

Pharmacology

Drugs

Drugs Have Three Names

Chemical Name - scientific name typically given to a drug when it's discovered that describes the molecular structure of the drug.

Generic Name - non-proprietary name or abbreviation of the chemical name such as Acetaminophen.

Trade Name or **Brand Name** - name given to the drug by the pharmaceutical companies that make the drug. In the case of Acetaminophen, the brand name most of us are familiar with is Tylenol.

Dose - amount of a drug or chemical entering the body. Usually given as mg of the chemical per kg of body weight.

Six Rights of Medication Administration

- ✓ Right Medication
- ✓ Right Dose
- ✓ Right Time
- ✓ Right Route
- ✓ Right Patient
- ✓ Right Documentation

Key Terms and Concepts

Affinity - describes the attraction between a drug and a receptor. Drugs with a High Affinity bind more easily to receptors. Drugs with a Low Affinity require a higher concentration of the drug to get a response.

Drug Potency - amount of the drug that's required to produce a therapeutic response.

Effective Dose - amount of the drug that produces a response in 50% of the people taking it.

Toxic Dose - amount of the drug that produces adverse effects in 50% of the people taking it.

LD50 or **Medial Lethal Dose** - dose required to kill half the members of a tested population after a specified test duration.

Margin of Safety - the ratio between the Toxic Dose and the Effective Dose and is called the **Therapeutic Index**. The higher the Therapeutic Index, the safer the drug is considered to be. In general, non-prescription drugs have a much higher Therapeutic Index than prescription drugs.

Cumulative Action - is the increasing effect that multiple doses of the same drug cause due to a buildup of the drug in the bloodstream.

Hypersensitivity - reaction to a drug that is more profound than expected. This often times leads to an exaggerated immune response.

Idiosyncrasy - a reaction to a drug that is significantly different from what is expected.

Indication - the medical condition for which the drug has therapeutic value.

Potentiation - enhancement of one drug's effect by another drug such as the way promethazine may enhance the effect of morphine. This should not be confused with Synergism which is defined as the combined action of 2 or more drugs that is greater than the sum of the 2 drugs acting independently.

Refractory - failure of a patient to respond as expected to a certain medication.

Therapeutic Action – the drug's intended action.

Tolerance - a decreased sensitivity or response to a drug that occurs after repeated doses. Increased doses may be required to achieve the desired effect.

Drug Schedules

Drugs with the highest abuse potential are placed in Schedule I, and those with the lowest abuse potential are in Schedule V. These schedules are commonly shown as C-I, C-II, C-III, C-IV, and C-V.

Schedule I drugs are considered by the government to have a high potential for abuse, no established medical use, and a lack of safety for use of the drug even under medical supervision. Examples include Heroin, LSD, Cocaine, and Marijuana.

Schedule II drugs have a High abuse potential and severe dependence liability although they do have accepted medical use but with severe restrictions. These class of drugs are available through signed prescription only and in limited quantities. Examples include Opium, Ritalin, Morphine and Methadone.

Schedule III drugs have less abuse potential than Schedule I and II, and accepted medical use by prescription only. Abuse of the drug or other substance may lead to moderate or low physical dependence or high psychological dependence. Examples include Codeine, short-acting barbiturates, amphetamines, Pentobarbital, as well as Anabolic Steroids.

Schedule IV drugs have a low potential for abuse relative to the drugs or other substances in Schedules III and accepted medical use by prescription. Abuse of these drugs or other substances may lead to limited physical or psychological dependence relative to the drugs or other substances in Schedule III. Examples include Xanax, Valium, Ativan, and Ambien.

Schedule V drugs are considered to have a low potential for abuse, a currently accepted medical use in the United States. Abuse of these drugs can lead to a mild physical dependence. Prescriptions may not be necessary, but transactions must be recorded. An example would be cough suppressants with small amounts of codeine such as Robitussin as well as other prescription drugs with small amounts of opiates.

Pharmacodynamics

Pharmacodynamics - the study of the biochemical and physiological EFFECTS of drugs in the body. Most drugs work through interactions with receptor sites which are protein coatings found on the outer surface of the cell membrane. Receptor sites receive a signal from the body's chemicals such as neurotransmitters, hormones and enzymes which cause a molecular event to occur within the cell. Drugs either Enhance (**Agonist**), Diminish (**Partial Agonist**), or Block (**Antagonist**) the generation, transmission or receipt of the signal.

