Clinical Perspective

Medical Management of Adult Obesity

Zhao Liu, MD

[N A J Med Sci. 2008;1(1):17-19.]

Introduction

Obesity has become a major public health problem. More than 300 million adults are affected world wide, and among them 20% are Americans (1). Obesity causes over 300,000 deaths yearly, making it the second most common cause of preventable death in the United Sates (2). Currently nearly two thirds of Americans are overweight and half of them are obese, the number of which has doubled since 1980. The prevalence of overweight and obesity among American children and adolescents (age 6 – 19 years) has tripled since 1963. On average, American adults are one inch taller and 25 lbs heavier today than they were in 1960. How did we become so fat?

Definition

Obesity is an abnormal accumulation of fat, usually 20% or more over the ideal body weight. The National Institute of Health (NIH) defines obesity using body mass index (BMI), a measurement of weight in relation to height and is calculated by weight in kilograms divided by height in meters squared (Kg/m^2). BMI between 25 and 29.9 is defined as overweight, and 30 or more as obesity.

Pathogenesis and Mechanism of Weight Gain

Energy Balance

Obesity is caused by ingesting more energy than is expended over a long period of time. The excess calories lead to an accumulation of body fat. In general, ingesting 3500 kcal more than expended will lead to a gain of approximately one pound of fat. Consistent differences, even if minor, between energy intake and energy expenditure can lead to large changes in body fat mass over time. If energy balance is positive by as little as 0.5% (12 kcal/day), 1 pound of fat would be gained in one year. Daily ingestion of only 8 kcal more than expended over 30 years could lead to an increase of 22 lbs in body weight, which is the average amount of weight gained by American adults from 25 to 55 years of age.[3]

Energy metabolism

Many obese individuals attribute their failure of weight loss efforts to abnormally low metabolism. As a matter of fact, most obese persons do not have an abnormal reduction in energy metabolism. Both total energy expenditure (TEE) and resting energy expenditure (REE) are usually greater in obese than lean persons who are of the same height and gender because of greater body cell mass in obese persons. Therefore obese persons must consume more calories than lean persons to maintain their larger body size.[4] Research has shown most people under-report their actual energy intake and over-report their actual physical activity even when they report good compliance with their diet and activity program in a closely monitored environment (5). An important clinical question is whether weight loss in obese persons causes an abnormal decline in energy expenditure, which could become an obstacle to long-term successful weight management. The answer to this question is not entirely clear because of conflicting data from different studies. However, the results from most studies support the notion that REE and TEE in reduced-obese subjects are normal for their new body size and composition.[6]

Genetics

Genetic factors may influence the amount of weight gained with overfeeding. In one study, weight gained varied greatly among12 monozygotic twin pairs who were chronically overfed 1000 kcal/day. However, weight gains were very similar within each member of a twin pair.[7] Data obtained from adoption studies also demonstrate a strong genetic influence in the pathogenesis of obesity. A Danish study involving 540 adoptees showed a strong positive correlation between the adoptee weight and the weight of their biologic parents, but not of their adoptive parents.[8] More than 250 genes, markers, and chromosomal regions have been linked with human obesity,[9] but the clinical importance of each association is not yet known.

Environment

Although genetics is an important factor in the pathogenesis of obesity, the recent increase in the prevalence of obesity cannot be attributed to genetics alone and must be a result of interactions between environment and genetics. The Pima Indians of Arizona, for example, has seen an unprecedented epidemic of obesity and diabetes during the last 50 years. Today, the Pimas of Arizona consume a high-fat diet (50% of energy as fat) provided by government surplus commodities rather than their traditional low-fat diet (15% of energy as fat), and they are much more sedentary than when they were farmers. The Pimas of Mexico, on the other hand, isolated from the Western influences, eat a traditional Pima diet and are physically active as farmers and sawmill workers. They have a much lower incidence of obesity and diabetes than their genetic kindred in Arizona.

A most recent study suggested that obesity is "contagious". Same sex friend, sibling and spouse of an obese person are more likely to be obese also because they tend to follow their partner's lead.[10] You are indeed whom you associate with.

