17/MHS/06/049

Obikpo Chisom

Medical Biochemistry IV

BCH 313

MBBS 300 level

Assignment

1. What do you understand by primary or simple obesity
2. How does congenital syndrome and drug therapy affect obesity
3. Outline the aetiology of cancer and it’s molecular basis
4. Primary/ simple obesity has been defined as a state of excess adipose tissue in the body. Primary obesity is obesity that is not associated with prior medical conditions or diagnosis. According to studies, no other cause exists other than the normal imbalance between energy intake and energy expenditure. Obesity is not just a cosmetic consideration. It is a chronic medical disease that can lead to diabetes, high blood pressure; obesity associated cardiovascular disease such as heart disease, gallstones, and other chronic illnesses.

Obesity is a chronic condition defined by an excess amount of body fat. A certain amount of body fat is necessary for storing energy, heat insulation, shock absorption, and other functions.

People are generally considered obese when their body mass index (BMI), a measurement obtained by dividing a person's weight by the square of the person's height, is over 30 kg/m2; the range 25–30 kg/m2 is defined as overweight.

1. **Effect of congenital syndrome**

The syndromic forms of obesity are often associated with phenotypes in addition to the early-onset severe obesity. This may be caused by change in a single gene or a larger chromosomal region encompassing several genes. Obesity is a feature of almost 100 syndromes; a little over half are not yet named, and 13.9% have more than one name. The co-presenting phenotypes often include intellectual disability, dysmorphic facies, or organ-system specific abnormalities. The most frequent forms of syndromic obesity are Bardet Biedl and Prader Willi syndrome.

*Prader Willi syndrome-*A person with Prader-Willi Syndrome (PWS) has extreme difficulty controlling their body weight, as they spend a long time eating and have a powerful compulsion to eat as much food as possible. PWS is the most common genetic cause of morbid obesity in children. People with PWS have seven genes on chromosome 15 that are either deleted or inactive. They will often have low muscle tone, incomplete sexual development, and chronic hunger. Their metabolism tends to burn fewer calories when compared to people who do not have the condition. Many individuals with PWS have short stature. A new-born infant with PWS tends to have a lower-than-usual birth weight, weak muscles, and difficulties with sucking. Muscle weakness is known as hypotonia. Individuals start developing a strong appetite called hyperphagia between 2 and 5 years of age and sometimes later. This characteristic occurs due to a significantly decreased feeling of fullness after eating. Once hyperphagia begins, it tends to be a lifelong condition.

*Bardet Biedl syndrome-* Bardet-Biedl syndrome (BBS) is a genetic disorder with obesity as one of the major phenotypic criterion, which is proposed to be of neuroendocrine origin. Therefore, disturbances in appetite-regulating hormones have been considered as causative factors. Acyl ghrelin is an orexigenic hormone, whereas its desacylated form, obestatin, and leptin have the opposite functions. Ghrelin is negatively regulated in relation to nutritional status. BBS patients lack the negative regulatory mechanisms of appetite-regulating hormones with respect to nutritional status and exhibit resistance to anorexigenic leptin. This results in a shift towards the orexigenic effects of this self-regulating system. These alterations may in part be responsible for the disturbed appetite regulation in BBS patients. Obesity is present in the vast majority (72–86%) of the individuals, although the birth weight may be normal. There is a high prevalence of Type 2 diabetes, hypogonadism, cognitive deficit, labile behavior, speech deficit, renal and cardiac anomalies The biological defect for the syndrome is an abnormality in immotile cilia that primarily function as the sensory organelle regulating signal transduction pathways.

