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Primary (simple) Obesity

Obesity is a nutritional disorder in which excess body fat has accumulated. It is defined by body mass index (BMI) and further evaluated in terms of fat distribution via the waist–hip ratio. Obesity occurs when excess metabolic fuel is stored as fat in the body. This excess metabolic fuel is gotten when intake of metabolic fuel is consistently greater than energy expenditure. This is caused by increased consumption of fatty food, genetics, junk food, food addiction, medication, congenital diseases and many more. Obesity is classified into two;

1. Primary obesity
2. Secondary obesity

Primary Obesity

Primary obesity is the class of obesity that is not associated with a clinical situation i.e. it doesn't occur as a result of an underling disease. This refers to obesity that is causes by fatty food, genetics, junk food, food addiction and so on. It is obesity that occurs due to life style and eating habits. It does not involve obesity that occurs as a result of medication or congenital diseases. Primary obesity accounts for 95% of obese people. To understand primary obesity more, we'll look at secondary obesity. Secondary obesity is obesity that occurs either as the side effect of a medication used to treat an illness or as the manifestation of a disease (e.g. Prader Willi syndrome). Medications such as antidepressants, antipsychotic, diabetes medication and generally drugs in class known as thiazolidinediones can lead to weight gain and an increase in fat. While congenital syndromes such as Prader Willi syndrome, Lawrence-Moon-Bardet syndrome and more will present obesity as one of their characteristics. This accounts for 5% of obese people. Hence primary obesity will involve every other thing that will lead to obesity which are listed as fatty food, genetics, junk food, food addiction and more. **In simple terms, when a normal healthy person adapts to a lackadaisical way of life and becomes obese, it is referred to as primary obesity. Whereas, when a person is born with a disorder that present obesity as a characteristic or when a person becomes obesity due to the used of certain medications, it is referred to as secondary obesity**.

The Effect of Congenital Syndrome and Drug Therapy on Obesity

Effect of Congenital Syndrome on Obesity

Congenital diseases, also known as birth defects, are conditions present at birth regardless of the cause. Examples are Fragile X syndrome, Down syndrome, Prader Willi syndrome, Lawrence-Moon-Bardet syndrome and so on. These disease exhibit certain characteristics which are known as symptoms. Some congenital diseases will present **obesity** as a symptom. An example is Prader Willi syndrome. Children with this syndrome present a metabolic rate that is **lower** than normal and mental problems such as a **constant sense of hunger** among other symptoms. Metabolism or metabolic rate is defined as the series of chemical reactions in a living organism that create and break down energy necessary for life. More simply, it's the rate at which the body expends energy or burns calories. A high metabolism means that more calories is needed to maintain weight. However, a person with a low (or slow) metabolism will burn fewer calories at rest and during activity and therefore has to eat less to avoid becoming overweight. In Prader Willi syndrome, one of the symptoms is a constant sense of hunger which will result in **compulsive overeating**. Because of their slow metabolic rate, they become overweight. **Although this is true for Prader Willi syndrome, it is not the same for all congenital diseases that present obesity as a symptom**. Some congenital diseases and the reason they present obesity are given below;

- Prader Willi syndrome: People with this disorder become obese as a result of a mental disorder that will result to overeating which together with their slow metabolic rate will lead to obesity.
- Lawrence-Moon-Bardet syndrome: People with this disorder become obese as a result of leptin resistance in fat cells (leptin is responsible for decrease in the number of adipocytes). Because the adipocytes do not respond to leptin, they continue to increase in number and lead to obesity.
- Down syndrome: Obesity in down syndrome occurs due to the same reason as that of Lawrence-Moon-Bardet syndrome.
- Pseudohypoparathyroidism: People with this disorder become obese as a result of leptin deficiency.
- Turner syndrome: People with this disorder become obese as a result of insulin resistance. Excess insulin, due to insulin resistance, can lead to weight gain and eventually obesity.
- Cohen syndrome: People with this disorder become obese as a result of increased response of adipocytes to insulin.

