

Introduction to Pharmacology

History, Types of pharmacology, sources of
Drug information etc.

INTRODUCTION TO PHARMACOLOGY

- Pharma=Drugs, Logos = Knowledge
(Pharmacology = The study or science of drugs)
- **Pharmacology:** It is the science of drugs derived from two Greek words: *Pharmakon* (Greek word for drugs) and *logos* (the Greek word for science). It is the study of the actions of drugs on living system.
- It includes physical and chemical properties, biochemical and physiological effects, mechanism of action, therapeutic uses and adverse effects of drugs.

Drug

- Any chemical that affects the processes of a living organism

Pharma=Drugs, Logos = Knowledge

Pharmacology

- The study or science of drugs

History of Pharmacology

HISTORY OF PHARMACOLOGY

- Knowledge of drugs and their uses in diseases are as old as history of mankind.
- Primitive men gather the knowledge of healing and medicines by observing the nature, noticing the animals while ill and personal experience after consuming plants and herbs as remedies.
- Ancient civilizations discovered that extracts from plants, animals, and minerals had medicinal effects on body tissue. These discoveries became the foundation of pharmacology.

Pharmacology in the present form is relatively recent branch about hundred years old.

Historical developments in Pharmacology

- **PEN PSAO (2700 BC)** It was the great herbal materia medica written in china.
- **Kahun Papyrus (2000 BC)** is an oldest Egyptian document containing information about veterinary medicines and uterine diseases of women.
- **Ebers papyrus (1550 BC)** also an Egyptian document containing information about number of diseases and 829 prescription where castor oil, opium like drug are being used.

Historical developments in Pharmacology

- Hippocrates (460-375 BC) A greek physician consider **“father of Medicine”**. He was the first person who recognize disease as abnormal reaction of body. He introduce use of metallic salts for the treatment of disease.
- Theophrastus (380-287 BC) a great philosopher called father of Pharmacognosy. He classified medicinal plants on the base of medicinal characteristics.

Historical developments in Pharmacology

- **Dioscorides (AD 57)** a greek, produced one of the first materia medica of approximately 500 plants and remedies.
- **Claudius Galen (AD 129–200)** first attempted to consider the theoretical background of pharmacology.
- **Paracelsus (1493–1541)** a Swiss scholar and alchemist, often considered the “**grandfather of pharmacology**”. He introduces the use of chemicals for treatment of disease.
- **Valerius Cordus (1514-1544)** He compiled the first pharmacopeia where he described techniques for the preparation of drugs.

MODERN PHARMACOLOGY

- Conversion of old medicines into the modern pharmacology start taking shape following the introduction of animal experimentation and isolation of active ingredients from plants.
- **Francois Megendie (1783-1855)** a first pharmacologist established the foundation of modern pharmacology. He developed experiment to elucidate the physiological processes and action of drugs on the body.
- **Rudolph Buchheim (1820–1879)** German pharmacologist a key figure in the development of pharmacology, a who at the University of Dorpat, created the first pharmacological institute.

MODERN PHARMACOLOGY

- **Frederich Sertürner**, German pharmacist's assistant, isolated morphine—the first pure drug—in 1805
- **Claude Bernard (1813-1878)** considered Father of experimental Medicine. He identifies the site of action of curare (arrow Poisoning).

MODERN PHARMACOLOGY

- Oswald Schmiedeberg (1838–1921) “**Father of Pharmacology**” established pharmacology as an independent discipline. He start teaching Pharmacology in University of Strasbourg (France).
- John Jacob Abel (1857-1938) founded first department of pharmacology in USA in the University of Michigan in 1893. In 1897 he established pharmacology department at Johns Hopkins University. Abel also co-founded the Journal of Pharmacology and Experimental Therapeutics in 1909.

MODERN PHARMACOLOGY

- L. Mayer Jones (1912-2002) regarded as father of modern veterinary pharmacology. He authored first book of veterinary pharmacology therapeutics in 1954.

SCOPE OF PHARMACOLOGY

- It provides the rational basis for the therapeutic use of the drug. Before the establishment of this discipline, even though many remedies were used, but doctors were reluctant to apply scientific principles to therapeutics.
- In 1920s, many synthetic chemicals were first introduced and the modern pharmaceutical companies began to develop.

SCOPE OF PHARMACOLOGY

- Scientific understanding of drugs enables us to predict the pharmacological effect of a new chemical that will produce a specified therapeutic effect.
- The scope of pharmacology has expanded greatly over the last decade to incorporate many new approaches such as computer-assisted drug design, genetic screens, protein engineering and use of novel drug delivery vehicles including viruses and artificial cells.
- Our society needs pharmacologists who understand the basis of modern therapeutics for careers within academic, pharmaceutical and governmental laboratories to study and develop tomorrow's drugs.

Sources of Drug information

- The sources of drug information is received by pharmacopeia, that is a book which contains a list of established and officially approved drug with description of their physical and chemical characteristics and tests for their identification, purity, methods of storage etc. some of the pharmacopeia's are:
 - Indian Pharmacopeia.(I.P.)
 - British Pharmacopeia (B.P.)
 - European Pharmacopeia.(E.P)
 - United states Pharmacopeia.(U.S.P).

contd

- Other sources of drug information are
- National formulary (NF), Martindale – The extra Pharmacopeia,
- Physician desk Reference (PDR),
- American Medical Association drug Evaluation,
- Textbook & Journal of pharmacology and therapeutics, Drug bulletins, data bases like drug Micromedex, Medline, Cochrane library etc.
- Sources of drug information is also present in Formulary which provides information about available drugs – their use, dosage, adverse effect, contraindications, precautions, warnings and guidance on selecting right drugs for a range of conditions.

The background of the slide features three blurred pills. At the top left is a white pill, at the top right is a pink pill, and at the bottom center is a yellow pill. The text is centered over the white and pink pills.

Definitions:
Terminology uses.

Definitions

Pharmacology	Detailed study of drugs
Pharmacognosy	Science of identification of drug
Pharmacy	Science of identification,selection, preservation, standardization, compounding and dispensing of medical substances

Definitions (Contd)

Therapeutics

**Branch of medicine concerned
With cure of disease or relief of
Symptoms and includes drug
Treatment**

Toxicology

**Science of poisons.
Measurement / detections of
poisons
Treatment of poisoning**

Definitions

Chemotherapy

Effect of drugs upon micro-organisms and parasites, living and multiplying in a living organism

Pharmacopoeia

An official code containing a selected list of the established drugs and medicinal preparations with description of their physical properties and tests for their identity, purity and potency

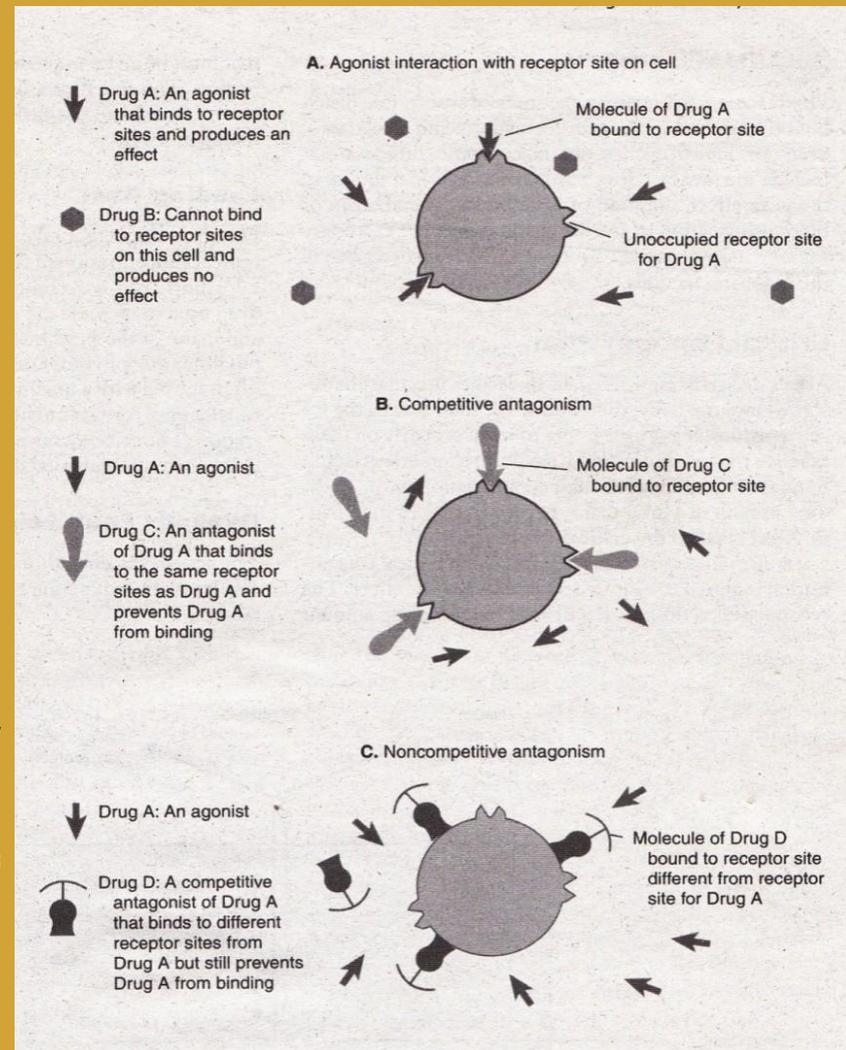


Drug – WHO scientific group definition

**Any substance or product that is used/
intended to be used to modify or
explore physiological systems or
pathological systems or pathological
states for the benefit of the recipient**

Drug Attachment

- Medication chemically binds to specific sites called “receptor sites”
 - **Agonist**-chemical fits at receptor site well
 - **Antagonist**- a chemical blocks another chemical from getting to areceptor
 - **Partial agonist** - attach to the receptor but only produce a small effect



Basics of Drug Action

- *Desired action* – the expected response of a medication
- *Side effects* – known and frequently experienced, expected reaction to drug.
- *Adverse reaction* – unexpected, unpredictable reactions that are not related to usual effects of a normal dose of the drug.

