Lifestyle interventions for the treatment of class III obesity: a primary target for nutrition medicine in the obesity epidemic^{1–4}

George L Blackburn, Samuel Wollner, and Steven B Heymsfield

ABSTRACT

Although rates of obesity have increased universally in the United States over the past 30 y, it is clear that certain individuals are more susceptible to weight gain than others. Extreme obesity [body mass index (in kg/m²) > 40] is increasing at rates greater than any other class of obesity in the United States. Severely obese patients often suffer from a wide variety of comorbidities. Although weight-loss surgery is the most effective treatment, it offers little in the way of large-scale containment due to its costly and invasive nature. Lifestyle interventions that induce modest weight loss and improve fitness can significantly lower disease risk. As medical professionals in the field of nutrition, we must focus first on the patient cohort that suffers most from the modern obesogenic environment. Lifestyle interventions specifically targeted toward the class III obese cohort should be a high priority in nutrition medicine. Am J Clin Nutr 2010;91(suppl):289S-92S.

INTRODUCTION

Estimated energy requirement is defined by the Institute of Medicine as the average dietary energy intake that is predicted to maintain energy balance in an adult (1). Estimated energy requirement is dependent on several variables such as health, age, sex, weight, height, and level of physical activity. To maintain energy balance, an adult must consume and expend calories in equal amounts over time. Energy imbalance occurs when more calories are expended than consumed or, conversely, when more calories are consumed than expended. In the United States today, energy imbalance often occurs in the latter form. Recently, Swinburn et al (2) provided an analysis of the energy imbalance that has driven the obesity epidemic from its beginning in the 1970s to today. By their estimates (3), a caloric gap of \approx 400 kcal/d now exists between the 2 eras. Whereas Swinburn argues that this positive energy imbalance is driven largely by increased food intake, others contend that decreases in physical activity have also contributed significantly to the obesity public health crisis (4, 5).

Far from just a number, the 400-kcal energy gap has created a public health crisis in the obesity epidemic (6). More than ever, obesity is viewed as a metabolic disease with an etiology much more complex than a simple lack of willpower to control eating (7, 8). Whereas rates of obesity have increased universally in the United States for the last 30 y, it is also clear that certain individuals are more susceptible to weight gain than others. Patients with class III obesity [body mass index (BMI; in kg/m²) >40] are the fastest growing segment of the obese population (9). Over the

last 20 y, the number of individuals in the United States with BMIs >40 and 50 has quadrupled and quintupled, respectively, with resulting body-composition and metabolic changes (10). Severe obesity is associated with a broad range of health issues from comorbidities such as insulin resistance and hypertension, to psychiatric disorders such as depression and hopelessness (11–13). Although weight-loss surgery is currently the most effective treatment (14), it is unwise to suggest that bariatric surgery is the only solution (15). Surgery currently offers little in the way of large-scale containment due to its costly and invasive nature (9). Followup studies are needed to determine the safety and long-term efficacy of the procedures, the complications associated with surgery, and the cost-benefit for the patient and provider (16).

In the meantime, we in nutrition medicine must develop lifestyle interventions tailored to the specific needs of patients who suffer most from our obesogenic environment: the class III obese cohort. Although public health efforts to prevent obesity (especially in the pediatric and minority populations) are equally important causes, nutrition medicine should target those persons who suffer from severe obesity as a patient cohort in dire need of immediate and effective medical treatment. Preliminary evidence suggests that lifestyle interventions with modest weight-loss goals can achieve significant long-term health benefits (17), but more research is necessary to determine the most effective way to reduce morbidities and disease risk in severe, class III obesity. Research must strive toward developing programs that achieve practical and medically significant outcomes. Comprehensive treatment programs might also address the psychology of motivation, the role of weight loss medications, and the changes in body composition and metabolism that are caused by weight fluctuations over time. Rather than providing an exhaustive review of best practices in the treatment of severe obesity, we hope to highlight only a few promising areas of research for lifestyle interventions in the class III obese cohort.

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¹ From the Beth Israel Deaconess Medical Center, Center for the Study of Nutrition Medicine, Boston, MA (GLB and SW), and Merck Research Laboratories, Center for Scientific Affairs, Rahway, NJ (SBH).

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⁴ Address correspondence to GL Blackburn, 330 Brookline Avenue, FD 880, Boston, MA 02215. E-mail: gblackbu@bidmc.harvard.edu.

