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Pharmacology

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Basic principles of Pharmacology

- Pharmacokinetic terms.
- Pharmacodynamics.
- Drug-drug and drug-food interactions.
- Adverse drug reactions.
- Individual variations in drug responses

Pharmacokinetic terms

Pharmacokinetics involves drug movement through the body. Specific processes are **absorption**, **distribution**, **metabolism**, and **excretion**. Overall, these processes largely determine

- **serum drug levels**;
- **onset**, **peak**, and
- **duration of drug actions**;
- **therapeutic and adverse effects**; and

other important aspects of drug therapy

Absorption is the process that occurs from the time a drug enters the body to the time it enters the bloodstream to be circulated. **Onset of drug action** is largely determined by the **rate of absorption**; **intensity** is determined by the **extent of absorption**.

Numerous factors affect the **rate and extent of drug absorption**, including ;

- dosage form,
- route of administration,
- blood flow to the site of administration,
- GI function,
- the presence of food or other drugs, and other variables

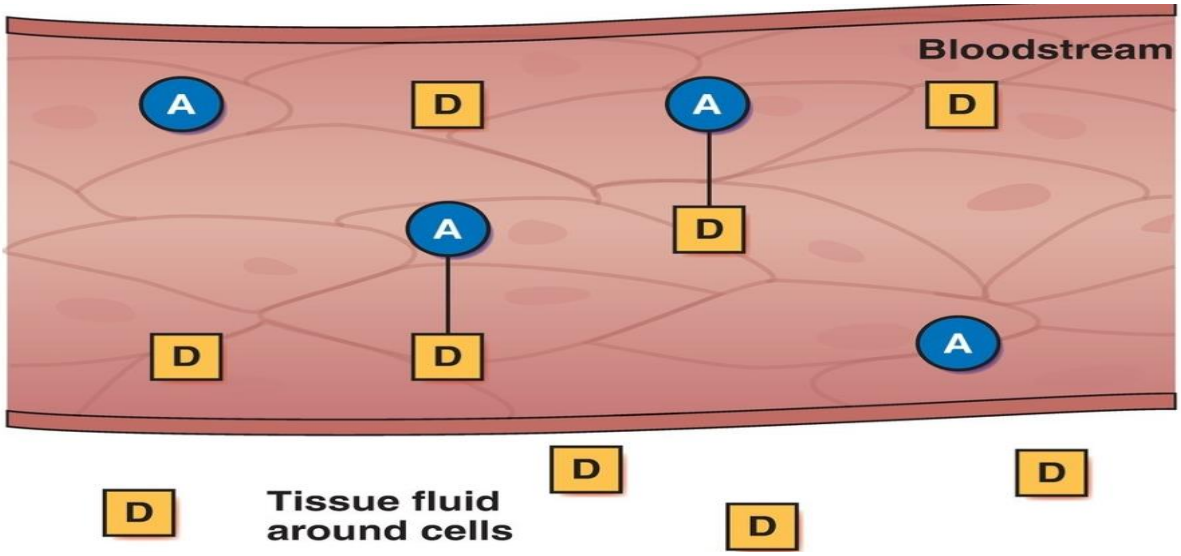
- **Dosage form** is a major determinant of a drug's **bioavailability** (the portion of a dose that reaches the systemic circulation and is available to act on body cells). An intravenous (IV) drug is virtually 100% bioavailable. In contrast, an oral drug is virtually always less than 100% bioavailable because some of it is not absorbed from the GI tract and some goes to the liver and is partially metabolized before reaching the systemic circulation.

Distribution involves the transport of drug molecules within the body. After a drug is injected or absorbed into the bloodstream, it is carried by the blood and tissue fluids to its sites of action. Distribution depends largely on the

- **adequacy of blood circulation**. Drugs are distributed rapidly to organs receiving a large blood supply, such as the heart, liver, and kidneys. Distribution to other internal organs, muscle, fat, and skin is usually slower.
- **Protein binding** is an important factor in drug distribution

(A) **albumin**

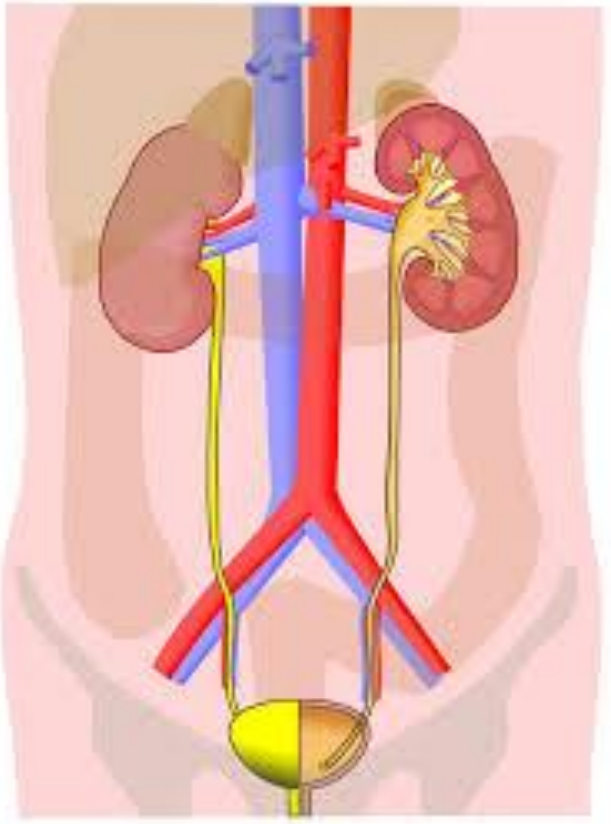
drug molecules (D)



Metabolism, or **biotransformation**, is the method by which drugs are inactivated or biotransformed by the body. Most often, an active drug is changed into inactive metabolites, which are then excreted. Some active drugs yield metabolites , Other drugs (called **prodrugs**) are initially inactive and exert no pharmacologic effects until they are metabolized.

