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1. Discuss in details the factors affecting drug metabolism

Factors affecting Drug Metabolism can be divided into two

* Internal Factors (Physiological and pathological):  species, genetic (strain), sex, age, hormones, pregnancy, disease
* External Factors (Exogenous): Diet and Environment

1. Internal Factors subdivided into:

**Physiological Factors** include:

1. ***Age***: As you get older, your metabolic rate generally slows. This is 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
2. ***Nutrition***: Foods can enhance, delay, or decrease drug absorption. Foods impair absorption of many antibiotics. They can alter metabolism of drugs; eg, high-protein diets can accelerate metabolism of certain drugs by stimulating cytochrome P-450. Eating grapefruit can inhibit cytochrome P-450 34A, slowing metabolism of some drugs (eg, amiodarone, carbamazepine, cyclosporine, certain Ca channel blockers)
3. ***Genetic variation*** (polymorphism) : Genetic differences are the result of genetically based variation in alleles for genes that code for enzymes responsible for the metabolism of drugs.
4. ***Species differences***: Species differences occur in both phase I and phase II metabolism and can be either quantitative (same metabolic route but differing rates) or qualitative (differing metabolic routes)
5. ***Intestinal flora***: The **consequences** of xenobiotic **metabolism** by **intestinal** microbiota would be increased toxicity by the production of toxic or carcinogenic metabolites, decreased toxicity or detoxication, delayed **excretion** of xenobiotics by enterohepatic circulation, production of pharmacologically active metabolites
6. ***Sex differences***: Men generally have faster metabolisms than women.

**Pathological factors** can also influence drug metabolism, including.

**Effects of Liver Disease**: The Liver is the main site of Drug Metabolism. The capacity of the liver to metabolise drugs depends on hepatic blood flow and liver enzyme activity, both of which can be affected by liver disease (e.g acute or chronic hepatitis, cirrhosis). In addition, liver failure can influence the binding of a drug to plasma proteins. These changes can occur alone or in combination; when they coexist their effect on drug kinetics is synergistic, not simply additive

**Effects of Kidney Disease**: Renal failure may influence hepatic drug metabolism either by inducing or inhibiting hepatic enzymes, or by its effect on other variables such as protein binding, hepatic blood flow and accumulation of metabolites.

**Effects of Heart Disease:** The pathologic changes occurring in cardiovascular disease can affect the absorption, distribution, metab- olism, and elimination of drugs in several different ways. Patients with heart disease can have decreased gastric emptying and intestinal motility, reduced splanchnic blood flow, and bowel edema.

1. External Factors

* ***Environment***: Environmental changes such as increased heat or cold, or harmful chemical substances forces the body to work harder to maintain its normal temperature and internal chemical environment and increases the BMR likewise the rate of Drug Metabolism will be increased too Eg. In twenty‐six men occupationally exposed to a mixture of insecticides, mainly lindane and DDT, antipyrine had a significantly shorter plasma half‐life than in 33 control sub;ects. If the mechanism is the same as that in animals, these studies indicate that insecticides can induce microsomal drug metabolism in man.
* ***Diet***: Metabolic food-drug interactions occur when the consumption of a particular food modulates the activity of a drug-metabolising enzyme system, resulting in an alteration of the pharmacokinetics of drugs metabolised by that system. Foods that contain complex mixtures of phytochemicals, such as fruits, vegetables, herbs, spices and teas, have the greatest potential to induce or inhibit the activity of drug-metabolising enzymes, although dietary macroconstituents (i.e. total protein, fat and carbohydrate ratios, and total energy intake) can also have effects