Pharmacology and Medication Administration

We’ll learn about drugs by Classification

• The broad group to which a drug belongs. Knowing classifications is essential to understanding the properties of drugs.

What we’ll talk about!

• Drug Names
• Sources of Drug Products
• Drug Classifications
• Food & Drug Administration
• Medication Administration
• Properties of Drugs

Drugs are chemicals used to diagnose, treat, and prevent disease.

Names of Drugs

• Chemical
  – States its chemical composition and molecular structure
• Generic
  – Usually suggested by the manufacturer
• Official
  – As listed in the U.S. Pharmacopeia
• Brand
  – The trade or proprietary name

Pharmacology is the study of drugs and their actions on the body.
Chemical Name 7-chloro-1, 3-dihydro-1, methyl-5-phenyl-2h-1
Generic Name diazepam
Official Name diazepam, USP
Brand (Trade) Name Valium®

Sources of Drug Information
- United States Pharmacopeia (USP)
- Physician’s Desk Reference (PDR)
- Drug Information
- Monthly Prescribing Reference
- AMA Drug Evaluation
- EMS field guides

Legal
- Knowing and obeying the laws and regulations governing medications and their administration is an important part of an EMT’s career.
- These include federal, state, and agency regulations.

Federal
- Pure Food & Drug Act of 1906
- Harrison Narcotic Act of 1914
- Federal Food, Drug, & Cosmetic Act of 1938
- Comprehensive Drug Abuse Prevention & Control Act of 1970

State vs. Local Standards
- They vary widely.
- Always consult local protocols and with medical direction for guidance in securing and distributing controlled substances.

New Drug Development
Components of a Drug Profile
- Name
  - Generic, trade
- Classification
- Mechanism of Action
- Indications
- Pharmacokinetics
- Side Effects/adverse reactions
- Routes of Administration
- Contraindications
- Dosage
- How Supplied
- Special Considerations

Providing Patient Care Using Medications
- Have current medication references available.
- Take careful drug histories including:
  - Name, strength, dose of prescribed medications
  - Over-the-counter drugs
  - Vitamins
  - Herbal medications
  - Allergies

Providing Patient Care Using Medications
- Evaluate the patient’s compliance, dosage, and adverse reactions.
- Consult with medical direction as needed.

The 6 Rights of Medication Administration
- Right medication
- Right dosage
- Right time
- Right route
- Right patient
- Right documentation

Special Considerations
- Pregnant patients
- Pediatric patients
- Geriatric patients

Case # 1
- You are dispatched on a “chest pain” call. First responders are on scene and you arrive in 8 minutes. A woman meets you at the front door and tells you she is the patient’s wife; she takes you to the patient who is a 42 year old minister. He is CAO PPTE, but is in obvious distress. He is breathing at a rate of 24/min., with some difficulty.
Case 1, cont.

• His skin is pale, cool, diaphoretic. His radial pulse is strong and regular at a rate of 84.
• Rev. Allen’s BP is 150/90. He is on 15 LPM/NRB oxygen by the first responders.
• Rev. Allen tells you that he had a sudden onset of heaviness in his chest as well as some SOB ~ 15 minutes ago. He rates the discomfort as 8/10. He has no PMH, no meds, NKA. What is your DDX?

Case 1, cont.

• Ok, now what will you do for him?
  – ECG
    • SR w/ ST elevation, frequent PVC’s
  – ASA, 325 mg PO
  – IV NS tko
  – NTG SL x 3
  – MS 2 mg increments, titrated to pain relief
  – Reassess vitals

De-Mystifying Pharmacology

• Drugs do not do anything new.
  – They can only alter functions that are already occurring in the body.
    • Replace a function, enhance a function or interrupt a function
  • Drugs will always leave residual effects.
    – Even selective-site drugs!
      • Albuterol and muscle tremors

De-mystifying Pharmacology

• Drugs usually have to bind to something before anything can occur.
  – Antacids bind to receptors in the stomach
  – Morphine binds to euphoria receptors, nausea and vessel control receptors in the brain

The EMT-Intermediate’s responsibilities with medication administration
EMT-I Responsibilities

• Understand how drugs in your scope of practice work in the body
  – How they alter body functions
  – Binding sites of drug classes and expected actions
  – Residual effects of specific drug classes
• Keep your knowledge base current!
  – New drugs are approved for use every day
    • Top 200 prescriptions per year

EMT-I Responsibilities in Patient Care

• Perform a comprehensive drug history
  – Prescribed medications
  – Over-the-counter medications
  – Vitamins or herbal supplements
  – Recreational/illicit substances and alcohol
  – Drug interactions/reactions

Remember!

