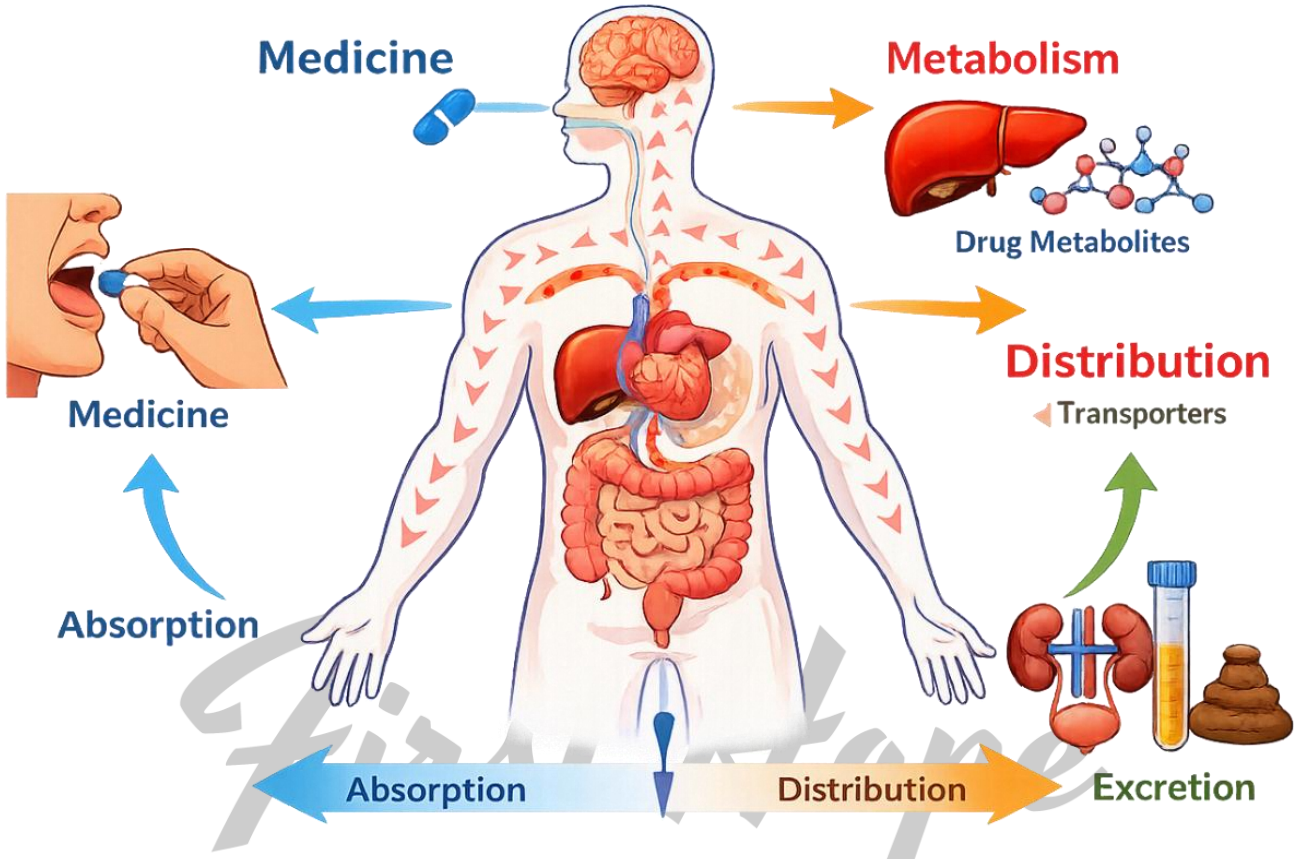
Pharmacokinetics

Pharmacokinetics: Basic Considerations

- Pharmacokinetics (PK) describes what the body does to a drug over time.



