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Obesity as a disease of the twenty-first century
Otyłość jako choroba XXI wieku

Summary
The present time appears to be a growing number of people suffering from obesity. Although a number of studies has not been known so far that eventually the molecular mechanisms conducive to the occurrence of overweight. This article introduces the current state of knowledge in this area.

Key words:obesity, metabolic syndrome, FTO

Streszczenie
W obecnym czasie odnotowuje się coraz większą rzeszę ludzi cierpiących na otyłość. Mimo licznych badań nie poznano do tej pory ostatecznie jakie mechanizmy molekularne sprzyjają występowaniu nadwagi. Poniższy artykuł przybliża aktualny stan wiedzy z tej dziedziny.

Słowa kluczowe: otyłość, zespół metaboliczny, gen podatności na otyłość.

Introduction

Obesity is defined as body weight increased significantly above normal values established for the age, gender and race, caused by excessive growth of body fat (Lang, 2012). This process leads to impairment of various organs and an increased risk of morbidity. In adults, it is recognized when the fat content is higher than 30% of ideal body weight in females and 25% males. In children, the content of fat in the body is highly dependent on age and sex (Berkowitz et al. 2005; Galal, Hulett, 2005). To assess the degree of obesity and the present distribution of anthropometric data used centile charts and so. BMI (Body Mass Index) is calculated by dividing body weight (in kilograms) and the square of the body length (in meters). A BMI of 25-29.9 kg/m2 is overweight while the value above 30 kg/m2 is called obesity (Poskitt, 1995).

A more accurate indicator of obesity is to assess the amount of fat, made with electronic equipment or calculated with the following formula: the amount of body fat [%] = (1.2 xBMI) + (0.23 xwiek) - (10.8 xpłeć) -5.4. Based on a mathematical calculation of the value of above 15-20% in men and more than 25-30% of women confirmed obesity (where the number of points for sex is 1.0 for men and 0 for women) (Barao, Fornes, 2012).

To assess the nutritional status and risk of certain diseases of civilization is evaluate the distribution of body fat compared to the rate of waist circumference to hip circumference ratio (WHR, waist to hipcircumference ratio). WHR (by Bjontropa) above 1 for men is called a androidal and less than 1 - gynoidal; WHR above 0.8 for women is the type of androidal, and below 0.8 is a type of gynoidalny. Androidal type is a risk factor for diseases of civilization (Białkowska, 1994; Barao, Fornes, 2012).

Obesity has been officially recognized as a chronic disease, not just a cosmetic defect since 1985 (Health implications of obesity. National Institutes of Health Consensus Development Conference Statement, 1985). In 1997, the World Health Organization (WHO) officially announced the worldwide epidemic involving adults and children, recognizing it as one of the greatest threats to human health (Wojcicki, 1994). In Europe, the prevalence of obesity affects approximately 30% of adults and about 20% of children and adolescents, although there are differences between the northern countries (10 - 20% of obesity in the general population) and southern (30 - 35% of obesity in the general population) (Lobstein, Frelut, 2003). In Poland, based on growth charts developed by the Institute of Mother and Child, and carried out in 1994-1995, obesity was observed in 3.4% and overweight in 8.7% of children and adolescents aged 6 - 17 years (Oblacińska, 1997). This percentage has increased noticeably in the second half of the nineties and was 18% in children aged 7 - 11 years and 12% in children aged 14 - 17 years (Lobstein, Frelut, 2003).

Terminology

Depending on the arrangement of the subcutaneous tissue is distinguished by obesity androidalną and gynoidal. Androidal obesity (abdominal, visceral, ‘apple’) is characteristic of a male in which the fat is localized mainly in the stomach. In this type of risk is particularly high coexistence of metabolic diseases (insulin resistance syndrome, hyperinsulinemia, hyperuricemia, elevated levels of fibrinogen in the blood, hypercholesterolemia, hypertriglyceridemia), hypertension, diabetes and cardiovascular diseases (coronary heart disease, stroke, limb ischemia, embolic disease thromboembolism). Obesity gynoidal (gluteal-femoral, a “pear”) occurs primarily in females, in which the fat is localized mainly on the hips, buttocks and thighs (Baghi, Preuss, 2007; Haslam, James, 2005).

