PHARMACOLOGY

بسم الله الرحمن الرحيم

MID – Lecture 1

Pharmacokinetics (Pt.1)

﴿ وَإِن تَتَوَلَّوْا يَسْتَبْدِلْ قَوْمًا غَيْرَكُمْ ثُمَّ لَا يَكُونُوا أَمْثَالَكُم ﴾

اللهم استعملنا ولا تستبدلنا

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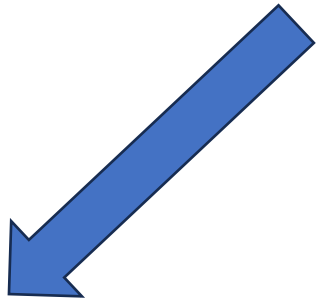
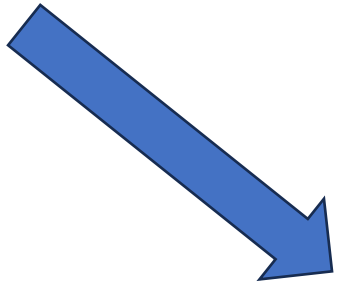
Pharmacology The science of drugs.





Pharmacokinetics:
The Effect of the Body on the Drug

Pharmacodynamics:
The Effect of the Drug on the Body

Introduction to Pharmacokinetics

- Definition:
- Pharmacokinetics is the study of how the human body affects the drug, including
  - the processes of absorption, distribution, metabolism, and excretion - ADME).
- Importance: Understanding pharmacokinetics is crucial for determining
  - drug dosage, timing, and potential side effects

- **Visuals**: Diagram of the ADME process (simplified body diagram showing drug absorption, metabolism, distribution, and excretion).

Key Processes of Pharmacokinetics

Absorption: How the drug enters the bloodstream

- Distribution: How the drug spreads through the body's tissues

  (moving through body fluids until reaching targeted tissue)

- Metabolism (Detoxification): How the body breaks down the drug, usually in the liver. Drugs are toxic if accumulated, therefore they should be taken in certain frequences and certain doses – to get metabolized (inactivated) and prevent accumulation in bloodstream and tissues.

- Excretion: How the drug or its metabolites are removed from the body (mostly by the kidneys as urine, and feces by the
- biliary system)

Individual, ethnic and gender-related physiological variability and pharmacokinetics.

Investigating one's genome could provide us with crucial information regarding physiological variability that determines the most suitable drug dose, frequency and timing for each individual.

P450 enzymes (to be discussed in the few coming slides), which are the principal enzymes involved in drug metabolism in the liver, vary in the number of their encoding gene copies among different individuals, therefore some people are termed Fast metabolizers, whereas others are slow metabolizers.

The difference lies in the fact that Fast metabolizer, who has more gene copies, needs a larger drug dose and higher frequency that slow metabolizer could handle to have the same effects on both.

The why behind this is that in the latter one, the active form of the drug remains longer in their body fluids performing its function in the site of action and thus showing its effectiveness on the targeted tissue, before it is being metabolized or inactivated and eventually excreted into the urine or by any other means.

Ethnicity plays essential role in this phenomenon as well. Several ethnic groups exhibit different drug-metabolic activity of the liver regarding Beta-blockers as a treatment for hypertension as just an example.

Also, gender is one of the primary factors to determine such variables (drug dosage and timing). Physiologically, men are fast metabolizers of alcohol and nicotine compared with women.

Absorption

Absorption is the **first** step in "making use" of the drug

- Definition: The process by which a drug passes from its site of administration into the bloodstream

Factors Affecting Absorption:

- Route of administration (oral, IV, etc.)

The Intravenous route (IV) is the only route by which we can guarantee the most possible absorption of the dosage, unlike all other means. The route of administration is significant in several cases and particularly critical ones.

(1) Severe Hyperglycemia-suffering individuals must receive insulin injection intravenously rather than tablets orally to ensure rapid onset of the drug and thus prevent falling into diabetic coma.
(2) Another example is when we counter epileptic episode, where oral administration is not a solution, and we must immediately use the IV route to cope with the critical condition.

Excessive administration of drugs over a short-time period results in extremely serious conditions including liver toxicity, which can eventually lead to acute liver failure.

- Drug formulation

Considering physical and chemical properties of the drug in the pharmaceutical industry to provide the final active form of the drug.

- Blood flow to the absorption site

Not to be confused with blood flow to the "organ or site of action", it is completely different concept. ***see the following slide.***

- Gastric pH

most drugs are designed such that we have small weak acids that can dissolve with ease in the acidic gastric environment. Individuals on medications like antacids or anti-ulcers have more basic gastric media than normal, therefore ingested drugs might take longer to dissolve and be absorbed.