- It explains how a drug moves through the body using four main processes: **ADME (Absorption, Distribution, Metabolism, Excretion).**

Absorption

Absorption is how a drug enters the bloodstream from its site of administration it is Important for all routes except IV (because IV goes directly into blood).

Factors affecting absorption:

- **Route of administration:** Oral, IV, IM, subcutaneous, etc.
- **Blood flow:** More blood flow = faster absorption.
- **Surface area:** Larger surface area (like intestine) increases absorption.
- **Drug properties:**
  - Lipid-soluble drugs cross membranes easily
  - Ionized drugs cross poorly
- **pH and pKa:**
  - Weak acids absorb better in acidic environments
  - Weak bases absorb better in basic environments

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Distribution

Distribution is how the drug **spreads from blood to tissues**.

Key points:

- **Drugs travel in blood either:**
  - Free (active form)
  - Bound to plasma proteins (inactive form)

Factors affecting distribution:

- **Blood flow to tissues:** Brain, liver, kidney get drug faster
- **Capillary permeability:** Some tissues (brain) restrict entry (blood-brain barrier)
- **Protein binding:** Highly bound drugs stay in plasma
- **Tissue binding:** Some drugs accumulate in fat or bone

Metabolism (Biotransformation)

Conversion of drug into **more water-soluble forms for elimination** it is mainly occurs in the liver.

Two phases:

1. **Phase I (functionalization):**
   - Oxidation, reduction, hydrolysis
   - Often involves CYP450 enzymes
2. **Phase II (conjugation):**
   - Drug combines with another molecule (e.g., glucuronide)
   - Makes drug more water-soluble

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Excretion

Removal of drug from the body.

Main routes:

- Kidneys (urine) – most important
- Bile (feces)
- Lungs (for gases)
- Sweat, saliva, breast milk (minor)

Important PK Parameters

1. **Half-life (t½)**
   - Time required for drug concentration to reduce by half
2. **Clearance (Cl)**

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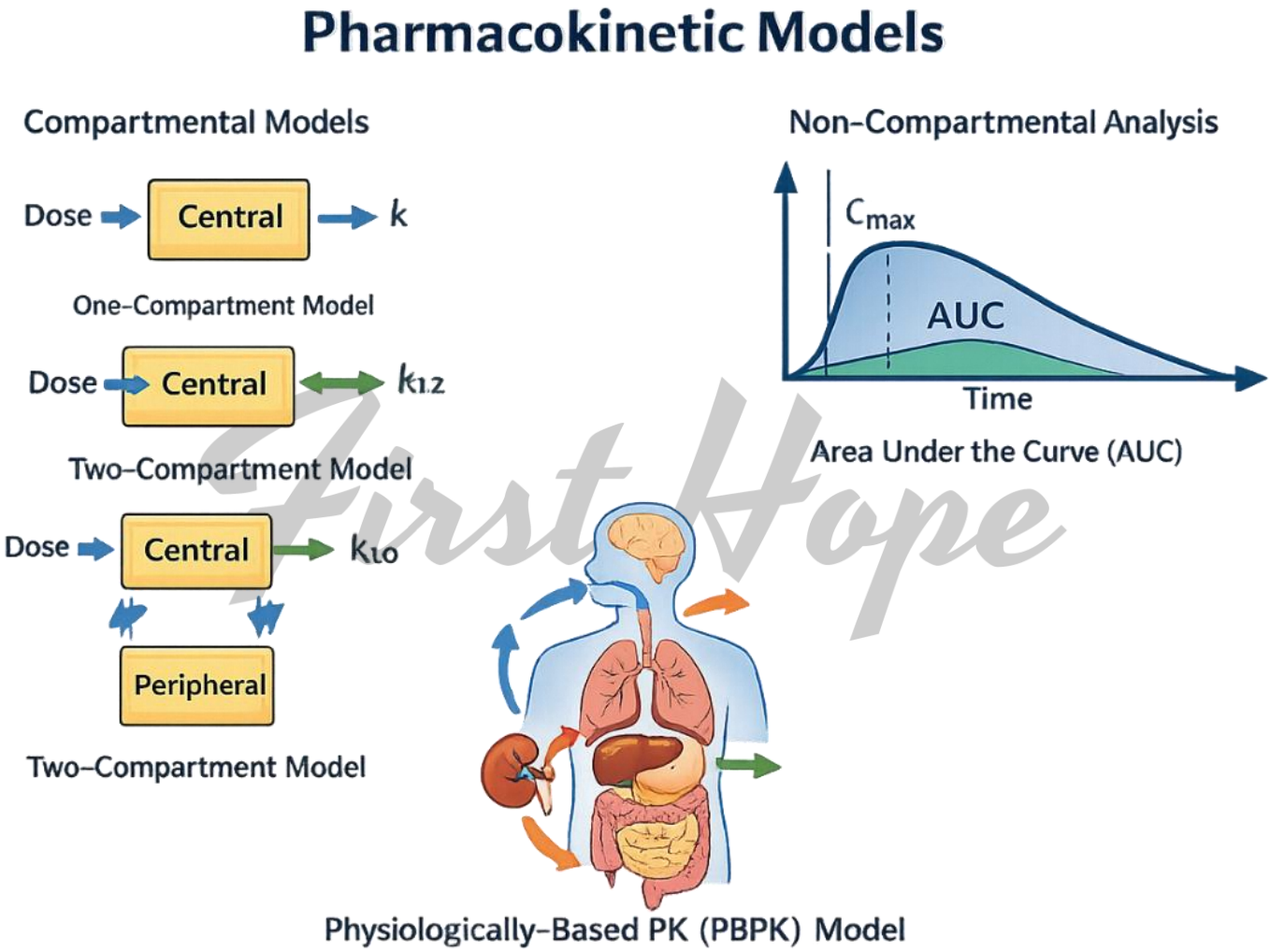
- Volume of plasma cleared of drug per unit time

