Pharmacokinetics & Pharmacodynamics

Drugs are chemicals used to diagnose, treat, and prevent disease.

Pharmacology is the study of drugs and their actions on the body.

Lecture 1

ROUTES OF ADMINISTRATION, DISTRIBUTION

Learning Outcomes

By the end of this lecture, students should be able to:

- Mention mechanisms of passage of drugs across membranes
- Enumerate routes of administration of drugs
- Define drug distribution
- Describe plasma protein binding, tissue binding and storage

Definitions

- **Pharmacokinetics is what the body does to the drugs**, for almost all drugs the magnitude of pharmacological effect depends on its concentration at its site of action.

- **Pharmacodynamics is what the drug does to the body**, ideally including the molecular mechanism (s) by which the drug acts.

Drug Routes (1 of 2)

Enteral:

- Delivers medications by absorption through the gastrointestinal tract.
- Includes oral, orogastric/nasogastric, sublingual, buccal, rectal.

- Parenteral:
  - Delivers medications via routes other than the GI tract.
  - Includes intravenous, intramuscular, subcutaneous, inhalation, topical.

Enteral – Examples (1 of 2)

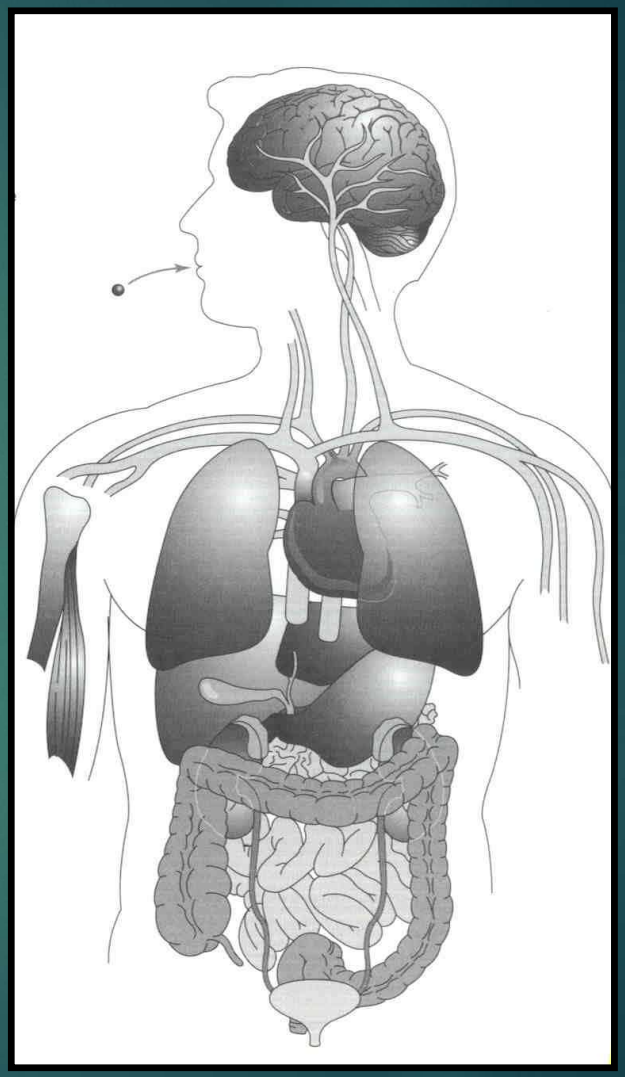
- Oral (PO)
  - Good for self-administering drugs
- Nasogastric (NG)
  - Alternate method to providing PO medications
- Sublingual (SL)
  - Excellent absorption without problems of gastric acidity
- Buccal
  - Between the cheek/gum
  - Similar to sublingual
- Rectal (PR)
  - Reserved for unconscious or vomiting patients

Parenteral – Examples (1 of 3)

- Intravenous (IV)
  - Preferred route in emergencies
- Endotracheal (ET)
  - Alternate route in emergencies for select medications
- Intraosseous (IO) –In to the bone
  - Alternative use in emergencies, mostly in pediatrics
- Umbilical
  - Provides alternate access in newborns
- Intramuscular (IM)
  - Slower absorption than IV
- Subcutaneous (SC)
  - Slower absorption than IM
- Inhalation
  - Very rapid absorption via the lungs
- Topical
  - Delivers drugs directly to the skin

Most emergency medications are given intravenously to avoid drug degradation in the liver.