• Drug administration
  – Use the correct precautions and administration rates
  – Observe for expected and unexpected effects of the drug
  – Document patient responses from the drug
    • Good and bad!
    • Pertinent vital signs
• Use the Rights of Drug Administration

The Basics of Drug Classes

Cells talk to each other

• Three distinct languages
  – Nervous system
    • neurotransmitters
  – Endocrine system
    • hormones
  – Immune system
    • cytokines
In disease, all systems are affected

- The three systems can’t exist without each other
- The actions of one impact the actions of the others
  - I.e., stress (nervous system) disrupts endocrine system which may respond with glucocorticoid production = suppressed immune response

Drug Classifications

- Drugs are classified 3 different ways:
  - By body system
  - By the action of the agents
  - By the drug’s mechanism of action

Drug Class Examples

- Nitroglycerin
  - Body system: “Cardiac drug”
  - Action of the agent: “Anti-anginal”
  - Mechanism of action: “Vasodilator”
- Indications for nitroglycerin
  - Cardiac chest pain
  - Pulmonary edema
  - Hypertensive crisis
- Which drug class best describes this drug?

Another way to classify drugs

- Mechanism of Action
  - Drugs in each category work on similar sites in the body and will have similar specific effects/side effects
    - Beta blockers: metoprolol
    - ACE inhibitors: lisinopril
    - Alpha blockers: prazosin
    - Calcium-channel blockers: verapamil
- Example: beta blocker actions and impacts
  - Suppress the actions of the sympathetic nervous system
  - Prehospital administration of epinephrine may not produce as dramatic effects with a patient taking a drug in this class

Prehospital example: Hyperglycemias

- Dextrose 50% and glucagon
  - Both will raise blood glucose
- Mechanism of action
  - Glucagon: hormone that works in the liver to convert stored chains of carbohydrate to glucose
  - Dextrose 50%: ready-made simple sugar that is ready to enter into the cell
- Which drug is considered first-line for hypoglycemia? Why?
- What are some limitations for glucagon in the presence of severe hypoglycemia?
Autonomic Nervous System

- Responsible for control of involuntary actions.
- Exit the central nervous system and enter structures called the autonomic ganglia
  - nerve fibers from CNS interact with nerve fibers from the ganglia to target organs
  - Pre-ganglionic nerves - exit CNS and terminate in autonomic ganglia
  - Post-ganglionic nerves - exit ganglia and terminate in target tissues
  - No actual connection between nerve cells - a synapse

Two functional divisions of autonomic nervous system

- Parasympathetic - Vegetative functions - feed or breed
- Sympathetic - Fight or Flight

Two functional divisions of autonomic nervous system

- The space between nerve cell and target organ is a neuroeffector junction.
- Neurotransmitters - specialized chemicals to conduct impulse
- Neurotransmitters released from pre-synaptic neurons and act on post-synaptic neurons or target organ.

the two neurotransmitters of the autonomic nervous system

- Acetylcholine - used in pre-ganglionic nerves of the sympathetic system and in pre and post-ganglionic nerves of the parasympathetic system
- Norepinephrine - the post-ganglionic neurotransmitter of the sympathetic nervous system.

Sympathetic nervous system stimulation

- Sweating
- Peripheral vasoconstriction
- Increased blood flow to skeletal muscle
- Increased HR and cardiac contractility
- Bronchodilation
- Energy

- Cholinergic synapses - use acetylcholine as neurotransmitter
- Adrenergic synapses - use norepinephrine as neurotransmitter
• Reduced blood flow to abdominal organs
• Decreased digestion
• Relaxation of bladder smooth muscle
• Release of glucose stores
• Also stimulation of the adrenal medulla
  - release of hormones norepinephrine and epinephrine

Adrenergic receptors
norepinephrine crosses synaptic cleft and interacts
  – alpha 1-peripheral vasoconstriction, mild bronchoconstriction, stimulation of metabolism
  – alpha 2-inhibitory - prevent over-release of norepinephrine in synapse
  – beta 1 - increased heart rate, cardiac contractility, automaticity, conduction
  – beta 2 - vasodilation, bronchodilation

• Dopaminergic receptors
  – not fully understood - believe to cause dilation of renal, coronary, cerebral arteries
• Sympathomimetics -
  – meds that stimulate the sympathetic nervous system
• Sympatholytics
  – inhibit the sympathetic nervous system

