate relationship between concentration of drug in plasma and effectiveness of drug over time
  - Profiles depend on rate of absorption, distribution, biotransformation, excretion after drug administration
Drug-Response Assessment

- Therapeutic range for most drugs
  - Concentration with highest probability of response
  - Least risk of toxicity
  - Dosage factors
    - Age
    - Body mass
    - Gender
    - Pathological state
    - Genetic factors
    - Psychological factors

Drug-Response Assessment

- Therapeutic range for most drugs
  - Therapeutic doses have high probability of producing desired effect, low probability of toxicity
    - Some people fail to respond to doses in therapeutic range
    - Others may develop drug toxicity

Biological Half-Life

- Determined by rate of biotransformation, excretion of drug
- Time it takes to metabolize or eliminate 50% of drug in body
  - 100-mg injection of drug given, half-life = 4 hours
  - Drug considered to be eliminated from body after five half-lives have passed
### Biological Half-Life

- Crucial when determining administration frequency
  - Drug with short half-life (2 to 3 hours) administered more often than drug with long half-life (12 hours)
  - Lengthened in persons with liver dysfunction/renal disorders
    - Require drug dosage reduction or longer intervals between doses

### Adenosine

Adenosine, an intravenous antidysrhythmic medicine, has a half-life of only 1 to 3 seconds. How will this brief half-life influence the speed and frequency of administration of this drug?

### Therapeutic Index (TI)

- Measurement of relative safety of drug
- Represents ratio between two factors
  - Lethal dose 50 (LD50)
    - Dose is lethal in 50% of laboratory animals tested
  - Effective dose 50 (ED50)
    - Dose that produces therapeutic effect in 50% of similar population
    - Calculated as: $\text{TI} = \frac{\text{LD}_{50}}{\text{ED}_{50}}$
**Therapeutic Index (TI)**

- Large TI indicates drug is fairly safe
- Narrow TI means distance between where drug is effective and where it is lethal is small
  - Not much room for error
  - Easy to get to toxic range
  - The closer ratio is to 1, narrower TI, greater danger in administering drug
  - Drugs such as digoxin (Lanoxin), difference between effective dose and lethal dose is small
  - Drugs such as naloxone (Narcan) have wide margin between effective dose and lethal dose

**Drug Interactions**

- Variables can influence drug interactions
  - Intestinal absorption
  - Competition for plasma–protein binding
  - Biotransformation
  - Action at receptor site
  - Renal excretion
  - Electrolyte balance alteration
Drug Interactions

• Not all drug interactions are dangerous, may be beneficial
• Clinically significant and can be dangerous
  – Be aware of common drug–drug interactions
  – Seek medical direction before giving drugs concurrently

Drug Interactions

• Drugs associated with clinically significant drug–drug interactions
  – Blood thinners
  – Tricyclic antidepressants (TCAs)
  – Monoamine oxidase (MAO) inhibitors
  – Amphetamines
  – Digitalis glycosides
  – Diuretics
  – Antihypertensives

Drug Interactions

• Factors that can influence drug interactions
  – Drug-induced malabsorption of food, nutrients
  – Food-induced malabsorption of drugs
  – Enzyme alterations that affect metabolism of food/drugs
  – Alcohol consumption
  – Cigarette smoking
  – Food-initiated alteration of drug excretion
Drug Interactions

• Some drugs are incompatible with each other
  – Calcium chloride will precipitate (or crystallize) when mixed with sodium bicarbonate

Drug Forms, Preparations, Storage

• Many forms
  – Have specific indications, advantages, disadvantages
  – Rules guide securing, storage, distribution, accounting
    • Follow agency protocol, local, state regulations
    • Temperature, light, moisture, shelf life can affect drug potency, effectiveness

Drug Profiles

• Be familiar with drug profiles
  – Not all aspects can be committed to memory
  – Make regular use of pharmacology references (handbooks, pocket guides), seek medical direction as needed
  – Paramedics are legally, morally, ethically responsible for safe, effective drug administration
Drug Profiles

- Professional practice of patient management
  - Use correct precautions, techniques when administering medications
  - Observe, document drug effects
  - Be current in knowledge base regarding changes in pharmacology trends
  - Establish, maintain professional relationships with other health care team members
  - Understand pharmacodynamics of drugs administered
  - Evaluate patients to identify drug indications, contraindications

Drug Profiles

- Professional practice of patient management
  - Take drug history from patients
  - Prescribed medications (name, strength, daily dosage)
  - Over-the-counter medications
  - Vitamins
  - Alternative drug therapies
  - Drug allergies, adverse drug reactions
  - Strictly adhere to standing orders/protocols for drug administration or consult with online medical direction

Components of Drug Profile

- Drug names
  - Usually generic and trade names
  - May include chemical names
- Classification
  - Group to which drug belongs
Components of Drug Profile

- Mechanism of action
  - Drug pharmacodynamic properties
- Indications
  - Conditions for which drug is administered as approved by FDA

Components of Drug Profile

- Pharmacokinetics
  - How body handles drug over time
    - Absorption
    - Distribution
    - Biotransformation
    - Excretion
    - Onset
    - Duration

Components of Drug Profile

- Side/adverse effects
  - Untoward or undesired effects
- Dosages
  - Amount of drug to be administered
- Administration routes
  - How drug is given
Components of Drug Profile

- Contraindications
  - Conditions in which it may be harmful to administer drug
- Special considerations
  - How drug may affect pediatric, geriatric, pregnant patients, other special groups
- Storage requirements
  - How drug should be stored

Pregnant Patients

- Consider benefits, possible risks to fetus
- Drugs may cross placental barrier, harm fetus
- May be communicated to newborn during breast feeding

Pregnant Patients

- FDA drug scale
  - Category A
    - No risk in first trimester
    - Fetal harm remote
  - Category B
    - No risk in animal studies, no controlled studies in humans
    - Adverse effect in controlled studies in first trimester, no risk in later trimesters
Pregnant Patients

- FDA drug scale
  - Category C
    - Adverse effects in animals, no controlled studies in women
    - Studies in women, animals not available
    - Drugs given only if potential benefit outweighs fetal risk
  - Category D
    - Human fetal risk, but benefits acceptable despite risk
  - Category X
    - Studies in animals, humans cause fetal abnormalities
    - Risk clearly outweighs benefits
    - Contraindicated in pregnant women

Pediatric Patients

- Age
  - Effects unpredictable among infants
  - Variation in development, maturation of different organ systems

Pediatric Patients

- Absorption
  - Follows same principles as in adults
  - Influenced by blood flow at site of intramuscular or subcutaneous administration
    - Blood flow determined by cardiovascular function
    - Physiological conditions might reduce blood flow to muscle and subcutaneous tissue
    - Shock
    - Vasoconstriction
    - Heart failure
Pediatric Patients

• Absorption
  – Smaller muscle mass causes diminished peripheral perfusion
  – For orally administered drugs, underlying gastrointestinal function may influence drug absorption
  – Liquids, suspensions disperse quickly in gastrointestinal fluids
    • Increases in peristalsis, lowered GI enzymes decrease overall absorption of orally/rectally administered medications

• Distribution
  – Most are distributed in body water
    • Increases body water and extracellular volume increases volume of distribution
    • Infants have proportionately higher volumes of total body water
    • Infants also have higher ratio of extracellular to intracellular fluid (40% compared with 30%)
    • Higher dosages of water-soluble drugs may be needed for effective blood levels in the newborn

• Distribution
  – Protein binding of drugs is reduced in the infant; therefore, the concentration of free drug in plasma is increased
    • Can result in greater drug effect or toxicity
  – Regarding CNS effects, the blood-brain barrier in infants is much less effective than in adults
    • Allows drugs greater access to area
Pediatric Patients

- Biotransformation
  - Metabolism enzyme systems mature unevenly
    - Infant has decreased ability to metabolize drugs
    - Can develop toxicity from drugs metabolized by liver
    - Many drugs have slower renal clearance times, longer half-lives in body
  - Must adjust dosages based on age, weight

Pediatric Patients

- Elimination
  - Glomerular filtration rate is much lower in newborns
    - Drugs eliminated through renal function cleared slowly in first few weeks of life
    - Renal excretory mechanisms progress to maturity after 1 year of age
    - Before that, excretion of some substances through renal system may be delayed because of immaturity
    - Result in higher serum levels, longer duration of action

Older Adult Patients

- Key changes in drug responses occur
- Factors that affect pharmacokinetics
  - Multiple diseases, multiple drug use
  - Nutritional problems decrease ability to metabolize drugs
  - Decreased drug dosing compliance
Older Adult Patients

• Age
  - Have less physiological reserves
    • Physiological function decreases after age 45
    • Decreased renal function
    • Impact on medication administration, drug clearance

Older Adult Patients

• Absorption
  - Little evidence exists of major changes in drug absorption with age
  - Conditions associated with age may alter rate at which some drugs are absorbed
    • Altered nutritional habits
    • Greater consumption, nonprescription drugs
    • Changes in gastric emptying
    • Reduced production of gastric acid and slowed gastric motility may have impact
    • Result in unpredictable rates of dissolutions, absorption of weakly acidic drugs

Older Adult Patients

• Distribution
  - Changes in body composition
  - Reduced lean body mass
  - Reduced total body water
  - Increased fat as percentage of body mass
  - Decline of serum albumin levels
    • Affects drug distribution
    • Decreases protein binding of drugs
    • Increase in amount of free drug in circulation
    • Ratio of bound to free drug may be significantly altered
Older Adult Patients

• Biotransformation
  – Ability of liver to metabolize drugs does not decline consistently with age for all drugs
    • Disorders common with aging can impair liver function
    • Hepatic recovery from injury declines

Older Adult Patients

• Biotransformation
  – Certain drugs metabolized more slowly
    • Due to decreased liver blood flow
    • Possible drug accumulation, toxicity
    • Use caution when administering repeated medication doses in patients with history of liver disease
    • Severe nutritional deficiencies may have impaired hepatic function

Older Adult Patients

• Elimination
  – Renal function critical factor for clearance of drugs
  – Decreased renal function, impairment
    • Caused by loss of functioning nephrons, decrease in blood flow
    • Result in decreased GFR
  – Prolongation of half-life of many drugs, possibility of toxic levels
Older Adult Patients

- Drug administration problems
  - Noncompliance
    - Rarely affects administration of emergency drugs
    - May be factor in patient’s condition

Older Adult Patients

- Drug administration problems
  - Common causes of noncompliance, medication errors
    - Expense of drugs with fixed incomes
    - Forgetfulness or confusion
      - Especially with several prescriptions and different dosing intervals
    - Do not complete because symptoms have disappeared
    - Physical disabilities (arthritis, visual impairment)
    - May be deliberate
    - Opposed to drug from past experiences
    - Drug history especially important
    - Patient has right to refuse medication

Lesson 13.4

Drugs that Affect the Nervous System
Learning Objective

• Outline drug actions and care considerations for a patient who is given drugs that affect the nervous, cardiovascular, respiratory, endocrine, and gastrointestinal systems.

Nervous System Drugs

• Actions depend on which branch of ANS is affected
  – If branch is stimulated/inhibited by drug therapy
  – Central nervous system (CNS)
    • Consists of brain, spinal cord
    • Collection point for nerve impulses
  – Peripheral nervous system
    • Consists of cranial, spinal nerves and their branches
    • Nerves outside CNS
    • Connects all parts of body to CNS
Nervous System Drugs

• Actions depend on which branch of ANS is affected
  – Somatic nervous system
    • Controls functions under conscious, voluntary control
  – Autonomic nervous system
    • Comprised mostly of motor nerves
    • Controls functions of involuntary smooth muscles, cardiac muscles, glands

Nervous System Drugs

• Four types of nerve fibers found in most nerves
  – Visceral afferent (sensory) fibers
    • Convey impulses from internal organs to CNS
  – Visceral efferent (motor) fibers
    • Convey impulses from CNS to internal organs, glands, smooth and cardiac (involuntary) muscles

Nervous System Drugs

• Four types of nerve fibers found in most nerves
  – Somatic afferent (sensory) fibers
    • Convey impulses from head, body wall, extremities to CNS
  – Somatic efferent (motor) fibers
    • Convey impulses from CNS to striated (voluntary) muscles
Nervous System Drugs

• Peripheral (sensory) nervous system
  – Receives stimuli from body
    • CNS interprets these stimuli
  – Initiates responses to stimuli

• Visceral afferent and efferent nerve fibers form autonomic nervous system

Nervous System Drugs

• Somatic afferent and somatic efferent nerve fibers form somatic nervous system

• Autonomic nervous system, somatic nervous system are subdivisions of peripheral nervous system

Autonomic Division of PNS

• Provides organs with double set of nerve fibers: sympathetic (adrenergic) and parasympathetic (cholinergic)
  – Cell bodies located in different areas of CNS
    • Also exit spinal cord at different levels
    • Sympathetic from thoracic, lumbar regions of spinal cord
    • Parasympathetic from cranial, sacral portions of spinal cord
Autonomic Division of PNS

- Sympathetic, parasympathetic systems work as physiological antagonists on effector organs
  - Sympathetic system
    - Prepares body for vigorous muscular activity, stress, emergencies (fight or flight)
    - Affects widespread areas of body for sustained time periods
  - Parasympathetic system
    - Lowers muscular activity
    - Operates during nonemergency situations
    - Produces selective, localized responses of short duration
    - Sympathetic, parasympathetic systems operate at same time
      - One usually has more dominant effects at any given time

Autonomic innervation by sympathetic, parasympathetic nervous systems viewed as involving two-neuron chain

- Chain exists in series between CNS and effector organs
  - Two-neuron chain
    - Preganglionic neuron, located in CNS
    - Postganglionic neuron, located in periphery
Autonomic Division of PNS

• Synapse
  – Area that serves as functional junction between two neurons

• Preganglionic fibers
  – Pass between CNS and nerve cell bodies in peripheral nervous system (ganglia)

