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**Department: MBBS**

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**Course Title: Medical Biochemistry**

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**Assignment**

Discuss in details the factors affecting drug metabolism.

INTERNAL FACTORS

1. **AGE**: newborns’ drug metabolism enzymes are not fully developed and older peoples’ metabolism rate is reduced due to change in hormonal and neurological processes. So for this reason, drugs are slowly metabolized in them. Their metabolism rate is not as active as it is in normal adults.
2. **GENDER**: men have a faster metabolism rate than women. This is due to sex hormones. Men have more glutathione than women.
3. **GENETIC VARIATIONS**: there are significant differences in enzyme activities between individuals, some of which are due to genetic factors. With N-acetyltransferases, there are individuals who acetylate quickly. These individuals are spit roughly 50:50 in some populations. Slow acetylators are more prone to drug toxicity. Approximately slow and rapid acetylators are found among whites and blacks whereas the slow acetylators dominate Japanese and Eskimo populations.
4. **BODY MASS**: people with greater body mass have a larger body metabolic rate.
5. **DISEASES**: diseases that affect metabolism of drugs include cirrhosis of the liver, diabetes mellitus, acromegaly, liver disease, viral infections, etc. These diseases affect the activities of drug metabolism enzymes, sometimes necessitating the adjustment of dosage of various drugs for patients with this disorder. Some of these diseases can also alter the hepatic blood flow or hypoalbuminanemia. Oxidation of vitamin D and hydrolysis of procaine are impaired to kidney disease.
6. **HORMONAL INBALANCE**: higher levels of one hormone can inhibit the activity of some enzymes while inducing others. Growth hormones also decrease the rate of drug metabolism
7. **ENZYME INDUCTION AND INHIBITION**: enzyme inducers are agent that increases drug metabolism enzymes. Enzyme inducers cause increase in liver size and liver blood flow, increase in total and microsomal protein content, increased stability of cytochrome P-450, increased stability of enzymes, and decreased degradation of cytochrome P-450, proliferation of smooth endoplasmic reticulum. Enzyme inhibition is decrease in drug metabolism of an enzyme directly or indirectly. Direct inhibition may result from interaction of enzyme at a site an there would be a change in enzyme activity. Competitive inhibition occurs when structurally similar compounds compete in the same site on an enzyme. Non-competitive inhibition occurs when a structurally unrelated agent interacts with the enzyme and prevents the metabolism of drugs. Product inhibition occurs when the metabolic products competes with the substrate for the same enzyme.

Indirect inhibition is caused repression or altered physiology. Repression may be due to the fall in the rate of enzyme synthesis or rise in the rate of enzyme degradation. Altered physiology may be due to nutritional deficiency or hormonal imbalance. It is important to know whether or not an individual has been exposed to these inducing agents in evaluating biochemical responses to xenobiotics. Metabolites of some xenobiotics can inhibitor stimulatethe activities of xenobiotic-metabolizing enzymes. Again, this can affect the doses of certain drugs that are administered to patients.

1. **SPECIES**: metabolism of drugs is usually affected by the half-life and duration of such drugs in specie. The activities of some enzymes might also differ substantially between species. The metabolisms of drugs in these different species are usually qualitative or quantitative. Human liver contains less cytochrome P-450 per gram than liver of other species.
2. **PREGNANCY**: pregnancy affects hepatic drug metabolism. This is due to the physiological changes associated with pregnancy such as elevated levels of hormones such as estrogen, progesterone, prolactin and placental growth hormone.

EXTERNAL FACTORS

1. **ENVIRONMENTAL CHEMICALS:** several environmental agents influence drug metabolizing ability of enzymes. Halogenated enzymes such as DDT and polycyclic aromatic hydrocarbons contained in cigarette smokes have enzyme induction effect. Organophosphate insecticides and heavy metals such as mercury, nickel, cobalt and arsenic inhibit drug metabolizing ability of enzymes. Other environmental factors that affect drug metabolism include temperature, pressure, altitude, atmosphere, etc.
2. **DIET**: certain foods can enhance, delay or decrease drug absorption. High protein diets can accelerate metabolism of certain drugs by stimulating cytochrome P-450. Fat free diet depresses cytochrome P-450**.** Dietary deficiency of vitamins like A, B2, B3, C and E and minerals such as Zn, Ca, Mg, Fe retard the metabolic rates of enzymes.Starvation results in decreased amount of glucuronides formed then under normal conditions.