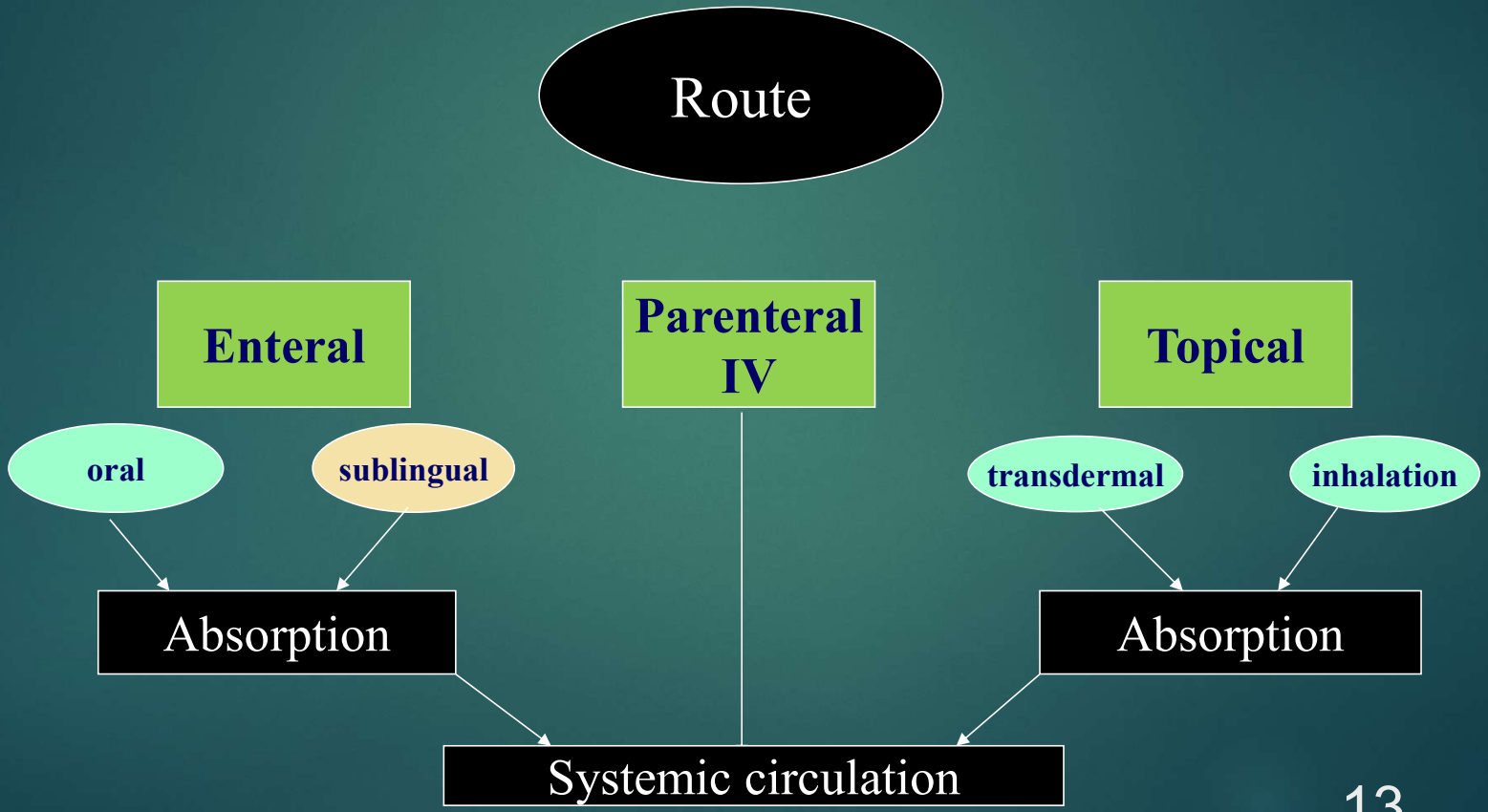
Absorption
Distribution
Metabolism
Excretion



- Pharmacokinetics refers to the handling of a drug within the body and includes " the bodies response to medication".
- To achieve the pharmacological response desired, the drug must first be in an available and suitable form and then administrated by an appropriate route.
- Unless the drug acts locally it will need to be absorbed, distributed and circulated before reaching the site of action.
- For the effect of the drug to wear off, it must be metabolised and the metabolic products excreted.

