**ADEBAYO ADETUTU MERCY**

**17/MHS01/012**

**MEDICINE AND SURGERY**

**BIOCHEMISTRY ASSIGNMENT**

**FACTORS THAT AFFECT DRUG METABOLISM**

***INTERNAL FACTORS***

1**. Muscle mass**: The amount of muscle tissue on your body. Muscle requires more energy to function than fat. So the more muscle tissue you carry, the more energy your body needs just to exist. (Resistance or strength training is most effective for building and maintaining mass.)

2**. 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.

With aging, there are changes in all these areas;

Absorption

Distribution across body compartments

Metabolism

Excretion

Some changes are more clinically relevant. The metabolism and excretion of many drugs decrease, requiring that doses of some drugs be decreased. Toxicity may develop slowly because concentrations of chronically used drugs increase for 5 to 6 half-lives, until a steady state is achieved. For example, certain benzodiazepines (diazepam, flurazepam, chlordiazepoxide), or their active metabolites, have half-lives of up to 96 h in older patients; signs of toxicity may not appear until days or weeks after therapy is started.

3**. Body size**. Those with bigger bodies have a larger BMR because they have larger organs and fluid volume to maintain.

Physiological alterations to the body, such as increased adipose (fat) tissue, can affect distribution, metabolism and clearance of drugs from the body. In particular, different considerations need to be given to hydrophilic (‘water-loving’) and lipophilic (‘fat-loving’) drugs, as these have different distributions in obese and lean people. Body size may also have an effect on liver and kidney function, with obesity believed to increase clearance of drugs.

However, the complex interaction between different drugs and body size means that a standard calculation would be difficult to establish. There are many factors that could be relevant, such as body mass index (BMI), total weight, adjusted weight (fraction of excess body weight added to ideal weight), lean body weight and body surface area. For different drugs, different factors may need to be considered to calculate the right dose. This is also the case for underweight people.

Based on the class of drug and its weight-dependent body distribution and clearance, some drugs may need to be given at greater or lesser amounts than the standard adult dose. Some drugs may need their starting dose adjusted, while others may need to have their maintenance dose changed. Others may benefit from being given at the standard dose but for a shorter or longer duration.

4. **Gender/Sex**: Men generally have faster metabolisms than women. Biologic differences exist between men and women that can result in differences in responses to drugs. Both pharmacokinetic and pharmacodynamic differences between the sexes exist, with more data on pharmacokinetic differences. On average, men are larger than women. Body size differences results in larger distribution volumes and faster total clearance of most medications in men compared to women. Greater body fat in women (until older ages) may increase distribution volumes for lipophilic drugs in women. Total drug absorption does not appear to be significantly affected by sex although absorption rates may be slightly slower in women. Bioavailability after oral drug dosing, for CYP3A substrates in particular, may be somewhat higher in women compared to men

5. **Genetics**: Some families have faster BMR than others with some genetic disorders also affecting metabolism. Differences in genetic (inherited) makeup among individuals affect what the body does to a drug and what the drug does to the body. The study of genetic differences in the response to drugs is called pharmacogenetics. In some cases, the level of an enzyme that metabolizes medications can be measured before starting the therapy. This should be considered before prescribing. Because of their genetic makeup, some people process (metabolize) drugs slowly. As a result, a drug may accumulate in the body, causing toxicity. Other people metabolize drugs so quickly that after they take a usual dose, drug levels in the blood never become high enough for the drug to be effective that we make can also increase BMR and reduce interference to the nervous system allowing your body to thrive

6. **Physical activity**: Exercise increases muscle mass and powers up your metabolic engines burning kilojoules at a faster rate, even when at rest

The increasing popularity of sporting events, even for people on drug treatment, has raised the question of the interaction of exercise and pharmacokinetics. Exercise reduces splanchnic blood flow, but possible changes in the absorption of orally given drugs seem tol significance. Absorption from intramuscular, subcutaneou and transdermal application sites may be accelerated by exercise, possibly causing harmful consequences, e.g. in diabetics treated with insulin. Exercise or physical work increases the rate and depth of respiration thus increasing alveolar exchange of gases and vapours. Physical activity increases muscular blood flow and the binding of digoxin to muscular structures, with a simultaneous fall in the concentration of serum digoxin. Reduction in blood flow to adipose and other inactive tissues may delay the distribution of some drugs that are stored or removed by these tissues. The change from supine to upright position can affect the distribution of a drug. Exercise reduces the blood flow in the liver and deactivation of drugs with flow-limited (high clearance) hepatic metabolism such as nitrates and lidocaine. Metabolism of capacity-limited (low clearance) drugs, e.g. antipyrine, diazepam and amobarbital, is not influenced by exercise. Renal plasma flow, urine excretion rate and urine pH are also reduced by exercise. This is an important reason why the serum levels of drugs eliminated through the kidneys increase during physical stress. The changes in parenteral absorption and distribution volume of some drugs caused by exercise, as well as the short half-life of drugs, are properties resulting in altered therapeutic/toxic response in those drugs with a narrow therapeutic range.

7. **Hormonal factors**: Hormonal imbalances such as hypo & hyperthyroidism can affect your metabolism. Cytochrome P450 (CYP) is a group of enzymes that metabolize drugs to a more water-soluble form, rendering them available for renal excretion. The major site of CYP expression is the liver. Nearly 50% of all medications currently on the market are metabolized by the enzyme CYP3A4, while metabolism of another 35-40% occurs through enzymes CYP1A2, CYP2C19, CYP2D6, CYP3A5 CYP3A6, and CYP3A7. Here, we summarize the current knowledge of the effects of hormones on the CYP family. The term "hormone" is used in its broad sense and includes products of the major endocrine glands (i.e., thyroid, adrenals, gonads, pancreas) and compounds that are not classically considered hormones, such as neurogenic amines, cytokines, interleukins, and eicosanoids. In addition, we comment on the effects on CYP expression of states associated with profound hormonal changes, such as pregnancy, malnutrition, obesity, diabetes mellitus, systemic inflammation, and conditions of altered extracellular fluid volume or osmolality.

***EXTERNAL FACTORS***

1**. DIET**: Food changes your metabolism. What and how you eat has a big influence on your BMR.

2. **ENVIRONMENT**: Environmental changes such as increased heat or cold forces the body to work harder to maintain its normal temperature and increases BMR

3. **DRUGS**: Caffeine and nicotine can increase your BMR whilst medications such as antidepressants and steroids increase weight gain regardless of what you eat.

This list shows us that some things you can change to alter your BMR and some things you can’t. The good news is that you can do plenty to alter the balance.

Chiropractic principles tell us that working to create a body that works well without interference will powerfully affect health. The food, exercise and activity choices that we make can also increase BMR and reduce interference to the nervous system allowing your body to thrive. A win-win situation.