Parasympathetic nervous system
• Acetylcholine release - very short-lived - deactivated by chemical acetylcholinesterase
• Parasympathetic actions
  – Pupils constrict
  – Secretions by digestive glands
  – Increased smooth muscle activity along digestive tract
  – Bronchoconstriction
  – Reduced heart rate and contractility

• Parasympatholytics
  – Anticholinergics
  – block the actions of the parasympathetic nervous system
    • Atropine
• Parasympathomimetics
  – Cholinergics
  – Stimulate the parasympathetic nervous system
Autonomic Nervous System

Sympathetic

Parasympathetic

Receptor Sites

Alpha-1
Vessel Constriction
Arterioles
Veins

Alpha-2
Nerve-to-Nerve Connections
Minimal EMS Significance

Beta-1
Cardiac Effects
Increase in HR, conductivity
Increase in contractions

Beta-2
Dilation of bronchioles
Skeletal muscle tremors
Inhibition of uterine contractions

Neurotransmitters:

Norepinephrine
Epinephrine

Sympathetic Neurotransmitter:

Acetylcholine (ACh)

Parasympathetic

“Sympathomimetics”

“Adrenergics”

“Beta Blocker”

Beta-2 Agonist” “Non-Specific Beta Agonist”

The Parasympathetic NS

• What organs will help out the typical couch potato?
  – Digestion
  – Slow heart rate
  – Smaller bronchioles
  – Pupil size
    • Normal or constricted
• This system works best at rest

Over-stimulation of the Parasympathetic NS

• A little is a good thing, but too much stimulation of this system leads to trouble
  – Very slow heart rates
  – Bronchoconstriction
  – Major gastrointestinal actions
    • Vomiting
    • Diarrhea

Autonomic Nervous System

Sympathetic Receptor Site Action

1) Brain sends out the response via nerve paths
2) Nerve moves the response: depolarization
3) Depolarization stimulates norepinephrine sacks
   • Sacks move to the end of the nerve and dump out their contents
4) Norepinephrine travels across the synapse
   • Attaches to a receptor on the organ, organ responds to the signal

5) Norepinephrine detaches and is deactivated
   • 2 options: destroy it or move it back into its sack

The nervous system master system
• Makes thought and movement possible
• Axons and dendrites are the wiring – neurons send and receive messages
  – Axons carry messages from neurons
  – Dendrites receive messages
• Neurons produce chemical messenger molecules and secrete them into the synapse
• Neurotransmitters lock onto receptors on dendrites of neurons upstream or downstream

The nervous system master system, cont.
• Neuronal communication is based on the shape of neurotransmitters and receptors
  – Key & lock – must fit receptor sites
• Insertion of neurotransmitter sets off a chain reaction;
  – Sodium and chloride outside the membrane enters the cell through channels
  – Potassium exits the cell through its channel
  – = wave of energy; at the end of the energy sweep, calcium enters axon and pushes neurotransmitters out of their storages into other synapse

Spinal cord
• Most primitive structure of nervous system
  – Carries messages back and forth
  – Also contains reflex arcs – pain response
  – Under control of brain stem, cerebellum, basal ganglia, & cerebral cortex.

The brain stem
• Tops off spinal cord and sends messages to provide most basic functions; breathing, vasoconstriction, cardiac action
• Reticular activating system rises up from brain stem
  – Rouses us into consciousness
• Limbic system
  – Acts as gatekeeper of memory
    • Food, sex, fight & flight

The brain stem, cont.
• Twin hippocampal structures are responsible for encoding new memory
• Amygdalae – on each side of the limbic system; react to threatening stimuli with fear
• The thalamus – in the center of the limbic system; aids in memory – stores memory for ~ 3 yrs, then other structures take over
The brain stem, cont.
- Hypothalamus – monitors and controls hormonal activities
  - Maternal bonding, etc
  - Oversees endocrine functions
  - Serves as connection between mind and body
- Cortex – wraps around limbic structures
  - Rises up from thalamus & is folded & wrinkled
  - Conscious control over movement, sensory interpretation, speech, cognitive function
  - Prefrontal lobes – anticipate the future, make plans, realize our mortality

The cerebellum
- Under cortex
  - Source of athletic grace

The sensory (peripheral) system
- Sends constant information back to brain
  - I.e., pressure, position, temperature

The motor system
- Somatic system
  - Long single axons to specific skeletal muscles
  - Can override the autonomic system
- Autonomic system
  - Controls vegetative function
  - Divides into sympathetic & parasympathetic systems
  - Uses two neurons – preganglionic neurons & postganglionic neurons
  - Sympathetic & parasympathetic systems are a TEAM

