Bratisl Lek Listy 2008; 109 (5)
224 – 230

SURVEILLANCE

Adult obesity at the beginning of the 21st century: epidemiology, pathophysiology and health risk

Ginter E[1], Simko V[2]

Institute of Preventive and Clinical Medicine, Bratislava, Slovakia. **ginter.emil@mail.t-com.sk**

Abstract: Obesity is defined as increased body weight caused by excessive accumulation of fat. Due to a very long period of undernutrition in human history, the contemporary human body•s regulation mechanisms seem to be biased in favor of preserving fat rather to eliminate it. At the highest risk are populations that suddenly gained wealth. The shift from undernutrition to overnutrition has occurred in a very short time, in many population groups in less than in one generation. The increase of obesity prevalence observed in the 20th century continues until present and it appears this trend will further continue in almost all countries in the world. Contemporary prevalence of adult obesity is very high in USA (33 % in both gender), in oil-rich Arabian countries (30 % in males, 40 % in females) and in European Union (up to 25 % in both gender). The aim of contemporary research is to understand the molecular and neural systems which the body uses to regulate its storage of energy in the form of fat and how these systems can become unbalanced, leading to obesity. In spite of discovery of new hormones (e.g. leptin produced in adipose tissue) and of new mechanisms, the prevention and treatment of obesity remains an open problem. Obesity is associated with an increased risk of numerous comorbidities such as type 2 diabetes, metabolic syndrome, hypertension, cardiovascular diseases and osteoarthritis. In USA the impact of obesity on mortality may have decreased over time, perhaps because of improvements in public health and medical care. New data from USA and China suggest the lowest all-cause mortality in persons with a body mass index, BMI between 23.0 and 27.0 *(Fig. 6, Tab. 1, Ref. 29).* Full Text (Free, PDF) *www.bmj.sk.*
Key words: obesity, BMI, metabolic syndrome, diabetes, heart disease, overweight.

This review aims to summarize the most recent information on obesity in the world, its pathogenesis and health consequences. The main source are informations published after the year 2000 by the World Health Statistics WHO 2007 (1), National Center for Health Statistics USA 2007 (2), Medline journals, American Association of Clinical Endocrinologists (*Endotext.org*), Scientific American (*sciamdigital.com*), and CDC (Centers of Disease Control and Prevention) (3). This review predominantly uses contemporary diagnostic measure, the body mass index (BMI= body weight/square of body height=kg/m^2), because most medical organizations have endorsed the WHO guidelines supporting the use of BMI to define and classify obesity: moderate, class I (BMI 30–34.9), severe, class II (BMI 35–40) and morbidly obese, class III (BMI>40).

Obesity trends observed in the 20th century continue and most probably will reflect a further increase in the developed as well as in the underdeveloped and post-communist countries. In the USA a remakable increase in obesity occurred in the mid-20th century, in the area of present European Union (EU) somewhat later. At least four factors have been decisive: decrease in energy expenditure (increase of automobilism and computers, televison viewing, increase of low-energy office occupations, growing affluence (consumption of more and higher-energy food); intensive advertising of cheap, visually appealing and tasty foods, as well as the decline in breast-feeding which tends to increase the risk of obesity in later life.

Epidemiology of obesity

The data on obesity prevalence have been intensively reported in the USA (2, 3). The prevalence of obesity among American men increased significantly during the 6-year period from 1999 to 2004; among women, no overall increases were observed (4). These estimates suggest that there may be leveling off in US women. Only four states of USA had in 2006 a prevalence of obesity less than 20 %. Twenty-two states had prevalence equal or greater than 25 %; two of these states (Mississippi and West Virginia) were equal to or greater than 30 % (Fig. 1). The situation in Europe is somewhat better (5). The prevalence of adult obesity in the states of EU is lower than in the USA: in males between 8–25 %, in females between 8–27 % (Fig. 2). The highest obesity prevalence is in Central Europe, especially in the Czech Republic (about 25 % of adult male and female population are obese) and in England. The Czech population unfortunately is

[1]Institute of Preventive and Clinical Medicine, Bratislava, Slovakia, and [2]State University New York, Downstate Medical Center at Brooklyn, USA

Address for correspondence: E. Ginter, RNDr, DSc, Racianska 17, SK-831 02 Bratislava, Slovakia.

