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

 **Simple obesity** is characterized by a normal or increased growth rate with an acceleration of bone age maturation. 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.

Simple obesity of children is influenced by selected environmental factors such as parents' level of education, familial inclination to obesity and health habits, chosen and accepted by the child and/or its mother/parents programme of dietary treatment in the form of low-energy diet with elements of low glycemic index results in the loss of body mass in children. Implemented dietary treatment translates into the modification of basic anthropometric features--body mass, body height, thickness of skin and adipose folds on arm, below shoulder blade (scapula), on abdomen as well as arm circumference and anthropometric parameters of examined children--body mass index BMI, waste-hip ratio, body fat content. Implemented dietary treatment has an impact on modification of certain biochemical indicators--lipid profile of children with increased indicators of lipid metabolism.

The main risk factors for simple obesity in examined children (n=236) aged 3-15 yrs were familial and environmental conditions. A significant correlation was found between the children's obesity expressed by a normalized body mass index BMI z-score, unrelated to age and sex, and mother's level of education and father's obesity (Chi(2) test, p<0.05). A positive correlation was demonstrated between the normalized relative body mass index (BMI z-score) and children's anthropometrical parameters--thickness of skin and adipose folds on the arm, below the shoulder blade (scapula), on the abdomen and their sum, arm circumference, waste-hip ratio and body fat content and the children's parents body mass index (father's BMI, mother's BMI). In boys with simple obesity the tendency to central obesity was observed since early childhood. In the examined group of children no distortions of metabolism of carbohydrates were observed (correct fasting levels of glucose), while in children with obesity the irregularities of metabolism of fats were noted. The implemented dietary treatment (low energy diet with elements of low glycemic index) had a significant impact on improvement of lipid metabolism in all children in whom the irregularities of metabolism of fats were noted. Modification of the diet of children aged 3-6 by implementing dietary recommendations, including the increased frequency of meals and the choice of products with low glycemic index, did not have a significant impact on the decrease of the body mass index in 95% of examined children. A considerable number of children aged 3-6 (n=12) continued to eat only three meals a day and their model of nutrition, including the selection of products, was not significantly modified. The introduced low energy diet with elements of low glycemic index in children of school age (7-15 years) with simple obesity positively influenced the decrease of analyzed features and parameters (p<0.0001). During dietary treatment statistically significant decrease of the children's body mass was observed as well as a decrease of the thickness of skin and adipose folds on the arm, below the shoulder blade (scapula), on the abdomen and a decrease of arm circumference and body fat content. The change of the energy content of a daily food ration, the amount of consumed carbohydrates and products from the group of sugar and sweets, cereal foodstuffs and fat and products from the group of other fats was positively correlated with body mass loss expressed as the difference between z-score BMI before and after the dietary treatment. The modification of the eating habits--increased frequency of meals and reduction or elimination of eating between the meals during the nutrition intervention were not significantly linked to the change of normalized body mass index in the examined children. Only the frequency of eating sweets was related to the change of z-score BMI (p<0.05). The implemented dietary treatment in obese children aged 7-15 years significantly influenced the body mass loss. In children (n=38/236) with lipid metabolism abnormalities, the low energy diet with elements of low glycemic index had a favorable impact on the lipid profile. The increased levels of total cholesterol, LDL cholesterol and triglycerides returned to normal.