Drug Interaction

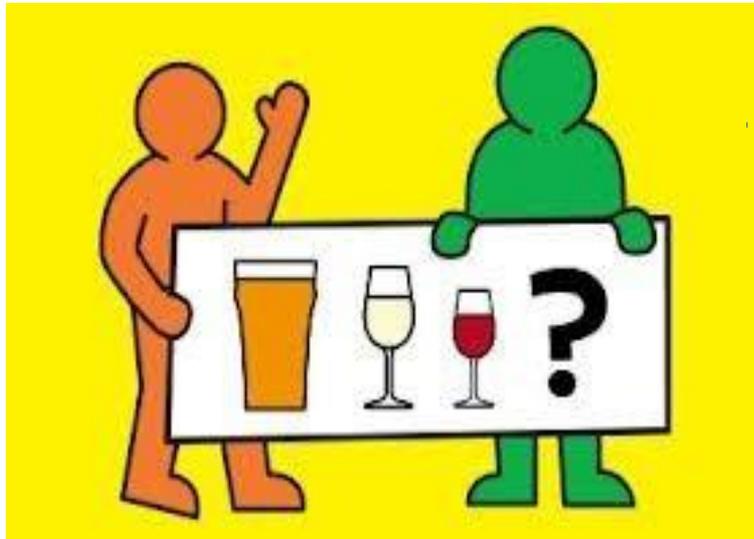
- Takes place when one drug alters the action of another drug.
- Some are helpful but often produce adverse effects.



Common Drug Interactions

- **Additive effect-** takes place when 2 drugs are given together & double the effect is produced.

Alcohol + aspirin = Pain relief



Common Drug Interactions

- **Antagonist**- a chemical blocks another chemical from getting to a receptor
- **Antagonistic effect**- takes place when 1 drug interferes with the action of another drug.
- **Eg. Protamine sulphate to counteract heparin toxicity**



Common Drug Interactions

- **Displacement effect** - takes place when 1 drug replaces another at the drug receptor site, increasing the effect of the 1st drug.

Common Drug Interactions

- **Incompatibility** –occurs when 2 drugs mixed together in a syringe produce a chemical reaction so they cannot be given.
e.g. Protamine sulfate & vitamin K

Common Drug Interactions

- **Interference**- occurs when 1 drug promotes the rapid excretion of another, thus reducing the activity of the 1st.
- **Synergistic effect** takes place when the effect of 2 drugs taken at the same time is greater than the sum of each drug given alone.

E.g. combining diuretics & adrenergic blockers to lower the BP

Pharmacognosy: Sources of Drugs

Pharmacognosy

- The study of natural (plant and animal) drug sources

Sources of Drugs

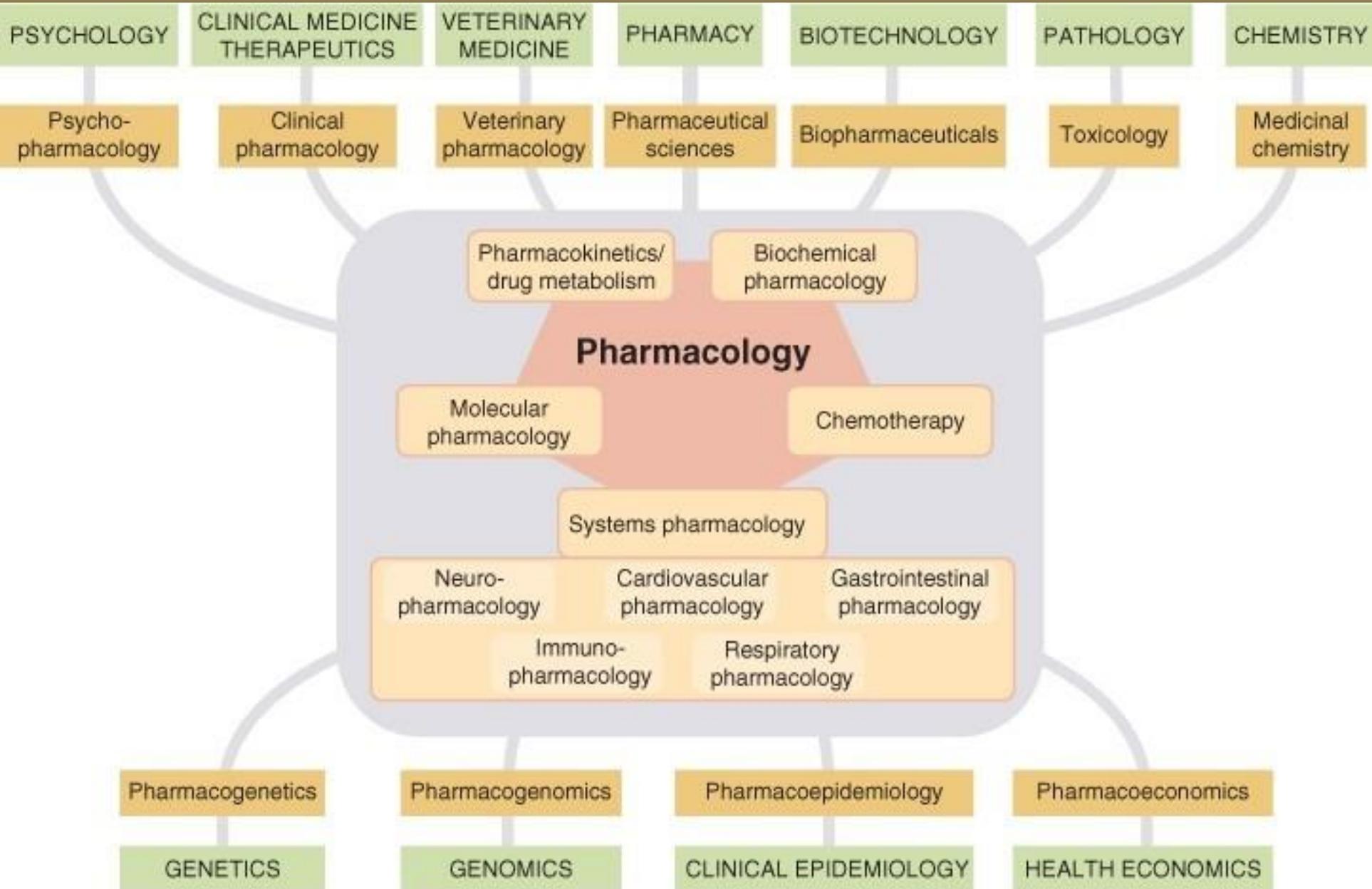
- The different sources of drugs are:
- Plants:
- *Alkaloids*: eg. Morphine, Atropine, Quinine, reserpine, ephedrine.
- *Glycosides*: eg. Digoxin, Digitoxin.
- Animals: Insulin, Heparin.
- Minerals: ferrous sulphate, Magnesium sulphate.
- Microorganisms: Penicillins, Streptomycin, Grisiiofulvin.
- Semisynthetic: Hydromorphone, Hydrocodone.
- Synthetic: Most of the drugs used today are synthetic.
Eg. Aspirin, paracetamol.

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- Drugs are also produced by genetic engineering (DNA recombinant technology) eg. Human insulin, Human growth hormone and Hepatitis B Vaccine.

Types: Classification of Pharmacology.

PHARMACOLOGY, Link to other biomedical principles



Types of Pharmacology

- 1. Experimental Pharmacology:** Done in the laboratory on experimental animals such as rodents and non rodents.
- 2. Clinical Pharmacology:** On human subjects normal or deceased

CLASSIFICATION OF DRUGS

- 1. Chemical Nature**
- 2. Source**
- 3. Target organ/Site of Action**
- 4. Mode of Action**
- 5. Therapeutic Uses**
- 6. Physiological system**
- 7. Physical Effects**

1. CLASSIFICATION BASED ON CHEMICAL NATURE

- Chemical Nature of drug is discussed by a Chemist and based on chemical nature we divide drugs into
- **INORGANIC DRUGS**
 - **Metals and their Salts** (Ferrous Sulphate, Zinc Sulphate, Magnesium Sulphate).
 - **Non Metals** Includes Sulphur.
- **ORGANIC DRUGS**
 - **Alkaloids** (atropine, Morphine, Strychnine)
 - **Glycosides** (Digitoxin, Digoxin).
 - **Proteins** (Insuline, Oxytocin)
 - **Esters, Amide, Alcohol, Glycerides.**

2. CLASSIFICATION BASED ON SOURCE

Sources of drugs are discussed by a Pharmacologist and Pharmacist

Natural Source

- **Plants** (Morphine, Atropine, Digitoxin)
- **Animals** (Insuline, eCG)
- **Micro organism** (Penicillin)
- **Mineral** (Sodium Chloride)

Synthetic Source

- (Sulphonamide, Procaine).

Semi-synthetic Source

- ▣ Amoxicillin, Ampicillin, Doxycycline

Bios-ynthetic Source

- ▣ Recombinant Human erythropiotin, Recombinant bovine somattotropine

3. CLASSIFICATION BASED ON TARGET ORGAN

Classification based on target organs are done by the Physicians.

- **Drugs acting on CNS** (Diazepam, Phenobarbitone).
- **Drugs acting on Respiratory System** (Bromhexaine).
- **Drugs acting on CVS** (Digitoxin, Digoxin).
- **Drugs acting on GIT** (Omeprazole, Kaoline, Sulphadimidine).
- **Drugs acting on Urinary System** (Magnesium Sulphate, Lasix)
- **Drugs acting on reproductive system** (Oxytocin, Estrogen)

4. CLASSIFICATION BASED ON MODE OF ACTION

Classification based on mode of action is done by Physicians & Pharmacologists.

- **Inhibitor of bacterial cell wall synthesis**
(penicillin)
- **Inhibitor of bacterial protein synthesis**
(Tetracycline)
- **Calcium Channel blocker** (Verapamil, nifedipine)

5. CLASSIFICATION BASED ON THERAPEUTIC USE

Classification based on mode of action is done by Physicians & Pharmacologists.

- **Antimicrobials/Antibacterials** (Penicillin, Streptomycin, Quinolones, Macrolides).
- **Antihypertensive** (Clonidine, hydralazine, Enalapril).
- **Antidiarrheal** (Lopramide, Kaoline).
- **Antiemetics** (Domperidone, Meclizine and Metoclopramide).