Adult obesity prevalence (%) in the USA in 2006
(CDC Behavioral Risk Factor Surveillance System)

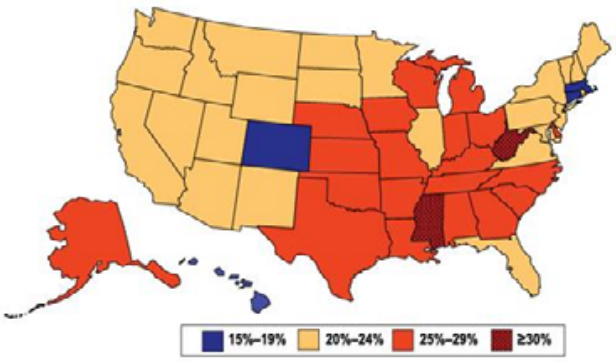


Fig. 1. Last available data on adult obesity prevalence in USA (3).

Adult obesity prevalence (%) in the European Union at the beginning of 21. century

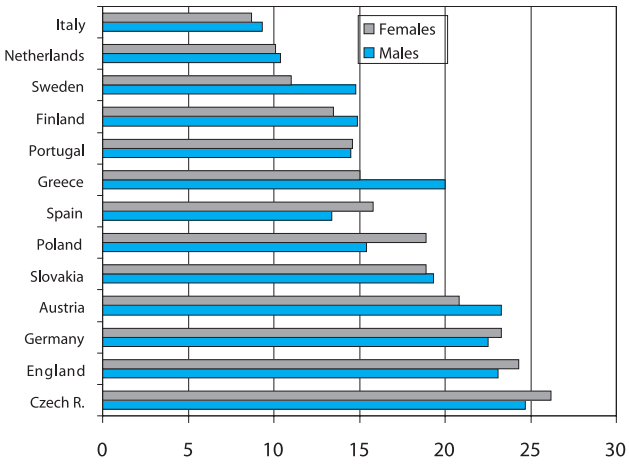


Fig. 2. Last available data on adult obesity prevalence in European Union (5, 6).

getting close to the American. The best situation is in Scandinavia and in the Mediterranean countries with the exception of Greek men. Slovakia presents trends that existed in the USA ten years ago.

According to the WHO estimates (6), there are extreme differences in obesity prevalence in various parts of the world: from about 60 % in the small Pacific island Nauru to 2–3 % in the Chinese population. The countries with highest obesity prevalence are either economically prosperous states like USA, New Zealand and Australia, or oil-rich countries (Kuwait, United Arab Emirates and Saudi Arabia). Nauru is a small Pacific island in which extremely rich stocks of phosphates were found. Enormous increase of the economic prosperity of this island led to an explosion of obesity (about 70 % obesity prevalence). After the phosphate deposits were exhausted, the decline of prosperity resulted in decrease in obesity. The impact of globalization arrived in the undeveloped countries together with the unhealthy Western diet rich in empty calories. Over the past twenty years, people in the Third World have greatly increased their consumption of animal-source foods (meat, poultry, eggs and dairy products), sweetened beverages and the vegetable oils. These people also adopted Western lifestyles that contributed to obesity. For these countries obesity has now emerged as a more serious health threat than the hunger. In South Africa, Mexico and Egypt more than half of the adults are overweight or obese.

The increase of obesity prevalence observed in the 20th century continues until present and it appears this trend will further continue in almost all countries. At the highest risk are populations that suddenly gained wealth from newly discovered mineral or oil deposits, also migrants from poor to affluent parts of the world (central Americans moving to the USA, Asian population from destitute rural areas settling in big cities) as well as poorly educated aborigines socially supported by central government (Australia). Similar problems have gypsies in Slovakia (7, 8). At least three factors are decisive: growing affluence (consumption of more and better food); production of cheap, high-energy and tasty foods; and decrease in energy expenditure. The shift from undernutrition to overnutrition has occurred in a very short time, in many population groups in less than in one generation. Genetic factors may contribute to such explosion of obesity. It is probable that millions of years ago, when food was not easily available, individuals developed a very efficient system to utilize and store energy. Conversely, descendants of those same individuals, living in a new environment of plentitude develop obesity and potentially other characteristics of the metabolic syndrome. Due to a very long period of the lean environment the contemporary human body's regulation mechanisms seem to be biased in favor of preserving fat as a source of energy rather than to eliminate it.