Agonists – Drugs that bind or attach to a receptor site which initiates a chemical reaction causes the desired physiological or therapeutic response.

Antagonist – Drugs that work by partially or completely blocking the chemical event through the principle of Antagonism. In such cases, the drug competes with another drug or chemical for position at a receptor site. A classic example of this is Naloxone (or Narcan) which competes with narcotic drugs. In this case Narcan would be an Antagonist.

Pharmacokinetics

Pharmacokinetics - study of the metabolism and action of drugs.

- ✓ How drugs enter the body
- ✓ How they move through the body
- ✓ How they are eliminated from the body.

Once exposed, the drug must get into the body and to its target site in an active form in order to cause an effect. The body's defenses include; Membrane barriers, Biotransformation enzymes, Antioxidants, and Elimination mechanisms.

ADME(**A**bsorption, **D**istribution, **M**etabolism (or Biotransformation) and **E**xcretion)

Absorption

Absorption - movement of a drug from its point of entry into the body into systemic circulation.

Factors that influence the rate of Absorption:

- ✓ Concentration of the drug
- ✓ Site of absorption
- ✓ pH of the drug
- ✓ Status of the person's circulation
- ✓ Solubility of the drug

Routes of Absorption Include:

Inhalation - drug is readily absorbed by gases and into the blood stream via the alveoli. Enhanced by the Large surface area of the alveolar surface, high blood flow, and the proximity of blood to alveolar air.

Ingestion - absorption occurs through the GI tract. In the stomach, the drug has to compete with stomach acids. If it makes it to the small intestine, the prolonged contact time with the large surface make this good location for absorption.

Distribution

Distribution - manner in which a drug is transported from the site of absorption to the site of action. Blood carries the drug to and from its site of action, storage depots, organs of transformation, and organs of elimination.

Distribution is influenced by cardiovascular function (heart rate and blood pressure) as well as physical barriers (blood brain barrier and the placenta barrier).

Biotransformation

Biotransformation - process by which drugs are inactivated and transformed into a form that can be eliminated from the body. These inactive forms are called metabolites.

Rate of transformation determines how often a drug needs to be administered to maintain its desired effect. *e.g. - Epinephrine transforms in 3-5 minutes.*

Key organs in biotransformation; LIVER (which is the most significant), the lungs, the kidneys and the intestines.

Excretion

Excretion - process of eliminating drugs from the body. Accomplished primarily through the kidneys. May also involve the liver, the lungs, intestines, sweat and mammary glands.

Routes of Administration

Ingestion (via the Gastrointestinal Tract), **Inhalation** (via the Lungs), **Dermal or Topical** (via the Skin) and **Injection** either intravenous, intramuscular or intraperitoneal (which is the injection of a substance into the peritoneum or abdomen).

MOST effective route to the **LEAST** effective route are:

- ✓ IV
- ✓ Inhalation
- ✓ Intraperitoneal
- ✓ Intramuscularly
- ✓ Ingestion
- ✓ Topical

MEDICATIONS THAT AFFECT THE NERVOUS SYSTEM

Autonomic Nervous System

Controls blood pressure, heart rate, respiratory rates, body temperature, digestion, metabolism, the balance of water and electrolytes, the production of body fluids (saliva, sweat, and tears), urination, defecation, sexual response, and other processes.

Two main divisions: **Sympathetic** and the **Parasympathetic**.

Sympathetic - prepares the body for stressful or emergency situations—fight or flight.

- ✓ Increases the heart rate
- ✓ Increases force of heart contractions
- ✓ Opens (or dilates) the airways
- ✓ Stimulates the body to release stored energy for increased muscular strength.

Also causes palms to sweat, pupils to dilate, and hair to stand on end while at the same time, slowing body processes that are less important in emergencies, such as digestion and urination.

Parasympathetic - controls body process during ordinary situations---rest and digest or feed and breed. In general, its job is to conserve and restore.

