Treatment of Pediatric and Adolescent Obesity

Jack A. Yanovski, MD, PhD

Susan Z. Yanovski, MD

THE PREVALENCE OF OVERWEIGHT IN US CHILDREN AND adolescents has reached alarming levels. The proportion of children and adolescents who are overweight, defined as a body mass index exceeding the 95th percentile for age and sex based on norms from the 1960s, has tripled in the past 3 decades.[1] This dramatic increase in overweight has not been confined to US children and adolescents; pediatric overweight is also increasing in other countries.[2-4] Greater body weight has been found to predispose children and adolescents to many of the medical complications of obesity found in adults, such as hypertension,[5] dyslipidemia,[6] impaired glucose homeostasis,[7,8] steatohepatitis,[9] sleep apnea,[10] and intracranial hypertension,[11] and to problems unique to childhood and adolescence, including accelerated pubertal[12] and skeletal[13] development and orthopedic disorders, such as slipped capital femoral epiphysis.[14]

In this issue of THE JOURNAL, Schwimmer and colleagues[15] report that severely obese children and adolescents who seek obesity treatment have more than a 5-fold increased risk of reporting a low health-related quality of life compared with a reference sample of healthy children and adolescents—a risk similar to that previously described for children and adolescents diagnosed as having cancer. Overweight during childhood and adolescence also appears to be an important independent predictor of health risks and mortality in later life, even when adult weight is taken into account.[16] Thus, it seems clear that one of the most compelling medical challenges of the 21st century is to develop effective strategies to prevent and treat pediatric obesity.

Successful methods to prevent pediatric overweight remain elusive, but some innovative approaches, such as techniques to decrease television viewing by children and adolescents,[17] are being actively investigated. Although some data suggest that behavioral treatment of obesity may be more effective for children and adolescents than for adults,[18] even the best of studies find long-term weight reductions maintained in only about half of young children and adolescents treated with intensive behavioral modification.[18,19] Successful behavioral programs are labor intensive, are not yet translated into versions that can be easily applied on the primary care level, and require intensive parental involvement which, for many families, is simply not realistic. Many clinicians also believe that behavioral treatment alone is not as effective in severely obese children and adolescents compared with those with lesser degrees of obesity. As a result, some investigators have turned to the study of pharmacotherapy for amelioration of pediatric obesity. Even though obesity is now viewed as a chronic disorder that requires continued treatment,[20] few controlled studies lasting more than a few weeks have examined the efficacy of medications to reduce body weight in children or adolescents.[21]

Also in this issue of THE JOURNAL, Berkowitz et al[22] present a 6-month randomized controlled trial of sibutramine, an anorexiant medication that blocks the reuptake of the neurotransmitters norepinephrine and serotonin. Sibutramine appears to be modestly effective for weight reduction in adults over periods as long as 2 years.[23] During the first 6 months of treatment, adults who follow a reduced-calorie diet and take sibutramine typically lose 5% to 8% of their initial body weight vs 1% to 4% in placebo-treated patients.[20] The major adverse effects of sibutramine include increases in blood pressure and pulse rate great enough to warrant discontinuation of sibutramine in up to 5.3% of treated adults.

Berkowitz et al randomly assigned 82 adolescents with a body mass index between 32 and 44—the majority of whom had evidence of obesity-related comorbid conditions (R. Berkowitz, written communication, March 14, 2003)—to receive intensive behavioral therapy and placebo or intensive behavioral therapy and sibutramine for 6 months. The investigators then offered all study participants open-label

See also pp 1805 and 1813.

Author Affiliations: Unit on Growth and Obesity, Developmental Endocrinology Branch, National Institute of Child Health and Human Development, Bethesda, Md (Dr J. A. Yanovski); Division of Digestive Diseases and Nutrition, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Department of Health and Human Services, Bethesda, Md (Dr S. Z. Yanovski).

Financial Disclosure: Dr J. Yanovski is principal investigator of a controlled trial of orlistat sponsored by the National Institute of Child Health and Human Development. For this study, orlistat and its matching placebo are supplied by Roche Laboratories under a material transfer agreement with the National Institute of Child Health and Human Development. Dr J. Yanovski received an honorarium from Strategic Implications International in 2001.