Zhao Liu, MD
From Department of Endocrinology, Berverly Hospital, MA

Medical Complications of Obesity

The fat cells are endocrine cells and they produce a variety of hormones and numerous adipocytokines and inflammatory molecules, such as free fatty acids, plasminogen activator inhibortor-1 (PAI-1), interleukin 6, tumor necrosis factor-α, angiotensinogen, and prostaglandin. These inflammatory molecules in turn lead to insulin resistance, metabolic syndrome and cardiovascular disease. The adipose tissue is by far the largest endocrine organ.

Obesity is associated with numerous co-morbidities, including coronary heart disease (CHD), dyslipidemia, type 2 diabetes mellitus (T2DM), hypertension, stroke, obstructive sleep apnea, nonalcoholic fatty liver disease, liver cirrhosis, gallbladder disease, pancreatitis, gout, venous stasis, osteoarthritis, chronic lower back pain, and many types of cancers, such as breast, uterus, colon, prostate, kidney, esophagus, and pancreas. The incidence and mortality of T2DM, hypertension, CHD, cholelithiasis and many types of cancers increase with increasing BMI.[11,12] Childhood obesity is also associated with an increased risk of having a CHD in adulthood.[13] Research has unequivocally demonstrated all-cause mortality increases with increasing BMI, and the trend even goes into the non-obese population.[14]

Benefits of Weight Loss

Data from many clinical studies have shown that with a modest weight loss of 5 to 10% of body weight, obese individuals can experience improvements in insulin sensitivity,[15] glycemic control,[16] blood pressure,[17] and lipid abnormalities.[18] It also reduces cardiovascular events, CHD-related mortality, and risk of developing T2DM. But does the improvement in these risk factors translate into a longer life? For many years, people were skeptical about mortality benefits of weight loss. Recent studies however have demonstrated that 10 to 15 years after bariatric surgery, not only the risk factors are significantly improved, but more importantly the all- cause mortality is reduced by 29% to 40% in the surgery group.[19,20]

Obesity Therapy

The clinical approach to obesity can be viewed as a pyramid consisting of several levels of therapeutic options (**Figure 1**). All patients should be involved in an effort to change their lifestyle behaviors to decrease energy intake and increase physical activity. Lifestyle modification should be a component of all other levels of therapy. Pharmacotherapy can be a useful adjunctive measure for properly selected patients. Bariatric surgery is an option for patients with severe obesity, who have not responded to less-intensive interventions.

Weight-Reducing Diet

NIH proposed dietary guidelines[21] recommending a daily 500 kcal deficit for overweight persons (BMI 25.0-29.9) who have obesity-related complications, and for persons with class I obesity (BMI 30-34.9). This energy deficit will result in approximately a 1 lb (0.45 kg) weight loss per week and about a 10% weight reduction at 6 months. A daily 500-1000 kcal deficit is recommended for those with class II (BMI 35.0-39.9) or class III (BMI ≥40) obesity, which will produce about a 1 to 2 lbs weight loss per week and a 10% weight loss at 6 months. The recommended macronutrient composition for a low-calorie weight loss diet includes 55% or more of daily calories from carbohydrates, 15% from protein, and 30% or less from fat (**Figure 2**). Regarding the composition of fat ingestion, 8%-10% of total energy intake should be from saturated fat, 10% or less from polyunsaturated fats, and 15% or less from monounsaturated fats. Daily cholesterol intake should not exceed 300 mg, and daily fiber intake should be between 20 and 30 g.

Behavior Modification

The purpose of behavior modification therapy is to help patients change behaviors that contribute to their obesity and initiate new dietary and physical activity behaviors needed to lose weight. Behavioral therapy for obesity should involve 1) developing specific and realistic goals that can be easily measured (such as walking for 20 minutes, three times per week), 2) developing a reasonable plan for reaching those goals and to prevent relapse, and 3) making incremental changes rather than large changes, so patients can have successful experiences that can be used as a foundation for additional lifestyle alterations. Specific behaviors associated with successful long-term weight loss have been identified by National Weight Control Registry (NWCR).[22] Participants enrolled in the registry must have maintained a weight loss of ≥13.6 kg (≥30 lb) for at least 1 year; on average, subjects have maintained a 32 kg (70 lb) weight loss for 6 years. The major behaviors reported by approximately 3000 NWCR participants were: 1) self-monitoring of food intake and body weight; 2) consuming a low-calorie (1300–1400 kcal/d) and low-fat diet (20%–25% of daily energy intake from fat), 3) eating breakfast every day, and 4) performing regular physical activity that expends 2500 to 3000 kcal per week (such as walking 4 miles per day).

