PHARMACOLOGY

AN INTRODUCTION

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Contents

What is Pharmacology ?

- From the Greek Pharmacon (Drug) and Logos (a discourse or treatise).
- It is defined as how chemical agents affect living processes i.e., Hormones, neurotransmitter, growth factors, drugs (pharmaceuticals), toxic agents in the environment.
- The medicinal/organic chemists may create the candidate compound (sometimes referred to as a new chemical entity), it is the pharmacologist who is

What is Drug ?

- A single active chemical entity present in a medicine that is used for diagnosis, prevention and treatment of diseases.
- WHO- in 1966 – " Drug is any substance or product which is used or intended to be used to modify or explore physiological systems or

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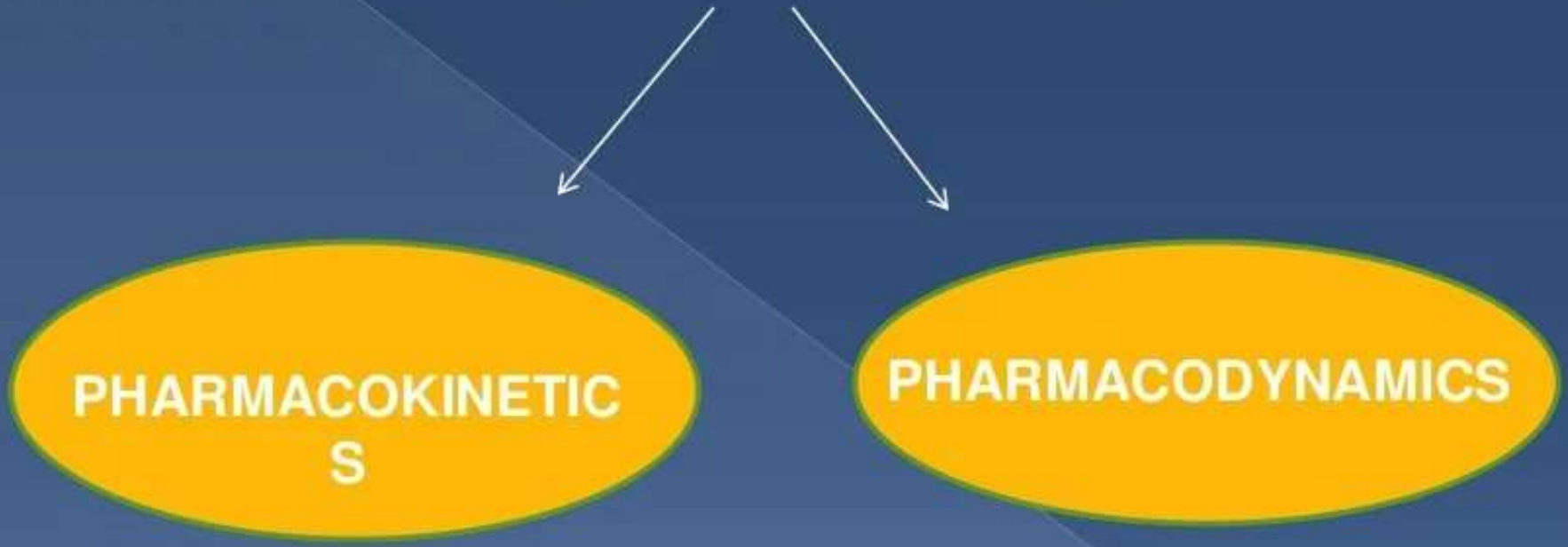
- Pharmacology studies the effect of drugs and how they exert their effects:
- Paracetamol can reduce body temperature in case of fever by inhibiting an enzyme known as cyclooxygenase in in CNS, which is responsible for the synthesis of a number of inflammatory mediators

Branches of Pharmacology

Two main branches



Branches related to Pharmacology

- Pharmacotherapeutics: Use of drugs for prevention and cure of diseases (clinical management of diseases).
- Pharmacoepidemiology: Study of effect of drugs on population.
- Pharmacoeconomics: Study of cost

- **Toxicology:** Science of poison which includes detection and measurement of poisons as well as treatment of poisoning.
- **Pharmacopoeia:** It is 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.