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LIFESTYLE INTERVENTIONS FOR SEVERE OBESITY

Contextualizing the energy gap

Dietary interventions need not induce complete excess weight loss to induce medically significant health benefits (18). Therefore, caloric restriction (CR) should be modest and in line with the unique energy demands of class III obesity. Two weight classes for the same 1.75-m (69-inch) man and corresponding BMIs are shown in Table 1. By using this reference male as an example, the Harris-Benedict equation reveals that a patient with a BMI >40 has a higher basal energy expenditure (BEE) compared with a normal-weight individual (Table 1). In more precise terms, a class III obese male has a BEE that is 464 kcal greater than a normal-weight male. This caloric difference is interesting for 2 reasons. First, it is close to the energy gap of 400 kcal/d proposed by Swinburn et al (2). Second, current guidelines recommend lowering intake by 500-1000 kcal/d to achieve a weight loss of 1-2 lbs/wk (14, 19) A 500-kcal/d reduction in total energy intake would mean that a class III obese man would essentially be feeding his normal-weight self. On the basis of an average caloric expenditure of 3507 kcal/d for a patient with a BMI of 40 and low activity levels, nonsurgical interventions that can create and sustain a daily energy deficit of 500 kcal/d could induce a 10% reduction in total body weight in 6 mo. This would represent a medically significant change in body weight, as it is likely to reduce the risk of diabetes and hypertension (14, 20, 21). It also represents a practical, achievable goal for patients and practitioners.

Improving dietary composition

Whereas weight loss via CR is essential to achieving health benefits, it can have negative consequences if fat-free mass (FFM) is metabolized along with adipose tissue. Reductions in FFM can reduce BEE due to losses in metabolically active lean

TABLE 1

Basal energy expenditure (BEE) in a 1.75-m (69-inch) man aged 30 y at normal weight and with class III obesity with varying physical activity levels¹

	BMI (kg/m ²)	
	25 (179 lbs)	40 (286 lbs)
	kcal	
BEE	1753	2217
Sedentary	2540	3192
Low active	2776	3507
Active	3071	3899
Very active	3602	4607

¹ Setting a negative caloric balance goal (\approx 464 kcal/d) on the basis of a patient's normal-weight energy requirement could induce medically significant weight loss for a class III obese patient. This caloric prescription is in line with the current dietary guidelines for weight loss. In normal-weight, overweight, and obese men aged \geq 19 y, total energy expenditure (TEE) = 864 – [9.72 × age (y)] + physical activity (PA) × [14.2 × weight (kg) + 503 × height (m)], where PA is the physical activity coefficient: PA = 1.00 if PA level (PAL) is estimated to be \geq 1.0 and <1.4 (sedentary); PA = 1.12 if PAL is estimated to be \geq 1.4 and <1.6 (low active); PA = 1.27 if PAL is estimated to be \geq 1.6 and <1.9 (active); PA = 1.54 if PAL is estimated to be \geq 1.9 and <2.5 (very active). The BEE, TEE, and Harris-Benedict data were adapted from reference 1. tissue (22, 23). Therefore, dietary programs that support FFM maintenance and skeletal muscle biogenesis are advisable. Low-protein, calorie-restricted diets are associated with increased loss of FFM (24). Conversely, higher-protein diets can preserve FFM and improve blood lipid profiles (25).

Decreasing fat intake should be of particular concern in any lifestyle intervention. By decreasing exogenous fat intake, a lowfat diet might help facilitate fat oxidation stimulated by CR and exercise. If muscle glycogen synthesis decreases due to high concentrations of circulating free fatty acids, ingested carbohydrates are diverted away from muscles and into the liver for de novo lipogenesis (26). Whereas the mechanism is still debated, elevated free fatty acid concentrations are associated with decreased myocellular insulin sensitivity (27, 28). Petersen et al (29) have suggested that insulin resistance due to atherogenic dyslipidemia in skeletal muscle may be the primary driving force in the development of the metabolic syndrome. Chronically elevated serum free fatty acid concentrations could lead to further metabolic complications and morbidity. Low-fat diets, such as the one used in the Women's Intervention Nutrition Study, have been implemented in the long term to successfully decrease disease risk (30).

Increasing physical activity

Sedentary behavior and poor fitness are important factors in the pathogenesis of metabolic disease in obesity (31). Conversely, physical activity (PA) and improved fitness ameliorate the health hazards of obesity in most studies, regardless of obesity measures, sex, or baseline health status (32). Severely obese patients who increase their PA have a higher quality of life than those who do not (33). Therefore, increasing PA levels should be a primary objective in any treatment strategy.

