

ENYONG, RUTH KINGSLEY

17/MHS01/119

MEDICINE AND SURGERY

MEDICAL BIOCHEMISTRY IV (BCH313)

DISCUSS IN DETAILS THE FACTORS AFFECTING DRUG METABOLISM

The factors affecting drug metabolism include:

I. AGE:

Generally, older age is associated with increased blood concentrations of drugs and altered metabolism, reduced effectiveness, and increased risk of adverse reactions for many medications. Advancing age reduces the effect of cytochrome P450 on drug metabolism.

II. SEX DIFFERENCES:

Many cytochrome P450 enzymes (phase I metabolism) show a sex-dependent difference in activity. Most of the phase II enzymes have a higher activity in men than in women. Activities of these enzymes can also change during pregnancy and with the use of oral contraceptives.

III. BODY MASS:

Physiological alterations to the body, such as increased adipose (fat) tissue, can affect distribution, metabolism and clearance of drugs from the body. In particular, different considerations are to be given to hydrophilic and lipophilic drugs as they have different distributions in lean and obese people. Body size may also have an

effect on liver and kidney function, with obesity believed to increase clearance of drugs.

IV. GENETIC DIFFERENCES

V. EXERCISE:

Exercise reduces the blood flow in the liver and deactivation of drugs with flow-limited (high clearance) hepatic metabolism such as nitrates and lidocaine. Metabolism of capacity-limited (low clearance) drugs, e.g. antipyrine, diazepam and amobarbital, is not influenced by exercise.

VI. HORMONAL FACTORS:

Growth hormones are known to reduce the function of cytochrome p450 isoenzymes.

VII. ENVIRONMENTAL FACTORS:

Environmental or external factors like alcohol can affect drug metabolism especially when ingested together. It can increase drug absorption by enhancing gastric solubility of drugs and by increasing gastrointestinal blood flow.

VIII. DISEASE:

Although the liver is the main site of drug metabolism, conflicting results have been reported on drug elimination during liver diseases. Drug metabolism may depend on histological changes in the liver (acute or chronic hepatitis, cirrhosis) but may also depend

on their origin (viral, toxic or immunological). In the case of liver diseases, drug metabolism is reduced.

IX. DIET:

Food can enhance, delay or decrease drug absorption. They impair absorption of many antibiotics. E.g. high protein diets can accelerate metabolism of certain drugs by stimulating cytochrome P450 while grapefruit inhibits cytochrome P450 thereby slowing drug metabolism.

X. NUTRITIONAL DEFICIENCIES:

Severe energy and protein deficiencies reduce enzyme tissue concentration and may impair response to drugs by reducing absorption or protein binding leading to liver dysfunction. Vitamin C deficiency decreases the activity of drug metabolizing enzymes especially in the elderly.