Sources of Drugs

- Plant Sources: Morphine, digoxin, quinine, atropine, paclitaxel, reserpine, vinca alkaloids.
- Animal Sources: Insulin, thyroid extract, heparin, gonadotrophins and sera.
- Minerals: Liquid paraffin, magnesium sulfate, magnesium trisilicate, ferrous sulphate and kaolin.
- Microorganism: Penicillin, Streptomycin.
- Synthetic: Analgesics, hypnotics, anticancer drugs, antimicrobials.

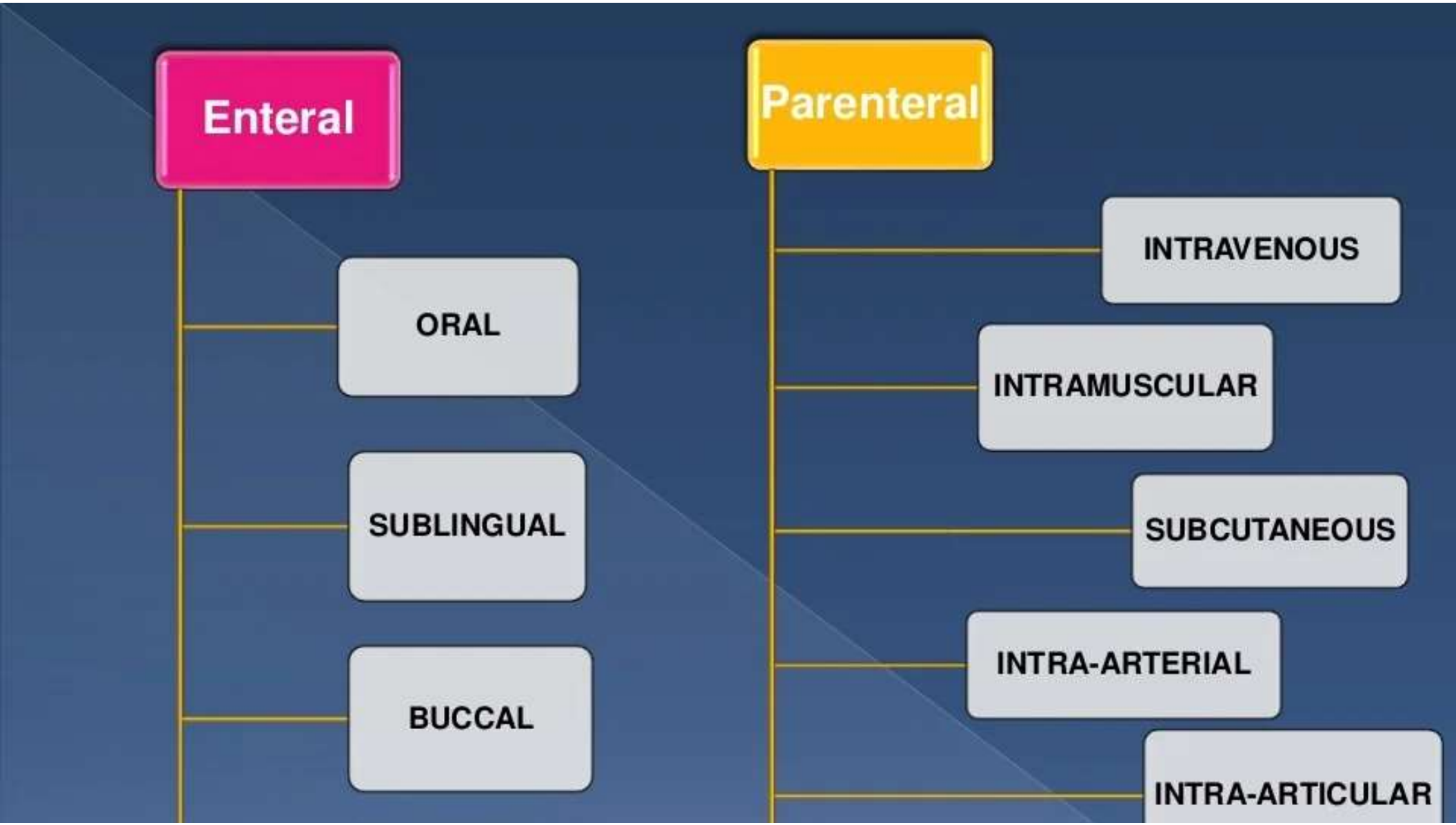
Essential Medicines

WHO - “Essential medicines are those that satisfy the priority healthcare needs of the population. Essential medicines are intended to be available within the context of the functioning health systems at all times and in adequate amounts, in appropriate dosage forms, with assured quality and adequate