Effective exercise protocols for class III obesity should consider the unique barriers faced by severely obese patients. These patients often suffer from locomotive handicaps and muscle quality deterioration (34, 35). To date, exercise interventions have focused on endurance training for its large effect on total energy expenditure and coronary heart disease reduction. Whereas the cardiovascular benefits of endurance training are irrefutable, exercise interventions designed to enhance weight loss via aerobic exercise and increased caloric expenditure may be misguided. Patients with severe obesity can struggle to achieve levels of aerobic exercise that are sufficient to reap health benefits. Clinically, we have found that $\approx 80\%$ of bariatric patients are unresponsive to doctors' recommendation to perform >150 min of moderate-intensity PA/ wk. Because extremely obese patients have innately high resting and total energy expenditure levels (36), creating a negative energy balance through CR may be a more viable target for inducing 5-10% weight loss. The exercise component of a lifestyle intervention should instead focus primarily on improving metabolic fitness and decreasing disease risk independent of weight loss.

For example, progressive resistance training (PRT) is a safe and effective form of exercise that has been well received in many complex patient cohorts, including those with mobility impairments and type 2 diabetes (37). Recently published guidelines from the American College of Sports Medicine and the Department of Health and Human Services recommend PRT for its health benefits and unique ability to improve fitness by increasing muscle strength (38, 39). Preliminary evidence suggests that PRT can improve cardiovascular disease risk factors in the absence of significant weight loss (38). A review by Tresierras and Balady (40) confirmed that PRT should be a focus of translational research for the treatment of obesity because of its favorable effects on body composition and insulin sensitivity.

A synergistic approach to diet and exercise

Exercise and diet should be paired synergistically in a lifestyle intervention. Exercise protocols that facilitate larger energy deficits without preserving or enhancing skeletal muscle biogenesis may be counterproductive to long-term treatment. The addition of a muscle-strengthening exercise program to a weightloss intervention may help conserve FFM and BEE and facilitate weight-loss maintenance (41). On the basis of the success of the Why WAIT program's diet and evidence that higher-protein diets support muscle hypertrophy, we recommend that patients receive $\approx 30\%$ of calories through protein intake (42). The remaining 70% of calories should be divided into 30% from mono- and polyunsaturated fats and 40% from carbohydrates (nutrient- and fiber-dense foods such as fruit and vegetables).

Broadening outcomes analysis

The primary outcomes of lifestyle interventions should include the most accurate surrogates for metabolic fitness and disease risk (43). Nontraditional markers of cardiovascular risk, such as highsensitivity C-reactive protein concentrations and plasminogen activator-1, may provide additional accuracy to traditional markers of BMI, blood pressure, lipids, and central adiposity (44). Glycated hemoglobin concentrations and homeostasis model assessment scores will also be important diagnostic measures for prediabetes and metabolic disorders (45, 46). Because cardiovascular disease, diabetes, and chronic illness represent the most relevant risks for this cohort, these markers could also serve as important outcomes in assessing the efficacy of lifestyle interventions to lower disease risk.

Strength and fitness could also help identify patients most in need of medical treatment. Recently, the six-minute-walk test was identified as a safe, simple, and effective tool for measuring functional status in obese patients of a bariatric clinic (47). Muscle-strength tests, such as the one-repetition maximum test, have also been used to stratify risk of mortality along with adiposity across BMI groups (48).

CONCLUSIONS

A positive energy balance has driven and perpetuated the obesity epidemic in the United States as Americans eat more and move less. Whereas this trend has caused a universal shift toward a higher average BMI in the United States, it is clear that some individuals suffer more than do others in our obesogenic environment. Patients who develop class III, severe obesity should be a primary target for nutrition medicine professions. The high costs and widespread pain and suffering inflicted by extreme obesity should serve as the rationale for aggressive lifestyle interventions. The goals of these interventions should be achievable, practical, and medically significant. As experts in nutrition medicine, we are best prepared to provide the sciencebased evidence for innovative and effective lifestyle interventions to treat severe obesity and comorbid chronic disease. (Other articles in this supplement to the Journal include references 49–51.)

