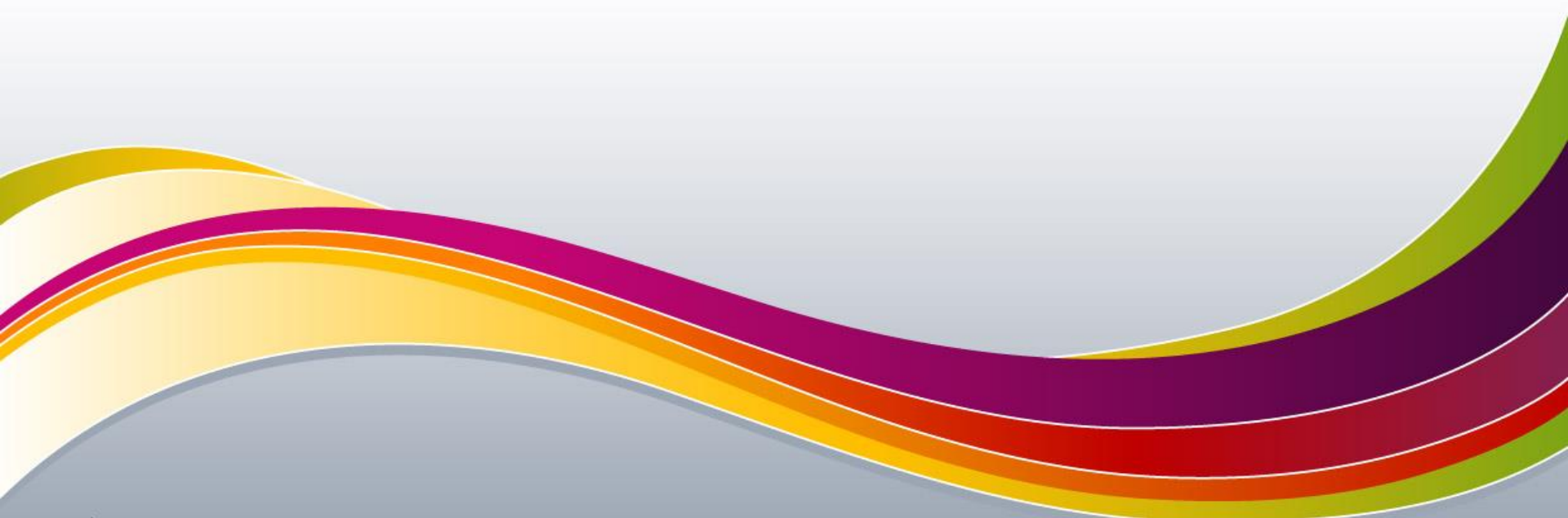


# Chapter 1

# General Principles of Pharmacology



# Introduction to Pharmacology

- Pharmacology: study of drugs, their action on living organisms
- Sound knowledge of basic pharmacologic principles
  - Enables safe medicine administration and monitoring of patients



# Drug Names and Categories

- Categories: chemical; generic; nonproprietary; official; trade or brand name
- Several trade names: use generic name to avoid confusion
- After drug approval FDA assigns categories:
  - prescription
  - nonprescription
  - controlled substance



# Question #1

What occurs during Phase 2 of clinical drug development?

- A. 20 to 100 volunteers involved to see what drug does to health tissue
- B. Test performed on people having the disease for which drug might be effective
- C. Drug given to large numbers of patients in medical research centers that provided information about adverse reactions

# Answer to Question #1

- B
- Phase 1: 20 to 100 volunteers involved to see what drug does to healthy tissue
- Phase 2: test performed on people having the disease for which drug might be effective
- Phase 3: drug given to large numbers of patients in medical research centers that provided information about adverse reactions
- Phase 4: postmarketing surveillance

# Drug Development #1

- Process of drug development: long and arduous—7 to 12 years or longer
- FDA: approves new drugs, monitors current drugs—adverse/toxic reactions
- Development of drug:
  - pre-FDA phase
  - FDA phase

# Drug Development #2

- Clinical testing: four phases
  - Phase 1: 20 to 100 volunteers involved to test drug on health tissue
  - Phase 2: test performed on people having the disease for which drug might be effective
  - Phase 3: drug given to large numbers of patients in medical research centers for information about adverse reactions

