

ASSIGNMENT ON MEDICAL BIOCHEMISTRY

DIABETES, OBESITY AND CANCER

BY

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17/MHS01/223

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APRIL, 2020

Question 1: What do you understand by primary or simple obesity

Obesity is the condition of being much too heavy for one's height so that one's health is affected. In other words, it means to be too overweight. Also known as being fat. It is considered a disease and has been described as an epidemic.

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%). The simple obesity is generally caused by the heredity factor, the nutrition surplus and a lack of exercise, and characterized by the even distribution of the whole body fat.

Question 2: How does congenital syndrome and drug therapy affect obesity

Severe obesity is a characteristic feature of many congenital and genetic disorders. Congenital syndromes like Prader-Willi syndrome, Cohen syndrome, Down syndrome, Bardet-Biedl syndrome and Turner syndrome are associated with obesity in children.

Children with Down syndrome are more likely to have higher levels of hormones associated with obesity; hormones such as leptin. The normal role of leptin is to suppress appetite and regulate body weight. Obese people do not respond to leptin properly because they have some leptin resistance. Down syndrome may have a genetic predisposition to more severe leptin resistance.

Prader-Willi syndrome (PWS) is a complex neurodevelopmental disorder due to errors in genomic imprinting with loss of imprinted genes that are paternally expressed from the chromosome region. PWS is considered most commonly known genetic cause of morbid obesity in children. The subject is frequently unable to sense when they are full after eating and this leads to weight gain. Unless food intake is strictly controlled, subject with PWS will be severely obese. PWS results in constant and inexorable hunger that drives patients to engage in problematic hunger behaviors with affected individuals who do not feel satisfied after completing a meal. Most patients have reduced

GH secretion and hypogonadotropic hypogonadism, suggesting hypothalamic–pituitary dysfunction. Nevertheless, encouraging results have been observed with the early administration of GH, resulting in accelerated growth and decreased body fat; sex hormone replacement may also be beneficial.

Drug therapy and obesity

A number of drugs are capable causing obesity; drugs such as birth control pills, steroids and antidepressants. This is because these drugs possess varying abilities to increase and appetite stimulate carbohydrate craving and cause weight gain over prolonged periods of administration. Psychotropic drugs with more pronounced amitriptyline induce weight gain. Selective serotonin reuptake inhibitors decrease transiently bodyweight during the first few weeks of treatment and may then increase body weight; weight gain tends to be most prominent some mood stabilizers. Atypical antipsychotic tends to cause more weight gain than the conventional ones. Some of the medications might interfere with central nervous functions regulating energy balance which are neurotransmitters, neuromodulators, cytokines and hormone interacting with the hypothalamus.

Question 3: Outline the aetiology of cancer and its molecular basis

Aetiology is the investigation or attribution of the cause or reason for something. It is the study of the causes or origin of a disease.

Cancer is a disease caused by genetic changes leading to uncontrolled cell growth and tumour formation. A minority of cancers are due to inherited genetic mutations. Most cancers are related to environmental, lifestyle, or behavioural exposures.

Cancer is generally not contagious in humans, though it can be caused by oncoviruses and cancer bacteria. Over one third of cancer deaths worldwide (and about 75–80% in the United States) are potentially avoidable by reducing exposure to known factors.

Common environmental factors that contribute to cancer death include exposure to different chemical and physical agents (tobacco use accounts for 25–30% of cancer deaths), environmental pollutants, diet and obesity (30–35%), infections (15–20%), and radiation (both ionizing and non-ionizing, up to 10%). These factors act, at least partly, by altering the function of genes within cells.

A). Physical and chemical agents

Particular substances, known as carcinogens, have been linked to specific types of cancer. Common examples of non-radioactive carcinogens are inhaled asbestos, certain dioxins, and tobacco smoke. Although the public generally associates carcinogenicity with synthetic chemicals, it is equally likely to arise in both natural and synthetic substances.

i). Smoking

Tobacco smoking is associated with many forms of cancer, and causes 80% of lung cancer. Decades of research has demonstrated the link between tobacco use and cancer in the lung, larynx, head, neck, stomach, bladder, kidney, esophagus and pancreas.

Tobacco smoke contains over fifty known carcinogens, including nitrosamines and polycyclic aromatic hydrocarbons. Tobacco is responsible for about one in three of all cancer deaths in the developed world, and about one in five worldwide.