Biochemistry and molecular biology of obesity

1) Regulation of food intake

Almost during the entire existence of mankind only those individuals survived who adjusted to meager food intake. The advent of agricultural improvements somewhat eased the conditions of starvation but essential progress occurred only in the 19th and 20th century, thanks to industrial and scientific advances. How could mankind adjust to the excess in food supply in such a short time?

Obesity became one of the most prominent health problems and hundreds of research centers search for adequate solutions. Our search for "obesity" in the data base brought 50.000 PubMed citations published in the last 10 years. However, it appears that despite this enormous interest the mechanisms leading to abnormal fat deposition are still unclear. We will summarize some basic information, aiming it more at the practical therapist in internal medicine, diabetes and nutrition rather than addressing it to a basic scientist.

The key aim is to understand the systems which the body uses to regulate its storage of energy in the form of fat and how these systems can become unbalanced and lead to obesity (9, 10). Hypothalamus connected with many other regions of the brain is responsible for controlling hunger, thirst, emotions, body temperature regulation, and circadian rhythms (10). Hypothalamus is central to these energy-regulating activities and therefore must receive updated information about how much stored energy is available. Many different molecules, mostly small peptides, have been shown to inuence appetite. An important message is brought to the hypothalamus by a 146 amino acid hormone, leptin produced directly in the adipocytes (9). Serum leptin concentration increases with increasing adipose tissue and is therefore a signal of energy stores. A reduction in adipose tissue with weight loss results in a decrease in leptin levels. Serum leptin is thus a dynamic signal to the hypothalamus of the amount of energy stored in the adipose tissue. Leptin has been tested as a potential weight loss therapy in humans. Leptin treatment produced suppression of appetite, but experiments failed to find significant changes in body weight. The discovery of leptin opened the door to exploration of a whole new biological pathway of cellular signaling and responses.

In addition to the gastrointestinal tract and the adipose tissue, other systems participate in controlling energy balance. For glucose control, a surprising finding was that the skeletal tissue produces calcineurin and osteocalcin, a noncollagenous protein secreted by which acts as a, causing β-cells in the to release more and at the same time directing to release the hormone, which increases sensitivity to insulin (11). Future research may show that the majority of cells produce substances directed to control energy homeostasis.

2) Regulation of energy expenditure

The abnormalities in energy expenditure contribute to the development of obesity. There are two main issues to explain: Is obesity caused by deficiencies in energy expenditure, and if so, what mechanisms, besides inadequate physical exercise, are abnormal in obese individuals? How is energy expenditure regulated and what molecular mechanisms are responsible for this regulation?

According to recent findings from Karolinska Institutet (Sweden), key enzyme, adenosine monophosphate (AMP)-activated protein kinase (AMPK) is an energy sensor that regulates cellular metabolism (12). When activated by a low energy intake, AMPK stimulates glucose uptake and lipid oxidation to produce energy, while turning off energy-consuming processes. AMPK controls whole-body glucose homeostasis by regulating metabolism in peripheral tissues, such as skeletal muscle, liver, adipose tissues, and pancreatic ß cells – key tissues in the pathogenesis of type 2 diabetes. AMPK serves as an intertissue signal integrator among peripheral tissues, as well as the hypothalamus, in the control of whole-body energy balance (12). The same research team identified a ‚fat-burning' gene, the products of which are required to maintain the cells insulin sensitivity. Reduced diacylglycerol kinase (DGK) expression and DGK activity in skeletal muscle from type 2 diabetic patients was found (13). In the absence of DGK, muscles have reduced insulin sensitivity and impaired fat burning ability, which leads to an increased risk of developing obesity.

