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Adolescent Obesity and Bariatric Surgery

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Obesity has become the most common nutritional disorder of children and adolescents in the United States. Along with this epidemic, there has been an increase in associated potentially life-threatening diseases. The World Health Organization classification in adults defines overweight as a body mass index (BMI) of 25 to 30 kg/m^2 and obesity as a BMI of 30 kg/m^2 or more. The BMI, which takes into account the relationship of weight and height, correlates with the amount of body fat in children and adults [1]. In children, the ratio of weight to height changes with growth. For that reason BMI growth charts have been developed for children by the US Centers for Disease Control and Prevention. The definition of obesity for children is ninety-fifth percentile or more of BMI for age. Children with a BMI between the eighty-fifth and ninety-fifth percentile are considered overweight [2]. Using these criteria, the prevalence of being obese doubled among children aged 6 to 11 years and tripled among children aged 12 and 17 years in the United States between 1980 and 2000. Currently more than 1 million adolescents and young adults in the United States are considered severely obese (BMI $\geq$40 kg/m^2). Groups that are at particularly high risk for morbid obesity include African Americans, Hispanics, Pima Indians, and other Native Americans.

The epidemic of obesity has multiple causes. Human beings are genetically predisposed to store fat, a survival mechanism that served well during lean times for our prehistoric ancestors. Currently our lifestyles, unlike those of our ancestors, are much more sedentary. Food in modern

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society also is plentiful, processed, and energy dense. In general, it is thought that genetic predisposition plays a permissive role, interacting with environmental factors to promote obesity. It is estimated that 30% to 50% of the tendency toward excess adiposity can be explained by genetic variations [3]. Although numerous genetic markers are linked with obesity and its metabolic consequences, identifiable hormonal, syndromic, or molecular genetic abnormalities are present in less than 5% of obese individuals [4,5]. More than 430 genes, markers, and chromosomal regions have been associated or linked with human obesity phenotypes [6]. Every chromosome, except the Y chromosome, has a locus linked with the phenotype of obesity. The most frequent mutations that result in the obesity phenotype have been found in the melanocortin receptor 4, occurring in up to 4% of early-onset and severe childhood obesity [7]. Given recent genetic findings, it is highly probable that severe childhood obesity is polygenic, with susceptibility conferred via complex interactions among genetic factors, behavioral factors, and the environment.

Comorbidities of obesity

Obesity in many children is not a problem of ''willpower'' or ''discipline'' but is a potentially life-threatening disease. A dose-response relationship between BMI during young adulthood and the risk of death has been demonstrated, with extreme obesity resulting in a reduction of 20, 13, 5 and 8 years of life expectancy for black men, white men, white women, and black women, respectively [8]. Importantly, the loss of 5% to 10% of body weight results in a significant improvement of risk and comorbidities [9].

Metabolic abnormalities

Over the past decade, an alarming increase in the appearance of type 2 diabetes in children has occurred. Type 2 diabetes is responsible for approximately one fifth of the new diagnoses of diabetes in pubertal children. By some estimates, up to one third of all children and half of Hispanic and black children develop type 2 diabetes in their lifetime [10]. Diabetes can be diagnosed by a fasting plasma glucose >125 mg/dL in the presence of diabetes symptoms or two fasting plasma glucose values >125 mg/dL in the absence of symptoms or by measuring a serum glucose concentration >200 mg/dL 2 hours after an oral load of 75 g of glucose (oral glucose tolerance test).

In adults, the metabolic syndrome is defined by the US National Cholesterol Education Program's Adult Treatment Panel III as requiring three of five characteristics:

1. Abdominal obesity with a waist circumference more than 102 cm in men and 88 cm in women
2. Triglyceride concentration >150 mg/dL or 1.7 μmol/L

3. Abnormal cholesterol profile with high-density lipoprotein cholesterol <40 mg/dL or 1 μmol/L in men and <50 mg/dL or 1.3 μmol/L in women
4. Blood pressure $>130/85$ mm Hg
5. Impaired fasting glucose ≥ 100 mg/dL or 5.5 μmol/L [11]

