بسم الله وبه نستعين

كلية التمريض – جامعة تكريت

المرحلة الثانية \ أدوية

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2024-2025 \ First Term

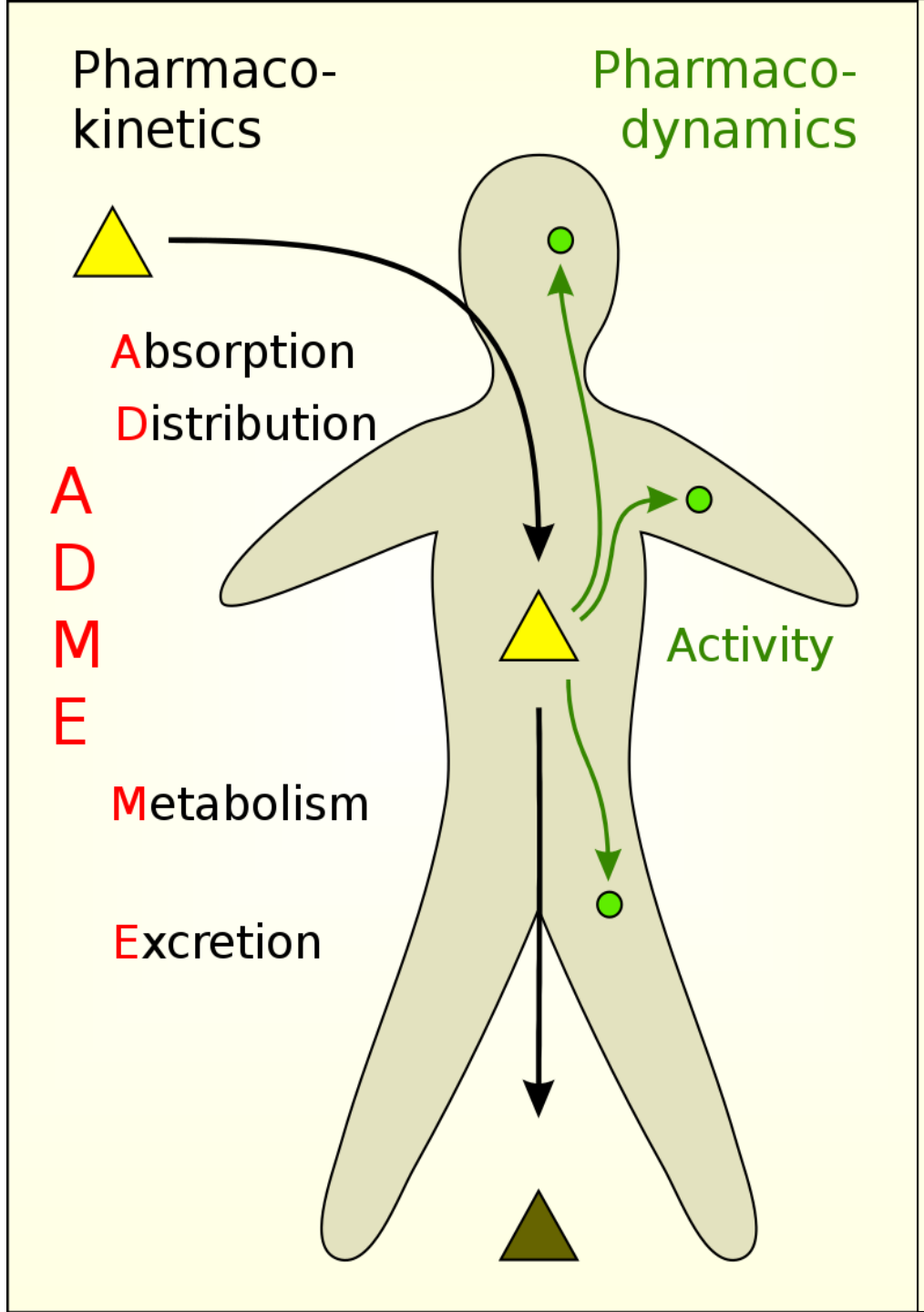
INTRODUCTION & ROUTES OF ADMINISTRATION

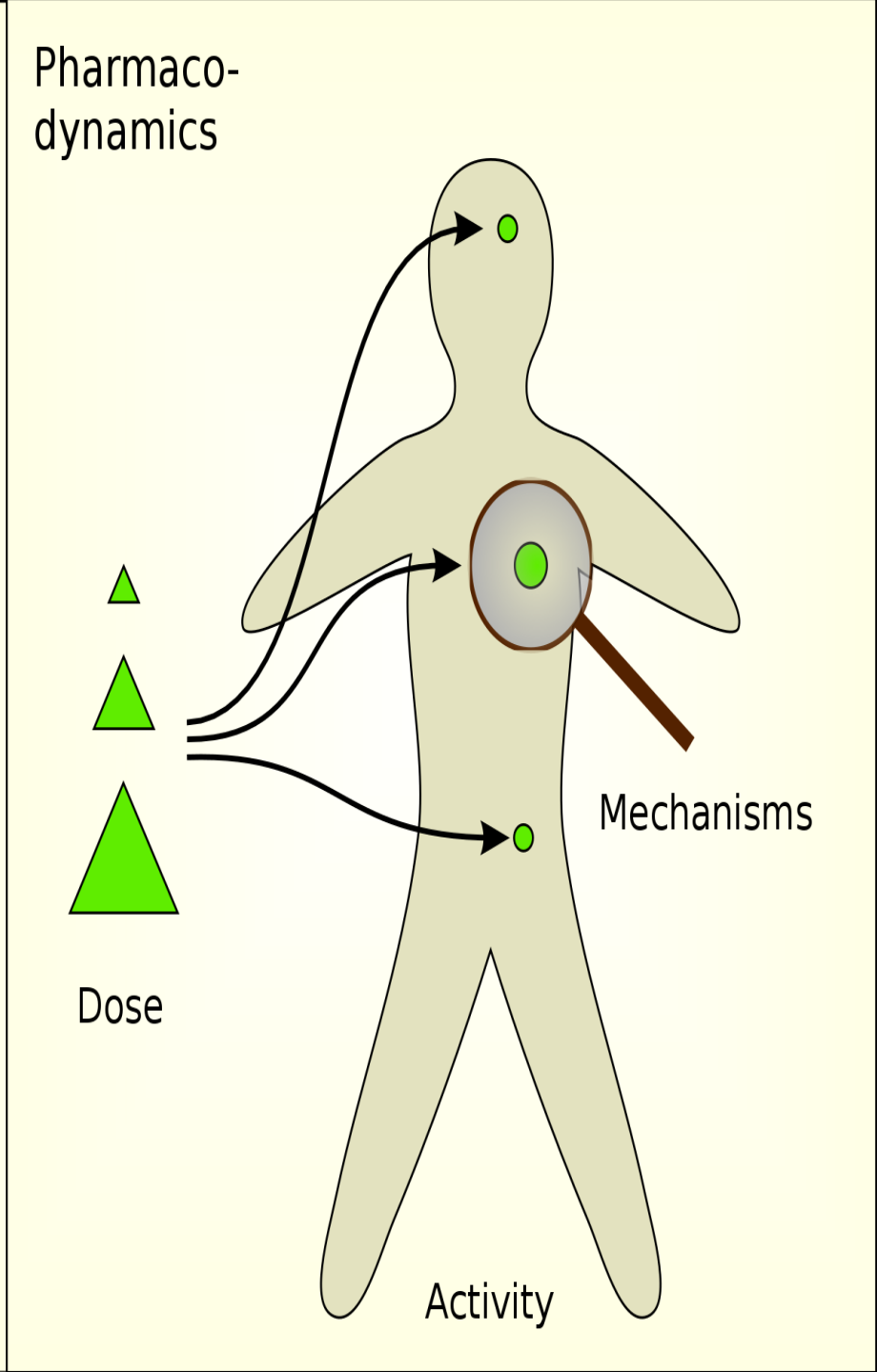
What is pharmacology

- **Pharmacology**: the study of substances (drugs) that interact with living systems through chemical processes. It is the science that deals with the mechanism of action, uses, adverse effects of drugs.
- **A drug**: a chemical substance of known structure, other than a nutrient, when administered to a living organism, produces a biological effect. It can be natural, synthetic, or genetic engineering product.

- **Toxicology:** study of harmful effects of drugs
- The interaction between drugs & the body can be divided into:

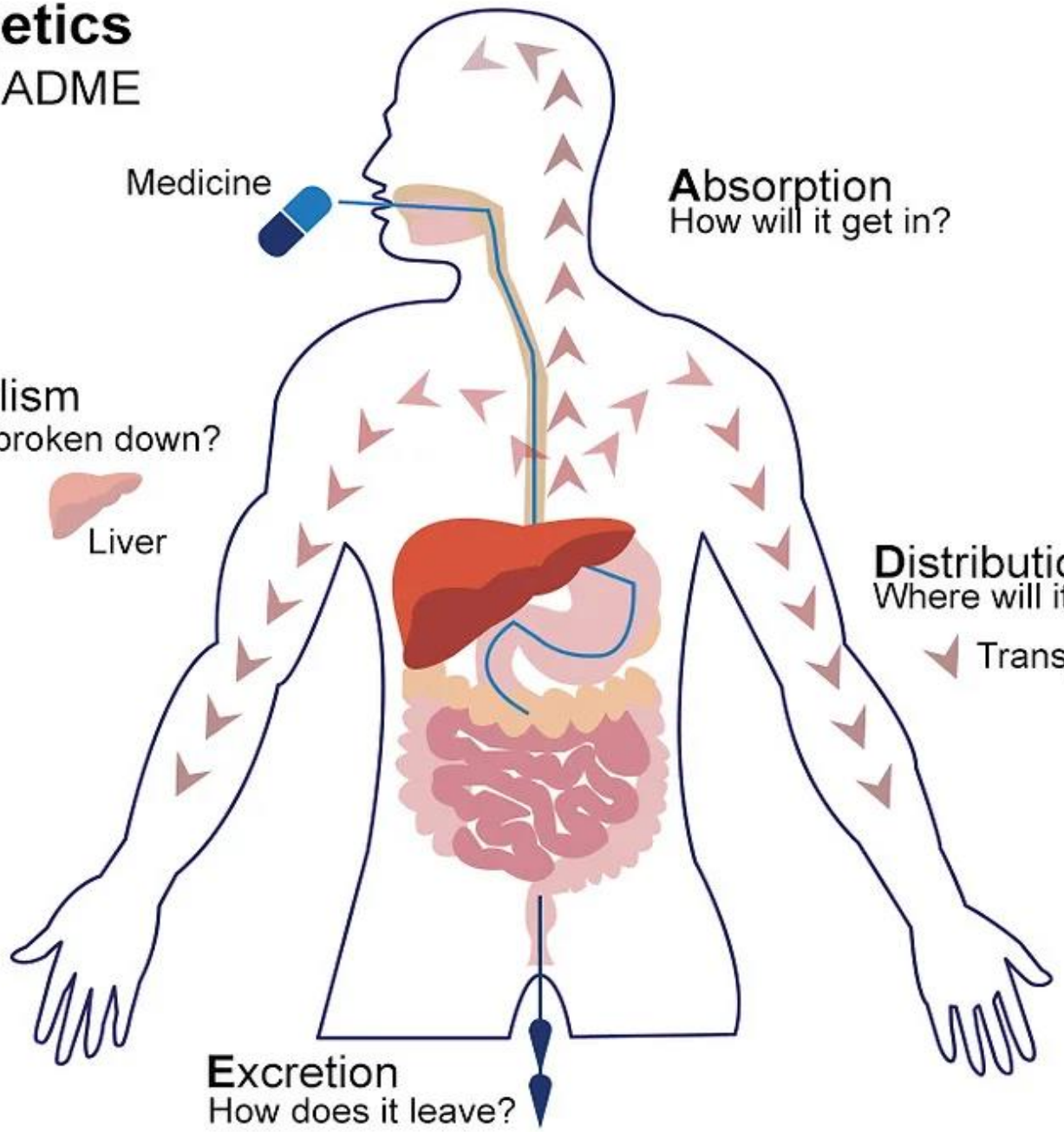
1. **Pharmacodynamics**: is the action of the drug on the body. It includes drug-receptor interaction, mechanism of action & dose response phenomena.
2. **Pharmacokinetics**: The action of the body on the drug. It includes Absorption, Distribution, Metabolism & Excretion (ADME)