1. How does congenital syndrome and drug therapy affect obesity?

Development of metabolic syndrome depends on two elements: firstly adult weight gain, with body fat accumulation and secondly a predisposition to locate fat in intra-abdominal sites, including ectopic fat in liver, pancreas and heart. The metabolic syndrome is strongly linked to a lifestyle characterized by an easy access to unlimited supply of high caloric, low nutrient-dense, foods and physical inactivity. This exposure is most potent during early period of life resulting in childhood obesity which is a major risk for metabolic syndrome in adults. Psychosocial stress has also been suggested to contribute, with most metabolic components are more prevalent in socioeconomically deprived populations. Not all individuals go on to develop the metabolic syndrome because of the high individual variation and genetic/epigenetic factors for both the components of the syndrome, for example insulin resistance and dyslipidaemia and body compositionand their expression varies with changes in external environment. It is estimated that genetic factors contribute about 30% of the observed variance in BMI but about 70% of the variance in fat distribution that relates more to the metabolic syndrome. The lifestyle factors that increase intra-abdominal fat and metabolic risk factors are weight gain, a diet high in saturated fat, smoking, inactivity and excess alcohol intake. 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) in 2007. *FTO* gene 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 higher 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. The predisposition to deposit excess body fat in intra-abdominal and ectopic sites appears mainly to be determined very early in life. Poor intra-uterine growth is a recognized factor, suggesting an epigenetic mechanism. There is scattered evidence for other exposures during pregnancy or early infancy, for example maternal smoking, Aside from certain drug effects (e.g. antiretroviral agents promote central fat accumulation, thiazolidinediones reduce it) there is little evidence that any factors in later life can modify fat distribution.

1. Discuss the aetiology of cancer and its molecular basis

**Overview**

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. Cancer often has the ability to spread throughout your body.

Cancer is the second-leading cause of death in the world. But survival rates are improving for many types of cancer, thanks to improvements in cancer screening and cancer treatment.

**Symptoms**

Signs and symptoms caused by cancer will vary depending on what part of the body is affected.

Some general signs and symptoms associated with, but not specific to, cancer, include:

* Fatigue
* Lump or area of thickening that can be felt under the skin
* Weight changes, including unintended loss or gain
* Skin changes, such as yellowing, darkening or redness of the skin, sores that won't heal, or changes to existing moles
* Changes in bowel or bladder habits
* Persistent cough or trouble breathing
* Difficulty swallowing
* Hoarseness
* Persistent indigestion or discomfort after eating
* Persistent, unexplained muscle or joint pain
* Persistent, unexplained fevers or night sweats
* Unexplained bleeding or bruising

**Causes**

Cancer is caused by changes (mutations) to the DNA within cells. The DNA inside a cell is packaged into a large number of individual genes, each of which contains a set of instructions telling the cell what functions to perform, as well as how to grow and divide. Errors in the instructions can cause the cell to stop its normal function and may allow a cell to become cancerous.

**What do gene mutations do?**

A gene mutation can instruct a healthy cell to:

* **Allow rapid growth.** A gene mutation can tell a cell to grow and divide more rapidly. This creates many new cells that all have that same mutation.
* **Fail to stop uncontrolled cell growth.** Normal cells know when to stop growing so that you have just the right number of each type of cell. Cancer cells lose the controls (tumor suppressor genes) that tell them when to stop growing. A mutation in a tumor suppressor gene allows cancer cells to continue growing and accumulating.
* **Make mistakes when repairing DNA errors.** DNA repair genes look for errors in a cell's DNA and make corrections. A mutation in a DNA repair gene may mean that other errors aren't corrected, leading cells to become cancerous.

These mutations are the most common ones found in cancer. But many other gene mutations can contribute to causing cancer.

**What causes gene mutations?**

Gene mutations can occur for several reasons, for instance:

* **Gene mutations you're born with.** You may be born with a genetic mutation that you inherited from your parents. This type of mutation accounts for a small percentage of cancers.
* **Gene mutations that occur after birth.** Most gene mutations occur after you're born and aren't inherited. A number of forces can cause gene mutations, such as smoking, radiation, viruses, cancer-causing chemicals (carcinogens), obesity, hormones, chronic inflammation and a lack of exercise.

Gene mutations occur frequently during normal cell growth. However, cells contain a mechanism that recognizes when a mistake occurs and repairs the mistake. Occasionally, a mistake is missed. This could cause a cell to become cancerous.

**How do gene mutations interact with each other?**

The gene mutations you're born with and those that you acquire throughout your life work together to cause cancer.

For instance, if you've inherited a genetic mutation that predisposes you to cancer, that doesn't mean you're certain to get cancer. Instead, you may need one or more other gene mutations to cause cancer. Your inherited gene mutation could make you more likely than other people to develop cancer when exposed to a certain cancer-causing substance.