Obesity as a risk factor for chronic diseases

Obesity is associated with an increased risk of numerous comorbidities, predominantly type 2 diabetes, hypertension, cardiovascular diseases and osteoarthritis (14, 15) and some types of cancer. While excess body weight (BMI>30) is clearly associated with increased risk of mortality, the optimal body weight to minimize mortality risk is equivocal. Several studies have reported a U- or J-shaped association between overweight and mortality (see the next chapter). Though the curve's shape is debatable, studies consistently report that adults with a BMI greater than 30 kg/m^2 have higher mortality rates.

1) Metabolic syndrome, diabetes type 2 and heart disease

Metabolic syndrome (syndrome X or syndrome of insulin resistance) is a combination of disorders that increase risk for diabetes and cardiovascular disease. It affects a large number of people in a clustered fashion. The prevalence of syndrome X in many economically developed countries is calculated as being up to 40% of the adult population. This syndrome is characterized by a group of metabolic risk factors concentrated in one person (16, 17). They include: abdominal obesity, atherogenic dyslipidemia (high triglycerides and low HDL cholesterol), elevated blood pressure, insulin resistance with glucose intolerance, prothrombotic state (e.g., high fibrinogen or plasminogen activator inhibitor-1 in the blood), proinflammatory state (e.g., elevated C-reactive protein in the blood). The dominant underlying risk factors for this syndrome appear to be abdominal obesity and insulin resistance. Other conditions associated with the syndrome include aging, physical inactivity, genetic predisposition and specific hormonal imbalance. Acquired factors, such as excess body fat and physical inactivity, can elicit insulin resistance and the metabolic syndrome in these people. The criteria for diagnosing the metabolic syndrome proposed by the US National Cholesterol Education Program are currently recommended and widely used (Tab. 1).

What is the meaning of serum total cholesterol? Note that total cholesterol levels are not included into criteria for metabolic syndrom diagnosis. Nevertheless, not only in popular but

Tab. 1. The criteria for diagnosing the metabolic syndrome proposed by the US National Cholesterol Education Program.

Abdominal obesity	Men: Waist circumference ≥102 cm Women: Waist circumference ≥88 cm
Blood pressure	≥130/80 mmHg
Triglycerides	≥1.7 mmol/L
Fasting glucose	≥5.6 mmol/L
HDL cholesterol	Men <1.0 mmol/L Women <1.3 mmol/L

The metabolic syndrome is present when 3 or more of the 5 criteria are met.

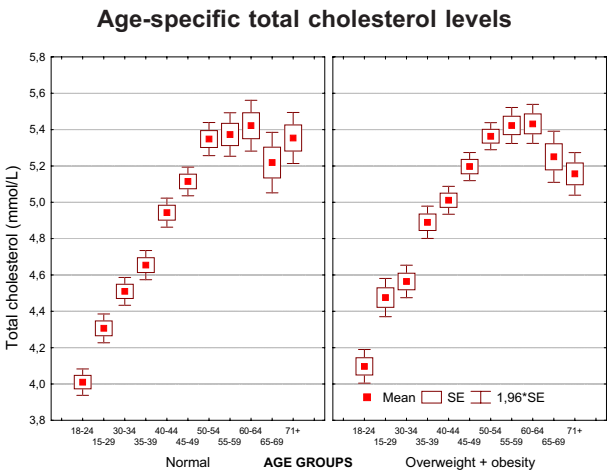


Fig. 3. Age-specific plasma cholesterol levels are very similar in the control and obesity-overweight groups (unpublished data from Slovakia).

also in some scientific articles there appear claims that overweight and obesity are associated with elevated cholesterol. Formal statistics indicates a correlation between BMI and the total cholesterol, however a multifactorial analysis of a represenative all-Slovak sample of more than 11.500 adult men and women aged 18–84 indicated that the main cause of this correlation was a close relation of BMI and blood cholesterol with age (Fig. 3). Age-specific values of total cholesterol levels are mildly elevated only in younger overweight individuals and remarkably, at certain higher age intervals cholesterol is lower in individuals with overweight and obesity.

