Available online at www.sciencedirect.com
SCIENCE DIRECT®
Meat Science 71 (2005) 2–7
MEAT SCIENCE
www.elsevier.com/locate/meatsci

Review

Epidemiology, risks and pathogenesis of obesity

George A. Bray *

Pennington Biomedical Research Center, Lousiana State University, 6400 Perkins Road, Baton Rouge, LA 70808-4124, USA

Abstract

Obesity is operationally defined using a relationship of height and weight called the body mass index. Using this measure, more than 60% of Americans are overweight and over 30% are obese. To determine the importance of the body mass index, which would also label many athletes "overweight", we also need assessment of central fatness, and the medical conditions present in any given person. A problem of this magnitude is expensive, costing between 3% and 8% of health budgets in various countries. An increasing body weight increases the risk of early mortality, and enhances the risk of developing diabetes, gall bladder disease, high blood pressure, heart disease, osteoarthritis and certain forms of cancer. Although obesity results from an imbalance between what is eaten and what the body needs for its daily activities, these relationships are complex, and it is the "devil in the details" that is needed to provide clear public health strategies to prevent the progression of what some have called an epidemic.

Keywords: Energy balance; Food intake; Overweight; Mortality; Morbidity; Diabetes

Contents

* Tel.: +1 225 763 3140; fax: +1 225 763 3045.
E-mail addresses: brayga@pbrc.edu, brayga@mhs.pbrc.edu.

0309-1740/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.meatsci.2005.04.009

1. Introduction

I start with the premise that all of us want to have a healthy weight, and that no one wants to be obese. Interest in obesity has taken a sharp up-turn in recent years and the prevalence of this problem by any standards has increased rapidly. An unhealthy weight can be viewed as the result of a chronic, stigmatized, neurochemical disease. In this context, the goal is to return body weight to a healthy level and to remove the stigma associated with the use of the word obesity. To consider it in the context of a neurochemical derangement has the advantage of focusing on the underlying mechanisms that produce the distortion in energy balance that produces the unhealthy weight (Bray & Champagne, 2005).

2. Definition of obesity

2.1. Body mass index

Throughout the past 50 years there has been a steady rightward shift in the distribution curve for body weight. This trend can be most effectively traced using the BMI, defined as the weight in kilograms divided by the height in meters squared [$W/(H)^2$], which provides a useful operating definition of overweight. A normal BMI is between 18.5 and <25 kg/m^2, a BMI between 25 and 29.9 kg/m^2 is operationally defined as overweight, and individuals with BMI >30 kg/m^2 are obese, after taking into consideration muscle builders, and other resistance trained athletes. BMI also provides one way to estimate the risk associated with obesity (NHLBI, 1998; WHO, 2000). However, to interpret it properly, several other pieces of information are needed. These include information about the ethnicity of the individual. For Asians, a BMI of more than 23 is considered overweight, and the cut-point for obesity is a BMI of greater than 25 kg/m^2, well below that of the Caucasian population. Age is also an important consideration. A high BMI at a young age implies longer years of excess weight and a higher lifetime risk. Whether the BMI is rising, falling or stable is also important. A rising BMI carries more risk than a stable one. Whether the individual is physically active is also important. Higher levels of physical activity reduce the detrimental effects of any given BMI and all Americans should be encouraged to have a regular program of physical activity. The final piece of information needed to interpret the BMI is whether it is associated with an increase in central adiposity.

2.2. Central adiposity

Centrally distributed body fat carries more risk for health than fat located primarily on the hips and thighs. The waist circumference is a practical measure of central adiposity and is a surrogate for more precise measures such as a CT or MRI scan of the abdomen at the L-4-5 position. When BMI and waist circumference were used to predict the risk of hypertension, dyslipidemia and the metabolic syndrome, the waist circumference was shown to be a better predictor than the BMI (Bray, 2004; Janssen, Katzmarzyk, & Ross, 2004).

