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MATRIC NO: 17/MHS01/131

COURSE TITLE: MEDICAL BIOCHEMISTRY IV

COURSE CODE: BCH 313

ASSIGNMENT TITLE: DIABETES, OBESITY AND CANCER

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QUESTION 1: What do you understand by simple or primary obesity?

ANSWER: Primary obesity is a medical condition in which excess body fat has accumulated to an extent that it has a negative effect on health. This is the common form of obesity that is seen in most cases. This type of obesity has no secondary cause i.e. it is not disease-based. It occurs in about 95% of all cases. Its causes include:

- Dietary intake
- Physical inactivity
- Eating patterns
- Food availability
- Sedentary lifestyle
- Snacking
- Fast food consumption linked to adiposity

QUESTION 2: How does congenital syndrome and drug therapy affect obesity?

ANSWER: CONGENITAL SYNDROME: such as Prader-Willi, Down's, bradet-biedi, cohen and carpenter syndrome. Although, it is thought that hypothalamic-pituitary axis abnormalities are possible causative mechanism in some of these disorders, current knowledge is insufficient to explain the pathophysiologic mechanism of obesity in most multiple congenital anomaly. Individuals with Prader-Willi syndrome, whose blood levels of ghrelin are exceptionally high, have an uncontrollable appetite, leading to extreme

obesity that often results in death before the age of 30. In all these syndromes listed above, we have congenital obesity common to them and this obesity is the excessive accumulation and storage of fat in the body that is present during infancy and/or in childhood. We also have congenital leptin deficiency which is rare and is caused by the mutation of the leptin gene. This disorder is autosomal recessive and manifested by severe obesity. It is exquisitely sensitive to leptin injection with reduced dietary intake and profound weight loss.

DRUG THERAPY: Therapies are arrived at by identifying an enzyme or receptor involved in the process and discovering an inhibitor that interferes with its action. Proteomics will play an increasing role in identifying such potential drug targets. Drug therapy for obesity has at least one of the following effects: reduce appetite or nutrient absorption. Increase resting or activity-related energy expenditure. Their effects on weight reduction tend to be modest, and weight regain upon termination of drug therapy is common. There are series of drugs that are used during drug therapy for obesity. We have drugs that alter fat digestion such as ORLISTAT (xenical, alli), drugs that are GLP-receptor agonist such as LIRAGLUTIDE (saxenda), combination drugs such as PHENTERMINE-TOPIRAMATE (qsymia), NALTREXONE-BUPROPION (contrave) and LORCASERIN (belviq). We also have sympathomimetic drugs and some which do not require therapy. These drugs, if stopped usage will cause relapse and the obesity will come back worse. Drugs used do not replace physical activity and healthy eating habit. These drugs are given based on what is wrong with the person, the family history and so on. Because obesity is chronic, the patient may need to continue changes to eating and physical activity habit and other behaviors for years. There are also drugs to curb the desire to eat. They include: phentermine, benzphetamine, diethylpropion and phendimetrazine

QUESTION 3: Outline the etiology of cancer and its molecular basis.

ANSWER: Cancer arises from factors within the cell and external factors within the environment e.g. inherited mutations or mutations due to metabolism in an environment. Etiology of cancer is, thus, multifactorial. Physical, chemical, hormonal, metabolic, genetic and environmental factors all have a role in the causes of cancer. They cause mutation of genes during replication causing cancer. Thus, carcinogens are mutagens i.e. whatever causes mutations causes cancer. Carcinogens, whether physical or chemical, cause DNA damage which leads to mutation and mutation causes cancer. Carcinogens and hereditary mutations affect the repair genes and since DNA repair mechanism cannot take place, cancer occurs.

ETIOLOGY (CAUSES) OF CANCER

1. Carcinogens: Physical carcinogens include x-ray, UV light, gamma rays e.t.c. Chemical carcinogens are aniline, asbestos, tobacco (benzose pyrine), food additives and coloring agents. Natural chemicals like aflatoxin B found in fungus that are found in mold that grows in moist and deep food.
2. Hormones: Like steroid hormones
3. Hereditary/genetic: a mutated gene causing cancer has 50% chance of being passed to offspring as parent chromosomes are passed to offspring. E.g. a form of skin cancer (Xeroderma Pigmentosa), familial adenomatous polyposis coli (FAP) - cancer of colon. These two cancers are known to be highly hereditary.
4. Oncogenic viruses: these viruses are integrated into the host DNA leading to multiplication of viral gene overtaking normal host's host thereby, causing uncontrollable multiplication of cancer cells. Four examples of typical oncogenic viruses.

| HUMAN VIRUS | ABBREVIATION | ASSOCIATED CANCER |
|---|---|---|
| Epstein-barr virus | EBV | • Lymphoma<br>• Nasopharyngeal carcinoma ($Ca^{-}$) |
| Hepatitis B virus | HBV | • Hepatoma/ hepatocellular carcinoma |
| Human-papilloma virus | HPV | • Uterocervical carcinoma |
| Human immuno-deficiency virus | HIV | • Kaposis sarcoma(cancer of muscle)<br>• Non-hodgkins lymphoma |

We also have some oncogens which are normal constituents of the DNA but are capable of causing cancer if activated. For example, BRCA1 (associated with familial breast cancer).

MOLECULAR BASIS OF CANCER

Normally, cells replicate and when they get older, the old cells are removed by APOPTOSIS (programmed cell death). The molecular basis of this is seen in shortening of telomeres on the chromosomes in normal cells. Cancer cells are able to escape apoptosis of normal cell cycle. They accomplish this by production of enzymes, telomere polymerase which lengthen the telomeres of chromosomes. By lengthening the telomeres, cell life is being prolonged. In this way, apoptosis is prevented and cancer cells are immortalized. All cancer cells receive signals for apoptosis. Chemicals that causes cancer destroys these signals, hence cells that cause cancer continue to multiply uncontrollably.