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Medicine and Surgery 300lvl

Biochemistry, Xenobiotics

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

Drug metabolism can be affected by chemical factors, biological factors and physiochemical properties of the drug.

1. Chemical factors
2. Enzyme induction: this is the phenomenon of increasing drug metabolizing ability of enzymes by several drugs and chemicals. This causes a decrease in pharmacological activity of drug and alters the physiological status due to enhanced metabolism of endogenous compounds.
3. Enzyme inhibition: This is the decrease in the drug metabolizing activity of an enzyme. This process might be direct or indirect. It is considered direct when it occurs from an interaction at the enzyme site, the net outcome being a change in enzyme activity. Indirect enzyme inhibition is caused by repression or altered physiology which might be due to nutritional deficiency.
4. Environmental chemicals: Several environmental factors affect drug metabolism such as insecticides, pesticides, halogens, altitude, pressure and temperature.
5. Biological factors
6. Age: In neonates, the microsomal enzyme system is not well developed. In young children, metabolism of drug is much more rapid than in adults. In old, liver size and function reduces leading to decreased metabolism of drug.
7. Sex: In 1932, Nicholas and Baron discovered that half of the hexobarbitone required to male sleep is required to make the females sleep. Women metabolize benzodiazepines slower than men. In general, women on contraceptives metabolize drugs slower than men.
8. Hormones: Growth hormones are known to cause a reduction or repress some isoenzymes of cytop450. High levels of one hormone can inhibit the activity of few enzymes while inducing that of others.
9. Diet: Most isoenzymes are preterous. Hence, diet can either induce or repress drug metabolism. Low protein diet decreases drug metabolism process while high protein diet increases it. Grapefruit increases rate of drug metabolism. Deficiency of essential vitamins and minerals reduces it.
10. Species difference: Rate of drug metabolism varies within various species of animals. In humans, amphetamine and epinephrine are predominately metabolized by oxidative deamination while in rats, aromatic oxidation is the route. Similarly, phenol is excreted mainly as glucuronide and as sulphate conjugates in cats.
11. Altered physiological factors: In pregnancy, metabolism of promazine and pethidine is reduced. In disease states such as cirrhosis of liver, alcoholic liver disease diabetes mellitus, etc, the liver is badly damage therefore causing a decrease in the rate of drug metabolism.
12. Physiochemical properties of the drug

Molecular size and shape, pKa, acidity/basicity, steric and electronic characteristics of a drug influence in interaction with the active sites of enzyme and the metabolism to which it is subjected.