BIOCHEMISTRY ASSIGNMENT by MR AKAWA

NAME: Awoniyi Gloria Funmilola

MATRIC NO: 17/MHS01/070

QUESTION 1. WHAT DO YOU UNDERSTAND BY PRIMARY OR SIMPLE OBESITY

Simple Obesity also called as primary obesity& is due to excessive energy intake and too little consumption, also known as diet-induced obesity and has the largest proportion in all types of obesity(95%). Simple obesity is characterized by a normal or increased growth rate with an acceleration of bone age maturation. 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 GH secretion evaluated by standard provocative tests, the administration of GH-releasing hormone or spontaneous 24-hour secretion. In obese children GH secretion may be as low as in poorly growing children with classical GH deficiency. The endocrine abnormalities along the GH axis seem to involve complex mechanisms at the hypothalamic, pituitary and peripheral level. Recent data suggest that simple obesity is associated with an increase in GH clearance and a decrease in GH synthesis and secretion. It is also associated with high insulin and insulin-like growth factor I levels which may interfere in the complex endocrine interactions. In conclusion, simple obesity is characterized by normal growth in the presence of 'hyposomatotropism'.

QUESTION 2. HOW DOES CONGENITAL SYNDROME AND DRUG THERAPY AFFECTS OBESITY

Congenital syndrome: An often-inherited medical condition that occurs at or before birth.

Drug therapy: Treatment with any substance, other than food, that is used to prevent, diagnose, treat, or relieve symptoms of a disease or abnormal condition. So how does these two affect obesity? Genes give the body instructions for responding to changes in its environment. Studies of resemblances and differences among family members, twins, and adoptees offer indirect scientific evidence that a sizable portion of the variation in weight among adults is due to genetic factors. Other studies have compared obese and non-obese people for variation in genes that could influence behaviors (such as a drive to overeat, or a tendency to be sedentary) or metabolism (such as a diminished capacity to use dietary fats as fuel, or an increased tendency to store body fat.

The development of obesity in syndromic conditions typically occurs after infancy. Examples include Prader-Willi syndrome, Bardet-Biedl syndrome, Alström syndrome, Albright's hereditary osteodystrophy, and WAGR (Wilms' tumor, aniridia, genitourinary anomalies, and retardation) syndrome. These syndromes are characterized by cognitive impairment, dysmorphic features, and anomalies of major organs.at). These studies have identified variants in several genes that may contribute to obesity by increasing hunger and food intake.

Using Prader-Willi syndrome (PWS) as an example, it is caused by functional absence of the paternal allele of 15q11-13, affects one in every 15,000 to 30,000 births.2,11 Birth weight is

normal or slightly low, and infants fail to gain weight, often requiring tube feedings, due to hypotonia and poor suck.11,22 Following a period of limited catch-up weight gain from 6 to 18 months, children develop an insatiable appetite, resulting in obesity by age 6.22 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.2,11 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.22 Affected children often have a fair complexion and suffer from developmental delay, delayed puberty, and poor linear growth secondary to growth hormone deficiency.2,22 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.

Rarely, a clear pattern of inherited obesity within a family is caused by a specific variant of a single gene (monogenic obesity). Most obesity, however, probably results from complex interactions among multiple genes and environmental factors that remain poorly understood (multifactorial obesity). There is an urgent need for effective pharmacological therapies to help tackle the growing obesity epidemic and the healthcare crisis it poses. The past 3 years have seen approval of a number of novel anti-obesity drugs. The majority of these influence hypothalamic appetite pathways via dopaminergic or serotoninergic signalling. Some are combination therapies, allowing lower doses to minimize the potential for off-target effects. An alternative approach is to mimic endogenous satiety signals using long-lasting forms of peripheral appetite-suppressing hormones. There is also considerable interest in targeting thermogenesis by brown adipose tissue to increase resting energy expenditure. Obesity pharmacotherapy has seen several false dawns, but improved understanding of the pathways regulating energy balance, and better-designed trials, give many greater confidence that recently approved agents will be both efficacious and safe. Nevertheless, a number of issues from preclinical and clinical development continue to attract debate, and additional large-scale trials are still required to address areas of uncertainty.

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.

QUESTION 3. OUTLINE THE AETIOLOGY OF CANCER AND ITS MOLECULAR BASIS

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. Majority of cancer cases we cannot attribute the disease to a single cause.

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 carcinogens such as many chemicals, radioactive materials and asbestos.
4. Lifestyle-related factors like 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 fibers, tar and pitch, polynuclear hydrocarbons (e.g. benzopyrene), some metal compounds and 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 e.g. Cervical cells), EBV (Epstein-Barr virus, the herpes virus that causes inflammation of the throat lymphoid).

Radiation can cause cancer: ionizing radiation (e.g. X-ray radiation, soil radon), non-ionized 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.

Cellular oncogenes Genes that promote autonomous cell growth in cancer cells are called oncogenes, and their normal cellular counterparts are called proto-oncogenes. Proto-oncogenes are physiologic regulators of cell proliferation and differentiation while oncogenes are characterized by the ability to promote cell growth in the absence of normal mitogenic signals. Their products, oncoproteins, resemble the normal products of proto-oncogenes with the exception that oncoproteins are devoid of important regulatory elements. Their production in the transformed cells becomes constitutive, that is, not dependent on growth factors or other external signals. Proto-oncogenes can be converted to oncogenes by several mechanisms including point mutation and gene amplification resulting in:

Overproduction of growth factors

Flooding of the cell with replication signals

Uncontrolled stimulation in the intermediary pathways

Cell growth by elevated levels of transcription factors

The RAS oncogene is the most frequently mutated oncogene in human cancer. It encodes a GTP-binding protein Ras that functions as an on-off ‘switch’ for a number of key signalling pathways controlling cellular proliferation. In a normal cell, Ras is transiently activated and recruits Raf, to activate the MAP-kinase pathway to transmit growth-promoting signals to the nucleus. The mutant Ras protein is permanently activated leading to continuous stimulation of cells without any external trigger.