Electronic cigarettes or e-cigarettes are handheld electronic devices that simulate the feeling of tobacco smoking. Daily long-term use of high voltage (5.0 V) electronic cigarettes may generate formaldehyde-forming chemicals at a greater level than smoking, which was determined to be a lifetime cancer risk of approximately 5 to 15 times greater than smoking.[26] However, the overall safety and long-term health effects of electronic cigarettes is still uncertain.

ii). Materials

Some substances cause cancer primarily through their physical, rather than chemical, effects on cells. A prominent example of this is prolonged exposure to asbestos, naturally occurring mineral fibers which are a major cause of mesothelioma, which is a cancer of the serous membrane, usually the serous membrane surrounding the lungs. Other substances in this category, including both naturally occurring and synthetic asbestos-like fibers such as wollastonite, attapulgite, glass wool, and rock wool, are believed to have similar effects.

Non-fibrous particulate materials that cause cancer include powdered metallic cobalt and nickel, and crystalline silica (quartz, cristobalite, and tridymite). Usually, physical carcinogens must get inside the body (such as through inhaling tiny pieces) and require years of exposure to develop cancer. Common occupational carcinogens include:

- arsenic
- asbestos
- benzene
- beryllium
- cadmium

- chromium
- ethylene oxide
- nickel
- Plutonium

B). Lifestyle

Many different lifestyle factors contribute to increasing cancer risk. Together, diet and obesity are related to approximately 30–35% of cancer deaths. Dietary recommendations for cancer prevention typically include an emphasis on vegetables, fruit, whole grains, and fish, and avoidance of processed meat, red meat, animal fats, and refined carbohydrates. The evidence to support these dietary changes is not definitive.

i). Alcohol

Alcohol is an example of a chemical carcinogen. The World Health Organization has classified alcohol as a Group 1 carcinogen. In Western Europe 10% of cancers in males and 3% of cancers in females are attributed to alcohol. Worldwide, 3.6% of all cancer cases and 3.5% of cancer deaths are attributable to alcohol.

In particular, alcohol use has been shown to increase the risk of developing cancers of the mouth, esophagus, pharynx, larynx, stomach, liver, ovaries, and colon. The main mechanism of cancer development involves increased exposure to acetaldehyde, a carcinogen and breakdown product of ethanol. Other mechanisms have been proposed, including alcohol-related nutritional deficiencies, changes in DNA methylation, and induction of oxidative stress in tissues.

ii). Diet

Some specific foods have been linked to specific cancers. Studies have shown that individuals that eat red or processed meat have a higher risk of developing breast cancer, prostate cancer, and pancreatic cancer.

This may be partially explained by the presence of carcinogens in food cooked at high temperatures.

Several risk factors for the development of colorectal cancer include high intake of fat, alcohol, red and processed meats, obesity, and lack of physical exercise. A high-salt diet is linked to gastric cancer. Aflatoxin B1, a frequent food contaminate, is associated with liver cancer. Betel nut chewing has been shown to cause oral cancers

The relationship between diet and the development of particular cancers may partly explain differences in cancer incidence in different countries. For example, gastric cancer is more common in Japan due to the frequency of high-salt diets and colon cancer is more common in the United States due to the increased intake of processed and red meats

iii). Obesity

Cancers related to obesity

Men	Women
Colorectal cancer	Colorectal cancer
Esophageal adenocarcinoma	Endometrial cancer
Kidney cancer	Esophageal adenocarcinoma
Pancreatic cancer	Gallbladder cancer
Thyroid cancer	Kidney cancer
	Pancreatic cancer
	Post-menopausal breast cancer

In the United States, excess body weight is associated with the development of many types of cancer and is a factor in 14–20% of all cancer deaths. Every year, nearly 85,000 new cancer diagnoses in the United States are related to obesity.

There is an association between obesity and colon cancer, post-menopausal breast cancer, endometrial cancer, kidney cancer, and esophageal cancer.

Obesity has also been linked with the development of liver cancer. The current understanding regarding the mechanism of cancer development in obesity relates to abnormal levels of metabolic proteins (including insulin-like growth factors) and sex hormones (estrogens, androgens and progestogens). Adipose tissue also creates an inflammatory environment which may contribute to the development of cancers.

