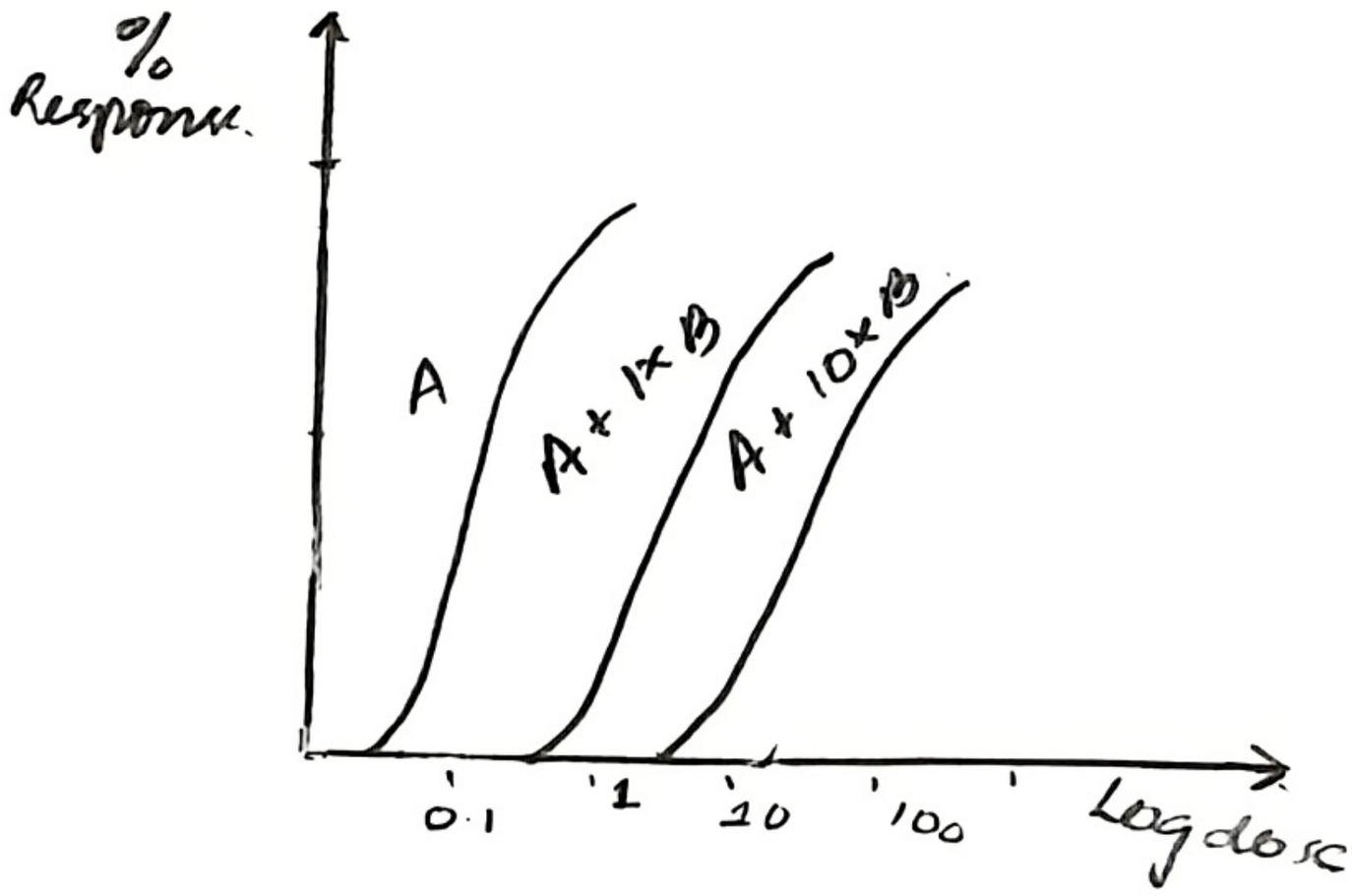
COMPETITIVE AND NON COMPETITIVE ANTAGONISM

(A) COMPETITIVE.

the antagonist is chemically similar to agonist competes with it, & binds at the same site to the exclusion of agonist molecules. Because antagonist has affinity but no intrinsic activity; no response is produced and log DRC of agonist is shifted to right.

Since antagonist binding is reversible and depends on relative conc of agonist and antagonist molecules, higher conc of agonist progressively overcomes block - a RTL shift of agonist DRC with no suppression of maximal response is obtained.

- Extent of shift is dependent on affinity & conc of antagonist.



(B) NONCOMPETITIVE / ALLOSTERIC

Antagonist is chemically unrelated to agonist, binds to a diff allosteric site altering the receptor in such a way that it is unable to combine with the agonist or is unable to transduce the response, so that the downstream chain of events are uncoupled. This is called allosteric antagonism.