Controversial reports on clinical significance of elevated total cholesterol carry a potential risk: An obese individual who finds his cholesterol to be as low as of his normal-weight counterpart, may underestimate his cardiovascular risk. Obese individuals have to understand that their cardiovascular risk depends on other risk factors, such as their waist circumference, their serum "good" HDL-cholesterol, serum triglycerides and their blood pressure. An elevation in low-density lipoprotein (LDL) cholesterol levels is not a part of the metabolic syndrome, although abnormalities in LDL particle size are. Measurement of the total number of LDL particles and the number of small LDL particles by nuclear magnetic resonance (NMR) appeared to be better related to the metabolic syndrome than were measurements of apolipoprotein B. The most important causes of metabolic syndrome in the following order are aging, genetics and lifestyle (physical activity and caloric intake). There is a debate regarding whether obesity or insulin resistance is the cause of the metabolic syndrome or a by-product of a more far-reaching metabolic derangement. A number of inflammatory markers (e.g. C-reactive protein) are often increased in persons with metabolic syndrome (16, 17).

Numerous cross-sectional and prospective cohort studies have consistently found strong positive association between BMI and risk for type 2 diabetes mellitus. The relative risk of diabetes for obesity group increased 20 fold, and for heavy obesity inreased 39 fold, compared with control group of women (18). Numerous other studies have found that the risk for developing diabetes increases exponentially in both men and women with increasing BMI. It is probable that in the USA about 70 % incident cases of diabetes type 2 could be prevented if BMI's were below 25 kg/m^2.

Obesity is an independent risk factor for cardiovascular diseases (CVD). Obesity could affect CVD through its influence on known risk factors such as metabolic syndrome (low HDL-cholesterol, hypertriglyceridemia, glucose intolerance and hypertension), inflammatory markers, prothrombotic state and obstructive sleep apnoe. Obesity and diabetes have overtaken hypertension, smoking and dyslipidemia as a risk factors for CVD (15, 19). Besides an altered metabolic profile, a variety of alterations in cardiac structure and function occur in the morbidly obese persons.

2) Obesity and cancer

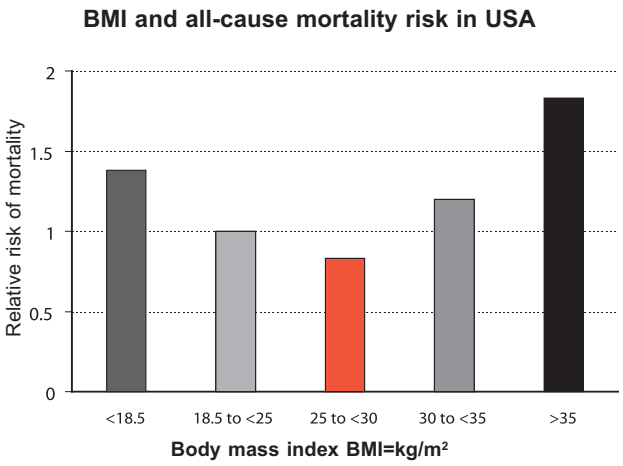
Obesity has been linked with increased risk of some cancers. Analysis of the association between BMI and colon cancer mortality over a 12-year follow-up in about 850 000 persons found that the relative risks of colon cancer mortality increased linearly across all categories of BMI in men but not women (20). A 13-year prospective cohort study of 750 000 persons found that gallbladder cancer mortality rates were significantly higher among obese women, but not in men. Reeves et al (21) recently published results of a prospective cohort study in 1.2 million women followed 7 years for cancer mortality in United Kingdom. Increasing BMI was associated with a significant increase in the risk of cancer for 10 out of 17 specific types examined. In a prospectively studied population of more than 900 000 U.S. adults, death rates from all cancers combined were significantly higher in obese men and women than in control groups (22).

3) Morbidity associated with obesity

Obesity is a potent risk factor for obstructive sleep apnea, asthma, gallbladder disease and osteoarthritis, particularly of weight bearing joints such as the hip and knee. The health consequences of obesity are substantial, with diabetes type 2, heart disease and gallbladder disease among the more common obesity-related diseases. There are also considerable psychosocial consequences of obesity.