Orphan Drugs

These are the drugs or the biological products for diagnosis, prevention and treatment of a rare disease or a more common disease for which there is no reasonable expectation that the cost of developing and marketing will be recovered

Routes of Drug Administration


Enteral
ORAL
SUBLINGUAL
BUCCAL
Parenteral
INTRAVENOUS
INTRAMUSCULAR
SUBCUTANEOUS
INTRA-ARTERIAL
INTRA-ARTICULAR

ORAL ROUTE

- Oral refers to two method of administration:
  - applying topically to the mouth
  - swallowing for absorption along the gastrointestinal (GI) tract into systemic circulation
- po (Latin term "*per os*") is the abbreviation used to indicate oral route of medication administration
- Common dosage forms for oral administration are:

Advantages

- Convenient - can be self- administered, pain free, easy to take
- Absorption - takes place along the whole length of the GI tract
- Cheap- compared to

Disadvantages

- Destruction of drugs by gastric acid and digestive juices
- Effect too slow for emergencies
- Unpleasant taste of some drugs
- Unable to use in

First Pass Effect

- The first-pass effect is the term used for the hepatic metabolism of a pharmacological agent when it is absorbed from the gut and delivered to the liver via the portal circulation. The greater the first-pass effect, the less the agent will reach the systemic circulation (in case of drug administered orally)

SUBLINGUAL ROUTE

Sublingual administration is where the dosage form is placed under the tongue and is rapidly absorbed by sublingual mucosa.

BUCCAL ROUTE

- Buccal administration is where the dosage form is placed between gums and inner lining of the cheeks and is absorbed by buccal mucosa

Advantages	Disadvantages
• Avoid first pass effect	• Inconvenience

RECTAL ROUTE

Advantages

- Used in children
- Little or no first pass effect
- Higher concentration

Disadvantages

- Inconvenient
- Absorption is slow and erratic
- Irritation and inflammation of

Systemic - Parenteral

- Parenteral administration is injection or infusion by means of a needle or catheter inserted into the body.
- The term parenterals comes from a greek word para (meaning outside) and enteral (meaning the intestine).
- This route of administration bypasses the

INTRAVENOUS

ADVANTAGES

- Bioavailability 100%
- Desired blood concentration achieved
- Large quantities
- Vomitting & diarrhoea
- Emergency situation

DISADVANTAGES

- Irritation & cellulities
- Thrombophelebitis
- Repeated injections not always feasible.
- Less safe
- Techinical assistance required

INTRAMUSCULAR

ADVANTAGES

- Absorption resonably uniform
- Rapid onset of action
- Mild irritants can be given

DISADVANTAGES

- Only upto 10ml drug given
- Local pain and abcess
- Expensive
- Infection

SUBCUTANEOUS

- Injected under the skin.
- Absorption is slow, so action is prolonged.

IMPLANT: A tablet or porous capsule is inserted into the loose tissues by incision of the skin, which is then stitched up.

INTRA - ARTERIAL

- Rarely used
- Anticancers drugs are given for localised effect.
- Drugs used for diagnosis of peripheral vascular diseases.

INTRA - ARTICULAR

- Injections of antibiotics and corticosteroids are administered in inflammed joined cavities by experts.

  Example: Hydrocortisone in rheumatoid arthritis.

INTRADERMAL

- Drug is given within skin layers (dermis).
- Painful
- Mainly used for testing sensitivity to drugs.

Example: Penicillin, ATS (Anti tetanus serum).

Topical Route of Administration

- Topical administration is the application of a drug directly to the surface of the skin.
- Includes administration of drugs to any mucous membrane.
- Dose forms of topical administration include: cream, ointment, lotion, gels, transdermal

Advantage & Disadvantages of topical route.