Considering the division we can distinguish pathogenic regulatory and metabolic obesity. Regulatory Obesity occurs when the under the influence of various factors (psychological, hormonal, economic) is disturbed normal feeding mechanism (excessive stimulation of the appetite center). Obesity and metabolic caused by a congenital or acquired disorder in carbohydrate or lipid (Knerr, 2004; Stawiarska-Heel et al. 2007).

Depending on the etiology of obesity distinguish simple, youthful and secondary or pathological. Obesity simple (idiopathic, one-symptom, source) arises from an imbalance between the amount of energy supplied with food and its consumption. In 20% of cases it is genetically determined and is probably associated with low basal metabolic rate of the family members with which it occurs. Juvenile obesity is mainly due to release of dense growth in this age group. Obesity is associated with secondary endocrinological diseases or nerve side effects of the treatment of chronic and genetic defects (Kosti, Panagiotakos,

2006; Lange, 2001). Among the bands genetic and chromosomal predisposing to obesity include disclosure of the teams: Willy-Pradera, Moon Bardet-Biedl, Alstrom-Hallgren, Cohen, Carpenter, Turner, Klinefelter, storage diseases and Down syndrome.

Etiologic agent

The most common reasons for increasing the amount of fat include abnormal eating habits, low physical activity, emotional problems and abnormal nutrition of pregnant women.

Improper eating habits (overeating, improper composition of the diet with lots of sugars and fats, nutrition in fast food) leads to the accumulation in the body of significant amounts of saturated fat and trans isomers at the expense of antioxidants, trace minerals, fiber and mineral water (Agras, Kramer, 1987; Elliott et al. 2004; Haslam, James, 2005; Komorowski, Pawlikowski, 1992; Lange et al. 2001).

Low physical activity ("couch potato kid") and abnormally shaped family lifestyle in which most of the time is spent in front of the TV or computer, snacking high-calorie snacks. Physical activity in the open air in such a case is limited to a short walk to the car or to the supermarket. It is shown that the muscular stagnation due to a lack of physical activity leads to clumping of fat droplets in adipocytes, compacted and thus fat is broken down harder. In addition, reduction of physical activity and prolonged immobilization reduces the consumption of energy supplied from food (Gutin, Manos, 1993; Nazar, Kaciuba-Uściłko, 1995).

Emotional problems, abnormal family relationships, stressful lifestyle with great psychological stress ("being unwanted and unnecessary", "lives in his own world" is not always understood by the environment). Long-term negative factors are offset psycho-pleasure which is the food. In addition, they may interfere with the proper functioning of the hunger centers in the hypothalamus (medial and lateral), and the cerebral cortex, resulting in a continuous binge (Goodman, Whitaker, 2002; Szajewska, 2002).

Improper nutrition of pregnant women. The results suggest that maternal obesity and excessive energy delivery prenatal promote childhood obesity, increasing the risk of metabolic syndrome, changes in vascular reactivity and hypertension. Additionally, it is believed that the early introduction of artificial infant milk (increased protein intake) promote excessive growth of body weight compared to breast-fed children (Breier et al. 2001).

Pathophysiology

Control over the amount of food intake exercise of hunger and satiety centers located in the hypothalamus, rhinencephalon, the limbic system and the cerebral cortex. The main structure of the system is the arcuate nucleus and ventromedial nucleus, including both producing neurons excitatory neurotransmitters (neuropeptide Y, agouti protein) as well as appetite suppressants (substances antyoreksygenne) - Proopiomelanocortin, transcripts of cocaine and amphetamines. Nutritional information centers are replaced by the chemical nature of the energy substrates (glucose, free fatty acids, amino acids) as well as by neurotransmitters such as gamma-aminobutyric acid (GABA), acetylcholine, dopamine, epinephrine, serotonin, endorphins. Stimuli continuously reach the regulatory

centers that affect glucose, insulin release, food intake and thermogenesis. Additionally, the appetite is affected certain neurotransmitters stimulate (norepinephrine, increases the appetite for carbohydrates) and serotonin-inhibiting (reducing cravings for carbohydrates) and dopamine (inhibits fat intake) (Baghi, Preuss, 2007; Haslam, James, 2005).