Parasympathetic nervous system
- Uses only the neurotransmitter acetylcholine
  - Controls behaviors
    - Thoughts & feelings
    - Visceral activities
    - Muscle actions
    - Also – thoughts, dreams, hallucinations
  - Enzyme acetylcholinesterase breaks down acetylcholine

Sympathetic nervous system
- Controls our responses to stress – good and bad
- Neurons produce catecholamines; dopamine, epinephrine, norepinephrine
  - Dopamine – reward-motivated behaviors
- The enzyme Monoamine oxidase (MAO) breaks down catecholamines
- The adrenal medulla is also part of the symp. nerv. sys. – also makes catecholamines
Nervous System Review

• You are to give a dose of a parasympatholytic. What is it expected to do?
  – Bronchodilation
  – Increase GI motility
  – Stimulate vomiting
  – Increase HR
• Is a parasympatholytic the same as a sympathomimetic?

Nervous System Review

5 minutes after you gave a non-specific beta agonist, you notice that the patient is complaining of palpitations. This effect is considered to be:
  A desired effect of the drug
  An expected side effect of the drug
  An unpredictable, adverse effect of the drug

Nervous System Review

• What other side effects or adverse reactions would you expect to see in a patient after giving them an adrenergic drug?
  – Muscle tremors
  – Tachycardia
  – Elevated BP
  – Chest discomfort

Nervous System Review

• A patient is taking atenolol, a Beta-1 specific blocker. What is the expected effects of this drug?
  – Lowered HR
  – Decrease in contraction and conduction
• What would be an expected side effect of the drug?
  – Dizziness when standing

Antiarrhythmic drugs and local anesthetics work on action potential

So, which drugs do this – in our world?
Antiarrhythmic drugs and local anesthetics work on action potential

- We are a walking sea of cells bathed in a solution of sodium and chloride ions
  - Cells contain potassium ions
  - Cells have trapdoors (channels)
    - Widen or narrow to allow or bar ions
      - Chloride
      - Potassium
      - Sodium

- A cascading domino effect – action potential
  - Energy washes over nerve cell membranes to axons
  - Neurotransmitters flood synapses
    - Lock into nerve endings, relaying message & action potential to downstream neurons
    - Depolarization
      - Nodes of Ranvier

Drugs that affect sodium and chloride concentrations can stabilize cells that emit ectopic electrical discharges

- Side effects would include nervous system conduction responses
  - Flushing, dizziness, nausea, SOB
- Parasympathetic system is affected by sodium channel interference
  - Anticholinergic side effects

Drugs that affect calcium, phosphorus, and the completion of the action potential

Lidocaine

- Remember….Lidocaine is considered a sodium channel blocker
  - Lidocaine suppresses automaticity, excitability, spontaneous depolarization of ventricle
  - We’ll use it for VT, VF, PVC’s

So, which drugs do this – in our world?
• No thought, feeling, or muscle movement can occur without calcium

• In muscle cells, calcium is stored just under the cell membrane
  – When the action potential stimulates the cell membrane, calcium channels open and calcium goes deeper into the cell
• In the fibrils & sarcoplasm, calcium binds with troponin, causing muscle contraction
• In the heart muscle cells, calcium creates greater muscle contractility & enhanced current

Nitroglycerine
• Remember, NTG affects calcium, phosphorus, and the completion of the action potential
  – decreases preload, afterload, systemic vascular resistance
  – dilates coronary arteries
  – improves blood flow through coronary vasculature
  – dilates arterial, venous beds systematically

Cholinergic & Anticholinergic drugs
• Acetylcholine makes possible routine functions
  – Dreaming, digestion, pupil constriction, etc
• Cholinergic and anticholinergic drugs have the potential to activate or block both the sympathetic and parasympathetic systems
• Acetylcholinesterase

So, which drugs do this – in our world?
• Muscarinic receptors
  – In all effector cells stimulated by postganglionic neurons of parasympathetic system
    • Including potassium channels in heart cells
• Nicotinic receptors
  – In synapses between pre & post ganglionic neurons or both parasympathetic and sympathetic neuromuscular junctions
  – Can be blocked by curare derivatives
Cholinergic drugs

• Two drug strategies make more acetylcholine available
  – Inhibition of acetylcholinesterase
  – Replacement of acetylcholine

Atropine

• Remember, Atropine is an anticholinergic/parasympatholytic
  – Blocks the action of acetylcholine at postganglionic receptor sites in smooth muscle, secretory glands, CNS, SA and AV nodes, and cardiac muscle

Drugs of the sympathetic nervous system

So, which drugs do this – in our world?