6. CLASSIFICATION BASED ON PHYSIOLOGICAL SYSTEM

- **Sympathomimetics** (Adrenaline, Noradrenaline).
- **Parasympathomimetics** (Carbachol, Pilocarpine, Neostigmine).
- **Neuromuscular blockers** Suxamethonium, Gallamine).

7. CLASSIFICATION BASED ON PHYSICAL EFFECTS

- **Emollients** (Lanolin, Vaseline)
- **Caustics** (Silver nitrate)
- **Demulcents** (Zinc Oxide, Tannic Acid).

Site/Type of Action



This is another way of classifying drugs according to the system of the body on which it acts

- **Vioxx would fall into the class called Musculo-Skeletal and Joint Diseases**
- **MIMS sets out these classes**
- **Use MIMS to find your drug's classification**

Drug Nomenclature



Naming of drugs (Drug Nomenclature)

Three Names

- # The Chemical Name - technical description of the actual molecule e.g. Cozaar is 2-Butyl, 4 Chloro-tetrazol, 5 Phenylbenzylimidazole, 5 Methanol sodium
- # The Generic Name - The official medical name
Cozaar's generic name is Losartan
- # The Brand or Propriety Name - The name under which the product is marketed i.e. Cozaar

Pharmaco-dynamics:
Actions, therapeutic
Adverse, toxic.

Pharmacotherapeutics: Types of Therapies

- Acute therapy
- Maintenance therapy
- Supplemental therapy
- Palliative therapy
- Supportive therapy
- Prophylactic therapy

Pharmacotherapeutics: Monitoring

- The effectiveness of the drug therapy must be evaluated.
- One must be familiar with the drug's
- intended therapeutic action (beneficial)
- and the drug's unintended but potential side effects (predictable, adverse drug reactions).

Pharmacotherapeutics: Monitoring

- Therapeutic index
- Drug concentration
- Patient's condition
- Tolerance and dependence
- Interactions
- Side effects/adverse drug effects

Pharmacotherapeutics: Monitoring

Therapeutic Index

- The ratio between a drug's therapeutic benefits and its toxic effects

Pharmacotherapeutics: Monitoring

Tolerance

- A decreasing response to repetitive drug doses

Dependence

- A physiologic or psychological need for a drug

Pharmacotherapeutics: Monitoring

Interactions may occur with other drugs or food

- Drug interactions: the alteration of action of a drug by:
 - Other prescribed drugs
 - Over-the-counter medications
 - Herbal therapies

Pharmacotherapeutics:

Interactions Monitoring

- Additive effect
- Synergistic effect
- Antagonistic effect
- Incompatibility

Pharmacotherapeutics: Monitoring

Medication Misadventures

Adverse drug events

- ALL are preventable
- Medication errors that result in patient harm

Adverse drug reactions

- Inherent, not preventable event occurring in the normal therapeutic use of a drug
- Any reaction that is unexpected, undesirable, and occurs at doses normally used

Pharmacotherapeutics: Monitoring

Some adverse drug reactions are classified as side effects.

- Expected, well-known reactions that result in little or no change in patient management
- Predictable frequency
- The effect's intensity and occurrence is related to the size of the dose

Pharmacotherapeutics: Monitoring

Adverse Drug Reaction

An undesirable response to drug therapy

- Idiosyncratic
- Hypersensitivity reactions
- Drug interactions

Pharmacotherapeutics: Monitoring

Iatrogenic Responses

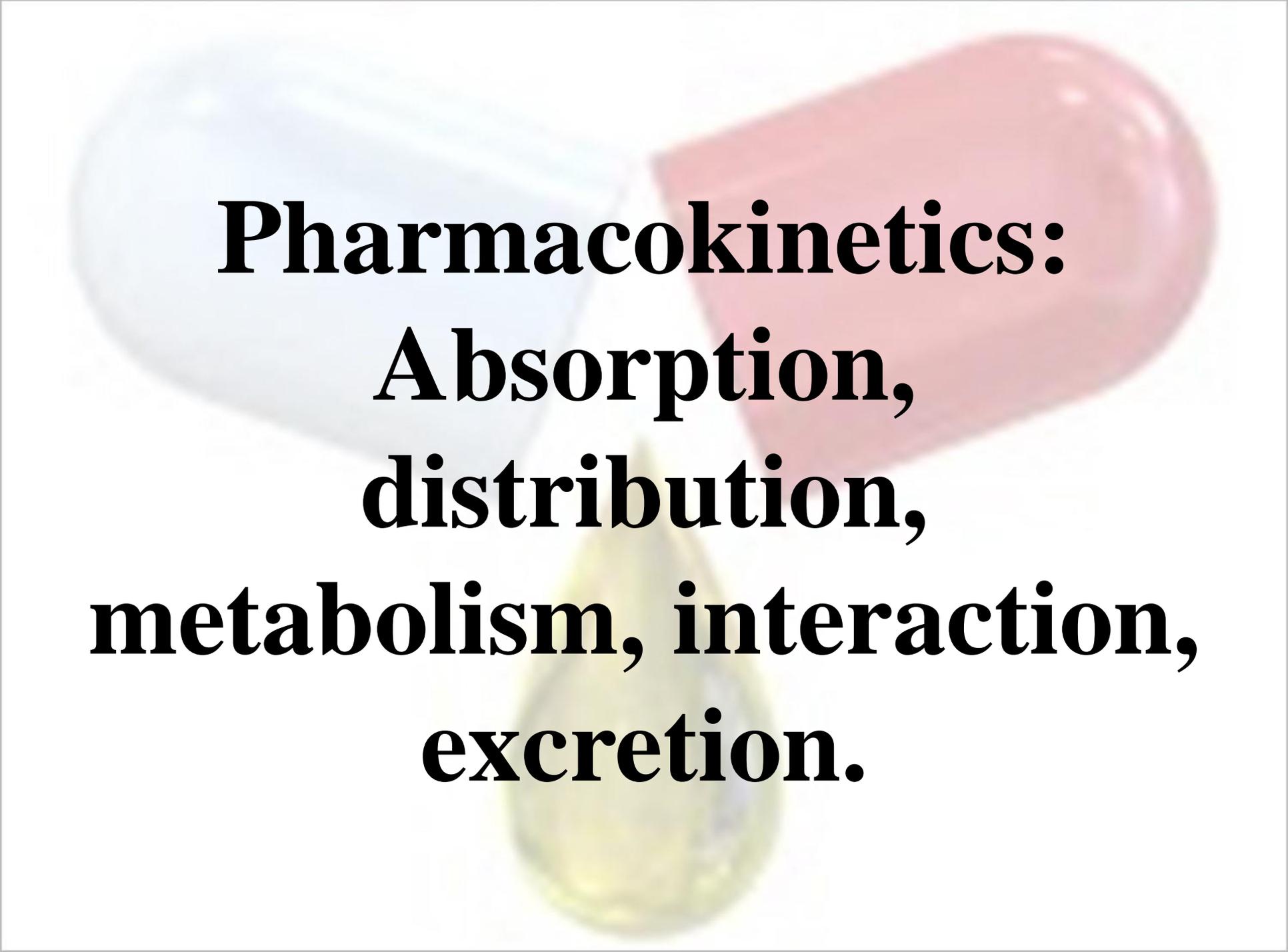
Unintentional adverse effects that are treatment-induced

- Dermatologic
- Renal damage
- Blood dyscrasias
- Hepatic toxicity

Pharmacotherapeutics: Monitoring

Other Drug-Related Effects

- Teratogenic
- Mutagenic
- Carcinogenic



**Pharmacokinetics:
Absorption,
distribution,
metabolism, interaction,
excretion.**

Factors influencing the efficacy of a drug are:

- **The route of Administration**
- **The rate of Absorption**
- **The distribution of the drug to the required site**
- **The rate of biotransformation or metabolism**
- **The presence of active metabolites**
- **The rate of excretion**

Absorption

- # To be effective a drug must be absorbed - except for topical and IV**
- # This means drugs have to cross cell membranes**
- # The ability of the drug to cross the cell membrane is influenced by its solubility in water or fat, its size and shape**

Drug Absorption of Various

Oral Preparations

Liquids, elixirs, syrups

Fastest

Suspension solutions

?

Powders

?

Capsules

?

Tablets

?

Coated tablets

?

Enteric-coated tablets

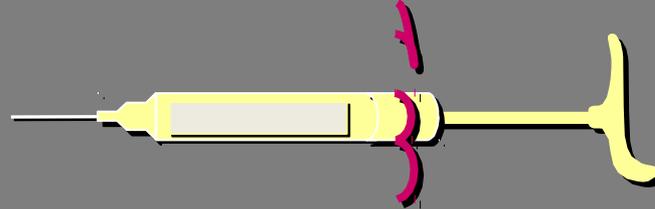
Slowest

Absorption

- **Drugs cross membranes by:**
 - **Filtration** - only small water-soluble molecules which flow through the hydrophilic pores
 - **Passive Transport** - Diffusion i.e. from high concentrations to low concentrations
 - **Active Transport** - Energy and carriers are required to move non-fat soluble substances across the cell membrane e.g against concentration gradient

Absorption

IV injection



delivered straight to bloodstream
rapid action

All other routes

need to be *absorbed* from site of administration

speed of action depends on *absorption rate* (ka)

Absorption

Factors affecting the absorption rate (k_a)

#Route of administration

Blood supply to the site of absorption

Formulation of the drug

Gut transit time

pH in the gut

Solubility of the product

Distribution

Drug in bloodstream is distributed to body:

Central compartment

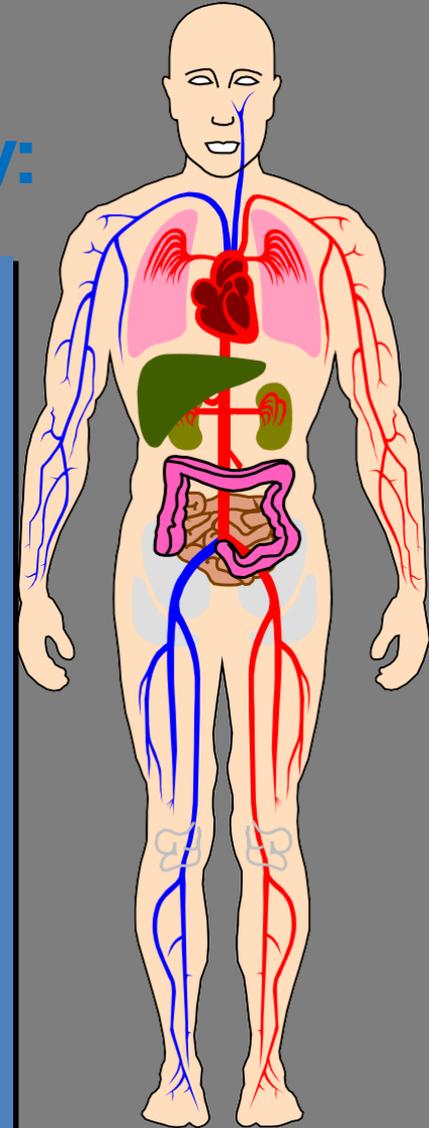
-(major organs & blood vessels)

