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Biochemistry Assignment

1. Simple obesity also known as Primary obesity is when caloric intake exceeds energy expenditure. A medical condition defined by excess amount of fat in the body. The Body Mass Index (BMI) calculated as Weight in KG divided by Height in M squared is the measure of obesity. Individuals with a BMI of 18.5-24.9 are normal, 25-29.9 are overweight, > 30 are obese and > 4o are morbidly obese. Amongst the causes of obesity are overeating, physical inactivity or leading a sedentary lifestyle and genetics It tends to increase the susceptibility of the body to conditions such as Cancer, Osteoarthritis, heart problems e.t.c. Solutions include physical activity and eating clean.

2. Congenital syndromes refer to conditions present at birth regardless of the cause. Some congenital syndromes affecting obesity include; The Prader-willi Syndrome, Bardet-Biedl syndrome, Cohen syndrome and MOMO syndrome.

***The Prader-willi*** syndrome is an abnormality in chromosome 15, diagnosed by genetic testing. Research has shown that it is the most common genetic cause of life-threatening childhood obesity. It affects the hypothalamus: the organ that controls hunger and satiety amongst other things by making it dysfunctional. It causes obesity as a result of hyperphagia, reduced physical activity related to decreased muscle tone, increased metabolic activity related to decreased muscle mass and the inability to vomit.

***The Bardet-Biedl syndrome***: this is a disorder affecting many parts of the body with obesity being its characteristic feature. Abnormal weight gain typically begins in early childhood and continues to be an issue throughout life. Complications of obesity can include type 2 diabetes, high blood pressure and

***MOMO syndrome***: this is an extremely rare genetic disorder which belongs to the overgrowth syndromes. It is characterized by obesity and Macrosomia amongst others.

**Drug therapy** is the general term for using medication to treat diseases. Certain drugs or classes of drugs are known to cause weight gain and in the long run, obesity some of them include; anti-depressants, anti-histamines, anti-psychotic, beta blockers and birth control pills.

Generally the mechanism of weight gain for this medications include:

* Stimulation of appetite
* Stimulation of fat storage
* Slowed metabolism
* Fluid retention
* Impaired exercise tolerance

***Anti-depressants:*** the theory is that it may affect metabolism and hunger levels. They work by increasing serotonin levels, the neurotransmitter responsible for the regulation of mood, anxiety and the controlling of the appetite. These changes may increase cravings for Carbohydrate-rich food which in turn is accompanied by weight gain and if uncontrolled can lead to obesity.

 Antidepressants, known as tricyclic antidepressants (TCAs) are well known for their ability to increase appetite and cause weight gain. TCAs affect neurotransmitters in the brain. TCAs are also used to treat migraine headaches, and other conditions.

 Examples of TCAs that can commonly lead to weight gain are amitriptyline (Elavil), trimipramine (Surmontil), and imipramine (Tofranil).

Antidepressants may also cause weight loss for example (Wellbutrin) is an antidepressant that is actually associated with weight loss; it's also linked with less sexual side effects than others.

***Antihistamines*** are a group of drugs commonly used to treat conditions such as allergic rhinitis (hay fever), cold or flu symptoms, food allergies, hives (urticaria), drug allergies, and insect bites or stings. They affect obesity by causing weight gain. They do this by increasing appetite or may cause sedation and fatigue that lower levels of activity.

***Anti-psychotic and mood disorder treatments***: These drugs are used to treat mental health conditions such as schizophrenia, bipolar disorder, or as an add-on treatment with an antidepressant for more severe depression. Although all of the drugs in the antipsychotic class have been shown to produce some metabolic changes, each drug has its own specific risk profile. Many antipsychotics are well-known to cause weight gain. Research has shown an enzyme called AMP-kinase is elevated in the brain of patients who use antipsychotics. AMP-kinase can block the brain histamine-1 receptor, which will boost appetite and may lead to weight gain. However, for many mental health disorders, drug treatment may be absolutely necessary and the risk of stopping the drug may be greater than the risk associated with weight gain. Examples in this drug class include the atypical antipsychotics such as olanzapine (Zyprexa), risperidone (Risperdal), aripiprazole (Abilify) and quetiapine (Seroquel).

