**NAME:** SUOWARI OYINEBI PASCHELIA

**MATRIC NUMBER**: 17/MHS01/299

**DEPARTMENT**: MEDICINE AND SURGERY

**BIOCHEMISTRY ASSIGNMENT**

1. What do you understand by primary or simple obesity
2. how does congenital syndrome and drug therapy affects obesity
3. Outline the aetiology of cancer and its molecular basis.

**ANSWERS**

1. **PRIMARY OR SIMPLE OBESITY**

 Obesity is a disorder of body weight regulatory systems characterized by an accumulation of excess body fat. In primitive societies, in which daily life required a high level of physical activity and food was only available intermittently, a genetic tendency favouring storage of excess calories as fat may have had a survival value. Today, however, the sedentary lifestyle and abundance and wide variety of palatable, inexpensive foods in industrialized societies has undoubtedly contributed to an obesity epidemic. As adiposity has increased so has the risk of developing associated diseases, such as arthritis, diabetes, hyper tension, cardiovascular disease, and cancer.

 Primary Obesity has been defined simply as a state of excess adipose tissue in the body. This condition is variously stated as affecting 5-30% of the adult population, depending upon the standards used and populations studied.

1. **CONGENITAL SYNDROME AND DRUG THERAPY EFFECTS ON OBESITY**

**CONGENITAL SYNDROME**: Unlike in monogenic disorders, where obesity begins very early in infancy, in obesity-related syndromes it begins after infancy. Other than obesity, basic syndrome features include dysmorphia, psychomotor retardation and anomalies of certain organ systems. They can occur due to gene or larger chromosomal abnormalities. Some Syndromes include:

* Alström’s syndrome (AS) is a rare autosomal recessive disorder due to the mutation of the ALMS1 gene located on chromosome 2p13, which also disrupts ciliary function. In addition to early central obesity like in children with BBS, children with AS also have visual impairment and deafness. Central obesity develops by 5 years of age, and the affected children have acanthosis nigricans and type 2 diabetes more often than children with BBS. Other endocrinopathies include hypothyroidism, primary hypogonadism in boys and GH deficiency. Intellectual development is normal (8).
* Carpenter syndrome besides obesity, includes mental retardation, short stature, brachicephalus, polydactyly, foot syndactyly, cryptorchidism, hypogonadism in boys, umbilical hernias and high palate. The RAB23 gene is located on chromosome 6p11. Like in Alström’s and Bardet-Biedl’s syndromes, this gene mutation also causes an impaired function of proteins involved in the ciliary body important for intercellular communication in mammals. The disorder also seems to disrupt communication between the neurons involved in the leptin signal pathway, crucial for energy homeostasis (31).
* Cohen’s syndrome is characterised by hypotonia and failure to thrive during infancy, and the central obesity develops in mid-childhood. The clinical features include microcephaly, mental retardation, cryptorchidism, small hands and feet with long, thin fingers as well as marked central incisors. The COH1 gene, whose mutation causes these disorders, is located on chromosome 8q22 and encodes a transmembrane protein with a still unknown function (32).
* WAGR syndrome includes Wilms tumour, aniridia, genitourinary tract abnormalities and mental retardation, while obesity is present only in some patients. The syndrome is caused by a deletion on chromosome 11p11.4, near the gene responsible for BDNF production. BDNF is regulated by nutritional status and included in the leptin signal pathway in the hypothalamus where it stimulates the production, differentiation and survival of neurons, but also body mass regulation. Most WAGR syndrome patients with the deletion which includes BDNF are obese, unlike those with no deletion, in whom the frequency of obesity is consistent

**DRUG THERAPY:** Obese people have larger absolute lean body masses as well as fat masses than non-obese individuals of the same age, gender and height. However, the percentage of fat per kg of total bodyweight (TBW) is markedly increased, whereas that chrome P450 isoforms are altered, but no clear overview of drug hepatic metabolism in obesity is currently available. Pharmacokinetic studies provide differing data on renal function in obese patients. This review analyses recent publications on several classes of drugs: antibacterial, anticancer drugs, psychotropic drugs, anticonvulsants, general anaesthetics, opioid analgesics, neuromuscular blockers, beta-blockers and drugs commonly used in the management of obesity. Pharmacokinetic studies in obesity show that the behaviour of molecules with weak or moderate lipophilicity (e.g. lithium and vecuronium) is generally rather predictable, as these drugs are distributed mainly in lean tissues. The dosage of these drugs should be based on the ideal bodyweight (IBW). However, some of these drugs (e.g. antibacterial and some anticancer drugs) are partly distributed in adipose tissues, and their dosage is based on IBW plus a percentage of the patient's excess bodyweight. There is no systematic relationship between the degree of lipophilicity of markedly lipophilic drugs (e.g. remifentanil and some beta-blockers) and their distribution in obese individuals. The distribution of a drug between fat and lean tissues may influence its pharmacokinetics in obese patients. Thus, the loading dose should be adjusted to the TBW or IBW, according to data from studies carried out in obese individuals. Adjustment of the maintenance dosage depends on the observed modifications in clearance. Our present knowledge of the influence of obesity on drug pharmacokinetics is limited. Drugs with a small therapeutic index should be used prudently and the dosage adjusted with the help of drug plasma concentrations.

