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BIOCHEMISTRY ASSIGNMENT

FACTORS THAT AFFECT DRUG METABOLISM

Drug metabolism is the metabolic breakdown of drugs. It can also be the chemical alteration of a drug by the body. There are various factors which constitute drug metabolism and are categorised under external and internal.

INTERNAL FACTORS

1. GENETICS: genetic differentiation is one of the main causes of rate of drug metabolism. It may be divided into two: ethnic variation and pharmogenetics
* Ethnic variation: these are differences observed in the metabolism of drug among different races. Such variations may be monomorphic or polymorphic. For example the difference in the rate of acetylation: rapid acetylators have more hepatic acetyl N-transferase than the slow acetylators. 90% of Eskimos and Asians are rapid acetylators while Egyptians and Mediterranean are slow acetylators. The rate of acetylation is clinically important in terms of toxicity and therapeutic response.
* Pharmogenetics: this is the study of inter subject variability in drug response. They may either be monogenetically or polygenetically controlled. A polygenetic control is observed in twins.
1. HORMONES: higher level of ones hormones may inhibit the activity of few enzymes while inducing that of others. Thyroidectomy, adrenalectomy and alloxan-induced diabetes in animals showed impairment in the enzyme activity with subsequent fall in the rate of metabolism.
2. AGE: in fetal, neonatal, elderly humans and animals drugs are metabolised more slowly than in adults. Drug metabolic rate in different age groups differ due to variations in the enzyme content, enzyme activity and hemodynamic. In neonates and infants, the microsomal enzyme system is not fully developed. Many drugs are metabolised slowly, take for example caffeine, which has a half-life of 4 days in neonates compared to 4 hours in adults. Children between a year and 12 years metabolise 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 large mg/kg compared to adults. In elderly persons, the liver size is reduced, the microsomal enzyme is decreased and hepatic blood flow also declines as a result of reduced cardiac output, all of which contributes to decreased metabolism of drugs.
3. DISEASE: there are many disease states that affect the metabolism of drugs. Some include: malaria, diabetes mellitus, cirrhosis of liver, jaundice, acromegaly, alcoholic liver disease, etc. it can be noted that major effects are seen in the disease affecting the liver as liver is quantitavely the important site for metabolism. The possible cause in the effect of metabolism due to the diseases may be hypoalbuminemia, decreased enzyme activity in liver, altered hepatic blood flow.

EXTERNAL FACTORS

1. Diet: number of dietary components can be altered due to enzyme content and activity. Generally, low protein decreases and high protein diet increases the drug metabolizing ability as enzyme syntheses 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, minerals such as iron (Fe), calcium (Ca), magnesium (Mg) and zinc (Zn) retard the metabolic activity of enzymes.
2. Environment: several environmental agents influence the drug metabolizing ability of enzymes. Example includes:
* Organophosphate insecticides and heavy metals such as mercury, nickel, cobalt and arsenic inhibit drug metabolizing ability of enzymes
* Halogenated pesticides such as polycyclic aromatic hydrocarbons and dichlorodiphenyltrichloroethane (DDT) contained in cigarette smoke have enzyme induction effect.
* Other environmental factors that may influence drug metabolism are temperature, altitude, pressure, and atmosphere and so on.