• Amiodarone
• Epinephrine

The Sympathetic Nervous System Responds to Stress

• Catecholamines are derived from the amino acid tyrosine
  – Dopamine is basic catecholamine
  • Norepinephrine, epinephrine evolves

– Receptors
  • Alphas – excite
    – Bronchial constriction – decrease congestion & edema
    – Intestinal sphincter contraction
    – Bladder sphincter contraction
    – Pupil dilation
  • Betas inhibit
    – Bronchial relaxation
    – B-1
      » Affinity for norepinephrine and epinephrine
      » Increased heart rate, contractility
    – B-2
      » Affinity for epinephrine
      » Vasodilation, bronchodilation, glycogenolysis
Amiodarone

- Remember, Amiodarone is a sympathetic nervous system drug
  - Prolongs duration of action potential and effective refractory period
  - Is a weak non-competitive α- and β- adrenergic blocker
  - Increases PR and QT intervals
  - Decreases sinus rate
  - Decreases peripheral vascular resistance

Epinephrine

- Remember, Epinephrine is a sympathetic nervous system drug
  - Is an Alpha – and Beta – agonist
  - Increased heart rate, conductivity
  - Increased contractility
  - Bronchodilation
  - Causes peripheral vasoconstriction

Histamine, Antihistamines, and H2 blockers

- The neurotransmitter histamine is an alerting neurotransmitter in the brain
  - Influences N/V and BP as well as alertness
  - Requires calcium to release
  - Many antihistamines also have anticholinergic activity
  - Can antagonize histamine, acetylcholine, and dopamine

So, which drugs do this – in our world?

- Diphenhydramine

- Mast cells and basophils in immune system contain histamine
  - Release it in response to trauma or foreign invasion
  - Capillaries become more permeable, possibly = hypovolemic shock
  - In GI tract, histamine affects H2 receptors and mediates the release of hydrochloric acid

Benadryl

- Remember, Benadryl is an antihistamine (1st generation, non-selective)
  - Acts on blood vessels, GI tract, respiratory system by competing with histamine for H1 and H2 receptor sites
Opiates & Opiate Blockers

- 2200 B.C., Sumerians documented Poppy’s “Joy Juice”
- Nervous system, Immune and endocrine systems respond to pain signals

![Image of a person with hands on head]

So, which drugs do this – in our world?

- Morphine sulfate
- Nalbuphine hydrochloride
- Naloxone

Types of pain

- Fast sharp pain – impulse directly to thalamus;
  - Brief, immediate, phasic pain
  - Responds well to opiate analgesics
- Referred pain
  - Visceral pathways

Opiate receptors

- Limbic system
  - Amygdala and hypothalamus
    - Opiate receptors
- Brain stem
  - Locus ceruleus
    - Opiate receptors
- Spinal cord
  - Opiate receptors

- Opiate receptors have differing shapes
- We make our own analgesia
  - Endorphins
Morphine versus Nubain

- Morphine binding to 2 receptors
  - Activates both

- Nubain binds to both
  - Activates only one
  - Sits in the other and blocks agonists from stimulating it

Morphine Sulfate

- Remember, Morphine is an Opioid analgesic (Schedule II drug)
  - Depresses pain impulse transmission at the spinal cord level by interacting with opioid receptors

Nubain

- Remember, Nubain is a Synthroid opioid agonist AND antagonist
  - Depresses pain impulse transmission at the spinal cord level by interacting with opioid receptors
  - Has antagonistic effects similar to Narcan
  - Is not currently regulated under the controlled substance act of 1970

Narcan

- Remember, Narcan is an opioid antagonist
  - Competes with opioids at receptor sites
  - Lasts for 60 – 100 minutes

Drugs to treat disorders of the Islets of Langerhans

- Glucagon
• Islets of Langerhans
  – Alpha cells
    • Glucagon
      – Turns glycogen back into glucose
  – Beta cells
    • Insulin
  – Delta cells
    • Somatostatin
      – Suppresses secretions of alpha and beta cells and slows digestion

• At junctures of the triads of these cells
  – Blood glucose sensor monitors blood sugar levels

• When blood glucose drops to fasting levels
  – Insulin production ceases
  – Glucagon release from alpha cells is triggered
    • Turns stored liver glycogen into glucose

Glucagon

• Remember, Glucagon stimulates an increase in blood glucose levels by
  – Stimulating the release of stored glucose
  – Has positive inotropic and chronotropic effects on the heart independent of beta receptors – indicated for beta blocker overdose