# Drug Development #3

- Phase 4: postmarketing surveillance
  - Ongoing review: particular attention to adverse reactions
- Health care professionals: help with surveillance; report adverse effects to FDA using MedWatch

# Question #2

- Is the following statement true or false?
- Orphan Drug Act: passed to encourage development and marketing of products for common diseases

# Answer to Question #2

- False
- Orphan Drug Act: passed to encourage development and marketing of products for rare diseases, not common diseases

# Orphan Drug Program

- Orphan Drug Act: passed to encourage development and marketing of products for rare diseases
- Rare disorders: Tourette syndrome; ovarian cancer; amyotrophic lateral sclerosis
- Drug approved: manufacturer gets 7 years of exclusive marketing rights
- Orphan drugs: Velcade for amyloidosis; enzyme replacement therapy for Gaucher disease; atiprimod for multiple myeloma

# Accelerated Programs

- Accelerated approval/provisional approval
- Diseases that are a threat to public health: AIDS—considered for shorter IND approval process
- Allows primary care providers to administer medications with positive results in early Phase 1 and 2 clinical trials
- Waiting until final approval not required: drug continues to prove beneficial—process of approval accelerated

# Drug Activity Within the Body

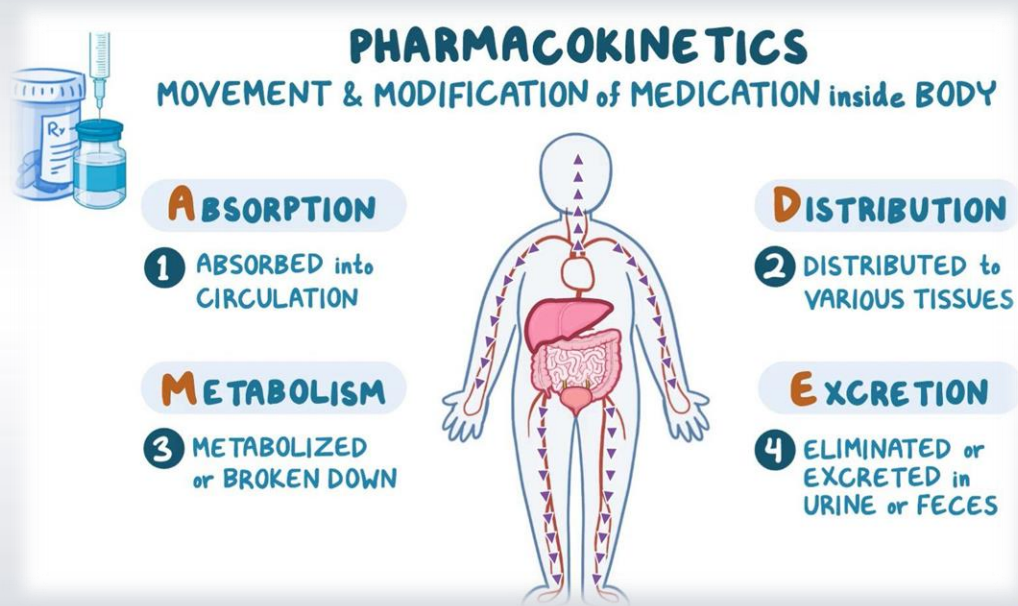
- Drugs: act in various ways in the body
- Oral drugs: three phases
  - Pharmaceutic: dissolution of drug occurs; drugs must be soluble to be absorbed
  - Pharmacokinetic: absorption; distribution; metabolism; excretion
  - Pharmacodynamics: deals with drugs action and effect on body

# Pharmaceutic Phase

- Liquid and parenteral drugs: already dissolved—quickly absorbed
- Solid forms of drugs: tablets or capsules—disintegrate into small particles; dissolve into body fluids in GI tract
- Enteric-coated tablets: disintegrate after reaching alkaline environment of small intestine

# Pharmacokinetic Phase

- Pharmacokinetics: activities within the body after a drug is administered
  - Absorption
  - Distribution
  - Metabolism
  - Excretion



