

Chapter 3

A Brief Introduction to the Science of
Pharmacology

The Prime Effect and Side Effects of Chemicals

- Prime Effects—what the drug is intended to do
- Secondary effects or side effects-things the user must endure to get the Prime Effect; these can be relatively minor or life threatening.
- There are desired primary effects and unwanted side effects of every compound.

The Method by which a compound is administered

- The method in which the drug is administered will influence the intensity of the prime effect and side effects
- Enteral forms of drug administration (gastrointestinal)
 - Orally
 - Tablet/capsule
 - Sublingually (under the tongue)
 - nitroglycerin
 - Rectally

The Method by which a compound is administered

- Parenteral forms of administration (Injecting drugs)
 - Subcutaneous
 - Skin-popping (Injected just under the skin)
- Intramuscular
 - Injected into muscle tissue
- Intravenous (IV)
 - Injected directly into a vein

Other forms of drug administration

- Transdermal
 - Absorbed through the skin
- Intranasal
 - Snorting
- Inhalation
 - Passing chemicals to the lung
 - The lungs offer a blood-rich, extremely large surface area, allowing for the rapid absorption of many compounds

Bioavailability

- Is the concentration of the unchanged chemical at the site of action (Bennett & Brown, 2003)
- Is influenced by:
 - Absorption-involves drug molecules moving from site of entry through various cell boundaries to the circulatory system, where it is transported to the site of action
 - The process of drug absorption is variable depending on:
 - Method of administration
 - Rate of blood flow at site of entry
 - Molecular characteristics of compound

Bioavailability

- Distribution-how chemical molecules are transported within the body
 - The chemical may be water-, lipid (fat), or protein-soluble
 - A compound that is lipid soluble will be concentrated in the brain tissues fairly rapidly since the brain is over 50% lipid molecules (Cooper, Bloom, & Roth, 2002)
 - May form basis of synergistic effect (the effects of one compound reinforce the effects of a second compound)

Bioavailability

- Biotransformation-helps the organism cope with potentially dangerous compounds found in food sources.
 - These are defensive detoxification systems
 - Usually carried out in the liver
 - Zero order biotransformation process
 - First Order Biotransformation process
- Elimination-Usually carried out by the kidneys
 - Does not happen instantly, depends on the speed at which the process of biotransformation is carried out

Drug half-life

- Rough estimate of the period of time that a drug remains active in the human body
- Distribution half-life: time it takes for a compound to work its way into general circulation into body tissues
- Therapeutic half-life: time needed for body to inactivate 50% of a compound
- Biological half-life: time needed for the individual's body to reduce the amount of single dose of a compound by one-half

Effective Dose

- Approximate dose at which a given percentage of the population will respond to a designated dose of a compound
- Lethal dose
 - Percentage of general population would die as a result of being exposed to a certain dose of a chemical
- Therapeutic window/index
 - A ratio of the effective dose and lethal dose
- Peak effects
 - the effects within the body develop over a period of time (therapeutic threshold)
 - Strongest possible effects are reached

The Site of Action

- The Central Nervous System-where most psychoactive pharmaceuticals and drugs of abuse have their main effects.
- The Receptor Site-the structure of the neurotransmitter molecule fits into the receptor site like a key in a lock.
 - Neurotransmission-*Inotropic* or *metabotropic*
- Neurotransmitter may then be retrieved by upstream neuron, destroyed by enzymes near receptor site, or diffused into surrounding areas

Upregulation/down-regulation

- Neurons are constantly adjusting to allow for greater/reduced sensitivity to the neurotransmitter activity
- If a receptor site is constantly exposed to high levels of a given neurotransmitter, it might decrease the sensitivity and/or number of receptor sites available to those molecules (down-regulate)
- The opposite effect, an up-regulation of receptor number/sensitivity, might result from lower levels of a given transmitter

Drug agonists/antagonists

- A drug agonists is a compound that activates a receptor site by being able to mimic or enhance the actions of a neurotransmitter (Wilson, et al., 2007)
- Antagonists are able to fit into the receptor site, without activating it
- Partial agonists are able to only weakly activate receptor sites, while preventing other drug molecules the opportunity to bind at that receptor site

Tolerance/Neuroadaptation

- When a compound has a shortened duration of effect because neurons have learned to compensate for the presences of that compound
 - Metabolic tolerance
 - Behavioral tolerance
 - Cross tolerance
 - Reverse tolerance

Potency

- The ratio between the size of a dose and the desired response
- Some compounds are more likely, with smaller doses, to achieve an action that may take another compound a much larger dose to achieve

The Blood Brain Barrier

- A thin layer of endothelial cell tissue and astrocytes of the brain, which separate the brain from direct contact with the circulatory system
- The Blood Brain Barrier is a screen that keeps unwanted substances from circulating in the brain.