Overweight is not obesity – an open problem of optimum BMI values

There appears an important difference related to stratification of an abnormal excessive body weight. According to many reports, overweight and obesity are associated with an increased risk of morbidity and mortality as well as reduced life expectancy. Nobody doubts that obesity, especially in its extreme forms, does seem to be a serious factor in premature deaths. On the other side, a growing number of dissenting researchers disagree about the health consequences of rising body weights (23). These experts warn against the simplifying weight reduction campaigns



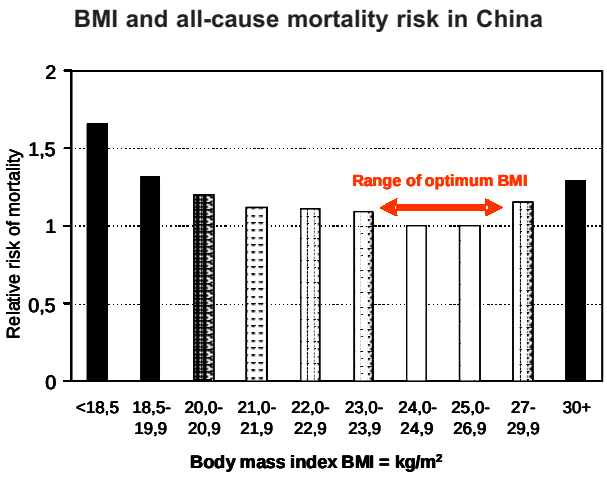


Fig. 4. BMI and relative risk of all-cause mortality in US adults. Graph is based on data of Flegal et al (24).

Fig. 5. BMI and relative risk of all-cause mortality in China adults. Graph is based on data of Gu et al (25).

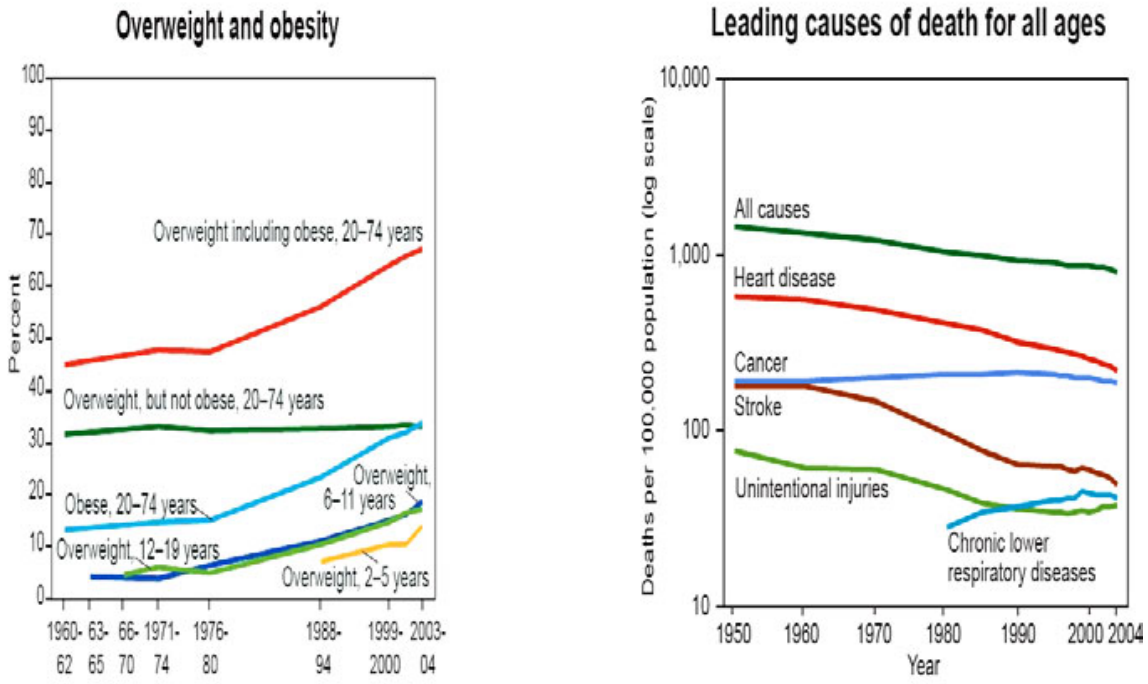


Fig. 6. USA paradox: increase of obesity prevalence and decrease of all cause-, heart disease- and stroke-deaths. Chartbook from the National Center for Health Statistics USA (2).