Drugs that maintain Mineral and Fluid Balance

Rule:
Water follows Salt

• Furosemide
• Vasopressin

So, which drugs do this – in our world?
• Originally, edema was tx by bleeding the pt with leeches or scalpels
• Most diuretics simply get rid of sodium
• Diuretics are first-line drugs in tx of hypertension and CHF

Vasopressin

• Commonly used during surgery to maintain organ perfusion, fluid balance
• Is effective in cardiac arrest because it
  – increases coronary perfusion pressure, vital organ blood flow
  – decreases defibrillation threshold
  – promotes reabsorption of water by action on renal tubules

Lasix

• Remember, it’s a loop diuretic
  – Inhibits reabsorption of sodium and chloride at tubules and in loop of Henle
  • WATER FOLLOWS SALT

Nonsteroidal Anti-inflammatories (NSAIDs)

• Willow bark – first NSAID
  – Salicin, first used to treat rheumatic fever – 1874 (body converts salicin into salicylic acid)
• NSAIDs relieve pain by inhibiting local production of prostaglandin
• Also appears to act on nervous system at the level of the hypothalamus

So, which drugs do this – in our world?

• Acetylsalicylic acid
• Toradol
• Note; acetaminophen is considered a NSAID but has no antiinflammatory activity – and can damage the liver

New Info!
New England Journal of Medicine, 3/05

• Men 50 y/o or more (no clinical evidence of coronary disease).
  • ASA - Risk of MI 44% less
  • No significant effect on risk of stroke and no effect on mortality from cardiovascular causes

• Women 65 y/o or more (no history of cardiovascular disease)
  • ASA - No significant effect on risk of MI or risk of death from cardiovascular causes
  • BUT 24% reduction in risk of ischemic stroke and 17% reduction in stroke risk overall

Conclusion of study

• Women < 65 y/o
• Reasonable to avoid prescribing low-dose aspirin (75-100mg) as a preventative measure for coronary disease
• Rx for stroke - left to pt and Dr

Aspirin

• Remember, Aspirin is a non-opioid analgesic, NSAID, antiplatelet
  – Blocks pain impulses in CNS
  – Reduces inflammation by inhibition of prostaglandin synthesis
  – Inhibits platelet aggregation for the life of the platelet (7 – 10 days)

Toradol

• Remember, Toradol is a NSAID and non-opioid analgesic
  – Inhibits prostaglandin synthesis by decreasing an enzyme needed for biosynthesis
  – Has anti-inflammatory, antipyretic effects

Drugs that work in the intestinal lumen
So, which drugs do this – in our world?

- Activated charcoal
- Drugs to treat poison ingestion
  - Acts externally to the surface of the bowel to absorb toxins from the mucosa
  - Increases drug diffusion rate from plasma into GI tract for absorption

Activated Charcoal

- Remember, Activated Charcoal is an absorbant
  - Binds poisons, increases adsorption in the GI tract
  - Iron, lithium, alcohol, petroleum products will not bind

Respiratory Medications

How do they work?

- Albuterol
  - Causes bronchodilation by acting on B-2 receptors (B-agonist)
- Atrovent (Ipratropium)
  - Causes bronchodilation by inhibiting acetylcholine at receptor sites on bronchial smooth muscle

Drug Mechanisms of Action
Phases of Drug Activity

• Pharmaceutical
  – Disintegration and dissolution
• Pharmacokinetic
  – How the drug gets in, how it reaches the target and how it gets out of the body
• Pharmacodynamic
  – The response of the tissue to the drug

Pharmaceutical Phase

• Disintegration
  – Breakdown of the solid form of the medication
• Dissolution
  – Drug goes into solution form and is able to be absorbed
  – The more rapid this step, the faster the drug will be absorbed

Pharmacokinetics

• Absorption
• Distribution
• Metabolism
• Excretion

Absorption

Drug Factors That Impact Absorption

• Fast, efficient absorption is achieved with the following:
  – High surface area of the tissue
  – Rich blood supply at the tissue
  – Thin membranes between the tissue and the bloodstream
• Drug solubility
  – Lipid soluble drugs absorb faster in tissues and cells than water soluble drugs

Other Drug Factors That Impact Absorption

• Drug concentration
  – High concentrations of the drug at the tissue will achieve better absorption as well
• pH of the drug
  – Glucagon does not absorb into cells readily
    • Requires very low or very high pH to break it down
Patient Factors Impacting Absorption