2.3. Prevalence of obesity

Using the BMI, it is clear that there is an epidemic of obesity that began in the 1980s and which continues unabated. It affects children as well as adults. We are now seeing a rise in the prevalence of Type 2 diabetes in adolescents that is directly related to obesity. Obesity and overweight now affect more than 60% of adult Americans. Diabetes mellitus, hypertension, heart disease, gall bladder disease and some forms of cancer result from obesity. Whether these diseases are yet present or not, the obese patient should be encouraged to lose weight by appropriate methods in order to reduce the future likelihood that they will develop. More females than males are overweight at any age. The frequency of overweight increases with age to reach a peak at 45–54 years in men and at age 55–64 in women.

At birth, the human infant contains about 12% body fat. During the first year of life, body fat rises rapidly to reach a peak of about 25% by 6 months of age and the declines to 18% over the next 10 years. At puberty, there is a significant increase in the percentage of body fat in females and a fall in males. By age 18, males have approximately 15–18% body fat, and females 25–28%. Between ages 20 and 50, the fat content of males

approximately doubles and that of females goes up by about 50%. Total body weight, however, rises by only 10–15% indicating that fat is accounting for a larger part by the rise in body weight and is accompanied by a reduction in lean body mass.

Obesity has a higher prevalence in Latino and African–American populations (Flegal, Carroll, Ogden, & Johnson, 2002; Ogden, Flegal, Carroll, & Johnson, 2002). The rising prevalence is shown in Fig. 1.

Recent data (CDC, 2005) show a continued increase in the prevalence of obesity. Both height and weight have increased in adults aged 20–74 between 1960 and 2002. Men increased from 172.7 cm (68 in.) to 176.5 cm (69.5 in.) and women from (160 cm) (63) to 162.5 cm (64 in.) during this period. For men weight rose from 75.6 kg (166.3 lbs) to 86.8 kg (191 lbs) and for women from 63.7 kg (140.2 lbs) to 74.7 kg (164.3 lbs), for an average increase of BMI from 25.2 to 28 kg/m^2 for men and from 24.8 to 28.2 kg/m^2 for women during this 42 year period. The increase in weight was greater in older men than younger ones, but the reverse was true for women with older women gaining less than younger ones. Similar effects are seen in children with the weight of 10 year old boys rising from 33.7 kg (74.2 lbs) in 1963 to 38.6 kg (85 lbs) in 2002 and for 10 year old girls rising from 35.2 kg (77.4 lbs) to 40 kg (88 lbs) in this same interval. These increases in weight were associated with increases in BMI for both boys and girls. For a 7-yr-old boy the BMI increased from 15.8 to 17.0 kg/m^2 between 1963 and 2002 and for 7-yr-old girls it rose from 15.8 to 16.6 kg/m^2. For 16-yr-old boys it rose from 21.3 to 24.1 kg/m^2 in this interval and for girls from 21.9 to 24.0 kg/m^2.

2.4. Costs

Obesity is expensive, costing between 3% and 8% of health budgets (Finkelstein, Fiebelkorn, & Wang, 2004). Hospital costs and use of medication have also been shown to increase with the increasing BMI (Quesenberry, Caan, & Jacobson, 1998).

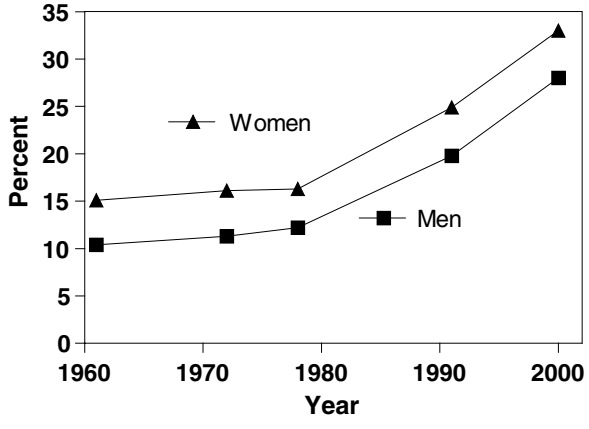

Fig. 1. Prevalence of obesity.

3. Risks related to obesity

3.1. Obesity and excess mortality

As the BMI increases, there is a curvilinear rise in excess mortality. This excess mortality rises more rapidly when the BMI is above 30 kg/m^2. A BMI over 40 kg/m^2 is associated with a further increase in overall risk and for the risk of sudden death. The principal causes of the excess mortality associated with overweight include hypertension, stroke and other cardiovascular diseases, diabetes mellitus, certain cancers, reproductive disorders, gall bladder disease, and sudden death.