Corresponding Author and Reprints: Jack A. Yanovski, MD, PhD, Unit on Growth and Obesity, National Institutes of Health, 10 Center Dr, Bldg 10, Room 10N262, MSC 1862, Bethesda, MD 20892 (e-mail: yanovskj@mail.nih.gov).

sibutramine for an additional 6 months along with a somewhat less intensive behavioral therapy. The study had excellent retention with all but 8 participants returning for follow-up at 6 months. Adolescents treated with behavioral therapy and sibutramine lost significantly more weight (mean [SD] of –7.9 [6.3] kg) than those who received behavioral therapy and placebo (mean [SD] of –3.2 [6.1] kg) over the first 6 months. Further, a substantial portion of adolescents treated with behavioral therapy and sibutramine had weight losses that are considered medically significant. A decrement in initial body mass index by 10% was found in 40% of adolescents treated with behavioral therapy and sibutramine vs 15% of adolescents treated with behavioral therapy and placebo. Weight losses were largely maintained by those who continued taking sibutramine for another 6 months while attending behavioral therapy sessions.

These data are encouraging, but have some important limitations. First, the study design excluded adolescents who had a body mass index of more than 44 or who had already developed type 2 diabetes. Thus, those adolescents most severely affected by their obesity were not studied, and no conclusions can be drawn regarding the efficacy of sibutramine for reducing body weight in such adolescents. Second, adolescents participated in an intensive behavior modification program that included 13 weekly group sessions, followed by 6 biweekly group sessions over the first 6 months. Berkowitz et al found that adherence to the program independently accounted for a significant portion of the variance in lost body weight—more than that explained by sibutramine vs placebo. Intensive behavioral programs are costly, require specially trained staff, and are not often available in the community setting.

Third, and perhaps most important, sibutramine therapy caused increases in systolic blood pressure at 3 months (vs a decline in blood pressure in placebo-treated adolescents). The medication dose had to be reduced or discontinued in 44% of the sibutramine-treated adolescents during the first 6 months. Fourth, the improvements observed in the comorbid conditions associated with obesity, such as insulin resistance and dyslipidemia, were not different in the adolescents receiving sibutramine or placebo despite the greater weight losses of those taking sibutramine. Although the failure to detect a difference between groups may have been due to the study's relatively small sample size, given the increases in pulse rate and blood pressure observed in this study, it is not clear whether behavioral therapy and sibutramine improve the surrogate markers for cardiovascular disease in adolescents more than behavioral treatment alone.

Fifth, the study data are informative only for the effects of sibutramine over 6 to 12 months. Obesity is a chronic condition that requires lifelong efforts to control. It remains unknown whether sibutramine will continue to be effective for reducing body weight in adolescents in the long term and diminish the medical complications of their obesity. Nonetheless, this study is important because it indicates that pharmacotherapy, in combination with intensive behavioral treatment, can lead to clinically significant decreases in body weight in an adolescent population and can serve as a model for future studies.

As the number of children and adolescents with severe obesity and concomitant medical problems increases, the inclination for clinicians to consider intensive treatments, including pharmacotherapy and surgery,[24] becomes greater. Given the many ways in which children and adolescents differ from adults, physicians must not conclude that treatments found safe and effective in adults will have similar safety and effectiveness in pediatric and adolescent populations.

While it is appropriate to consider intensive treatments in severely obese adolescents with comorbid conditions,[20,21] such treatments should be regarded as investigational at this time and should be performed as part of a closely monitored research study. Clinicians should consider referring severely obese children and adolescents to experienced, specialized pediatric obesity centers, so that intensive treatment can be performed by a team of professionals that may include physicians, dietitians, behaviorists, and exercise specialists with expertise in pediatric and adolescent medicine. Evidence-based guidelines[25] for treatment of pediatric and adolescent obesity would be useful, but current data are insufficient to generate them for children or adolescents. For now, expert opinion must serve as a guide for pediatric and adolescent obesity treatment.[26]

Rapid advances in basic and clinical science are elucidating the complex genetic, psychosocial, metabolic, and environmental factors that contribute to the development of obesity and its comorbid conditions. This research will lead to improved methods for prevention and treatment of obesity in the years ahead. Researchers should be encouraged to include children and adolescents in clinical research studies of obesity prevention and treatment, so that the risks and benefits from therapeutic advances can be established in pediatric and adolescent populations.

