

PHARMACOLOGY

I. Pharmacology

- definition: the interaction of chemical agents with living organisms
- consists of two areas: (1) pharmacodynamics and (2) pharmacokinetics

II. Pharmacodynamics

- definition: the study of drug action at the biochemical or physiological level
→ “mechanism of action” of a drug
- there are 2 major types of pharmacological actions:
 - A. drugs which change the environment of body cells
 - example: antacids (Mylanta) → neutralize excess stomach acid
 - B. drugs which alter or modify function of body cells by binding to receptors located on cell membranes
 - (1) drug-receptor interaction (“lock-and-key mechanism”)
 - a. agonist - drug which binds to a specific receptor and produces a biological effect by stimulating the receptor
 - example: amphetamines → stimulate receptors in the CNS (central nervous system)
 - b. antagonist - drug which binds to a specific receptor and prevents substances from stimulating the receptor
 - example 1: antihistamines (e.g., Benadryl) → block histamine receptors → block allergic reactions
 - example 2: naloxone (Narcan) → blocks opiate (morphine) receptors → reverses respiratory depression

Pharmacodynamics (continued)

(2) competitive inhibition

- agonist and antagonist which bind to the same receptor may compete for occupation at the receptor site
- examples 1: Valium (agonist) \leftrightarrow Romazicon (antagonist)
- example 2: morphine (agonist) \leftrightarrow Narcan (antagonist)

II. Pharmacokinetics

- definition: the study of how drugs enter the body, reach their site of action, and are excreted from the body
- consists of : (1) drug absorption, (2) drug distribution, (3) drug biotransformation, and (4) drug excretion

A. Drug Absorption (how drugs enter the bloodstream)

i. oral

- drug is taken orally and is absorbed from the stomach and/or intestine
- the oral route is convenient and economical
- once absorbed into the bloodstream, the drug enters the liver, where it may be metabolized

ii. sublingual

- drug is dissolved and absorbed under the tongue
- the sublingual route is convenient and economical
- the drug will enter the general circulation and interact with its receptor before entering the liver, where it may be metabolized or inactivated

iii. transdermal

- drug is absorbed through the skin
- drug patch provides continuous drug dosing
- local skin irritation may occur
- the drug will enter the general circulation before passing through the liver

iv. rectal

- drug is inserted into rectum as a suppository and diffuses through the mucous membranes into the bloodstream
- route is convenient in unconscious or vomiting patients
- disadvantage: drug may be incompletely or erratically absorbed
- the drug will interact with its receptor before subjected to the metabolic processes of the liver

A. Drug Absorption (continued)

v. inhalation

- drug is inhaled as a gas or aerosol into the lungs where it either exerts a localized effect (bronchodilation) or enters the bloodstream (anesthetics)
- tobacco and marijuana smoke pass through the lung membrane and enter the bloodstream
- inhaled drugs produce a rapid onset since they circulate to the brain shortly after being absorbed into the bloodstream from the lungs
- absorbed drug will enter the general circulation before entering the liver

vi. intranasal

- drug is absorbed into the bloodstream through the mucous membranes of the nasal cavity
- absorbed drug interacts with its receptors before undergoing metabolism by the liver

vii. parenteral (by injection)

(1) subcutaneous (SQ) is an injection under the skin (“skin-popping”)

(2) intramuscular (IM) is an injection into muscle mass

(3) intravenous (IV) is an injection into a vein (“mainlining”)

- drug response: $IV > IM > SQ$
- parenteral route produces a more rapid onset of effect than oral or rectal administration
- drug formulation must be sterile to avoid infections
- route may be used in unconscious or uncooperative patients
- disadvantage: once injected, a drug cannot be retrieved
- drug bypasses the unpredictable absorption processes which may occur in the stomach and/or intestine of some patients
- injected drug enters the general circulation before passing through the liver

B. Drug Distribution

- once absorbed into the bloodstream, a drug is distributed throughout the body
- the degree of drug distribution depends on the drug’s physical and chemical properties
- as a general rule, small and highly lipid-soluble drug molecules will penetrate cell membranes, capillaries, and physiological barriers (e.g., placenta, blood-brain barrier, etc...) more readily than larger, polar (non-lipid soluble) drug molecules

B. Drug Distribution (continued)

(1) Blood-Brain Barrier (BBB)

- only lipid-soluble drugs and very small molecules are capable to crossing the BBB to exert an effect on the brain
- example: heroin crosses the BBB more readily than morphine because of its greater lipid-solubility factor

