MATRIC NO: 17/MHS01/302

DEPT.: MBBS

COURSE TITTLE: BIOCHEMISTRY 3

QUESTION 1:

What do you understand by primary or simple obesity?

ANSWER

OBESITY: obesity is a disorder of body weight regulatory system characterized by an accumulation of excess body fat, lifestyle availability of high calories food etc. in mammals a complex set of hormonal and neural signals act to keep fuel and energy expenditure in balance so as to hold he amount of adipose tissue in a suitable level. Obesity occurs when energy intake exceeds energy expenditure.

Simple obesity: simple obesity is one of the classes of obesity characterized by a normal or increased growth rate with an acceleration of bone age maturation. It is simply obesity that results when caloric intake exceeds energy expenditure. When longitudinal growth slows down in the presence of obesity, a hormonal disturbance should be sought. Despite normal growth, simple obesity is characterized by a reduced growth hormone secretion. It is also associated with high insulin and insulin-like growth factor 1 levels which may interfere in the complex endocrine secretions. It is not associated with clinical disorders.

QUESTION 2

How does congenital syndrome and drug therapy affect obesity?

ANSWER

EFFECTS OF CONGENITAL SYNDROMES ON OBESITY:

Unlike in monogenic disorders, where obesity begins very early in infancy, in obesity-related syndromes it begins after infancy. Other than obesity, basic syndrome features include dysmorphia, psychomotor retardation and anomalies of certain organ systems. They can occur due to gene or larger chromosomal abnormalities. Autosomal or X chromosomes can be affected. They include:

1. **Bardet-Biedl Syndrome (BBS):** (BBS) is a heterogeneous autosomal recessive disorder due to mutations in one of the 15 possible genes that control cilliary function. The role of cilia in regulating body mass has been confirmed in mice. Primary cilliary disorders by inactivating mutations of the Tg737 and Kif3a genes in POMC neurons, i.e. the leptin signal pathway, lead to hyperphagia and obesity. Classical clinical features include severe

early-onset obesity, retinitis pigmentosa, hypogonadism, mental retardation, glucose intolerance, postaxial polydactyl, deafness and kidney disorders. Mortality is a consequence of obesity and kidney disease complications.

2. **Alström's syndrome:** (AS) is a rare autosomal recessive disorder due to the mutation of the ALMS1 gene located on chromosome 2p13, which also disrupts cilliary function. In addition to early central obesity like in children with BBS, children with AS also have visual impairment and deafness. Central obesity develops by 5 years of age, and the affected children have acanthosis nigricans and type 2 diabetes more often than children with BBS. Other endocrinopathies include hypothyroidism, primary hypogonadism in boys and GH deficiency. Intellectual development is normal.
3. **Carpenter syndrome:** besides obesity, includes mental retardation, short stature, brachiocephalus, polydactyly, foot syndactyly, cryptorchidism, hypogonadism in boys, umbilical hernias and high palate. The RAB23 gene is located on chromosome 6p11. Like in Alström's and Bardet-Biedl's syndromes, this gene mutation also causes an impaired function of proteins involved in the cilliary body important for intercellular communication in mammals. The disorder also seems to disrupt communication between the neurons involved in the leptin signal pathway, crucial for energy homeostasis.
4. **Cohen's syndrome**: is characterized by hypotonia and failure to thrive during infancy, and the central obesity develops in mid-childhood. The clinical features include microcephaly, mental retardation, cryptorchidism, small hands and feet with long, thin fingers as well as marked central incisors. The COH1 gene, whose mutation causes these disorders, is located on chromosome 8q22 and encodes a transmembrane protein with a still unknown function.
5. **Prader-Willi syndrome (PWS)**: a rare and complex genetic disorder that affects many organ systems, is a consequence of the lack of expression of paternal genes in the 15q11-q13 region. From the earliest age it causes reduced muscle tone that impairs feeding and development. Due to excessive food intake, severe obesity develops. In spite of the obesity these children lag in growth and are of short stature, there is no sexual development and psychomotor development is also delayed. The disease is characterized by numerous complications, primarily obesity associated, which significantly impair the quality of life and shorten life expectancy. First of all, it is necessary to ensure control of food intake and thereby prevent the development of severe obesity and, by applying habilitation measures, to enhance the psychomotor development of the child.
6. **Albright's hereditary osteodistrophy:** involves a phenotype with short stature and obesity, along with a shortening of the 4th metacarpal bone as well as pseudohypoparathyroidism type 1a (PHP 1a) and pseudopseudohypoparathyroidism (PPHP). In case of PHP 1a with hypocalcaemia and mental retardation, hypothyroidism can develop due to TSH resistance and delayed puberty or hypogonadism due to gonadotropin resistance. The responsible GNAS1 gene is located on chromosome 20q13.2. Patients have an inactivating mutation in the stem cells involving the α-subunit