↑ strng concn of antagonist progressively flatten agonist DRC

Factors Affecting Drug Action.

The factors modifying drug action either

(a) Quantitatively.
(b) Qualitatively.

The various factors affecting dose/action of drug are.

1) Body size
2) Age
3) Sex
4) Race.
5) Genetics.
6) Route of administration
7) Environmental factors & time of administration.
8) Psychological Factor
9) Pathological state.
10) Other drugs
11) Cumulation
12) Tolerance.

① Body Size.

It influences the concn of drug attained at site of action. The average adult dose refers to individuals of medium built. For exceptionally obese or lean individuals and for children dose may be calculated on body weight basis.

$$\text{Individual dose} = \frac{\text{Bw (kg)}}{70} \times \text{average adult.}$$

② Age.

Age of patient, particularly at two extremities has profound bearing on drug dose and in some cases on drug action as well.

→ the processes, particularly those which govern pharmacokinetics of drug change rapidly during infancy and at a slower pace during childhood.

Few basic features of pediatric pharmacology are:
eg: Hepatic drug metabolising systems is inadequate in newborns. Blood barrier is more permeable drugs attain higher conc in CNS.

→ geriatric popn suffers from a host of chronic disease. Multiple drugs are often prescribed to same patient, setting the stage for drug interactions and adverse drug effects. Great caution needed to be exercised when prescribing the elderly.

③ SEX.

Females have a smaller body size and requires doses that are on the lower side of the range. Subjective effects of drugs many differs in females because of their mental makeup.
eg: Women get intoxicated with smaller quantities of alcohol than men because of both higher bioavailability as well as slower hepatic oxd^{n} of alcohol by them.

④ RACE.

Among human beings, some racial diff have been observed
eg: blacks require higher and Mongols requires lower conc of atropine and ephedrine to dilate their pupil.

⑤ GENETICS.

Pharmacogenetics and pharmacogenomics.

⑥ ROUTES OF ADMINISTRATION.

It governs the speed & intensity of drug response, parenteral administration is often resorted to for more pronounced drug action.

⑦ ENVIRONMENTAL FACTORS & TIME OF ADMINISTRATION

eg: Hypnotics taken at night and in the familiar surroundings may work more easily.

⑧ PSYCHOLOGICAL FACTOR.

Efficacy of drug can be affected by patients belief, attitude & expectations, particularly applicable to

drug action of CNS

⑨ PATHOLOGICAL STATES.

Not only drug modify disease process, several diseases can influence drug disposition and drug action.

Eg: certain GI diseases can alter absorption of orally administered drugs.

⑩ OTHER DRUGS: Drugs can modify the response to each other by pharmacokinetics/pharmacodynamic interaction b/n them.

⑪ CUMULATION

Any drug will cumulate in the body of route of administration is more than rate of elimination.

⑫ TOLERANCE:

MICROSOMAL ENZYMES - INDUCTION & INHIBITION.

Microsomal enzymes, predominantly located in ER of liver cells, play a critical role in drug metabolism. They are essential for biotransformation of various xenobiotics and endogenous compounds. Induction and inhibition properties can significantly influence drug efficacy & toxicity.

Def^{n}: Microsomal enzymes refer to a group of enzymes, including cytochrome P450 (CYP) isoenzymes that are involved in oxd^{n} of drugs & other substances.

Function : They facilitate phase I reactions, which introduce or expose functional gps on drugs making them more polar & often preparing them for phase II conjugation.

(a) Induction of Microsomal Enzymes.

Induction refers to increased synthesis of microsomal enzymes leading to enhanced metabolic activity.

Mechanism:

Induction typically occurs through activation of nuclear receptors (eg: CAR, PXR) which bind to specific response elements in promoter regions of target genes. common inducers which includes drugs, environmental chemicals & dietary components.

eg: phenobarbitol: A classic inducer of CYP450 enzymes.

Rifampicin: Induces CYP 3A4 affecting metabolism of other drugs.

(b) Inhibition of Microsomal enzymes

Inhibition refers to decreased activity of microsomal enzymes, resulting in reduced metabolism of drugs.

Mechanisms

Inhibition can be competitive, non competitive or irreversible.

Inhibition can either bind to enzymes active site or allosteric enzyme's conformation.

eg: Ebrmetidine: A competitive inhibitor of

CYP1A2, CYP2CA & CYP3A4

Inhibition can lead to ↑ed plasma conc of drugs heightening risk of toxicity & adverse effects.

Factors affecting induction & inhibition

- Genetic variability
- Age and gender
- Diet & lifestyle [Alcohol, tobacco etc]

eg: A patient on warfarin who starts taking rifampicin may experience sub therapeutic effects due to induction of CYP2C9.