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COURSE TITLE : CELLULAR BIOCHEMISTRY

QUESTIONS

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

1. 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

It is not associated with clinical condition .It is characterised by a normal or increased growth rate with an acceleration of bone age maturation. It is characterised by a reduced growth hormone secretion evaluated by standard provocative tests, the administration of growth hormone 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 endocrine interactions.

1. 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.

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

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 taking fluoxetine 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).

1. Cancer is caused by accumulated damage to genes. Such changes may be due to chance or to exposure to a cancer causing substance.

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.

We should bear in mind, though, that in the majority of cancer cases we cannot attribute the disease to a single cause.

The causes of cancer can be categorized into the following:

1. Biological factors

a. Inherited genetic defects

b. Viruses

c. Bacteria

2. Chemical factors

a. Aflatoxin B

b. Nickel

c. Tobacco smoke

d. Industrial pollutants

3. Physical factors

a. UV Ray's

b. X-rays

c. Beta and gamma rays.

**Molecular basis of cancer**

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’.