• Postganglionic fibers
  – Pass between ganglia and effector organ

Autonomic Division of PNS

• Sympathetic ganglia
  – Some lie close to spinal cord
  – Others lie midway between spinal cord and effector organ

• Parasympathetic ganglia
  – Lie close/within walls of effector organs

• Difference in location of ganglia is anatomical reason for widespread responses caused by sympathetic division versus localized responses caused by parasympathetic division
Neurochemical Transmission

- Neurotransmitters
  - Help fibers communicate
  - Chemicals released from one neuron at presynaptic nerve fiber
  - Cross synapse where accepted by next neuron at specialized site (receptor)
  - Bind only to specific receptors on postsynaptic membranes that recognize them
  - Then deactivated or taken up into presynaptic neuron

- Acetylcholine
  - Neurotransmitter for preganglionic fiber at junction between preganglionic fiber and synapse
  - Neurotransmitter at junction between parasympathetic postganglionic fiber and effector cell

- Norepinephrine
  - Between sympathetic postganglionic fiber and effector cell
  - Member of catecholamine family
  - Released by adrenergic fibers
Neurochemical Transmission

• Neurotransmitters
  – Adrenergic fibers
    • Fibers that release norepinephrine
    • Most postganglionic neurons of sympathetic division

Neurochemical Transmission

• Autonomic nervous system actions
  – Depend on interaction between neurotransmitter released by ganglionic cells and receptor effector cells
    • Sympathetic stimulation causes excitatory effects in some organs, inhibitory effects in others
    • Parasympathetic stimulation causes excitation in some organs, inhibition in others

Neurochemical Transmission

• Parasympathetic, sympathetic systems function continuously
  – Innervate many of the same organs at the same time
  – Opposing actions balance one another
    • Most organs controlled predominantly by one or the other system
Nerve Impulse Transmission in ANS

- Both branches have multiple receptors
  - Variety accounts for differences in response to stimulation of sympathetic, parasympathetic nerves (excitatory or inhibitory)

Parasympathetic Nervous System

- Nicotinic receptors
  - Stimulated by nicotine
  - Found at neuromuscular junctions of skeletal muscles
  - Also found on postganglionic neurons of parasympathetic nervous system
Parasympathetic Nervous System

• Muscarinic receptors
  – Stimulated by mushroom poison, muscarine
  – Found at neuromuscular junction of cardiac and smooth muscle
  – Also found on glands and postganglionic neurons of sympathetic nervous system

Parasympathetic Nervous System

• Drugs that activate nicotinic receptors do not activate muscarinic receptors
• Difference between nicotinic and muscarinic receptors is crucial in drug therapy

Parasympathetic Nervous System

• Acetylcholine
  – When binds to nicotinic receptors, excitatory response occurs
  – When binds with muscarinic receptors, excitation/inhibition occurs
    • Depends on where target tissue receptors are found
    • In cardiac muscle, heart rate slows
    • In smooth muscle of GI tract, contraction rate, amplitude increase
Parasympathetic Nervous System

- Atropine
  - Blocks muscarinic but not nicotinic receptor sites
  - Affects heart rate but does not cause paralysis
- Curare
  - Nicotinic receptor blocker
  - Causes paralysis

Sympathetic Nervous System

- Receptors
  - Alpha adrenergic, subgroups
  - Beta adrenergic, subgroups
- Norepinephrine
  - Binds to, activates both receptor molecule types
  - Has more affinity for alpha receptors

- Epinephrine
  - Produced by adrenal medulla
  - Classified as adrenergic substance
  - Equal affinity for both receptors
- Tissues containing alpha and beta receptor cells
  - One type is more abundant
  - As a result, that type has a predominant effect
- Both receptors can be excitatory or inhibitory
  - Beta receptors are stimulatory in cardiac muscle, inhibitory in intestinal smooth muscle
Drugs that Affect the ANS

- Nervous and endocrine systems
  - Control, coordinate body functions
  - Share characteristics
    - High level of integration in brain
    - Ability to influence functions in distant regions of body
    - Extensive use of negative feedback mechanisms
  - Difference
    - Information mode of transmission

Drugs that Affect the ANS

- Endocrine system transmission
  - Chiefly chemical
  - Moves via blood-borne hormones
    - Not targeted for specific organ
    - Diffusely affect many cells, organs at same time

Drugs that Affect the ANS

- Nervous system transmission
  - Rapid electrical transmission over nerve fibers
  - Chemical impulses carry signals only between nerve cells and their effector cells in localized manner, affecting only a few cells
Drugs that Affect the ANS

• Drug classifications
  – Autonomic drugs mimic/block effects of sympathetic and parasympathetic divisions of ANS
  – Cholinergic
    • Parasympathomimetic
    • Mimic actions of parasympathetic nervous system

Drugs that Affect the ANS

• Drug classifications
  – Cholinergic blocking
    • Parasympatholytic
    • Block actions of parasympathetic nervous system
  – Adrenergic
    • Sympathomimetic
    • Mimic actions of sympathetic nervous system or adrenal medulla
  – Adrenergic blocking
    • Sympatholytic
    • Block actions of sympathetic nervous system or adrenal medulla

Cholinergic Drugs

• Acetylcholine
  – Nicotinic effect on ganglia, adrenal medulla, and skeletal muscle
  – Muscarinic effect at postganglionic nerve endings in cardiac muscle, smooth muscle, glands
Cholinergic Drugs

- Ganglionic stimulating drugs
  - Drugs that affect nicotinic or cholinergic receptor sites on autonomic ganglia
- Act directly with cholinergic receptors on postsynaptic membranes

Cholinergic Drugs

- Act indirectly by inhibiting enzyme that destroys acetylcholine
  - Results in accumulation of acetylcholine
  - Causes longer, more intense response at various effector sites

Cholinergic Drugs

- Little therapeutic value
  - Not emergency drugs
  - Main exception, physostigmine (Antilirium), indirect-acting drug
    - Works to elevate concentration of acetylcholine at myoneural junctions
    - Increases muscle strength, function
Cholinergic-Blocking Drugs

• Block muscarinic effects of acetylcholine
• Decrease action of acetylcholine on effector organ

Cholinergic-Blocking Drugs

• Atropine
  – Belladonna alkaloid
  – Competitive antagonist
  – Occupies muscarinic receptor sites
  – Prevents/reduces muscarinic response to acetylcholine
  – Large doses
    • Dilate pupils
    • Inhibit accommodation of eyes
    • Increase heart rate by blocking cholinergic effects of heart

Cholinergic-Blocking Drugs

• Atropine synthetic substitutes
  – Created to obtain only antispasmodic effects of drug
  – Treats gastric, duodenal ulcers
  – Dicyclomine (Bentyl)
  – Glycopyrrolate (Robinul)
Adrenergic Drugs

- Produce activities like neurotransmitters
  - Direct-acting drugs
    - Catecholamines
      - Epinephrine: emergency hormone, adrenalin
      - Norepinephrine: critical neurotransmitter of nerve impulses, levophed

Adrenergic Drugs

- Direct-acting drugs
  - Dopamine
    - Precursor of epinephrine, norepinephrine
    - Has neurotransmitter in certain parts of CNS
    - Intropin
      - Depend on ability to act directly with alpha, beta receptors

Adrenergic Drugs

- Direct-acting drugs
  - Alpha2 receptors
    - Postsynaptic receptors
    - Located on effector organs
    - Stimulate contraction of smooth muscle
    - Increase BP
Adrenergic Drugs

• Direct-acting drugs
  – Alpha2 receptors
    • Found on presynaptic, postsynaptic nerve endings
    • When stimulated, presynaptic receptors inhibit further release of norepinephrine
    • Produce vasoconstriction to increase resistance in blood vessels, increase BP

Adrenergic Drugs

• Direct-acting drugs
  – Beta receptors
    • Subdivided based on their response to drugs
    • Follow anatomical distinctions
    • Beta1 receptors located mainly in heart
    • Beta2 receptors located mainly in bronchiolar, arterial smooth muscle
    • Stimulate heart
    • Dilate bronchioles
    • Dilate blood vessels in skeletal muscle, brain, heart
    • Aid in glycogenolysis (breakdown of glycogen to glucose)

When would each of these beta effects be helpful to a patient?
Adrenergic Drugs

• Direct-acting drugs
  – Norepinephrine
    • Acts on alpha receptors
    • Causes vasoconstriction of blood vessels
  – Epinephrine
    • Acts on alpha and beta receptors
    • Produces mixture of vasodilation and vasoconstriction
    • Depends on number of alpha, beta receptors in target tissue

Adrenergic Drugs

• Direct-acting drugs
  – Alpha activities
    • Vasoconstriction of arterioles in skin and splanchnic area
    • Increased BP
    • Peripheral shunting of blood to heart, brain from shifting of blood volume
    • Pupil dilation
    • Relaxation of gut

Adrenergic Drugs

• Direct-acting drugs
  – Beta activities
    • Cardiac acceleration, increased contractility
    • Vasodilation of arterioles supplying skeletal muscle
    • Bronchial relaxation
    • Uterine relaxation
Adrenergic Drugs

- Indirect-acting and dual-acting drugs
  - Act indirectly on receptors
  - Trigger release of catecholamines, norepinephrine, epinephrine
    - Activate alpha and beta receptors
  - Dual-acting adrenergic drugs have indirect, direct effects
    - Ephedrine (ephedrine sulfate)

Adrenergic Drugs

- Adrenergic-blocking agents may be classified into alpha- and beta-blocking drugs
  - Alpha-blocking drugs
    - Block vasoconstricting effect of catecholamines
    - Used in hypertension
    - Used to help prevent necrosis when norepinephrine or dopamine has leaked into tissues

Adrenergic Drugs

- Beta-blocking agents
  - Greater clinical application
  - Often used in emergency care
  - Inhibit action of beta receptors at effector site
Adrenergic Drugs

• Beta-blocking agents
  — Selective
    • Block beta1 or beta2 receptors
    • Cardiovascular blockers
    • Block beta2 receptors in heart with minimal beta1 activities in lungs
    • Metoprolol (Lopressor, Toprol-XL)
    • Atenolol (Tenormin)
    • Manage hypertension
    • Suspected MI
    • High-risk unstable angina

Adrenergic Drugs

• Beta-blocking agents
  — Nonselective
    • Block beta1 and beta2 receptor sites
    • Inhibit both beta receptors in smooth muscle of bronchioles, blood vessels
    • Nadolol (Corgard)
    • Propranolol (Inderal)
    • Labetalol (Normodyne, Trandate)
    • Also has some alpha-blocking activity

Narcotic Analgesics and Antagonists

• Analgesics
  — Relieve pain

• Antagonists
  — Reverse effects of some narcotic analgesics
Narcotic Analgesics and Antagonists

• Pain components
  – Sensation of pain
    • Involves nerve pathways, brain
• Emotional response to pain
  – May be result of
    • Anxiety level
    • Previous pain experience
    • Age
    • Gender
    • Culture

Narcotic Analgesics and Antagonists

• Pain classifications
  – Acute
    • Sudden onset
    • Usually subsides with treatment
  – Chronic
    • Persistent or recurrent pain
    • Difficult to treat
  – Referred
    • Visceral pain felt at site different from origin

Narcotic Analgesics and Antagonists

• Pain classifications
  – Somatic
    • Arises from skeletal muscles, ligaments, vessels, joints
  – Superficial
    • Arises from skin or mucous membrane
  – Visceral
    • “Deep” pain arising from smooth musculature or organ system
    • May be difficult to localize
    • Dull or aching
Narcotic Analgesics and Antagonists

• Opiates
  – Drugs that contain or are extracted from opium

Narcotic Analgesics and Antagonists

• Opioid
  – Refers to synthetic drugs
  – Have pharmacological properties similar to opium or morphine
  – Morphine is chief alkaloid of opium
  – Work by binding with opioid receptors in brain, other body organs
    • Alters patient’s pain perception, emotional response to pain-causing stimulus

Narcotic Analgesics and Antagonists

• Opioid analgesics
  – Morphine
  – Codeine (Methylmorphine)
  – Hydromorphone (Dilaudid)
  – Meperidine (Demerol)
  – Fentanyl (Duragesic, Sublimaze)
  – Methadone (Dolophine, Methadose)
  – Oxycodone (Oxycontin, Percodan, Tylox, Percocet)
  – Hydrocodone (Lortab, Vicodin)
  – Propoxyphene (Darvon, Dolene)
Narcotic Analgesics and Antagonists

- Opioid analgesics
  - May produce undesirable effects
  - Nausea
  - Vomiting
  - Constipation
  - Urinary retention
  - Orthostatic hypotension
  - Respiratory depression
  - CNS depression
  - Most can be overcome by careful administration, patient monitoring

Narcotic Analgesics and Antagonists

- Opioid antagonists
  - Block effects of opioid analgesics
    - Displaces analgesics from their receptor sites
    - Opioid-induced respiratory depression
    - Sedation
  - Naloxone (Narcan)
  - Naltrexone (Trexan)
  - Nalmefene (Revex)

Narcotic Analgesics and Antagonists

- Opioid agonist-antagonists
  - Analgesic and antagonist effects
  - Pharmacokinetic, adverse effects similar to morphine
  - Antagonize some opioid receptors competitively
  - Varying degrees of agonist effect at other opioid receptor sites
Narcotic Analgesics and Antagonists

- Opioid agonist-antagonists
  - Pentazocine (Talwin)
  - Nalbuphine (Nubain)
  - Lower potential for creating dependency than opioid analgesics
  - Withdrawal symptoms not as severe as opioid agonist drugs
  - May bring out withdrawal symptoms in addicts

Nonnarcotic Analgesics

- Act by peripheral mechanism that interferes with local mediators released when tissue is damaged
  - Mediators stimulate nerve endings, cause pain
  - Nerve endings in damaged tissues stimulated less often with use
    - Differs from the mechanism of narcotic analgesics that act at the level of CNS

Nonnarcotic Analgesics

- Ketorolac (Toradol)
  - Nonsteroidal antiinflammatory drug (NSAID)
  - Exhibits analgesic activity
- Tramadol (Ultram)
Nonnarcotic Analgesics

• Cyclooxygenase (COX) inhibitors
• Oral NSAIDs
  – Ibuprofen (Advil)
  – Naproxen (Aleve)
  – Acetaminophen

A nonnarcotic analgesic may be selected instead of a narcotic for a paramedic returning to work on the ambulance. Why?

