MATRIC NO: 17/MHS01/275

NAME: OSUBOR STEPHANIE

COURSE: BCH 313

**QUESTION 1**

**PRIMARY/SIMPLE OBESITY**

This is obesity based on nutritional factors, resulting when caloric intake exceeds energy expenditure. There will be accumulation of excess body fat(TAGs) which leads to increase in the number and size of adipocytes.

**QUESTION 2**

**2a) HOW CONGENITAL SYNDROME AFFECT OBESITY**

Congenital obesity is the excessive accumulation and storage of fat in the body that is present during infancy and/or childhood. Obesity may be diagnosed as an isolated clinical finding or as a part of syndromic findings. Monogenic forms of childhood obesity are very rare. Mutations in only a few genes controlling appetite and metabolism are known to cause the development of severe obesity in early childhood.
Syndromic causes of congenital and early-onset obesity include:

* Albright hereditary osteodystrophy
* Alstrom syndrome
* Bardet-Biedl syndrome
* Borjeson-Forssman-Lehmann syndrome
* Cohen syndrome
* Schaaf-Yang syndrome (also called Prader-Willi-like syndrome)
* Leptin deficiency
* Leptin receptor deficiency
* MC4R (melanocortin 4 receptor) deficiency

**CONGENITAL LEPTIN DEFICIENCY**: is a condition that causes severe obesity beginning in the first few months of life. Affected individuals are of normal weight at birth, but they are constantly hungry and quickly gain weight. Without treatment, the extreme hunger continues and leads to chronic excessive eating (hyperphagia) and obesity. Beginning in early childhood, affected individuals develop abnormal eating behaviors such as fighting with other children over food, hoarding food, and eating in secret.

People with congenital leptin deficiency also have hypogonadotropic hypogonadism, which is a condition caused by reduced production of hormones that direct sexual development. Without treatment, affected individuals experience delayed puberty or do not go through puberty, and may be unable to conceive children (infertile). It is a rare disorder.

Congenital leptin deficiency is caused by mutations in the *LEP* gene. This gene provides instructions for making a hormone called leptin, which is involved in the regulation of body weight. Normally, the body's fat cells release leptin in proportion to their size. As fat accumulates in cells, more leptin is produced. This rise in leptin indicates that fat stores are increasing.

Leptin attaches (binds) to and activates a protein called the leptin receptor, fitting into the receptor like a key into a lock. The leptin receptor protein is found on the surface of cells in many organs and tissues of the body including a part of the brain called the hypothalamus. The hypothalamus controls hunger and thirst as well as other functions such as sleep, moods, and body temperature. It also regulates the release of many hormones that have functions throughout the body. In the hypothalamus, the binding of leptin to its receptor triggers a series of chemical signals that affect hunger and help produce a feeling of fullness (satiety).

*LEP* gene mutations that cause congenital leptin deficiency lead to an absence of leptin. As a result, the signaling that triggers feelings of satiety does not occur, leading to the excessive hunger and weight gain associated with this disorder. Because hypogonadotropic hypogonadism occurs in congenital leptin deficiency, researchers suggest that leptin signaling is also involved in regulating the hormones that control sexual development. However, the specifics of this involvement and how it may be altered in congenital leptin deficiency are unknown.

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

2b) **HOW DRUG THERAPY AFFECT OBESITY**

Drug therapy involves the use of anti-obesity drugs which reduce or control weight. These medications alter one of the fundamental processes of the human body, weight regulation, by altering either appetite, or absorption of calories. Anti-obesity drugs can be classified into three main categories according to their mode of action and are as follows:

1. Drugs inhibiting intestinal fat absorption
2. Drugs suppressing food intake: This includes medications which modulate the production of neurotransmitters or act on their receptors in the central nervous system so as to suppress appetite. E.g.: noradrenergic, serotoninergic, serotoninergic and adrenergic drugs and selective cannabinoid type-1 (CB1) receptor antagonist.
3. Drugs increasing energy consumption and thermogenesis

**QUESTION 3**

3a) **ETIOLOGY OF CANCER**

The etiology of cancer is multifactorial, which means different factors play a role in the cause of cancer. These factors can be classified into:

* Factors within the cell e.g. Inherited factors
* External factors e.g. environmental factors

 The causes of cancer are:

1. **Carcinogens**: These are mutagens that cause DNA damage which leads to mutation and also affect DNA repair gene which causes cancer. About 50% of human cancer is as a result of mutation/deletion of this repair gene called antioncogene/onco-suppressor gene

Physical carcinogens; x-ray, UV light, gamma rays etc.

Chemical carcinogens; aniline, abestors, tobbacco, food additives, natural chemicals etc.

1. **Hormones**: e.g. steroid hormones
2. **Hereditary gene**: a mutated gene causing cancer has 50% chance of being passed to the offspring e.g. xerodermal pigmentosa, familial adenonatous polypocoli.
3. **Oncogenic Viruses/onco virus:** These viruses get integrated into the host’s DNA leading to multiplication of viral gene, overtaking that of the host’s gene leading to uncontrolled multiplication of cells.

3b) **MOLECULAR BASIS OF CANCER**

Cancer is a disease of uncontrolled growth and proliferation whereby cells have escaped the body’s normal growth control mechanisms and have gained the ability to divide indefinitely. It is a multi-step process that requires the accumulation of many genetic changes over time. These genetic alterations involve activation of proto-oncogenes to oncogenes, deregulation of tumour suppressor genes and DNA repair genes and ‘immortalisation.’

**Cell cycle regulation and the importance of apoptosis**

Normal cells replicate normally and later the old cells are removed by a natural process, apoptosis. The molecular basis of this is seen in the shortening of telomeres on the chromosomes in normal cells. Cancer cells are able to escape apoptosis of the normal cell cycle. All normal cells receive signals for apoptosis while chemicals that cause cancer, destroy the signals hence cancer cells continue to multiply uncontrollably.

**Cell immortalisation and tumourigenesis**

Immortalisation is defined as the acquisition of an infinite lifespan. Normal mammalian **somatic** cells proliferate a limited number of times before undergoing senescence. Senescent cells may remain metabolically active even though they have permanently ceased proliferation. Immortalisation is an essential step in the malignant transformation of normal cells and can be attributed, in part, to the presence of **telomerase**, the enzyme responsible for maintaining telomeres at the ends of chromosomes. By extending telomeric DNA, telomerase is able to counter the progressive telomere shortening that would otherwise lead to cell death. Unlike normal cells that lack detectable levels of telomerase activity, approximately 90% of human tumours consist of cells that contain an active telomerase enzyme.