Physical Activity

Regular physical activity is an important component of every weight loss program. However, exercise alone, without concomitant dietary therapy, does not produce significant weight loss. Moreover, adding exercise to dietary therapy does not significantly increase short-term weight loss compared with dietary therapy alone.[23]

Although it may not improve short-term weight loss, physical activity may be very important for long-term weight management and has beneficial health effects, such as reducing the incidence of CHD and T2DM, which are independent of weight loss itself.[24,25] Most society guidelines including American College of Sports Medicine and the Centers for Disease Control and Prevention recommend 30 to 60 minutes of moderate-intensity exercise on most days of the week. Unfortunately only 15% of Americans perform the recommended amount of physical activity.

Pharmacotherapy

Currently there are three FDA approved anti-obesity agents in the US. Sibutramine is a serotonin and norepinephrine reuptake inhibitor, and is approved for long term use. It

induces feeling satisfied with less food, less preoccupied with food, and greater control of food intake. The most common side effects are headache, dry mouth, constipation and insomnia. Blood pressure needs to be monitored. The use of Sibutramine is contraindicated in patients with poorly controlled hypertension, CHD, congestive heart failure, arrhythmias, stroke, severe renal or liver dysfunction, or concomitant monoamine oxidase inhibitor therapy. Orlistat is a selective gastric and pancreatic lipase inhibitor and reduces 30% of dietary fat absorption. Hence fat passes undigested causing adverse side effects such as frequent defecation, oily or liquid stool, flatulence, fecal urgency or incontinence. Concomitant therapy with a gel-forming fiber can prevent many of the gastrointestinal side effects. Individual taking orlistat should supplement a multivitamin 2 hours before or after to prevent fat-soluble vitamin (A, D, E) deficiency. Phentermine is a norepinephrine and dopamine releasing agent, and is approved only for short-term (3 months) weight loss given its abuse potential. However it is the most commonly prescribed anorexant medication in the US, presumably because it is the least expensive. Most US insurance plans do not cover for these anti-obesity agents, therefore casting heavy financial burden on patients given the chronic nature of obesity, and making these medications less available and less frequently prescribed. Phentermine is the least expensive, costing less than $40 a month. Orlistat costs about $120 a month if taken at each meal (3 times daily). Sibutramine costs $100 to $140 a month depending on the dosage used.

Comprehensive Weight Management

To lose weight is hard, but to maintain the weight loss is much harder. Obesity is a chronic disease that requires long-term therapy for successful long-term weight management. Often, patients who are able to lose weight with obesity therapy regain their lost weight after therapy is discontinued. A maintenance program is essential in successful long-term weight loss. A comprehensive weight management program that includes behavioral modification, exercise, and dietary plan in addition to pharmacotherapy achieves the most significant weight loss and most lasting result.[26] The provider's goal is not only to encourage a 5 to 10% of body weight loss, but also to prevent weight regain, maintain healthy weight over long term, and hence promote risk reduction, cardiovascular health, and active longevity.

