FACTORS MODIFYING DRUG ACTION

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FACTORS MODIFYING DRUG ACTION

- I. Physiological Factors.
- II. Pathological Factors (Diseases).
- III. Genetic Factors.
- IV. Environmental Factors.
- V. Interaction with other drugs.

I. Physiological Factors

- Age
- Sex
- Pregnancy
- Body weight
- Lactation
- Food

I. <u>Physiological Factors</u>

1. AGE

Newborn: Decreased

- J gastric acid secretion.
- liver microsomal enzymes (glucuronyl transferase).
- Plasma protein binding.
- − ↓ GFR & tubular secretion.
- Immaturity of BBB in neonates.

- GIT absorption of ampicillin and amoxicillin is greater in neonates due to decreased gastric acidity.
- Chloramphenicol --- Grey baby syndrome Inadequate glucouronidation of chloramphenicol with drug accumulation).
- Sulfonamides ----- Hyperbilirubinemia & Kernicterus

CHILDREN

- Tetracyclines
 Permanent teeth staining
- Corticosteroids
 Growth & development retardation
- Antihistaminics
 Hyperactivity.

Old Age $-\downarrow$ Liver function. diazepam, theophylline. $-\downarrow$ Kidney function. Digoxin, lithium. – ↓ Plasma protein binding diazepam, morphine

2. SEX.

• Testosterone increases the rate of biotransformation of drugs.

Decreased metabolism of some drugs in female (Diazepam).

 Females are more susceptible to autonomic drugs (estrogen inhibits choline estrase).

3. Pregnancy

- ↑ Cardiac output
- ↑ GFR and renal elimination of drugs.
- 1 Vd
- ↑ Metabolic rate of some drugs.
- Lipophilic drugs cross placental barrier & slowly excreted.

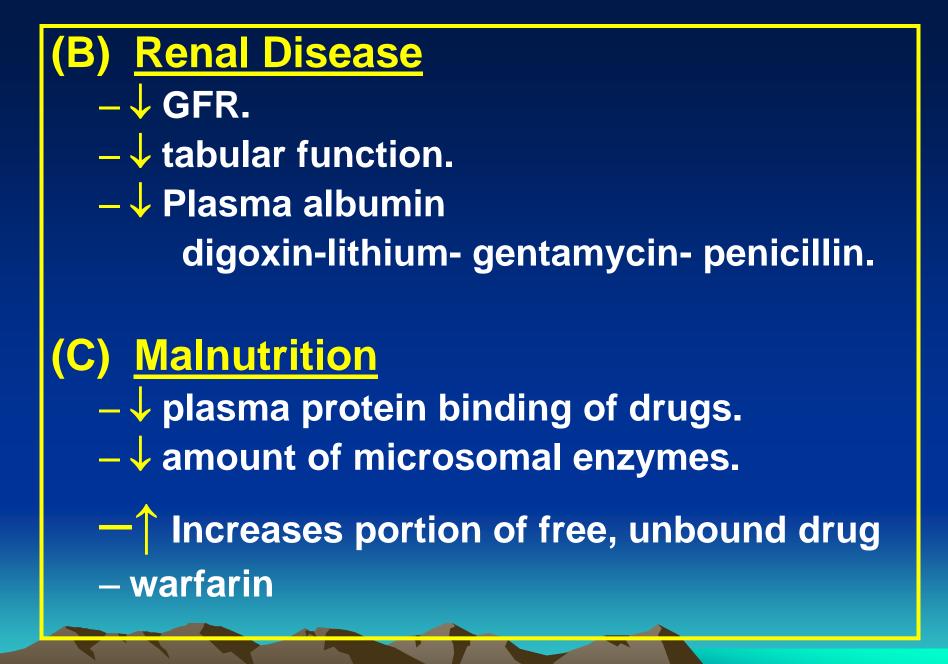
4. Plasma Protein Binding – Malnutrition. – Drug Interaction.

II. Pathological Factors

Diseases cause individual variation in drug response

(A) Liver Disease

- Prolong duration of action $= \uparrow$ (t1/2).
- Vertication Plasma protein binding for warfarin, tolbutamide –> adverse effects.
- –↓ Hepatic blood flow →↓ clearance of morphine- propanolol.
- Impaired liver microsomal enzymes
- Diazepam- rifampicin- theophylline



III. Genetic Factors Pharmacogenetics is the study of the relationship b/w genetic factors and drug response. **Idiosyncrasy** abnormal drug reaction due to genetic disorder. - Acetylation. - Oxidation.

- Succinylcholine apnea.
- Glucose 6-phosphate dehydrogenase deficiency.

III. Genetic Factors GENETIC POLYMORPHISM The existence in a population of two or more phenotype with respect to the effect of a drug.

Acetylation enzymes deficiency

- acetyl transferase (non-microsomal).
- Isoniazid, sulphonamides, etc.
- Slow acetylator phenotype → peripheral neuropathy.
- Rapid acetylator phenotype \rightarrow hepatitis.

Pseudocholinesterase deficiency.

Succinyl choline (Sk.muscle relaxant)
 → Succinylcholine apnea due to
 paralysis of respiratory muscles.

Malignant hyperthermia

- By succinyl choline due to inherited inability to chelate calcium by sarcoplasmic reticulum.
- ↑ Ca release, muscle spasm, ↑ Temp.

Oxidation Polymorphism Debrisoquine.

- Extensive metabolizers (EM) need larger dose.
- poor metabolizers (PM) need smaller dose.

Porphyria

Deficiency of Glucose–6 phosphate dehydrogenase (G-6-PD).

G-6-PD Deficiency in RBCs → hemolytic anemia upon exposure to some oxidizing drugs.

- Antimalarial drug, primaquine.
- Long acting sulphonamides.
- Fava beans (favism).

IV. Environmental Factors

Microsomal Enzyme Inducers

– Tobacco Smoke

 Smokers metabolize drugs more rapidly than non smoker.