- low lipid solubility (hydrophilic)
- low volume of distribution (low V_d)

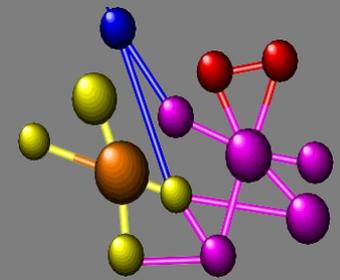
Peripheral compartment

• (skin & fat stores)

- high lipid solubility (lipophilic)
- high volume of distribution (high V_d)



Distribution



Plasma protein binding:

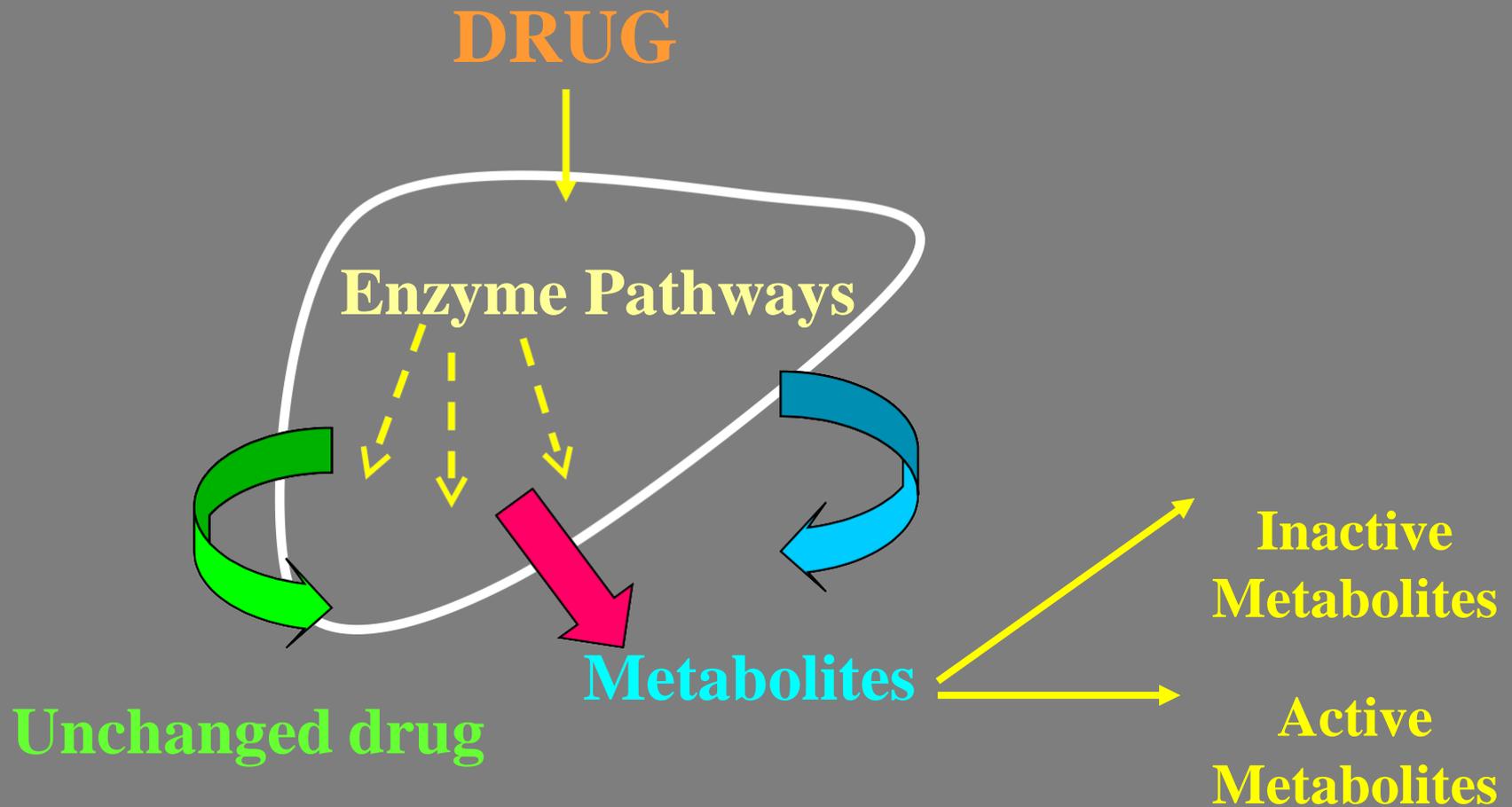
#Only 'free fraction' can move to target site (e.g. 80% bound / 20% free)

#Dynamic process i.e. as free drug moves into tissues, protein-bound drug is released into plasma to maintain ratio (*ratio of 'free fraction' : 'plasma protein bound' remains constant*)

#Drugs vary in the degree to which they are plasma protein bound (< 99.9%)

Metabolism

Major organ of metabolism - LIVER



Metabolism

Major organ of metabolism - LIVER

- **Active metabolites :**
Clinical or side effects
- **Inactive metabolites**

N.B. Patients with hepatic impairment may require:

- *higher doses (where metabolism → active metabolites)*
- *lower doses (where metabolism → inactive metabolites)*

Metabolism



**Factors affecting metabolism
(i.e. compete for enzyme pathways in the liver)**

Genetic factors

Other drugs e.g. *Cimetidine / Ciprofen*

Smoking

Enzyme induction/inhibition (CYP450/others)

Some foods

Liver disease

Age

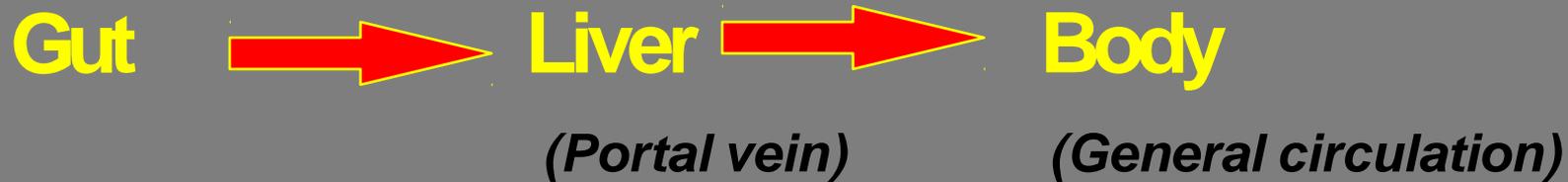
First-Pass Effect

The metabolism of a drug and its passage from the liver into the circulation.

- A drug given via the oral route may be extensively metabolized by the liver before reaching the systemic circulation (high first-pass effect).
- The same drug—given IV—bypasses the liver, preventing the first-pass effect from taking place, and more drug reaches the circulation.

Metabolism

First pass metabolism



the breakdown of a drug in the liver before it reaches the site of action

oral dose may need to be higher than parenteral dose

Prodrug

First Pass (Presystemic) Metabolism

- # Metabolism of orally administered drugs in a single passage thru the gut wall and (principally) the liver.
- # Drugs for which presystemic elimination is significant – Isosorbide dinitrate, Propranolol etc.
- # First pass elimination is reduced in severe hepatic cirrhosis

First-Pass Effect

- Routes that bypass the liver:
 - Sublingual
 - Buccal
 - Rectal
 - Intravenous
 - Intranasal
 - Transdermal
 - Vaginal
 - Intramuscular
 - Subcutaneous
 - Inhalation
- *Rectal route undergoes a higher degree of first-pass effects than the other routes listed.

Elimination

Elimination

=

Metabolism

+

Excretion

Excretion

#The process by which drug is removed from the body.

Primary

via the kidneys (in urine) also

via the gut (faeces), the skin (sweat), the lungs (breath), saliva

N.B. Patients with renal disease or dysfunction (elderly/heart disease) may require lower doses as the drug will be retained for longer than in 'normal' patients

Bioavailability

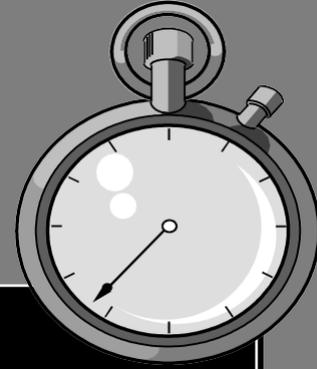
- It is defined as the extent to which active ingredients *are absorbed and transported* to sites of action.
- *Factors*
 1. Drug solubility
 2. Pharmaceutical formulation
 3. pH
 4. Food

Dose regimes

- *Factors determining Dosage :*
 - Half Life
 - Age
 - Sex
 - Body Weight and Surface area
 - Tolerance
 - Specific disease