Physical inactivity is believed to contribute to cancer risk not only through its effect on body weight but also through negative effects on immune system and endocrine system.[30] More than half of the effect from diet is due to overnutrition rather than from eating too little healthy foods.

iv). Hormones

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.

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. For example, the daughters of women who have breast cancer have significantly higher levels of estrogen and progesterone than the daughters of women without breast cancer. These higher hormone levels may explain why these women have higher risk of breast cancer, even in the absence of a breast-cancer gene.

Similarly, men of African ancestry have significantly higher levels of testosterone than men of European ancestry, and have a correspondingly much higher level of prostate cancer. Men of Asian ancestry, with the lowest levels of testosterone-activating androstenediol glucuronide, have the lowest levels of prostate cancer.

Other factors are also relevant: obese people have higher levels of some hormones associated with cancer and a higher rate of those cancers. Women who take hormone replacement therapy have a higher risk of developing cancers associated with those hormones. On the other hand, people who exercise far more than average have lower levels of these hormones, and lower risk of cancer. Osteosarcoma may be promoted by growth hormones.

v). Infection and inflammation

Worldwide, approximately 18% of cancer cases are related to infectious diseases. Viruses are the usual infectious agents that cause cancer but bacteria and parasites also contribute. Infectious organisms that increase the risk of cancer are frequently a source of DNA damage or genomic instability.

Inflammation triggered by the worm's eggs appears to be the cancer-causing mechanism. Certain parasitic infections can also increase the presence of carcinogenic compounds in the body, leading to the development of cancers.

C). **Viruses**

Viral infection is a major risk factor for cervical and liver cancer.[52] A virus that can cause cancer is called an oncovirus.

These include human papillomavirus (cervical carcinoma), Epstein–Barr virus (B-cell lymphoproliferative disease and nasopharyngeal carcinoma).

D). Bacteria and parasites

Certain bacterial infections also increase the risk of cancer, as seen in *Helicobacter pylori*-induced gastric carcinoma. Parasitic infections strongly associated with cancer include *Schistosoma haematobium* (squamous cell carcinoma of the bladder) and the liver flukes, *Opisthorchis viverrini* and *Clonorchis sinensis* (cholangiocarcinoma).

E). Radiation

Up to 10% of invasive cancers are related to radiation exposure, including both non-ionizing radiation and ionizing radiation. Major damage normally results in the cell dying, but smaller damage may leave a stable, partly functional cell that may be capable of proliferating and developing into cancer, especially if tumor suppressor genes were damaged by the radiation.

i). Non-ionizing radiation

Not all types of electromagnetic radiation are carcinogenic. Low-energy waves on the electromagnetic spectrum including radio waves, microwaves, infrared radiation and visible light are thought not to be because they have insufficient energy to break chemical bonds.

Unlike chemical or physical triggers for cancer, ionizing radiation hits molecules within cells randomly. If it happens to strike a chromosome, it can break the chromosome, result in an abnormal number of chromosomes, inactivate one or more genes in the part of the chromosome that it hit, delete parts of the DNA sequence, cause chromosome translocations, or cause other types of chromosome abnormalities.

Non-ionizing radio frequency radiation from mobile phones, electric power transmission, and other similar sources have been described as a possible carcinogen by the World Health Organization's International Agency for Research on Cancer.

Higher-energy radiation, including ultraviolet radiation (present in sunlight), x-rays, and gamma radiation, generally is carcinogenic, if received in sufficient doses. Prolonged exposure to ultraviolet radiation from the sun can lead to melanoma and other skin malignancies.

ii). Ionizing radiation

Sources of ionizing radiation include medical imaging, and radon gas. Ionizing radiation is not a particularly strong mutagen. Medical use of ionizing radiation is a growing source of radiation-induced cancers. Ionizing radiation may be used to treat other cancers, but this may, in some cases, induce a second form of cancer.

Molecular Basis of Cancer

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'.

Normal cells tend to replicate normally and when they get older, they are removed by apoptosis (programmed cell death). The molecular basis of this is seen in the shortening of telomeres on the chromosomes of 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 lengthens the telomeres on the chromosome. In this way, apoptosis is escaped and immortality is attained by cancer cells. All normal cells receive signals for apoptosis; chemical compounds that because cancer destroy these signals hence, cells continue to multiply uncontrollably.