Absorption

Distribution



Absorption

Process of drug movement from the administration site to the systemic circulation.

The amount and rate of absorption are determined by several factors:

- Physical nature of the dosage form
- Presence or absence of food in the stomach
- Composition of the GI contents
- Gastric or intestinal pH
- Mesenteric blood flow
- Concurrent administration with other drugs

- E..g. Migraine – reduced rate of gastric motility = delayed response to oral analgesia. Delay can be lessened by the use of **metoclopramide** which increases gastric emptying.

Bioavailability

- "Bioavailability is the proportion of the administered dose that reaches the systemic circulation."

- Refers to the amount and the rate of appearance of the drug in the blood after administration in its initial dose form.

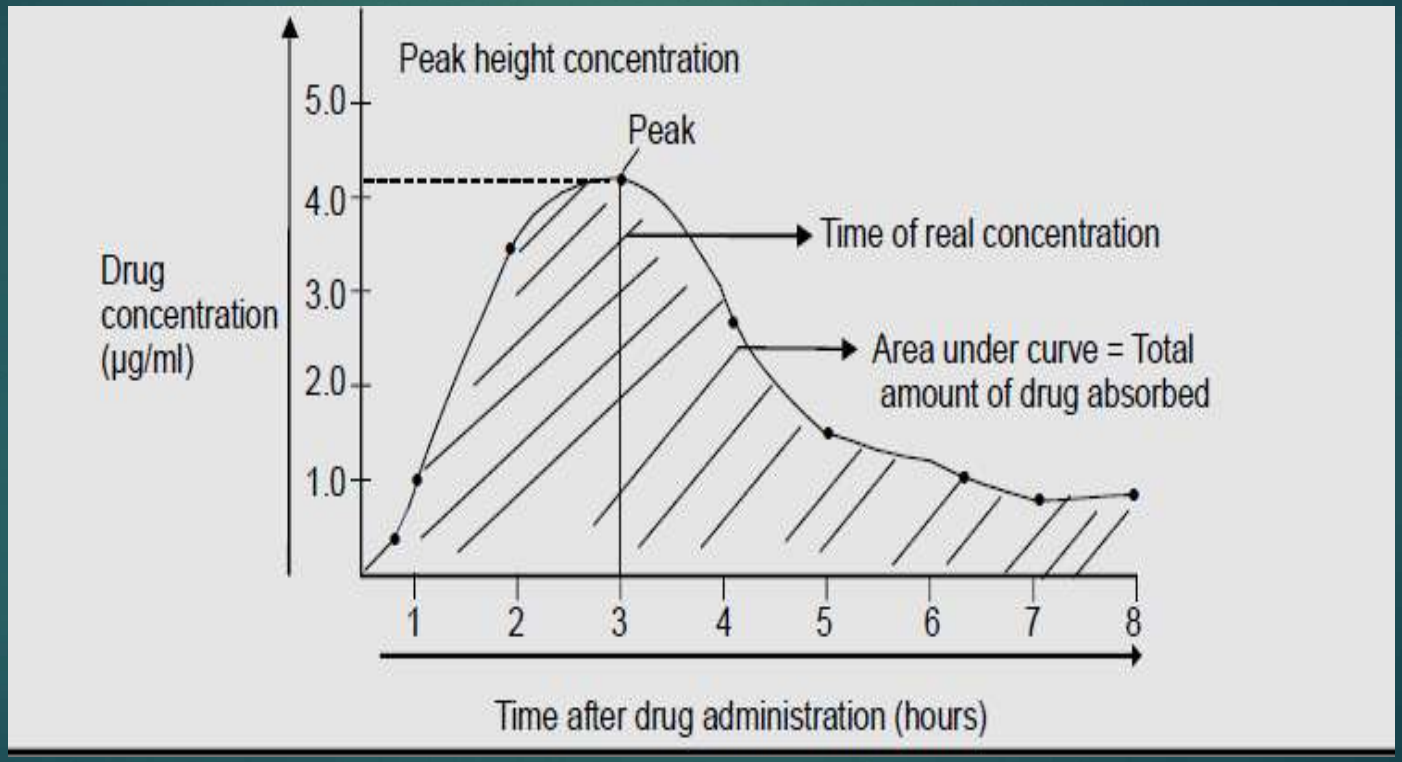
- Orally administered drug bioavailability is directly related to the individual solubility in body fluids.