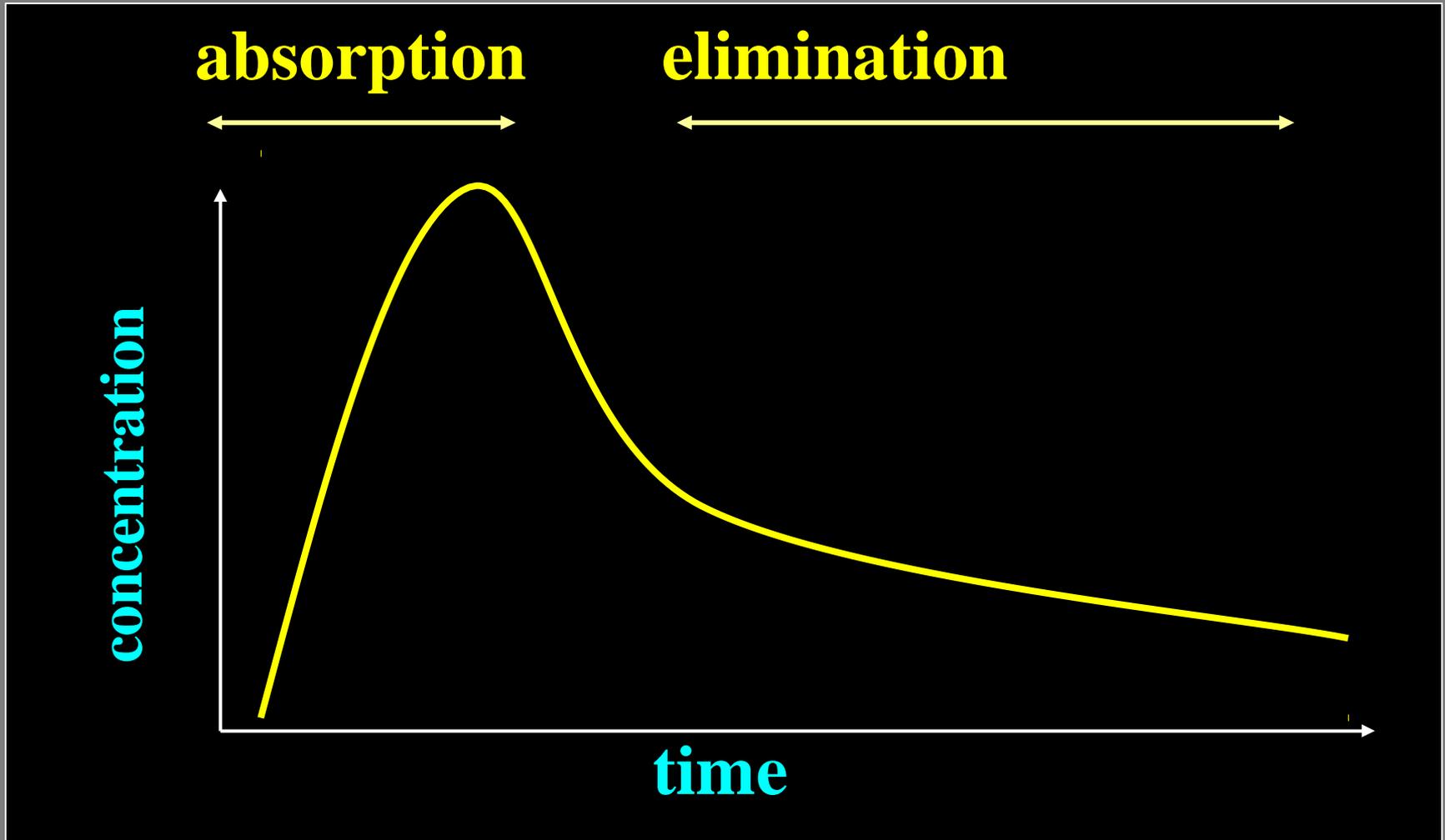
Dose regimes



- **OD** (*mane / nocte*)
- **BD** (*12 hourly*)
- **TDS** (*8 hourly*)
- **QDS** (*6 hourly*)
- **PRN** (*as required*)
- **Depot** (*weekly / monthly / quarterly*)
- **Stat** (*immediately*)

Plasma profiles

- Single dose plasma profile

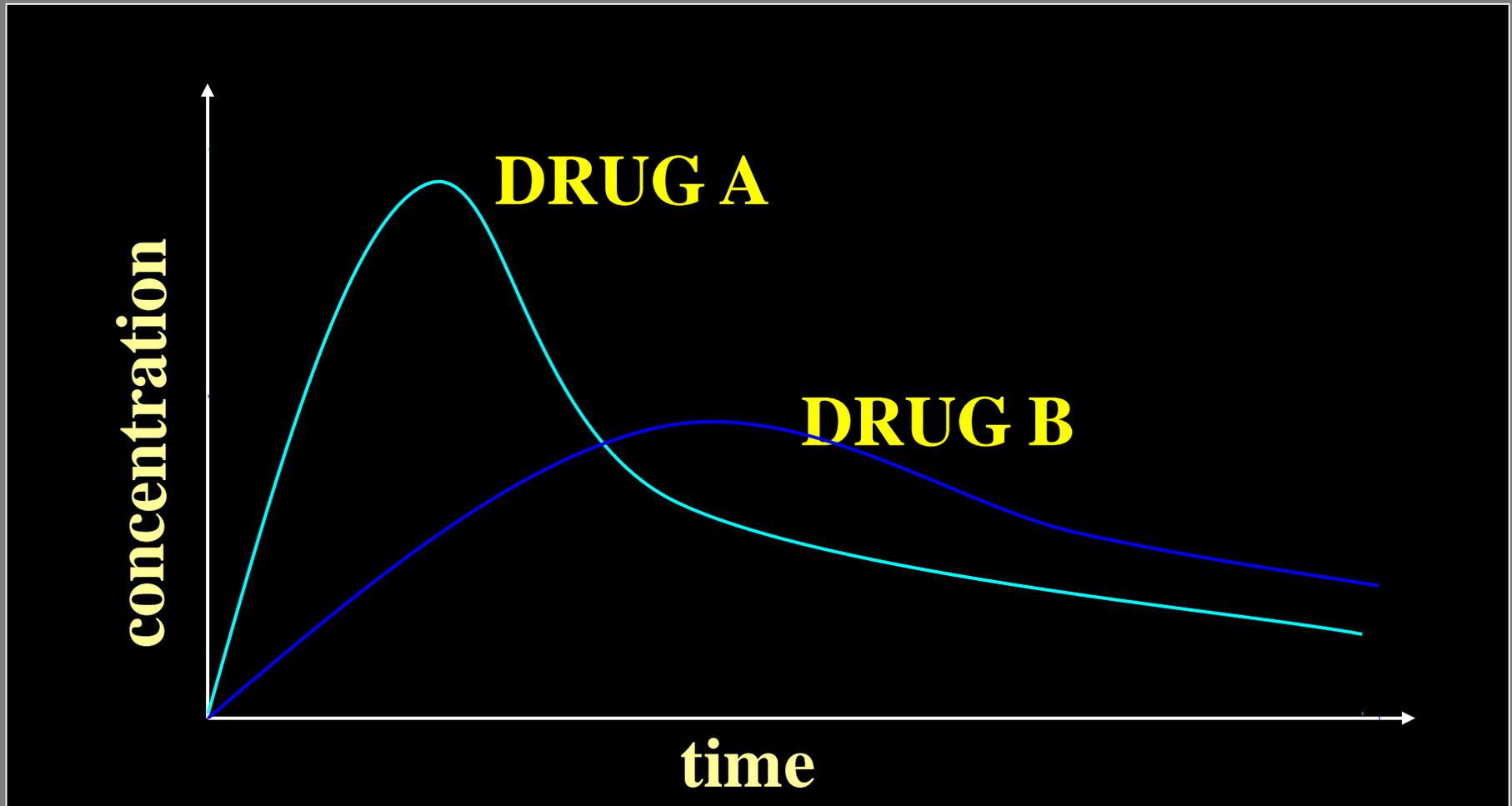


Plasma levels

- **Constant plasma levels only with constant I.V. infusion.**
- **Peaks & troughs in plasma levels with all other routes of administration (due to absorption & elimination)**
- **Dose regimes are calculated to maintain therapeutic plasma levels**

Plasma profiles

Dose plasma profile



Half-life

- Refers to the time required for the body to eliminate 50% of the drug.
 - It is important in planning the *frequency* of dosing.
- Short half-life (2-4 hours) : needs to be given frequently
- Long half life: (21-24 hours): requires less frequent dosing

Note: It takes 5 to 6 half lives to eliminate approximately 98% of a drug from the body

Half-life

- Liver and kidney disease patients may have problems of excreting a drug.
- Difficulty in excreting a drug increases the half-life and increases the risk of toxicity.
- Implication: may require frequent diagnostic tests and measuring renal and hepatic function.

Half Life = 1/2

Time in which a measure (concentration effects) declines by one half

Measured in 3 ways : -

- 1) Plasma half life
- 2) Biological effect half life
- 3) Biological half life

Plasma – Half Life

- # Time in which the plasma concentration falls by one half
- # Influenced by various factor – tissue diffusion, protein binding , renal excretion

