

# Obesity in Childhood and Adolescence

## Part 1: Physiology, Genetics, and Growth

---

Linda G. Bandini, RD, PhD, and  
William H. Dietz, MD

*Department of Pediatrics  
Division of Gastroenterology and  
Nutrition*

*New England Medical Center  
Boston, Massachusetts*

### Introduction

Childhood obesity is a multifactorial disease resulting from an imbalance of energy intake and expenditure. Environmental and hereditary factors play a role in the development of obesity. Environmental factors particularly contribute to increased food (energy) intake and to expenditure of energy through activity. In this review, we will consider the physiology of obesity, the evidence that genetic factors operate to produce obesity, how these factors may be expressed, and how growth may be affected in obesity.

### Physiology

An individual is in energy balance when energy intake equals energy expenditure. When energy intake exceeds expenditure, the storage of body fat increases. Conversely, when energy intake is lower

than expenditure, the depots of body fat decrease. Relatively small excesses in energy intake that are maintained for long periods produce significant increases in body fat. For example, an excess energy intake of 100 cal/d for a year results in 10 pounds of accumulated fat.

Food (or energy) intakes have been reported to be comparable among obese and nonobese adults,<sup>1,2</sup> thus suggesting that obese individuals have a reduced energy expenditure. However, others have reported that in obese individuals energy intake is significantly lower than energy expenditure, which casts doubt on the reliability of dietary records to provide a valid measure of energy expenditure.<sup>3</sup>

Daily total energy expenditure (TEE) is calculated based on 4 components: (1) the basal metabolic rate (BMR); (2) the thermic effect of food (TEF); (3) the energy spent in physical activity ( $E_A$ ); and (4) the energy required for growth ( $E_G$ ). Under normal circumstances in adolescence, the BMR accounts for 55% to 60% of TEE, TEF for approximately 10% of TEE, and

$E_A$  for approximately 25% of TEE;  $E_G$  is extremely variable according to growth velocity and/or replacement of tissue. Heredity *may* produce obesity by decreasing TEE through decreased BMR and/or decreased TEF and, possibly, through the energy necessary for activity ( $E_A$ ) and growth ( $E_G$ ).

TEE can be determined by the doubly labeled water method ( $^2\text{H}_2^{18}\text{O}$ ) described by Schoeller.<sup>4</sup> Because  $^{18}\text{O}$  is lost as both water and carbon dioxide ( $\text{CO}_2$ ) and  $^2\text{H}$  is lost as water, the differential loss of the 2 isotopes from body water over time is a measure of the rate of  $\text{CO}_2$  production. With the knowledge of the food quotient of the diet, TEE can be measured within 5% of that determined by respiratory gas exchange. This method is ideal for children and adolescents because no equipment or confinement is necessary.

BMR can be measured continuously using indirect calorimetry with a ventilated hood.<sup>5</sup> Calculations are made from measures of oxygen consumption and  $\text{CO}_2$  production according to the modified Weir's formula.<sup>6</sup> In

adolescents, BMR accounts for 55% to 60% of TEE. The BMR is affected by fat-free mass (FFM), fat mass, age, stage of sexual development, and familial characteristics. However, the *principal determinant* of the BMR is FFM. Increase in Tanner staging and in age improve the correlation between the BMR and the FFM ( $r = 0.93$ ) in adolescents.<sup>7</sup>

A different relationship between FFM and BMR has been shown for males and females and obese and nonobese adolescents, which suggests that *both* sex and fat mass contribute to the variability in the BMR.<sup>7</sup> Bogardus et al reported that familial characteristics also contributed significantly to the BMR in a group of Southwestern Indians.<sup>8</sup> Presumably, the same could occur in other family groups.

Because the BMR contributes significantly to the total metabolic rate, decreases in BMR will reduce total energy needs. In a study of obese and nonobese adolescents,<sup>7</sup> the BMR adjusted for differences in body composition was increased in the obese group (Table 1). These findings suggest that the normal obese adolescent does not have a reduction in

metabolic rate. Bogardus et al<sup>8</sup> found no significant differences in fat mass in individuals from families with high and low metabolic rates.

Although a reduction in BMR does not seem to be a factor in the *maintenance* of adolescent obesity, it theoretically could contribute to the *development* of obesity.

Prospective studies by Ravussin et al<sup>9</sup> in adults suggest a significant relationship between TEE and weight gain. Specifically, Ravussin et al demonstrated greater weight gains in those Pima Indians who had low adjusted BMRs and TEEs. Following weight gain the metabolic rates increased. These data suggest that individuals with a low metabolic rate may gain weight as a compensatory mechanism to normalize the BMR and increase energy expenditure.

The TEF is reflected in the rise in metabolic rate after eating. This increase in energy expenditure is the energy necessary to process the food. The TEF has a genetic component<sup>5,10</sup> and contributes approximately 10% to the TEE. Small decreases in the TEF over a prolonged period of time could lead to a significant energy imbalance and an increase in body fat stores.