The insulin resistant state or metabolic syndrome is strongly associated with visceral fat. It may include consequences such as glucose intolerance or Type 2 diabetes mellitus, hypertension, polycystic ovarian syndrome, dyslipidemia and other disorders. These are often responsive to weight loss, especially when this is achieved early and the loss is maintained.

4. Pathophysiology

4.1. The fat cell as an endocrine cell

Two mechanisms can explain the pathophysiological effects of obesity: the first is increased fat mass which can explain the stigmatization of physically obvious obesity, and the accompanying osteoarthritis and sleep apnea. The second mechanism is the increased amount of peptides that may produce associated diseases by acting on distant organs. The discovery of leptin catapulted the fat cell into the arena of endocrine cells (Kershaw & Flier, 2004). In addition to leptin, there are increased amounts of cytokines, angiotensinogen, adipsin (Complement D), etc., and metabolites such as free fatty acids and lactate. In contrast, adiponectin release is decreased in obesity (Fig. 2). The products of the fat cell in turn modify the metabolic processes in the host. For the susceptible host, these metabolic changes lead in turn to a variety of other processes, including hyperinsulinemia, atherosclerosis, hypertension, and physical stress on bones and joints.

4.2. Visceral fat

A considerable body of data suggests that visceral fat has a stronger relationship with the complications associated with obesity than total body fat (Kanaya et al., 2003). Central adiposity is one of the key components of the metabolic syndrome whose diagnostic criteria

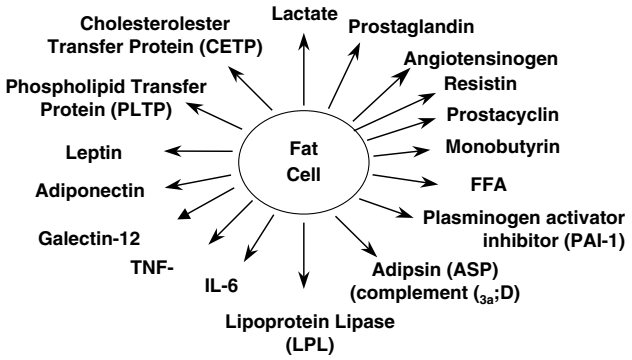

Fig. 2. The fat cell as an endocrine cell.

based on the recommendation of the National Cholesterol Education Program Adult Treatment Panel III are shown in Table 1 (Expert Panel, 2001; Park et al., 2003).

5. Complications

5.1. Death

The complications associated with obesity are related to the increased mass of fat and the enlarged size of fat cells and contribute to the 112,000 to 565,000 excess deaths per years (Mokdad, Marks, Stroup, & Gerberding, 2004; Flegal, Graubard, Williamson, & Gail, 2005). Obesity is associated with shortened life span. Using either the NCHS data (CDC, 2005) or the Framingham data (Peeters et al., 2003) a BMI of 30 or more reduces years of life by 3–5 compared to normal weight. This effect has ethnic differences with black women showing fewer years of life lost for a given increase in BMI than black men or white men or women (Fontaine, Redden, Wang, Westfall, & Allison, 2003; Peeters et al., 2003).

5.2. Diseases

The curvilinear, "J"-shaped relationship of BMI to risk of complications, which has been known for 100 years, applies to Caucasian males more than Caucasian females and to a much lesser extent to African–American females (Calle, Thun, Petrelli, Rodriguez, & Heath, 1999). The prevalence of diabetes mellitus is high in all ethnic groups, but the risk of cardiovascular events shows highly significant ethnic differences. For example, increasing BMI shows only a small increase in mortality among Black women, in contrast to the rise in death rate with increasing BMI observed in White men and women. Many kinds of cancers are related to obesity (Calle, Rodriguez, Walker-Thurmond, & Thun, 2003). Recently, obesity has been added to the group of diseases where inflammatory markers, such as C-reactive protein, are increased (Esposito et al., 2003; Weisberg et al., 2003).