- ✓ Slows the heart rate
- ✓ Decreases blood pressure
- ✓ Stimulates the gastrointestinal tract to process food and eliminate waste.

The energy obtained from the processed food is used to restore and build tissues during this time of rest and digest.

An analogy is that the parasympathetic division is like the brake while the sympathetic division acts like the accelerator. The sympathetic division functions during actions that require a rapid response and the parasympathetic division functions during actions that don't require such an immediate reaction.

Naturally occurring **Catecholamines** (Norepinephrine, Epinephrine and Dopamine) act as hormones or neurotransmitters and are used to communicate primarily with the **Sympathetic** branch of the Autonomic Nervous System.

Acetylcholine also acts as a chemical messenger communicating with the Autonomic Nervous System, but generally speaking, Acetylcholine deals primarily with the **Parasympathetic** branch.

Nerve fibers that secrete norepinephrine are called **adrenergic** nerve fibers and nerve fibers that secrete acetylcholine are called **cholinergic** nerve fibers. **Don't get the terms Catecholamine and Cholinergic confused.**

Drugs or chemicals that enter our body can act on cholinergic or adrenergic receptors which can have similar effects as Acetylcholine and Norepinephrine.

Sympathetic Nervous Systems Drugs

Adrenergics

Classification of drugs used to mimic the naturally occurring catecholamines (epinephrine, norepinephrine and dopamine) **OR** stimulate the release of norepinephrine, thus causing a sympathetic response. Think **Adrenaline** and **Dry**.

- ✓ Pupils will be dilated
- ✓ Vasoconstriction results in reduced mucous secretion in the nose, ↓ decreased salivation and dry-mouth
- ✓ Constipation
- ✓ Intestines relax
- ✓ Bronchial dilation in the lungs
- ✓ Coronary artery dilation
- ✓ Increase in the contractile force and rate of the heart

Adrenergics are used to combat life-threatening disorders such as...

- ✓ acute attacks of bronchial asthma
- ✓ shock
- ✓ cardiac arrest
- ✓ allergic reactions
- ✓ also used in nasal decongestants and appetite suppressants.

In simple terms, adrenergic drugs stimulate Alpha, Beta 1 and/or Beta 2 receptor sites.

- ✓ **Alpha receptor stimulation** - will constrict vessels
- ✓ **Beta 1 receptor stimulation** - will ↑ Increase the automaticity of the heart, ↑ increase the heart rate, ↑ increase conductivity, ↑ increase the force of the heart contractions and releases rennin
- ✓ **Beta 2 receptor stimulation** - relaxes bronchial smooth muscles which results in bronchodilation and increases the conversion of stored liver glycogen to glucose for energy

Remember This General Rule:
Alpha 'typically' affects our vessels
Beta 1 'typically' affects our heart
Beta 2 'typically' affects our lungs

Think...

Alpha for Veins, Beta 1 we have one heart and Beta 2, we have two lungs.

Alpha Adrenergic Agonists - used to treat Hypotension typically in life-threatening situations through Vasoconstriction. e.g. -Norepinephrine (Levophed).

FYI - Pseudoephedrine is a sympathomimetic used as a nasal decongestant and is commonly found in Dimetapp, Sudafed, Cenafed and Triaminic.

Beta 1 Adrenergic Agonists are used to treat...

- ✓ Bradycardia
- ✓ Low Cardiac Output
- ✓ Paroxysmal atrial or nodal tachycardia
- ✓ Ventricular Fibrillation
- ✓ Cardiac Output

e.g. - *Dobutamine Hydrochloride (Dobutrex)*

Beta 2 Adrenergic Agonists are used to treat...

- ✓ Acute and Chronic Bronchial Asthma
- ✓ Emphysema
- ✓ Bronchitis
- ✓ Acute Hypersensitive or Allergic Reactions to Drugs
- ✓ Aids in delaying delivery in premature labor

Examples include: Albuterol Sulfate (also known as Proventil, Ventolin or Volmax), Metaproterenol Sulfate and Terbutaline.

Dopamine

The catecholamine **Dopamine** improves blood flow to the kidneys by vasodilating renal and mesenteric arteries. FYI – Dopamine cannot cross the blood-brain barrier therefore does not **DIRECTLY** affect the central nervous system. Dopamine is used primarily to treat...