At the present time, however, it remains exceedingly difficult for overweight children and adolescents to lose weight, and even more difficult for them to sustain that weight loss long term. The ultimate goal must be prevention of the development of overweight in children and adolescents.[27]

Funding/Support: Dr J. Yanovski is a commissioned officer in the US Public Health Service, Department of Health and Human Services. His research is supported by the National Institute of Child Health and Human Development grant ZO1 HD-00641 and the National Center on Minority Health and Health Disparities.
Disclaimer: The opinions expressed herein are those of the authors, and do not necessarily reflect the views of the National Institutes of Health, the US Public Health Service, or the Department of Health and Human Services.

REFERENCES

1. Ogden CL, Flegal KM, Carroll MD, Johnson CL. Prevalence and trends in overweight among US children and adolescents, 1999-2000. *JAMA.* 2002;288:1728-1732.

2. Moreno LA, Sarria A, Fleta J, Rodriguez G, Bueno M. Trends in body mass index and overweight prevalence among children and adolescents in the region of Aragon (Spain) from 1985 to 1995. *Int J Obes Relat Metab Disord.* 2000;24:925-931.
3. Hughes JM, Li L, Chinn S, Rona RJ. Trends in growth in England and Scotland, 1972 to 1994. *Arch Dis Child.* 1997;76:182-189.
4. Esposito-Del Puente A, Contaldo F, De Filippo E, et al. High prevalence of overweight in a children population living in Naples (Italy). *Int J Obes Relat Metab Disord.* 1996;20:283-286.
5. Sorof JM, Poffenbarger T, Franco K, Bernard L, Portman RJ. Isolated systolic hypertension, obesity, and hyperkinetic hemodynamic states in children. *J Pediatr.* 2002;140:660-666.
6. Chu NF, Rimm EB, Wang DJ, Liou HS, Shieh SM. Clustering of cardiovascular disease risk factors among obese schoolchildren: the Taipei Children Heart Study. *Am J Clin Nutr.* 1998;67:1141-1146.
7. Sinha R, Fisch G, Teague B, et al. Prevalence of impaired glucose tolerance among children and adolescents with marked obesity. *N Engl J Med.* 2002;346:802-810.
8. Uwaifo GI, Elberg J, Yanovski JA. Impaired glucose tolerance in obese children and adolescents. *N Engl J Med.* 2002;347:290-292.
9. Rashid M, Roberts EA. Nonalcoholic steatohepatitis in children. *J Pediatr Gastroenterol Nutr.* 2000;30:48-53.
10. de la Eva RC, Baur LA, Donaghue KC, Waters KA. Metabolic correlates with obstructive sleep apnea in obese subjects. *J Pediatr.* 2002;140:654-659.
11. Scott IU, Siatkowski RM, Eneyni M, Brodsky MC, Lam BL. Idiopathic intracranial hypertension in children and adolescents. *Am J Ophthalmol.* 1997;124:253-255.
12. Kaplowitz PB, Slora EJ, Wasserman RC, Pedlow SE, Herman-Giddens ME. Earlier onset of puberty in girls: relation to increased body mass index and race. *Pediatrics.* 2001;108:347-353.
13. Russell DL, Keil MF, Bonat SH, et al. The relation between skeletal maturation and adiposity in African American and Caucasian children. *J Pediatr.* 2001;139:844-848.
14. Loder RT, Aronson DD, Greenfield ML. The epidemiology of bilateral slipped capital femoral epiphysis: a study of children in Michigan. *J Bone Joint Surg Am.* 1993;75:1141-1147.
15. Schwimmer JB, Burwinkle TM, Varni JW. Health-related quality of life of severely obese children and adolescents. *JAMA.* 2003;289:1813-1819.
16. Must A, Jacques PF, Dallal GE, Bajema CJ, Dietz WH. Long-term morbidity and mortality of overweight adolescents: a follow-up of the Harvard Growth Study of 1922 to 1935. *N Engl J Med.* 1992;327:1350-1355.
17. Robinson TN. Reducing children's television viewing to prevent obesity: a randomized controlled trial. *JAMA.* 1999;282:1561-1567.
18. Epstein LH, Valoski AM, Kalarchian MA, McCurley J. Do children lose and maintain weight easier than adults: a comparison of child and parent weight changes from six months to ten years. *Obes Res.* 1995;3:411-417.
19. Epstein LH, Valoski A, Wing RR, McCurley J. Ten-year outcomes of behavioral family-based treatment for childhood obesity. *Health Psychol.* 1994;13:373-383.
20. Yanovski SZ, Yanovski JA. Obesity. *N Engl J Med.* 2002;346:591-602.
21. Yanovski JA. Intensive therapies for pediatric obesity. *Pediatr Clin North Am.* 2001;48:1041-1053.
22. Berkowitz RI, Wadden TA, Tershakovec AM, Cronquist Y. Behavior therapy and sibutramine for the treatment of adolescent obesity: a randomized, placebo-controlled trial. *JAMA.* 2003;289:1805-1812.
23. James WP, Astrup A, Finer N, et al, for the STORM Study Group. Effect of sibutramine on weight maintenance after weight loss: a randomised trial (Sibutramine Trial of Obesity Reduction and Maintenance). *Lancet.* 2000;356:2119-2125.
24. Sugerman HJ, Sugerman EL, DeMaria EJ, et al. Bariatric surgery for severely obese adolescents. *J Gastrointest Surg.* 2003;7:102-108.
25. National Institutes of Health. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults—The Evidence Report. *Obes Res.* 1998;6(suppl 2):51S-209S.
26. Barlow SE, Dietz WH, for the Maternal and Child Health Bureau, Health Resources and Services Administration, and the Department of Health and Human Services. Obesity evaluation and treatment: expert committee recommendations. *Pediatrics.* 1998;102:E29.
27. Jackson Y, Dietz WH, Sanders C, et al. Summary of the 2000 Surgeon General's listening session: toward a national action plan on overweight and obesity. *Obes Res.* 2002;10:1299-1305.