Table 1
Criteria for the Metabolic Syndrome, which is present if an individual has any three of the risk factors

Risk factor	Defining level
Abdominal obesity (waist circumference)	
Men	>102 cm (>40 in.)
Women	> 88 cm (>35 in.)
HDL-cholesterol	
Men	<40 mg/dL
Women	<50 mg/dL
Triglycerides	⩾150 mg/dL
Fasting glucose	⩾110 mg/dL
Blood pressure (SBP/DBP)	⩾130/⩾85 mmHg

6. Pathogenesis of obesity

6.1. Neuroendocrine obesity

Several mechanisms lead to obesity. Obesity can follow damage to the ventromedial part of the hypothalamus in the brain, but this is rare. Cushing's disease is somewhat more common and can present with obesity. Treatment should be directed at the cause of the increased formation of adrenal corticosteroids.

6.2. Drug-induced weight gain

Treatment of diabetics with insulin, sulfonylureas or thiazolidinediones, but not metformin can increase hunger and food intake, resulting in weight gain. Treatment with some antidepressants, antiepileptics and neuroleptics can also increase body weight, as can cyproheptadine, probably through effects on the monoamines in the central nervous system.

6.3. Dietary obesity

Eating a high-fat diet and excessive consumption of sugar-sweetened beverages and the prevalence of abundant varieties of food in cafeterias or supermarkets are dietary factors in the development of obesity. Larger portion sizes increase the amount we eat. It would seem a simple enough behavioral change to "eat less", but the programs that have tried to introduce behavior change strategies have made few effective inroads yet. Pushing oneself away from the table is easier to say than it is to do in practice when good tasting food is abundantly available at cheap prices.

6.4. Reduced energy expenditure

Reduced energy expenditure relative to energy intake is the other major component in the cause of obesity in

modern society. Energy expenditure can be divided into four parts: resting metabolism ranges from 3.37 to 3.76 MJ/m^2/24 h (800–900 kcal/sq m/24 h). It is lower in females than in males, and declines with age. This decline with age could account for much of the increase in fat stores if food intake does not decline similarly. Physical exercise is variable but on average is responsible for about one-third of the daily energy expenditure. From a therapeutic point of view, this component of energy expenditure is most easily manipulated. Dietary thermogenesis is the energy expenditure that follows the ingestion of a meal. Heat produced by eating may dissipate up to10% of the ingested calories. Protein appears to have the largest effect. These thermic effects of food are one type of metabolic "inefficiency" in the body, that is, where dietary calories are not available for "useful" work. In the obese, the thermic effects of food are reduced particularly in individuals with impaired glucose tolerance or diabetes. Acute over- or underfeeding will produce corresponding shifts in overall metabolism, which can be as large as 15–20%. Thus increasing physical activity, and energy expenditure would seem a good way of "preventing" obesity. However, it must be more difficult than it seems, otherwise the US Army would not have to discharge large numbers of men and women from military service each year because they do not continue to meet the military's weight standards. If losing your job and support for your family is not sufficient motivation to increase physical activity enough to lose weight, the problem must be more intransigent that it would seem on the surface.

6.5. Genetic factors in obesity

6.5.1. Syndromes of obesity

Genetic factors can produce some types of obesity that are easily recognized. Among these type of obesity are: (1) The Bardet-Biedl syndrome, characterized by retinal degeneration, mental retardation, obesity, polydactyly, and hypogonadism (Sheffield et al., 1994); (2) the Alstrom syndrome, characterized by pigmentary retinopathy, nerve deafness, obesity, and diabetes mellitus (Alstrom, Hallgren, Nilsson, & Asander, 1959); (3) Carpenter syndrome, characterized by acrocephaly, mental retardation, hypogonadism, obesity, and preaxial syndactyly (Robinson, James, Mubarak, Allen, & Jones, 1985); (4) the Cohen syndrome, characterized by mental retardation, obesity, hypotonia, and characteristic facies (Kolehmainen et al., 2004); (5) the Prader-Willi syndrome, characterized by hypotonia, mental retardation, hypogonadism, and obesity (Smith, 1999); and (6) the pro-opiomelanocortin (POMC) syndrome, characterized by defective production of POMC that is recognized as a red-headed fat child with a low plasma cortisol (Krude et al., 1998).