Biological effect half life

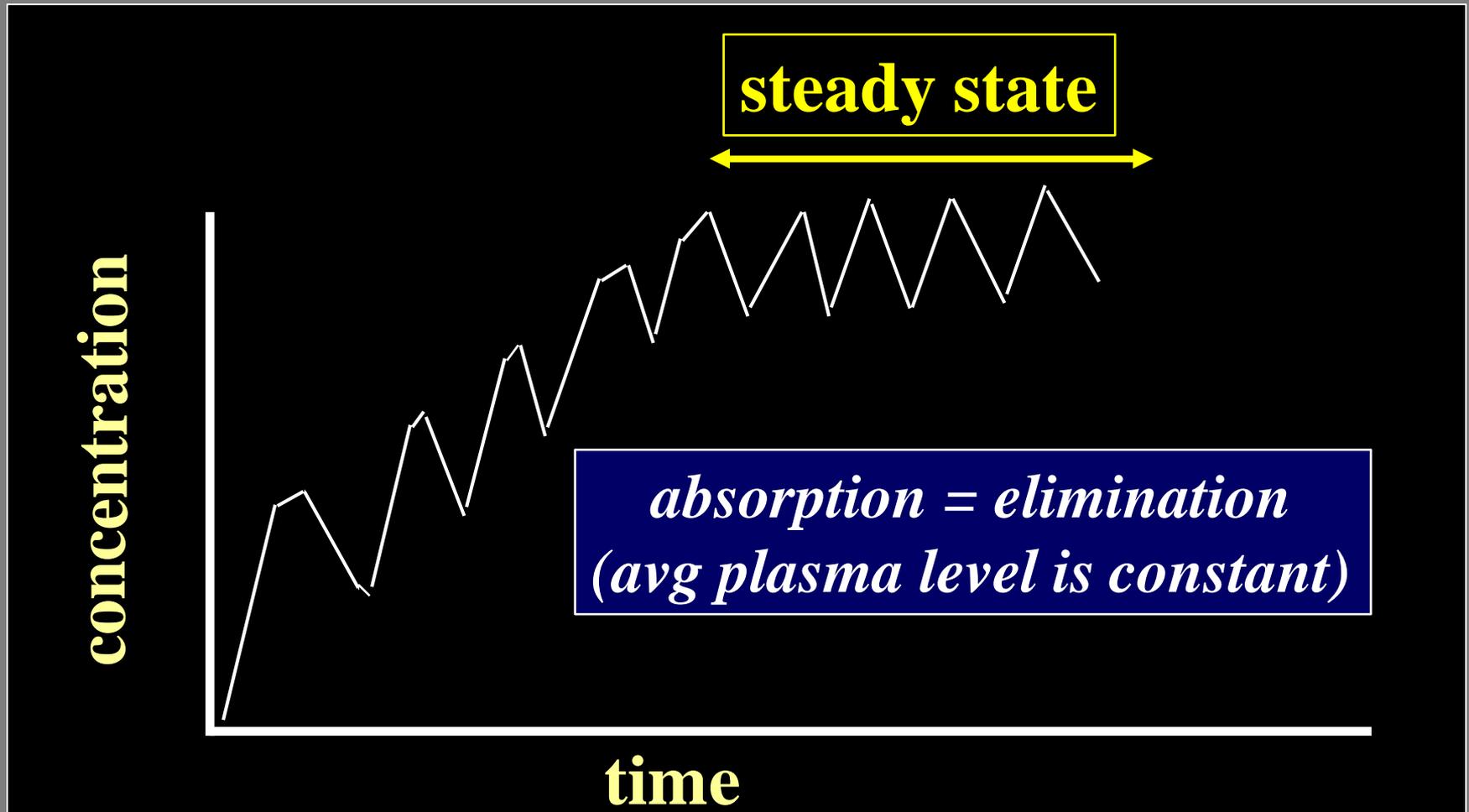
- # Time in which a the pharmacological effect of the drug, and of any of the active metabolites, has declined by one half
- # Eg. For antibiotics, varies with each infection

Biological half life

- # **Time in which a the total amount of drug in the body after equilibrium of plasma with other compartments (fat, muscle) is halved**
- # **Measured using radioisotopes, rates of excretion**

Plasma profiles

Multiple dose plasma profile



Steady state concentration

- # **Plateau concentration**
- # **Rate of input of drug to the body is matched by rate of elimination**
- # **Has to be in therapeutic range to maintain effect**
- # **Affected by half life of drug**

Therapeutic Index/Ratio

- # Devised by Ehrlich
- # Maximum tolerated dose / minimum curative dose
- # Gives indication of safety
- # Especially applicable to antibiotics
- # Defines safety in relation to efficacy

Review: Routes and principles of administration of drugs

Routes of Administration

To be effective a drug must :

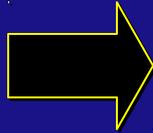
- Be present in an active form**
- At the correct site**
- At the right concentration**
- For the right duration of time**

The formulation of the product for each delivery route is vital to ensure optimal activity and consistent delivery

Thus choose the right Route of Administration and Formulation

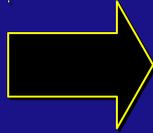
Route of Administration & Formulation (Dosage forms)

Oral



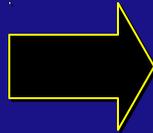
**Tablets / Capsules / Elixirs / Syrups /
Suspensions / Granules / Powders /
Caplets / Drops**

Parenteral



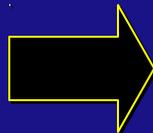
**Intra-dermal / Subcutaneous /
Intra-muscular / Intra-venous /
Intra-thecal / Epidural / Spinal /
Depot**

Sub-lingual / buccal



Tablets / Sprays

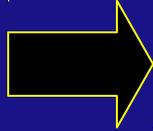
Inhaled



**Aerosol inhalers / Dry powder inhalers /
Nebuliser solutions / Spacers**

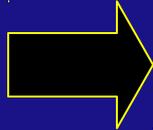
Route of Administration & Formulation (Dosage forms)

Rectal (PR)



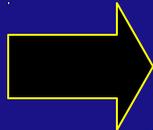
Suppositories / Enemas

Vaginal (PV)



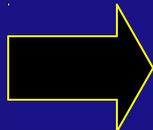
Pessaries / Creams / Vaginal tablets

Transdermal



Creams / Gels / Patches

Topical



**Creams / Lotions / Gels / Nasal sprays /
Shampoos / Suppositories / Peccaries**

Oral Route

- # Absorption hampered by food
- # Drug may be destroyed (insulin)
- # Drug may not be absorbed
(Streptomycin)
- # First pass metabolism

Sublingual route

- # **Abundant blood supply**
- # **Quick effect**
- # **No degradation by digestive juices**
- # **No first pass metabolism**
- # **Irritation of mucous membranes**

Rectal Route

- # Rich blood supply**
- # No irritation of GIT**
- # Useful in patients who cannot swallow/vomiting / uncooperative patient**

Effects of Protein Binding on Drugs

Assists oral absorption of a drug

Delays metabolic degradation

Delays excretion

Diminishes penetration into the CNS

**Significance – acts as reservoir and thereby prolongs
action of drug**

Enteric Coating

Pills or tablets are coated with substances which resist the acid juice of the stomach but permit disintegration in intestinal juices.

- # To prevent gastric irritation & alteration of drug in stomach**
- # To get desired concentration of the drug in small intestine**
- # To retard the absorption of the drug.**

SR Preparations

$$SR = TR = XL$$

**Sustained release or time release preparations
for oral use**

- # Release the active drug over an extended period of time.**
- # Particles of drug covered with coatings which dissolve at different time intervals.**

Basic pharmacology - Agenda

#Classification of Drugs

#Routes of administration & drug formulations

#A.D.M.E.

#Dose regimes & plasma levels

#Package insert information

#Scheduling of drugs

#Pharmacodynamics

#Drug uses & ADR

#Clinical pharmacology



Storage and Maintenance of Drugs

Introduction

- The Drugs which are supplied to ward are stored in drug cupboards to provide a uniform supply of drugs to the patients.
- The drugs are stocked in containers, such as boxes and on flexible racks and shelves etc.
- It must be ensure that drugs which are stored remain preserved during their storage.
- There should not be any damage due to high temperature or exposure to sunlight.
- The drugs are to be stored as per the prescribed conditions of their storage.

Introduction - contd

- The drugs stored in a drug store be arranged in such a way that they are easily traceable as and when required.

1. According to pharmacological action
2. Alphabetically

Drug Storage

1. Proper drug storage
2. Storage Environment
3. Arrangement of drugs on shelves
4. The storeroom
5. The dispensary



1. Proper drug storage

Drugs are stored in a specially designed secure area or space of a building in order to:

- Avoid contamination or deterioration,
- Avoid disfiguration of labels,
- Maintain integrity of packaging and so guarantee quality and potency of drugs during shelf life,
- Prevent or reduce pilferage, theft or losses,
- Prevent infestation of pests and vermin.

- The storage should not hinder the cleaning and should have sufficient space for movement of stocks and handling.
- Products are to be stored in a manner that prevents damage due to excessive vertical stacking heights and not to exceed eight stacks.
- Store the products as per product storage condition (As per label) to prevent deterioration of finished product on storage.
- Monitor and record the temperature of storage area on daily basis.

2. Storage Environment

The storage environment should possess the following:

- Adequate temperature,
- Sufficient lighting,
- Clean conditions,
- Humidity control,
- Cold storage facilities,
- Adequate shelving to ensure integrity of the stored drugs.

Storage and Maintenance

- Drugs to be stored under condition that prevent contamination & as far as possible, deterioration.
- **“Well closed container”** precautions to be taken in relation to the effects of the atmosphere, moisture, heat & light.
- **“Protected from moisture”** means that the product is to be “stored in air tight container”

Protected from light

- **“Protected from light”** the product is to be stored either in a container made of material that absorbs actinic light sufficiently to protect the contents from change induced by such light.

Temperature

- In a deep freeze (-15°C)
- In a refrigerator 2°C -8°C
- Cold or cool 8°C-15°C
- Room temperature 15°C-25°C

Storage Premises

- The Storage area must be free from unsanitary conditions(Ex Rodents, insects, Birds, litter etc).
- The floor of the warehouse should be made of hard floor (Concrete /Kota/Epoxy) and must be in a good state of repair and appearance at all times.
- The floors are kept clean and free of trash, dirt, sippage water, drain water etc.
- The area must be kept clean and free of refuse.

Storage Premises

- The area used for storage of IV fluids should have adequate space and to prevent exposure to direct sunlight.
- Secured area availability for damaged, rejected and expired goods.
- Ensure adequate pest control program in place and shall be carried out at a minimum frequency of a year.
- The Pest control shall cover treatment for Termite and Rodents.

3. Arrangement of drugs on shelves

- Shelves should be made of steel or treated wood.
- Shelves should be strong.
- Drugs are arranged in alphabetical order of generic names.
- Each dosage form of drug is arranged in separate and distinct areas.
- Sufficient empty space should demarcate one drug or dosage form from another.

- Most recently received drugs are placed behind old stock on the shelf except where new drugs have shorter expiration dates.
- Always put lids properly on tins always and at the close of the day.

- Put drugs in a dry place protected from light and heat.
- Store liquids on a pallet on the floor or on the lowest shelf.
- The store must be cleaned daily and mopped at least once a week.

4. The store-room

- A well-arranged store enables easy identification of drugs and saves time when picking a drug from the shelves.
- This helps remove drugs quickly and makes for easy inventory control.

- The rule of **FIRST IN FIRST OUT (FIFO)** should be applied always.
- So, drugs that were received first should be used first, except where the new stock has shorter expiration dates than the old stock.
- In this regard, the principle of **FIRST TO EXPIRE FIRST OUT (FEFO)** should apply.
- To have access to drugs with shorter expiration dates first, put these in front of the shelves.
- Those with longer expiration dates should be placed behind those with shorter dates.

5. The dispensary

- Clean after each use tablet counters and place within easy reach on the table.
- Avoid dispensing wrong drugs by arranging drugs on the table in alphabetical order so that the drug being dispensed is not confused with another.
- Always close drug containers from which drugs are not being dispensed to prevent spillage or dispensing the wrong drug.