- Local therapeutic effects.
- Not well absorbed into the deep layers of the skin or mucous membrane.
- Low risk of side effects.
- Transdermal route offers steady level of drug in the system

TRANSDERMAL

- Absorption of drug through the skin (systemic action)
- Stable blood levels
- No first pass metabolism
- Drug must be potent or patch becomes too large.

Selection of Route

- The route of administration is determined by:
- The physical characteristics of the drug.
- The speed which the drug is absorbed and/or released.
- The need to bypass hepatic metabolism.
- To achieve high concentration at particular sites.

Ligands and its Types

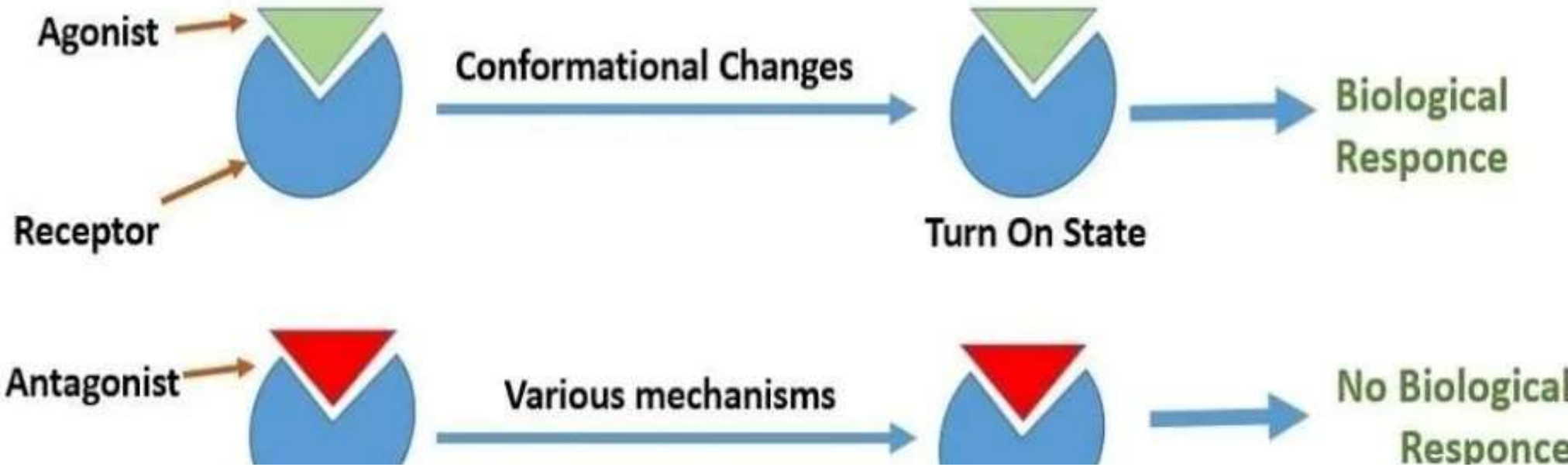
- Ligand is usually a molecule which produces a signal by binding to its specific receptor.
- Ligands are classified by effect upon binding to the receptor.

