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MATRIC NO: 17/MHS01/115

1. DISCUSS IN DETAILS THE FACTORS AFFECTING DRUG METABOLISM.

There are various physiological and *pathological* factors can also affect drug metabolism.

A. Physiological factors that can influence drug metabolism include:

- Age

- Sex differences

- Diet

1. Age.

Drug metabolism in different age group differs mainly due to variations in the enzyme content, enzyme activity and haemodynamics.

In neonates, the microsomal enzyme system is not fully developed,therefore many drugs are metabolized slowly.

In ederly persons, the liver size is reduced, the microsomal enzyme activity is decreased and hepatic blood flow also declines as a result of reduced cardiac output, all of which contributes to decreased metabolism of drugs.

In general, drugs are metabolized more slowly in fetal, neonatal and elderly humans and animals than in adults.

1. Diet.

The enzyme content and activity is altered by a number of dietary components. Generally,

* Low protein deit decreases and high protein diet increases the drug metabolizing ability as enzyme synthesis is promoted by protein diet and also raises the level of amino aids for conjugation with drugs.
* Fat free diet depresses cytochrome P-450 levels since phospholipids, which are important components of microsomes become deficient.
* Dietary deficiency of vitamins like Vitamin A, B2, B3,C and E, and minerals such as Fe, Ca, Mg, Zn retard the metabolic activity of enzymes.
* Starvation results in decreased amount of glucuronides formed than under normal conditions.

1. Sex differences.

Sex related differences in the rate of metabolism may be due to sex hormones. In humans, women metabolize benzodiazepines slowly than men.

1. Pathological factors can also influence drug metabolism, including liver, kidney or heart diseases. Thyroid diseases:

* Hyperthyroid- increases metabolism
* Hypothyroid- decreases metabolism.

1. Chemical factors include;

* Induction of drug metabolizing enzymes: the drug causes an increase in the activity of an enzyme, often due to increased amounts of newly synthesized enzymes which would result in increased drug metabolism and decreased rate of drug action
* Inhibition of drug metabolizing enzymes
* Environmental chemicals: the activity of drug metabolizing enzyme can be induced or inhibited by chemicals contained in environmental contaminants and drugs e.g organophosphate pesticides.