Drug expiry

- **Shelf life**- the time where a given product stored under reasonable condition, is expected to remain stable (>90% potency)
- **Essential drugs**- drugs that satisfy the health care needs of the majority of the population.
- Essential drugs should there fore available at all times in adequate amounts & in appropriate dosage forms.

Expiry dates

- Medications must not be administered, and products and equipment must not be used beyond their expiry dates.
- All medical equipment, dressings and solutions used during invasive procedures must be sterile.
- Single-use devices are meant for single use only and must not be re-used.

Storage, Maintenance & Security

- All drugs, including samples, should be maintained separate from non-medications in a locked cabinet which is sufficiently secure to deny access to unauthorized persons.
- Key should be available only to authorized personnel who are assigned medication-related responsibilities.
- Store medications that are “for external use only” separate from medications intended for internal use.

Storage, Maintenance & Security

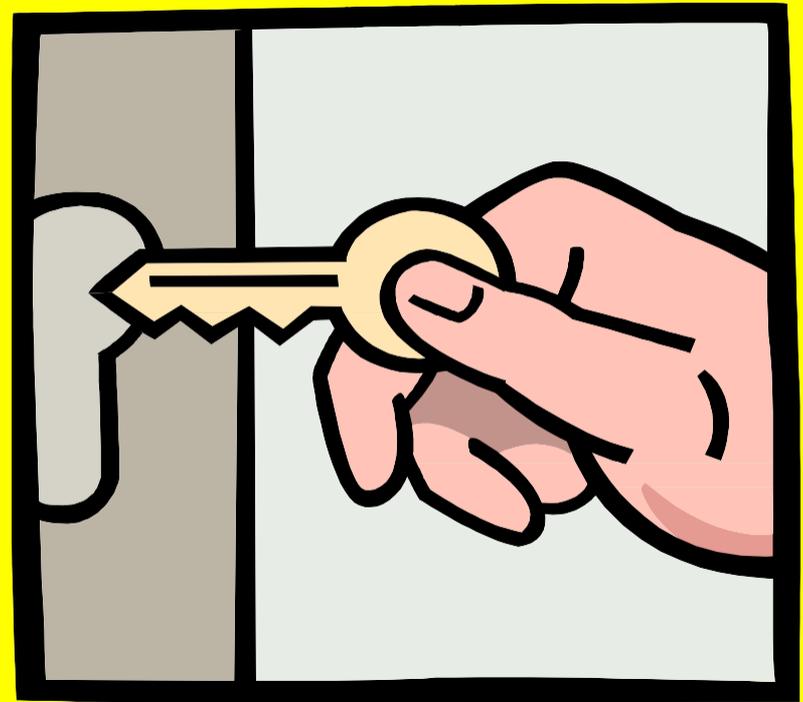
- Store look-alike and sound-alike drugs separately.
- Maintain temperature between 59 degree and 86 degrees Fahrenheit for non-refrigerated medications.
- Where refrigeration is necessary use a “Medications Only” refrigerator and maintain temperature between 36 degrees and 46 degrees Fahrenheit.

Storage, Maintenance & Security

- On daily basis check, verify and document the proper temperature.
- All multiple-dose injectable medications should be initialed and have the date of first entry recorded on the label.
- Rotate medication stock monthly employing a “FIFO” (first in/first out) process.

Controlled Drug Regulations

- Double Locked Container



Controlled Drug Regulations

- 2 licensed personnel count (or verify any discrepancies) every shift (8 hours)
- Witness to all discards
- Record on Control Substance Sheet all administrations and wastes.



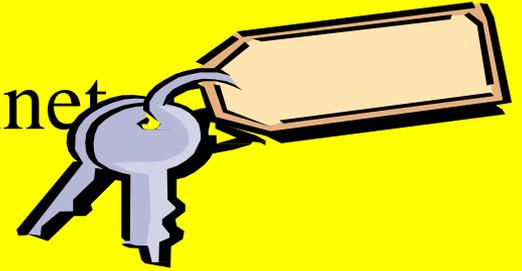
Controlled Drugs

All details must be completed in the Doctors own handwriting, like:

- Name of drug
- Dose of drug
- Number of doses or length of course
- Signature of prescribing doctor and date

Storage of Controlled Drugs

- They must be kept in a locked cabinet or cupboard
- The keys to the cabinet must be in the possession of an authorised person
- Authorised person, refers to Ward Manager or deputy who must be a Trained Nurse or Midwife
- Students should not be responsible for the controlled drug cupboard keys



Recording of Controlled Drug Use

- Records in the form of **CONTROLLED DRUG REGISTERS** must be kept
- Each drug must have its own specified page which is Headed with the Drugs name and Strength
- The Number of Ampoules of a drug must be entered and updated with every use.

Recording of Controlled Drug Use

- Must record:

- Date
- Time
- Dose of every administration
- Name of receiving patient/client
- Number of ampoules at start and finish of administration

Entry must be signed by 2 people **one of who must be registered**

No alterations must be made to the entry

All entries must be in **Black Ink**

Rational use of drugs & Calculation of drug dosage

Rational use of drugs

- Any drug is made with help of combination or mixture of the chemicals which some times harm to the other parts of body.
- Rational use: Eg. Patient is having hypertension then the goal is to reduce blood pressure to the normal level in order to prevent prolonged hypertension, thus creating complication.
- Once identifying the person suffering from specific disease, the physician or nurse should find out other factors contribution the ill effect of the prescribed drug.

- Any drug required good renal or hepatic system to pass drug and to be drain out or metabolize in the body.
- The choice of drug has to be make wisely by the physician or nurse to avoid side effects, drug interaction, contraindication.
- Nurse should follow the 6 Rights of drug administration to avoid wrong administration of drug.
- Use of combination drug can be one option in treatment, eg. Ibufen (Brufen+Paracetamol)

Conclusion

- Rational use of drugs requires that the patients receiving medications appropriate to their clinical needs, in does that meet their own requirement of an adequate period for time and at lowest cost to them and their community.

Drug Calculations

Pharmacotherapeutics: Principles of therapeutics

Drug –
WHO scientific group definition

**Any substance or product that is used/
intended to be used to modify or
explore physiological systems or
pathological systems or pathological
states for the benefit of the recipient**