Significant impact on the development of obesity protein leptin is as a result of the expression of the ob gene located on chromosome 7. This substance is produced by adipose tissue, together with the flow of blood reaches the hypothalamus, where it is combined with the specific receptor (dimerization) causes inhibition of the synthesis and release of neuropeptide Y. Leptin increases satiety, reduces appetite, increases thermogenesis and processes leading to the loss of energy, than is lowers blood glucose and insulin in the blood. Due to the fact that the concentration of leptin in the blood of obese people is higher compared to those of normal weight, it is believed there are certain of those substances that act as antagonist to leptin (leptin-resistance action). If overweight people, the concentration of leptin in the blood drops to control values after four weeks of acute diet (400 kcal / day), it is only then they can expect to restore the feeling of fullness after a meal. Note, however, that this type of diet is not always safe because of the fact that leptin also regulates immune function. The study also observed that there are significant fluctuations in the ob gene expression during starvation and return to a normal diet. During fasting serum leptin concentration is reduced to undetectable values and increases to very high during the commutation of increased caloric (anorexia nervosa). The resulting condition may cause difficulties in maintaining a normal body weight, to reduce appetite and increase energy expenditure. The situation is different in different situation: in obese patients using caloric restriction reduced leptin levels in the blood, and thus increases appetite, reduces thermogenesis and energy expenditure, which may hamper obtained with difficulty reduced body weight (Breier et al. 2001; Romer, 1997; Świerczyński et al. 1997; Tatoń et al. 2007).

The other causes of obesity are mentioned also reduce postprandial thermogenesis. Mature people react to welcome meal in the form of increased heat dissipation by up to 10% of the supplied energy (called diet-induced thermogenesis). The essence of this process is the protein-termogenin which dissipates in the form of a substantial part of the heat energy generated during the processes included in the respiratory chain. Uncoupling can be found in the mitochondria of brown adipose tissue (BAT), which in the form of small aggregates are distributed in a normal white adipose tissue. In the absence of BAT or impairment of the function in obese postprandial thermogenesis is very limited or does not exist. The process of creating protein in the BAT is adjusted such with the participation of sympathetic fibers, dense tangle cells of that tissue. b-3-adrenergic receptors in BAT, which in turn stimulates the breakdown of fat in adipose tissue, glucose transport to BAT and postprandial thermogenesis.Which is a neurotransmitter norepinephrine stimulates end here. It has been shown that the primary defect that leads to the development of obesity, is often associated with reduced sensitivity of adrenergic receptors in brown adipose tissue. The visceral obesity sympathetic activity at the beginning of the disease is increased, and, with increasing insulin resistance decreases. The highest number of b-3 adrenergic receptors found an area with high metabolic activity in intra-abdominal and perirenal adipose tissue. b-3-adrenergic receptor has about 40% of the human population.

It has been shown that the synthesis of the mutant gene encoding b-3adrenergic receptors. This mutation is inherited as a recessive trait.If the individual inherits from both parents, it is predisposed to obesity, due to defective. Changes in their construction may impair thermogenesis and lipolysis, including peritoneal adipose tissue leading to the development of visceral obesity and type 2 diabetes with all its consequences metabolic (Walston et al. 1995).

Some types of obesity, in response to a high-calorie diet, accompanied by excessive secretion of acylation stimulating proteins (ASP). To increase their production runs associated with activation of protein-adypsyn whose expression increases during differentiation to adipose tissue cells. In the obesity gynoidal, the concentration of ASP in blood plasma is increased, the higher is the ability of the subcutaneous adipose tissue deposition. An inverse relationship is observed in abdominal obesity as cell response in visceral fat in ASP protein is impaired. This condition results in an increase in free fatty acids in serum decreased ability to remove from the blood plasma postprandial triglyceride-rich lipoproteins and increased the flow to the liver. All this leads to increased synthesis of atherogenic lipoproteins and increase in the concentration of ASP in blood plasma (Kielar, 1995).