Anesthetics

• CNS depressants
  – Have reversible action on nervous tissue
• Major types of anesthesia
  – General anesthesia
    • Achieved by IV or inhalation routes
    • Most common type during surgery to induce unconsciousness
Anesthetics

- Major types of anesthesia
  - Regional anesthesia
    - Inject local anesthetic near nerve trunk or specific sites in large region of body
    - Spinal block
  - Local anesthesia
    - Achieved topically to produce loss of sensation
    - Achieved by injection to block area surrounding operative field, making it insensitive to pain

Antianxiety, Sedative-Hypnotic Agents

- Antianxiety agents used to reduce
  - Apprehension
  - Nervousness
  - Worry
  - Fearfulness

Antianxiety, Sedative-Hypnotic Agents

- Sedatives, hypnotics
  - Depress CNS
  - Produce calming effect
  - Help induce sleep
  - Difference between them is degree of CNS depression induced by agent
    - Small dose administered to calm is sedative
    - Larger dose of same to induce sleep is hypnotic
Alcohol

- Has actions characteristic of sedative-hypnotic or antianxiety drugs
- Major source of drug abuse, dependency

Reticular Formation

- Group of nuclei scattered throughout the brainstem
- With its neural pathways, make up reticular activating system
  - Involved with sleep-wake cycle
  - Collects incoming signals from senses, viscera
  - Processes, passes signals to higher brain centers
  - Determines level of awareness to environment
    - Governs actions, responses to environment
      - Antianxiety, sedative-hypnotic agents and alcohol act by depressing this system

Classifications

- Treat anxiety or induce sleep
- Benzodiazepines
  - Most often used to treat anxiety, insomnia
  - Introduced in 1960s as antianxiety drugs
  - Among most widely prescribed drugs in clinical medicine
  - Wide therapeutic index
  - Mortality and morbidity from oral overdose are rare unless taken with other CNS depressants
Classifications

- Benzodiazepines
  - Bind to specific receptors in cerebral cortex, limbic system
  - Together govern emotional behavior
  - Highly lipid soluble, distributed widely in body tissues
  - Highly bound to plasma protein, usually more than 80%
- Actions
  - Anxiety reducing
  - Sedative-hypnotic
  - Muscle relaxing
  - Anticonvulsant

Classifications

- Benzodiazepines
  - Schedule IV drugs
  - Potential for abuse
  - Commonly prescribed
    - Alprazolam (Xanax)
    - Clonazepam (Klonopin)
    - Diazepam (Valium)
    - Flurazepam (Dalmane)
    - Midazolam (Versed)
    - Lorazepam (Ativan)
    - Temazepam (Restoril)

Why would a benzodiazepine be preferred over a narcotic when preparing to reduce a dislocated shoulder?
Classifications

• Barbiturates
  – Once most commonly prescribed for sedative-hypnotic effects
    • Replaced by benzodiazepines
  – Divided into classes according to duration of action
    • Differences depend on lipid solubility, protein-binding properties

• Barbiturates
  – Ultrashort-acting
    • Used as IV anesthetics
    • Act rapidly, can produce state of anesthesia in a few seconds
    • Pentobarbital (Nembutal)
    • Secobarbital (Seconal)

• Barbiturates
  – Short-acting
    • Produce effect in short time (10 to 15 minutes)
    • Peak over short period (3 to 4 hours)
    • Rarely used to treat insomnia
    • Preanesthesia sedation
    • In combination with other drugs for psychosomatic disorders
    • Pentobarbital (Nembutal)
    • Secobarbital (Seconal)
Classifications

- **Barbiturates**
  - Intermediate-acting barbiturates
    - Onset of 54 to 60 minutes
    - Peak in 6 to 8 hours
    - Short-acting and intermediate-acting produce similar patient responses
    - Amobarbital (Amytal)
    - Butabarbital (Butisol)

Classifications

- **Barbiturates**
  - Long-acting barbiturates
    - 60+ minutes for onset
    - Peak over 10 to 12 hours
    - Treat epilepsy, other chronic neurological disorders
    - Used to sedate patients with severe anxiety
    - Mephobarbital (Mebaral)
    - Phenobarbital (Luminal)

Classifications

- **Miscellaneous sedative-hypnotic drugs**
  - Many antianxiety, sedative-hypnotic drugs are not barbiturates or benzodiazepines
  - Generally shorter acting
    - Chloral hydrate (Noctec)
    - Eszopiclon (Lunesta)
    - Zolpidem (Ambien)
    - Antihistamine hydroxyzine (Vistaril, Atarax)
    - Etomidate (Amidate)
Alcohol Intake and Behavioral Effects

- General CNS depressant
- Can produce
  - Sedation
  - Sleep
  - Anesthesia

Alcohol Intake and Behavioral Effects

- Enhances sedative-hypnotic effects of other drug classes
  - General CNS depressants
  - Antihistamines
  - Phenothiazines
  - Narcotic analgesics
  - Tricyclic antidepressants

Alcohol Intake and Behavioral Effects

- If taken with other drugs, enhancement could result in coma or death
- Blood alcohol measured in milligrams per deciliter (mg/dL)
  - Characteristic behavioral effects can be predicted
    - Amount of alcohol consumed
    - Blood alcohol levels
Anticonvulsants

- Used to treat seizure disorders
- Epilepsy
  - Neurological disorder
  - Recurrent pattern of abnormal neuronal discharges within brain
    - Cause sudden loss or disturbance of consciousness
    - Sometimes associated with motor activity, sensory phenomena, inappropriate behavior

Anticonvulsants

- Epilepsy
  - Occur in 0.5% to 1% of population
  - Primary or idiopathic
    - 50% of cases, cause unknown
  - Secondary epilepsy traced to
    - Trauma
    - Infection
    - Cerebrovascular disorder
    - Some other illness

Anticonvulsants

- Work by depressing excitability of neurons that fire to initiate seizure
  - Suppress neurons responsible for spread of seizure discharge
  - Presumed to modify ionic movements of sodium, potassium, or calcium across nerve membrane
    - Reduce response to incoming electrical or chemical stimulation
  - Benzodiazepines also stimulate major inhibitory neurotransmitters in CNS
  - Many need drug therapy throughout their lives to control seizure disorders
Anticonvulsants

- Drug choice
  - Depends on type of seizure disorder
    - Generalized
    - Partial
    - Status
  - Depends on patient’s tolerance, response to prescribed medication

CNS Stimulants

- Classified by where they exert major effects in nervous system
  - Cerebrum region
  - Medulla and brainstem region
  - Hypothalamic limbic region
- Increase excitability
  - Block activity of inhibitory neurons or their neurotransmitters
  - Enhance production of excitatory neurotransmitters

CNS Stimulants

- Anorexiants
  - Appetite suppressants
    - Treat obesity
  - Produce direct stimulant effect on hypothalamic and limbic regions
    - Phendimetrazine (Plegine)
    - Mazindol (Mazanor, Sanorex)
CNS Stimulants

- Anorexiant
  - Gastrointestinal lipase inhibitors or fat blockers
    - New class of drugs
    - Block about 30% of dietary fat absorption
    - Sometimes used to manage obesity with reduced-calorie diet
    - Orlistat (Xenical)

CNS Stimulants

- Amphetamines
  - Stimulate cerebral cortex and reticular activating system
    - Increase alertness, responsiveness to environmental surroundings
  - Used for attention deficit hyperactivity disorder (ADHD)
    - Mostly in children, adolescents
    - Short attention span
    - Impulsive behavior

CNS Stimulants

- Amphetamines
  - Treat attention deficit disorder (ADD)
- Nonamphetamine CNS stimulants
  - Methylphenidate (Ritalin, Concerta)
  - Atomoxetine (Strattera)
  - Pemoline (Cylert)
CNS Stimulants

• Amphetamines
  – Have calming effect on persons with ADHD
    • Increase neurotransmitter levels of dopamine

CNS Stimulants

• Amphetamines
  – Treat narcolepsy
    • Excessive drowsiness
    • Sudden sleep attacks during daytime hours
    • Sometimes sleep paralysis
    • Methamphetamine (Desoxyn)
    • Amphetamine-mixed salts (Adderall)
    • Dextroamphetamine tablets and elixir

Psychotherapeutic Drugs

• Used for psychoses and affective disorders
  – Schizophrenia
  – Depression
  – Mania
Psychotherapeutic Drugs

• CNS and emotions
  – Neurotransmitters with major effect on emotion
    • Acetylcholine
    • Norepinephrine
    • Dopamine
    • Serotonin
    • Monoamine oxidase
  – Drug therapy alleviates symptoms by temporarily modifying unwanted behavior

Psychotherapeutic Drugs

• Antipsychotic agents
  – Main use, treat schizophrenia
    • Only clearly effective treatment
  – Other psychiatric indications
    • Treat Tourette’s syndrome
    • Treat senile dementia associated with Alzheimer’s
  – Block dopamine receptors in specific areas of CNS
Psychotherapeutic Drugs

- **Antipsychotic agents**
  - Classified into groups
  - Phenothiazine derivatives
    - Chlorpromazine (Thorazine)
    - Thioridazine (Mellaril)
    - Fluphenazine (Prolixin)
  - Butyrophenone derivatives
    - Haloperidol (Haldol)
  - Dihydroindolone derivatives
    - Molindone (Moban)

Psychotherapeutic Drugs

- **Antipsychotic agents**
  - Dibenzoazepine derivatives
    - Loxapine (Loxitane)
  - Thienbenzodiazepine derivatives
    - Olanzapine (Zyprexa)
  - Atypical agents
    - Clozapine (Clozaril)
    - Risperidone (Risperdal)

Psychotherapeutic Drugs

- **Continued use of certain antipsychotics**
  - Can develop super sensitivity of dopamine receptors
  - Can lead to tardive dyskinesia
    - Potentially irreversible neurological disorder
    - Involuntary repetitive movements of muscles of face, limbs, trunk
    - Excessive blinking
    - Lip smacking
    - Tongue protrusion
    - Foot tapping
    - Rocking side-to-side
Psychotherapeutic Drugs

• Continued use of certain antipsychotics
  – Can lead to dystonia
  – Local or diffuse changes in muscle tone, resulting in
    • Painful muscle spasms
    • Unusually fixed postures
    • Strange movement patterns

Psychotherapeutic Drugs

• Antidepressants
  – Treat affective disorders (mood disturbances)
    • Depression
    • Mania
    • Elation
  – Prescribed for depression
    • Tricyclic antidepressants
    • Selective serotonin reuptake inhibitors
    • MAO inhibitors
    • Lithium (antimanic drug) (preferred treatment for mania)

Psychotherapeutic Drugs

• Antidepressants
  – Tricyclic antidepressants
    • Treat depression by increasing levels (blocking reuptake) of neurotransmitters norepinephrine and serotonin
    • Nortriptyline (Pamelor)
    • Amitriptyline (Elavil)
  – Excessive doses carry potential for cardiac dysrhythmias, cardiovascular collapse
You know that tricyclic antidepressants increase the levels of norepinephrine. Thus what side effects might you expect in an overdose?

**Psychotherapeutic Drugs**

- Selective serotonin reuptake inhibitors
  - Block reabsorption, reuptake of serotonin
    - Make more available to brain
  - Side effects
    - Insomnia
    - Headache
    - Diarrhea

**Psychotherapeutic Drugs**

- Selective serotonin reuptake inhibitors
  - Examples
    - Fluoxetine (Prozac)
    - Sertraline (Zoloft)
    - Paroxetine (Paxil)
    - Escitalopram (Lexapro)
    - Fluvoxamine (Luvox)
    - Citalopram (Celexa)
Psychotherapeutic Drugs

- Monoamine oxidase inhibitor antidepressants
  - Central-acting monoamines
  - Norepinephrine, serotonin
  - Cause depression, mania
  - Monoamine oxidase is enzyme found in nerve cells
    - Produced during tense emotional states
    - Responsible for metabolizing norepinephrine within nerve
    - Monoamine oxidase inhibitors block enzyme
    - Leads to increased levels of norepinephrine
  - Examples
    - Isocarboxazid (Marplan)
    - Phenelzine (Nardil)
    - Tranylcypromine (Parnate)
    - Also used as antihypertensive agents

Psychotherapeutic Drugs

- Lithium
  - Cation closely related to sodium
  - Both cations are transported actively across cell membranes
    - Lithium cannot be pumped as effectively out of cell as sodium
    - Accumulates in cells
    - Results in decrease in intracellular sodium, improvement in symptoms of manic state
Psychotherapeutic Drugs

• Lithium
  – Enhances some actions of serotonin
  – May decrease levels of norepinephrine, dopamine
  – Block development of dopamine receptor super sensitivity
  – Lithium carbonate used to treat manic disorders
    • Bipolar disorders
  – Narrow therapeutic range, toxicity common

CNS-Peripheral Dysfunction Drugs

• Parkinson's disease
  – Chronic disabling
  – Rigidity of voluntary muscles
  – Tremor of fingers, extremities
  – Most often affects people over 60

• Parkinson's disease
  – May occur especially after
    • Acute encephalitis
    • Cases of carbon monoxide poisoning
    • Metallic poisoning
    • Use of illicit drugs
    • Result of abnormally low concentration of dopamine
CNS-Peripheral Dysfunction Drugs