It's not clear just how many mutations must accumulate for cancer to form. It's likely that this varies among cancer types.

**Risk factors**

While doctors have an idea of what may increase your risk of cancer, the majority of cancers occur in people who don't have any known risk factors. Factors known to increase your risk of cancer include:

**Your age**

Cancer can take decades to develop. That's why most people diagnosed with cancer are 65 or older. While it's more common in older adults, cancer isn't exclusively an adult disease — cancer can be diagnosed at any age.

**Your habits**

Certain lifestyle choices are known to increase your risk of cancer. Smoking, drinking more than one alcoholic drink a day (for women of all ages and men older than age 65) or two drinks a day (for men age 65 and younger), excessive exposure to the sun or frequent blistering sunburns, being obese, and having unsafe sex can contribute to cancer.

You can change these habits to lower your risk of cancer — though some habits are easier to change than others.

**Your family history**

Only a small portion of cancers are due to an inherited condition. If cancer is common in your family, it's possible that mutations are being passed from one generation to the next. You might be a candidate for genetic testing to see whether you have inherited mutations that might increase your risk of certain cancers. Keep in mind that having an inherited genetic mutation doesn't necessarily mean you'll get cancer.

**Your environment**

The environment around you may contain harmful chemicals that can increase your risk of cancer. Even if you don't smoke, you might inhale secondhand smoke if you go where people are smoking or if you live with someone who smokes. Chemicals in your home or workplace, such as asbestos and benzene, also are associated with an increased risk of cancer.

**Complications**

Cancer and its treatment can cause several complications, including:

* **Pain.** Pain can be caused by cancer or by cancer treatment, though not all cancer is painful. Medications and other approaches can effectively treat cancer-related pain.
* **Fatigue.** Fatigue in people with cancer has many causes, but it can often be managed. Fatigue associated with chemotherapy or radiation therapy treatments is common, but it's usually temporary.
* **Difficulty breathing.** Cancer or cancer treatment may cause a feeling of being short of breath. Treatments may bring relief.
* **Nausea.** Certain cancers and cancer treatments can cause nausea. Your doctor can sometimes predict if your treatment is likely to cause nausea. Medications and other treatments may help you prevent or decrease nausea.
* **Diarrhea or constipation.** Cancer and cancer treatment can affect your bowels and cause diarrhea or constipation.
* **Weight loss.** Cancer and cancer treatment may cause weight loss. Cancer steals food from normal cells and deprives them of nutrients. This is often not affected by how many calories or what kind of food is eaten; it's difficult to treat. In most cases, using artificial nutrition through tubes into the stomach or vein does not help change the weight loss.
* **Chemical changes in your body.** Cancer can upset the normal chemical balance in your body and increase your risk of serious complications. Signs and symptoms of chemical imbalances might include excessive thirst, frequent urination, constipation and confusion.
* **Brain and nervous system problems.** Cancer can press on nearby nerves and cause pain and loss of function of one part of your body. Cancer that involves the brain can cause headaches and stroke-like signs and symptoms, such as weakness on one side of your body.
* **Unusual immune system reactions to cancer.** In some cases the body's immune system may react to the presence of cancer by attacking healthy cells. Called paraneoplastic syndrome, these very rare reactions can lead to a variety of signs and symptoms, such as difficulty walking and seizures.
* **Cancer that spreads.** As cancer advances, it may spread (metastasize) to other parts of the body. Where cancer spreads depends on the type of cancer.
* **Cancer that returns.** Cancer survivors have a risk of cancer recurrence. Some cancers are more likely to recur than others. Ask your doctor about what you can do to reduce your risk of cancer recurrence. Your doctor may devise a follow-up care plan for you after treatment. This plan may include periodic scans and exams in the months and years after your treatment, to look for cancer recurrence.

