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ASSIGNMENT

1. What do you understand by primary or simple obesity?

Obesity occurs when excess fat accumulation increases risk to health. Simple obesity, also called primary obesity, is due to excessive energy intake and too little consumption. It is also known as diet-induced obesity and has the largest proportion in all types of obesity (95%). Research has shown that problems such as simple obesity may in fact be linked to immune dysfunction that begins with a “failure to communicate” in the human gut. Simple obesity is characterized by a normal or increased growth rate with an acceleration of bone age maturation.

2. How does congenital syndrome and drug therapy affect obesity

Congenital syndrome may refer to individuals with cardiovascular disease (CVD). They often have a constellation of aetiologically linked cardiometabolic risk factors including dyslipidaemia, high blood pressure and high fasting plasma glucose. A name ‘syndrome X’ was coined and it is used by cardiologists to indicate angina-like chest pain in association with reversible electrocardiographic signs of myocardial ischemia in the absence of flow-limiting stenosis on coronary angiography, a condition also more often found in obese individuals. Other terms have been used previously in the literature such as insulin resistance syndrome, but ‘metabolic syndrome’ has gained international acceptance.

Metabolic syndrome has shown extensively to promote the development of diabetes and cardiovascular disease. The appearance of the metabolic syndrome phenotype is provoked by weight gain, particularly an increase in intra-abdominal fat accumulation which is mirrored by a large waist circumference. The prevalence of the metabolic syndrome and CVD is expected to rise dramatically in parallel to the global obesity epidemic. Metabolic syndrome doubles the risk of CVD but since its components are all reversible, the diagnosis of metabolic syndrome offers an effective treatment approach- principally weight management.

Increasingly, new insights into genetic basis of obesity have been gained from genome wide association studies (GWAS). The first single nucleotide polymorphism (SNP) associated with increased BMI was mapped to a gene now known as FTO (fat mass and obesity associated). FTO acts by regulating appetite and energy expenditure. Over 40 genetic variants since have been identified to associate with BMI, fat distribution or risk of obesity and metabolic syndrome. Although only a small proportion of variance in BMI (<2%) is observed to be attributable to common allelic variants, these risk alleles make substantial contribution to obesity in a polygenic manner such that people who carry a high number of variants (more than 10) will

likely to gain extra weight than those who carry only one or two variants. While certain excessively rare single gene mutations (e.g. leptin deficiency, leptin-receptor defects) can cause massive obesity, usually manifest in early childhood, genetic factors which affect BMI appear to contribute little to the very substantial weight gain needed to generate obesity.

3. Outline the aetiology of cancer and its molecular basis

Cancer is a group of diseases characterized by an autonomous proliferation of neoplastic cells which have a number of alterations, including mutations and genetic instability. Cellular functions are controlled by proteins, and because these proteins are encoded by DNA organized into genes, molecular studies have shown that cancer is a paradigm of acquired genetic disease. The process of protein production involves a cascade of several different steps, each with its attendant enzymes, which are also encoded by DNA and regulated by other proteins. Most steps in the process can be affected, eventually leading to an alteration in the amount or structure of proteins, which in turn affects cellular function. However, whereas cellular function may be altered by disturbance of one gene, malignant transformation is thought to require two or more abnormalities occurring in the same cell. Although there are mechanisms responsible for DNA maintenance and repair, the basic structure of DNA and the order of the nucleotide bases can be mutated. These mutations can be inherited or can occur sporadically, and can be present in all cells or only in the tumor cells. At the nucleotide level, these mutations can be substitutions, additions or deletions. Several of the oncogenes discussed below, including the p53, c-fms, and Ras genes, can be activated by point mutations that lead to aminoacid substitution in critical portions of the protein.

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.

We can roughly divide 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.

Lifestyle-related factors that cause cancer include:

- tobacco
- alcohol
- UV radiation in sunlight
- some food-related factors, such as nitrites and poly aromatic hydrocarbons generated by barbecuing food).

Lifestyles can prevent cancer

Cancer causing factors related to work and living environments include:

- asbestos fibres
- tar and pitch
- polynuclear hydrocarbons (e.g. benzopyrene)
- Some metal compounds
- Some 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 eg. Cervical cells)
- EBV (Epstein-Barr virus, the herpes virus that causes inflammation of the throat lymphoid)

Radiation can cause cancer:

- ionising radiation (e.g. X-ray radiation, soil radon)
- non-ionised 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.