Pharmaco-
kinetics
Pharmaco-
dynamics
Absorption
Distribution
A
D
M
E
Metabolism
Excretion
Activity


Pharmaco-
dynamics
Mechanisms
Dose
Activity

Pharmacokinetics

The principles of ADME



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European Patients' Academy
on Therapeutic Innovation
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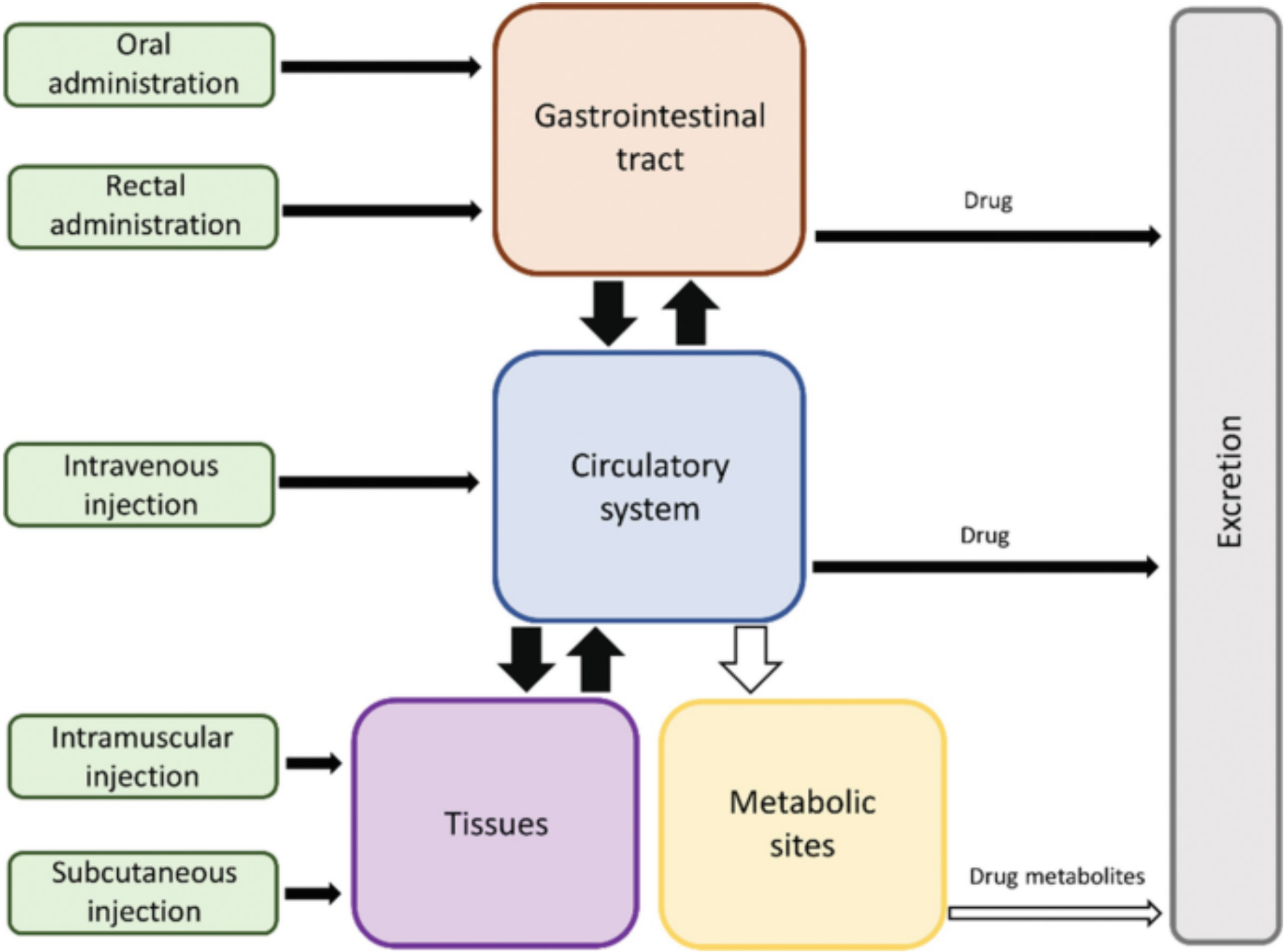
- **Routes of drug administration:**
  - **Enteral routes (oral, sublingual, & rectal)**
  - **Parenteral route: Administering medication by the parenteral route is defined as medications placed into the tissues and the circulatory system by injection.**
  - **Inhalation**
  - **Topical application**


Oral administration
Rectal administration
Gastrointestinal tract
Drug
Excretion
Intravenous injection
Circulatory system
Drug
Intramuscular injection
Subcutaneous injection
Tissues
Metabolic sites
Drug metabolites

1. ***<u>Oral route (P.O.):</u>***

- **Advantages:**
- Safe, most convenient & economical.
- May provide local effect in the gut (vancomycin)
- **Disadvantages:**
- Can not be used in emergency and for patient with vomiting and diarrhea.
- Requires patient co-operation.
- May cause GIT mucosal irritation.
- Poorly soluble, gastric pH unstable drugs and drugs interact with food components → incomplete absorption.

DRUG AWARENESS

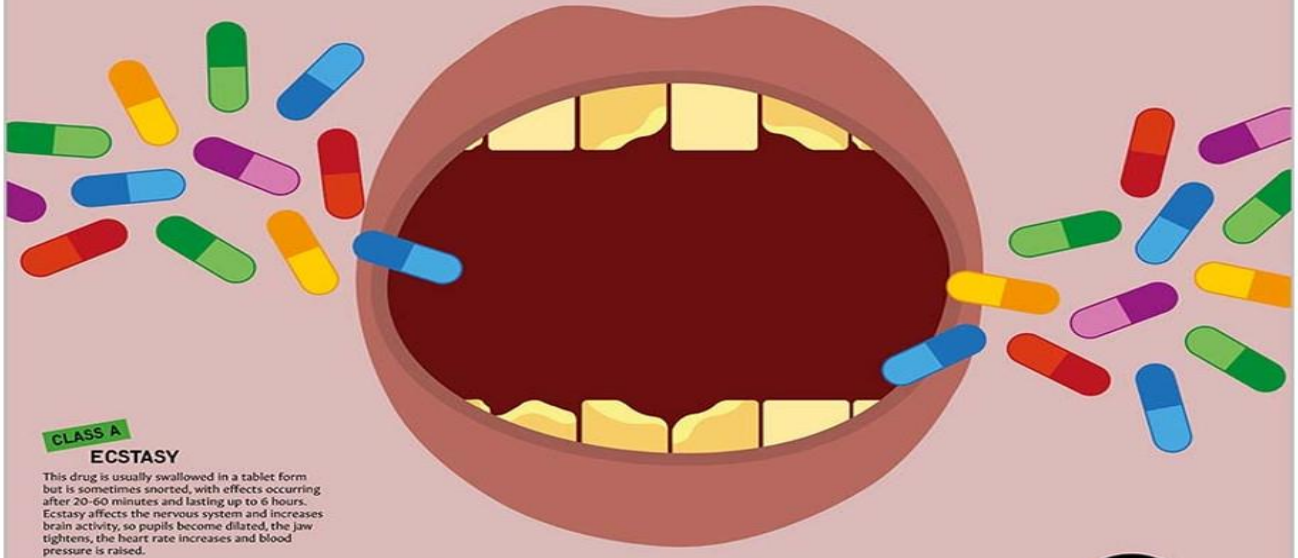
Drugs are chemicals that have a wide range of short and long term effects on the human body. The type and severity depends on the type of drug taken, how long it is taken for, and the user's existing health factors.

SHORT TERM EFFECTS

The possible short-term side effects from substance abuse range from changes in appetite, sleeping patterns, heart rate and blood pressure to heart attack, stroke, psychosis, overdose and death. Serious side effects can occur after just one use. Drugs like cocaine cause a short intense high that is immediately followed by a feeling of depression and edginess that can lead to a craving for more of the drug.

LONG TERM EFFECTS

Longer term effects include heart and lung disease, cancer, mental illness, HIV, and hepatitis. Drug addiction is also a risk. Not everyone who uses drugs will become addicted, but for some, drugs can change how certain brain circuits work. These changes interfere with how people experience normal things such as food, sex, the ability to control stress levels, decision-making and the ability to learn and remember.



CLASS A

ECSTASY

This drug is usually swallowed in a tablet form but is sometimes snorted, with effects occurring after 20-60 minutes and lasting up to 6 hours. Ecstasy affects the nervous system and increases brain activity, so pupils become dilated, the jaw tightens, the heart rate increases and blood pressure is raised.

CLASS A

COCAINE

Processed as a white powder, cocaine is usually inhaled through the nose, but is sometimes made into a solution and injected. The effects of cocaine are similar to those of amphetamines in that they create physical and mental arousal, but it peaks and fades within 15-30 minutes. Because the high is quick, users tend to repeat the drug intake every 20 minutes to maintain the feeling.

Cocaine use can alter sleep patterns, cause nose bleeds or collapse, high blood pressure, stroke, seizure and a shrinking brain size.

CLASS A

CRACK

Crack is very similar to cocaine although the effects are more extreme, felt more quickly and last for around 10 minutes. Smoked like cannabis, users may experience feelings of exhilation and increased confience.

However, crack is extremely addictive and can cause aggressive and paranoid behaviours, loss of appetite, hallucinations and in some cases death from overdose.