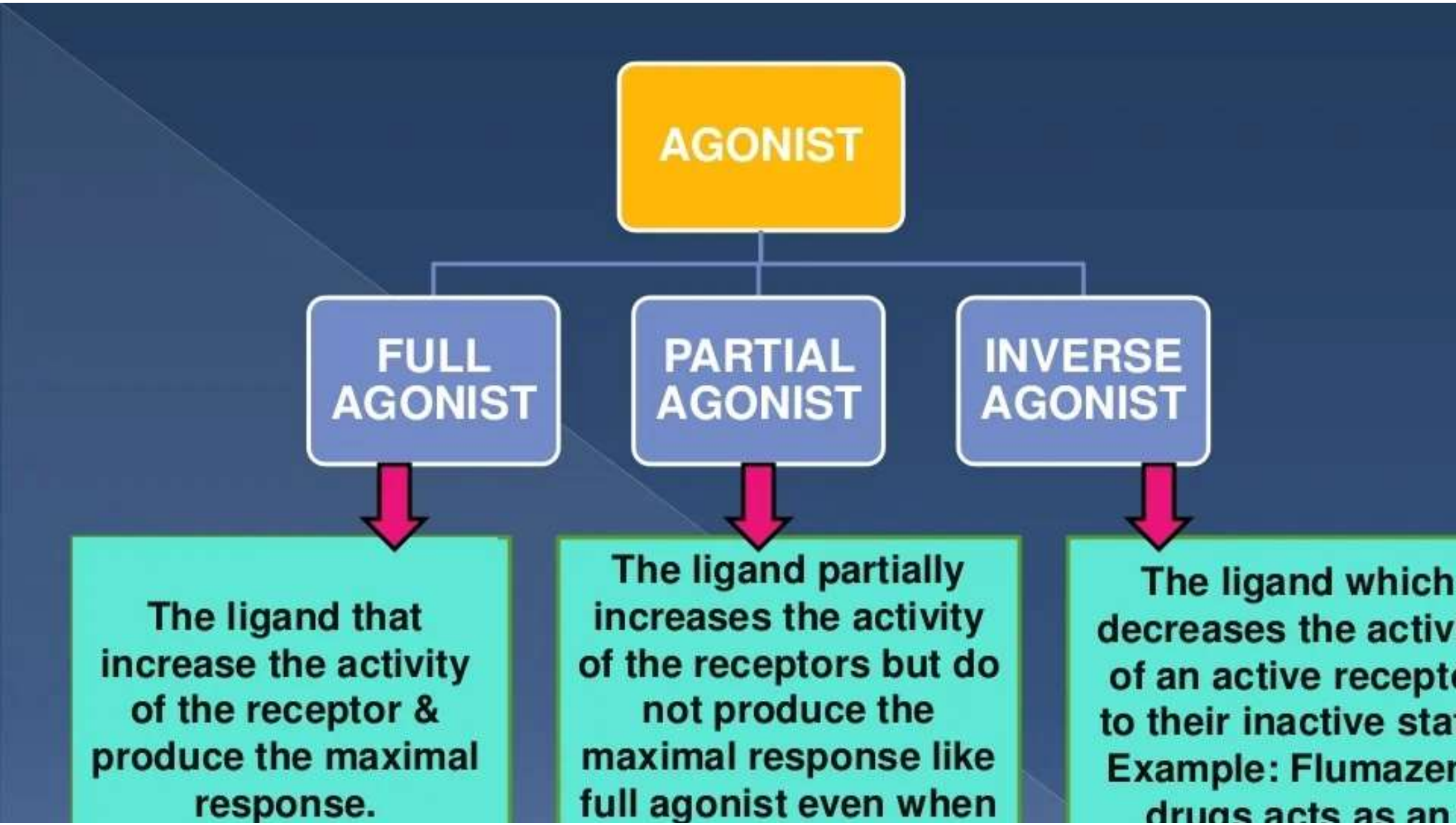
Agonist and Antagonist