# Absorption

- Drug particles within gastrointestinal tract: move into body fluids
- Factors influencing rate of absorption: route of administration; solubility of drug
- First-pass effect: drug absorbed by small intestine; liver first metabolizes drug; remaining drug not sufficient to produce therapeutic effect
  - patient needs higher dosage for desired effect

# Distribution

- Systematic circulation: drug distributed to various body tissues and target sites—interact with specific receptors in body
- Factors affecting distribution: protein binding (free/bound drugs); blood flow; solubility (lipid-soluble drugs/water-soluble drugs)
- Quick distribution: heart; liver; kidneys
- Slow distribution: internal organs; skin; muscle

# Metabolism and Excretion

- Metabolism: body changes drug to a more or less active form for excretion
- Excretion: elimination of drugs from the body
- Patients with kidney disease: require dosage reduction and careful monitoring of kidney function
- Older adults: diminished kidney function—require careful monitoring and lower dosages

# Half-Life

- Time required for the body to eliminate 50% of the drug
- Drugs with short half-life: administered frequently
- Drugs with long half-life: require less frequent dosing
- Difficulty in drug excretion: increases half-life and risk of toxicity

# Onset, Peak, and Duration

- Onset of action: time between drug administration and beginning of therapeutic effect
- Peak concentration: absorption rate equals elimination rate
- Duration of action: time for drug to produce therapeutic effect

# Pharmacodynamic Phase

- Pharmacodynamics: study of drug mechanisms producing biochemical/physiologic changes in body
- Primary effect of drug: desired or therapeutic effect
- Secondary effect of drug: other desirable or undesirable effects
- Drugs exert action—two mechanisms: alteration in cellular form/environment

# Alteration in Cellular Environment

- Physical changes: osmotic pressures; lubrication; absorption; conditions—surface of cell membrane
  - Mannitol; sunscreen; activated charcoal; docusate
- Chemical changes: inactivation of cellular functions; alteration of chemical components of body fluid—change in the pH
  - Antacids; cancer drugs or some antibiotics

# Receptor-Mediated Drug Action

- Drug interacts with receptor; function of a cell alters; drug molecule joins with reactive site (receptor) on surface of cell
- Agonist: binds with and stimulates receptor—therapeutic response
- Antagonist: joins with but does not stimulate receptors; prevents drug response; competitive/noncompetitive
- Effects of number of available receptor sites; potent drugs

# Drug Use and Pregnancy

- Drugs administered during the first trimester: may cause teratogenic effects
- Most drugs: contraindicated unless benefits outweigh risk
- Pregnant women: use drugs/herbal supplements only after consultation
- Risks of smoking and drinking: low birth weight; premature birth; fetal alcohol syndrome
- Addictive drugs: children born with addiction

# Various Drug Reactions

- Allergic drug reactions
- Drug idiosyncrasy
- Drug tolerance
- Cumulative drug effect
- Toxic reactions
- Pharmacogenetic reactions

# Allergic Drug Reactions (Hypersensitivity Reactions)

- Usually begin after more than one dose of the drug is given; body views drug as antigen
- Signs and symptoms: itching; skin rashes; hives; wheezing; cyanosis; sudden loss of consciousness; swelling of eyes, lips, or tongue
- Anaphylactic shock; hypotension and shock; angioedema



# Drug Idiosyncrasy

- Unusual, abnormal reaction to drug; different from expected reaction
- Cause: believed to be due to genetic deficiency

# Drug Tolerance

- Decreased response to a drug: requires increased dosage for desired effect
- Example: narcotics or tranquilizers taken for a long time

# Cumulative Drug Effect

- Patients with liver and kidney disease: body is unable to metabolize and excrete one dose of drug before next dose is given
- Dose lowered to prevent toxic drug reaction

# Toxic Reactions

- Drug is administered in large dosages; blood concentration levels exceed therapeutic levels
- Reverse drug toxicity: Administer another drug as antidote; monitor drugs with low safety margin

# Pharmacogenetic Reactions

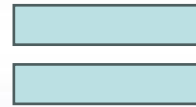
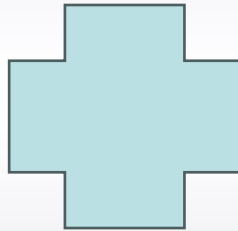
- Pharmacogenetic disorder
  - Genetically determined abnormal response to normal doses of a drug
  - Inherited traits cause abnormal metabolism of drugs
- Patients with G6PD deficiency: Drugs cause hemolysis (aspirin; chloramphenicol; sulfonamides)

