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**MATRIC NO: 17/MHS03/014**

**COURSE TITLE: CELLULAR BIOCHEMISTRY**

**COURSE CODE; BCH308**

1.what do you understand by primary obesity.

2.How does drug therapy and congenital syndrome affect secondary obesity

3.Discuss the aetiology of cancer and its molecular basis

ANSWERS

**PRIMARY OBESTIY**

Obesity is a medical condition in which excess body fat has 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

Primary obesity is due to excessive energy intake and too little consumption. It's also known as diet-induced obesity and has the largest proportion in all types of obesity( about 95%).Primary obesity is characterized by a normal or increased growth rate with an acceleration of bone age maturation, It is not associated with clinical condition . 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 evaluated by standard provocative tests, the administration of growth releasing hormone or spontaneous 24-hour secretion. It is also associated with high insulin and insulin-like growth factor I levels which may interfere in the complex endocrineinteractions. It is not associated with clinical condition.

HOW CONGENITAL SYNDROME AFFECTS OBESITY

Syndromic obesity corresponds to severe obesity associated with additional phenotypes (mental retardation, dysmorphic features, and organspeciﬁc developmental abnormalities). Prader-Willi (PWS) and BardetBiedl (BBS) syndromes are the 2 syndromes most frequently linked to obesity, but more than 100 syndromes are now associated with obesity.

- Prader-Willi: some clinical features associated to obesity; neonatal hypotonia, mental retardation, hyperphagia, facial dysmorphy, hypogonadism, shoet stature.

- Bardet- Biedl: some clinical features associated with obesity; mental retardation, renal dystrophy or pigmentary retinathy, dysmorphic extremeities, hypogonadism, kidney anomalies.

HOW DRUG THERAPY AFFECTS OBESITY

Drug therapy plays an important complementary role in an integrated strategy for managingobesity**.**

• Medication treatment of obesity should be used only in patients who have health risks related to obesity. Medications should be used in patients with a BMI greater than 30 or in those with a BMI of greater than 27 who have other medical conditions (such as high blood pressure, diabetes, high blood cholesterol) that put them at risk for developing heart disease. Medications should not be used for cosmetic reasons.

• Medications should only be used as an adjunct to diet modiﬁcations and an exercise program.

Various pharmacologic agents, referred to as anorectic drugs, are used as adjuncts to behavioral therapy in weight reduction programs. The two classes of anorectic drugs currently available are the noradrenergic and the serotonergic agents.

1. Noradrenergic drugs affect weight loss through action in the appetite center.Phenylpropanolamine (Dexatrim), a sympathomimetic drug and a synthetic derivative of ephedrine, is available as an over-the-counter appetite suppressant and decongestant. In studies lasting 14 weeks, the subjects who took phenylpropanolamine had a greater weight loss than those who took placebo, although the difference was minimal.

2. The serotonergic drugs partially inhibit the reuptake of serotonin and release serotonin into the synaptic cleft, thus acting on the hypothalamus to decrease satiety.

Fluoxetine (Prozac) is a highly selective serotonin reuptake inhibitor (SSRI) that has been studied in the treatment of obesity. Fluoxetine may increase energy expenditure by raising basal body temperature; however, weight loss has not been consistent among subjects in clinical trials. In a three-month study, fluoxetine did not significantly reduce weight when compared with placebo. In a longer clinical trial, significantly greater weight loss was achieved in the subjects takingfluoxetine at 20 weeks, compared with the subjects taking placebo. However, after one year, weight loss was not different in the two groups.

3. Adrenergic/Serotonergic Agents. Sibutramine (Meridia) is an adrenergic/serotonergic agent recently labeled by the FDA for use in the management of obesity.Sibutramine and its metabolite inhibit monoamine uptake, suppressing appetite in a fashion similar to SSRIs. Sibutramine may also stimulate thermogenesis by activating the beta3-system in brown adipose tissue. Initially tested for its antidepressant activity, sibutramine was found to cause weight loss 1 to 2 kg (2.2 to 4.4 lb) in healthy and depressed patients. In six-month studies, weight loss in subjects taking sibutramine, although modest, was found to be significantly greater than the loss in subjects taking placebo, and weight loss increased with increasing dosages. In a continued, open-label, 96-week extension study, weight was regained even in subjects taking high-dose sibutramine.

Sibutramine is indicated for the management of obesity, including weight loss and maintenance of weight loss, and should be used in conjunction with a reduced calorie diet. It is recommended for obese patients with an initial BMI of greater than 30 kg per m2, or greater than 27 kg per m2 in the presence of other risk factors (e.g., hypertension, diabetes, hyperlipidemia).

**the aetiology of cancer and its molecular basis**

MOLECULAR BASIS

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’.

Normally, normal cells replicate and remove from the body through apoptosis, a natural process - The molecular basis of this is seen in the shortening of the telomeres on the chromosomes on the normal cells - Cancer cells are able to escape apoptosis of the normal cell cycle. They accomplish this by production of the enzyme, TELOMERE POLYMERASE, which tends to lengthen the telomere which prolongs life. In this way cancer cells are immortalised because they escaped apoptosis - All normal cells receive signal for apoptosis, chemicals that cause cancer destroy signals hence cells continue to multiply uncontrollably .