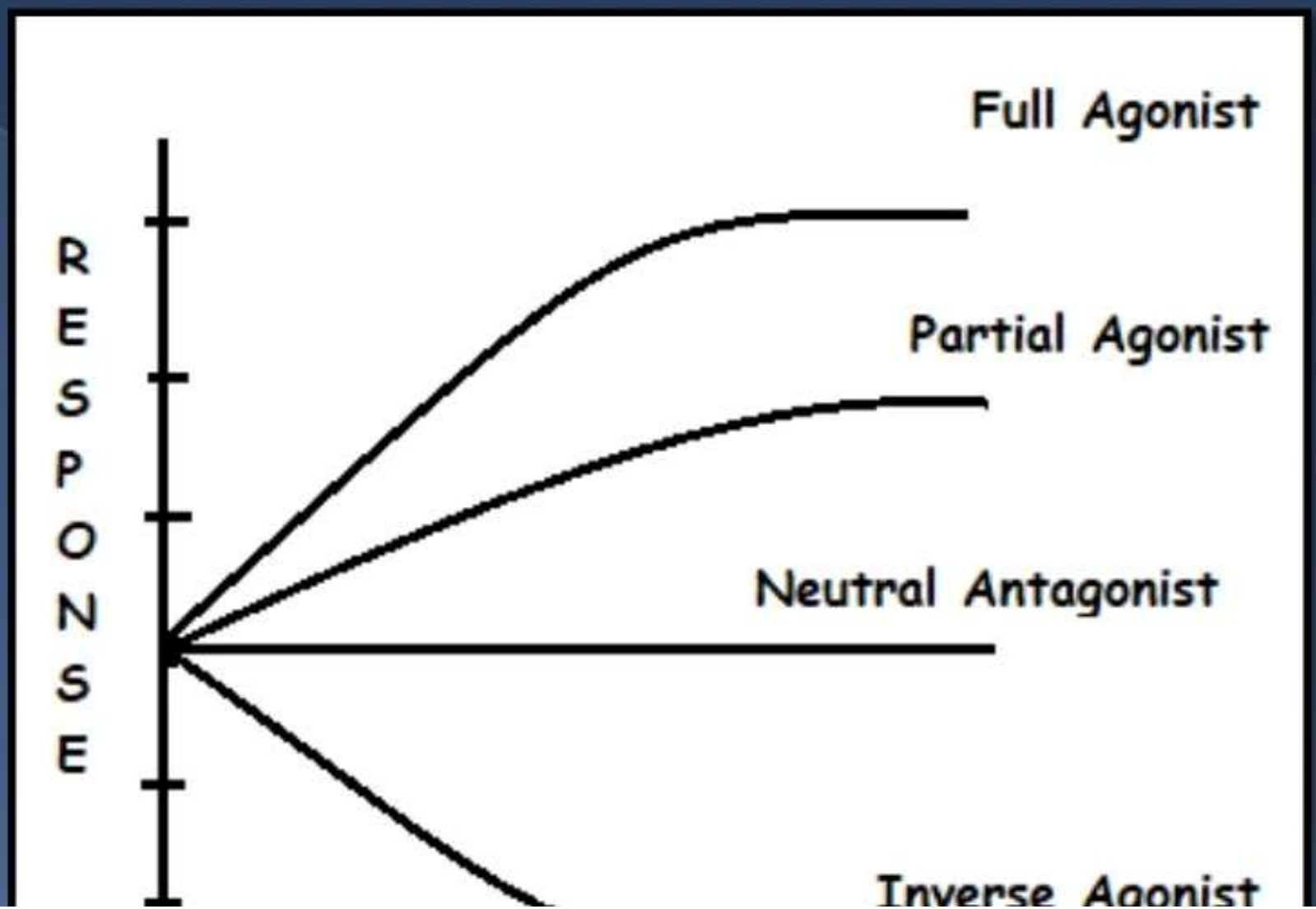
Agonist: Drugs that occupy receptors and activate them.

