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Matric. number: 17/mhs01/164

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Course: Medical Biochemistry

1.What do you understand by primary or simple obesity

Primary obesity is most commonly caused by a combination of [excessive food intake](https://en.wikipedia.org/wiki/Gluttony), lack of physical activity, and [genetic susceptibility](https://en.wikipedia.org/wiki/Quantitative_trait_locus). It is not caused as a result of any medical condition. It is the most common type of obesity found in humans. Obesity is mostly preventable through a combination of social changes and personal choices. Changes to [diet](https://en.wikipedia.org/wiki/Diet_%28nutrition%29) and [exercising](https://en.wikipedia.org/wiki/Physical_exercise) are the main treatments. Diet quality can be improved by reducing the consumption of energy-dense foods, such as those high in fat or sugars, and by increasing the intake of [dietary fiber](https://en.wikipedia.org/wiki/Dietary_fiber). [Medications](https://en.wikipedia.org/wiki/Anti-obesity_medication) can be used, along with a suitable diet, to reduce appetite or decrease fat absorption. If diet, exercise, and medication are not effective, a [gastric balloon](https://en.wikipedia.org/wiki/Gastric_balloon) or [surgery](https://en.wikipedia.org/wiki/Bariatric_surgery) may be performed to reduce stomach volume or length of the intestines, leading to feeling full earlier or a reduced ability to absorb nutrients from food

Secondary obesity means that one has a medical condition that has caused you to gain weight. These diseases include endocrine disorders, hypothalamic disorders and some congenital conditions. While few patients fit into this category, it is important to get a clean bill of health before starting any new nutrition or exercise regimen. Some of the more common endocrine disorders include a deficiency in thyroid hormone(hypothyroidism) and polycystic ovarian syndrome(pcos). There are alsosome rare causes of secondary obesity like cushings disease(hypercortisolism),hypothalamic injury or disorders and genetic mutations.

2. how does congenital syndrome or drug therapy affects obesity

 some cases of obesity are “endogenous”, associated with hormonal, genetic, or syndromic disorders such as hypothyroidism, Cushing’s syndrome, growth hormone deficiency, defective leptin signaling, mutations in the melanocortin 4 receptor, and Prader-Willi and Bardet-Biedl syndromes.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. Some congenital syndrome that affects obesity are 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. Prader-Willi syndrome (PWS), caused by functional absence of the paternal allele of 15q11-13, affects one in every 15,000 to 30,000 births. Birth weight is normal or slightly low, and infants fail to gain weight, often requiring tube feedings, due to hypotonia and poor suck. Following a period of limited catch-up weight gain from 6 to 18 months, children develop an insatiable appetite, resulting in obesity by age 6.The relatively high levels of ghrelin in children with PWS may contribute to hyperphagia and excess weight gain because ghrelin has been shown to stimulate food intake in adults. Physical features include small hands and feet and dysmorphic facies characterized by almond-shaped palpebral fissures and a downturned mouth with a thin upper lip. Affected children often have a fair complexion and suffer from developmental delay, delayed puberty, and poor linear growth secondary to growth hormone deficiency. Growth hormone replacement improves body composition in children with PWS and has beneficial effects on linear growth. Diagnosis of PWS is made through methylation studies.Bardet-Biedl syndrome is a heterogeneous autosomal recessive disorder caused by a defect in one of 15 genes involved in ciliary function. The prevalence of this group of disorders is one in 13,500 to 160,000 individuals depending on geographic location. Energy dysregulation is thought to arise from defective leptin activity. Classic features include early-onset obesity, cognitive impairment, delayed puberty, renal anomalies (calyceal clubbing, parenchymal cysts, vesicoureteral reflux, hydronephrosis), post-axial polydactyly, and rod-cone dystrophy.Hearing loss, diabetes mellitus, and congenital heart disease may also occur. Complications from morbid obesity and renal disease are the most common causes of mortality.Alström syndrome (AS) is a rare autosomal recessive disorder affecting fewer than one in every 1,000,000 people. It is caused by a mutation in ALMS1, resulting in defective ciliary function. Children typically develop obesity by age 5 years. Like children with Bardet-Biedl syndrome, children with AS have visual impairment and sensorineural hearing loss, although the incidence of deafness is higher in those with AS and typically occurs in the first decade of life. Another distinguishing feature is the high incidence of type 2 diabetes, which occurs in up to 70% of individuals by age 20 years.[26](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4369917/#R26) Other endocrinopathies include growth hormone deficiency, hypertriglyceridemia, pubertal delay, and hyperandrogenism. AS is also associated with renal anomalies and cardiomyopathy, the most common cause of mortality in affected individuals.Albright’s hereditary osteodystrophy is caused by a mutation in GNAS1, leading to a defect in the alpha subunit of G proteins (Gαs) coupled to transmembrane receptors. Genomic imprinting in tissues including the kidney, thyroid, pituitary somatotropes, gonads, and chondrocytes results in wide phenotypic variability. Excess weight gain may occur during infancy and is thought to arise from Gαs deficiency in imprinted regions of the hypothalamus. Round facies, brachydactyly, metacarpia of hands and/or feet, and heterotopic ossifications are classic characteristics. Other features include early-onset hypothyroidism without goiter due to TSH resistance, short stature from a defect in growth hormone–releasing hormone (GHRH) action, and pubertal delay due to TSH, GHRH, and gonadotropin resistance. Pseudohypoparathyroidism, characterized by hypocalcemia and hyperphosphatemia despite high levels of PTH, may also occur.WAGR syndrome, characterized by Wilms’ tumor, aniridia, genitourinary anomalies, and mental retardation, is another disorder that may be associated with both obesity and cognitive impairment. It is caused by a deletion on 11p14.1, located near the gene responsible for brain-derived neurotrophic factor (BDNF) production. BDNF is regulated by nutritional status and MC4R signaling and is expressed in the hypothalamus, where it facilitates neuronal proliferation, survival, and differentiation. Interestingly, the majority of patients with WAGR and BDNF deletions are obese; in contrast, the rate of obesity in those without BDNF deletions is comparable to that of the general United States population.Genome-wide association studies have identified other genetic variants thought to predispose to obesity. Many are associated with intellectual disability or developmental delay, demonstrating the critical role of affected genes in maintaining neurologic function and energy balance. Of particular interest are variants on chromosome 1 and the short arm of chromosome 16 (1q21.1, 16p11.2, and 16p12.1 microdeletions). In addition to obesity and developmental delay/intellectual disability, these genetic variants have been associated with autism, schizophrenia, and cardiac and renal anomalies. Continued advances in the field may uncover additional genes implicated in obesity, promoting our understanding of the complex nature of this disorder and leading to the discovery of new obesity-related syndromes.