- **Genetic polymorphisms**
- **enzyme induction**
- **enzyme inhibition**,
- **first-pass effect (**drugs are extensively metabolized in the liver, with only part of a drug dose reaching the systemic circulation for distribution to sites of action.)

Excretion refers to elimination of a drug from the body. Effective excretion requires adequate functioning of the **circulatory system** and of the **organs of excretion** (kidneys, bowel, lungs, and skin). Factors impairing excretion, especially severe **renal disease**, lead to accumulation of numerous drugs and may cause severe adverse effects if dosage is not reduced



❑ Pharmacodynamics.

Pharmacodynamics involves drug actions on target cells and the resulting alterations in cellular biochemical reactions and functions (i.e., “what the drug does to the body”).

Receptor Theory of Drug Action

When drug molecules bind with receptor molecules, the resulting drug receptor complex initiates physiochemical reactions that stimulate or inhibit normal cellular functions

- One type of reaction involves activation, inactivation, or other alterations of intracellular enzymes.
- A second type of reaction involves changes in the permeability of cell membranes to one or more ions.
- A third reaction may modify the synthesis, release, or inactivation of the neurohormones (e.g., acetylcholine, norepinephrine, serotonin) that regulate many physiologic processes.

Non-receptor Drug Actions

Drugs that do not act on receptor sites include the following:

- **Antacids**, which act chemically to neutralize the hydrochloric acid produced by gastric parietal cells and thereby raise the pH of gastric fluid
- **Osmotic diuretics** (e.g., mannitol), which increase the osmolarity of plasma and pull water out of tissues into the bloodstream
- Drugs that are structurally similar to **nutrients** required by body cells (e.g., purines, pyrimidines) and that can be incorporated into cellular constituents, such as nucleic acids, which interfere with normal cell functioning. Several anticancer drugs act by this mechanism.
- **Metal chelating agents,** which combine with toxic metals to form a complex that can be more readily excreted

❑ Drug-drug and drug-food interactions.

The action of a drug may be increased or decreased by its interaction with another drug in the body. Most interactions occur whenever the interacting drugs are present in the body; some, especially those **affecting the absorption** of oral drugs, occur when the interacting drugs are taken at or near the same time. The basic cause of many drug–drug interactions is **altered drug metabolism**. For example, drugs metabolized by the same enzymes compete for enzyme binding sites, and there may not be enough binding sites for two or more drugs. Also, some drugs **induce or inhibit the metabolism** of other drugs. **Protein binding** is also the basis for some important drug–drug interactions

Interactions that can increase the therapeutic or adverse effects of drugs include the following

- ✓ **Additive effects**
- ✓ **Synergism**
- ✓ **Interference by one drug with the metabolism of a second drug**
- ✓ **Displacement**

Interactions in which drug effects are decreased include the following

- ✓ **An antidote drug**
- ✓ **Decreased intestinal absorption of oral drugs,**
- ✓ **Activation of drug-metabolizing enzymes in the liver**,

❑ Adverse drug reactions

refers to any undesired responses to drug administration, as opposed to therapeutic effects, which are desired responses.

Common or Serious Adverse Drug Effects

- ❖ Central Nervous System Effects
- ❖ Gastrointestinal Effects
- ❖ Hematologic Effects
- ❖ Hepatic Effects
- ❖ Nephrotoxicity
- ❖ Hypersensitivity
- ❖ Drug Fever
- ❖ Idiosyncrasy
- ❖ Drug Dependence
- ❖ Carcinogenicity

❑ Individual variations in drug responses

Several factors that can cause individual variation in drug responses, including;

- **body weight,**
- **age,**
- **gender,**
- **pre-existing medical conditions,**
- **drug tolerance, and**
- **placebo effects.**

It discusses how drug absorption and a patient's adherence to the prescribed dosage regimen can also impact the variability of drug responses.

Black Box Warnings (BBW)

some prescription drug groups and individual drugs that may cause serious or life-threatening adverse effects,

A BBW is the strongest warning that the FDA can give consumers and often includes prescribing or monitoring information intended to improve the safety of using the particular drug or drug group. BBWs have been added to antidepressant drugs, nonopioid analgesics, and immediate-release opioid analgesics.

Pregnancy Categories

The FDA has categorized drug risk in a range from A (safest) to X (known danger). The five categories that will be phased out over time are

Category A. Risk to the fetus in the first trimester

Category B. Animal reproduction studies have not demonstrated risk to the fetus, and there are no well-controlled studies in pregnant women.

Category C. Animal reproduction studies have not demonstrated risk to the fetus, and there are no well-controlled studies in pregnant women; however, potential benefits may outweigh **potential risk in use of drug** in pregnant women.

Category D. Evidence of risk to the fetus has been demonstrated..

Category X. Studies in humans or animals have demonstrated fetal abnormalities or evidence of fetal risk, The drug is contraindicated in women who are pregnant or in those who may become pregnant


Thank
you!