**Effect of drug therapy**

Medical treatment of obesity is advised for patients with a BMI of over 30 or for patients with a BMI greater than 27 possessing possible risks like high blood pressure, diabetes and high blood cholesterol. The medication put in place is solely for dietary purposes or exercise programs in weight loss and will only work if taken in the right doses. At first, weight loss could occur beginning from the loss of 5-10 pounds in the first month. The first class (category) of medication used for weight control cause symptoms that mimic the sympathetic nervous system. They cause the body to feel "under stress" or "nervous." As a result, the major side effect of this class of medication is high blood pressure. This class of medication includes sibutramine and phentermine. These medications also decrease appetite and create a sensation of fullness. Hunger and fullness (satiety) are regulated by brain chemicals called neurotransmitters. Examples of neurotransmitters include serotonin, norepinephrine, and dopamine. Anti-obesity medications that suppress appetite do so by increasing the level of these neurotransmitters at the junction (called synapse) between nerve endings in the brain. .

**Etiology of cancer**

Cancer arises from factors within the cells and other external factors within the environment e.g inherited mutations and mutations from the environment

Etiology of of cancer is multifactorial i.e. physical, chemical, metabolic, hormonal, genetic factors they all have to do with the development and generation of cancer. All the factors causing mutation of genes during replication leading to cancer. Thus, carcinogens are mutagens and vice versa. In summary, carcinogens whether physical or chemical causes DNA damage which leads to mutation which causes cancer.

Every normal cell has DNA repair gene mechanism that corrects the defects that occur during replication

Carcinogens and hereditary mutations affect this repair of genes and hence, cause cancer

about 50% of human cancer is due to mutation or deletion of this repair gene called ANTIONCOGENE and ONCOSUPPRESSOR GENE.

**Causes of cancer**

1. Carcinogens- visible carcinogens include x-rays UV light, gamma rays etc.

Chemical carcinogens include aniline, tobacco, carbon monoxide, nitrogen oxide,

food additives and coloring agents

natural chemicals like AFLATOXIN B, found in fungus aspergilius

1. Hormones- some hormones like steroid hormones are carcinogenic
2. Hereditary- a mutated gene causing cancer has 50% , that is one and two chances of being passed to the child because each gene of the parents is passed to the child e.g xerodema pigmentosa (cancer of the skin).
3. Organic viruses and oncoviruses- these viruses get integrated into the host DNA leading to multiplication of viral genes overtaking the host and causing uncontrollable multiplication of cells.
4. Mutations in Genes That Regulate Apoptosis Allow Cancer Cells to Escape Suicide- To achieve net cell proliferation, it is necessary not only to drive cells into division, but also to keep cells from committing suicide by apoptosis. There are many normal situations in which cells proliferate continuously, but the cell division is exactly balanced by cell loss. In the germinal centers of lymph nodes, for example, B cells proliferate rapidly but most of their progeny are eliminated by apoptosis. Apoptosis is thus essential in maintaining the normal balance of cell births and deaths in tissues that undergo cell turnover.
5. Mutations in the p53 Gene Allow Cancer Cells to Survive and Proliferate despite DNA Damage- The p53 gene-named for the molecular mass of its protein product-may be the most important gene in human cancer. This tumor suppressor gene is mutated in about half of all human cancers. What makes p53 so critical? The answer lies in its triple involvement in cell-cycle control, in apoptosis, and in maintenance of genetic stability-all aspects of the fundamental role of the p53 protein in protecting the organism against cellular damage and disorder.

**Molecular basis of cancer**

Most of the genes found to be mutated in cancer, both oncogenes and tumor suppressor genes, code for components of the pathways that regulate the social and proliferative behavior of cells in the body—in particular, the mechanisms by which signals from a cell's neighbors can impel it to divide, differentiate, or die. Other cancer-critical genes are involved in maintaining the integrity of the genome and guarding against damage. The molecular changes that allow cancers to metastasize, however, escaping the parent tumor and growing in foreign tissues, are still largely unknown. A protein known as protein p53 has dual roles which are both very important the first being regulating both progression through the cell cycle and the second role being initiation of apoptosis. So loss or inactivation of p53, which occurs in about half of all human cancers, is doubly dangerous: it allows genetically damaged and senescent cells to continue to replicate their DNA, increasing the damage, and it allows them to escape apoptosis. The loss of p53 function may contribute to the genetic instability of many full-blown metastasizing cancers.