The metabolic syndrome is a clustering of risk factors for later cardiac disease and diabetes. Approximately 47 million adults meet criteria for this syndrome, which elevates one's risk of later heart diseases twofold and the risk of diabetes fivefold. There is as yet no definition of metabolic syndrome for the pediatric age group, but using the adult criteria, the overall prevalence of metabolic syndrome among 12- to 19-year-old individuals in the United States was found to be 4.2% [12]. Using modified criteria, Weiss and colleagues [13] found that nearly 50% of severely obese adolescents met criteria for the metabolic syndrome and that the risk increased as BMI increased. Currently, there is a lack of certainty about the pathogenesis of the syndrome, and considerable controversy exists about whether the metabolic syndrome poses a greater health risk than the sum of its parts, especially for pediatric patients.

Acanthosis nigricans, another frequent manifestation of insulin resistance, is characterized by hyperpigmented, hyperkeratotic, velvety plaques on the dorsal surface of the neck and hands. Insulin resistance also stimulates ovarian and adrenal androgen and estrogen production. These hormonal perturbations place obese adolescent girls at high risk of menstrual disorders and early onset of polycystic ovary syndrome. Polycystic ovary syndrome, previously called Stein-Leventhal syndrome, is a complex metabolic disease that may present in adolescents and is associated with obesity. This syndrome is manifested by oligomenorrhea or amenorrhea associated with obesity, insulin resistance, hirsutism, acne, and acanthosis nigrans [14]. It is reasoned that weight loss, which results in decreases in insulin resistance, can be an important adjunct to treatment of polycystic ovary syndrome and menstrual abnormalities in obese patients [15].

Cardiac risk factors

Cardiac risk factors are common in obese children and include atherogenic dyslipidemia (low high-density lipoprotein cholesterol and elevated triglycerides or low-density lipoprotein cholesterol), hypertension, sleep apnea, and left ventricular hypertrophy. Fifty percent of overweight adolescents have one risk factor for developing cardiovascular disease and 20% have two factors [15]. Childhood obesity is the leading cause of pediatric hypertension. Systolic blood pressure correlates positively with BMI, skinfold thickness, and waist-to-hip ratio in children and adolescents [16]. Clinical hypertension is ten times more common in obese children than lean children, with up to 30% of obese children having elevated systolic or diastolic blood pressure [17,18]. Significant, irreversible consequences of

hypertension, such as hypertensive cardiac disease, can present in childhood. In one study, 38% of children who had hypertension had left ventricular hypertrophy by echocardiography [18]. Others have noted that the prevalence of left ventricular hypertrophy increases as a function of overweight, with 3% of normal weight, 25% of overweight, 52% of obese, and 86% of morbidly obese youth fulfilling echocardiographic criteria for left ventricular hypertrophy (Thomas Kimball, MD, personal communication, 2005). Hyperlipidemia in obese children is most often manifested by elevated low-density lipoprotein cholesterol, elevated triglycerides, and decreased high-density lipoprotein cholesterol [19].

Obstructive sleep apnea syndrome

There is a strong association between obesity and obstructive sleep apnea syndrome (OSAS), because obese children are four to six times more likely to have OSAS when compared with lean subjects [20]. Symptoms of OSAS may include snoring, poor school performance because of daytime sleepiness, enuresis, and hyperactivity [21]. OSAS is diagnosed by an overnight sleep study to measure the apnea-hypopnea index. Twenty-six percent to 37% of obese children have an abnormal sleep study, although not all have significant obstruction [22]. We have found that OSAS correlates directly with BMI: 40%, 50%, and 70% of adolescents with BMI of 40 to 49, 50 to 59, and >60, respectively, meet polysomnographic criteria for OSAS [23]. For obese children, weight reduction improves obstructive sleep apnea, although it is important to rule out other anatomic causes of sleep apnea, such as tonsillar hypertrophy [24]. Obese children with sleep disorders may benefit from an evaluation by an otorhinolaryngologist.