CLASS A

HEROIN

Derived from the opium poppy, heroin comes in the form of white powder that is snorted or smoked. Users report feeling warm, drowsy and calm, with reduction in feelings of anxiety or pain. Heroin is extremely addictive and puts the user at risk of sedation, loss of speech and death.

CLASS B

AMPHETAMINES

This drug is often referred to as 'speed' and is snorted or swallowed, taking effect after around half an hour. The effects include feelings of wakefulness and increased confidence but as the body's energy levels reduce the user is prone to feelings of anxiety, irritability and dizziness.

CLASS B

CANNABIS

Called 'marijuana', 'pot', or 'weed', cannabis is usually smoked, sometimes mixed with tobacco. The effects of the drug are varied and include laughter, vivid sensations, increased appetite, hallucinations and paranoia. These will vary depending on the person, environment and amount of the drug taken by the user.

Regular use of cannabis can decrease fertility and increase the risk of developing a psychotic illness, such as schizophrenia. Nicotine addiction and the negative health effects of smoking can also occur if the cannabis is smoked with tobacco.

AnatomyStuff

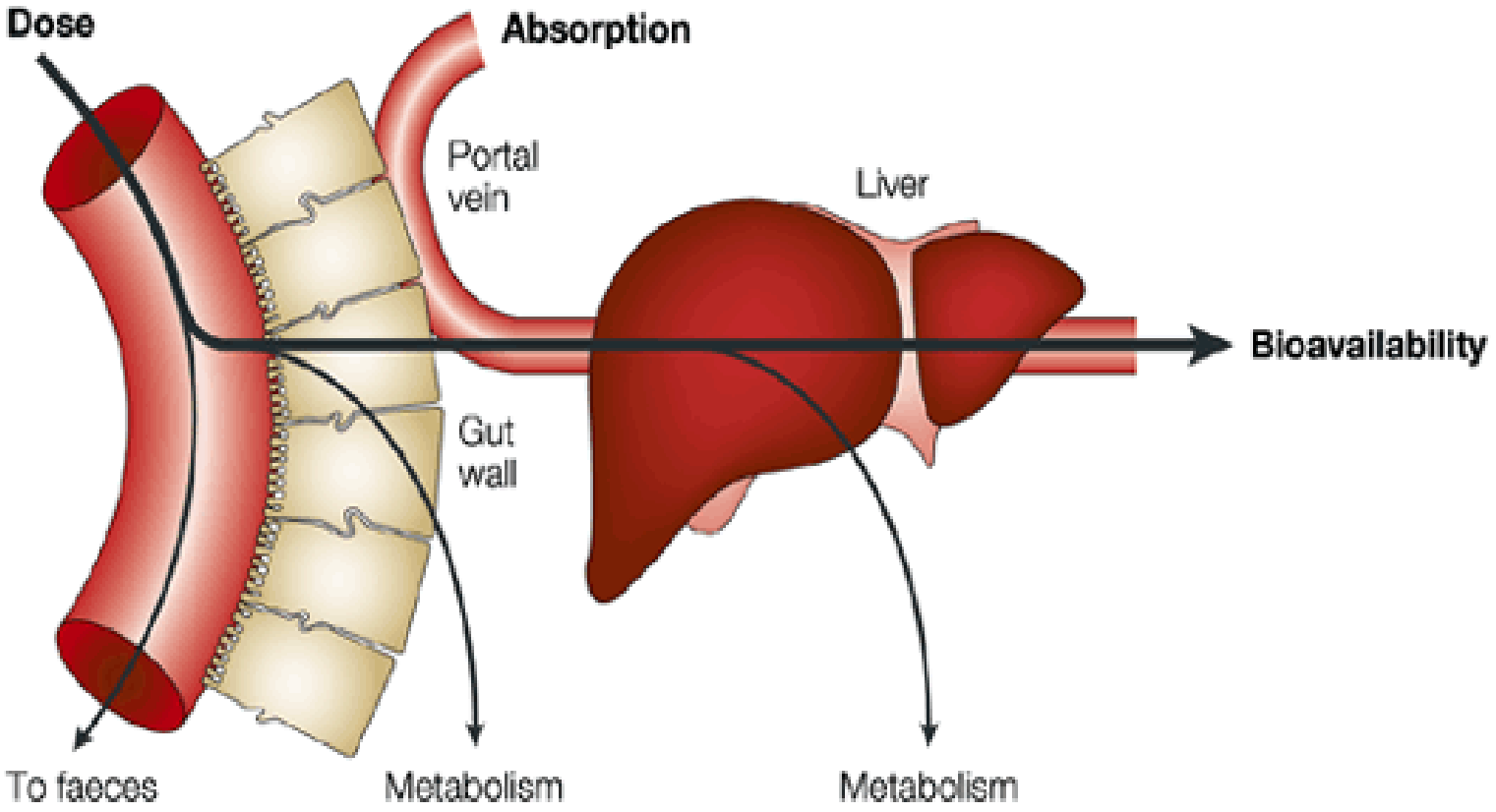
- May be subjected to **first pass metabolism**:

  The drug may be subjected to extensive metabolism in the GIT or the liver during their first passage through the liver before reaching the systemic circulation (↓amount reaches the systemic circulation) e.g glyceryl trinitrate, propranolol, levodopa & aspirin

2. ***Sublingual*** *(under the tongue)* ***& buccal*** *(inside the cheek) route:*

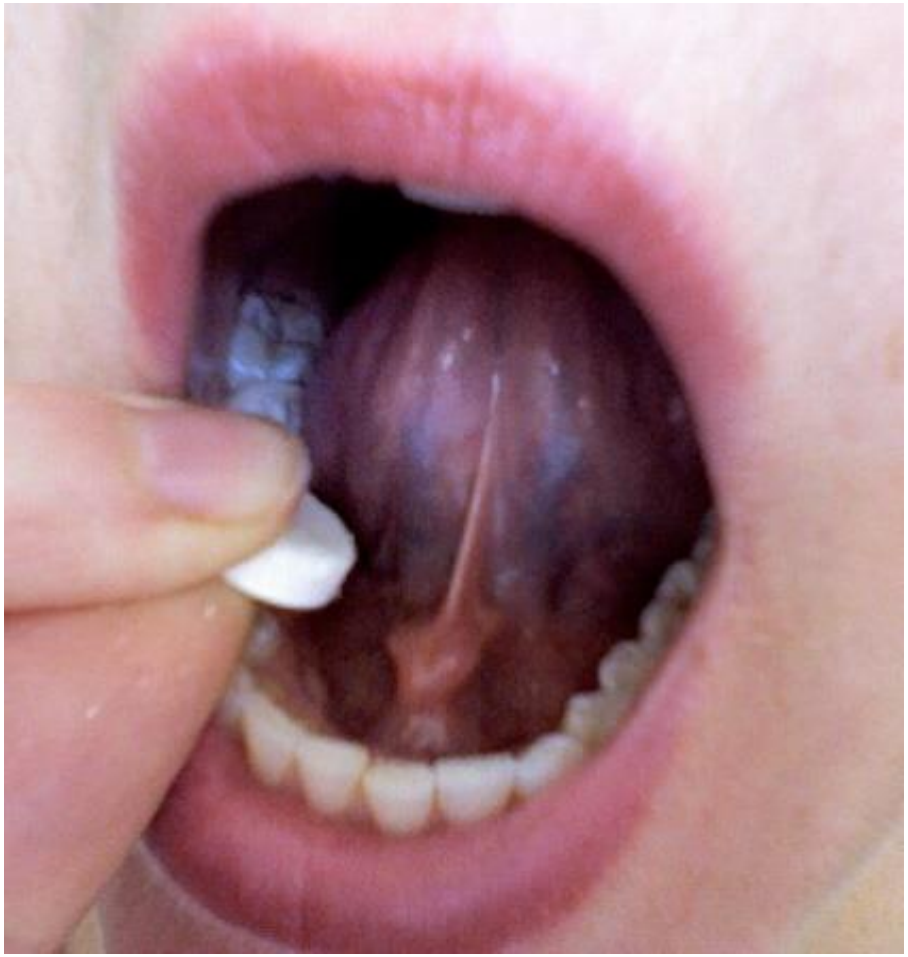
- **Advantages:**
- Produces quick response
- Escape first pass metabolism & GIT hydrolysis e.g. nitoglycerin
- **Disadvantages:**
- Not suitable for comatose patient

First pass effect (metabolism)



Nature Reviews | Drug Discovery

Inconvenient, stimulate salivation (promote swallowing) and may cause mucus membrane irritation



3. ***Rectal route:***

- Suppositories or enema
- Produces systemic or local effect e.g paracetamol, artesunate & corticosteriod.

Advantages:

- Escape 1st pass metabolism (local effect)
- Fast absorption due to large vascularity of the rectum.
- Useful for patient with vomiting & comatose patient.
- Useful for drugs that are irritant to the GIT mucosa (indomethacin).

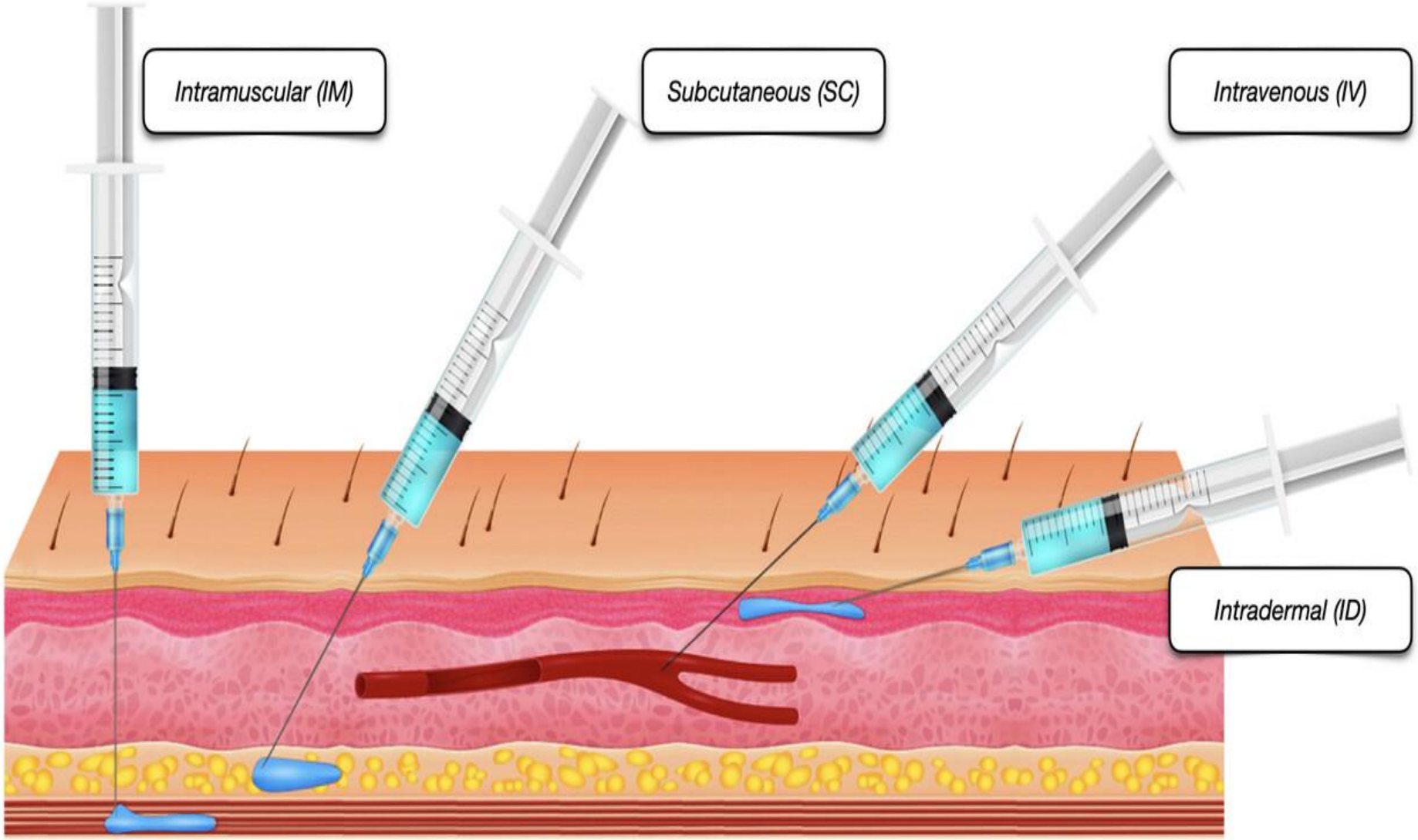
- **Disadvantages:**
- Not suitable for patient with diarrhea
- Inconvenient & may cause irritation to rectal mucosa (highly irritating drugs are contraindicated)
- Irregular & incomplete absorption.