Distribution

- Definition: The dispersion of a drug throughout the fluids and tissues of the body
- Factors Influencing Distribution:
  - Plasma protein binding (the more the binding--> the less the effect, therefore by knowing the affinity of a drug to a specific protein; increasing the dosage can overcome this association)
  - Tissue permeability (the plasma membrane is a bilayer, so we need drugs that are more liposoluble to get better diffusion (passive diffusion). However, size also matters: some drugs may need channels (facilitated diffusion), and some drugs require energy to be transported (active transport))
  - Blood flow to organs (More blood inflow to vital organs such as the heart, brain and kidney directs great deal of active drug to the site of action and thus more effectiveness. For instance, antidepressants targeting the brain, prescribed to treat depression which arises from the serotonin deficiency)
  - Volume of distribution (Vd) (its calculations will be discussed later, but it's simply the whole body's volume through which the drug diffuses in relation to the protein binding)
    - the theoretical volume that a drug would need to occupy if it were evenly distributed at the same concentration as in the blood plasma.

Metabolism

- Definition: The chemical alteration of the drug in the body, often in the liver (to reduce toxicity or to make the drug benign)
- Phase I Reactions: Oxidation, reduction, hydrolysis (usually cytochrome P450 enzymes) some drugs require only phase 1 , while some others requires both phases .
- Phase II Reactions: Conjugation (glucuronidation, sulfation) Also some of drugs enter phase 2 directly without passing through phase 1.
- First-pass effect: Liver metabolism reduces the drug's concentration before it reaches systemic circulation considering other means of administration can overcome this effect.

Excretion

- Definition: The removal of drugs and their metabolites from the body, primarily via the kidneys
- Routes of Excretion:
  - Renal (urine)
  - Biliary (feces)
  - Others: sweat, saliva, exhalation

Most common form of excretion is renal excretion; urine discoloration is a normal and a widespread side effect
Fecal discoloration is also relatively normal.

Examples mentioned throughout the lecture; to clarify.

1- Revanin example to simply show the meaning of (ADME).

- Absorption (the Revanin – for example – goes to the small intestine)
- Distribution (crosses the bloodstream and goes to the site of action)
- Metabolism(detoxification by the liver)
- Excretion (by kidneys – most of the drugs)

2- Intravenous VS. Oral Administration (Slide 6)

We lose about 25% of oral administered drugs. IV drugs are usually used in critical cases in which we need a fast administration of a dose.

3- Capsules VS. Tablets (Slide 6)

Capsules generally dissolve faster than tablets; that's why we use them in antibiotics. (ie. Gelatin capsules are more easily digested and absorbed)

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1	5	-------	newly added slide
	6	-------	Rephrasing and adding new information under the subheading: “factors affecting absorption”
	7	-------	addition new information under the subheading; “blood flow to organs”
V1 → V2	6	The Intravenous route (IV) is the only route by which we can guarantee the most possible absorption of the dosage, unlike all other means. Sometimes it is important to take a combination of different Routes of administration. Severe Hyperglycemia-suffering individuals must receive tablets orally, alongside insulin injection intravenously to prevent falling into diabetic coma. Excessive administration of drugs over a short-time period results in extremely serious conditions including liver toxicity, which can eventually lead to acute liver failure.	The Intravenous route (IV) is the only route by which we can guarantee the most possible absorption of the dosage, unlike all other means. The route of administration is significant in several cases and particularly critical ones. (1) Severe Hyperglycemia-suffering individuals must receive insulin injection intravenously rather than tablets orally to ensure rapid onset of the drug and thus prevent falling into diabetic coma. (2) Another example is when we counter epileptic episode, where oral administration is not a solution, and we must immediately use the IV route to cope with the critical condition. Excessive administration of drugs over a short-time period results in extremely serious conditions including liver toxicity, which can eventually lead to acute liver failure.

Additional Resources:

Extra References for the Reader to Use:

1. Osmosis
2. High yield points
3. brief pharmacokinetics

رسالة من الفريق العلمي:

رجاءً ارحموا الافريج A.M
اسعوا جاهدا في طلب العلم, وتحصيل النافع ولا تيأسوا, لربما تكون الطريق وعرة ولكن لا يوجد انتصار دون ألم.
من لا يحب صعود الجبال يعش أبد الدهر بين الحفر.
مع تمنياتنا لكم بالتوفيق والسداد