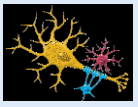
Chapter 5

The Actions of Drugs



Origins of Drugs

- Most drugs come from plants or are chemically derived from plants

Names of Drugs

- **Chemical name:** Complete chemical description of the molecule
  - *Example:* N'-[2-[[5-(dimethylaminomethyl)-2-furyl] methylsulfanyl]ethyl]-N-methyl-2-nitro-ethene-1,1-diamine
- **Generic name:** Official (legal) name, listed in the *United States Pharmacopoeia* (USP)
  - *Example:* ranitidine
- **Brand name:** Specific drug or formulation trademarked by manufacturer; can be patented for 20 years;
  - *Example:* Zantac® (an acid reflux drug)

Categories of Drugs

Categorization is "in the eye of the beholder" *(p 107)*

- **Stimulants** produce wakefulness, a sense of energy
- **Depressants** slow nervous system activity
- **Opioids** (narcotics) reduce pain
- **Hallucinogens** produce altered perceptions
- **Psychotherapeutics** control mental disorders
- Some drugs have effects typical of more than one category
  - **Marijuana**
  - **Nicotine**

Classification of Psychoactive Drugs

Drug Identification

- It is important that both legal and illicit drugs be **identifiable by appearance**
- The ***Physician's Desk Reference*** (*PDR*) includes color photographs of many legally manufactured pharmaceuticals
- **Illegal drugs** are sometimes shaped, marked, or packaged in an identifiable way
- Drugs can be tested and identified through **chemical analysis**

Valium

Types of Drug Effects

- **Nonspecific effects** derive from the user's unique background, expectations, perceptions, and environment (setting); e.g. a "bad acid trip"
- **Specific effects** depend on the presence of a chemical at certain concentrations
- **Placebo effects** are those produced by an inactive chemical that the user believes to be a drug
  - Especially important in treating pain and psychological depression

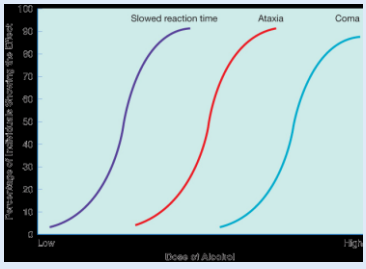
Double-Blind Procedure

- Because of nonspecific effects (for instance bias of subject to act in a way expected by a doctor or researcher) **double-blind tests** are needed to evaluate the effectiveness of a drug;
- Neither the test subjects nor the evaluators knows whether a subject is receiving an experimental drug or a placebo until the drug trial is over.

Dose-Response Relationship

- **Dose-response relationship** = correlation between the response and the quantity of drug administered
- **Threshold** = the dose at which an effect is first observed
- Some response systems have higher thresholds than others, so dose-response curves can be created for different drug effects
- Some drugs have an *all-or-none* dose-response relationship (for example, *ibuprofen* or *aspirin*) – **side effects** may accumulate but not drug response.

Dose-Response Curve



Dose-response graph showing size of response relative to amount of drug administered; different systems/effects have different response thresholds

Animal Testing: Effective and Lethal Doses

- **Effective dose** = the dose of a drug that produces a meaningful effect in some percentage of test subjects
  - ED_{50} refers to the effective dose for half the animal subjects in a drug test
- **Lethal dose** = the dose of a drug that has a lethal effect in some percentage of test subjects
  - LD_{50} refers to the lethal dose for half the animal subjects in a drug test
- **Therapeutic index** = LD_{50}/ED_{50}
  - Always greater than one

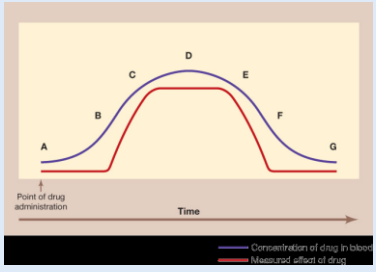
Potency, Toxicity, and Safety Margin

- **Potency** = measured by the amount of a drug required to produce a given effect
- **Toxicity** = capacity of a drug to do damage or cause adverse side effects
- **Safety margin** = difference between:
  - Dose that produces the desired therapeutic effect in most patients
  - Lowest dose that produces an unacceptable toxic reaction
- Most drugs have an LD_1 well above the ED_{95}

Time-Dependent Factors

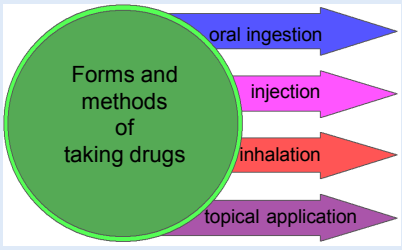
- Drugs vary in the timing of the onset, duration, and termination of their effects
- The time course of a drug **depends on how the drug is administered, how rapidly is it absorbed, and how it is eliminated from the** body
- Drug effects can be prolonged by taking additional doses at intervals determined by the time course of the drug (like ***time-release*** *capsules*)
- Taking multiple doses too close together will increase the maximum blood level of the drug (***cumulative effects.***)