Effect of Drug therapy on Obesity

Medications such as *antidepressants, antipsychotic, diabetes medication* and generally drugs in class known as **thiazolidinediones** (TZDs) can lead to weight gain and an increase in fat. This eventually will result in obesity. As in the case of congenital diseases, how these drugs will produce obesity is different. **Thiazolidinediones (TZDs)** are oral anti-diabetic drugs that act as insulin sensitizers. TZDs improve glycemic control and insulin sensitivity in patients with type 2 diabetes, despite their potential to cause weight gain. Studies have attempted to elucidate the mechanisms behind the apparent paradox of TZDs improving insulin sensitivity while causing weight gain. Data indicate that with TZD treatment, there is a favorable shift in fat distribution from visceral to subcutaneous adipose depots that is associated with improvements in hepatic and peripheral tissue sensitivity to insulin. Although weight gain may occur with TZD therapy, it is not inevitable. Experts do not fully understand why **antidepressants** lead to weight gain in some people. One theory is that both metabolism and hunger levels may be affected. Antidepressants interfere with serotonin, the neurotransmitter that regulates anxiety and mood while also controlling appetite. In particular, these changes may increase cravings for carbohydrate-rich foods, such as bread, pasta, and desserts. Also, depression itself may cause weight gain in some people and weight loss in others. When people are depressed, their appetites are affected. In some people, this may make them hungrier while others lose their appetite. It may be the case that when antidepressants take effect, a person's usual appetite returns and this has an impact on their weight.

The Etiology of Cancer and its Molecular Basis

Etiology of Cancer

Cancer is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body. Cancer is a caused by genetic changes (mutation) leading to uncontrolled cell growth and tumor formation. The basic cause of the genetic changes is DNA damage and genomic instability(refers to a high frequency of mutations within the genome of a cellular lineage). This accounts for about 80% of cancer cases. A minority of cancers are due to

inherited genetic mutations. Thus, the etiology of cancer is multifactorial. This means the cause of cancer can be genetic, physical, chemical, hormonal, metabolic and more. All these factors cause mutation in genes;

- <u>Genetics</u>:   Although the vast majority of cancers are non-hereditary ("sporadic cancers"), about 3-10% of cancers are hereditary. Hereditary cancers are primarily caused by an inherited genetic defect which causes cancer syndrome. 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.

- <u>Physical and chemical agents</u>:   Particular substances, known as carcinogens, have been linked to specific types of cancer. Common examples of non-radioactive carcinogens are inhaled asbestos, cobalt, tobacco smoke, alcohol, food additives, nickel, benzene, natural chemicals and so on. Millions of workers run the risk of developing cancers such as lung cancer and mesothelioma from inhaling asbestos fibers and tobacco smoke, or leukemia from exposure to benzene at their workplaces. Cancer related to one's occupation is believed to represent between 2–20% of all cases.

- <u>Lifestyle</u>: Many different lifestyle factors contribute to increasing cancer risk. Together, diet and obesity are related to approximately 30–35% of cancer deaths. The over consumption of high processed food, alcohol and a sedentary lifestyle in general can contribute to the cause of cancer.

- <u>Hormones</u>:   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 (development of cancer). 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.

- <u>Viruses</u>:   A virus that can cause cancer is called an *oncovirus*. These include human papillomavirus, Epstein–Barr virus, hepatitis B virus and human immunodeficiency virus. These viruses get integrated into the host DNA leading to multiplication of the viral gene and that multiplication takes over the host causing abnormal multiplication of cells

- <u>Bacterial and parasitic infections</u>:   Certain bacterial or parasitic infections also increase the risk of cancer. Some of these include *Helicobacter Pylori*, *Schistosoma haematobium*, *liver fluke*, *Opisthorchis viverrini*, *Clonorchis sinensis* and *mycobacterium M. tuberculosis*. The mechanism by which these bacteria causes cancer may involve chronic inflammation or the direct action of some of the bacteria's virulence factors, inflammation triggered by the worm's eggs. Certain parasitic infections can also

increase the presence of carcinogenic compounds in the body, leading to the development of cancer.

