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MATRICULATION NUMBER: 17/MHS03/025

DEPARTMENT: MBBS

COURSE: MEDICAL BIOCHEMISTRY IV

COURSE CODE: BCH313

ASSIGNMENT TITLE: XENOBIOTICS

1. Discuss in details the factors affecting drug metabolism.

**FACTORS AFFECTING DRUG METABOLISM**

The factors affecting drug metabolism can be classified into two, which are:

* INTERNAL FACTORS; and this includes:
1. Specie difference
2. Genetics/Strain difference
3. Age
4. Sex
5. Hormones
6. Diseases
7. Pregnancy
* EXTERNAL FACTORS; and this includes:
1. Diet
2. Environmental factors

**INTERNAL FACTORS**

1. SPECIE DIFFERENCE: Qualitative (Has to do with whether an enzyme is present or not) and quantitative (Involves the variations in amounts and localization of enzymes, amount of natural inhibitors and the competition between enzymes for specific substrates. For example, humans have the least amount of cytochrome P450 enzyme in one gram of tissue than any other specie) differences between species results in varying rate of drug metabolism (Phase I and II reactions) in their body systems.
2. GENETICS/STRAIN DIFFERENCE: Just like the difference in drug metabolism between different species is genetically determined, so also are the variations between strains of the same specie determined and can be studied under two headings:
* PHARMOGENETICS: This is the study of inter-subject variability in drug response. Inter-subject variations may be monogenetically or polygenetically controlled. Polygenetic control is observed in twins. In an experiment, Little or no difference in metabolism of some drug compounds e.g. Halothane, Dicoumaral, Antipyrine and phenylbutazone was observed but large variations were observed in fraternal twins.
* ETHNICAL VARIATIONS: This is the variation between different races and such differences could be monomorphic or polymorphic. Slow acetylators; dominated by the Japanese and Eskimos and includes 50% of African Americans and Caucasians while the rest of the races are generally rapid acetylators.
1. AGE: Fetuses, Neonates and elderly ones are more susceptible to drug action i.e. metabolize drug slowly compared to adults. Reasons for this are as follows:
* In fetuses and neonates, drug metabolic rate and systems are still underdeveloped. Hence, resulting in their slow metabolism of drugs while,
* In the elderly, the liver size is decreased, microsomal activity is also decreased and hepatic blood flow is also decreased due to decrease in cardiac output contributing to decrease in metabolic rate i.e. slow metabolism of drugs.
1. SEX: Males tend to have a higher metabolic capacity for most drugs than females. This variation is also as a result of different sex hormones.
2. HORMONES: Some hormones inhibit drug action e.g. Growth hormones which inhibits cytochrome P450 isozyme while others stimulate drug action.
3. DISEASES: Diseases especially those affecting the liver, generally leads to decreased drug metabolism
4. PREGNANCY: It is known to affect hepatic drug metabolism. Physiological changes during pregnancy causes this reported alteration in drug metabolism in that individual.

**EXTERNAL FACTORS**

1. DIET: Dietary components can depress or induce drug metabolism e.g. Low protein diet, Fat free diet, Grapefruit, starvation and dietary deficiency depresses or inhibits drug metabolism while high protein diet etc., stimulates drug metabolism.
2. ENVIRONMENTAL FACTORS: Environment, and several of its factors and agents influence the rate of drug metabolism in the body e.g. Halogenated pesticides e.g. DDT, Cigarette smoke containing polycyclic aromatic hydrocarbons results in enzyme induction effects while organophosphate insecticides and heavy metals e.g. mercury, cobalt, nickel, etc. causes inhibition of drug metabolism. Other environmental factors that may influence drug metabolism includes; Temperature, Altitude, Pressure, etc.