- Decreased circulation
  - Hypothermia
  - Shock
- Decreased cardiac output
  - CHF
  - Significant MI

Absorption Rates

<table>
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<tr>
<th>Oral Subcutaneous</th>
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<tbody>
<tr>
<td>Topical Intramuscular</td>
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<tr>
<td>Sublingual Rectal</td>
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<tr>
<td>Endotracheal Inhalation, IO, IV Intracardiac</td>
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Oral Absorption Speeds

- Elixirs, syrups
- Suspensions
- Powders
- Capsules
- Tablets
- Coated tablets
- Enteric-coated tablets

Absorption Principles for the EMT-I

- IV is used as the primary route
  - IV drugs already in solution form
  - Achieving drug levels are predictable
    - Everything that is administered is already in the circulation
    - Higher chance of toxicity
      - Absorption and delivery is immediate

Absorption Principles for the EMT-I

- Intramuscular (IM) – “second line” route
  - Highly vascular, but not as direct a route for administration
  - IM routes are utilized as a back-up when IV access is unobtainable
- SQ
  - Limited #s of BV and slower absorption
  - Drugs must have a higher concentration in order to be given in this route

More Applications of Absorption
Nitroglycerin

- How does the drug come packaged?
  - As a tablet, spray, ointment, liquid (IV)
- Nitroglycerin forms and absorption rates
  - SL: 1-3 minutes
  - Ointment/transdermal: 30 minutes
  - IV: immediate!

Epinephrine Absorption

- What is the concentration and dosing time for subcutaneous and IV epinephrine?
  - SQ: 1:1000 with repeat doses every 3-5 minutes
  - IV: 1:10,000 with repeat doses every 3-5 minutes
- Why is there a need for 2 different concentrations?
  - Epinephrine is a short-lived drug and will break down quickly
  - SQ absorption is significantly slower than IV
  - A higher concentration of the drug will assure that enough of the active drug will still be available after it is absorbed

Absorption at the Cell

Four Paths of Cellular Absorption

- Membrane pores
  - Drug must be very, very small in order to enter
  - Rare site of absorption
- Diffusion
  - Movement through the membrane with a concentration gradient
  - No energy required to move the drug
  - Most common route of entry for drugs (lipid soluble)

- Facilitated Diffusion
  - Commonly used for moderate-sized drugs and water soluble drugs
    - Morphine, dextrose, amiodarone, diphenhydramine
  - Drug forms a complex with a protein in the membrane, which allows the gates of the membrane to open
- Active Transport
  - Movement of a drug against a concentration gradient
  - Requires the use of energy to let the drug in
Facilitated Diffusion

Distribution

Pharmacokinetics: Distribution

- Definition: how the drug gets from the blood to the target cell or tissue
- Plight of the drug bolus
  - Some of the drug will seek out and bind with cell receptors
    - There may not be enough cell receptors for the drug
  - The rest of the drug will go to staging and utilized as replacements
    - Drug reservoirs

Pharmacokinetics: Distribution

- Types of drug reservoirs
  - Fat cells (for fat soluble drugs)
    - Longer storage time
    - Marijuana THC can stay in the body up to 6 months with just one dose
  - Plasma proteins (all other drugs)
    - "Mobile storage"
    - Release of the drug is more immediate and replacement at cell receptors is more rapid

Barriers to Distribution

- Blood-Brain Barrier
  - Selective site for drugs
  - Capillary cells packed tightly together
  - Only allows fat-soluble drugs and small molecules through
- Placental Barrier
  - Only lipid soluble or free-form drugs can get through

Biotransformation (Drug Metabolism)
Pharmacokinetics: Biotransformation

- Drugs must be in an active form before they can work at a cell receptor
  - Most prehospital drugs are packaged in an active form and result in a faster onset of the drug
    - “Active metabolite”
  - Other drugs must be transported to the liver to be “de-activated” before elimination

Factors Altering Drug Metabolism

- Age
  - Pediatric “growth spurts” may increase drug metabolism
  - The very young and very old have diminished liver function and may develop drug toxicity
- Body mass and gender
  - Fat distribution and percentage differences

Factors Altering Drug Metabolism

- Pathologic state
  - Circulatory problems, CHF may slow drug distribution
- Genetic factors
  - Enzyme systems in some may be slower
  - More susceptibility to adverse reactions or toxic effects

Excretion

- Bile
  - Drugs turned into inactive metabolites by the liver
  - Dumped into the duodenum and excreted by the feces
- Expired air
  - Alcohol and volatile gases
- Breast milk
  - Narcotics