Pharmacotherapy is a second step in the treatment of obesity, approved only when weight loss targets were not reached through lifestyle intervention. During the history of antiobesity drugs, many of them were withdrawn because of their side effects. Various guidelines recommend prescribing drug therapy for obesity through consideration of the potential benefits and limitations. Orlistat deactivates intestinal lipase and inhibits intestinal fat lipolysis. It is actually the only drug on the European market approved for the treatment of obesity. Orlistat therapy reduces weight to a modest extent, but it reduces the incidence of diabetes beyond the result achieved with lifestyle changes. Recently, some effective antiobesity drugs like sibutramine and rimonabant have been removed from the market due to their side effects. The new combination of topimarate and fentermine is approved in the US but not in Europe.

3. Outline the aeitiology of cancer and its molecular basis

1. The substances that cause cancer are called carcinogens. A carcinogen may be a chemical substance, such as certain molecules in tobacco smoke. The cause of cancer may be environmental agents, viral or genetic factors.The majority of cancer cases cannot be attributed the disease to a single cause.We can roughly divide cancer risk factors into the following groups: 1**.** biological or internal factors, such as age, gender, inherited genetic defects and skin type
2. environmental exposure, for instance to radon and UV radiation, and fine particulate matter
3. occupational risk factors, including carci nogens such as many chemicals, radioactive materials and asbestos
4. lifestyle-related factors.

**Lifestyle-related factors that cause cancer include:**

* tobacco
* alcohol
* UV radiation in sunlight
* some food-related factors, such as nitrites and poly aromatic hydrocarbons generated by barbecuing food).

**Cancer causing factors related to work and living environments include:**

* asbestos fibres
* tar and pitch
* polynuclear hydrocarbons (e.g. benzopyrene)
* Some metal compounds
* Some plastic chemicals (e.g. Vinyl chloride)

**Bacteria and viruses can cause cancer:**

* Helicobacter pylori (H. pylori, which causes gastritis)
* HBV, HCV (hepatitis viruses that cause hepatitis)
* HPV (human papilloma virus, papilloma virus, which causes changes eg. Cervical cells)
* EBV (Epstein-Barr virus, the herpes virus that causes inflammation of the throat lymphoid)

**Radiation can cause cancer:**

* ionising radiation (e.g. X-ray radiation, soil radon)
* non-ionised radiation (the sun’s ultraviolet radiation)

**Some drugs may increase the risk of cancer:**

* certain antineoplastic agents
* certain hormones
* medicines that cause immune deficiency

In 5 – 10 per cent of breast cancer genetic predisposition plays an important role in the emergence of the disease. Normally cell replicate and are removed from a natural process. Apoptosis at an old age. The molecular basis of the cell is seen in shortening of the telomeres at their chromosomes, cancer cell can escape apoptosis of normal cell cycle. The accomplish this by lengthening of telomeres through the enzyme, telomere polymerase. In this way cancer cells life is prolonged through prevention of apoptosis and thus cancer cells are immortalized. All cancer cells receive signal for apoptosis, chemicals that cause cancer to destroy the signals hence cell continue to multiply uncontrollably.