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**Factors affecting drug metabolism**

**Drug metabolism** is the metabolic breakdown of drugs by living organisms, usually through specialized (enzymatic) systems. Xenobiotic metabolism is the set of metabolic pathways that modify the chemical structure of xenobiotics which are foreign compounds to an organism's normal biochemistry E.g. drug or poison. These pathways are a form of biotransformation present in all major groups of organisms, and are considered to be of ancient origin but some factors are involved to affect these metabolism process:

1. Nutrition: it affect the body’s response to drugs the same way drugs can affect the body’s nutrition. Foods can enhance, delay, or decrease drug absorption, impair absorption of many antibiotics and alter metabolism of drugs; e.g., high-protein diets can **accelerate** metabolism of certain drugs by stimulating cytochrome P-450, Eating grapefruit can **inhibit** cytochrome P-450, slowing metabolism of some drugs (e.g., amiodarone, carbamazepine, cyclosporine).

- Nutritional deficiencies can affect drug metabolism e.g. severe energy and protein deficiencies reduce enzyme tissue concentrations and may impair the response to drugs by reducing absorption or protein binding and causing liver dysfunction.

* Changes in the GI tract can affect the response to a drug e.g. Vitamin C deficiency decreases activity of drug-metabolizing enzymes (especially in the elderly)

1. Age. As you get older, your metabolic rate generally slows because of a loss of muscle tissue and changes to hormonal and neurological processes. During development, children go through periods of growth with extreme rates of metabolism. Aging results in a number of significant changes in the body including reductions in blood flow, size and drug-metabolizing enzyme content. Drug metabolism is also influenced by diseases, frailty, concomitant medicines etc. These changes have the potential to alter the hepatic clearance of drugs but need to be interpreted in the context of the characteristics of the drug of interest. There is growing evidence that the age-related changes in the liver not only result in a decrease in the hepatic clearance of unbound drug but also influence variability in response to medicines in older people.
2. Body size: Those with bigger bodies have a larger BMR because they have larger organs and fluid volume to maintain. Physiological alterations to the body (i.e. increased adipose tissue) can affect distribution, metabolism and clearance of drugs from the body. Different considerations need to be given to hydrophilic and lipophilic drugs because these have different distributions in obese and lean people as it also have an effect on liver and kidney function, with **obesity believed to increase clearance of drugs.** It has been researched that several antimicrobial drugs that are currently given in standard doses (E.g. fluoroquinolones, linezolid, sulphonamides etc.) should be given in higher doses to patients with large body size to help attain target effects on the body. . For different drugs, different factors may need to be considered to calculate the right dose such as body mass index, total weight loss or gain, adjusted weight due to exercise etc.
3. Gender: Men generally have faster metabolisms than women, Drug absorption occur in different places across body surfaces (gastrointestinal tract, respiratory tract, or skin) which differ in sexes e.g. absorption time is shorter in men than in women, Men have higher concentrations of colic acid while women have higher concentrations of chenodeoxycholic acid etc. Women experience more side effects than men that are more serious. Generally Women are smaller and have a different body composition than men so the recommended dose may result in higher drug concentrations for them because the drug has lower clearance or smaller volume of distribution.
4. Genetics: Some families have faster Body mass ratio than others with some genetic disorders also affecting metabolism, People vary widely in their response to drugs and Genetic factors can account for most of patient variability because it affect what the body does to a drug and what the drug does to the body. In some cases, some people metabolize drugs slowly and the drug may accumulate in the body leading to toxicity while Other people metabolize drugs so quickly that after they take a usual dose, drug levels in the blood never become high enough for the drug to be effective. E.g. fewer African men and women have a deficiency of glucose-6-phosphate dehydrogenase (an enzyme that protects red blood cells from certain toxic chemicals), people with this deficiency, are affected by malaria drugs (chloroquine and primaquine) which destroy red blood cells and cause hemolytic anemia.
5. Environmental factors: Environmental changes such as increased heat or cold forces the body to work harder to maintain its normal temperature and increases BMR. Although various kinds of environmental factors may alter the activity of cytochrome P-450 enzymes in liver micromes, their effects will depend on the relative importance of excretory and metabolic mechanisms in the elimination of the drug, the relative importance of various metabolic reactions in different tissues, the extraction ratio of the drug by the liver and the route of administration of the drug. The activities of other drug-metabolizing enzymes and that the relative effects of the environmental factors of these enzymes may differ depending on the animal species or the animal strain
6. Muscle mass: The amount of muscle tissue on your body. Muscle requires more energy to function than fat. So the more muscle tissue you carry, the more energy your body needs just to exist. (Resistance or strength training is most effective for building and maintaining mass.)
7. Hormonal factors: Hormonal imbalances such as hypo & hyperthyroidism can affect your metabolism.