Routes of Elimination

- Urine
  - Drugs must be in a “deactivated” form before they are eliminated by the kidneys
  - Water-soluble drugs are removed easily
  - Fat soluble drugs must be more “water-friendly” if the kidneys are going to get rid of them
    - This transformation occurs in the liver
Pharmacodynamics: How the tissues and cells respond to a drug

Theories of Drug Action

Drug-Receptor Interaction

Drug classes are sometimes named by the type of cell receptor with which they interact

• “Beta blockers”
• “Opiate drugs”
• “Anticholinergics”

Drug classes are sometimes named by their actions on a cell receptor

• “Agonist” drugs – after binding, the drug will stimulate a response
  – Albuterol: “Beta-2 agonist”
• “Antagonist” drugs – after binding, the drug will prevent a response
  – Narcan: “narcotic antagonist”
  – Benadryl: anti-histamine

Drug-Response Relationship

• Drugs are studied for the following:
  – Plasma levels
    • How fast they reach active levels
  – Biologic half-life
    • How long it takes to break down half of the drug
  – Minimum effective concentration
    • How much of the drug it takes to create a response
  – Therapeutic threshold
    • How much of the drug is too much, or toxic
Drug Interaction Variables

- Intestinal absorption
- Competition for plasma protein binding
- Drug metabolism
  - “Biotransformation”
- Action at the receptor site
- Renal excretion
- Alteration of electrolyte balance
- Drug-drug interactions
- Other drug interactions
  - Alcohol consumption
  - Cigarette smoking

Pharmacology Case Study

Case Study

You respond to “Jan,” a 45 year-old female who was stung by a bee while at a family picnic. She is lying in the grass field. She is conscious but shaking, and has hives on her arms, chest and legs.

A family member tells you that they administered her Epi-Pen 5 minutes ago.

Her vital signs include a respiratory rate of 24, heart rate of 110 and a blood pressure of 156/70.

More Patient Information

Jan has a history of “severe” reactions to bee stings. Her lips appear swollen but her family members state that “her whole face was swollen before we gave her the Epi-Pen.”

Her lung sounds are clear.

Embellishment!

- Would you expect a change in Jan’s response to epinephrine if she…
  - Was 5 years old?
  - Was 20 and pregnant?
  - Was 65 (and not pregnant)?

  - Was old, pregnant, and acted like she was 5? Just Kidding!!

Drugs in Kids

- Less than one year
  - Lower levels of plasma protein
    - Increased likelihood for drugs to be in a free-form state
    - More potent effects of the drug
  - Kidneys and liver are less developed
    - Potentially slower activation and elimination of drugs
Kids and Drugs

- Over 1 year
  - Liver enzymes more active than an adult
  - Faster work in the kidneys than an adult
    - Later childhood causes a faster elimination of drugs
  - Dosing for drugs are based on the child’s weight
    - More proportional response

Pregnancy Considerations

- 1st trimester
  - Lipid soluble drugs can cross into the placenta
  - Immature fetal liver and kidneys may store drugs longer
- Later pregnancy
  - Higher HR, CO = faster absorption and onset of drugs
  - Increased fatty tissue may cause more storage of lipid-soluble drugs
  - Drug dependency by the fetus if the mother is addicted to opiate drugs
- During labor
  - May depress respirations in the neonate

The Elderly

- Decreased cardiac output and metabolism
  - Longer drug effects (pain medications)
  - Less filtration through the kidneys – keeps drugs in circulation longer
- More body fat and less total body water
  - Stores more fat-soluble drugs
  - Higher concentration of drugs in the body
- Decreased plasma proteins
  - More drugs circulating in their free-form state

The half-life of Valium in a 20 year-old lasts approximately 20 hours.

**For a person in their 80s, this half-life extends to 90 hours!**

Controlled substances

- Schedule I
  - Heroin, LSD
- Schedule II
  - Narcotics and cocaine
- Schedule III
  - Combinations of narcotics + NSAID
- Schedule IV
  - Enhance GABA’s affinity for its receptors, result in decreased anxiety or in sedation
- Schedule V
  - Small amounts of narcotics used in antidiarrheal and antitussive preparations
Managing Controlled Substances

- Ensuring the security of them
- Requirements for locking a controlled substance
- Accounting of drug inventory
- Wasting a controlled substance
- DEA forms
- Violation reporting

Pharmacology Activity

Find a partner and grab one medication out of the grab bag. Create a singles ad-style of profile for your medication, including indications, contraindications, precautions and how the drug works in the body.

Be prepared to share your "singles ad" to the class.