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ASSIGNMENT

1. What do you understand by primary or simply obesity?
2. How does Congenital Syndrome and Drug Therapy affect obesity?
3. Outline the aetiology of cancer and its molecular basis.

1) PRIMARY OR SIMPLE OBESITY

OBESITY

Obesity is a nutritional disorder in which excess body fat is accumulated to an extent that it may have a negative effect on health. People are generally considered obese when their **body mass index (BMI),** a measurement obtained by dividing a person's weight by the square of the person's height, is over **30 kg/m²**; the range **(25–30 kg/m²)** is defined as overweight.

If the intake of metabolic fuel is consistently greater than energy expenditure, there will be excess triacylglycerides (TAGs) production, which will lead to increased number of adipocytes.

Causes of Obesity

1. **Metabolic:** In metabolic, triacylglycerides accumulates when calorie intake exceeds the amount needed for body function leading to weight gain.
2. **Hormonal;** Obesity may result from endocrine disorders like hypothyroidism, hypogonadism and Cushing's Syndrome.

Classes of Obesity

a. Primary or Simple Obesity
b. Secondary Obesity.

PRIMARY OBESITY

Primary obesity can be defined simply as obesity that is gotten without any prior medical conditions such as endocrine disorders, hypothalamic disorder and even congenital disorders.

This is the class of obesity that is gotten through mainly metabolic causes and has no hormonal connection whatsoever. In this case, triacylglycerides accumulate when calorie intake exceeds the amount needed for normal body function and this will eventually lead to excess weight gain and eventually obesity.

However, though it may not be caused by any prior medical conditions, it eventually leads to other medical condition such as hypertension, diabetes, myocardial infarction and major cardiovascular events. Metabolic diseases most associated with primary obesity contribute to atherosclerosis, hypertension, dyslipidemia, diabetes type II, hyperandrogenemia in women and hypoandrogenemia/hyperestrogenemia in men.

2) How does Congenital Syndrome and Drug Therapy affect obesity?

Congenital Syndrome

Congenital anomalies can be **defined** as structural or functional anomalies (for example, metabolic **disorders**) that occur during intrauterine life and can be identified prenatally, at birth, or sometimes may only be detected later in infancy, such as hearing defects. Congenital disorders can be inherited or caused by environmental factors and their impact on a child's health and development can vary from mild to severe. A child with a congenital disorder may experience a disability or health problems throughout life.

The relationship between congenital syndrome and obesity has to do with secondary obesity (**Secondary obesity** means that you have a medical condition that has caused you to gain weight. These diseases include endocrine disorders, hypothalamic disorders and some congenital conditions).

Some congenital disorders include;

1. Prader–Willi syndrome,
2. Bardet–Biedl syndrome,
3. Cohen syndrome,
4. Albright hereditary osteodystrophy
5. Borjeson–Forssman–Lehmann syndrome
6. Alstrom syndrome
7. Carpenter syndrome,
8. MOMO syndrome,
9. Rubinstein-Taybi syndrome,

Most congenital syndromes associated with obesity usually have to do with the loss of imprinted genes on 15q11-13. This is the commonest cause obesity syndrome disorders.

DRUG THERAPY

NEGATIVE EFFECTS OF DRUG IN OBESITY

Drug-induced weight gain is a serious side effect of many commonly used drugs leading to noncompliance with therapy and to exacerbation of comorbid conditions related to obesity. Improved glycemic control achieved by insulin, insulin secretagogues or thiazolidinedione therapy is generally accompanied by weight gain. It is a problematic side effect of therapy due to the known deleterious effect of weight gain on glucose control, increased blood pressure and worsening lipid profile. Weight gain may be lessened or prevented by adherence to diet and exercise or combination therapy with metformin. Weight gain is also common in psychotropic therapy. The atypical antipsychotic drugs (clozapine, olanzepine, risperidone and quetiapine) are known to cause marked weight gain. Antidepressants such as amitriptyline, mirtazapine and some serotonin reuptake inhibitors (SSRIs) also may promote appreciable weight gain that cannot be explained solely by improvement in depressive symptoms. The same phenomenon is observed with mood stabilizers such as lithium, valproic acid and carbamazepine. Antiepileptic drugs (AEDs) that promote weight gain include valproate, carbamazepine and gabapentin. Lamotrigine is an AED that is weight-neutral, while topiramate and zonisamide may induce weight loss.

POSITIVE EFFECTS OF DRUGS IN OBESITY

A doctor may recommend weight-loss medication if other diet and exercise programs haven't worked and you meet one of these criteria:

- Your body mass index (BMI) is 30 or greater
- Your BMI is greater than 27, and you also have medical complications of obesity, such as diabetes, high blood pressure or sleep apnea.

Anti-obesity medication or **weight loss medications are** pharmacological agents that 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 medications approved by the Food and Drug Administration (FDA) include:

- Orlistat (Alli, Xenical)

- Phentermine and topiramate (Qsymia)
- Bupropion and naltrexone (Contrave)
- Liraglutide (Saxenda, Victoza)

A close medical monitoring while taking a prescription weight-loss medication will be needed in order to avoid overuse of the medication and dangerous side effects.. Also, keep in mind that a weight-loss medication may not work for everyone, and the effects may wane over time. When you stop taking a weight-loss medication, you may regain much or all of the weight you lost.

3) Outline the aetiology of cancer and its molecular basis.