References

1. http://www.who.int/nut/obs.htm.
2. US Dept of Health and Human Services. *The Surgeon General's Call to Action to Prevent and Decrease Overweight and Obesity*. Rockville, MD: US Dept of Health and Human Services, Public Health Service, Office of the Surgeon General; 2001. Available from: US GPO, Washington.
3. Rosenbaum M et al. Obesity. *N Engl J Med*. 1997;337:396-408.
4. Ravussin E, Burnand B, Schutz Y, Jequier E. Twenty-four-hour energy expenditure and resting metabolic rate in obese, moderately obese, and control subjects. Am J Clin Nutr 1982;35:566-573.
5. Lichtman SW, Pisarska K, Berman ER, et al. Discrepancy between self-reported and actual caloric intake and exercise in obese subjects. N Engl J Med. 1992;327:1893-1898.
6. Amatruda JM, Statt MC, Welle SL. Total and resting energy expenditure in obese women reduced to ideal body weight. J Clin Invest. 1993;92:1236-1242.
7. Bouchard C, Tremblay A, Despres JP, et al. The response to long-term overfeeding in identical twins. N Engl J Med. 1990;322:1477-1482.
8. Stunkard AJ, Sorensen TIA, Hanis C, et al. An adoption study of human obesity. N Engl J Med. 1986;314:193-198.
9. Rankinen T, Perusse L, Weisnagel SJ, et al. The human obesity gene map: the 2001 update. Obes Res. 2002;10:196-243.
10. Christakis N and Fowler J. N Engl J Med. 2007;357:370-379.
11. Willett WC, et al. N Engl J Med. 1999;341:427-34.
12. Reeves GK et al. BMJ. 2007;335(7630): 1134.
13. Baker et al. N Engl J Med. 2007;357(23):2329.
14. Adams et al. N Engl J Med. 2006;355(8):763.
15. Wing RR, Koeske R, Epstein LH, et al. Long-term effects of modest weight loss in type II diabetic patients. Arch Intern Med 1987;147:1749-1753.
16. Wing RR, Marcus MD, Epstein LH, Salata R. Type II diabetic subjects lose less weight than their overweight nondiabetic spouses. Diabetes Care. 1987;10:563-566.
17. Tuck ML, Sowers J, Dornfeld L, Kledzik G, Maxwell M. The effect of weight reduction on blood pressure, plasma renin activity, and plasma aldosterone levels in obese patients. N Engl J Med. 1981;304:930-933.
18. Dattilo AM, Kris-Etherton PM. Effects of weight reduction on blood lipids and lipoproteins: a meta-analysis. Am J Clin Nutr. 1992;56:320-328.
19. Adams et al. N Engl J Med. 2007;357(8):753.
20. Sjöström et al. N Engl J Med. 2007;357(8):741.
21. National Institutes of Health, National Heart, Lung, and Blood Institute. Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults – The Evidence Report. Obes Res. 1998;6(suppl 2): S51-S209.
22. Klem ML, Wing RR, McGuire MT, et al. A descriptive study of individuals successful at long-term maintenance of substantial weight loss. Am J Clin Nutr. 1997;66:239-246.
23. Wing RR. Physical activity in the treatment of the adulthood overweight and obesity: current evidence and research issues. Med Sci Sports Exerc. 1999;31(suppl)S547-S552.
24. Lee CD, Blair SN, Jackson AS. Cardiorespiratory fitness, body composition, and all-cause and cardiovascular disease mortality in men. Am J Clin Nutr. 1999;69:373-380.
25. Wei M, Gibbons L, Mitchell T, et al. The association between cardiorespiratory fitness and impaired fasting glucose and type 2 diabetes mellitus in men. Ann Intern Med. 1999;130(1):89-96.
26. Wadden TA, Berkowitz RI, Sarwer DB, et al. Benefits of lifestyle modification in the pharmacologic treatment of obesity. A randomized trial. Arch Intern Med. 2001;161:218-227.

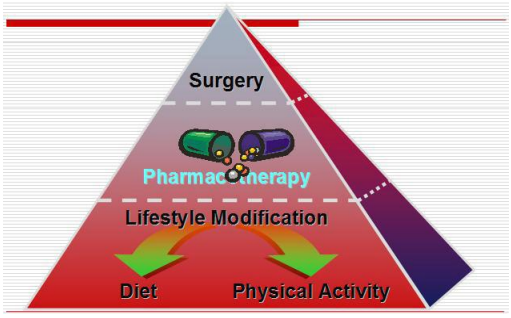

Figure 1. Obesity Treatment Pyramid.

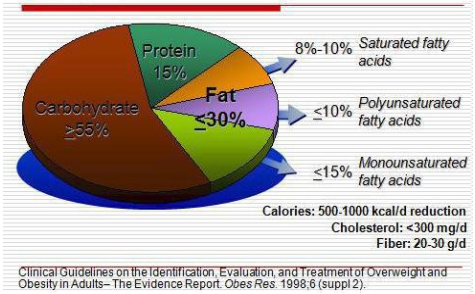

Figure 2. Recommended Nutrient Content of a Weight-Reducing Diet.