- ✓ Acute renal failure
- ✓ Heart failure
- ✓ Shock

Example is Dopamine Hydrochloride also known as Intropin.

Adrenergic Blocking Agent (Antagonist)

Drugs that selectively interact with Alpha and Beta Receptors to inhibit sympathetic stimulation or block the release of norepinephrine from storage sites. Depression of adrenergic nerves results in a vasodilation effect which ↓reduces Peripheral Vascular Resistance (PVR). Drugs in this category are mostly antihypertensive agents.

Parasympathetic Nervous System Drugs

Cholinergics

Cholinergics are **direct acting** agents that activate the cholinergic receptor sites by **mimicking the effects of acetylcholine**. Stimulation of cholinergic nerves can occur directly or indirectly.

Effects of cholinergic stimulation include...

- ✓ Vasodilation of blood vessels
- ✓ Slower heart rate (decreases the firing rate of the SA node)
- ✓ Constriction of bronchioles
- ✓ Constriction of the pupils
- ✓ Intestinal cramps
- ✓ Increased secretion of mucus in the respiratory tract
- ✓ Increased secretion of saliva; sweat and tears

When you think of Cholinergic, think of WET. An acronym often times used to summarize the functions of the parasympathetic nervous system is **SLUDD** (*Salivation, Lacrimation, Urination, Digestion and Defecation*). In general, Cholinergics have limited medical use, although some are used to relieve urinary incontinence and in eye surgeries.

Anticholinergics

Anticholinergics are **Cholinergic Blocking Agents** which compete with and prevent acetylcholine from stimulating the receptor site and thus act as antagonists (or against) the Parasympathetic Nervous System and indirectly causing a Sympathetic Nervous System response. By blocking acetylcholine receptors Anticholinergics result in a **drying effect**.

Effects of Anticholinergics include...

- ✓ Decreased bronchial secretions
- ✓ Decreased salivary secretions
- ✓ Decreased sweating
- ✓ Increased heart rate (Increases conduction through the myocardium)
- ✓ Pupil dilation

Examples of common Anticholinergics include Atropine and Atrovent.

Again remember that the Sympathetic and Parasympathetic divisions are always complementing each other. When one is reduced, the other takes over. This relationship is why an Anticholinergic that blocks a Parasympathetic response indirectly results in a Sympathetic response.

Cholinesterase Inhibitors

Once a cholinergic nerve is stimulated, it requires the enzyme Cholinesterase to return it to its normal resting state. Indirect stimulation of cholinergic nerves occurs by inhibiting the cholinesterase enzyme, thus permitting a build up of acetylcholine on the nerve receptor sites. As a result, acetylcholine increases in quantity with successive nerve impulses so that large amounts of acetylcholine can accumulate and repetitively stimulate receptors. The accumulation of acetylcholine that occurs by blocking cholinesterase (cholinesterase inhibitors) will cause an **over** stimulated parasympathetic response.

Cholinesterase inhibitors are commonly found in chemical warfare nerve agents and certain insecticides. FYI - Atropine blocks excess acetylcholine but does nothing to reverse the inhibition of the cholinesterase. This is why Atropine can be used as an antidote for organophosphate poisoning caused by the inhibition of cholinesterase.

**When you think of Cholinergic,
Think of WET**

Effects of Cholinergic include...

- ✓ Constricted Pupils
- ✓ Vasodilation results in ↑ increased mucous secretion in the nose, increased saliva secretions in the mouth
- ✓ Nausea/Vomiting
- ✓ Abdominal cramps
- ✓ Diarrhea
- ✓ Sphincter relaxation
- ✓ Bronchi constriction in the lungs
- ✓ Coronary artery contraction
- ✓ ↓ Decrease in the contractile force and rate of the heart.

**When you think of Adrenergic,
Think Adrenaline and DRY**

Effects of Adrenergic include...

