Discuss in details the factors affecting drug metabolism.
**ANSWER**

The factors affecting drug metabolism may be divided into two categories; internal factors and external factors.

The following are some factors(internal factors) affecting drug metabolism:

* AGE

The drug metabolic rate in the different age groups differs mainly due to variations in the enzyme content, enzyme activity and haemodynamics. In neonates (up to 2 months) and in infants (2 months to 1 year), the microsomal enzyme system is not fully developed. So, many drugs are metabolized slowly. For example; caffeine has a half-life of 4 days in neonates in comparision to 4 hrs in adults. However, children (between 1 year and 12 years) metabolize several drugs much more rapidly than adults as the rate of metabolism reaches a maximum somewhere between 6 months and 12 years. As a result they require a larger dose in comparison to adults. In elderly persons, the liver size is reduced, the microsomal enzyme activity is decreased and hepatic blood flow also declines as a result of reduced cardiac output, all of which contributes to decreased metabolism of drugs. For example, chlomethiazole shows a high bioavailability within the elderly, therefore they require a lower dose.

* SEX DIFFERENCE

Variations between male and female are observed following puberty. So, sex related differences in the rate of metabolism may be due to sex hormones. Such sex differences are widely studied in rats where male rats have greater drug metabolizing capacity. In humans, women metabolize benzodiazepines slowly than men. Several studies have shown that women on contraceptive pills metabolize a number of drugs at a slow rate.

* HORMONES

Hormones may either enhance or reduce the metabolizing effect of drugs. For example, growth hormones are known to cause a reduction or repress some isoenzymes of Cytochrome p450.

* SPECIES DIFFERENCE

Qualitative differences among species generally result from the presence or absence of specific enzymes in those species. Quantitative differences result from variations in the amount and localization of enzymes. Human liver contains less cytochrome p450 per gram of tissue than do the livers of other species. For example, rat liver contains approximately 30 to 50 nmol/g of Cytochrome P450, whereas human liver contains 10 to 20 nmol/g. Furthermore, human liver is 2 percent of body weight, whereas rat liver is approximately 4 percent.

Similarly,In men, amphetamine and ephedrine are predominantly metabolized by oxidative deamination, whereas in rats aromatic oxidation is the major route in Phase-II reactions.

The following are some factors (external factors) which affect drug metabolism:

* DIET

 The enzyme content and activity is altered by a number of dietary components. Generally Low protein diet decreases and high protein diet increases the drug metabolizing ability as enzyme synthesis is promoted by protein diet and also raises the level of amino acids for conjugation with drugs. Fat free diet depresses cytochrome P-450 levels since phospholipids, which are important components of microsomes become deficient. Dietary deficiency of vitamins (like Vitamin A, B2, B3, C and E) and minerals (such as Fe, Ca, Mg, Zn) retard the metabolic activity of enzymes. Starvation results in decreased amount of glucuronides formed than under normal conditions.

* ENVIRONMENT

There are. however. factors outside the body that can also have a profound influence on drug metabolism. The body can be exposed to these factors by design (e.g. substances taken as food. alcohol and tobacco smoke) or by accident (air. water and food contaminants or pollutants). Some physiological factors include pregnancy, stress, etc.

Examples of other biological factors are: a) Strain difference b) Altered physiological factors (such as pregnancy, hormonal imbalance and disease states)

There are also some chemical factors which affect drug metabolism such as: a) Enzyme induction b) Enzyme inhibition c) Environmental chemicals