4. ***Parenteral routes by injection:***

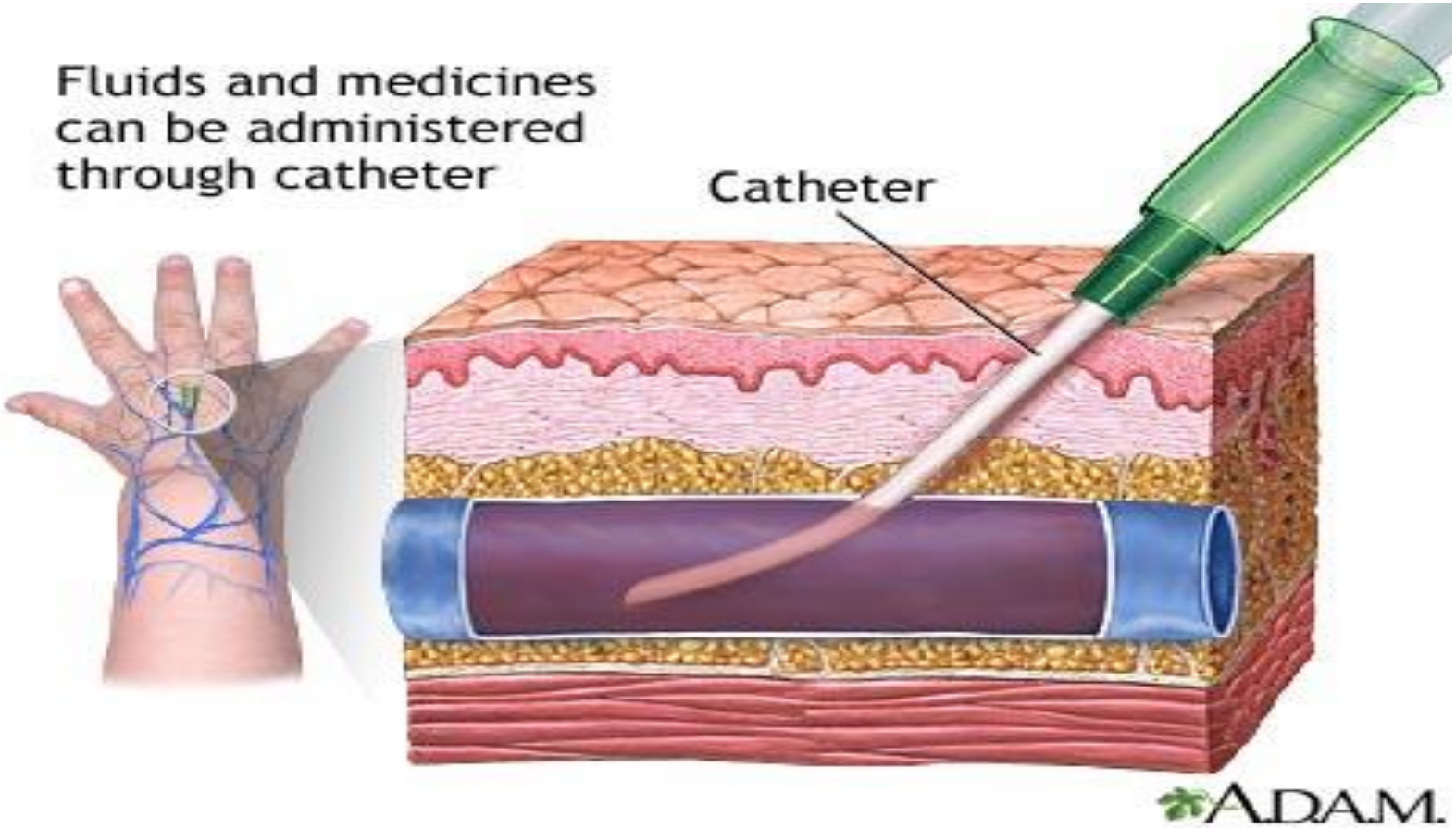
a. Intravenous route (I.V):

Advantages:

- 100% bioavailable & escape 1st pass metabolism
- Useful in emergency, in comatose patient & patient with vomiting &/or diarrhea
- Suitable for large volumes & produces steady state concentration by continuous I.V. infusion.


Intramuscular (IM)
Subcutaneous (SC)
Intravenous (IV)
Intradermal (ID)

- **Disadvantages:**
- Increases the risk of adverse effects (↑concentrated drugs → cardiac & respiratory complications)
- Not suitable for oily solutions or insoluble substances.
- Causes pain, irritation, necrosis & thrombosis at the site of injection.
- No retreatment once the drug is injected.
- Risk of infection.
- Need skills and not economical.


Fluids and medicines
can be administered
through catheter
Catheter
A.D.A.M.

b. Intramuscular (I.M.):

Advantages:

- Faster than the oral route and escape 1st pass metabolism
- Suitable for moderate volumes and oily solutions.
- Useful in comatose & patient with vomiting &/or diarrhea
- Suitable for irritant drugs and depot preparations (benzathine penicillin)

- **Disadvantages:**
- Painful, may cause local inflammation or abscess

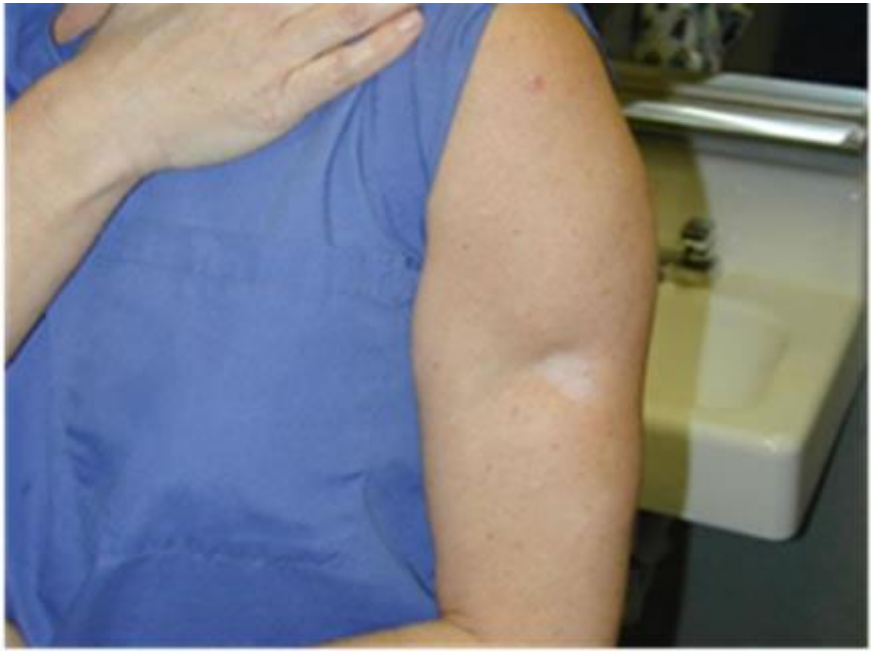
c. Subcutaneous (S.C) and local tissue infilteration:

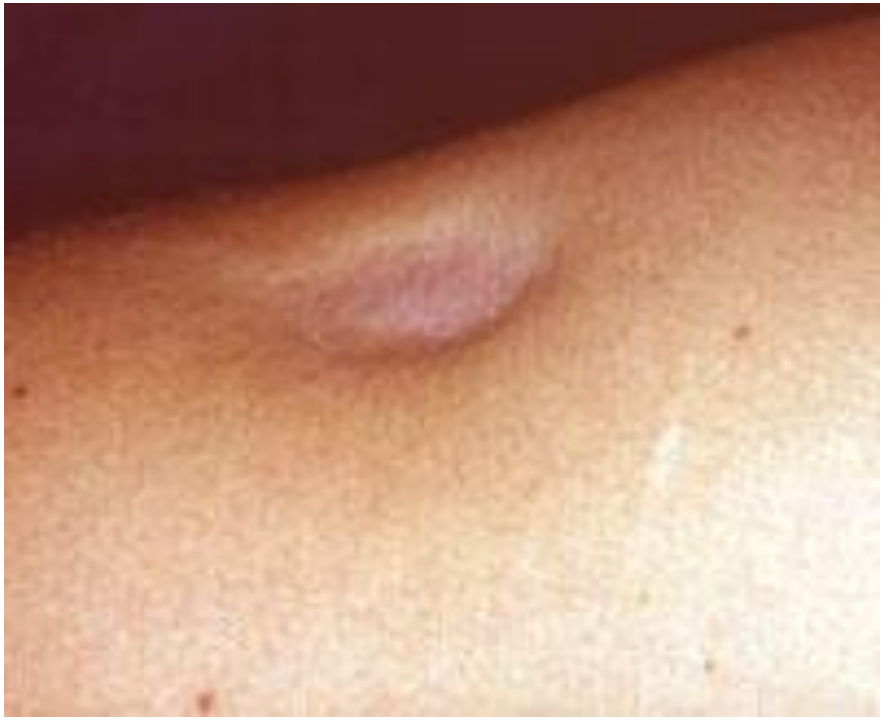
Advantages:

- Faster than the oral.
- Suitable for insoluble suspension (insulin) & implantation of solid pellets (estradiol contraceptive).
- Reliable and is acceptable for self-administration.