6.5.2. Genetic susceptibility to obesity

If both parents are obese, about 80% of the offspring will be obese. If only one parent is obese, the likelihood of obesity in the offspring falls to less than 40%. Studies with identical twins suggest that inheritance accounts for up to 70% and environmental factors (diet, physical inactivity, or both) account for the rest of the variation in body weight. What this means is that if pairs of twins who have identical genetic make-up are put into our food toxic environment, each member of a pair will respond very similarly to the other member, but that there will be large differences between the pairs of twins. Thus, some pairs will gain weight, others not, but at the end the heavier twins will gain almost exactly as much and the lighter pairs will gain less, but also similar amounts (Bouchard et al., 1990).

6.5.3. Single gene causes of obesity

Leptin deficiency and deficiency of the leptin receptor are rare, but are associated with massive human obesity. Absence of convertase also has been associated with obesity in one family.

The most common defects associated with massive obesity are abnormalities in the melanocortin receptor system where up to 5% of massively obese young people may have this type of defect.

7. Conclusions

This brief review of the epidemiology and pathogenesis of obesity has pointed out the obesity epidemic that current plagues most part of the world. A number of the mechanisms that underlie the epidemic were discussed. Although the solution for individuals of eating less and exercising more sounds good, it is not currently working. As the costs of the epidemic of human and economic terms begin to "bite" into our economic fabric, serious steps may be taken to curb this latent hazard to our way of life.

References

Alstrom, C. H., Hallgren, B., Nilsson, L. B., & Asander, H. (1959). Retinal degeneration combined with obesity, diabetes mellitus and neurogenous deafness. *Acta Psychiatrica Scandinavia, 34*(Suppl. 129), 1–35.

Bouchard, C., Tremblay, A., Despres, J. P., Nadeau, A., Lupien, P. J., Theriault, G., et al. (1990). The response to long-term overfeeding in identical twins. *New England Journal of Medicine, 322*(21), 1477–1482.

Bray, G. A. (2004). Obesity is a chronic, relapsing neurochemical disease. *International Journal of Obesity and Related Metabolic Disorders, 28*(1), 34–38.

Bray, G. A., Champagne, C. (2005). Beyond energy balance: there's more to obesity than calories. *Journal of the American Dietetic Association* [in press].

Calle, E. E., Rodriguez, C., Walker-Thurmond, K., & Thun, M. J. (2003). Overweight, obesity, and mortality from cancer in a prospectively studied cohort of US adults. *New England Journal of Medicine, 348*(17), 1625–1638.

Calle, E. E., Thun, M. J., Petrelli, J. M., Rodriguez, C., & Heath, C. W. Jr., (1999). Body-mass index and mortality in a prospective cohort of US adults. *New England Journal of Medicine, 341*(15), 1097–1105.

CDC (Centers for Disease Control). (2005). *Overweight and obesity*. National Center for Health Statistics. Centers for Disease Control. <http://www.cdc.gov/nccdphp/dnpa/obesity/> Accessed 30.03.05.

Esposito, K., Pontillo, A., Di Palo, C., Giugliano, G., Masella, M., & Marfella, R. (2003). Effect of weight loss and lifestyle changes on vascular inflammatory markers in obese women: a randomized trial. *Journal of the American Medical Association, 289*(14), 1799–1804.

Expert Panel (2001). Executive summary of the third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). *Journal of the American Medical Association, 285*(19), 2486–2497.

Finkelstein, E. A., Fiebelkorn, I. C., & Wang, G. (2004). State-level estimates of annual medical expenditures attributable to obesity. *Obesity Research, 12*(1), 18–24.

Flegal, K. M., Carroll, M. D., Ogden, C. L., & Johnson, C. L. (2002). Prevalence and trends in obesity among us adults, 1999–2000. *Journal of the American Medical Association, 288*(14), 1723–1727.

Flegal, K. M., Graubard, B. I., Williamson, D. F., & Gail, M. H. (2005). Excess deaths associated with underweight, overweight, and obesity. *Journal of the American Medical Association, 293*(15), 1861–1867.