that are ever so popular in lay press and against unscientific definition of overweight and obesity. Between 2005–2007 Journal of American Medical Assocciation (JAMA) published three important papers (24–26) which throw doubt on the BMI definition of life-shortening overweight. Flegal et al (24) estimated relative risks of mortality associated with different levels of BMI from the nationally representative National Health and Nutrition Examination Survey (NHANES) I, II and III, with follow-up through 2000. These relative risks were applied to the distribution of BMI and other covariates from NHANES 1999–2002 to estimate attributable fractions and number of excess deaths, adjusted for confounding factors and for effect modification by age. Relative to the "normal" weight category (BMI 18.5 to <25), obesity (BMI>30) and underweight were associated with excess deaths. Overweight (BMI 25 to 30) was not associated with excess mortality, on the contrary, the mortality in this group was the lowest (Fig. 4). Gu et al (25) performed similar research in China with almost the same results (Fig. 5). Their findings are consistent with observations from Western populations that have identified the lowest all-cause mortality in persons with a BMI

between 23.0 and 27.0. Flegal et al (26) analyzed cause-specific relative risks of mortality from the NHANES with underlying cause of death information for 2.3 million adults 25 years and older from 2004 vital statistics data for the USA. Underweight and obesity were associated with significantly increased total mortality, obesity was associated with significantly increased cardiovascular mortality, but not with cancer. Overweight was associated with significantly decreased mortality from noncancer, non-CVD causes but not associated with cancer or CVD mortality. McGee (27) published meta-analysis based on person-level data from twenty-six observational studies on BMI and mortality. These results do question whether the current classification of individuals as "overweight" is acceptable in the sense, since there is little evidence of increased risk of mortality in this group.

These data indicate a paradox in the US epidemiological reports. Overweight and obesity rates have increased in USA over the past 25 years. On the other hand, number of deaths caused by cardiovascular disorders has been decreased (Fig. 6). How is it possible that in the USA beside rapid increase of obesity prevalence, cardiovascular mortality decreased, and the life expectancy increased by almost 5 years during the period of the last 20 years? There are two explanations: 1) Better medical control of cardiovascular risk factors, 2) The population of overweight individuals was not under the increased risk of cardiovascular death.

Some inconsistency in the meaning of risk factors may be related to selection of an inadequate parameter for excess body weight, namely the BMI. Though many past observational studies have used BMI as a measure of overall adiposity, a growing evidence suggests that a central (abdominal) fat distribution pattern, as reflected by waist circumference or waist-to-hip ratio (WHR) may be more related to risk than elevated body weight (28). WHR of >1.0 in men and >0.85 in women identify subjects with abdominal fat accumulation reflected by the waist circumference. The waist circumference is the most convenient and simple measurement that correlates well with BMI, WHR and most importantly, with risk factors for cardiovascular disease. There is one important risk factor for overweight persons: with aging they will progress to the group of obese people. Therefore we quote the statement of US public health authorities (29): "Although the Social Security Administration recently raised its estimates of how long Americans are going to live in the 21st century, current trends in obesity in the United States suggest that these estimates may not be accurate. From our analysis of the effect of obesity on longevity, we conclude that the steady rise in life expectancy during the past two centuries may soon come to an end, unless effective population-level interventions to reduce obesity are developed. The youth of today may, on average, live less healthy and possibly even shorter lives than their parents. It is critical to remember that never before in the U.S. history have so many children been so heavy at such a young age. It is naive to believe that new drug therapy will enable an obese child to live a healthy life".

The same holds for Slovakia and for most countries forming the European Union.

References

1. World Health Statistics 2007, WHO, Geneva, 2007.

2. National Center for Health Statistics: Health, United States, 2007, Hayttsville, 2007.

3. CDC Behavioral Risk Factor Surveillance System, USA, 2007 (http://www.cdc.gov)

4. Prevalence of overweight and obesity in the United States, 1999—2004. J Amer Med Ass 2006; 295: 1549—1555.

5. The challenge of obesity in the WHO European Region and the strategies for response. WHO, Copenhagen, Denmark, 2007.

6. Global database on body mass index (BMI). WHO,Geneva, 2006.

7. Ginter E, Krajcovicova-Kudlackova M, Kacala O et al. Health status of Romanies (Gypsies) in the Slovak Republic and in the neighbouring countries. Bratisl Lek Listy 2001; 102: 479—484.