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REFERENCES

- Institute of Medicine. Dietary Reference Intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids. Washington, DC: National Academies Press, 2002.
- Swinburn BA, Sacks G, Lo SK, et al. Estimating the changes in energy flux that characterize the rise in obesity prevalence. Am J Clin Nutr 2009;89:1723–8.
- Heymsfield SB. How large is the energy gap that accounts for the obesity epidemic? Am J Clin Nutr 2009;89:1717–8.
- Booth FW, Gordon SE, Carlson CJ, Hamilton MT. Waging war on modern chronic diseases: primary prevention through exercise biology. J Appl Physiol 2000;88:774–87.
- Booth FW, Laye MJ, Lees SJ, Rector RS, Thyfault JP. Reduced physical activity and risk of chronic disease: the biology behind the consequences. Eur J Appl Physiol 2008;102:381–90.
- Hill JO, Wyatt HR, Reed GW, Peters JC. Obesity and the environment: where do we go from here? Science 2003;299:853–5.
- 7. Friedman JM. A war on obesity, not the obese. Science 2003;299:856-8.
- Allison DB, Downey M, Atkinson RL, et al. Obesity as a disease: a white paper on evidence and arguments commissioned by the Council of The Obesity Society. Obesity (Silver Spring) 2008;16:1161–77.
- Sturm R. Increases in morbid obesity in the USA: 2000-2005. Public Health 2007;121:492–6.
- Poirier P, Alpert MA, Fleisher LA, et al. Cardiovascular evaluation and management of severely obese patients undergoing surgery: a science advisory from the American Heart Association. Circulation 2009;120: 86–95.
- Must A, Spadano J, Coakley EH, Field AE, Colditz G, Dietz WH. The disease burden associated with overweight and obesity. JAMA 1999; 282:1523–9.
- Kolotkin RL, Crosby RD, Gress RE, Hunt SC, Engel SG, Adams TD. Health and health-related quality of life: differences between men and women who seek gastric bypass surgery. Surg Obes Relat Dis 2008;4: 651–8.
- Valtonen M, Laaksonen DE, Tolmunen T, et al. Hopelessness—novel facet of the metabolic syndrome in men. Scand J Public Health 2008;36: 795–802.
- Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults—the evidence report. National Institutes of Health. Obes Res 1998;6(suppl 2):2098–51S.
- Chipkin SR, Goldberg RJ. Obesity surgery and diabetes: does a chance to cut mean a chance to cure? Am J Med 2009;122:205–6.
- Blackburn GL, Hutter MM, Harvey AM, et al. Expert Panel on Weight Loss Surgery: executive report update. Obesity (Silver Spring) 2009;17: 842–62.
- Wadden TA, Butryn ML, Byrne KJ. Efficacy of lifestyle modification for long-term weight control. Obes Res 2004;12(suppl):151S–62S.
- Blackburn G. Effect of degree of weight loss on health benefits. Obes Res 1995;3(suppl 2):211s–6s.

- American Dietetic Association. Position of the American Dietetic Association: Weight management. J Am Diet Assoc 2009;109:330–46.
- Tuomilehto J, Lindström J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001;344:1343–50.
- Stevens VJ, Obarzanek E, Cook NR, et al. Long-term weight loss and changes in blood pressure: results of the Trials of Hypertension Prevention, phase II. Ann Intern Med 2001;134:1–11.
- Weiss EP, Racette SB, Villareal DT, et al. Lower extremity muscle size and strength and aerobic capacity decrease with caloric restriction but not with exercise-induced weight loss. J Appl Physiol 2007;102:634–40.
- Leibel RL, Rosenbaum M, Hirsch J. Changes in energy expenditure resulting from altered body weight. N Engl J Med 1995;332:621–8.
- Bopp MJ, Houston DK, Lenchik L, Easter L, Kritchevsky SB, Nicklas BJ. Lean mass loss is associated with low protein intake during dietaryinduced weight loss in postmenopausal women. J Am Diet Assoc 2008; 108:1216–20.
- Layman DK, Boileau RA, Erickson DJ, et al. A reduced ratio of dietary carbohydrate to protein improves body composition and blood lipid profiles during weight loss in adult women. J Nutr 2003;133:411–7.
- Savage DB, Petersen KF, Shulman GI. Disordered lipid metabolism and the pathogenesis of insulin resistance. Physiol Rev 2007;87:507–20.
- Roden M, Krssak M, Stingl H, et al. Rapid impairment of skeletal muscle glucose transport/phosphorylation by free fatty acids in humans. Diabetes 1999;48:358–64.
- Chiu JD, Kolka CM, Richey JM, et al. Experimental hyperlipidemia dramatically reduces access of insulin to canine skeletal muscle. Obesity (Silver Spring) 2009 Epub ahead of print;
- Petersen KF, Dufour S, Savage DB, et al. The role of skeletal muscle insulin resistance in the pathogenesis of the metabolic syndrome. Proc Natl Acad Sci USA 2007;104:12587–94.
- Hoy MK, Winters BL, Chlebowski RT, et al. Implementing a low-fat eating plan in the Women's Intervention Nutrition Study. J Am Diet Assoc 2009;109:688–96.
- Vanhecke TE, Franklin BA, Miller WM, deJong AT, Coleman CJ, McCullough PA. Cardiorespiratory fitness and sedentary lifestyle in the morbidly obese. Clin Cardiol 2009;32:121–4.
- Lee DC, Sui X, Blair SN. Does physical activity ameliorate the health hazards of obesity? Br J Sports Med 2009;43:49–51.
- Bond DS, Evans RK, DeMaria E, et al. Physical activity and quality of life improvements before obesity surgery. Am J Health Behav 2006;30: 422–34.
- Ferraro KF, Su Y, Gretebeck RJ, Black DR, Badylak SF. Body mass index and disability in adulthood: a 20-year panel study. Am J Public Health 2002;92:834–40.
- Hittel DS, Berggren JR, Shearer J, Boyle K, Houmard JA. Increased secretion and expression of myostatin in skeletal muscle from extremely obese women. Diabetes 2009;58:30–8.