Fontaine, K. R., Redden, D. T., Wang, C., Westfall, A. O., & Allison, D. B. (2003). Years of life lost due to obesity. *Journal of the American Medical Association, 289*, 187–193.

Janssen, I., Katzmarzyk, P. D., & Ross, R. (2004). Waist circumference and not body mass index explains obesity-related health risk. *American Journal of Clinical Nutrition, 79*(3), 379–384.

Kanaya, A. M., Vittinghoff, E., Shlipak, M. G., Resnick, H. E., Visser, M., & Grady, D. (2003). Association of total and central obesity with mortality in postmenopausal women with coronary heart disease. *American Journal of Epidemiology, 158*(12), 1161–1170.

Kershaw, E. E., & Flier, J. S. (2004). Adipose tissue as an endocrine organ. *Journal of Clinical Endocrinology and Metabolism, 89*(6), 2548–2556.

Kolehmainen, J., Wilkinson, R., Lehesjoki, A. E., Chandler, K., Kivitie-Kallio, S., Clayton-Smith, J., et al. (2004). Delineation of Cohen syndrome following a large-scale genotype–phenotype screen. *American Journal of Human Genetics, 75*(1), 122–127.

Krude, H., Biebermann, H., Luck, W., Horn, R., Brabant, G., & Gruters, A. (1998). Severe early-onset obesity, adrenal insufficiency and red hair pigmentation caused by POMC mutations in humans. *Nature Genetics, 19*(2), 155–157.

Mokdad, A. H., Marks, J. S., Stroup, D. F., & Gerberding, J. L. (2004). Actual causes of death in the United States, 2000. *Journal of the American Medical Association, 291*(10), 1238–1245.

NHLBI (1998). *Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults*. Washington (DC): National Heart, Lung, and Blood Institute.

Ogden, C. L., Flegal, K. M., Carroll, M. D., & Johnson, C. L. (2002). Prevalence and trends in overweight among US children and adolescents, 1999–2000. *Journal of the American Medical Association, 288*(14), 1728–1732.

Park, Y. W., Zhu, S., Palaniappan, L., Heshka, S., Carnethon, M. R., & Heymsfield, S. B. (2003). The metabolic syndrome: prevalence and associated risk factor findings in the U.S. population from the third National Health and Nutrition Examination Survey, 1988–1994. *Archives of Internal Medicine, 163*(4), 427–436.

Peeters, A., Barendregt, J. J., Willekens, F., Mackenbach, J. P., Al Mamun, A., & Bonneux, L. (2003). Obesity in adulthood and its consequences for life expectancy: a life-table analysis. *Annals of Internal Medicine, 138*(1), 24–32.

Quesenberry, C. P., Jr., Caan, B., & Jacobson, A. (1998). Obesity, health services use, and health care costs among members of a health maintenance organization. *Archives of Internal Medicine, 158*(5), 466–472.

Robinson, L. K., James, H. E., Mubarak, S. J., Allen, E. J., & Jones, K. L. (1985). Carpenter syndrome: natural history and clinical spectrum. *American Journal of Medical Genetics, 20*(3), 461–469.

Sheffield, V. C., Carmi, R., Kwitek-Black, A., Rokhlina, T., Nishimura, D., Duyk, G. M., et al. (1994). Identification of a BardetBiedl syndrome locus on chromosome 3 and evaluation of an efficient approach to homozygosity mapping. *Human Molecular Genetics, 3*(8), 1133–1135.

Smith, A. (1999). The diagnosis of Prader-Willi syndrome. *Journal of Paediatric Child Health, 35*(4), 335–337.

Weisberg, S. P., McCann, D., Desai, M., Rosenbaum, M., Leibel, R. L., & Ferrante, A. W. (2003). Obesity is associated with macrophage accumulation in adipose tissue. *Journal of Clinical Investigation, 112*(12), 1796–1808.

WHO (World Health Organization). (2000). Obesity: preventing and managing the global epidemic. *Report of a WHO consultation*. World Health Organization Technical Reprints Ser. 894, i–xii, pp. 1–253.