**Prevention**

There's no certain way to prevent cancer. But doctors have identified several ways of reducing your cancer risk, such as:

* **Stop smoking.** If you smoke, quit. If you don't smoke, don't start. Smoking is linked to several types of cancer — not just lung cancer. Stopping now will reduce your risk of cancer in the future.
* **Avoid excessive sun exposure.** Harmful ultraviolet (UV) rays from the sun can increase your risk of skin cancer. Limit your sun exposure by staying in the shade, wearing protective clothing or applying sunscreen.
* **Eat a healthy diet.** Choose a diet rich in fruits and vegetables. Select whole grains and lean proteins.
* **Exercise most days of the week.** Regular exercise is linked to a lower risk of cancer. Aim for at least 30 minutes of exercise most days of the week. If you haven't been exercising regularly, start out slowly and work your way up to 30 minutes or longer.
* **Maintain a healthy weight.** Being overweight or obese may increase your risk of cancer. Work to achieve and maintain a healthy weight through a combination of a healthy diet and regular exercise.
* **Drink alcohol in moderation, if you choose to drink.** If you choose to drink alcohol, limit yourself to one drink a day if you're a woman of any age or a man older than age 65, or two drinks a day if you're a man 65 years old or younger.
* **Schedule cancer screening exams.** Talk to your doctor about what types of cancer screening exams are best for you based on your risk factors.
* **Ask your doctor about immunizations.** Certain viruses increase your risk of cancer. Immunizations may help prevent those viruses, including hepatitis B, which increases the risk of liver cancer, and human papillomavirus (HPV), which increases the risk of cervical cancer and other cancers. Ask your doctor whether immunization against these viruses is appropriate for you.
* *The Molecular Basis of Cancer*;

The text is divided into four main sections: malignant transformation,
growth and spread of cancer, molecular abnormalities of specific
malignancies, and the molecular basis of cancer therapy. The first
section on malignant transformation is comprised of introductory
chapters on such topics as cell-cycle regulation, viral carcinogenesis,
tumor-suppressor genes, specific oncogenes, and signal transduction.
The chapters on viral carcinogenesis and tumor-suppressor genes
are well-written and comprehensive with extensive reference lists,
but the chapter on molecular genetics of hematopoietic malignancies
is inappropriate for the introductory section and is redundant,
since much of the information is repeated in two later chapters.

* The second section, entitled "Growth and Spread of Cancer,"
includes chapters on cytokinetics, cell adhesion mechanisms, tumor
angiogenesis, and molecular mechanisms of metastasis. The chapters
on cell adhesion and angiogenesis are excellent; the text is clear
and well-written, and each chapter has over 340 references.
* The third section is comprised of chapters on specific tumors,
including hematopoietic malignancies, childhood malignancies,
lung cancer, breast cancer, and colorectal cancer. Certain cancers
with well-defined molecularly based origins have been omitted,
such as genitourinary cancers (renal cell cancers, bladder cancers,
germ cell tumors), sarcomas, ovarian cancer, melanoma, and endocrine
cancers (eg, medullary thyroid cancer). All the omitted cancers
have fascinating, well-established molecular mechanisms, and the
textbook would be more complete with additional chapters on these
cancers.
* Cancer therapy is the main topic of the fourth and final section,
and chapters on chemotherapy, radiation therapy, growth factors,
monoclonal antibody therapy, cellular immunity, and gene therapy
are included. One chapter I was disappointed with was that on
cellular immunity, which consists of 18 pages of uninterrupted
text with no diagrams. Most of the chapter focuses on natural
killer and tumor-infiltrating leukocyte (TIL) cells with a rather
long historical description of past immunotherapy trials. I was
surprised to find no discussion of tumor antigens, T-cell costimulation,
or T-cell anergy, and how these concepts may relate to the escape
of cancers by the immune system. Importantly, manipulation of
the immune system may lead to novel anticancer therapies, which
was not discussed.
* One significant shortcoming of the book as a whole is the paucity
and poor quality of the illustrations. Conceptual understanding
of the molecular biology discussed in the text would be facilitated
by clear diagrams, which should serve to confirm points described
more fully in the text. In *The Molecular Basis of Cancer*,
the text bears the full responsibility of explaining detailed,
complex concepts. Diagrams, when present, are often small, rudimentary,
and sometimes even appear hand-drawn. This textbook would benefit
from larger, clearer, computer-generated, and more frequent diagrams.