Nonalcoholic fatty liver disease

Obesity is related to a spectrum of liver abnormalities, referred to as nonalcoholic fatty liver disease. This disease may present as isolated fatty infiltration of the liver to steatohepatitis (termed "NASH" for nonalcoholic steatosis/hepatitis) or may involve fibrosis and cirrhosis. Up to 40% of obese children have ultrasound findings that suggest infiltration of the liver, and up to 40% of these children also have abnormal liver function test results [17]. Because characteristic biochemical findings do not always correlate with histology, diagnosis requires a liver biopsy [25]. Nonalcoholic fatty liver disease has been diagnosed histologically in up to 50% of obese children and in 83% of morbidly obese teenagers [25a]. Nonalcoholic fatty liver disease in childhood may be characterized by a benign clinical course without progression. With escalating rates of pediatric obesity, however, there is concern that the prevalence and severity of NASH also may increase because of earlier and prolonged exposure to obesity and associated

inflammation [26]. The long-term outcome of untreated NASH acquired in childhood is unknown, but the literature notes that 25% of adult patients who have NASH develop cirrhosis [27]. Currently, antioxidants are being used for the treatment of NASH, but weight loss may prove to be the only effective treatment for nonalcoholic fatty liver disease [28].

Orthopedic disorders

Overweight children are susceptible to developing orthopedic problems. Excess weight may cause injury to the growth plate and result in slipped capital femoral epiphysis, genu valga, tibia vara (Blount's disease), flat kneecap pressure/pain, spondylolisthesis, scoliosis, and osteoarthritis [29]. Blount's disease (tibia vara) is overgrowth of the medial aspect of the proximal tibial metaphysis, which occurs in response to and then accentuates bowing of the legs under the pressure of excess weight [19].

Pseudotumor cerebri

Pseudotumor cerebri is a rare disorder characterized by a gradual increase in intracranial pressure, which, if untreated, may result in visual impairment or even blindness. The usual presentation is headaches, but patients also may experience dizziness, unsteadiness, or diploplia [21]. Approximately 50% of children who have pseudotumor cerebri are obese [19]. There is no effective long-term therapy other than weight loss [19].

Psychology

Although not a life-threatening comorbidity, morbid obesity has a profound impact on normal adolescent development. In a recent study, Schwimmer and Varni demonstrated that the health-related quality of life experienced by obese children and adolescents was the same as that of children undergoing chemotherapy for cancer [30]. The challenge of adolescence is to make the transition to an emotionally and physically mature adult who is able to work and have meaningful relationships [31]. Obese children are more at risk for poor self-esteem, withdrawal from social interaction, depression, and anxiety [32]. The impact of peer teasing and changed body image can be profound in adolescents [33]. Among severely obese adolescents, 48% have moderate to severe depressive symptoms and 35% report a high level of anxiety. Extreme obesity is associated with an increased risk of suicide and suicidal ideation among adolescents [33,34]. This is particularly true for obese adolescent girls [35]. Obese adolescents are more likely to remain unmarried, have lower incomes, and live in poverty than their matched normal weight controls [17]. They are less likely to be accepted into college than normal weight adolescents with comparable scholastic achievement [36].

Treatment of morbid obesity in adolescence

Without question, obesity results from an imbalance in energy intake and expenditure. The ideal treatment for obesity involves decreasing caloric intake while increasing caloric expenditure through exercise or nonexercise thermogenesis. Successful weight loss and maintenance require great effort and commitment but are occasionally possible. In general, patients who are successful in keeping weight off long-term exercise consistently, eat breakfast regularly, control portions and fat in their diet, monitor their weight, and eat consistently during weekdays and weekends [37]. Although weight loss success is possible, most studies have shown that behavior modification and dieting are associated with poor weight loss, high attrition rates, and a high probability of weight regain [38]. For morbidly obese teenagers with comorbidities, failure in one of these programs leaves little chance to achieve and maintain a healthy weight into adulthood.