  Poor solubility = low bioavailability

- To become affective i.e. produce a therapeutic effect, a drug must reach an adequate concentration in the blood. Drugs administered by the IV route are bio available in 100% of cases as it is administered directly into the blood.

- Some drugs with the same active principle, made by different manufacturers may differ in the bioavailability, dependant on the degree of compression or nature of excipients (added substances), that may affect the disintegration and dissolution of the drug.

- Drugs administered by the IV route are bio available in 100% of cases as it is administered directly into the blood.


Peak height concentration
Peak
Time of real concentration
Area under curve = Total amount of drug absorbed
Drug concentration (µg/ml)
5.0
4.0
3.0
2.0
1.0
1
2
3
4
5
6
7
8
Time after drug administration (hours)

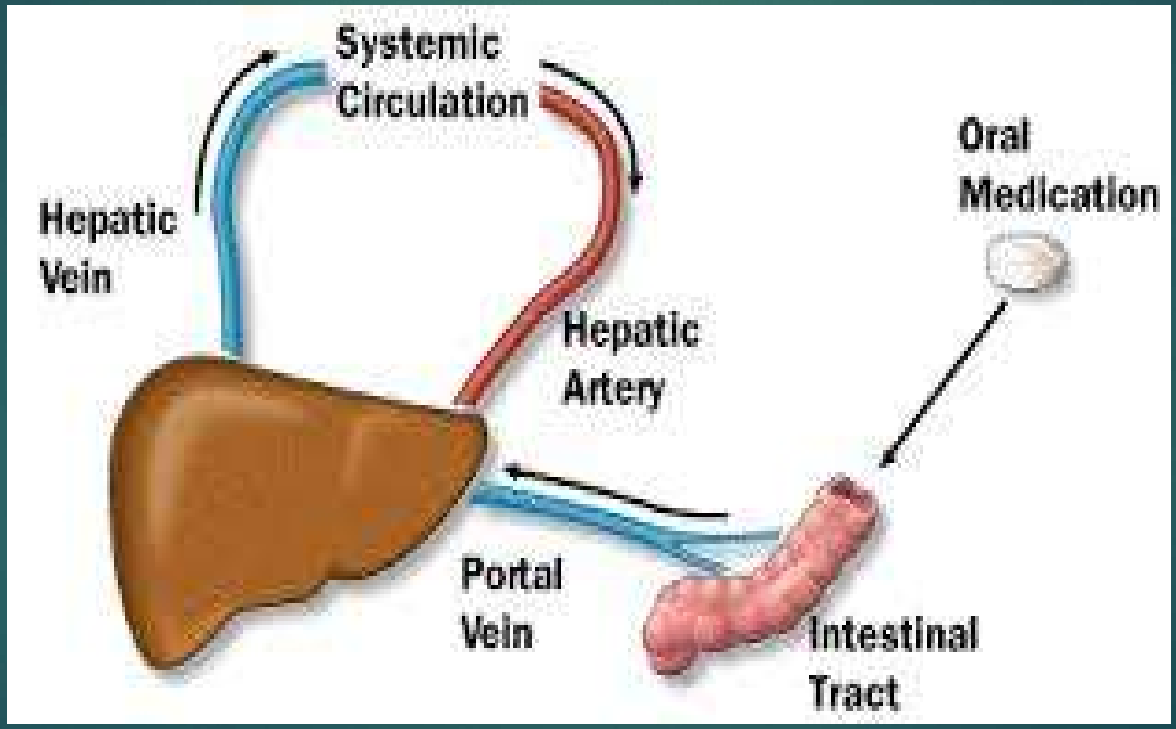
Effect of Food

- Bioavailability of some drugs is affected by the presence of food. E.g penicillin's, erythromycin, rifampicin, thyroxine.
- Some drugs are taken before meals to allow time for drug to act before food is taken: sildenafil absorption slowed down by fatty food.
- Gastric irritation can be caused by drugs taken on an empty stomach: metformin and levodopa-Better give with food.

