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**Medicine and Surgery**

**300level**

**17/MHS01/185**

**Biochemistry assignment (BCH313)**

**Questions**

1. Outline the etiology of cancer and its molecular basis
2. How does congenital syndrome and drug therapy lead to obesity?
3. What do you understand by primary or simple obesity?

**Answers**

1. Cancer arises from factors within the cell and the external factors within the environment. Thus, etiology of cancer is multifactorial. They include genetic (mutation), hormonal (steroid hormones), physical (X-rays, UV-rays, gamma rays, e.t.c), chemical (aniline, asbestos), metabolic and environmental factors. All these factors have a role in development of cancer. They cause mutation of genes during replication and this replication causes cancer. Mutated gene causing cancer has 50% chance of being passed to offspring e.g. Xeroderma pigmentoza, familial adenomatous polypscoli. Most human cancers are spontaneous.
* The incidence of many cancers increases with age. All cancers originate usually from one aberrant cell, which goes on to multiply and produce a tumor mass. One mutation occurs out of 106 cell divisions. By the time the person reaches adulthood, about 1026 cell divisions have occurred. Usually, these aberrant cells are destroyed by the immune system but as age advances, these mutations accumulate, hence the statistical probability of the incidence of cancer is increased. Carcinogens are mutagens and mutagens are carcinogens. Carcinogens, whether physical or chemical, cause DNA damage which leads to mutation. Every normal cell has DNA repair mechanism that corrects the defects that occur during replication. Carcinogens and hereditary mutations affect these DNA repair mechanisms genes and hence, cancer results. About 50% of human cancer is due to mutation or deletion of these repair genes called antioncogenes or oncosupressor genes. Oncogenic viruses get integrated into the host DNA leading to multiplication of viral gene overtaking the normal host causing uncontrollable multiplication of cells.

**Molecular basis**

Normal cells tend to replicate normally and when they get older, they are remove by apoptosis (programmed cell death). The molecular basis of this is seen in the shortening of telomeres on the chromosomes of normal cells. Cancer cells are able to escape apoptosis of the normal cell cycle. They accomplish this by production of the enzyme telomere polymerase which lengthens the telomeres on the chromosome. In this way, apoptosis is escaped and immortality is attained by cancer cells. All normal cells receive signals for apoptosis; chemical compounds that cause cancer destroy these signals hence, cells continue to multiply uncontrollably.

1. **Congenital syndrome and obesity**

Severe obesity is a characteristic feature of many congenital and genetic disorders. Congenital syndromes like Prader-Willi syndrome, Cohen syndrome, Down syndrome, Bardet-Biedl syndrome and Turner syndrome are associated with obesity in children.

 Children with Down syndrome are more likely to have higher levels of hormones associated with obesity; hormones such as leptin. The normal role of leptin is to suppress appetite and regulate body weight. Obese people do not respond to leptin properly because they have some leptin resistance. Down syndrome may have a genetic predisposition to more severe leptin resistance.

Prader-Willi syndrome (PWS) is a complex neurodevelopmental disorder due to errors in genomic imprinting with loss f imprinted genes that are paternally expressed from the chromosome region. PWS is considered most common known genetic cause of morbid obesity in children. The subject are frequently unable to sense when they are full after eating and this leads to weight gain Unless food intake is strictly controlled, subject with PWS will be severely obese. PWS result to constant and inexorable hunger that drives patients to engage in problematic hunger behaviors with affected individuals who do not fill satisfied after completing a meal. Most patients have reduced GH secretion and hypogonadotropic hypogonadism, suggesting hypothalamic–pituitary dysfunction. Nevertheless, encouraging results have been observed with the early administration of GH, resulting in accelerated growth and decreased body fat; sex hormone replacement may also be beneficial.

**Drug therapy and obesity**

A number of drugs are capable causing obesity; drugs such as birth control pills, steroids and antidepressants. This is because these drugs posses varying abilities to increase and appetite stimulate carbohydrate craving and cause weight gain over prolonged periods of administration. Psychotropic drugs with more pronounced amitripyline induce weight gain. Selective serotonin reuptake inhibitors decrease transiently bodyweight during the first few weeks of treatment and may then increase body weight; weight gain tends to be most prominent some mood stabilizers. Atypical antipsychotic tend to cause more weight gain than the convenient ones. Some of the medications might interfere with central nervous functions regulating energy balance which are neurotransmitters, neuromodulators, cytokines and hormone interacting with the hypothalamus.

1. Primary or simple obesity is characterized by a normal or increased growth with an acceleration of bone maturation. When longitudinal growth slows down in the presence of obesity, a hormonal disturbance should be sought. At this stage, it is not associated with clinical conditions.