(2) Tissue Trapping

- certain tissues in the body are capable of trapping or storing drugs temporarily or permanently, converting them into inactive (bound) forms
- when drugs leave the tissue-binding site, they become physiologically active again

C. Drug Biotransformation (Drug Metabolism)

- the liver is the major organ responsible for metabolizing drugs
- the complex liver enzyme system is effective in transforming lipid-soluble substances (e.g., drugs) into water-soluble compounds so they may be excreted from the body by the kidneys

(1) "First-Pass" Effect (Liver)

- foods, drugs, toxins, and other substances absorbed from the gastrointestinal (GI) tract into the bloodstream, enter the liver before entering the general circulation
- the "first-pass" effect of the liver allows the body to chemically inactivate potentially harmful chemicals before they are extensively distributed throughout the body
- biologically active drugs are chemically transformed into less active or
 - example: heroin (more potent) → morphine (less potent)

(2) Induction / Inhibition of Drug Metabolism

- liver enzymes which metabolize drugs may be induced or inhibited by other drugs → drug-drug interactions

i. induction of enzymes

- example: smoking tobacco induces (increases) the metabolism of theophylline (breathing medication used in asthma)
→ subtherapeutic effect → wheezing

(3) Induction / Inhibition of Drug Metabolism (continued)

ii. inhibition of enzymes

- example: Tagamet (cimetidine) inhibits the metabolism of Theo-Dur (theophylline) → theophylline toxicity

D. Drug Elimination (Kidneys)

- the three main routes of drug elimination are: kidneys, liver, and bowel; however, most drugs are excreted by the kidneys
- it has been estimated that kidney function decreases by 10% per decade of life after 20 years of age

III. Factors Influencing Drug Actions

A. Age

- (1) infants → underdeveloped abilities to metabolize and excrete drugs
- (2) elderly → impaired abilities to metabolize and excrete drugs

B. Body Weight

- heavier individuals possess greater volumes of body fluids to dilute drugs

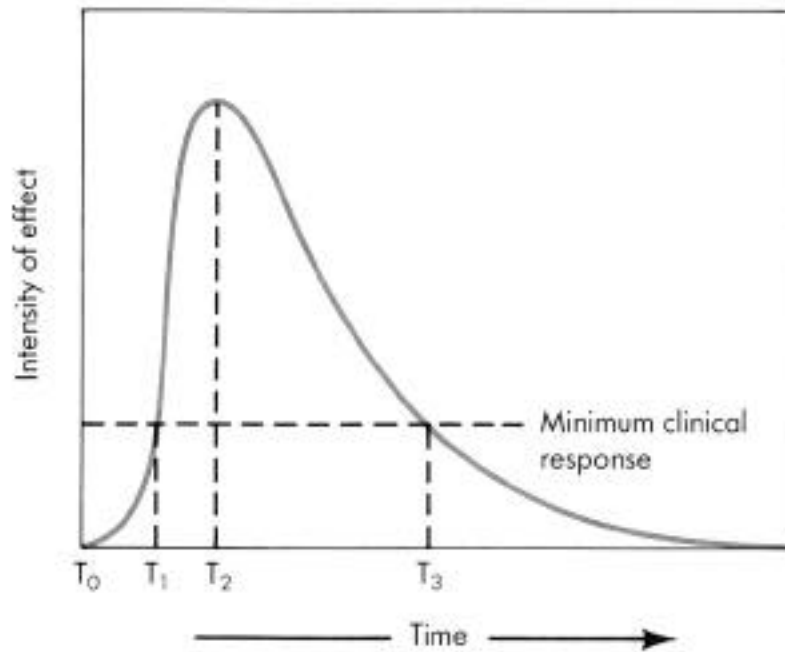
C. Gender

- females, in general, tend to be more sensitive to the effects of some drugs than males

D. Disease

- patients with and liver and/or kidney diseases will have compromised abilities to metabolize and excrete drugs → prolonged and toxic drug effects

E. Time Profile



- (1) onset of action $\rightarrow T_0$ to T_1
 \rightarrow time between taking a drug and observing its effect
- (2) peak $\rightarrow T_0$ to T_2
 \rightarrow time it takes for a drug to reach its highest blood concentration
- (3) duration of action $\rightarrow T_1$ to T_3
 \rightarrow time during which the drug is producing a response
- (4) half-life ($t_{1/2}$) \rightarrow time it takes for the body to reduce a drug blood level by one-half

IV. Overview of Pharmacodynamics & Pharmacokinetics