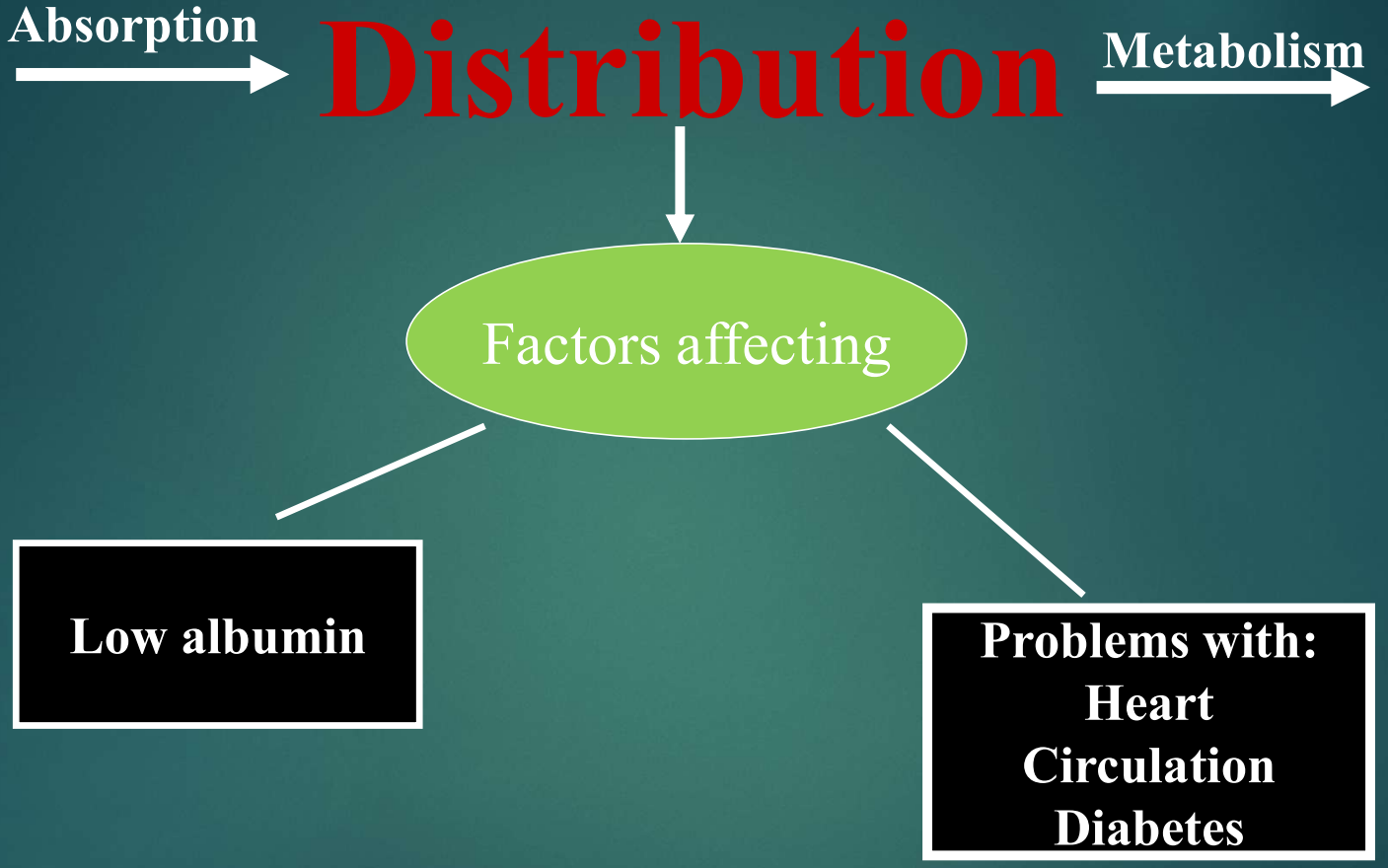
First Pass Effect

- Drugs that are absorbed via the GIT are circulated to the liver first via the hepatic portal vein.
- The liver then acts as a filter.
- Only part of the drug is circulated systemically.
- The combination of processes is termed the ‘First Pass’ effect.

First pass effect



- As a result only part of the administered drug reaches the systemic circulation via the hepatic artery.
- The extent can explain the difference between oral and injectable dose e.g propranolol, salbutamol verapamil undergo substantial first pass metabolism.
- Glyceryl trinitrate first-pass breakdown is complete so cannot be taken orally-sublingual preparation!!



Bound drugs are pharmacologically inactive because the drug-protein complex is unable to cross cell membranes.

Plasma proteins affect the distribution of drugs

- Plasma proteins can affect movement from blood to tissue, reduced in some diseases, role in polypharmacy.
- Additional factors that affect distribution: Cardiac output and regional blood flow.
- Bound drugs are pharmacologically inactive because the drug-protein complex is unable to cross cell membranes.

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Thank you