Behavioral and dietary measures have formed the cornerstone of treatment of obesity [39]. The abundance of diet books and programs available in our society reflects how ineffective most of these strategies are for adults, however. It is not surprising that 90% to 95% of adult patients who lose weight with dietary changes alone regain the weight. The lack of effective weight loss programs has intensified the ongoing search for effective and safe medications to aid in weight loss [39,40]. Currently, the only anorectic agent currently approved for use in obese adolescents (older than age 16) is sibutramine, a nonselective inhibitor of serotonin, norepinephrine, and dopamine. When combined with caloric restriction, exercise, and a comprehensive family-based behavioral program, sibutramine has been shown to be effective in the treatment of adolescent obesity. In a prospective, randomized trial of 60 adolescents, the group treated with sibutramine had an average weight loss of 10.3 kg compared with 2.4 kg in a placebo group [41]. Although previous trials had reported hypertension as a significant side effect, this was not a problem in this trial [41,42].

Orlistat also has been studied in the treatment of morbid obesity. Orlistat inhibits pancreatic lipase and increases fecal losses of triglyceride. In the United States, the Food and Drug Administration has approved orlistat in children older than age 12. In a 1-year, prospective, randomized trial of 539 adolescents, orlistat resulted in an improvement in weight control compared with a control group. BMI in patients on orlistat decreased by 0.55 compared with an increase of 0.31 in the control group, a statistically significant change but of no real clinical relevance [43]. Durable weight loss with orlistat requires maintenance of therapy; unfortunately, high study dropout rates occur because of unacceptable flatulence and diarrhea [44]. Metformin is a bisubstituted, short-chain hydrophilic guanidine derivative that activates AMP protein kinase and reduces fasting and postprandial insulin concentrations. It has been used primarily in obese adolescents

who have polycystic ovarian syndrome to decrease weight and insulin resistance [45]. In preliminary studies, it also has improved obesity-related NASH [46]. Metformin is fairly well tolerated and is approved by the US Food and Drug Administration for the treatment of type 2 diabetes. It is not approved for the treatment of childhood obesity.

Bariatric surgery in adolescents

Resorting to surgery to change the metabolism of a growing child is a profound new concept, but adolescents with morbid obesity who have life-threatening comorbidities probably warrant such a radical therapy. Ethically, it is important that all adolescents first be treated with aggressive nonoperative approaches and, once surgery is considered, that the indications for surgery are considered carefully. The indications for bariatric surgery in adults were derived by an National Institutes of Health consensus panel in 1991 based on known risks factors of obesity and its associated comorbidities [47]. In general, adults with a BMI >40 with or without comorbidities and BMI >35 with comorbidities who have failed multiple attempts at medical management of their obesity are considered candidates for bariatric surgery. This panel specifically avoided making a recommendation for the treatment of patients younger than 18 years of age. Objective data to demonstrate the medical risk of being severely obese as an adolescent and carrying that obesity into adulthood would provide important insight required for developing objective criteria for this unique set of patients. In the absence of these data, the question remains: Will any adolescent patients benefit from bariatric surgery? A task force convened by the American Pediatric Surgical Association addressed this issue, taking into account the noncompliant nature of this population of patients, nutritional and developmental requirements, the ethical issue of assent versus consent in children younger than age 18, and the overall lack of medical data supporting the role for bariatric surgery in severely obese adolescents. The indications for surgery described by this task force are much more conservative than those for adults and include the necessity of studying these patients for long-term outcome [48].

Adolescents being considered for bariatric surgery require careful preoperative testing and preparation. Preoperative testing should focus on identifying comorbidities associated with severe obesity. Routine screening laboratories often performed on patients being evaluated for bariatric surgery include a complete blood count, liver profile, lipid profile, fasting insulin and glucose, oral glucose tolerance test at baseline, and vitamin B_1, B_{12}, and folate levels. All patients undergo a sleep study and ultrasound evaluation of the abdomen to look for steatohepatitis, gallstones, and, in girls, ovarian pathology. In addition to a structured clinical interview with an adolescent psychologist, objective tests are performed to assess

personality traits, cognitive maturity, depression, eating behaviors, and weight-related quality of life, which may have a bearing on candidacy for bariatric surgery or postoperative adherence to medical and nutritional regimens. Screening evaluation of all patients by a pediatric dietitian and exercise physiologist who have experience with adolescent obesity has been helpful preoperatively and postoperatively. Participation in a monthly adolescent support group is also required as part of the preoperative preparation.