- **Disadvantages;**
- Not suitable for large volumes & irritant drugs
- May cause pain & necrosis at the site of injection.
- Repeated injections at one site can cause lipotrophy, resulting in irregular absorption (insulin).
- Drug absorption from the site of injection is increased by increasing local blood flow & rubbing.
- Drug absorption from the site of injection is reduced by:

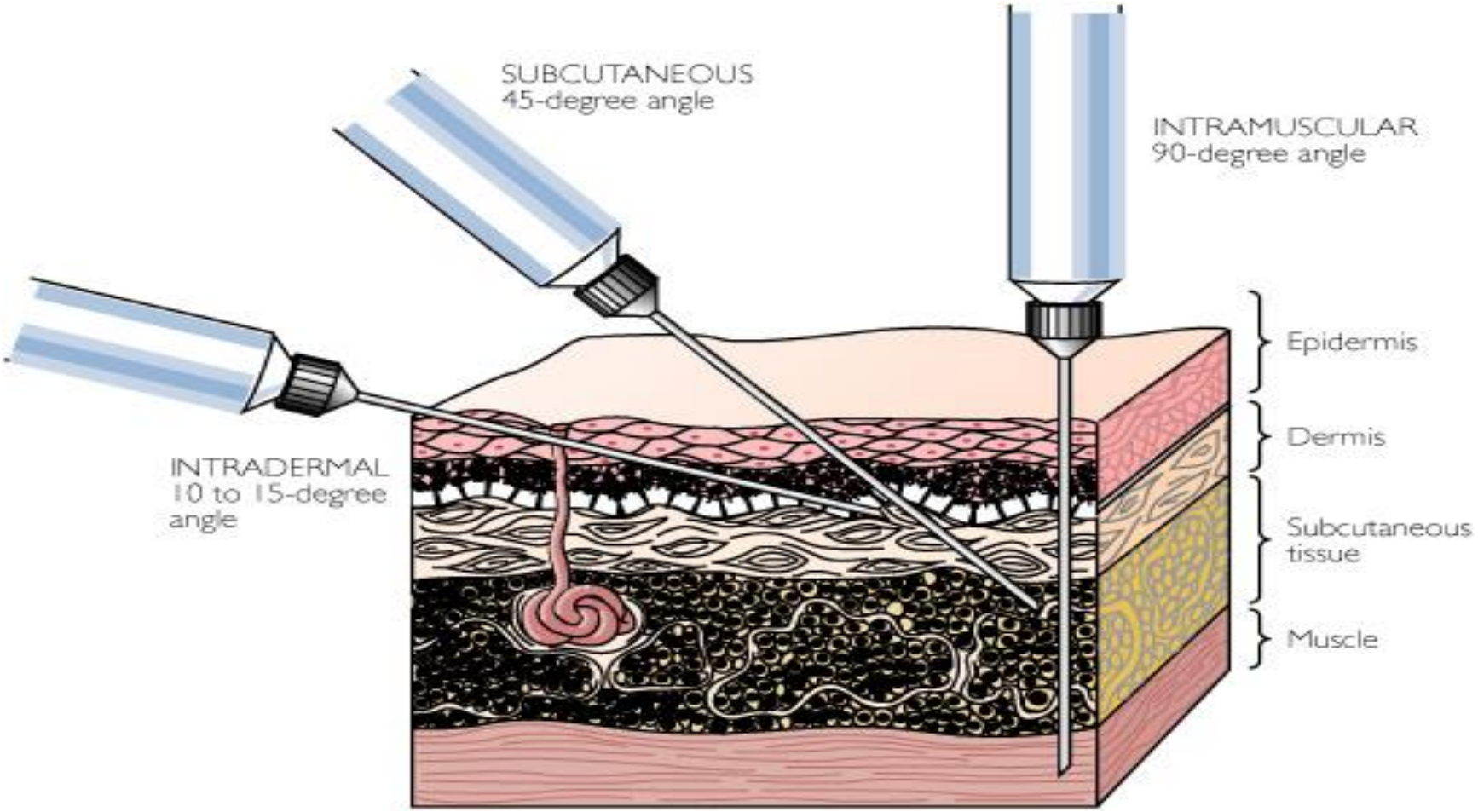
1. Decreasing local blood flow (addition of vasoconstrictors; adrenaline + local anesthetic).
2. Implantation of solid pellets.
3. The use of poorly soluble salts & oily solution. "slow-release" e.g. Procaine and benzathine penicillins, medroxy progesterone acetate.





d. Intradermal:

- Into the skin itself.
- Used for some allergen and also for mantoux test.


SUBCUTANEOUS
45-degree angle
INTRAMUSCULAR
90-degree angle
INTRADERMAL
10 to 15-degree
angle
Epidermis
Dermis
Subcutaneous
tissue
Muscle

e. Intrathecal:

(into the spinal canal) ,produces local & rapid effect on the meninges & cerebrospinal axis, most commonly used for spinal anesthesia (bupivacaine) and chemotherapy e.g methotrexate (leukemia), aminoglycoside (resistant CNS infection)

- Advantages:

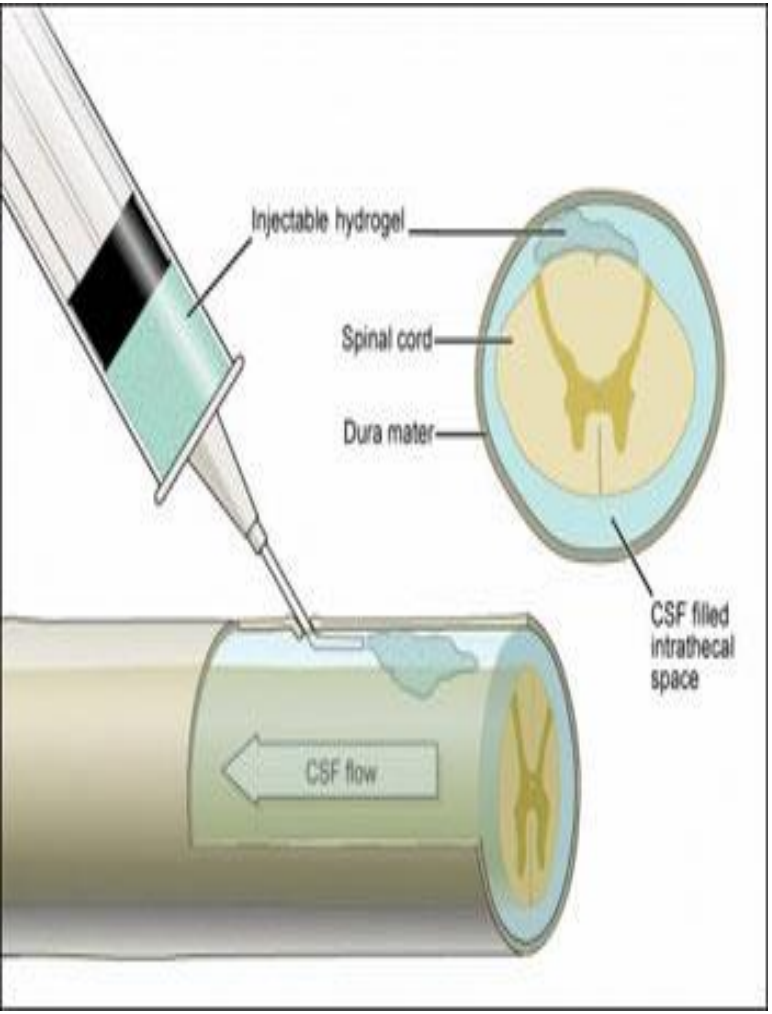
Rapid & localized effect.

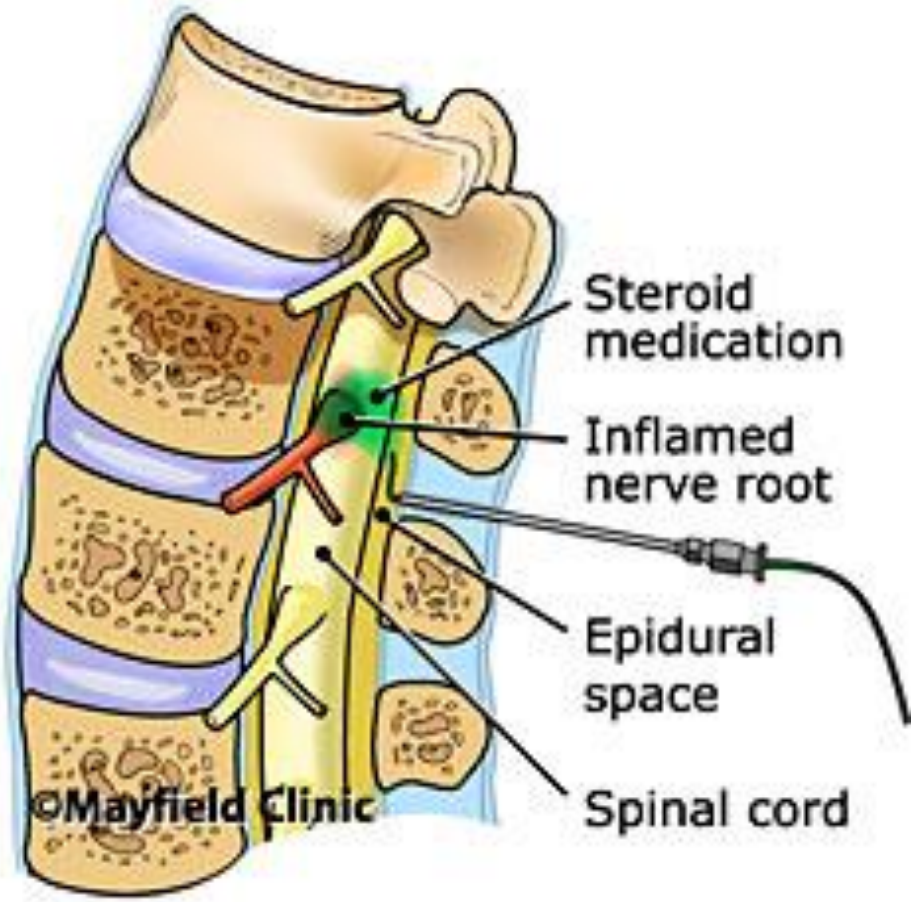
- Disadvantages:

- Needs high skills & carries some degree of risk.
- Not economical.

f. Intraperitoneal:

- into the peritoneum. Seldom to use clinically , but it is a common laboratory practice use to administer drugs to experimental animals. Advantages:
- Rapid absorption due to large surface area
- Disadvantages:
- High risk of infection, painful & may cause necrosis


Injectable hydrogel
Spinal cord
Dura mater
CSF filled intrathecal space
CSF flow


Steroid medication
Inflamed nerve root
Epidural space
Spinal cord
©Mayfield Clinic

g. Intra-arterial:

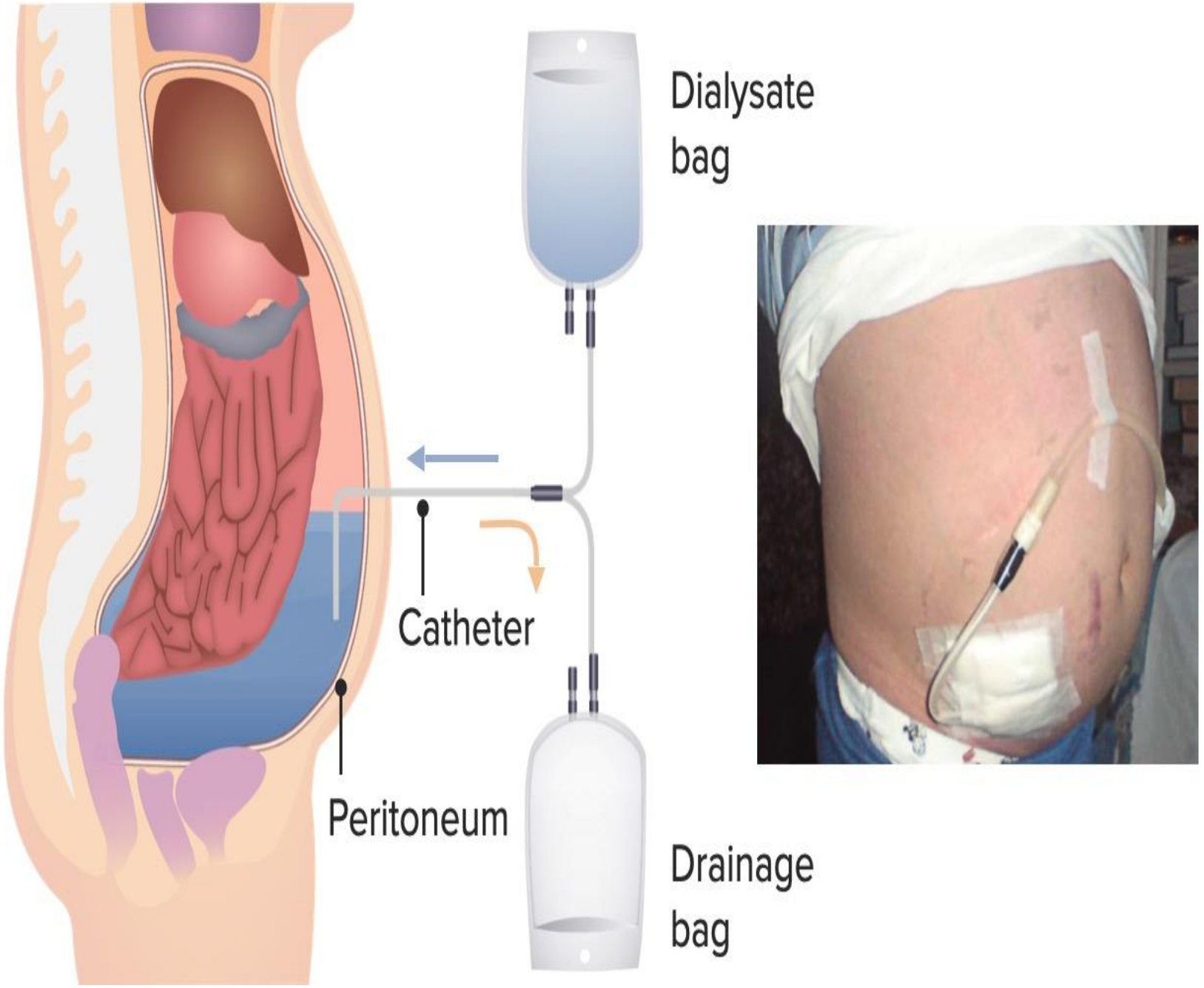
(into an artery), e.g. vasodilator drugs in the treatment of vasospasm.

- If needles are shared, there is risk of HIV and other infectious diseases

5. Inhalation:

Suitable for gases or volatile compounds (halothane), aerosol & nebulized solution (beclomethasone & salbutamol), powder (Na^+cromoglycate).

- Advantages:
- Rapid absorption due to large surface area Local application of the drug at the desired site of action (↓side effects)
- Avoid 1st pass metabolism.
- Disadvantages:
- Can cause side effects due to systemic absorption.
- May cause pulmonary irritation
- Poor ability to regulate the dose (inhaler).


Dialysate bag
Catheter
Peritoneum
Drainage bag

6. ***Topical application:***

a. Cutaneous application:

- For local effect (low lipid soluble drugs in the form of creams & ointments) e.g. betamethasone. For sustained systemic effect (lipid soluble drugs in the form of transdermal patches)

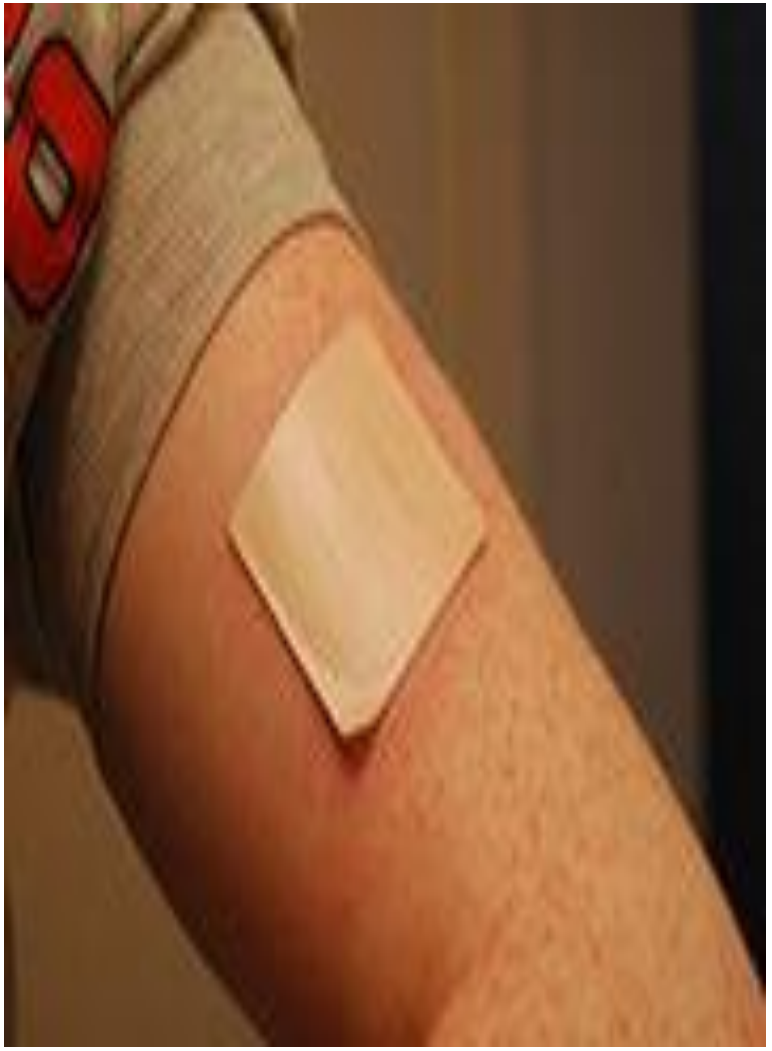
e. g. fentanyl skin patches, nicotine patches & estrogen skin patches

b. Application to the nasal mucosa e.g. Nasal decongestant → local effect. ADH (escape 1st pass effect & avoid destruction by gastric juice →systemic effect.

c. Application to the vaginal mucosa (pessaries).

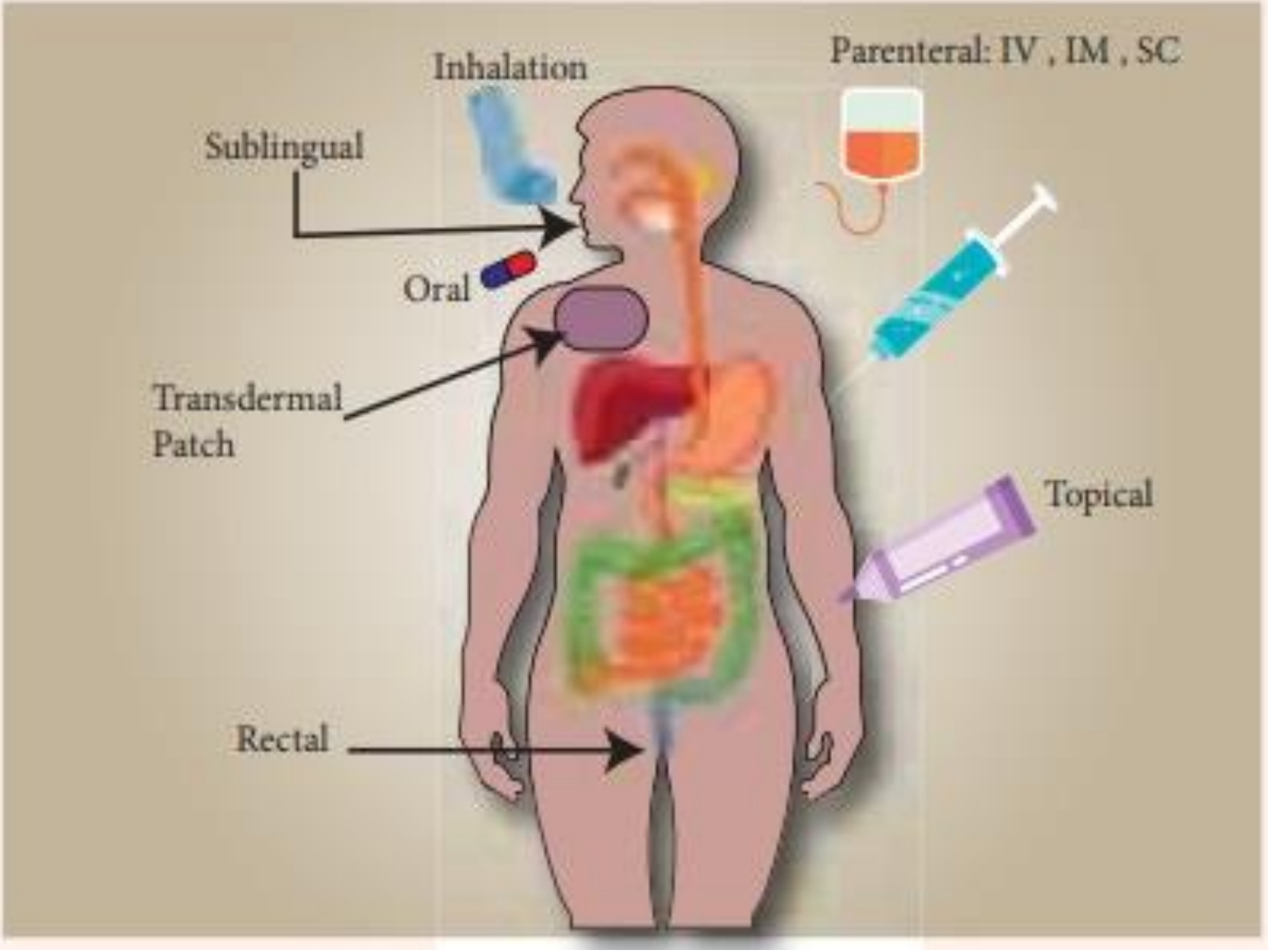
d. Application to the eye:

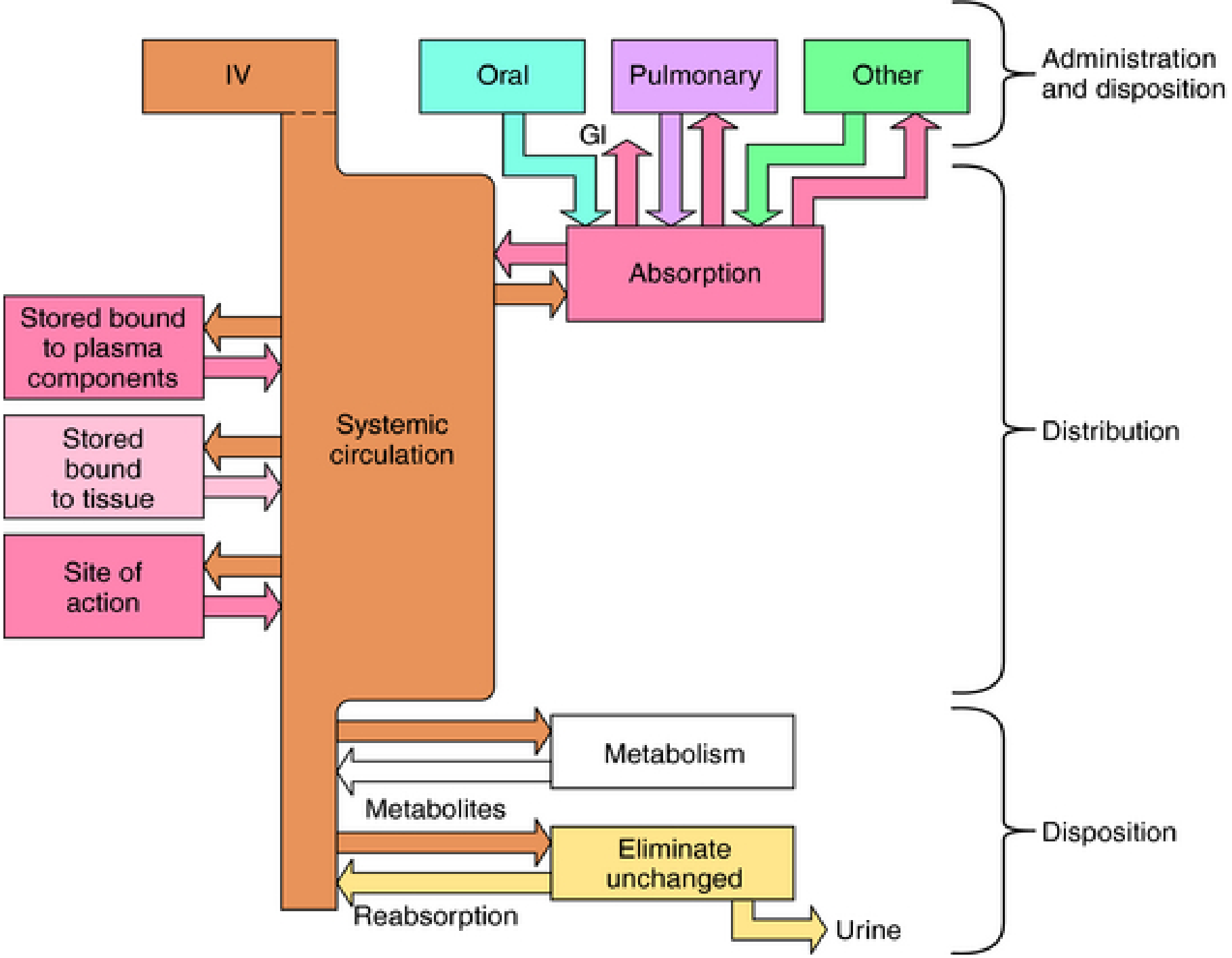
Gentamicin & timolol eye drops

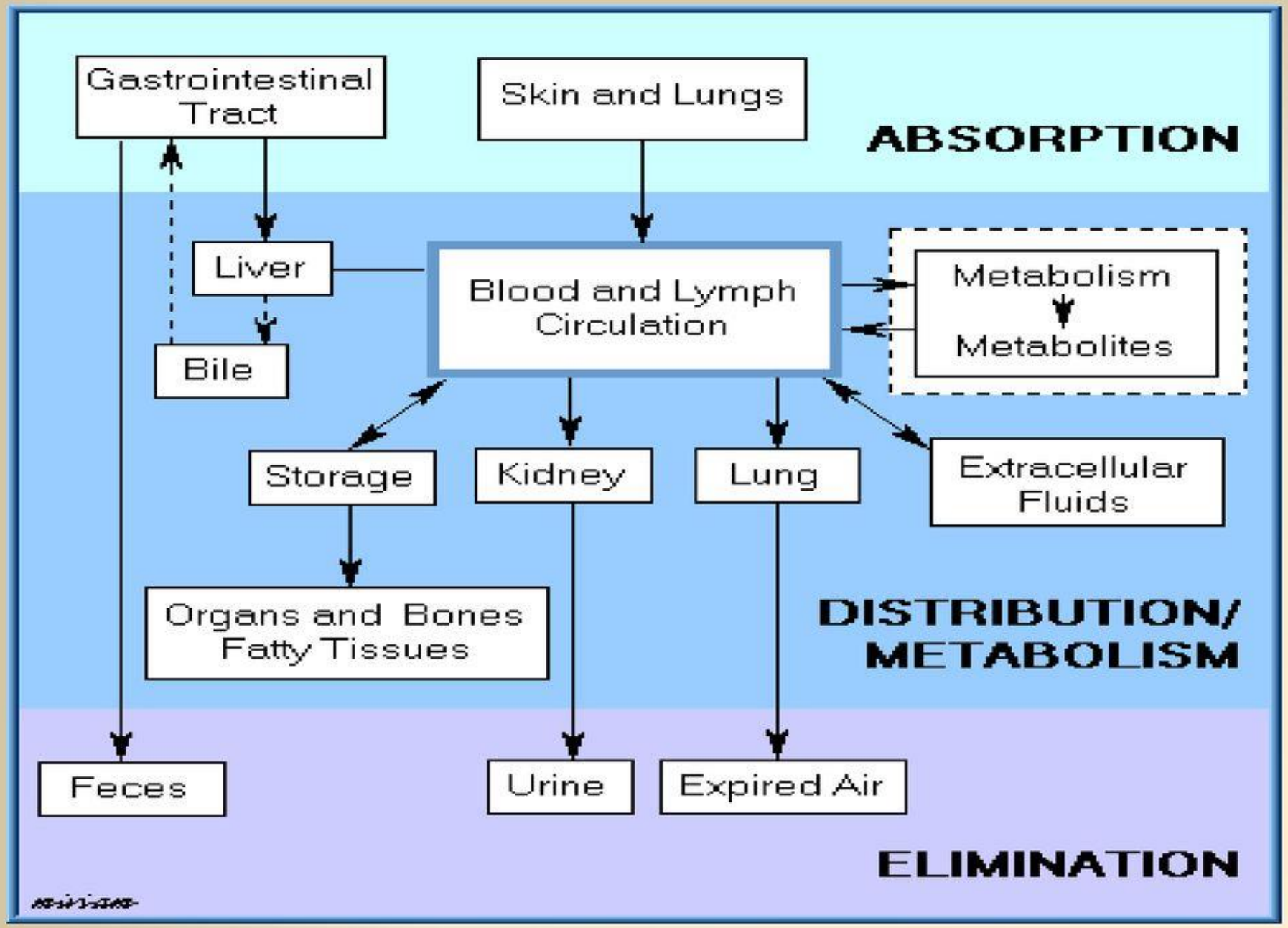


Route for administration
-Time until effect-

- *intravenous 30-60 seconds*
- *inhalation 2-3 minutes*
- *sublingual 3-5 minutes*
- *intramuscular 10-20 minutes*
- *subcutaneous 15-30 minutes*
- *rectal 5-30 minutes*
- *oral 30-90 minutes*
- *transdermal (topical) variable (minutes to hours)*


Inhalation
Parenteral: IV , IM , SC
Sublingual
Oral
Transdermal
Patch
Topical
Rectal


IV
Oral
Pulmonary
Other
Administration and disposition
GI
Absorption
Stored bound to plasma components
Stored bound to tissue
Site of action
Systemic circulation
Distribution
Metabolism
Metabolites
Eliminate unchanged
Reabsorption
Urine
Disposition


Gastrointestinal Tract
Skin and Lungs
ABSORPTION
Liver
Bile
Blood and Lymph Circulation
Metabolism
Metabolites
Storage
Kidney
Lung
Extracellular Fluids
Organs and Bones
Fatty Tissues
DISTRIBUTION/
METABOLISM
Feces
Urine
Expired Air
ELIMINATION

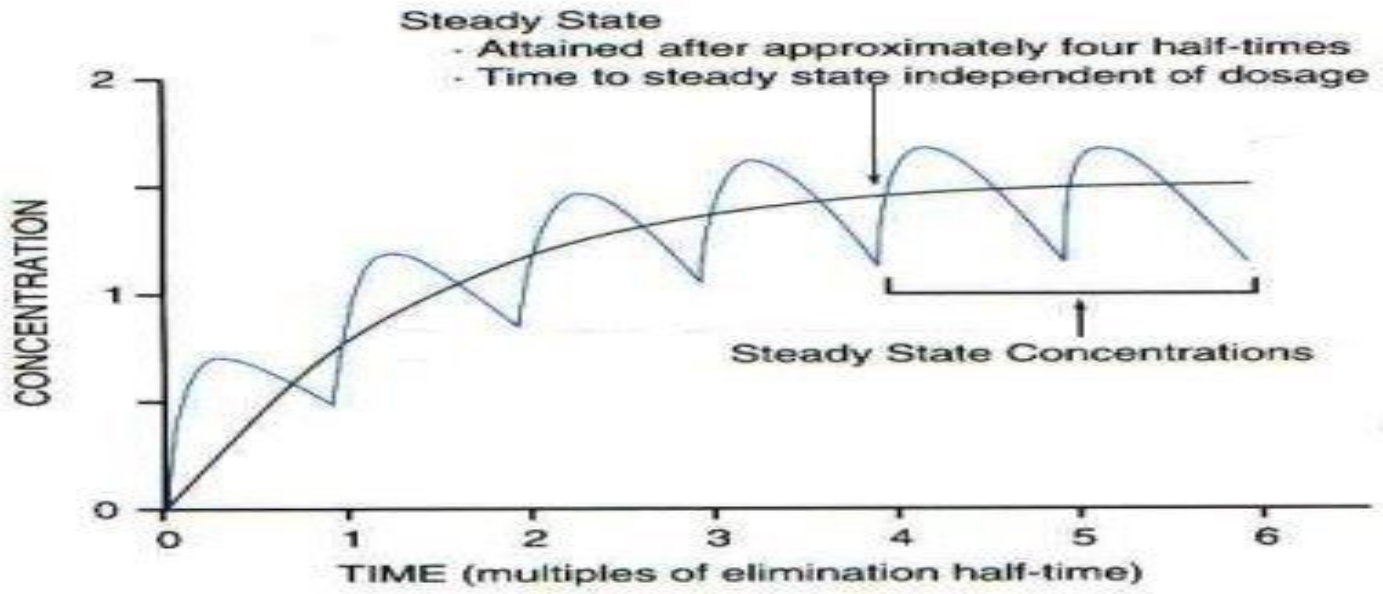
Pharmacokinetic Principles

Pharmacokinetic principles aid in the selection & adjustment of drug dosage schedules & facilitate interpretation of plasma drug concentration.