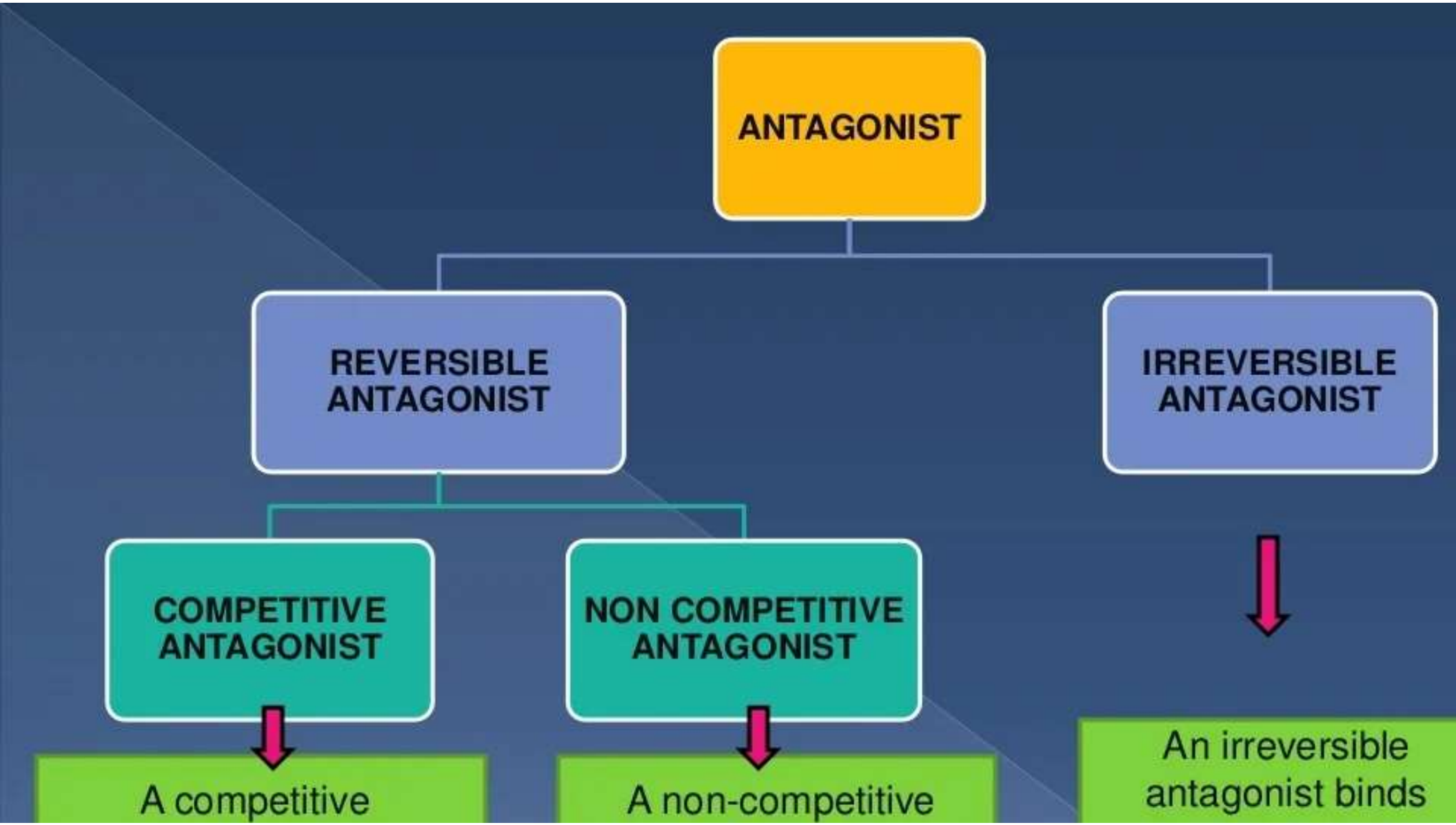
Antagonist: Drugs that occupy receptor but do not activate them. also block receptor activation by agonist.

Agonist and Antagonist




AGONIST
FULL AGONIST
PARTIAL AGONIST
INVERSE AGONIST
The ligand that increase the activity of the receptor & produce the maximal response.
The ligand partially increases the activity of the receptors but do not produce the maximal response like full agonist even when
The ligand which decreases the activ of an active recept to their inactive sta Example: Flumazen drugs acts as an


Full Agonist
Partial Agonist
Neutral Antagonist
Inverse Agonist
RESPONSE


ANTAGONIST
REVERSIBLE ANTAGONIST
IRREVERSIBLE ANTAGONIST
COMPETITIVE ANTAGONIST
NON COMPETITIVE ANTAGONIST
A competitive
A non-competitive
An irreversible antagonist binds

Factors Modifying Drug Response (Action)

- Responses variation to a Drug — (1)person to person; and (2) also same person on different occasions
- Individuals differ in pharmacokinetic handling of drugs —varying plasma/target site cone. — Metabolized drug Vs excreted unchanged drugs — Propranolol and Atenolol
- Variation in number or state of receptors, coupling proteins or other components of response effectuation. Variations in hormonal/neurogenic tone or concentrations —atropine, propranolol, captopril. Categories of factors: Genetic and Non genetic including environmental, circumstantial and personal variables.

1. Body Size

- The Conc. of the drug attained at the site of action- obese/lean/children – Body Weight (BW) and Body Surface Area (BSA).
- Individual dose = BW(kg)/70 X average adult dose
- Individual dose = BSA(m^2)/70 X average adult dose

2. Age

- Young's Formula

3. Sex

- Females have smaller body size - required doses are lower.
- Digoxin in Maintenance therapy of heart failure - mortality higher.
- Beta blockers, methyldopa, diuretics - sexual function disturbances in male.