# Drug Interactions

- One drug interacts and interferes with the action of another drug
  - Oral anticoagulants; oral hypoglycemics; anti-infectives; antiarrhythmics; cardiac glycosides; alcohol
- Effects: Additive; synergistic; antagonistic

# Additive Drug Reaction

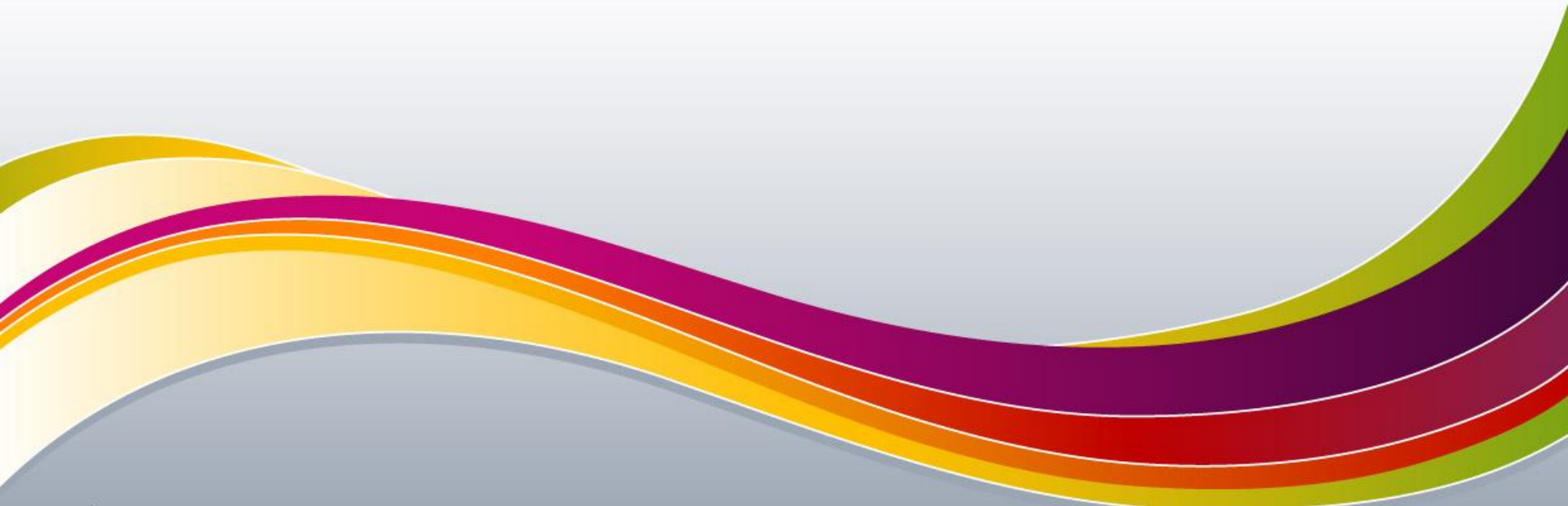
- Combined effect of two drugs is equal to sum of each drug given alone ( $1 + 1 = 2$ )