3. Area Under Curve (AUC)

- Represents total drug exposure

Pharmacokinetic Models

- Pharmacokinetic models are mathematical representations used to describe and predict drug concentration over time in the body.



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Why Models are Needed

- To understand drug behavior
- To design dosage regimens
- To predict concentration at different times

Types of Models

1. Compartment Models

- Body is divided into compartments
- Drug moves between compartments

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2. Non-compartment Models

- Do not assume compartments
- Use statistical methods

Compartment Concept

- A compartment is not a real organ.
- It is a theoretical space where the drug concentration is assumed to be uniform.
- **Example:** Blood and highly perfused organs may form one compartment

Assumptions

- Drug distributes instantly within a compartment
- Drug elimination follows certain kinetics
- Compartments are connected

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One-Compartment Model

Compartment Modeling: One-Compartment Model

- In this model, the body is treated as a **single, uniform compartment** where the drug distributes **instantly and evenly** after administration.

Basic Idea

- Simplest pharmacokinetic model
- Assumes instant distribution throughout the body
- Drug concentration changes are governed mainly by absorption (if any) and elimination

One-Compartment Model: IV Bolus Administration

Definition

- A **single, rapid injection** of drug directly into the bloodstream.

Key Features

- Drug enters instantly
- No absorption phase
- Highest concentration occurs at **time = 0**

Concentration-Time Profile

- Concentration declines exponentially over time
- Decline is due to elimination only
- Forms a straight line on a semi-log plot

Equation

$$C = C_0\, e^{-kt}$$

- **Where:**
  - **C** = concentration at time *t*
  - **C_0** = initial concentration
  - **k** = elimination rate constant

Important Pharmacokinetic Parameters

- **Half-life (t½):** Time required for concentration to reduce by half
- **Clearance (CL):** Volume of plasma cleared per unit time
- **Volume of Distribution (Vd):** Extent of drug distribution in the body

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