Low-Carbohydrate Diets and Realities of Weight Loss

George A. Bray, MD

OBESITY IS A WORLDWIDE EPIDEMIC AND WILL BE followed by a worldwide epidemic of diabetes.[1] While diet, lifestyle, and exercise are the cornerstones of current approaches to treat obesity, they have been ineffective in stemming the current epidemic. In this issue of THE JOURNAL, the article by Bravata et al[2] systematically reviews and synthesizes the literature on the use of low-carbohydrate diets for treatment of obesity. Their findings add to the review of popular diets published by Freedman et al.[3] Among the principal findings in the analysis by Bravata et al are that lower-carbohydrate (≤60 g/d of carbohydrate) diets were associated with reduced calorie intake and that weight loss was predicted by calorie intake, diet duration, and baseline body weight, but not by carbohydrate content. At the end of their analysis, Bravata et al note several gaps in the current literature on low-carbohydrate diets, including the need for better follow-up and for use of intent-to-treat analyses.

These findings are helpful in understanding whether low-carbodydrate diets work for obese individuals, but first several important lessons about obesity must be considered.[4] First, obesity is a chronic, relapsing, neurochemical disease that occurs in genetically susceptible people. Second, obesity can be conceptualized as an epidemiological disease with food as the agent that acts on the host to produce disease. Third, current treatments do not cure obesity and thus are only palliative. Fourth, 2 kinds of treatment are available for obesity: cognitive and noncognitive. Cognitive treatments, such as lifestyle change, diet,

See also p 1837.

Author Affiliation: Division of Obesity, Pennington Biomedical Research Center, Louisiana State University, Baton Rouge.
Corresponding Author and Reprints: George A. Bray, MD, Pennington Biomedical Research Center, Louisiana State University, 6400 Perkins Rd, Baton Rouge, LA 70808 (e-mail: brayga@pbrc.edu).