- ✓ Dilated Pupils
- ✓ Vasoconstriction results in ↓ reduced mucous secretion in the nose, decreased salivation and dry-mouth
- ✓ Constipation
- ✓ Intestines relax
- ✓ Bronchial dilation in the lungs
- ✓ Coronary artery dilation
- ✓ ↑ Increase in the contractile force and rate of the heart

Other CNS Medications

Opioids

Class of Analgesics that are used to primarily to relieve moderate to severe pain associated with acute and chronic disorders such as MIs, postoperative pain or terminal cancer as well as pulmonary edema, preoperative sedation, anesthesia, cough suppression and diarrhea. Cautionary side effects include sedation, respiratory depression, and constipation.

Opioid Agonists

Narcotic Analgesics which include morphine or morphine like drugs such as codeine, Darvon, Demerol, fentanyl, hydrocodone and methadone.

Non Opioid Agonists

Non-narcotic analgesics that some times also have anti-inflammatory and fever reducing properties. Such drugs include aspirin and Non-Steroidal Anti-Inflammatory (or NSAIDS) such as ibuprophen and acetaminophen (or Tylenol).

Opioid Antagonists

Receptor antagonists that act on opioid receptors by blocking the receiving signals from opioids. Naloxone (or Narcan) is a commonly used opioid antagonist that binds to opioid receptors with higher affinity than agonists but do not activate the receptors. This effectively blocks the receptor, preventing the body from responding to opiates and endorphins.

Anesthetics

Drugs that cause anesthesia or reversible loss of sensation. They are different than analgesics which relieve pain without eliminating sensation. Examples range from low level anesthetics like Nitrous Oxide (or Nitronox) to higher level benzodiazepines such as diazepam (or valium) and midazolam (or Versed).

Sedative and Antianxiety Medications

Commonly used to decrease anxiety and assist sleep by depressing the CNS system. The two main categories are Benzodiazepines and Barbiturates. As mentioned a moment ago, examples of Benzodiazepines include diazepam and midazolam. Examples of Barbiturates include Phenobarbital and Seconal. Barbiturates are typically less frequently used due to their more intense effect.

Psychiatric Medications

Work by increasing the amounts of the CNS neurotransmitters Norepinephrine, Dopamine and Serotonin in patients with psychiatric disorders. Such drugs are broken down into Antipsychotics, Antidepressants and Antimanics.

Antipsychotics

Also known as neuroleptics because they affect the nerves. Examples include; **Phenothazines** (or **Thorazine**), **Seroquel**, **Risperdal**, and **Haldol**.

Antidepressants

Depressive illness is caused by a decrease of the chemicals or neurotransmitters norepinephrine, dopamine and serotonin in the brain that are responsible for mood. Antidepressants work by stimulating chemical changes that increase the levels of these neurotransmitters. Different antidepressant medications affect one or more of these neurotransmitters. The three main categories of antidepressants are **Selective Serotonin Reuptake Inhibitors**, **Tricyclic Antidepressants** and **Monoamine Oxidase Inhibitors** (or MAOIs).

Selective Serotonin Reuptake Inhibitors

Block the reuptake of serotonin which increases the level of serotonin in the brain. Common Selective Serotonin Reuptake Inhibitors are **Celexa**, **Lexapro**, **Prozac** and **Zoloft**.

Tricyclic Antidepressants

Similar to Selective Serotonin Reuptake Inhibitors, Tricyclic Antidepressants (or TCAs) also block the reuptake of serotonin but are less specific and also block the reuptake of norepinephrine resulting in an increase of both neurotransmitters in the brain. Examples of common Tricyclic Antidepressants include; **Elavil**, **Adapin** and **Tofranil**.

MAOIs

Increase the availability of neurotransmitters by preventing the breakdown of neurotransmitter molecules by inhibiting the activity of monoamine oxidase, thus preventing the breakdown of monoamine neurotransmitters. Examples of MAOIs include **Tranylcypromine** and **Phenelzine** (also known as **Nardil**).

Antimanics

Used to treat bipolar disorders. Examples include lithium as well as **Tegretol** and **Depakote** which are also used to treat seizure disorders.

Anticonvulsants and Antiseizure

The goal of an anticonvulsant (often times referred to as Antiseizure) is to suppress the rapid and excessive firing of neurons that initiate a seizure. Medications used to treat seizures include, Barbiturates such as **Phenobarbital**, Benzodiazapines such **Diazepam** and others such as **Tegretol** and **Depakote**.