1. **AETIOLOGY OF CANCER**

 Cancer is a set of diseases in which cells escape from the control mechanisms normally limiting their growth. Cancer cells ignore the normal signals that operate the cell cycle and affect the body by dividing uncontrollably and invading surrounding tissues. The gene regulation systems that go wrong during cancer turn out to be the very same systems that play important roles in embryonic development, the immune response, and many other biological processes. The genes that normally regulate cell growth and division during the cell cycle include genes for growth factors, their receptors, and the intracellular molecules of signalling pathways. Mutations that alter any of these genes in somatic cells can lead to cancer.

 Cancer is simply the gain of oncogenes and the loss of tumor suppressor genes. Genetic abnormalities found in cancer typically affect two general classes of genes. Cancer-promoting oncogenes are typically activated in cancer cells, giving those cells new properties, such as hyperactive growth and division, protection against programmed cell death, loss of respect for normal tissue boundaries, and the ability to become established in diverse tissue environments. Activated oncogenes result from different types of mutations including point mutations, chromosomal translocations, promoter translocations, and amplifications. Point mutations increase proteins' activity and prevent it from being turned off. Chromosomal translocations encode fusion proteins that are hyper activated or inappropriately regulated or localized. Promoter translocations drive abnormally high levels of expression. Amplifications increase the copy number and expression of a gene. Tumor suppressor genes (TSG) are then inactivated in cancer cells, resulting in the loss of normal functions in those cells, such as accurate DNA replication, control over the cell cycle, orientation and adhesion within tissues, and interaction with protective cells of the immune system. Tumor suppressor genes can be inactivated by missense mutations that decrease the protein's activity, deletions, frameshifts, and promoter methylation.

 Cancer is caused by changes (mutations) to the DNA within cells. The DNA inside a cell is packaged into a large number of individual genes, each of which contains a set of instructions telling the cell what functions to perform, as well as how to grow and divide. Errors in the instructions can cause the cell to stop its normal function and may allow a cell to become cancerous. A gene mutation can instruct a healthy cell to:

1. Allow rapid growth: A gene mutation can tell a cell to grow and divide more rapidly. This creates many new cells that all have that same mutation.
2. Fail to stop uncontrolled cell growth: Normal cells know when to stop growing so that you have just the right number of each type of cell. Cancer cells lose the controls (tumor suppressor genes) that tell them when to stop growing. A mutation in a tumor suppressor gene allows cancer cells to continue growing and accumulating.
3. Make mistakes when repairing DNA errors: DNA repair genes look for errors in a cell's DNA and make corrections. A mutation in a DNA repair gene may mean that other errors aren't corrected, leading cells to become cancerous.

 These mutations are the most common ones found in cancer. But many other gene mutations can contribute to causing cancer. Gene mutations can occur for several reasons, for instance:

1. Gene mutations you're born with: You may be born with a genetic mutation that you inherited from your parents. This type of mutation accounts for a small percentage of cancers.
2. Gene mutations that occur after birth: Most gene mutations occur after you're born and aren't inherited. A number of forces can cause gene mutations, such as smoking, radiation, viruses, cancer-causing chemicals (carcinogens), obesity, hormones, chronic inflammation and a lack of exercise. Gene mutations occur frequently during normal cell growth. However, cells contain a mechanism that recognizes when a mistake occurs and repairs the mistake. Occasionally, a mistake is missed. This could cause a cell to become cancerous.

 The gene mutations you're born with and those that you acquire throughout your life work together to cause cancer. For instance, if you've inherited a genetic mutation that predisposes you to cancer, that doesn't mean you're certain to get cancer. Instead, you may need one or more other gene mutations to cause cancer. Your inherited gene mutation could make you more likely than other people to develop cancer when exposed to a certain cancer-causing substance.