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**FACTORS AFFECTING DRUG METABOLISM**

Drug metabolism is the metabolic breakdown of drugs by living organisms, usually through specialized enzymatic systems. The metabolism of pharmaceutical drugs is an important aspect of pharmacology and medicine. For example, the rate of metabolism determines the duration and intensity of a drug's pharmacologic action. Drug metabolism also affects multi-drug resistance in infectious diseases and in chemotherapy for cancer, and the actions of some drugs as substrates or inhibitors of enzymes involved in xenobiotic metabolism are a common reason for hazardous drug interactions.

Physiological factors that can influence drug metabolism include age, individual variation e.g., pharmacogenetics, enterohepatic circulation, nutrition, intestinal flora, or sex differences.

In general, drugs are metabolized more slowly in fetal, neonatal and elderly humans and animals than in adults. Dose, frequency, route of administration, tissue distribution and protein binding of the drug affect its metabolism.

Here are some other important factors that affect drug metabolism : genetic polymorphisms, enzyme inhibition, enzyme induction, and first pass metabolism. There is a great deal of variation in the metabolic reactions that produce drug metabolites. The extent to which a drug is metabolized by one individual can be dramatically different than that of another. Thus, the effect a drug will have on one individual can be dramatically different than the effect it has on another.

Note : The duration and intensity of pharmacological action of most lipophilic drugs are determined by the rate they are metabolized to inactive products. The Cytochrome P450 monooxygenase system is the most important pathway in this regard.

1. ENZYME INDUCTION : It refers to an increase in the rate of hepatic metabolism, mediated by increased transcription of mRNA encoding the genes for drug metabolizing enzymes. This leads to a decrease in the concentrations of drugs metabolized by the same enzyme. It, in other words, increases the rate of metabolism of a pharmacologically active metabolite and decreases the duration and intensity of the drug action.
2. ENZYME INHIBITION : It is the opposite of enzyme induction. However, in cases where an enzyme is responsible for metabolizing a pro-drug into a drug, enzyme induction can speed up this conversion and increase drug levels, potentially causing toxicity.
3. GENETIC POLYMORPHISM : This is when there are two or more possibilities of a trait on a gene. It accounts for some of the variability in the effect of drugs. With N-acetyltransferases (involved in Phase II reactions), individual variation creates a group of people who acetylate slowly (slow acetylators) and those who acetylate quickly. This variation may have dramatic consequences, as the slow acetylators are more prone to dose-dependent toxicity.
4. FIRST PASS METABOLISM : The first pass effect, also known as first-pass metabolism or presystemic metabolism, is a phenomenon of drug metabolism whereby the concentration of a drug, specifically when administered orally, is greatly reduced before it reaches the systemic circulation.