Stimulants

Stimulants is a name given to several groups of drugs that tend to increase alertness and physical activity often times used in treating ADHD. Examples include **Methylphenidate** also known **Ritalin** and **Metadate**.

MEDICATIONS THAT AFFECT THE CARDIOVASCULAR SYSTEM

Beta-Blockers

Used to decrease the workload of the heart by blocking sympathetic stimulation of the beta receptors on the SA node and myocardial cells, thus decreasing the force of the contractions and causing a reduction in heart rate. Examples include; **Metoprolol** , **Labetalol**, **Sotalol** and **Propranolol**.

Calcium Channel Blockers

Work by relaxing smooth muscles to provide vasodilation as well as reduce heart rate and stroke volume of the heart. Examples include; **Diltiazem** (or **Cardizem**), **Verapamil** and **Nicardipine**.

Sodium Channel Blockers

Work by impairing conduction of sodium ions through sodium channels used in the treatment of cardiac dysrhythmias. An example of this would be **Lidocaine**.

Diuretics

Control high blood pressure by increasing the rate of urination. Loop diuretics, such as **Furosemide** (also known as **Lasix**), do this by inhibiting the body's ability to reabsorb sodium at the ascending loop in the kidney resulting in a retention and excretion of water in the urine.

Other diuretics include **Thiazides** such as **Hydrochlorothiazide** as well as **Potassium-Sparing Diuretics** such as **Aldactone**.

Alpha-Adrenergic Blockers

Used to lower blood pressure by dilating peripheral blood vessels causes a decrease in peripheral vascular resistance (PVR). Common examples include; **Cardura**, **Minipress** and **Flowmax**.

ACE Inhibitors or Angiotensin-Converting Enzyme Inhibitors

Group of pharmaceuticals that are used primarily in treatment of hypertension and congestive heart failure. Examples include; **Benazepril Hydrochloride** also known as **Lotensin**, **Captopril** also known as **Capoten**, and **Lisinopril** also known as **Prinivil** or **Zestril**.

Angiotensin II Receptor Antagonists – aka Angiotensin Receptor Blockers (or ARBs)

Vasodilate arterioles by blocking the effects of Angiotensin II, enhancing renal clearance of sodium and water. Mainly used in hypertension, kidney damage due as a result of diabetes and congestive heart failure. Examples include; **Losartan** also known as **Cozaar** and **Valsartan** also known as **Diovan**.

Nitrates

Used to prevent and relieve chest pain associated with angina as well as ease the symptoms of congestive heart failure. Nitrates vasodilate blood vessels and improves blood flow which allows more oxygen-rich blood to reach the heart muscle. This also reduces the workload on the heart by reducing preload. Example is **Nitroglycerine**.

Antiplatelet and Anticoagulant

Used to prevent clot formation in patients with a-fib, pulmonary embolism, provide anticoagulation during hemodialysis, prevent clot formation post-surgery, decrease the risk of MIs in patients with atherosclerosis as well as decrease the risk of strokes. Examples include **Heparin** and **Lovenox** as well as **Thrombolytics** such as **Retaplaste**, **Alteplase** and **Streptokinase**.

Vitamin K Antagonists (VKA)

Class of anticoagulants that work to reduce blood clotting by inhibiting the action of vitamin K. The most commonly used is **warfarin** also known as **Coumadin**.

Steroids

Corticosteroids are steroid hormones produced within the adrenal cortex. Corticosteroids are involved in a range of physiologic systems such as immune response, stress response as well as carbohydrate metabolism, regulation of inflammation, blood electrolyte levels, protein catabolism and behavior.

Adrenocorticoids

Two types of Adrenocorticoids: **Glucocorticoids** and **Mineralocorticoids**.

Mineralocorticoids

Control electrolyte and water levels, mainly by promoting sodium retention in the kidney. Example is **Aldosterone**.

Glucocorticoids

Regulate carbohydrate, fat and protein metabolism, block inflammation by preventing phospholipid release, and regulate the body's immune response. Synthetic Glucocorticoids are commonly used in the treatment of joint pain or inflammation such as arthritis, dermatitis, allergic reactions and asthma. Examples include **Hydrocortisone** and **Prednisone**.