**AETIOLOGY OF CANCER**

About 50% of human cancer is due to mutation or deletion of repair gene called anti oncogensor oncosuppressor gene . Exposure to mutagens or radiation greatly increases the mutation rate and thus the probability of developing cancer

Commeon causes of cancers are;

* Carcinogens
* oncongenic virus
* multifactorial
* genetic factor
* environment factors
* **CARCINOGENS**

Carcinogens are agents which can induce cancer ***.*** Carcinogens are a variety of external agents which are divided into three groups:

1. Chemical carcinogens

2. Physical carcinogens

3. Biologic carcinogens

**Chemical carcinogens** comprise a quite disparate group of chemicals that modify DNA through a range of mechanisms, such as alkylation or deamination of DNA bases, or through intercalation between base pairs and formation of DNA adducts (e.g. aromatic hydrocarbons). Oxidative damage may also affect DNA integrity. Examples of chemical carcinogens alfatoxin b1, asbestos, tobacco.

**Physical Carcinogens**

Physical carcinogenic agent is radiant energy both **ultraviolet light** and **ionizing radiation,** i.e. **X-rays,** α**,** β and γ**-rays.** These rays damage DNA which is the basic mechanism of carcinogenicity with radiant energy.

The main source of UV radiation is the sunlight, others are UV lamps, welder’s arcs etc. In humans, excessive exposure of UV rays can cause various forms of skin cancers.

Ionizing radiation of all kinds like X-rays, α, β and γ-rays, radioactive isotopes, protons, and neutrons can cause cancer.

X-rays and radioactive radiation tend to induce DNA double-strand breaks, whereas UVradiatio**n** results in the formation of pyrimidine dimers, by cross-linking of adjacent pyrimidine bases.

**Biologic Carcinogens**

Biologic carcinogens are chiefly ***viruses, parasites*** and ***bacteria.*** The role of viruses in the causation of

cancer is more significant.

Oncogenic (carcinogenic) viruses contain either DNA or RNA as their genome. The two types of

carcinogenic viruses are:

1. DNA oncogenic viruses

2. RNA oncogenic viruses.

***DNA oncogenic viruses***

DNA oncogenic viruses are classified into five subgroups.

These are:

a. Papoviruses

b. Herpes viruses

c. Adenoviruses

d. Pox viruses

e. Hepadna viruses.

***Mode of action of DNA oncogenic virus***

The DNA virus infects the host cell. Then, DNA virusbinds tightly to host cell DNA and causes alterations in gene expression of host cell DNA and thus causes

cancer by altering the types of protein made in cell. Viral oncoproteins bind to tumor supressors and inactivate them.

**RNA oncogenic viruses**

The RNA viruses use RNA as the genome. RNA oncogenic viruses are **retroviruses** they contain the enzyme ***reverse transcriptase***. All retroviruses are not oncogenic. The examples of RNA oncogenic viruses are:

• Rous Sarcoma virus

• Leukemia sarcoma virus

• Mouse mammary tumor virus etc.

***Mode of action of RNA oncogenic virus***

The RNA viruses use RNA as the genome. The RNA gets copied by **reverse transcriptase** to produce single strand of viral DNA. Single strand of viral DNA is then copied to form another strand of complementary DNA, resulting in double stranded ***viral DNA*** or ***provirus***. The provirus is then integrated into the DNA of the host cell genome and may transform the cell into cancer cell

* **Viral causes of cancer**

Certain viruses, derived from quite different taxonomic groups, are able to induce cancer development. We distinguish the highly **oncogenic viruses**, which contain **viral oncogenes** in their genomes that are in most cases derived from cellular proto-oncogenes, whereas **slowly transforming viruses** do not contain such genes.

They tend to use one of the following mechanisms to stimulate proliferation of their host cells:

* Insertion of a strong promoter in the vicinity of a host cell proto-oncogene
* Expression of proteins that neutralise host cell tumour suppressor proteins
* Expression of proteins that prevent or delay apoptosis

Characteristics of viral carcinogenesis include:

Tumour viruses often establish persistent infections in the human host

Host factors are important determinants of virus-induced carcinogenesis

Viruses are rarely complete carcinogens; they require additional factors to fully activate carcinogenesis.

**. Human tumour viruses**

|  |  |
| --- | --- |
| **Virus (Group)** | **Associated Human Cancer** |
| **DNA VIRUSES** | |
| **Papilloma virus family**  Human papilloma virus (HPV)  (various subtypes) | Genital tumours, squamous cell carcinoma |
| **Herpes virus family**  Human herpes virus 8 (HHV8)  Epstein-Barr virus (EBV) | Kaposi sarcoma  Burkitt's lymphoma, Hodgkin's disease, Nasopharyngeal carcinoma |
| **Hepadnavirus family**  Hepatitis B virus | Hepatocellular carcinoma |
| **RNA VIRUSES** | |
| **Retrovirus family**  Human T-cell leukaemia virus  Human immunodeficiency virus | Adult T-cell leukaemia  AIDS-related malignancies |
| **Flavivirus family**  Hepatitis C virus | Hepatocellular carcinoma |

**GENETIC FACTOR**

Some types of cancer run in certain families, but most cancers are not clearly linked to the genes we

inherit from our parents. Gene changes that start in a single cell over the course of a person's life cause most cancers. Some faulty genes that increase the risk of cancer can be passed on from parent to child. These are called inherited cancer genes. This occurs when there is a mistake or a fault in the genes in an egg or sperm cell. Then the gene fault can be passed on to children. Genes that increase the risk of cancer are called cancer susceptibility genes.

These genes would normally protect us against cancer – they correct DNA damage that naturally occurs when cells divide. Inheriting a faulty copy of one of these genes means that it cannot repair damaged DNA in cells. This means the cells may become cancerous.

We inherit genes from both our parents. If a parent has a gene fault then each child has a 1 in 2 chance (50%) of inheriting it. So some children will have the faulty gene and an increased risk of developing cancer and some children won’t.

Being born with one inherited faulty gene doesn’t mean that a person will definitely get cancer. But they have a higher risk of developing particular types of cancer than other people.