of the widespread stimulating G protein, which is a component of many hormone receptors involved in the adenylate-cyclase signal pathway.

7. **WAGR syndrome**: includes Wilms tumor, aniridia, genitourinary tract abnormalities and mental retardation, while obesity is present only in some patients. The syndrome is caused by a deletion on chromosome 11p11.4, near the gene responsible for BDNF production. BDNF is regulated by nutritional status and included in the leptin signal pathway in the hypothalamus where it stimulates the production, differentiation and survival of neurons, but also body mass regulation. Most WAGR syndrome patients with the deletion which includes BDNF are obese, unlike those with no deletion, in whom the frequency of obesity is consistent with that in the general population.

EFFECT OF DRUG THERAPY ON OBESITY:

1. **Prader-Willi syndrome (PWS)**: In the last few years, growth hormone has been introduced in the treatment, since GH deficiency was recorded in approximately 80% of PWS children. This therapy accelerates growth, improves final height and has a positive effect on body composition, primarily by reducing the amount of fat tissue. Therapy is maintained until the final height is achieved, but its positive effect on the patient's metabolic status persists several years after its discontinuation. The appetite regulation disorder in PWS is manifested by the inability to stop eating, repeated food intake soon after the previous meal and consumption of inedible items. This is not a consequence of an increased sense of hunger, but of a lack of satiety because of a hypothalamic disorder and increased stimulation of the ventromedial prefrontal cortex region as a response to food, as evidenced by functional magnetic resonance studies. Due to the disorder that most likely primarily affects the hypothalamus, deficiencies of other pituitary and peripheral gland hormones can develop, almost always leading to hypogonadotropic hypogonadism and hypothyroidism or adrenal gland insufficiency.
2. **Treatment of obesity with Orlistat:** Orlistat deactivates intestinal lipase and inhibits intestinal fat lipolysis. Orlistat therapy reduces weight to a modest extent, but it reduces the incidence of diabetes beyond the results achieved with life style changes.

QUESTION 3

Outline the Etiology of cancer and its molecular basis

ANSWER

ETIOLOGY OF CANCER

Cancer arises from factors within the cell and external factors within the environment eg inherited mutations, thus etiology of cancer is multifactorial i.e. physical, chemical, hormonal,

metabolic, environmental and genetic factors all play a role. This factors cause gene mutation that results in cancer. Carcinogens are mutagens and vice versa. In summary, carcinogens whether physical or chemical cause DNA damage which leads to mutation and mutation causes cancer. Every normal cell has DNA repair mechanism that correct s defects which occur during replication. Carcinogens and inherited mutations affect DNA repair gene which results in cancer. About 50% of human cancer is due to mutation and deletion of this repair gene called **anti-oncogene** or **oncosupressant gene.**

MOLECULAR BASIS OF CANCER

Normal cells tend to replicate normally and as they get older, they are removed by a natural process called apoptosis. The molecular basis is seen in shortening of telomeres. Cancer cells are able to escape apoptosis of the normal cell cycle. They accomplish this by production of telomere polymerase which elongates the telomeres and thereby prolong the life span of the cancer cells, preventing apoptosis. All normal cells receives signal for apoptosis. Chemicals that cause cancer destroy this signals, hence cells continue to multiply uncontrollable.