• Parkinson’s disease
  – Parkinsonism syndromes mimic symptoms of Parkinson’s disease
    • Usually of an unknown cause (idiopathic)
    • May result from treatment with antipsychotic drugs (drug-induced parkinsonism) that block dopaminergic receptors
      – Haloperidol (Haldol)
      – Metoclopramide (Clopra, Emex)
      – Phenothiazines (Thorazine, Mellaril)

• Huntington’s disease
  – Inherited disorder
  – Progressive dementia
  – Involuntary muscle twitching (chorea)
  – Related to imbalance of dopamine, acetylcholine, other neurotransmitters
Central Anticholinergic Drugs

- Anticholinergic
  - Inhibit/block acetylcholine
  - Restore normal dopamine–acetylcholine balance in brain

Central Anticholinergic Drugs

- Common agents
  - Benztropine (tablets and injections)
  - Ethopropazine hydrochloride
  - Ipratropium (Atrovent)
  - Donepezil (Aricept)
    - Treats dementia in patients with mild-to-moderate Alzheimer’s disease

Drugs that Affect Brain Dopamine

- Classifications
  - Those that release dopamine
  - Those that increase brain levels of dopamine
    - Levodopa (L-dopa)
    - Drug of choice in movement disorders associated with dopamine-acetylcholine imbalance
  - Dopaminergic agonists
Monamine oxidase inhibitors
- Monoamine oxidase A
  - Metabolizes norepinephrine, serotonin
- Monoamine oxidase B
  - Metabolizes dopamine
  - Selegiline (Deprenyl) is a selective inhibitor
  - Retards breakdown of dopamine
  - Often used with levodopa
  - Enhances, prolongs antiparkinsonism effects of levodopa
  - Allows dose of levodopa to be reduced

Skeletal Muscle Relaxants
- Skeletal muscle contraction evoked by a nicotinic cholinergic transmission process
  - Contractions can be modified by drugs

Skeletal Muscle Relaxants
- Central-acting muscle relaxants
  - Treat muscle spasms
  - Produce CNS depression in brain, spinal cord
  - Antispastic agents
    - Carisoprodol (Soma)
    - Cyclobenzaprine (Flexeril)
    - Diazepam (Valium)
Skeletal Muscle Relaxants

• Direct-acting muscle relaxants
  – Work directly on skeletal muscles to produce muscle relaxation
    • Results in decrease in muscle contraction
    – Dantrolene (Dantrium)

• Neuromuscular blockers
  – Produce complete muscle relaxation, paralysis
  – Bind to nicotinic receptor for acetylcholine at neuromuscular junction
  – Block neuromuscular nerve transmission
    • Remains blocked for a variable period depending on type, amount used

• Neuromuscular blockers
  – Sometimes used to achieve total paralysis before endotracheal intubation
    • Relieve muscle spasms of larynx
    • Suppress tetany
    • Used during electroconvulsive therapy for depression
    • Allow for breathing control by respirator
  – Examples
    • Pancuronium (Pavulon)
    • Vecuronium (Norcuron)
    • Succinylcholine (Anectine)
Physicians usually will not prescribe a nonselective beta blocker such as propranolol (Inderal) for patients with a history of asthma. Explain why this is true.

Lesson 13.5
Drugs that Affect the Cardiovascular System

Learning Objective
- Outline drug actions and care considerations for a patient who is given drugs that affect the nervous, cardiovascular, respiratory, endocrine, and gastrointestinal systems.
Heart

- Many interconnected branching fibers, cells
  - Form walls of two atria, two ventricles
- Cells
  - Some conduct electrical impulses
  - Others have contraction as main role
  - All cells nourished through profuse network of blood vessels (coronary vasculature)
- Cardiac drugs classified by their effects on coronary vasculature

Cardiac Glycosides

- Naturally occurring plant substances
- Have characteristic effects on heart
- Contain carbohydrate molecule (sugar)

Cardiac Glycosides

- When combined with water, molecule converted into sugar and active substances
- Blocks certain ionic pumps in cellular membrane
- Indirectly increases calcium concentration of contractile proteins
- Digoxin (Lanoxin) used to treat heart failure, manage certain tachycardias
Cardiac Glycosides

- Digitalis glycosides affect heart
  - Increase strength of contraction
  - Positive inotropic effect
    - Effect on electrophysiological properties of heart
  - Modest negative chronotropic effect
    - Causes slight slowing of heart rate
  - Negative dromotropic effect
    - Decreases conduction velocity of impulses in heart

Cardiac Glycosides

- Side effects due to narrow therapeutic index of drugs
  - Symptoms often vague, can be attributed easily by patient to viral illness
    - Neurological
    - Visual
    - Gastrointestinal
    - Cardiac
    - Psychiatric

Cardiac Glycosides

- High index of suspicion in patients taking cardiac glycosides who report flulike symptoms important
  - Most common side effects
    - Anorexia
    - Nausea
    - Vomiting
    - Visual disturbances
      - Flashing lights
      - Altered color vision
    - Dysrhythmias, usually slowing with varying degrees of blocked conduction
Cardiac Glycosides

• Toxic effects are dose related
  – May be increased by other drugs, such as diuretics
  – May predispose patient to cardiac rhythm disturbances
  – Dysrhythmias
    • Bradycardias
    • Tachycardias
    • Ventricular fibrillation

• Treatment for digitalis toxicity
  • Correction of electrolyte imbalances
  • Neutralization of free drug
  • Use of antidysrhythmics
  – Patient with low potassium level likely to develop digoxin toxicity

Antidysrhythmics

• Treat, prevent disorders of cardiac rhythm
• Suppress dysrhythmias
  – By direct action on cardiac cell membrane
    • Vasopressin (Pitressin)
  – By indirect action that affects cells
    • Propranolol (Inderal)
  – Both direct and indirect action can occur
Antidysrhythmics

• Cardiac rhythm disturbance factors
  – Ischemia
  – Hypoxia
  – Acidosis or alkalosis
  – Electrolyte abnormalities
  – Excessive catecholamine exposure
  – Autonomic influences
  – Drug toxicity
  – Scarred, diseased tissue

Antidysrhythmics

• Dysrhythmias result from disturbances in impulse formation, conduction, or both
• Classifications
  – Based on fundamental mode of action on cardiac muscle
  – Drugs that belong to same class do not always produce identical actions
  – All drugs have some ability to suppress automaticity

Antidysrhythmics

• Classifications
  – Class I: sodium channel blockers
    • Slow conduction
    • Divided into subclasses (Ia, Ib, and Ic) based on extent of sodium channel blockade
  – Class Ia drugs
    • Quinidine (Quinaglute, Duraquin)
    • Disopyramide (Norpace)
    • Procainamide (Pronestyl)
Antidysrhythmics

- Classifications
  - Class Ib drugs
    - Decrease/have no effect on conduction velocity
    - Lidocaine (Xylocaine)
    - Phenytoin (Dilantin)
  - Class Ic drugs
    - Profoundly slow conduction
    - Indicated only for control of life-threatening ventricular dysrhythmias
    - Flecainide (Tambocor)

How might the signs of shock in a patient taking digoxin (Lanoxin) or propranolol (Inderal) vary from what might be expected normally?

Antidysrhythmics

- Classifications
  - Class II: beta-blocking agents
    - Reduce adrenergic stimulation of heart
    - Metoprolol (Lopressor)
Antidysrhythmics

- Classifications
  - Class III
    - Produce potassium channel blockade
    - Increase contractility
    - Do not suppress automaticity
    - No effect on conduction velocity
    - Cease dysrhythmias that result from re-entry of blocked impulses
    - Amiodarone (Cordarone)

Antidysrhythmics

- Classifications
  - Class IV
    - Calcium channel blockers
    - Block inflow of calcium through cell membranes of cardiac, smooth muscle cells
    - Depress myocardial and smooth muscle contraction
    - Decrease automaticity
    - Some cases, decrease conduction velocity
    - Verapamil (Isoptin)
    - Diltiazem (Cardizem)

Antihypertensives

- High BP affects 50 million adults, children in the United States
  - Related to increased incidence of
    - Stroke
    - Cerebral hemorrhage
    - Heart, renal failure
    - Coronary heart disease
  - Exact mechanism of action of many drugs is unknown
Antihypertensives

- Drug mechanisms
  - Maintain BP within normal limits
  - Maintain/improve blood flow without compromising tissue perfusion or blood supply to brain
  - Reduce workload of heart
  - Have no undesirable side effects
  - Permit long-term administration without intolerance

Antihypertensives

- Classifications
  - Given in low-dose combinations, titrated (gradually adjusted) to effect
  - Diuretics
    - Drug of choice in managing hypertension
    - Often used with other antihypertensive agents
    - Cause loss of excess salt and water from body by kidneys
    - Decrease in plasma and extracellular fluid volume decreases preload, stroke volume

Antihypertensives

- Classifications
  - Diuretics
    - Decrease in fluid volume has direct effect on size of arterioles, resulting in lowered BP
    - Response causes initial decline of cardiac output, followed by decrease in peripheral vascular resistance
    - Responses result in lowering of BP
Antihypertensives

- Classifications
  - Thiazides
    - Given concomitantly, prevents retention of sodium and water
    - Hydrochlorothiazide (HCTZ)

Antihypertensives

- Classifications
  - Loop diuretics
    - Strong, short-acting agents
    - Inhibit sodium and chloride reabsorption in loop of Henle
    - Cause excessive potassium loss
    - Cause increase in excretion of sodium and water

What medication might you expect a patient to be taking in addition to their loop diuretic?
Antihypertensives

• Classifications
  – Loop diuretics
    • Have fewer side effects than most other antihypertensives
    • Hypokalemia, profound dehydration can result from use
    • Prescribed for renal insufficiency
    • Given to patients who cannot take other diuretics
    • Furosemide (Lasix)

Antihypertensives

• Classifications: potassium-sparring agents
  – Effective as antihypertensive when used in combination with other diuretics
  – Promote sodium and water loss without loss of potassium
  – Indications
    • Hypokalemia from other diuretics
    • Patients resistant to antihypertensive effects of other diuretics
    • Edema
  – Spironolactone (Aldactone)

Sympathetic Blocking Agents

• Beta-blocking agents
  – Treat cardiovascular disorders
    • Suspected myocardial infarction
    • High-risk unstable angina
    • Hypertension
  – Decrease cardiac output
  – Inhibit renin secretion from kidneys
  – Drugs compete with epinephrine for available beta receptor sites
    • Inhibit tissue, organ response to beta stimulation
Sympathetic Blocking Agents

• Beta₁-blocking agents (cardioselective)
  – Acebutolol (Sectral)
  – Atenolol (Tenormin)
  – Metoprolol (Lopressor, Toprol-XL)

• Beta₁- and beta₂-blocking agents (nonselective)
  – Labetalol (Normodyne, Trandate) (also has alpha₁-blocking properties)
  – Nadolol (Corgard)
  – Propranolol (Inderal)

What should you anticipate when palpating the pulse of a patient who is taking a beta-blocking drug?

Adrenergic-Inhibiting Agents

• Modify actions of sympathetic nervous system
• Effective antihypertensive drugs
• Mechanism of work unknown
Adrenergic-Inhibiting Agents

• Centrally acting adrenergic inhibitors
  – Clonidine hydrochloride (Catapres)
  – Methyldopa (Aldomet)
  – Prazosin hydrochloride (Minipress)

Adrenergic-Inhibiting Agents

• Peripheral hydrochloride inhibitors
  – Doxazosin (Cardura)
  – Guanethidine sulfate (Ismelin)
  – Reserpine (Sandril, Serpasil)
  – Phentolamine (Regitine)
  – Phenoxycbenzamine (Dibenzyline)
  – Terazosin (Hytrin)

Vasodilator Drugs

• Act directly on smooth muscle walls of arterioles, veins, or both
• Lower peripheral resistance
  – Lower BP
• Stimulate sympathetic nervous system, activate baroreceptor reflexes
  – Increase heart rate, cardiac output, renin release
  – Drugs that inhibit sympathetic response are usually given with vasodilator drugs
Vasodilator Drugs

• Some treat angina pectoris (ischemic chest pain)
  – Nitrates dilate veins, arteries
    • Lead to venous pooling of blood
    • Reduce amount of blood return to heart
    • Reduce left ventricular end-diastolic pressure, volume
    • Subsequent decrease in wall tension helps to reduce myocardial oxygen demand, relieves chest pain of myocardial ischemia

Vasodilator Drugs

• Classified as arteriolar dilators and arteriolar and venous dilators
  – Arteriolar dilator drugs
    • Hydralazine (Apresoline)
    • Minoxidil (Loniten)

Vasodilator Drugs

• Classified as arteriolar dilators and arteriolar and venous dilators
  – Arteriolar and venous dilator drugs
    • Sodium nitroprusside (Nipride, Nitropress)
    • Nitrates and nitrates
    • Amyl nitrite inhalant
    • Isosorbide dinitrate (Isordil, Sorbitrate)
    • Nitroglycerin sublingual tablet (Nitrostat)
    • Nitropaste (Nitro-Bid ointment, Nitrostat, Nitrol)
    • Intravenous nitroglycerin (Tridil)
ACE Inhibitors

• Angiotensin-converting enzyme (ACE)
• Renin-angiotensin-aldosterone system key roles
  – Maintaining BP
  – Sodium, fluid balance
  – Disturbance in system causes
    • Hypertension
    • Edema
    • Congestive heart failure

ACE Inhibitors

• Kidney damage can result in inability to regulate release of renin through normal feedback mechanisms
  – Causes elevated BP in some patients
• Angiotensin II
  – Strong vasoconstrictor
  – Raises BP
  – Causes release of aldosterone
  – Contributes to sodium and water retention

ACE Inhibitors

• By inhibiting conversion of precursor angiotensin I to angiotensin II, renin-angiotensin-aldosterone system is suppressed and BP is lowered
• Captopril (Capoten)
• Enalapril (Vasotec)
ACE Inhibitors

- Benazepril (Lotensin)
- Fosinopril (Monopril)
- Lisinopril (Prinivil, Zestril)
- Quinapril (Accupril)