Half-life (t½):

Is the time required to decrease drug concentration in the body by 50%.

- It provides a good indication of the time required to reach steady state conc (4 X t½) & a means to estimate dosing interval in repeated doses.



- **Pharmacokinetics orders:**
- For a chemical reaction, the order of a reaction refers to the way in which the concentration of a drug or a reactant influences the rate of the reaction.

1. **First order kinetic**

The change in concentration with respect to time is directly proportional to the concentration of the reactants i.e the rate of the process (ADME) is directly proportional to the amount or concentration of the drug in the body.

Zero order kinetic :saturation kinetic

The rate of the process is constant regardless of the concentration.

Zero-order process occurs when an enzyme or carrier system is saturated, then the rate can not further increased by increasing the substrate conc. and consequently the rate remain constant i.e. It is a capacity-limited process e.g. ethanol, phenytoin, aspirin (↑dose), prednisolone elimination.

Most drug absorption or elimination follow first-order kinetics except when the process is saturated.

- Paracetamol (acetaminophen) is safe at therapeutic dose. [glucuronide and sulfate conjugation (95%). CYP450-dependent GSH conjugation. (5%)].
- Paracetamol overdose leads to saturation of glucuronidation and sulfation pathways and the CYP450-dependent pathway dominates, leading to accumulation of reactive intermediate (N-acetyl-p-benzoquinone imine).
- Little or no toxicity occurs as long as glutathione is available but when it is depleted, the accumulated reactive metabolites can produce hepatotoxicity.
- Cysteamine and N-acetylcysteine are used as antidote.

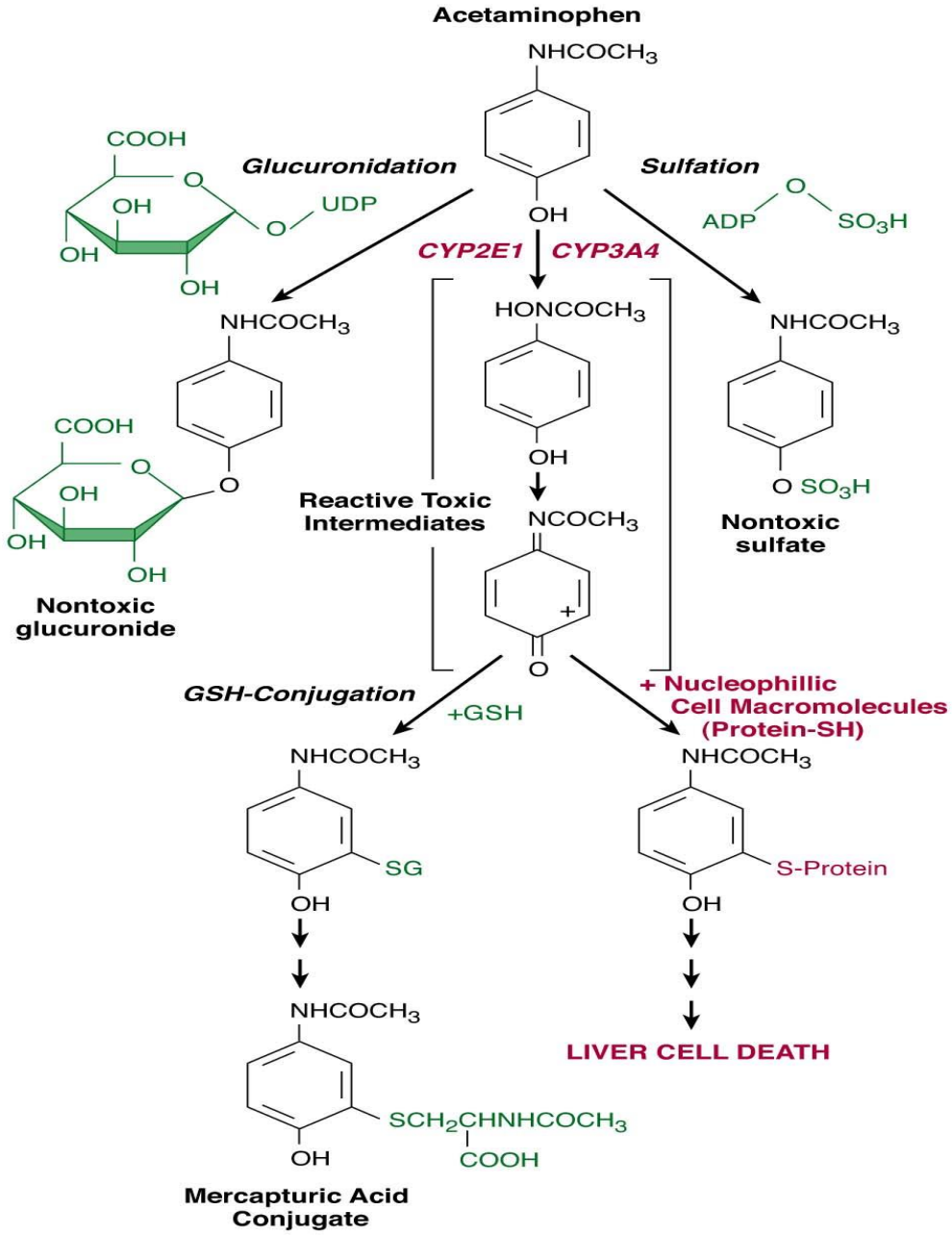
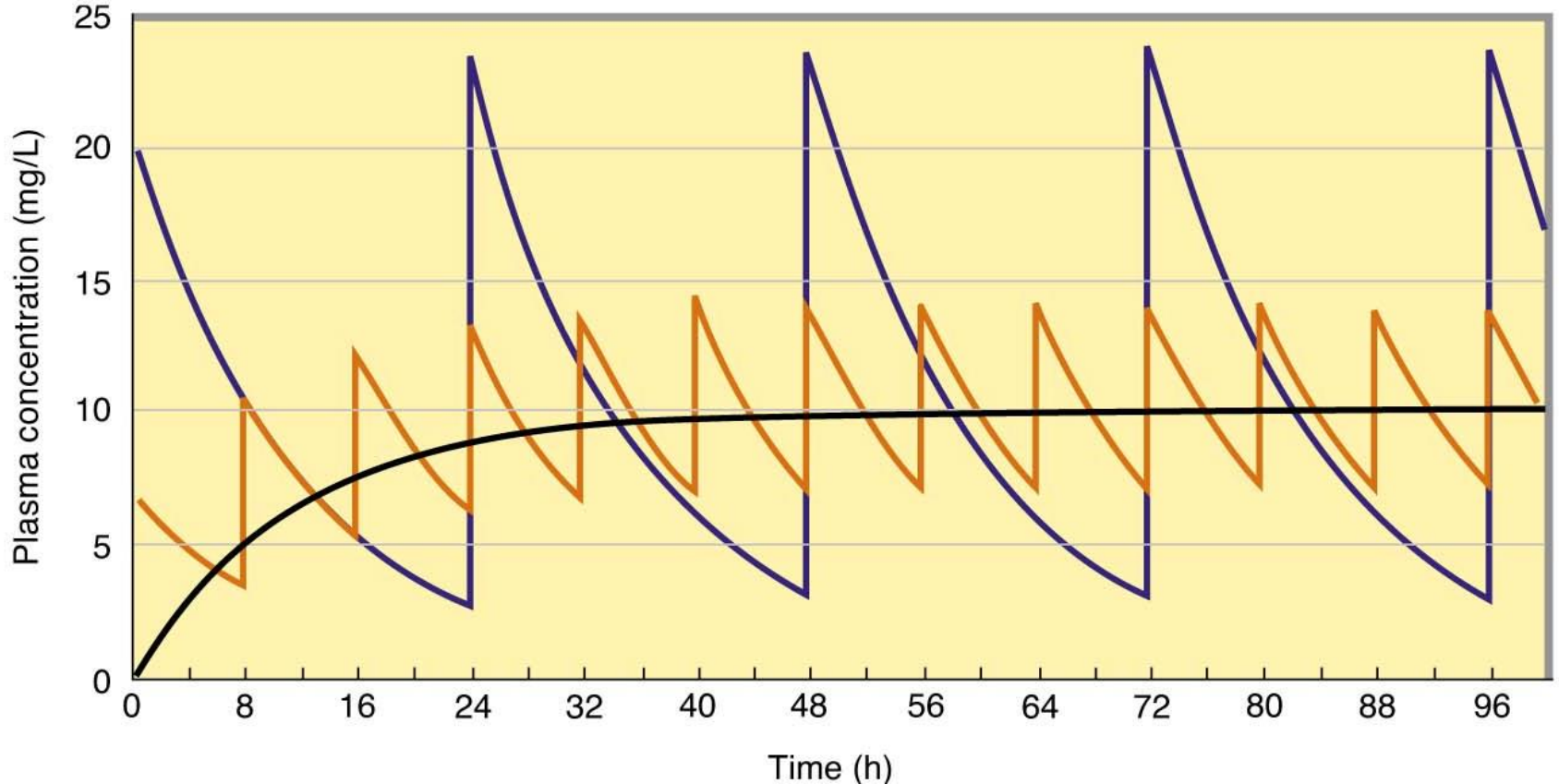


FIGURE 4–5 Metabolism of acetaminophen (top center) to hepatotoxic metabolites. GSH, glutathione; SG, glutathione moiety.

- At steady state , plasma drug concentration fluctuate between maximum (C^{ss}_{max}) and minimum (C^{ss}_{min}) plasma concentrations.
- The steady state conc. should be within the therapeutic window.



THANKS FOR LISTENING, ANY QUESTIONS?