A multidisciplinary adolescent bariatric review board should deliberate indications and contraindications before scheduling an adolescent for bariatric surgery. Such a board should consist minimally of a medical director (pediatrician), surgical director (bariatric surgeon), pediatric psychologist, anesthesiologist, gynecologist, dietician, and ethicist. Such a board has been developed at Cincinnati Children's and Texas Children's Hospital. It has facilitated the development of the adolescent bariatric program throughout the hospital and community and been instrumental in resolving potential controversial patient selection and management decisions.

All patients are told that the long-term consequences of bariatric surgery in adolescents are not known and that a long-term study of outcomes is an integral part of this surgery. All patients who undergo surgery are asked to participate in a 10-year outcome study. Operative consent for surgery includes requiring all patients to write a letter describing their indications for having a bariatric procedure, the short- and long-term risks of having the procedure, dietary restrictions and expectations, need to adhere to medical and exercise regimen, their understanding of the procedure, and the lifelong commitment that comes with the decision. The patient and parents/guardians are required to sign the letter and a formal operative consent.

Gastric bypass is considered the gold standard obesity surgery and is the most commonly performed operation worldwide for obesity. Gastric bypass can be performed by laparotomy or laparoscopy. Recent data suggested that the laparoscopic technique may have some advantages over the open technique, but only surgeons with advanced training and expertise in laparoscopic and bariatric surgery should perform it [49,50]. Laparoscopic gastric bypass surgery results in consistent initial weight loss in $>90\%$ of patients. Expected weight loss after laparoscopic gastric bypass surgery is 20 to 30 pounds in the first month and approximately 10 pounds/mo until the weight loss plateaus after 12 to 18 months. Preliminary data from adolescents demonstrated a decrease of BMI from 59 kg/m^2 to 38 kg/m^2 by 1 year [51,52]. If a patient complies with the postoperative diet and exercise program, a weight loss of 80% of excess body weight can be expected at 1 year. Recidivism in the form of weight gain occurs in 20% to 30% of adults. Durable weight loss occurs in most adolescents, yet up to 15% of these patients may have late weight regain [53]. More important than the specific weight loss, laparoscopic gastric bypass surgery results in reversal of nearly all studied comorbidities, with marked improvement in patient health and

long-term prognosis [53–55]. Treatment of morbid obesity with surgery results in improved educational and occupational status [56].

The ultimate success of all bariatric procedures depends on a patient's ability to adhere to a markedly changed and reduced diet. Given the propensity of adolescents to rebel against strict regimens, continued support must be available to all of these patients. Postoperative vitamin and mineral supplementation is critical and commonly consists of two pediatric chewable multivitamins, a calcium supplement (1500 mg calcium citrate/d), and supplementation of B-complex vitamins based on postoperative serum levels. All nonsteroidal anti-inflammatory medications should be avoided. Long-term nutritional complications can be avoided by the patient's adherence to the five basic rules: (1) Eat protein first. (2) Drink at least 64 ounces of liquids daily. (3) No snacking between meals. (4) Walk or exercise at least 30 minutes per day. (5) Always remember vitamins and minerals.

Early complications occur in 1% to 5% of patients who undergo a laparoscopic gastric bypass surgery and include death, acute gastric distention, pulmonary embolism (1%–2%), anastomotic leak (1%–2%), and wound infection (1%–5%) [57]. The mortality rate associated with gastric bypass is 0.5% to 1% in most reports. Population-based data from Washington suggest a mortality rate of up to 6% during a surgeon's first 20 bariatric procedures, decreasing to less than 0.4% beyond 100 procedures performed [58]. Acute gastric distention usually presents with hiccups, bloating, and left shoulder pain and is diagnosed by abdominal radiograph and ultrasound or CT scan demonstrating a dilated stomach. Differentiating this condition from a jejunojejunostomy anastomotic obstruction is important and often requires an experienced radiologist or bariatric surgeon to interpret the radiologic findings. Acute gastric distention may be treated by image-guided needle decompression, usually performed by an interventional radiologist. If distention recurs, an image-guided percutaneous gastrostomy tube can be placed. The diagnosis of an anastomotic leak in the early-postoperative period is difficult in obese patients who may not manifest peritoneal signs. To further complicate matters, an upper gastrointestinal series may not demonstrate the leak. The procedure of choice to evaluate a postoperative bariatric patient who has unexplained tachycardia, particularly in the presence of fever, shoulder, or pelvic pain, should be surgical re-exploration.