4. Species and Race

- Species variation in drugs responses do exists.
- Some strains of rabbits – resistant to atropine.
- Rat and mice are resistant to digitalis.
- Race – Racial differences have been observed.
- Black require higher doses of atropine and ephedrine, while mongols require lower doses.
- Africans – beta blocker are less effective.

5. Genetics

- Determinants of drug responses — transporter, enzymes, ion channels, receptors and couplers — controlled genetically –Individual variation of responses.
- Pharmacogenetics: Use of genetic information to guide the choice of drug and dose on an individual basis –to identify individuals who are either more likely or less likely respond to a drug
  - so far genetic abnormalities have been identified
  - Personalized medicine goal yet to achieve
  - G-6PD deficiency —Primaquine, chlroquin, quinine, dapsone, aspirin

6. Route of Administration

- Route determines the speed and intensity of drug response – Oral/ Enteral for slow & Parenteral for speedy action.
- Adrug may have different actions via different routes - Magnesium sulfate or anatacids.

7. Environmental Factors

- Drug metabolism may get induced – exposure to insecticides, carcinogens, tobacco smoke and charcoal broiled meat.

8. Psychological Factors

- Efficacy of a drug can be affected by patient's beliefs, attitudes and expectations — particularly CNS drugs — more GA in nervous and anxious patients — alcohol and performance
- Placebo: An *Inert* substance which is given in the garb of medicine. Works by psychodynamic effects (not pharmacodynamics) — sometimes responses equivalent to active drugs
- Placebo reactors
- Induce psychological responses — release of endorphins in brain
- Uses — Control device in clinical trials and to treat a patient
- Lactose tablet/capsules or water injections etc

9. Pathological State

- Diseases can influence drug deposition- GIT diseases, Liv diseases, kidney diseases, Congestive heart failure and Thyroid etc.
- **GIT:** Coeliac diseases- amoxicillin absorption decreas while Cephalexin and cotrimoxazole increase Achlorohydria – Reduced aspirin absorption – NSAI aggravate peptic ulcer.
- **Liver diseases:** Liver diseases (cirrhosis) influence dr action
- Increased bioavailability of drugs with high first pa

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- **Kidney diseases:** Pharmacokinetics of many drugs are affected
- Clearance of drugs in unchanged form (aminoglycosides digoxin, phenobarbitone) reduced - parallel to CL- loading dose not altered- dose should be reduced.
- Plasma protein, albumin reduced – binding of acidi drugs affected.
- Permeability of BBB is increased – Opiates etc, more CNS depression.

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- **CHF/ CCF:** (1) Alter drug kinetics by decreased absorption (Thiazide),(2)modifying Volume of distribution (Lignocaine),(3)retarding the elimination(Lignocaine).decreased perfusion and congestion of liver; reduced g.f.r, increased tubular reabsorption- doses need reduction.
- **Thyroid diseases:** Hypothyroid states- sensitive to digoxin, morphine, and CNS depressants; Hyperthyroid states- resistant to ionotropic action- prone to cause arrhythmia by digoxin.
- **Presence of other drugs:** Drug interaction- Pharmacokinetic and Pharmacodynamic.
- **Cumulation:** If Rate of administration> Rate of elimination

10. Tolerance

- The requirement of higher dose of a drug to produce a given response

  Example: Sulfonylureas in type 2 diabetes and beta-2 agonist in bronchial asthma – adaptive biological phenomena.

- Natural : Species or individual inherently less sensitive – rabbits to atropine and black to beta blocker.
- Acquired: Repeated use of a drug in an individual who was initially responsive become nonresponsive (tolerant) – CNS

...Contd. (tolerance mechanism)

- Pharmacokinetic/Drug disposition tolerance: effective concentration of the drug at the site of action is decreased – due to enhancement of elimination on chronic use – Barbiturates and Carbamazepine induce own metabolism.
- Pharmacodynamic tolerance: less drug action – cells of target organs become less responsive – morphine, barbiturates, nitrates etc,... Down regulation/desensitization of receptors

THANKYOU