Time-Dependent Factors

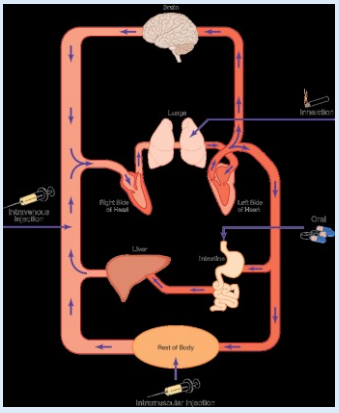


Possible relationship between drug concentration in the body and measured effect of the drug

Routes of Administration



Distribution of drugs through the body

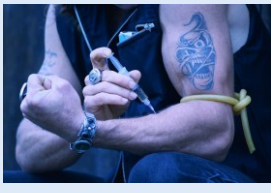


Routes of Administration: **Oral Ingestion**

- Absorption from the gastrointestinal (GI) tract is a complicated process
- **Drugs must withstand the digestive processes** and pass through the cells lining the GI tract into the bloodstream
- Drugs from the GI tract travel **through veins first to the liver**, where they may be metabolized

Routes of Administration: Injection

- **Intravenous (IV) injection** involves putting the drug directly into the bloodstream
  - Effects are **rapid**
  - **High concentrations** can be delivered
  - Irritating material can be injected this way
  - ***Veins can be damaged*** over time
  - ***Infections*** can be directly introduced into the bloodstream



Routes of Administration: Injection

- **Subcutaneous injection** (under the skin)
  - "Skin popping"
  - Can cause necrosis
- **Intramuscular injection** (into a muscle)
  - Absorption is more rapid from intramuscular injection due to the greater blood supply in muscles

Routes of Administration: Inhalation

- The drug moves from the **lungs into the bloodstream through capillary walls**
- Effects are rapid because **blood moves quickly from the lungs to the brain**

Routes of Administration: Topical Application

- Absorption through the skin can provide **slow, steady drug delivery**
- Absorption through the mucous membranes occurs more rapidly

When a user snorts cocaine, the drug is absorbed through the mucous membranes in the nose.

Transport in the Blood

- Some drug molecules attach to protein molecules; they are inactive in this state
- Free (unbound) drug molecules can move to sites of action in the body
- Drugs vary in their affinity for binding with proteins

Blood-Brain Barrier

- Some drugs can't cross the blood-brain barrier; they act only on peripheral nerves
- **Only lipid-soluble substances can leave capillaries in the brain**
- Many brain capillaries are covered with glial cells, also increasing the difficulty for compounds to pass out of the capillaries
- **Active transport systems** may be needed to move chemicals in and out of the brain
- Trauma and infections can impair the blood-brain barrier

Mechanisms of Drug Action

- Effects on all neurons
- Effects on specific neurotransmitter systems
  - **Drugs may alter** the availability of a neurotransmitter by changing the rate of **synthesis, metabolism, release, or reuptake**
  - Drugs may **activate or prevent the activation of a receptor**

Drug Interactions

- Combining **depressants** can cause respiratory depression
- **Stimulants + antidepressants** can lead to overexcitement, high blood pressure, and arrhythmia
- **Stimulants + depressants** can lead to explosive and dangerous behaviors
- **Cocaine + alcohol** produces a potent and toxic substance called cocaethylene

Drug Deactivation

- A drug ceases to have an effect when it is excreted unchanged from the body or is chemically changed
- The key **drug-metabolizing liver enzymes** are a group known as CYP450
  - The resulting metabolite no longer has the same action as the drug
  - The resulting metabolite can be excreted by the kidneys

Enzyme Induction

- When the body's cells detect the presence of foreign **drugs**, they **trigger production of more of the specific metabolizing enzyme:**
  - Causes **tolerance**
  - Causes **interaction of drugs broken down by the same enzyme**
- Enzyme activity returns to normal some time after the inducing drug is no longer being used
- **Enzyme induction** and tolerance can occur after use of prescription and OTC drugs, dietary supplements, or illicit drugs

Mechanisms of Tolerance and Withdrawal Symptoms

- **Drug disposition (pharmacokinetic) tolerance**
  - Increased metabolism reduces the effect of the subsequent dose
  - May relate to enzyme activity or alteration of urine pH

Mechanisms of Tolerance and Withdrawal Symptoms

- **Behavioral tolerance**
  - Drug may have the same biochemical effect but a reduced behavioral effect as a drug user learns to compensate for nervous system impairment
- **Pharmacodynamic tolerance**
  - Sensitivity of neurons change after repeated use of a drug
  - Can cause withdrawal reactions