- Das SK, Saltzman E, McCrory MA, et al. Energy expenditure is very high in extremely obese women. J Nutr 2004;134:1412–6.
- Willey KA, Singh MAF. Battling insulin resistance in elderly obese people with type 2 diabetes: bring on the heavy weights. Diabetes Care 2003;26:1580–8.
- Donnelly JE, Blair SN, Jakicic JM, Manore MM, Rankin JW, Smith BK. American College of Sports Medicine Position Stand. Appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults. Med Sci Sports Exerc 2009;41:459–71.
- US Department of Health and Human Services. 2008 Physical activity guidelines for Americans. Version current 21 November 2008. Available from: http://www.health.gov/paguidelines/guidelines/default.aspx (cited 14 June 2009).
- Tresierras MA, Balady GJ. Resistance training in the treatment of diabetes and obesity: mechanisms and outcomes. J Cardiopulm Rehabil Prev 2009;29:67–75.
- Hunter GR, Byrne NM, Sirikul B, et al. Resistance training conserves fat-free mass and resting energy expenditure following weight loss. Obesity (Silver Spring) 2008;16:1045–51.
- Hamdy O, Carver C. The Why WAIT program: improving clinical outcomes through weight management in type 2 diabetes. Curr Diab Rep 2008;8:413–20.
- Gellad WF, Detsky AS, Choudhry NK. Implications of recent clinical rials on pay-for-performance. Am J Health Syst Pharm 2009;66: 864–7.
- 44. Kahn SE, Zinman B, Haffner SM, et al. Obesity is a major determinant of the association of C-reactive protein levels and the metabolic syndrome in type 2 diabetes. Diabetes 2006;55:2357–64.
- Manley SE, Luzio SD, Stratton IM, Wallace TM, Clark PMS. Preanalytical, analytical, and computational factors affect homeostasis model assessment estimates. Diabetes Care 2008;31:1877–83.
- 46. Manley SE, Sikaris KA, Lu ZX, et al. Validation of an algorithm combining hemoglobin A(1c) and fasting plasma glucose for diagnosis of diabetes mellitus in UK and Australian populations. Diabet Med 2009;26:115–21.
- 47. Fabris de Souza SA, Faintuch J, Fabris SM, et al. Six-minute walk test: functional capacity of severely obese before and after bariatric surgery. Surg Obes Relat Dis 2009;5:540–3.
- Ruiz JR, Sui X, Lobelo F, et al. Muscular strength and adiposity as predictors of adulthood cancer mortality in men. Cancer Epidemiol Biomarkers Prev 2009;18:1468–76.
- 49. Apovian CM. The causes, prevalence, and treatment of obesity revisited in 2009: what have we learned so far? Am J Clin Nutr 2010;91(suppl): 277S–9S.
- Heber D. An integrative view of obesity. Am J Clin Nutr 2010; 91(suppl):280S–3S.
- Popkin BM. Recent dynamics suggest selected countries catching up to US obesity. Am J Clin Nutr 2010;91(suppl):284S–8S.