- Radiation: Radiation of certain wavelengths, called ionizing radiation, has enough energy to damage DNA and cause cancer. Ionizing radiation includes radon, x-rays, gamma rays, and other forms of high-energy radiation. Lower-energy, non-ionizing forms of radiation, such as visible light and the energy from cell phones, have not been found to cause cancer in people.
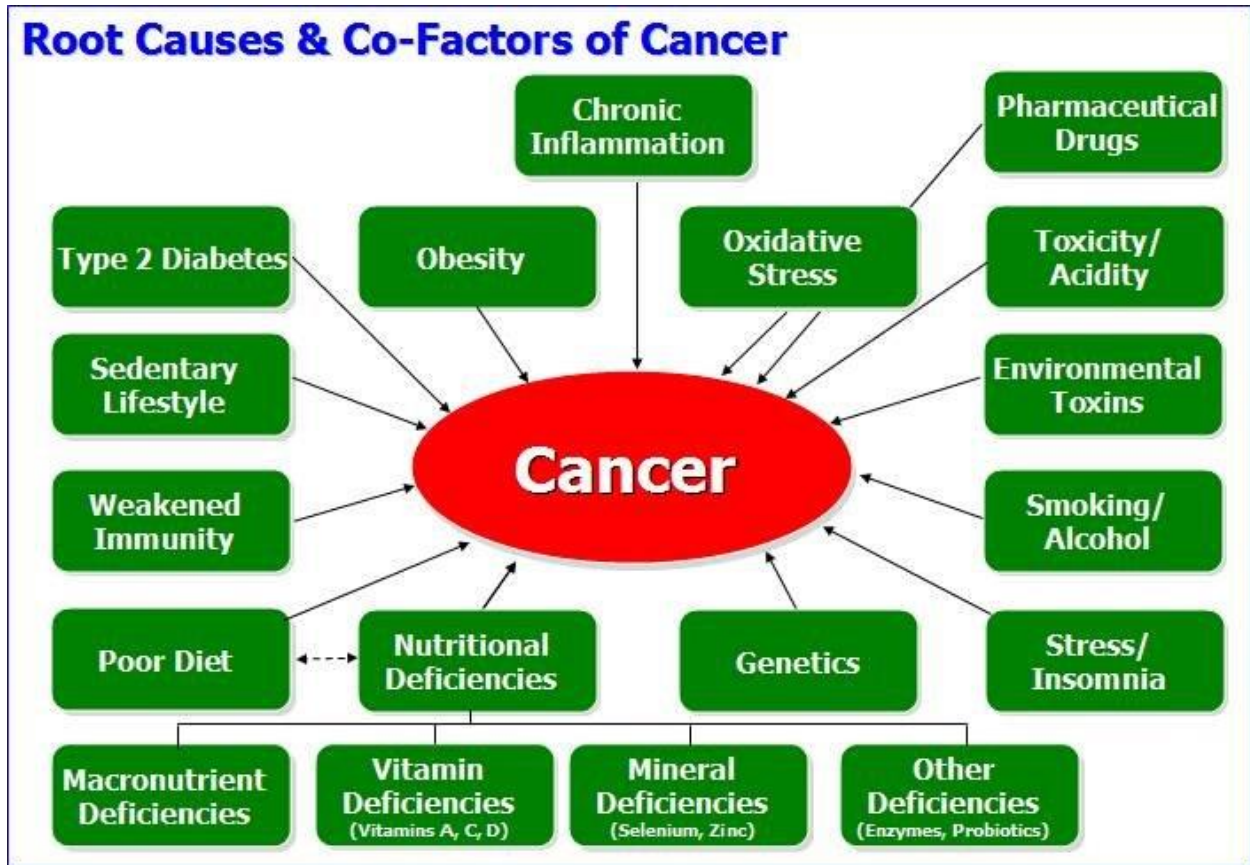
Molecular Basis of Cancer

Normal cells replicate by undergoing the cell cycle. Proliferation through the cell cycle is strictly regulated by groups of proteins that interact with each other in a specific sequence of events. Normal cells proliferate a limited number of times before undergoing senescence (the process of deterioration with age). These cells undergo apoptosis and are removed from the system. In normal tissue, there is a balance between the generation of new cells by cell division and the loss of cells by apoptosis. However, in cancer cells are able to escape apoptosis of the normal cell cycle. This is 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 tumors consist of cells that contain an active telomerase enzyme. The transformation of a normal cell to a cancer cell is accompanied by the loss of function of one or more **tumor suppressor genes** (genes that encode proteins that promote apoptosis DNA repair enzymes). and both gene copies must be defective in order to promote tumor development.