Late complications of laparoscopic gastric bypass surgery include anastomotic strictures, marginal ulcers, bowel obstructions from internal and incisional hernias, cholelithiasis, and dietary complications. Patients who have internal hernias often present with recurrent periumbilical abdominal pain or biliary colic in the absence of gallstones as their only symptom. Plain films and upper gastrointestinal scans are often normal, whereas a CT may demonstrate dilation of the biliary limb but also may be normal. The presence of persistent periumbilical pain, even in the face of normal imaging studies, mandates exploration [57]. Patients who have

postprandial vomiting after bariatric surgery are at risk of developing dry beriberi, which most often presents with numbness in the extremities and ataxia. If left untreated, the patient may develop irreversible encephalopathy [59,60]. Previously, as many as 38% of adult obese patients who underwent bariatric surgery developed postoperative cholelithiasis. This number can be reduced substantially by prophylaxis with ursodeoxycholic acid therapy [61,62]. Although previously a concern, the weight loss associated with bariatric surgery does not affect the outcome of subsequent pregnancies, as long as the mother has achieved a stable weight. For that reason, pregnancy is contraindicated in the first 1 or 2 years after surgery [63].

Other surgical options exist for the treatment of morbid obesity in adults. One of the more popular approaches is the laparoscopic gastric band, which was approved in the United States for use in adults in 2001 but has been performed around the world since the early 1990s. The adjustable gastric band offers an enticing alternative to the gastric bypass because it is potentially reversible and carries a lower morbidity and mortality rate (0.1%) [64]. The adjustable gastric band or "lap band" is a prosthetic band with an adjustable inner diameter that is placed around the proximal stomach, which restricts food intake. An adjustable gastric band is connected to a subcutaneous port, which is accessed via a needle through which saline solution is injected to alter the inner diameter. The laparoscopic gastric band has been reported to be successful in European and Australian trials [65,66]. These trials have yet to be reproduced in the United States, most likely because of the difference in abilities to provide week-to-week postoperative adjustments and follow-up. Weight loss with an adjustable gastric band occurs more slowly than with other procedures, with maximal loss occurring 2 to 3 years postoperatively, compared with 12 to 18 months in gastric bypass. Complications of gastric banding include exacerbation of gastroesophageal reflux, esophageal dilation and dysmotility, and mechanical failure of port or device. Complications leading to reoperation have been reported in up to 41% of patients [67].

Summary

Morbid obesity in the United States has reached epidemic proportions. Families, physicians, and the government are finally hearing the message that obesity is an issue of health and not of appearance. Treating this epidemic requires a multidisciplinary approach and a commitment on the part of legislators, health care executives, and medical professionals. Prevention is critical, and all efforts should be made to support increasing safe physical activity for children and adolescents. Children and families also should be educated about appropriate food choices and portion sizes in schools and by their physicians. Decisions about foods in the schools and at home should be driven by education and not by advertising or other outside forces.

The treatment of morbid obesity in adolescence first and foremost should be based on aggressive behavioral and dietary modification. With only a small daily increase in caloric expenditure and a relatively small decrease in caloric intake, many adolescents can achieve and maintain weight loss. This goal requires constant encouragement and surveillance on the part of a "coach," whether that be family, a commercial weight loss program, or a physician. For adolescents with severe morbid obesity who have failed attempts at weight loss, the options are medical therapy or bariatric surgery. Medical therapy is occasionally effective in some patients and should be considered. Bariatric surgery is currently the most effective method of weight loss for morbid obesity. Current indications for bariatric surgery in adolescence are more conservative than for adults, because the long-term consequences of this surgery in growing children are not known. The unique psychological and physical issues of adolescence add another layer of complexity to the management of these patients. For that reason, morbidly obese teenagers are best treated in centers with special expertise in the care of adolescents. Because the long-term outcomes of bariatric surgery in adolescents are not known, it is ethically and clinically important that these patients be enrolled, whenever possible, in long-term prospective outcome studies.

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