Pharmacology

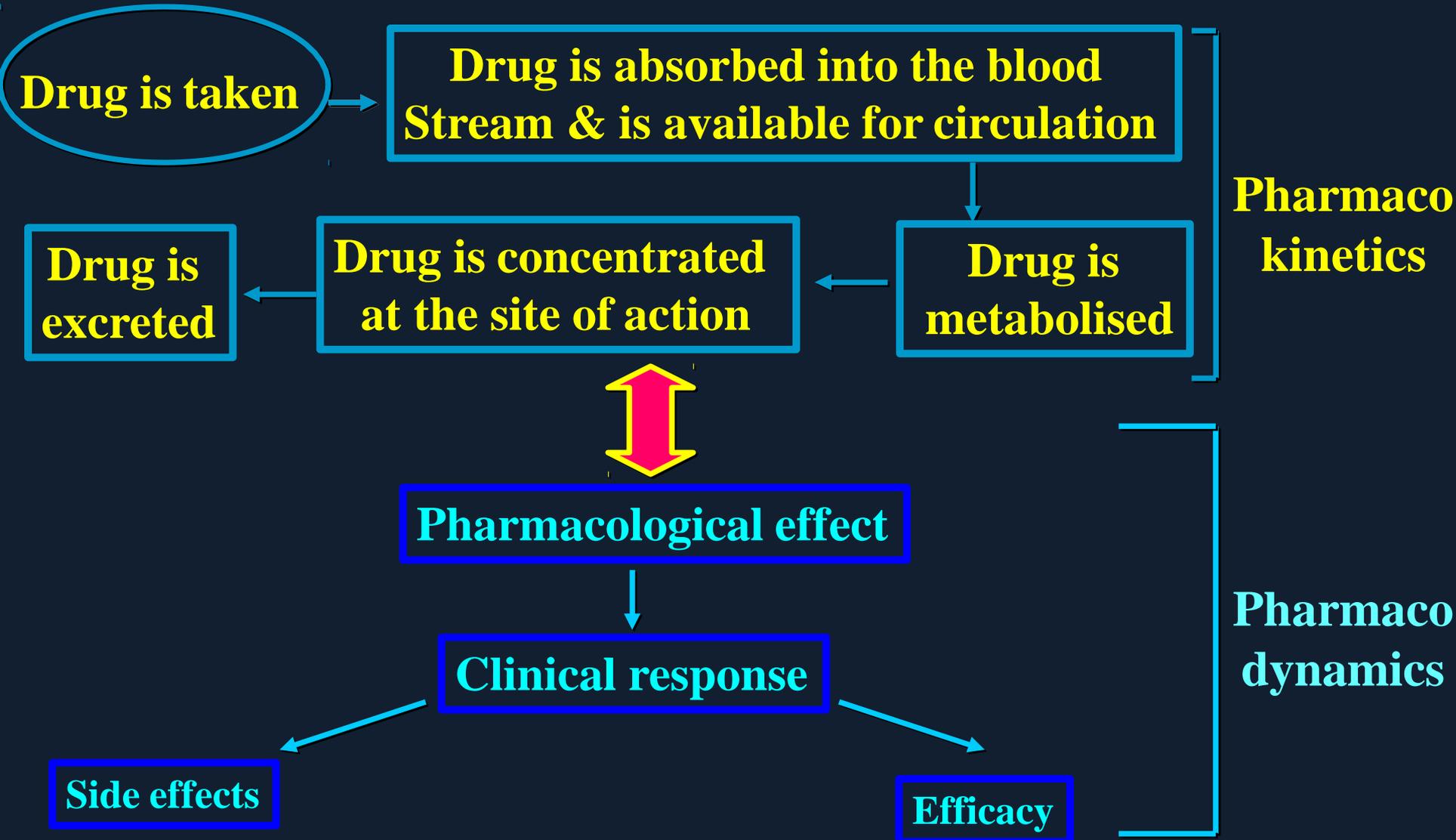
Pharmacodynamics

- **Biological and therapeutic effects of drugs**

pharmacokinetics

- **Absorption, Distribution, Metabolism & Excretion of drugs**

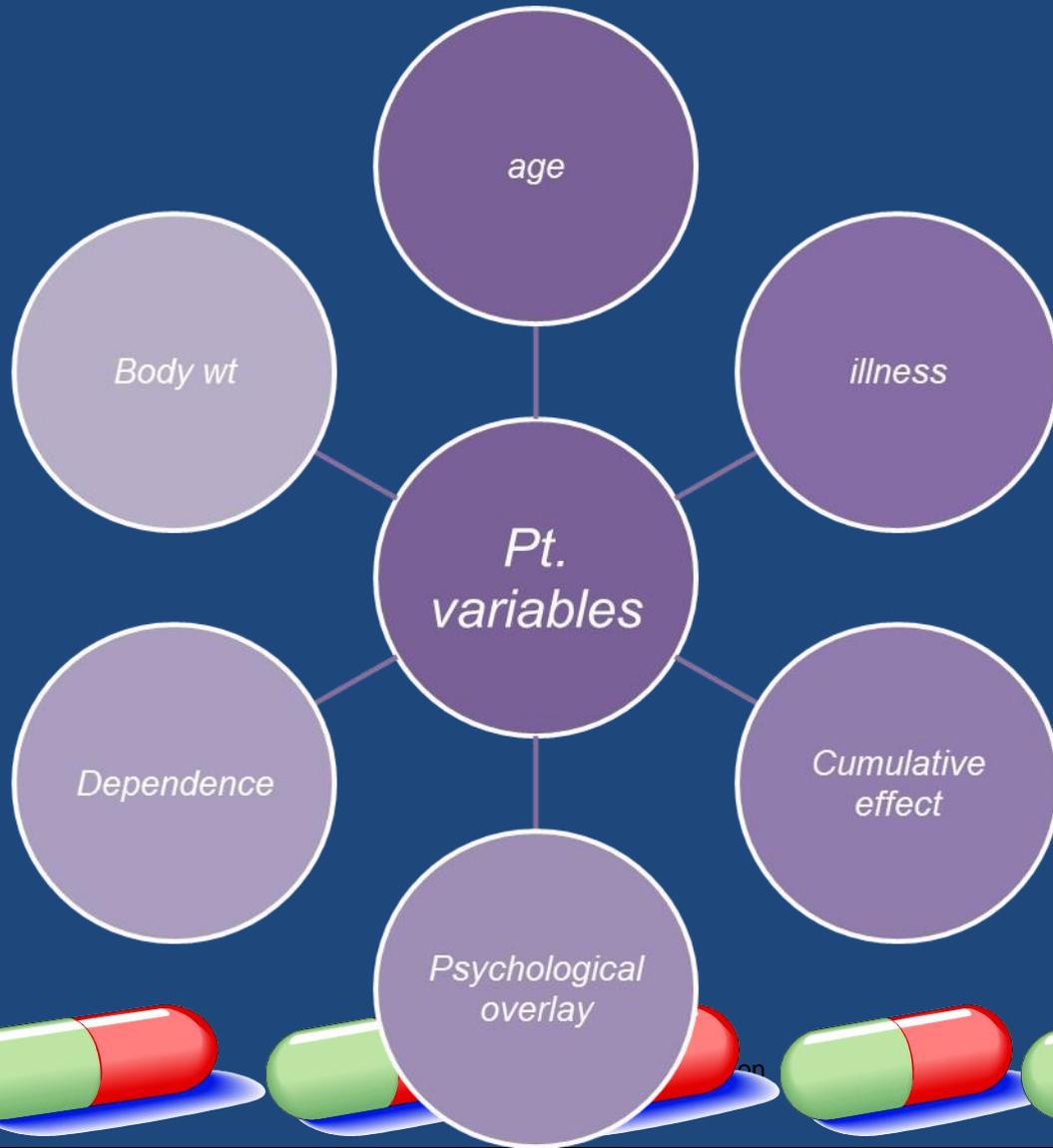
The Relationship between Pharmacokinetic and Pharmacodynamic processes



Drug – and – patient related factors.

- Drug and patient related factors determined the selection of routes for drug administration. These are:
- Characteristics of the drug.
- Emergency/ Routine use.
- Condition of the patient (Unconscious, Vomiting and Diarrhoea)
- Age of patient.
- Associated disease.
- Patients/ Doctors choice (Sometimes)

Patient Variables that may affect Drug Action



Pharmacokinetics

Absorption

Distribution

Metabolism

Excretion

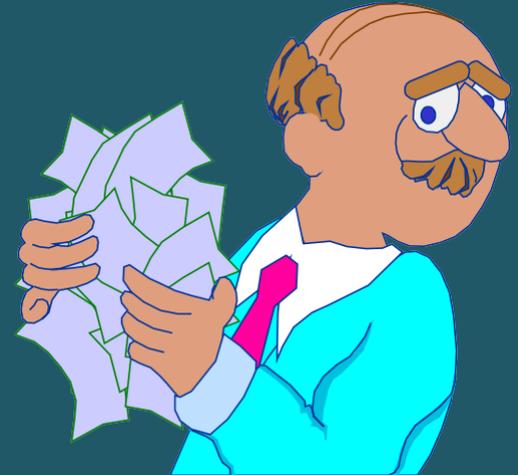
Basic pharmacology - Agenda

- **Definitions**
- **Classification of Drugs**
- **Routes of administration & drug formulations**
- **Dose regimes & plasma levels**
- **Package insert information**
- **Scheduling of drugs**
- **Pharmacodynamics**



Package insert information (Literature)

- **Composition (drug/dose per tablet)**
- **Schedule**
- **Pharmacological classification**
- **Pharmacological action**
- **Indications**
- **Contra-indications**
- **Dosage & directions for use**
- **Side effects & special precautions**
- **Known symptoms of overdose & particulars of its treatment**
- **Identification (physical description of tablet)**
- **Presentation (package details)**
- **Storage instructions**
- **Registration number**
- **Name of applicant**



Pharmacodynamics: Mechanisms of Action

The ways by which drugs can produce therapeutic effects:

- Once the drug is at the site of action, it can modify the rate (increase or decrease) at which the cells or tissues function.
- A drug cannot make a cell or tissue perform a function it was not designed to perform.

Pharmacodynamics

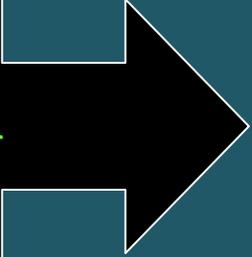
- **The effect the drug has on the body**
- **Based on either:**
 - **Non-specific action**
 - **Binding with a receptor**
 - **Enzyme interaction**

Pharmacodynamics

- # Non-specific action depends on the drug's accumulation in cell membranes**
- # Specific actions result from the drug becoming affixed to the receptor i.e. binding to receptors**
- # Drugs can only increase or decrease cell function - they cannot totally alter the action of the specific cell**

Mechanism of Action

**Mechanism
of action**



Cell membrane

**Metabolic processes
Within the cells**

Outside the cell

Cell Membrane

Specific receptors-agonists and antagonists on adrenoceptors

Interference with selective passage of ions across membranes eg: Calcium channel blockers

Outside the cell

- # Direct chemical interaction eg: chelating agents, antacids**
- # Osmosis with diuretics like mannitol**

Receptor

Protein macromolecules

Agonist to receptor  proteins

alter 

cell 

Agonists : activate receptors

Antagonists : blockers of receptors

Additive Effect

$$1 + 1 = 2$$

**When the total pharmacological action of
Two or more drugs administered together
Is equivalent to the summation of their
Individual pharmacological actions
Eg: ephedrine + aminophylline in treatment
of bronchial asthma**

Synergistic effect

$$1 + 1 = X (>2)$$

**When the total pharmacological action of
Two or more drugs administered together
Is more than the summation of their
individual pharmacological actions**

**Eg: cotrimoxazole(sulphamthoxazole
+pyrimethamine) Septran**

Terminology

Bioavailability

- *the extent of the drug which is delivered to the circulation (expressed as %)*

Bioequivalence

- *the rate and extent of absorption of two products is equivalent - 'no significant difference'*

Drug uses



- # **Curative, as primary therapy (bacterial / parasitic infections), or auxiliary therapy (anaesthetics, ergometrine and oxytocin in obstetrics)**
- # **Suppressive of disease/symptoms, used continually or intermittently to maintain health with out attaining cure as in hypertension, diabetes, epilepsy, asthma/ to control symptoms such as pain and cough, while awaiting recovery from cause**
- # **Preventive (prophylactic), as when a non-immune person enters a malarial area or contraception**

Using more than one drug simultaneously



Possible responses:

- The drugs have no effect on each other
- Antagonism - the combination results in a lower response than when either is given on its own
- Potentiation - the response rate of the two drugs when combined is more than the sum of their independent response rates
- Synergy - the combination offers greater effect than the sum of the two products given individually I.e. $1+1=3$ or more
- Globally there is a move away from polypharmacy

Adverse Drug Reaction (ADR)



An adverse reaction is a harmful or seriously unpleasant effect caused by a drug at doses intended for therapeutic effect/prophylaxis/diagnosis which warrants reduction of dose/withdrawal of the drug and/or foretells hazard from future administration

Degrees of certainty of (ADR)



Definite : time from taking drug is reasonable event corresponds to what is known of drug event ceases on stopping drug even returns on restarting drug

Probable: time sequence reasonable corresponds to what is known of drug ceases on stopping drug not reasonably explained by patient's disease

Degrees of certainty of (ADR)



Possible : time sequence reasonable
corresponds to what is known of
drug could be due to disease / other
therapy

Conditional : time sequence reasonable
corresponds not to what is known of
drug cannot be explained by patients
disease

Doubtful : event not meeting above criteria



Anaphylaxis

Systemic reaction in a sensitized human subject following repeat injection of a drug like penicillin characterized by laryngeal edema, severe bronchospasm leading to asphyxia, or circulatory collapse.

Eg: Penicillin

Placebo



Latin – “I will please”

Placebo are used for two purposes :

- As a control in scientific evaluation of drugs**
- To benefit or please a patient not by any pharmacological actions, but by psychological means**



Therapeutic evaluations

Whether a drug is of value and how it may

Best be used :

- a) formal therapeutic trials**
- b) surveillance studies for both efficacy and adverse effects**