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1. Factors affecting drug metabolism

Drugs, as well as other xenobiotics are metabolised via various pathways, including phase I and phase II reactions, which involve participation of numerous enzyme systems. Factors that have a role in the metabolism of a drug are divided into Internal & External factors

Internal factors include: species, sex, age, disease.

External factors include: diet, environment

INTERNAL FACTORS

* Species - the metabolism of a drug in species may involve the same route, but differ in the rate along that particular pathway (i.e. quantitatively different) or they may adopt different pathways (i.e. differing qualitatively). A well-known quantitative example is that of species variation in hexobarbitone metabolism, affecting half-life and sleeping time. Experiments have been made on man, dog, mice and the rat . The factors that influence drug biotransformation longest half-time was registered for man (~360 min). The sleeping time increased in the following order: mice, rats, dogs and man.
* SEX: Both qualitative and quantitative differences in both phases of drug metabolism are related to sex as well. For example Experiments show that female rats required half dosage of barbiturates to induce sleep compared to male rats . It was then concluded that the female rats couldn’t really metabolize barbiturates.
* AGE: in babies and children, they would be highly sensitive because of their poor ability to metabolize drugs. But in adults, the levels of enzyme activity is increased, thus improving drug metabolism activities. In the elderly, enzyme activities are reduced and it causes a decrease in drug metabolizing activity.
* Disease: The way in which the body clears drugs is affected by many disease states. Diseases like cirrhosis, diabetes mellitus , cholestatic jaundice, and liver carcinoma. In cirrhosis, parts replaced by fibrous tissue leads to a reduction in the number of functional hepatocytes and this impairs drug metabolism. In humans the cytochrome p450 (especially the CYP2A6 isoform) catalyse the bioactivation of various drugs and even carcinogens. In the case of cirrhosis, this isoform is overexpressed and it then becomes the main lover catalyst.

EXTERNAL FACTORS

* Environment : there are a large number of environmental chemicals that potentially could affect drug biotransformations, usually grouped into heavy metals, industrial pollutants and pesticides. The most important industrial pollutants are typically aromatic or aromatic polycyclic compounds and polychlorinated biphenyls. A lot of these environmental factors either have enzyme induction effect or inhibit enzyme activity
* DIET: Low protein diet decreases and high protein diet increases as enzyme synthesis is promoted by protein diet and also raises the level of amino acids for the conjugation of drugs. A fat free diet reduces levels of cytochrome p450.