A S S I G N M E N T

**BCH 308: Cellular Biochemistry**

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**300 Level.**

**Question**

1. WHAT DO YOU UNDERSTAND BY PRIMARY OBESITY?

2. HOW DOES DRUG THERAPY AND CONGENITAL SYNDROME AFFECT SECONDARY OBESITY?

3. DISCUSS THE AETIOLOGY OF CANCER AND ITS MOLECULAR BASIS.

**Answer**

1. Primary obesity is the most common form of obesity, caused by the accumulation of excess body fat as a result of excessive food intake, lack of exercise etc. that can have an adverse effect on the affected individual. This differs from secondary because, secondary obesity is caused by a pre-existing medical condition.
2. ***EFFECT OF DRUG THERAPY***: In the history of using drug as a therapy for obesity, many of them were withdrawn because of their side effects. These side effects are the causes of the weight gain, not the drug itself. Currently, only five drug therapies are approved for the specific treatment of obesity. Some drugs may for instance, have an effect on how the body stores and absorbs glucose and other substances. This can lead to it accumulating in strategic points in the body e.g. abdomen. Other drugs could bring about a large appetite by stimulating a part of the hypothalamus (arcuate nucleus), hence making more food to be consumed. Major drugs that have this ability are the mood stabilizer drugs e.g. clozapine; an antipsychotic drug that is known to cause a remarkable increase in weight after prolonged usage.

The use of glucagon-like peptide-1 (GLP-1) antagonists has been used to exploit the GLP-1 receptor, which is involved in the control of sugar level. There is also the use of sodium-glucose co-transporter-2 (SGLT-2) inhibitors, e.g. amylin, ghrelin antagonists etc., to suppress appetite. A major example of a drug used in therapy for obesity is Orlistat, which deactivates intestinal lipase and inhibits intestinal fat lipolysis.

***EFFECT OF CONGENITAL SYNDROME:*** Congenitally, there are rare genetic and syndromic forms of obesity. They are characterized by mental retardation, dysmorphic features, organ-specific abnormalities, hyperphagia, and/or other signs of hypothalamic dysfunction. These forms of obesity may be inherited in either an autosomal or an X-linked pattern. A major example of the congenitally acquired obesity is the monogenic obesity, described as a rare and severely-onset obesity with abnormal feeding behavior and endocrine disorders. It is mainly due to autosomal recessive mutations in genes of the leptin-melanocortin pathway that plays a key-role in the hypothalamic control of food intake. A child suffering from this form of obesity can be able to normalize their body weight after daily subcutaneous leptin administration. For instance, Sibutramine, a serotonin-noradrenaline reuptake-inhibitor which is really effective in the treatment of obesity (extensive metabolism of substances in the liver).

1. ***AETIOLOGY OF CANCER:*** Cancer is simply an uncontrolled division of abnormal cells in a part of the body. It is a malignant growth or tumor. All cancers are multifactorial in origin i.e. genetic, hormonal, metabolic, physical, chemical and environmental.
   * 1. Environmentally, the skin can be exposed to ionic radiation e.g. UV rays.
     2. Physically, this can be from lifestyle related factors such as tobacco smoking, alcohol, food additives and sweeteners.
     3. Chemically, it can be from exposure to some chemical substances e.g. asbestos, polynuclear hydrocarbons etc.

Apart from these, some bacteria and viruses can also cause cancer e.g. HIV (Human Immuno-deficiency Virus), HPV (Human Papilloma Virus), EBV (Epstein Bar Virus) etc.

***MOLECULAR BASIS OF CANCER:*** Every cell in the body is programmed to undergo apoptosis (programmed cell death) once there is detection of damaged DNA that cannot be repaired. This apoptosis is carried out by some genes e.g. P53, the most vital gene responsible for detecting DNA damage, chromosome abnormalities and arresting the cell cycle to initiate repair. Cancer cells however, are able to evade this apoptosis by responding to inbuilt cytokines that promote growth, weaken and reduce apoptosis and facilitate invasion and metastasis, allowing it to be easily spread to other normal, healthy cells. Also, in highly aggressive cancer cells, there can be a mutation and inactivation of the P53 gene protein, as well as the Retinoblastoma (another vital *gatekeeper* that controls cell division and cell death) by oncogenes and oncoproteins. All these represent a major breach in the anti-cancer defence mechanism, hence causing cancer.