Calcium Channel Blockers

- Reduce peripheral vascular resistance
- Inhibit contractility of vascular smooth muscle
- Dilate coronary vessels
- Verapamil (Isoptin)
- Amlodipine (Norvasc)
- Felodipine (Plendil)

Calcium Channel Blockers

- Diltiazem (Cardizem, Tiazac)
- Treat hypertension
- Decrease oxygen requirements of heart (through decreased afterload)
- Increase oxygen supply
  - Abolish coronary artery spasm
  - Relieve causes of angina pectoris
- Drugs differ in degree of selectivity for coronary (and peripheral) vasodilation or decreased cardiac contractility
Angiotensin II Receptor Antagonists

• Newer class of antihypertensive agent
• Block renin-angiotensin-aldosterone system more completely than ACE inhibitors

Angiotensin II Receptor Antagonists

• Lower BP by selectively inhibiting actions of angiotensin II receptors that include
  – Vasoconstriction
  – Renal tubular sodium reabsorption
  – Aldosterone release
  – Stimulation of central and peripheral sympathetic activity
• Used for those who cannot deal with adverse effects of ACE inhibitors (e.g., dry cough)

Angiotensin II Receptor Antagonists

• Being studied for effectiveness in treating
  – Congestive heart failure
  – Diabetic nephropathy
  – Vascular diseases
Angiotensin II Receptor Antagonists

- Candesartan (Atacand)
- Irbesartan (Avapro)
- Losartan (Cozaar, Hyzaar)
- Telmisartan (Micardis)
- Valsartan (Diovan)

Antihemorrhheologic Agents

- Treat peripheral vascular disorders caused by pathological or physiological obstruction
- Improve blood flow, delivery of oxygen to ischemic tissues
  - Restore red blood cell flexibility to traverse narrow vessels
  - Lower blood viscosity
    - Pentoxifyline (Trental)
Lesson 13.6
Drugs that Affect Blood, Blood Components, and the Respiratory System

Learning Objective

• Outline drug actions and care considerations for a patient who is given drugs that affect the nervous, cardiovascular, respiratory, endocrine, and gastrointestinal systems.

Anticoagulants

• Platelets
  — Small cell fragments in blood
  — Provide initial step in normal repair of blood vessels
• Blood coagulation
  — Forms stable fibrin clot that entraps platelets, blood cells, and plasma
    • End result is blood clot or thrombus
  — Abnormal thrombus formation
    • Major cause of myocardial infarction, stroke
Anticoagulants

- Thrombosis formation
  - Can occur in both venous and arterial systems
  - In venous system
    - Pulmonary embolus
    - Deep vein thrombosis (DVT)

Thromboses Risk Factors

- Stasis
  - Reduced blood flow
  - Results from immobilization or venous insufficiency
  - Responsible for increased incidence of DVT in bedridden patients
- Localized trauma
  - May initiate clotting cascade
  - May cause arterial and venous thrombosis

Thromboses Risk Factors

- Hypercoagulability
  - Increased likelihood of blood to become abnormally thick
    - Increases formation of fibrin complexes in blood vessels
  - Cause of increased incidence of DVT in women who take birth control pills
  - Factor in clotting problems for familial thrombotic disorders
Arterial Thrombi

- Associated with
  - Atherosclerotic plaques
  - Hypertension
  - Turbulent blood flow
- Damage endothelial lining of blood vessels
- Damage to endothelium causes platelets to stick, aggregate in arterial system

Arterial Thrombi

- Made up mostly of platelets
- Involve chemical substances that contribute to coagulation process
  - In particular, fibrinogen and fibrin
- Cause MIs, strokes

Agents that Affect Blood Coagulation

- Antiplatelet agents
  - Interfere with platelet aggregation
  - Indications
    - Prophylactically for patients at risk of arterial clots
    - Patients with MI or stroke
    - Valvular heart disease
    - Valvular prostheses
    - Intracardiac shunts
Agents that Affect Blood Coagulation

• Antiplatelet agents
  – Aspirin
  – Dipyridamole (Persantine)
  – Clopidogrel (Plavix)
  – Ticlopidine (Ticlid)

• Anticoagulant agents
  – Prevent intravascular thrombosis
    • Decrease blood coagulability
  – Used to prevent postoperative thromboembolism
  – Used during hemodialysis, reperfusion therapy

• Preventive measure against future clot formation
  – No direct effect on blood clot already formed
  – No effect on ischemic tissue injured by inadequate blood supply as result of thrombus

• Side effect
  – Hemorrhage
  – Bleeding complications

• Warfarin (Coumadin)
• Heparin
Fibrinolytic Agents

• Dissolve clots after formation
  — Promote digestion of fibrin
• Indications
  — MI in certain groups of patients
  — Stroke
    • Reestablish blood flow
    • Prevent ischemia and tissue death
  — Acute pulmonary embolism
  — DVT
  — Peripheral arterial occlusion

Fibrinolytic Agents

• Used in prehospital setting in some areas of the United States
• Anistreplase (APSAC, Eminase)
• Alteplase (t-PA)

If fibrinolytics have the potential to dissolve clots and reverse the catastrophic effects of myocardial infarction and stroke, why aren’t they given to everyone suspected of having these conditions?
Fibrinolytic Agents

- Reteplase (Retavase)
- Streptokinase (Streptase)
- Tenecteplase (TNKase)

Antihemophilic Agents

- Hemophilia
  - Hereditary bleeding disorders
  - Lack factors needed for blood coagulation
  - Persistent and uncontrollable bleeding
    - Can occur after minor injury
    - Bleeding may occur into joints, urinary tract, CNS

Antihemophilic Agents

- Hemophilia
  - Hemophilia A
    - Classic form of hemophilia
    - Caused by deficiency of factor VIII
  - Hemophilia B
    - Results from deficiency in factor IX complex
Antihemophilic Agents

- Hemophilia
  - Replacement therapy of missing clotting factor can be effective management
    - Factor VIII (Factorate)
    - Factor IX (Konyne)
    - Antiinhibitor coagulant complex (Autoplex)

Homostatic Agents

- Hasten clot formation
  - Reduces bleeding
- Systemic hemostatic agents
  - Control rapid blood loss after surgery by inhibiting fibrinolysis
    - Anicar
    - Cyklokapron

Homostatic Agents

- Topical hemostatic agents
  - Control capillary bleeding during surgical, dental procedures
    - Gelfoam
    - Novacell
- Used in prehospital setting, combat medical care
Homostatic Agents

- Celox, WoundStat, and QuickClot
  - Absorb plasma from blood
  - Reduce clotting times
- Chitosan
  - Substance derived from shrimp shells
  - Adheres to, seals wounds

Blood, Blood Components

- Healthy body maintains normal balance of blood, its components
  - Illness and injury affect balance
    - Hemorrhage
    - Burns
    - Dehydration

Blood, Blood Components

- Require replacement therapy
  - Whole blood
    - Red blood cells and plasma
    - Rarely used
  - Packed red blood cells
    - Red blood cells without plasma
  - Fresh-frozen plasma
    - Plasma without red blood cells or platelets
Blood, Blood Components

- Require replacement therapy
  - Plasma expanders (dextran)
  - Platelets
  - Cryoprecipitate
    - Multiple clotting factors
  - Fibrinogen
    - Found in fresh frozen plasma (FFP), cryoprecipitate
  - Albumin
  - Gamma globulins
    - Antibodies

Antihyperlipidemic Drugs

- Hyperlipidemia
  - Excess of lipids in plasma
  - Several types occur
  - Associated with elevated levels of cholesterol, triglycerides
  - Thought to play a role in the development of atherosclerosis
  - Used along with diet, exercise to control serum lipid levels

Respiratory System Drugs

- Includes all structures involved in exchange of oxygen and carbon dioxide
  - Narrowing of any portion of respiratory tract indication for drug therapy
  - Emergencies involving respiratory system usually caused by reversible conditions
    - Asthma
    - Emphysema with infection
    - Foreign body airway obstruction
Respiratory System Drugs

• Smooth muscle fibers line tracheobronchial tree
  — Directly influence diameter of airways
  — Bronchial smooth muscle tone is maintained by impulses from autonomic nervous system
  — Parasympathetic fibers from vagus nerve stimulate bronchial smooth muscle through release of acetylcholine
    • Interacts with muscarinic receptors on membranes of cell
    • Produces bronchoconstriction

Respiratory System Drugs

• Sympathetic fibers mainly affect beta2 receptors in lungs
  — Release epinephrine from adrenal medulla
  — Release norepinephrine from peripheral sympathetic nerves
  — Epinephrine
    • Reaches lungs by way of circulatory system
    • Interacts with beta2 receptors to produce smooth muscle relaxation, bronchodilation
    • Beta2 receptor plays dominant role in bronchial muscle tone

Bronchodilators

• Primary treatment for obstructive pulmonary disease
  — Asthma
  — Chronic bronchitis
  — Emphysema
• Many drugs administered by inhalation via nebulizer or pressure cartridge
Bronchodilators

• Sympathomimetic drugs
  – Grouped according to effects on receptors
    • Nonselective adrenergic drugs have alpha, beta_1 (cardiac), beta_2 (respiratory) activity
    • Nonselective beta adrenergic drugs have beta_1 and beta_2 effects
    • Selective beta_2 receptor drugs act primarily on beta_2 receptors in lungs (bronchial smooth muscle)

Bronchodilators

• Nonselective adrenergic drugs
  – Stimulate alpha and beta receptors
  – Alpha activity
    • Lessens vasoconstriction to reduce mucosal edema
  – Beta_2 activity
    • Produces bronchodilation and vasodilation
  – Undesirable beta_1 effects
    • Increased heart rate
    • Increased force of contraction

Bronchodilators

• Nonselective adrenergic drugs
  – Undesirable beta_2 effects
    • Muscle tremors
    • CNS stimulation
  – Nonprescription epinephrine inhalation aerosol
    • Bronkaid Mist
    • Primatene Mist
  – Epinephrine inhalation solution
    • Adrenalin
Bronchodilators

• Nonselective adrenergic drugs
  – Racemic epinephrine inhalation solution
    • MicroNephrin
    • Manages upper airway swelling associated with croup

Bronchodilators

• Nonselective beta adrenergic drugs
  – Not selective for beta₂ receptors
  – Wide range of effects
  – No longer recommended for asthma management
  – Epinephrine
    • Adrenalin
    • Asmolin
  – Ephedrine
    • Ephed II

Bronchodilators

• Nonselective beta adrenergic drugs
  – Ethynorepinephrine
    • Bronkephrine
    • Each of the above drugs has some alpha activity
  – Isoproterenol inhalation solution
    • Aerolone
    • Vapo-Iso
    • Isuprel
  – Isoproterenol inhalation aerosol
    • Isuprel Mistometer
    • Norisodrine Aerotrol
Bronchodilators

• Beta2 selective drugs
  - Lessen incidence of unwanted cardiac effects caused by beta, adrenergic agents
  - Patients with hypertension, cardiac disease, or diabetes can better tolerate this group of bronchodilators
    - Albuterol (Proventil, Ventolin)
    - Levalbuterol (Xopenex)
    - Pirbuterol (Maxair)
    - Bitolterol (Tornalate)
    - Salmeterol (Serevent)
    - Formoterol (Foradil aerolizer)
    - Isoetharine (Bronkosol)

• Xanthine derivatives
  - Caffeine
  - Theophylline
  - Theobromine
  - Relax smooth muscle, particularly bronchial smooth muscle
    - Stimulate cardiac muscle and CNS
    - Increase diaphragmatic contractility
    - Promote diuresis through increased renal perfusion

• Xanthine derivatives
  - Theophylline compounds
    - Action depends on concentration of theophylline
    - Active ingredient
    - Vary in absorption rate, therapeutic effects
    - Aminophylline (Amoline, Somophyllin, Theo-Dur, Aminophyllin)
    - Dyphylline (Dilor, Droxine, Lufyllin)
    - Theophylline (Bronkodyl, Elixophyllin, Somophyllin-T)
Bronchodilators

- Xanthine derivatives
  - Theophylline compounds
    - Not considered first-line drug in treatment of acute reactive airway disease (e.g., asthma)
    - High side-effect profile
    - Slow onset of action

Other Respiratory Drugs

- Prophylactic asthmatic agents
  - Cromolyn sodium (Intal, sodium cromoglycate)
- Aerosol corticosteroid agents
  - Beclomethasone dipropionate (Vanceril inhaler, Beclovent)
  - Dexamethasone (Decadron)

Other Respiratory Drugs

- Antileukotrienes
  - Montelukast (Singular)
  - Zafirlukast (Accolate)
- Muscarinic antagonists (anticholinergics)
  - Ipratropium (Atrovent)
  - Glycopyrrolate (Robinul)
Other Respiratory Drugs

- Reduce allergic or inflammatory response to variety of stimuli
- Have effect on bronchial smooth muscle
- In acute care setting, IV steroids may be given to decrease inflammatory response, improve airflow

Mucokinetic Drugs

- Move respiratory secretions along tracheobronchial tree
- Alter consistency of secretions
  - Can be removed from body more easily
- Used for COPD

Mucokinetic Drugs

- Help clear respiratory passages
- Improve ciliary activity in airways
- Diluents
  - Water
  - Saline
  - Solution
Mucokinetic Drugs

- Aerosols
- Mucolytic drugs or expectorants
  - Mucomyst

Respiratory Agents

- Oxygen
  - Mainly used to treat hypoxia, hypoxemia
  - Colorless gas
  - Odorless gas
  - Tasteless gas
  - Essential for sustaining life

Respiratory Agents

- Direct respiratory stimulants
  - Analeptics
  - Act directly on medullary center of brain to increase rate, depth of respirations
  - Inferior to mechanical ventilatory measures, counteract drug-induced respiratory depression caused by anesthetics
  - Doxapram (Dopram)
Respiratory Agents