8. Dolinska S, Kudlackova M, Ginter E. The prevalence of female obesity in the world and in the Slovak Gypsy women. Bratisl Lek Listy 2007; 108: 207—211.

9. Klok MD, Jakobsdottir S, Drent ML. The role of leptin and ghrelin in the regulation of food intake and body weight in humans: a review. Obesity Rev 2007; 8: 21—34.

10. Morton GJ, Cummings DE, Baskin GS et al. Central nervous system control of food intake and body weight. Nature 2006; 443: 289—295.

11. Long YC, Glund S, Garcia-Roves PM, Zierath JR. Calcineurin regulates skeletal muscle metabolism via coordinated changes in gene expression. J Biol Chem 2007; 282: 1607—1614.

12. Long YC, Zierath JR. AMP-activated protein kinase signaling in metabolic regulation. J Clin Invest 2006; 116: 1776—1783.

13. Chibalin AV, Leng Y, Vieira E et al. Down-regulation of diacylglycerol kinase delta contributes to hyperglycemia-induced insulin resistance. Cell 2008; 132: 375—386.

14. Raman RP. Obesity and health risks. J Amer Coll Nutr 2002; 21: 134S—139S.

15. Poirier P, Giles TD, Bray GA et al. Obesity and cardiovascular disease: pathophysiology, evaluation, and effects of weight loss. Circulation 2006; 113: 898—918.

16. Mohan C. Diabetes, insuline resistence, and the metabolic syndrome. Calbiochem Biologics 2006; 32 (2): 2—3.

17. Maraldi NM, Capanni C, Mattioli E et al. A pathogenic mechanism leasing to partial lipodystrophy and prospects for pharmacologic treatment of insulin resistance syndrom. Acta Biomed 2007; 78 (Suppl 1): 207—215.

18. Hu FB, Manson JE, Stampfer MJ et al. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. New Engl J Med 2001; 345: 790—797.

19. Smith SC Jr. Multiple risk factors for cardiovascular diseases and diabetes mellitus. Am J Med 2007; 120 (32 Suppl 1): S3—S11.

20. Murphy TK, Calle EE, Rodriguez C et al. Body mass index and colon cancer mortality in a large prospective study. Amer J Epidemiol 2000; 152: 847—854.

21. Reeves GK, Pirie K, Beral V et al. Cancer incidence and mortality in relation to body mass index in the Million Women Study: cohort study. Brit Med J 2007; 335: 1134, Epub 2007 Nov 6.

22. Calle EE, Rodriguez C, Walker-Thurmond K et al. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. New Engl J Med 2003; 348: 1625—1638.

23. Gibbs WW. Obesity. an overblown epidemics? SciAm 2005, June, pp. 70—77.

24. Flegal KM, Graubard BI, Williamson DF et al. Excess deaths associated with underweight, overweight, and obesity. J Amer Med Ass 2005; 293: 1861—1867.

25. Gu D, He J, Duan X et al. Body weight and mortality among men and women in China. J Amer Med Ass 2006; 295: 776—783.

26. Flegal KM, Graubard BI, Williamson DF et al. Cause-specific excess deaths associated with underweight, overweight, and obesity. J Amer Med Ass 2007; 298: 2028—2037.

27. McGee DL. Body mass index and mortality: a meta-analysis based on person-level data from twenty-six observational studies. Ann Epidemiol 2005; 15: 87—97.

28. Katzmarzyk PT, Janssen I, Ross R et al. The importance of waist circumference in the definition of metabolic syndrome. Diabet Care 2006; 29: 404—409.

29. Olshansky SJ, Passaro DJ, Hershow RC et al. A potential decline in life expectancy in the United States in the 21st century. New Engl J Med 2005; 352: 1138—1145.

Received February 29, 2008.
Accepted March 28, 2008.