***Hypertensives or Beta blockers***- Beta blockers are an older class of heart drug used to treat high blood pressure, chest pain (angina), and protect or prevent the heart from an attack. Beta blockers long been known to lead to weight gain. Common examples of this class are propranolol, metoprolol (Lopressor) and atenolol (Tenormin). Many of the older beta blocker drugs can lead to fatigue, which may be responsible for some of the weight gain. Patients may be tired, have lack of energy, and in general slowdown, which may affect the number of calories burned each day.

***Birth control pills***: In general, the birth control pill is not linked with weight gain, especially the newer pills with lower doses of estrogen and progestin. However, higher doses of estrogen or progestin-only birth control can cause weight gain.

* The birth control shot known as medroxyprogesterone (Depo-Provera) that is given every 3 months can cause significant weight gain in some women.

3. Cancer refers to any one of a large number of diseases characterized by the development of abnormal cells that divide uncontrollably and have the ability to infiltrate and destroy normal body tissue. It can be inherited. Genes are segments of DNA located on chromosomes, and can mutate over time to become cancerous. These mutations can result from a variety of causes, including diet and lifestyle choices as well as exposure to certain environmental factors. Overall, only 5 to 10 percent of all cancers are genetically inherited, although these are the cancers that tend to occur earlier in life. One such inheritable genetic disorder that is associated with increased cancer risk is **Lynch syndrome**, which prevents cells’ ability to repair their DNA when damage occurs. It can also be caused by behavior. An example of a behavioral risk factor is smoking, which can lead to lung cancer, or excessive exposure to the sun’s ultraviolet (UV) rays, which can cause skin cancer. Some dietary choices, including red meat and alcohol, have also been linked to certain types of cancer, while obesity is associated with higher rates of cancer as well. Exposure to certain factors in the environment, such as chemicals like asbestos and benzene, as well as talcum powder and various sources of radiation (including excessive X-rays), can also cause cancer. These substances capable of damaging DNA and triggering cancer are referred to as carcinogens.

**Molecular basis**: Genetic mutations are responsible for the generation of cancer cells and are thus present in all cancers. These mutations alter the quantity or function of protein products that regulate cell growth and division and DNA repair. Two major categories of mutated genes are Oncogenes and Tumor suppressor genes

***Oncogenes*** are abnormal forms of normal genes that regulate various aspects of cell growth and differentiation. Mutation of these genes may result in direct and continuous stimulation of the pathways that control cellular growth and division, cellular metabolism, DNA repair, angiogenesis, and other physiologic processes.

There are > 100 known oncogenes that may contribute to human neoplastic transformation. For example, the *RAS* gene encodes the ras protein, which carries signals from membrane-bound receptors down the RAS-MAPKinase pathway to the cell nucleus, and thereby regulates cell division. Mutations may result in the inappropriate activation of the ras protein, leading to uncontrolled cell growth. Other oncogenes have been implicated in specific cancers. These include

* *HER2* (amplified in breast and gastric cancer and less commonly in lung cancer)
* *CMYC* (Burkitt lymphoma)
* *NMYC* (small cell lung cancer, neuroblastoma)
* *EGFR* (adenocarcinoma of the lung)

Oncogenes typically result from; translocations, acquired somatic cell point mutations and gene amplification. These changes may either increase the activity of the gene product (protein) or change its function.

### Tumor suppressor genes

Genes such as *TP53*, *BRCA1*, and *BRCA2* play a role in normal cell division and DNA repair and are critical for detecting inappropriate growth signals or DNA damage in cells. If these genes, as a result of inherited or acquired mutations, become unable to function, the system for monitoring DNA integration becomes inefficient, cells with spontaneous genetic mutations persist and proliferate, and tumors result.

The important regulatory protein, p53, prevents replication of damaged DNA in normal cells and promotes cell death (apoptosis) in cells with abnormal DNA. Inactive p53 allows cells with abnormal DNA to survive and divide. *BRCA1* and *BRCA2* mutations that decrease function increase risk of breast and ovarian cancer.

Another example, the retinoblastoma (*RB*) gene encodes for the protein Rb, which regulates the cell cycle by stopping DNA replication. Mutations in the *RB* gene family occur in many human cancers, allowing affected cells to divide continuously.

As with oncogenes, mutation of tumor suppressor genes such as *TP53* or *RB* in germ cell lines may result in vertical transmission and a higher incidence of cancer in offspring.