**Double  
the  
strength**

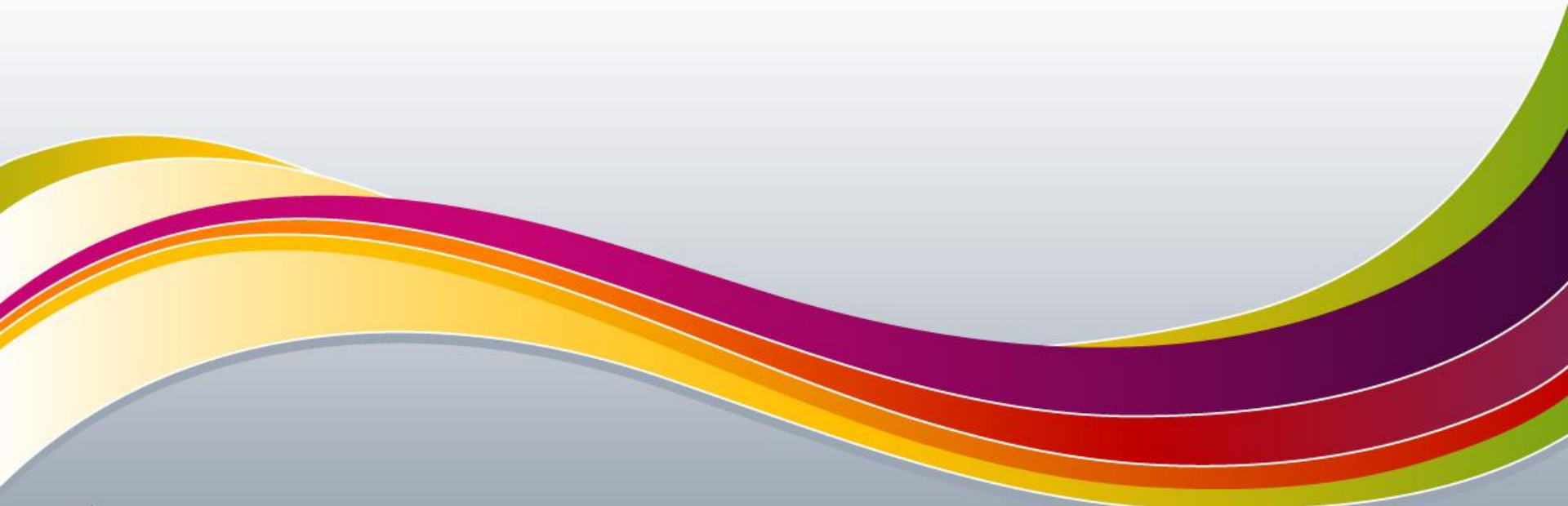
# Synergistic Drug Reaction

- Drugs interact with each other and produce a sum greater than the sum of their separate actions ( $1 + 1 = 3$ )



# Antagonistic Drug Reaction

- One drug interferes with action of another: neutralization/decrease in effect of one drug



# Drug–Food Interactions

- Food may impair or enhance drug's absorption
  - Drug taken on empty stomach (captopril)
  - Drugs that irritate stomach; cause nausea, vomiting, epigastric distress: given with meals (anti-inflammatory drugs; salicylates)
  - Drug–food mixture: drugs combine with a food forming an insoluble food (tetracycline administered with dairy products)



# Question #3

- Is the following statement true or false?
- Age is a factor that influences drug response.

# Answer to Question #3

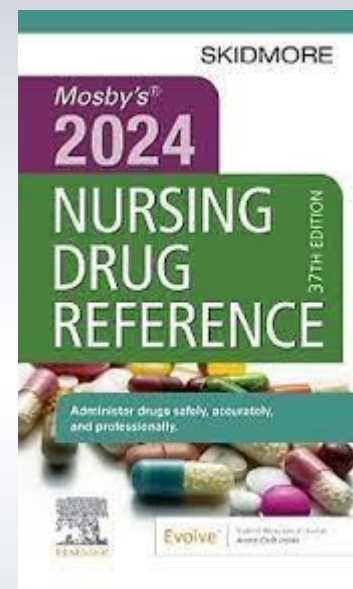
- True
- Age, weight, gender, disease, and route of administration are factors influencing drug response.

# Factors Influencing Drug Response

- Age
- Weight
- Gender
- Disease
- Route of administration

# Nursing Implications

- Consult appropriate references and hospital pharmacist
- Observe patients
- Report
- Use judgment
- Accurately observe and evaluate circumstances
- Record



# Herbal Therapy and Dietary Supplements

- Herbal therapy
  - Type of complementary/alternative therapy—using plants or herbs
  - Explain that “natural” is not necessarily safe
- Nutritional or dietary supplements
  - Substances not regulated as drugs by FDA; effective for promoting health

# National Center for Complementary and Alternative Medicine (NCCAM)

- Explores complementary and alternative healing practices: scientific research
- Trains CAM scientists and disseminates information gleaned from conducted research
- Develops programs; encourages scientists to investigate CAM treatments that show promise