In addition, among the factors affecting body weight and body fat distribution plays the following genes: a gene of peroxisomal proliferator-activated receptor gamma(PPAR-γ) is responsible for the differentiation of fibroblasts into the adipocytes and affecting the metabolism of mature cells; cannabinoid receptor (CNR1) is an integral part of the network that control appetite, fat mass and obesity associated gene(FTO) (Męczekalski et al. 2008).

FTO is located on chromosome 16 (16q12.2). It consists of 9 exons and covers an area of more than 400 kb (Loos and Bouchard, 2008). This gene encodes a 2-demethylase oxoglutaran, depending on the DNA, an enzyme present in many tissues (particularly the hypothalamus). FTO expression is inhibited by intermediates of the Krebs cycle metabolites, in particular by fumarate (Gerken et al. 2007). On the basis of studies have shown an association between the FTO risk allele carrier state and the components of metabolic syndrome, such as waist circumference, insulin sensitivity, the concentration glucose, triglycerides and cholesterol (Andreasen et al. 2008). It is now believed that the mechanism of action is related FTO:

- the control offood intakeand the type offood preferences, and to a lesserextentin the regulation ofenergy expenditure(Wardle et al. 2009);
- a change inmRNAexpressionin the hypothalamusFTO (arcuate nucleus) (Gerkenetal., 2007);
- withadipogenesisbychanges in insulin sensitivityin the cerebral cortex(Tschritter et al. 2007);
- direct influenceon the metabolismof fat cellsthrougheffects onlipolysisin adipocytes(FTO mRNAexpressionis activatedat an earlystage ofdifferentiation ofpreadipocytes) (Wahlenetal, 2008).

Complications

If left untreated, obesity entails a number of health consequences. Early complications associated with overweight in children and adolescents include: high blood pressure, stroke, atherosclerosis, insulin-resistance, type 2 diabetes, dyslipidemy, metabolic syndrome, non-alkoholic fatty liver disease (NAFLD), hypertransaminazemy, kidney bubble, glomerulosclerosis, obstructive sleep apnea (OSA), bronchial asthma, reduced exercise tolerance, diseases of the bone and joints (knee valgus, Blount disease, slipped capital femoral head, flat feet, scoliosis, postural problems, back pain, arthritis bones and joints), emotional disorders (low self-esteem). The consequence of untreated obesity results in the following complications in later life obesity, risk factors for the occurrence of cardiovascular (hypertriglyceridemy, hypercholesterolemy, high LDL cholesterol, low HDL cholesterol, hyperinsulinemy, hypertension), left ventricular hypertrophy, reduced life expectancy (Gawlik et al. 2009; Haslam, James, 2005).

Conclusions

At the present time appears to be an increasing number of people suffering from obesity. Although a number of studies has not been known so far that eventually the molecular mechanisms conducive to the occurrence of overweight. The study of genetic determinants of obesity give hope for the future. Perhaps this knowledge will help in the near future to develop new drugs that will be healed in certain of obesity and thus prevent the occurrence of many of its serious complications. However, in order to protect yourself from unpleasant consequences of untreated complications of obesity, you should pay special attention on the fight. Both parents and physicians should educate children to the need for proper, balanced diet, avoid situations conducive to weight gain and promote an active lifestyle. Addressed these recommendations should not only be obese, but thin as normal weight during childhood and adolescence does not protect against the development of obesity in later. American Society of Endocrinology recommends: breast-feeding for at least six months of age, the commitment of schools to organize daily hour of exercise in all age groups, information on the principles of optimal diet and the benefits of increasing physical activity, promoting the consumption of unhealthy food restriction and prohibition of advertising, as also create opportunities for safe walking to reach the school. In addition, the recommendations emphasize the particular importance of preventive measures in children with BMI> 85 th percentile (August et al. 2008).

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