AETIOLOGY OF CANCER

Cancer is a disease caused by genetic changes leading to uncontrolled cell growth and tumor formation. The basic cause of sporadic (non-familial) cancers is DNA damage and genomic instability. A minority of cancers are due to inherited genetic mutations. Most cancers are related to environmental, lifestyle, or behavioral exposures. Cancer is generally not contagious in humans, though it can be caused by oncoviruses and cancer bacteria. The term "environmental", as used by cancer researchers, refers to everything outside the body that interacts with humans. The environment is not limited to the biophysical environment (e.g. exposure to factors such as air pollution or sunlight), but also includes lifestyle and behavioral factors.

The aetiology of cancer is multifactorial; chemical, hormonal, metabolic, genetical and environmental factors all have a role in the development of cancer. They cause mutation of genes in the cancer and this eventually leads to multiplication. Thus carcinogens are mutagenes and vice versa, anything that causes cancer causes mutations though not everything that causes mutations cause cancer.

The aetiology of cancer can be divided into the following groups;

1. **GENETICS**

Although there are over 50 identifiable hereditary forms of cancer, less than 0.3% of the population, are carriers of a cancer-related genetic mutation and these make up less than 3–10% of all cancer cases. The vast majority of cancers are non-hereditary ("sporadic cancers"). Hereditary cancers are primarily caused by an inherited genetic defect. A cancer syndrome or family cancer syndrome is a genetic disorder in which inherited genetic mutations in one or more genes predisposes the affected individuals to the development of cancers and may also cause the early onset of these cancers.

Although cancer syndromes exhibit an increased risk of cancer, the risk varies. For some of these diseases, cancer is not the primary feature and is a rare consequence.

Many of the cancer syndrome cases are caused by mutations in tumor suppressor genes that regulate cell growth. Other common mutations alter the function of DNA repair genes, oncogenes and genes involved in the production of blood vessels. Certain inherited mutations in the genes **BRCA1** and **BRCA2** with a more than **75%** risk of **breast cancer** and **ovarian cancer.** Some of the inherited genetic disorders that can cause **colorectal cancer** include **familial adenomatous polyposis** and **hereditary non-polyposis colon cancer**; however, these represent less than 5% of colon cancer cases. In many cases, genetic testing can be used to identify mutated genes or chromosomes that are passed through generations. Other cancer syndromes include**; Von Hippel-Lindau disease, Werner syndrome, Xeroderma pigmentosum.**

2. CARCINOGENS

A carcinogen is any substance, radionuclide, or radiation that promotes carcinogenesis, the formation of cancer. This may be due to the ability to damage the genome or to the disruption of cellular metabolic processes.

a. Physical carcinogens which include; X-ray, UV light rays, Gamma rays.
b. Chemical carcinogens are aninine, obestos, arsenic, beryllium, tobacco (nicotine, benzopyrise, Carbon Monoxide).
c. Food additives and coluring agents.
d. Natural chemicals like aflotoxin B (which is found in fungus that is found in molds that grow in moist and damp food).

3. LIFESTYLE

Many different lifestyle factors contribute to increasing cancer risk. Together, diet and obesity are related to approximately 30–35% of cancer deaths. Dietary recommendations for cancer prevention typically include an emphasis on vegetables, fruit, whole grains, and fish, and avoidance of processed meat, red meat, animal fats, and refined carbohydrates. The evidence to support these dietary changes is not definitive.

4. HORMONES

Some hormones play a role in the development of cancer by promoting cell proliferation. Insulin-like growth factors and their binding proteins play a key role in cancer cell growth, differentiation and apoptosis, suggesting possible involvement in carcinogenesis.

Hormones are important agents in sex-related cancers such as cancer of the breast, endometrium, prostate, ovary, and testis, and also of **thyroid cancer** and **bone cancer.** For example, the daughters of women who have breast cancer have significantly higher levels of **estrogen** and **progesterone** than the daughters of women without breast cancer. These higher hormone levels may explain why these women have higher risk of **breast cancer**, even in the absence of a breast-cancer gene. Similarly, men of African ancestry have significantly higher levels of **testosterone** than men of European ancestry, and have a correspondingly much higher level of **prostate cancer.** Men of Asian ancestry, with the lowest levels of testosterone-activating androstanediol glucuronide, have the lowest levels of prostate cancer.

5. <u>ONCOGENIC VIRUSES</u>

These viruses get integrated in the host DNA leading to the multiplication of the viral gene and that multiplication overtakes the normal multiplication of the cells causing uncontrollable multiplication of the cancer gene.

HUMAN VIRUS	ABBREVIATION	ASSOCIATED CANCER
Epstein-Barr Virus	EBV	1. Burkitts Lymphoma 2. Nasopharyngeal Carcinoma
Hepatitis B Virus	HBV	Hepatoma/ Hepatocellullar carcinoma.
Human Papilloma Virus	HPV	Uterocervical carcinoma
Human Immuno Deficiency Virus	HIV	1. Kaposis Sarcoma 2. Non- Hodgkin Lymphoma

Other causes include;

- Organ transplantation
- Trauma
- Bacterial Infections
- Parasites
- Inflammation.

MOLECULAR BASIS OF CANCER

The molecular basis of cancer can be seen by their ability to avoid apoptosis(programmed cell death) by lengthening the telomeres of the carcinogenic cells which will eventually lead to immortalization.

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.