• Reflex respiratory stimulants
  – Spirits of ammonia
    • Given by inhalation
    • Act as stimulant
    • Noxious vapor sometimes used in fainting cases
    • Irritate sensory nerve receptors in throat, stomach
    • Nerve receptors send afferent messages to control centers of brain to stimulate respiration

Respiratory Agents

• Respiratory depressants
  – Opiates
  – Barbiturates
  – Side effect is respiratory depression
  – Seldom given to intentionally inhibit rate, depth of respiration

Respiratory Agents

• Cough suppressants
  – Cough
    • Protective reflex to expel harmful irritants
    • Productive when removing irritants or secretions from airway
    • Nonproductive when dry and irritating
    • When prolonged or secondary to underlying disorder, treatment with antitussive drugs may be indicated
Antihistamines

- Histamine
  - Chemical mediator found in almost all body tissues
  - Concentration is highest in skin, lungs, GI tract
  - Body releases when exposed to an antigen
    - Increased localized blood flow
    - Increased capillary permeability
    - Swelling of tissues

Antihistamines

- Histamine
  - Produces contractile action on bronchial smooth muscle
  - Allergic responses
    - Angioedema
    - Eczema
    - Rhinitis
    - Urticaria
    - Asthma
    - Systemic effects may result in anaphylaxis

Antihistamines

- Compete with histamine for receptor sites
  - Prevent physiological action of histamine
- Types of histamine receptors
  - $H_1$ receptors act mainly on blood vessels and bronchioles
  - $H_2$ receptors act mainly on gastrointestinal tract
Antihistamines

• Anticholinergic or atropine-like action
  – Tachycardia
  – Constipation
  – Drowsiness
  – Sedation
  – Inhibition of secretions
• Most have local anesthetic effect
  – May soothe skin irritations caused by allergic reaction

Antihistamines

• Clinical use
  – Allergic reactions
  – Motion sickness
  – Sedative
  – Antiemetic
• Dimenhydrinate
  – Dramamine
• Diphenhydramine
  – Benadryl

Antihistamines

• Hydroxyzine
  – Vistaril
• Promethazine
  – Phenergan
• Newer H1 receptor antagonists
  – Loratadine (Claritin)
  – Cetirizine (Zyrtec)
  – Fexofenadine (Allegra)
Serotonin

- Naturally occurring vasoconstrictor material
- Found in platelets, cells of brain, intestine
- Several pharmacological actions exerted on various smooth muscles, nerves

Serotonin

- Not administered as drug
  - Has major influence on other drugs, some disease states
- Helps repair damaged blood vessels

Serotonin

- Stimulates smooth muscle contraction
- Acts as neurotransmitter in CNS
  - Effect on sleep, pain perception, some mental illnesses
Antiserotonins

- Serotonin antagonists
- Inhibit responses to serotonin
  - Block smooth muscle contraction and vasoconstriction
  - Inhibit action of serotonin in brain
- Some used to treat vascular headaches, allergic disorders

Antiserotonins

- Cyproheptadine
  - Periactin
- Lysergic acid diethylamide
  - LSD
- Methysergide maleate
  - Sansert

Lesson 13.7
Drugs that Affect the GI and Endocrine Systems and the Eye and Ear
Learning Objective

- Outline drug actions and care considerations for a patient who is given drugs that affect the nervous, cardiovascular, respiratory, endocrine, and gastrointestinal systems.

GI System Drugs

- Components
  - Digestive tract
  - Biliary system
  - Pancreas

- Primary function
  - Provide body with water, electrolytes, other nutrients used by cells

- Drug therapy divided into groups
  - Drugs that affect stomach
  - Drugs that affect lower GI tract
GI System Drugs

• Drugs that affect stomach
  – Stomach conditions
    • Hyperacidity
    • Hypoacidity
    • Ulcer disease
    • Nausea
    • Vomiting
    • Hypermotility

GI System Drugs

• Antacids
  – Buffer or neutralize hydrochloric acid
  – Prescribed for symptom relief of hyperacidity
    • Peptic ulcer
    • Gastritis
    • Esophagitis
    • Heartburn
    • Hiatal hernia
  – Common over-the-counter antacids
    • Alka-Seltzer, Gaviscon, Rolaid

GI System Drugs

• Antiflatulents
  – Prevent formation of gas in GI tract
    • Gas retention is common with
      – Diverticulitis
      – Ulcer disease
      – Spastic or irritable colon
  – Sometimes used along with antacids
  – Simethicone (Mylicone)
GI System Drugs

- Digestants
  - Promote digestion in GI tract
  - Release small amounts of digestive enzymes in small intestine
  - Pancreatin (Creon)
  - Pancrelipase (Pancrease)

Emetics and Antiemetics

- Vomiting
  - Involuntary action coordinated by emetic center of medulla
  - May be initiated through the CNS
    - Secondary reaction to emotion, pain, disequilibrium
    - Through irritation of mucosa of GI tract or bowel
    - Through stimulation from chemoreceptor trigger zone of medulla by circulating drugs and toxins

- Emetics
  - Induce vomiting
  - Rarely administered today as part of treatment for drug overdoses, poisonings
  - Apomorphine
  - Syrup of ipecac
Emetics and Antiemetics

- Antiemetics
  - Drugs used to treat nausea, vomiting include antagonists of
    - Histamine
    - Acetylcholine
    - Dopamine
    - Other drugs
  - Work best when given before nausea, vomiting have begun

Emetics and Antiemetics

- Antiemetics
  - Scopolamine (Transderm-Scôp)
  - Dimenhydrinate (Dramamine)
  - Diphenhydramine (Benadryl)
  - Hydroxyzine (Vistaril)
  - Meclizine (Antivert)
  - Promethazine (Phenergan)
  - Prochlorperazine (Compazine)
  - Ondansetron (Zofran)

Cytoprotective Agents

- Protect cells from damage
- Treat peptic ulcer disease by protecting gastric mucosa
- Sucralfate (Carafate)
- Misoprostol (Cytotec)
H$_2$ Receptor Antagonists

- Histamine action mediated through H$_2$ receptors
  - Associated with gastric acid secretion
  - H$_2$ receptor antagonists block H$_2$ receptors
    - Reduce volume of gastric acid secretion and its acid content
    - Cimetidine (Tagamet)
    - Ranitidine (Zantac)
    - Famotidine (Pepcid)

Proton Pump Inhibitors

- Indications
  - Symptomatic gastroesophageal reflux disease
  - Short-term treatment of erosive esophagitis
  - Maintenance of erosive esophagitis healing
  - Some agents also approved for use with antibiotics to treat *Helicobacter pylori* infection

Proton Pump Inhibitors

- Proton pump
  - Potassium adenosine triphosphate enzyme system
  - Final pathway for secretion of hydrochloric acid by parietal cells of stomach
Proton Pump Inhibitors

- Decrease hydrochloric acid secretion
  - Inhibit actions of parietal cells
  - Gastric pH of stomach altered
  - Esomeprazole (Nexium)
  - Lansoprazole (Prevacid)
  - Omeprazole (Prilosec)
  - Pantoprazole (Protonix)
  - Rabeprazole (AciPhex)

Lower GI Tract Drugs

- Laxatives
  - Produce defecation
  - Evacuate bowel, soften hardened stool for easier passage

Lower GI Tract Drugs

- Laxatives
  - Indications
    - Constipation
    - Neurological diseases
    - Pregnancy
    - Rectal disorders
    - Drug poisoning
    - Surgery and endoscopic examination
Lower GI Tract Drugs

- Laxatives
  - Saline laxatives
    - Epsom salt
    - Milk of Magnesia
  - Stimulant laxatives
    - Dulcolax
    - Castor oil
    - Ex-Lax

- Bulk-forming laxatives
  - Mitrolan
  - Metamucil

- Lubricant laxatives
  - Mineral oil

- Fecal moistening agents
  - Colace
  - Glycerin suppositories

- Those used for bowel evacuation
  - GoLYTELY
  - Chronulac

- Regular/excessive use common in older adults, those with eating disorders
  - Abuse may result in permanent bowel damage, electrolyte imbalance
Lower GI Tract Drugs

- Antidiarrheal drugs
  - Reduce abnormal frequency of bowel evacuation
  - Common causes of acute, chronic diarrhea
    - Bacterial or viral invasion
    - Drugs
    - Diet
    - Numerous disease states

Lower GI Tract Drugs

- Antidiarrheal drugs
  - Adsorbents
    - Bismuth subsalicylate
    - Pepto-bismol
  - Anticholinergics
    - Donnatal

Lower GI Tract Drugs

- Antidiarrheal drugs
  - Opiates
    - Paregoric
    - Codeine
  - Other agents
    - Diphenoxylate (Lomotil)
    - Loperamide (Imodium)
Antiglaucoma Agents

• Glaucoma
  – Eye disease
  – Pressure of fluid in eye is abnormally high
  – Pressure causes compression or obstruction of small internal blood vessels of eye, fibers of optic nerve, or both
    • Causes nerve fiber destruction and partial/complete vision loss

Antiglaucoma Agents

• Glaucoma
  – Common eye disorder in persons over age 60
    • Responsible for 15% of blindness in adults in the United States
  – Agents include cholinergic and anticholinesterase drugs
    • Dilate pupil of eye

You are caring for an older adult patient who had mydriatic eye drops instilled by an ophthalmologist. If you didn’t know this history, what might you consider after your physical exam of this patient?
Antiglaucoma Agents

- Pilocarpine
  - Constricts pupil
  - Slows secretion of aqueous fluid
- Acetazolamide
  - If drug therapies fail, surgery may be indicated
    - If diagnosed early, drugs can control condition for a lifetime
    - Testing recommended every 2 years after age 35

Drugs that Affect the Eye

- Mydriatic and cycloplegic agents
  - Applied topically
  - Cause dilation of pupils, paralysis of accommodation to light
  - Used to treat inflammation, relieve ocular pain by putting eye to rest
  - Used during routine eye examinations, in ocular surgery
  - Atropine ophthalmic solution

Drugs that Affect the Eye

- Mydriatic and cycloplegic agents
  - Cyclopentolate hydrochloride ophthalmic solution
    - Cyclogyrl
  - Homatropine ophthalmic solution
    - Isopto Homatropine
  - Epinephrine
  - Oxymetazoline
    - Ocuclear
Antiinfective/Antiinflammatory Agents

- Treat eye conditions
  - Conjunctivitis
  - Sty
  - Keratitis
    - Corneal inflammation caused by bacterial infection

Antiinfective/Antiinflammatory Agents

- Bacitracin (Baciquent)
- Chloramphenicol (Chloroptic)
- Erythromycin (Ilotycin)
- Natamycin (Natacyn)

Topical Anesthetic Agents

- Local anesthetics
- Prevent pain in surgical procedures, eye examinations
- Used in treatment of some eye injuries
  - Corneal abrasion
Topical Anesthetic Agents

- Rapid onset
  - Within 20 seconds
  - Last 15 to 20 minutes
- Proparacaine
  - Ophthaine, Alcaine
- Tetracaine
  - Ak-T-Caine
  - Pontocaine

Topical Anesthetic Agents

- Artificial tear solutions
- Lubricants
- Irrigation solutions
- Antiallergic agents
  - Relieves itching, tearing, redness

Drugs that Affect the Ear

- Antibiotics used to treat infections
  - Chloramphenicol (Chloromycetin Otic)
  - Gentamicin sulfate (Garamycin)
- Steroid/antibiotic combinations used to treat superficial bacterial infections
  - Neomycin sulfate/polymyxin b sulfate/hydrocortisone (Cortisporin Otic)
  - Neomycin/polymyxin b sulfate/hydrocortisone (Coly-Mycin S Otic)
Drugs that Affect the Ear

• Miscellaneous preparations used to treat ear wax accumulation, inflammation, pain, fungal infections, other minor conditions
  – Boric acid in isopropyl alcohol
    • Aurocaine 2
  – Triethanolamine with chlorobutanol in propylene glycol
    • Cerumenex

Endocrine System Drugs

• Endocrine system
  – Controls, integrates body functions
  – Information from various parts of body carried via blood-borne hormones to distant sites

Endocrine System Drugs

• Hormones are natural chemical substances
  – Act after secreted into bloodstream from endocrine glands
  – Glands include
    • Anterior and posterior pituitary
    • Thyroid
    • Parathyroid
    • Adrenal glands
    • Thymus
    • Pancreas
    • Testes
    • Ovaries
Endocrine System Drugs

- Endocrine gland hormones work together to regulate vital processes, including:
  - Secretory, motor activities of digestive tract
  - Energy production
  - Composition, volume of extracellular fluid
  - Adaptation
    - Acclimatization
    - Immunity
  - Growth, development
  - Reproduction, lactation

Pituitary Gland Drugs

- Anterior pituitary gland drugs
  - Used to treat growth failure in children
  - Somatren (Protropin)
  - Somatropin (Humatrope)
- Posterior pituitary gland drugs
  - Used to treat symptoms of diabetes insipidus
  - Vasopressin (Pitressin)

Thyroid and Parathyroid Gland Drugs

- Thyroid hormone
  - Controls rate of metabolic processes
  - Required for normal growth and development
- Parathyroid hormone
  - Regulates level of ionized calcium in blood
  - Releases calcium from bone
  - Absorbs calcium from intestine
  - Controls rate of calcium excretion by kidneys
Thyroid and Parathyroid Gland Drugs

• Disorders of thyroid gland
  – Goiter
    • Enlargement of thyroid gland
  – Hypothyroidism
    • Thyroid hormone deficiency
  – Hyperthyroidism
    • Thyroid hormone excess

• Disorders of parathyroid
  – Hypoparathyroidism
  – Hyperparathyroidism

• Thyroid drugs
  – Treat hypothyroidism
  • Thyroid
  • Iodine products
    • Levothyroxine (Synthroid, Levoxyl)

• Parathyroid drugs
  – Treat hyperparathyroidism
  • Vitamin D
    • Calcium supplements
Adrenal Cortex Drugs

• Adrenal cortex secretes three major classes of steroid hormones
  – Glucocorticoids (cortisol)
    • Raise blood glucose
    • Deplete tissue proteins
    • Suppress inflammatory reaction
    • Betamethasone (Celestone)
    • Dexamethasone (Decadron)
    • Methylprednisolone (Solu-Medrol)
    • Triamcinolone (Aristocort)
  – Mineralocorticoids (primarily aldosterone)
    • Regulate electrolyte and water
    • Desoxycorticosterone acetate (Doca)
    • Fludrocortisone (Florinef)
  – Sex hormones
    • Estrogen, progesterone, testosterone
    • Produced in small amounts by men and women
    • Have little physiological effect under normal circumstances

• Adrenal cortex secretes three major classes of steroid hormones
  – Adrenal steroid inhibitors
    • Aminogluthethimide (Cytadren)
    • Metyrapone (Metopirone)
Adrenal Cortex Drugs

- Two disorders of adrenal cortex
  - Addison’s disease (adrenal cortical hypofunction)
  - Cushing’s disease (adrenal cortical hyperfunction)

Drugs that Affect the Pancreas

- Pancreas
  - Exocrine and endocrine gland
  - Exocrine portion
    - Secretes hormones into ducts
    - Provides digestive juices to small intestine
  - Endocrine portion
    - Consists of pancreatic islets (islets of Langerhans)
    - Produce hormones that directly enter the circulatory system

Drugs that Affect the Pancreas

- Hormones of pancreas
  - Regulate concentration of certain nutrients in circulatory system
  - Pancreas secretes two major hormones
    - Insulin
    - Glucagon
Drugs that Affect the Pancreas

- Hormones of pancreas
  - Insulin
    - Primary hormone that regulates glucose metabolism
    - Increases ability of liver, adipose tissue, muscle to take up and use glucose
    - Glucose not immediately needed for energy is stored in skeletal muscle, liver, other tissues
    - Stored form of glucose is glycogen

Drugs that Affect the Pancreas

- Hormones of pancreas
  - Glucagon
    - Mainly influences liver
    - Has some effect on skeletal muscle and adipose tissue
    - Stimulates liver to break down glycogen so glucose is released into blood
    - Inhibits uptake of glucose by muscle, fat cells

Drugs that Affect the Pancreas

- Hormones of pancreas
  - Balancing action protects body from hyperglycemia and hypoglycemia
    - Important when considering metabolic problems that can occur in diabetes mellitus
Lesson 13.8
Drugs that Affect the Reproductive and Immunological Systems, Used in Neoplastic and Infectious Diseases

Learning Objective

• Outline drug actions and care considerations for a patient who is given drugs that affect the nervous, cardiovascular, respiratory, endocrine, and gastrointestinal systems.

Reproductive System

• Drugs that affect the female reproductive system
  – Hormones
  – Oral contraceptives
  – Ovulatory stimulants
  – Infertility drugs
Reproductive System

- Drugs that affect the female reproductive system
  - Female sex hormones
  - Hormones secreted by ovary
    - Estrogen
    - Progesterone
  - Indications for supplemental estrogen
    - Estrogen deficiency or replacement
    - Treatment of breast cancer
    - Prophylaxis for osteoporosis in postmenopausal women

Reproductive System

- Drugs that affect the female reproductive system
  - Indications for progesterone (and synthetic progestins)
    - Hormonal imbalance
    - Endometriosis
    - Specific cancers
    - Prevent pregnancy when used properly

Female Reproductive System

- Oral contraceptives
  - Most effective form of birth control
  - "The pill"
  - Combination of estrogen and progesterone
    - Suppression of ovulation
  - Several types, combinations available
    - All nearly 100% effective when taken properly
Female Reproductive System

- Ovulatory stimulants, infertility drugs
  - Anovulation
    - Absence of ovulation
    - May be pathological in women with abnormal bleeding, infertility
  - Sometimes treated with
    - Gonadotropins
    - Thyroid preparations
    - Estrogen
    - Synthetic agents

Male Reproductive System

- Drugs that affect the male reproductive system
  - Testosterone
    - Male sex hormone
    - Adequate amounts needed for normal development, maintenance of male sex characteristics

Male Reproductive System

- Drugs that affect the male reproductive system
  - Indications for testosterone therapy
    - Hormone deficiency (testicular failure)
    - Impotence
    - Delayed puberty
    - Female breast cancer
    - Anemia
Male Reproductive System

- Drugs that affect the male reproductive system
  - Dosage, length of therapy depend on
    - Diagnosis
    - Patient’s age
    - Intensity of side effects/adverse reactions
  - Methyltestosterone (Metandren)

Sexual Behavior Drugs

- Factors affecting sexual drive (libido)
  - Psychological
  - Social
  - Physiological
  - Combination

Sexual Behavior Drugs

- Drugs that impair libido, sexual gratification
  - Some drugs interfere with nervous system mechanisms responsible for sexual arousal
    - Antihypertensives
    - Antihistamines
    - Antispasmodics
    - Sedatives and tranquilizers
    - Antidepressants
    - Alcohol
    - Barbiturates
Sexual Behavior Drugs

- Drugs that enhance libido, sexual gratification
  - Patient may change medicines (under physician supervision) to avoid drug-induced sexual dysfunction
    - May be prescribed drugs to enhance libido and sexual gratification
    - Levodopa (L-Dopa)
    - Tadalafil (Cialis)
    - Vardenifil (Levitra)
    - Sildenafil (Viagra)

Antineoplastic Agents

- Used in cancer chemotherapy
  - Prevent increase of malignant cells
  - Do not directly kill tumor cells
    - Interfere with cell reproduction or replication through various mechanisms

Antineoplastic Agents

- Agents are nonselective
  - Injurious to all cells in body
  - Side effects
    - Infection
    - Hemorrhage
    - Nausea
    - Vomiting
    - Changes in bowel habits
Antineoplastic Agents

- Agents are nonselective
  - Short-term toxicity from agents may affect
    - Pulmonary system
    - Cardiovascular system
    - Renal system
    - Integumentary system
- Prehospital care
  - Supportive
  - Providing comfort measures, emotional support

Antibiotics

- Treat local or systemic infection
  - Kill or suppress growth of microorganisms
    - Disrupt bacterial cell wall
    - Disturb functions of cell membrane
    - Interfere with metabolic functions of cell

Antibiotics

- Drug groups
  - Penicillins
  - Cephalosporins
  - Macrolide antibiotics
  - Tetracyclines
  - Fluoroquinolones
  - Miscellaneous agents
    - Metronidazole (Flagyl)
    - Spectinomycin (Trobicin)
Antibiotics

• More toxic to bacteria than they are to patient
  — Some may produce hypersensitivity
  • Can lead to fatal reaction if drug is given to sensitized patient

How can you help prevent the development of antibiotic-resistant strains of bacteria?

Antibiotics

• Penicillins
  — Active against gram-positive, some gram-negative bacteria
  — Treat many infections
  • Tonsillitis
  • Pharyngitis
  • Bronchitis
  • Pneumonia
Antibiotics

- Penicillins
  - Examples
    - Amoxicillin (Amoxil)
    - Ampicillin (Amcill)
    - Dicloxacillin (Dynapen)
    - Penicillin V Potassium (Pen-Vee K)
  - Can produce severe anaphylactic reactions

A person reports accidentally ingesting penicillin 5 minutes ago, forgetting that the last time he took it, he experienced hives and severe itching. What should you anticipate?

Antibiotics

- Cephalosporins (and related products)
  - Resemble penicillins
  - Active against gram-positive, gram-negative bacteria
  - Treat ear, throat, respiratory infections, urinary tract infections
    - Often caused by bacteria resistant to penicillin-type antibiotics
Antibiotics

- Cephalosporins (and related products)
  - Examples
    - Cefazolin (Ancef)
    - Cephalothin (Keflin)
    - Cephalexin (Keflex)
    - Cefotaxime (Claforan)
  - About 6% to 10% of people allergic to penicillins are also allergic to cephalosporins

Antibiotics

- Macrolide antibiotics
  - Treat infections of
    - Skin
    - Chest
    - Throat
    - Ears
  - Indications
    - Pertussis (whooping cough)
    - Legionnaires' disease
    - Pneumonia

Antibiotics

- Macrolide antibiotics
  - Examples
    - Eryc
    - EMycin
    - E.E.S. and Erythrocin
    - Azithromycin (Zithromax)
    - Clarithromycin (Biaxin)
Antibiotics

• Tetracyclines
  – Active against many gram-negative, gram-positive organisms (broad-spectrum)
  – Indications
    • Acne
    • Bronchitis
    • Syphilis
    • Gonorrhea
    • Certain pneumonia types

Antibiotics

• Tetracyclines
  – Examples
    • Demeclocycline (Declomycin)
    • Doxycycline (Vibramycin)
    • Tetracycline (Achromycin)
  – May discolor developing teeth
    • Usually are not prescribed for children under age 12 or pregnant women

Antibiotics

• Fluoroquinolones
  – Treatment of choice for some GI infections
    • Particularly severe food-borne illness caused by Campylobacter or Salmonella bacteria
  – Other indications
    • Urinary tract infections
    • Bone and joint infections
    • Some types of pneumonia
Antibiotics

- Fluoroquinolones
  - Examples
    - Ciprofloxacin (Cipro)
    - Gatifloxacin (Tequin)
    - Levofloxacin (Levaquin)

Antifungal Drugs

- Fungi
  - Harmlessly present at all times in body areas
    - Mouth
    - Skin
    - Intestines
    - Vagina
  - Prevented from multiplying through competition from bacteria

Antifungal Drugs

- Fungal infection causes
  - Long-term antibiotics use
  - Immunosuppressed as complication of illness
  - Corticosteroids or immunosuppressant drug use
- Fungal infections classified broadly
  - Superficial infections
  - Subcutaneous infections
  - Deep infections
Antifungal Drugs

• Examples
  – Tolnaftate (Tinactin)
  – Fluconazole (Diflucan)
  – Nystatin (Mycostatin)
• About 50 fungi species can cause illness, sometimes fatal disease

Antiviral Drugs

• Few effective drugs exist to treat minor viral infections
  – Due partly to relative delay in onset of symptoms of viral diseases
  • Makes drug therapy difficult once disease is established
  – Serious diseases
  • Influenza
  • Rabies
  • AIDS
  • Some cancers

Antiviral Drugs

• Examples
  – Acyclovir (Zovirax)
  – Valacyclovir (Valtrex)
  • Effective against herpes infection
  – Zidovudine (Retrovir, AZT, ZDV)
  – Lamivudine (Epivir)
  – Combination drug (Lamivudine)
  – Zidovudine (Combivir)
Protease Inhibitors

• Complete mechanism of action not understood
  – Appear to inhibit replication of retroviruses in acute and chronically infected cells

• Side effects, adverse reactions
  – Nausea, vomiting
  – Headache
  – Malaise
  – Fever
  – Flulike symptoms

Protease Inhibitors

• Examples
  – Indinavir (Crixivan)
  – Ritonavir (Norvir)
  – Saquinavir (Invirase)

Antimicrobial and Antiparasitic Drugs

• Treat atypical microbial infection and infection and disease caused by parasite and insect vector
  – Trichomoniasis
  – Malaria
Antiinflammatory Drugs

• Inflammation
  – Defense mechanism of body tissues in response to
    • Physical trauma
    • Foreign biological and chemical substances
    • Surgery
    • Radiation
    • Electricity

Antiinflammatory Drugs

• Inflammation
  – Regardless of event producing inflammation, response is similar
    • Chemical mediators released or activated
  – Cause vasodilation and increased blood flow
    • Brings phagocytes, other leukocytes to area
    • Prevents spread of infection by limiting infected site
    • Phagocytes clean area, damaged tissues are repaired

Antiinflammatory Drugs

• Inflammation
  – Local inflammation confined to specific area of body
    • Redness
    • Heat
    • Swelling
    • Pain
    • Loss of function
### Antiinflammatory Drugs

- **Inflammation**
  - Systemic inflammation occurs in many parts of body
  - Red bone marrow produces, releases large numbers of neutrophils
    - Promote phagocytosis
    - Pyrogens stimulate fever production
    - Increased vascular permeability in severe cases may result in decreased blood volume
  - Classified as analgesic-antipyretic drugs and nonsteroidal antiinflammatory drugs (NSAIDs)

### Analgesic-Antipyretic Drugs

- **Reduce fever**
  - Temperature-regulating mechanism of body located in hypothalamus
  - Normally, set point of hypothalamic center is about 98.6°F (37°C)
  - When inflammatory response occurs, endogenous pyrogens are released by phagocytic leukocytes, which produces fever

- **Reduction of fever**
  - Drugs work by reversing effect of pyrogen on hypothalamus
  - Set point of hypothalamus returned to normal
  - Analgesic effects of drugs act on peripheral pain receptors to block activation
**Analgesic-Antipyretic Drugs**

- Examples
  - Acetaminophen
    - Datril
    - Tylenol
    - Panadol
  - Aspirin/acetylsalicylic acid
    - A.S.A.
    - Aspergum
    - Bayer Aspirin

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**Analgesic-Antipyretic Drugs**

- Examples
  - Aspirin (buffered)
    - Aluprin
    - Bufferin
    - Alka-Seltzer

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**NSAIDs**

- Nonsteroidal antiinflammatory drugs
  - Aspirin is prototype
  - New drugs developed
    - Analgesic
    - Antipyretic
    - Antiinflammatory
NSAIDs

- Indications
  - Various inflammatory conditions
  - For those who cannot tolerate aspirin
  - Painful joint disorders (with or without inflammation)
    - Osteoarthritis
    - Low back pain
    - Gout

- Aspirin, other NSAIDs may decrease platelet activity
  - Could result in GI bleeding
  - Long-term use linked to increased risk for heart attack, stroke
  - Inhibit specific enzymes so prostaglandins are not formed

- Examples
  - Aspirin
    - Bayer timed-release
    - Bufferin
  - Diflunisal (Dolobid)
  - Ibuprofen
    - Advil
    - Motrin
    - Nuprin
  - Indomethacin (Indocin)
NSAIDs

- Examples
  - Naproxen
    - Anaprox
    - Aleve
    - Naproyn
  - Sulindac (Clinoril)
  - Ketorolac (Toradol)
  - Cyclooxygenase-2 inhibitors (cox-2 inhibitors)
    - Celecoxib (Celebrex)
    - Valdecoxib (Bextra)

Immunological System Drugs

- Composed of cells, organs
- Defend body against invasion by foreign substances
- Organs, tissues
  - Spleen
  - Tonsils
  - Lymph nodes
  - Thymus
Immunomodulating Agents

• Increase efficiency of immune system
• Activate immune defenses or modify biological response to unwanted stimulus

Immunomodulating Agents

• Include vaccines that protect against specific infectious agents
  – Interferons
    • Treat viral infections, certain cancers
  – Zidovudine (AZT, Retrovir)
    • Treat AIDS
• Some enhance ability of vaccine to stimulate immune system
  – Thus added to vaccine

Serums and Vaccines

• Serum
  – Clear fluid that separates from blood when blood clots
  – Contains salts, glucose, other proteins
  – Includes antibodies formed by immune system
    • Fight against infection
  – Serum from blood infected with microorganism usually contains antibodies
    • May protect against that microorganism if serum is injected into someone else
    • Forms basis for passive immunization
Serums and Vaccines

• Vaccines
  – Contain killed/modified microorganisms (live attenuated organisms) that usually do not cause disease
  – Given to produce specific immunity
  – May be for disease-causing bacterial toxin, virus, bacterium (active immunization)
  – Infectious agent may invade body at later time
  – Sensitized immune system quickly produces antibodies to destroy agent or toxin it produces

Serums and Vaccines

• Vaccines
  – Examples of live attenuated vaccines
    • Measles
    • Mumps
    • Rubella
    • Yellow fever
    • Polio

Serums and Vaccines

• Vaccines
  – Vaccines containing inactivated bacterial toxins
    • Diphtheria
    • Tetanus
Serums and Vaccines

- Vaccines
  - Vaccines containing killed organisms
    - Cholera
    - Typhoid fever
    - Pertussis
    - Rabies
    - Viral hepatitis B
    - Influenza
    - Salk injected polio

Summary

- A drug is any substance taken by mouth; injected into a muscle, blood vessel, or cavity of the body; or applied topically to treat or prevent a disease or condition
- Drugs can be identified by four types of names
  - Include the chemical name; generic or nonproprietary name; trade, brand, or proprietary name; and official name

Summary

- The Drug Enforcement Agency is the sole legal drug enforcement body in United States
  - Other regulatory bodies or services include the FDA; Public Health Service; Federal Trade Commission; in Canada, Health Protection Branch of the Department of National Health and Welfare; and for international drug control, International Narcotics Control Board
Summary

• Drugs do not confer any new functions on a tissue or organ; they only modify existing functions
  – Drug that interacts with a receptor to stimulate a response is known as an agonist
  – Drug that attaches to a receptor but does not stimulate a response is called an antagonist
• Pharmacokinetics is the study of how the body handles a drug over a period of time

Summary

• Degree to which drugs attain pharmacological activity depends partly on the rate and extent to which they are absorbed
  – Absorption depends on ability of drug to cross cell membrane
  – Rate and extent of absorption depend on nature of cell membrane drug must cross, blood flow to site of administration, solubility of drug, pH of drug environment, drug concentration, and drug dosage form

Summary

• Route of drug administration influences drug absorption
  – Can be classified as enteral, parenteral, pulmonary, and topical
Summary

• Distribution is the transport of a drug through the bloodstream to various tissues of the body and ultimately to its site of action
  – After absorption and distribution, the body eliminates most drugs
  – Body first biotransforms the drug and then excretes the drug
    • Kidney is the primary organ for excretion
    • Intestine, lungs, and mammary, sweat, and salivary glands also may be involved

Summary

• Blood-brain barrier and placenta are barriers to distribution of some drugs
• Many factors can alter the response to drug therapy, including age, body mass, gender, pathological state, time of administration, genetic factors, and psychological factors

Summary

• Most drug actions are thought to result from a chemical interaction
  – This interaction is between the drug and various receptors throughout the body
  – Most common form of drug action is the drug–receptor interaction
Summary

• Many variables can influence drug interactions, including intestinal absorption, competition for plasma–protein binding, biotransformation, action at the receptor site, renal excretion, and alteration of electrolyte balance

• Paramedics are held responsible for the safe and effective administration of drugs
  — Responsible for each drug they provide to a patient
    • Legally, morally, and ethically responsible

Summary

• Elements of drug profile the paramedic should know include drug names, classification, mechanism of action, indications, pharmacokinetics, side/adverse effects, dose, route of administration, contraindication, special considerations, and storage requirements

• Alterations in drug administration may be needed when caring for children, pregnant patients, or older adults

Summary

• Autonomic drugs mimic or block effects of sympathetic and parasympathetic divisions of the autonomic nervous system
  — Classified into four groups: cholinergic (parasympathomimetic) drugs, cholinergic blocking (parasympatholytic) drugs, adrenergic (sympathomimetic) drugs, and adrenergic blocking (sympatholytic) drugs
Summary

• Narcotic analgesics relieve pain
• Narcotic antagonists reverse the narcotic effects of some analgesics
• Nonnarcotic analgesics interfere with local mediators released when tissue is damaged in the periphery of the body
  – These mediators stimulate nerve endings and cause pain

Summary

• Anesthetic drugs are CNS depressants that have a reversible effect on nervous tissue
• Antianxiety agents are used to reduce feelings of apprehension, nervousness, worry, or fearfulness
• Sedatives and hypnotics are drugs that depress the CNS
  – Produce calming effect and help induce sleep
  – Alcohol is a general CNS depressant that can produce sedation, sleep, and anesthesia

Summary

• Anticonvulsant drugs are used to treat seizure disorders
  – Most notably they treat epilepsy
Summary

• All CNS stimulants work to increase excitability
  – They do this by blocking activity of inhibitory neurons or their respective neurotransmitters or by enhancing the production of the excitatory neurotransmitters
• Psychotherapeutic drugs include antipsychotic agents, antidepressants, and lithium
  – These drugs are used to treat psychoses and affective disorders, especially schizophrenia, depression, and mania

Summary

• Movement disorders such as Parkinson’s disease can result from an imbalance of dopamine and acetylcholine
  – Drugs that inhibit or block acetylcholine are referred to as anticholinergic
  – Three classes of drugs affect brain dopamine: those that release dopamine, those that increase brain levels of dopamine, and dopaminergic agonists
• Skeletal muscle relaxants can be classified as central acting, direct acting, and neuromuscular blockers

Summary

• Cardiac drugs are classified by their effects on specialized cardiac tissues
  – Cardiac glycosides are used to treat congestive heart failure and certain tachycardias
  – Antidyssrhythmic drugs are used to treat and prevent disorders of cardiac rhythm
Summary

• Cardiac drugs are classified by their effects on specialized cardiac tissues
  – Pharmacological agents that suppress dysrhythmias may do so by direct action on the cardiac cell membrane (lidocaine), by indirect action that affects the cell (propranolol), or both
  • Four classes of antidysrhythmic drugs are sodium channel blockers, beta blockers, potassium channel blockers, and calcium channel blockers

Summary

• Antihypertensive drugs used to reduce BP are classified into major categories: diuretics, sympathetic blocking agents (sympatholytic drugs), vasodilators, calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors, and angiotensin II receptor antagonists

Summary

• Antihemorrheologic agents are used to treat peripheral vascular disorders
  – Caused by pathological or physiological obstruction (e.g., arteriosclerosis)
  – These agents improve blood flow to ischemic tissues
Summary

• Drugs that affect blood coagulation may be classified as antiplatelet, anticoagulant, or fibrinolytic agents
  — Drugs that interfere with platelet aggregation are known as antiplatelet or antithrombic drugs
  — Anticoagulant drug therapy is designed to prevent intravascular thrombosis
    • Decreases blood coagulability
  — Fibrinolytic drugs dissolve clots after their formation
    • Work by promoting the digestion of fibrin

Summary

• Hemophilia is a group of hereditary bleeding disorders
  — Involve a deficiency of one of the factors needed for the coagulation of blood
  — Replacing the missing clotting factor can help manage hemophilia

Summary

• Hemostatic agents speed up clot formation, thus reducing bleeding
  — Systemic hemostatic agents are used to control blood loss after surgery
    • Work by inhibiting the breakdown of fibrin
  — Topical hemostatic agents are used to control capillary bleeding
    • Used during surgical and dental procedures
Summary

• Treatment of choice in managing loss of blood or blood components is to replace deficient blood component
  – Replacement therapy may include transfusing whole blood (rare), packed red blood cells, fresh-frozen plasma, plasma expanders, platelets, cryoprecipitate, fibrinogen, albumin, or gamma globulins
• Antihyperlipidemic drugs sometimes are used along with diet and exercise to control serum lipid levels, which may include high cholesterol and triglycerides

Summary

• Bronchodilator drugs are the primary form of treatment for obstructive pulmonary disease such as asthma, chronic bronchitis, and emphysema
  – May be classified as sympathomimetic drugs and xanthine derivatives
• Mucokinetic drugs are used to move respiratory secretions, excessive mucus, and sputum along the tracheobronchial tree

Summary

• Oxygen is used chiefly to treat hypoxia and hypoxemia
• Direct respiratory stimulant drugs act directly on the medullary center of the brain and are analeptics
  – Increase rate and depth of respiration
Summary

• A cough may be prolonged or result from an underlying disorder
  – Treatment with antitussive drugs may be indicated
• Main clinical use of antihistamines is for allergic reactions
  – Also used to control motion sickness or as a sedative or antiemetic

Summary

• Drug therapy for the GI system can be divided into drugs that affect the stomach and drugs that affect the lower GI tract
  – Antacids buffer or neutralize hydrochloric acid in the stomach
  – Antiflatulents prevent the formation of gas in the GI tract
  – Digestant drugs promote digestion in the GI tract by releasing small amounts of hydrochloric acid in the stomach
  – Drugs used to treat nausea and vomiting include antagonists of histamine, acetylcholine, and dopamine and other drugs, the actions of which are not understood clearly

Summary

• Cytoprotective agents and other drugs are used to treat peptic ulcer disease by protecting the gastric mucosa
  – H₂ receptor antagonists block the H₂ receptors
    • Also reduce the volume of gastric acid secretion and its acid content
  – Proton pump inhibitors decrease hydrochloric acid secretion by inhibiting the actions of the parietal cells
Summary

• Two common conditions of the lower GI tract may require drug therapy: constipation and diarrhea
  – Drugs used to manage conditions include laxatives and antidiarrheals
• Drugs used to treat eye disorders include antiglaucoma agents, mydriatics, cyclopletics, antiinfective/antiinflammatory agents, and topical anesthetics

Summary

• Drugs used to treat disorders of the ear include antibiotics, steroid/antibiotic combinations, and miscellaneous preparations
• Endocrine system works to control and integrate body functions
  – Number of drugs are used to treat disorders of the anterior and posterior pituitary, the thyroid and parathyroid glands, and the adrenal cortex

Summary

• Pancreatic hormones play a key role in regulating amount of certain nutrients in the circulatory system
  – Two main hormones secreted by the pancreas are insulin and glucagon
    • Imbalances in either of these may call for drug therapy
    • Therapy is meant to correct metabolic derangements
    • Oral hypoglycemic agents help lower blood glucose by a variety of mechanisms
Summary

- Drugs that affect the female reproductive system include synthetic and natural substances such as hormones (estrogen and progesterone), oral contraceptives, ovulation stimulants, and drugs used to treat infertility
- Male sex hormone is testosterone
  - Adequate amounts of this hormone are needed for normal development and maintenance of male sex characteristics

Summary

- Erectile dysfunction drugs are used to enhance sexual function
- Antineoplastic agents are used in cancer chemotherapy to prevent increase of malignant cells
- Antibiotics are used to treat local or systemic infection
  - Includes penicillin, cephalosporins, and related products; macrolide antibiotics; tetracyclines; fluoroquinolones and miscellaneous antibiotic agents

Summary

- Persons can be infected by bacterial organisms, fungi, and viruses
  - Examples of antifungal drugs include tolnaftate (Tinactin), fluconazole (Diflucan), and nystatin (Mycostatin)
- Few drugs exist for use in any viral infections
  - One antiviral drug is acyclovir (Zovirax), effective against herpes infection
  - Another is zidovudine (Retrovir, AZT), which is used to treat HIV infection
Summary

- Drugs used to treat inflammation or its symptoms may be classified as analgesic-antipyretic drugs and nonsteroidal antiinflammatory drugs
  - Number of medications have both properties
- Immunosuppressant drugs reduce activity of the immune system
  - Suppress production and activity of lymphocytes
  - Prescribed after transplant surgery, can help to prevent the rejection of foreign tissues
  - Sometimes given to halt progress of autoimmune disorders

Summary

- Immunosuppressant drugs reduce activity of the immune system
  - Suppress production and activity of lymphocytes
  - Prescribed after transplant surgery, can help to prevent the rejection of foreign tissues
  - Sometimes given to halt progress of autoimmune disorders

Summary

- Immunomodulating agents are drugs that help the immune system be more efficient
  - Activate immune defenses and by modifying a biological response to an unwanted stimulus

Summary

- Serum contains agents of immunity
  - These are antibodies
    - Can protect against an organism if the serum is injected into someone else
  - Vaccines are composed of killed or altered microorganisms
    - Administered to a person to produce specific immunity to a disease-causing bacterial toxin, virus, or bacterium (active immunization)
Questions?