Therefore, significant attention has recently focused on the TEF. However, these studies, which were performed primarily in adults, are inconclusive. Some studies reported a reduced TEF in the obese while others did not. However, there were significant differences in study designs, nutrients ingested, caloric content, criteria for obesity, heterogeneity of the subjects, and duration of the studies. For example, some investigators fed similar amounts of calories to obese and nonobese subjects, while others based the caloric intake on body weight, FFM, or a percent of BMR. Some of the differences in outcomes can be attributed to the altered body composition in obese subjects. Segal et al<sup>11</sup> controlled many of these variables by matching obese and nonobese subjects for FFM. Their results indicate that there is a blunted TEF in the obese. However, we were unable to demonstrate significant differences in the TEF in obese and nonobese adolescents, although FFM was similar in the 2 groups.<sup>5</sup>

$E_A$  is the most variable component of energy expenditure.  $E_A$  can be calculated if TEE, BMR, and TEF are known by using the formula  $E_A$

**Table 1**  
Fat-Free Mass and Energy Expenditure in Obese and Nonobese Adolescents<sup>†</sup>

	NONOBESE		OBESE		SIGNIFICANCE*	
	Females	Males	Females	Males	Females	Males
FFM (kg)	40.9	47.1	52.6	55.9	-	-
BMR (kcal/d)	1,441	1,742	1,918	2,253	yes	yes
TEE (kcal/d)	2,385	3,109	3,282	3,612	yes	yes
TEE-BMR <sup>+</sup>	944	1,367	1,364	1,359	yes	no
TEE/BMR <sup>-</sup>	1.69	1.79	1.68	1.68	no	no

+ Nonbasal energy expenditure (direct calculation)

- Nonbasal energy expenditure (relative or indirect calculation)

\* Obese vs nonobese

† Table modified from reference number 7

FFM, fat-free mass; BMR, basal metabolic rate; TEE, total energy expenditure.

= TEE - ( $E_{\text{BMR}} + E_{\text{TEF}}$ ). The energy costs of growth ( $E_{\text{G}}$ ) are very small and are considered negligible in this calculation. Another calculation that reflects  $E_{\text{A}}$  is the ratio TEE:BMR, which reflects the amount of energy spent above the BMR. The ratio of TEE:BMR did not differ significantly between obese and nonobese adolescents in our study,<sup>7</sup> although TEE was greater in the obese group (See Table 1, page 7). These results indicated that the proportion of  $E_{\text{A}}$  and TEF was not reduced in the obese groups. However, a significant reciprocal relationship existed between nonbasal energy expenditure and body fat,<sup>7</sup> suggesting that the amount of energy spent above basal level decreases with increased body fat and that obese and nonobese individuals are not equally active. Because an increase in body size requires an increased amount of energy be spent in performing the same physical activity, the overall or total physical activity level of obese individuals may be lower than that of comparable nonobese individuals. This finding supports the previously reported work by Bullen et al<sup>12</sup> who found obese girls to be less active than nonobese girls. Together, these data suggest that the obese adolescent is less active overall, although the energy spent in performing similar activities may be relatively equivalent. These observations are supported by studies of infants which demonstrate excess weight gain despite unaltered metabolic rates, when a lower TEE exists, ie, the infants who gained the most weight had decreased levels of physical activity.<sup>13</sup>

There is a theory that some individuals are able to overeat but burn the excess calories as heat, while others are more energy efficient and store the excess calories as fat. This

concept has been termed *facultative thermogenesis* or *luxus consumption*. In obese adolescents in whom BMR, TEF, and TEE were measured during a maintenance period and after 2 weeks of overfeeding, the thermogenic response to overeating was not reduced.<sup>5</sup> Additionally, the majority of overfeeding studies in which energy expenditure was measured do not support a role for facultative thermogenesis in the maintenance of body weight.<sup>14-17</sup>

### Genetics

Obesity occurs with a greater prevalence among children with 2 obese parents than among those with 1 obese parent or no obese parents.<sup>19</sup> Although studies of the resemblance in fatness between pets and their owners suggest a strong environmental component,<sup>20</sup> genetic factors play an important role. This has been demonstrated in studies of subcutaneous fatness, as determined from measures of skin-fold thickness of twins. Bouchard et al<sup>21</sup> examined subcutaneous skin-folds in adopted and biologic siblings, cousins, and monozygotic (MZ) and dizygotic (DZ) twins. The intraclass pair correlations were highest for MZ twins ( $r = 0.76$  to  $0.87$ ), followed by DZ twins ( $0.30$  to  $0.49$ ), biologic siblings ( $0.18$  to  $0.43$ ), and cousins ( $0.21$  to  $0.29$ ). The intraclass correlations for pairs of adopted siblings or unrelated siblings were essentially zero.

Because a similar environment existed for these twins, it is difficult to determine the genetic contribution in fat accumulation. More recently, definitive studies to determine the heritability of fatness and obesity have focused on MZ and DZ twins living in similar or dissimilar environments or on adoptees separated from biologic parents. For these studies, body mass index

(BMI) (weight in kilograms/body surface area in square meters), which is strongly correlated with body fatness in adults, was used as the parameter to determine the heritability of fatness. In both Stunkard et al's twin study<sup>22</sup> and adoption study,<sup>23</sup> heredity appeared to be a major determinant of BMI. In the adoption study, Stunkard et al found a strong relationship between the BMIs of Danish adoptees with the BMIs of their biologic parents, but not with the BMIs of their adoptive parents.

These findings were interpreted to suggest that childhood family environment alone has little or no effect on the development of obesity. Careful inspection of the data, however, suggested that the significance of the BMI relationship between adoptees and their biologic parents resulted from the resemblance of the BMIs of lean adoptees and their biologic parents.<sup>24</sup> No significant difference in the prevalence of obesity existed between obese and overweight adoptees and either their adoptive or biologic parents.

In a more recent (1990) study, Stunkard et al<sup>25</sup> compared the BMIs of Swedish adult MZ and DZ twins reared together or apart. The mean age of the population was 58 years but few members of the study were obese. Intrapair BMI correlations were  $0.66$  to  $0.77$  in MZ twins reared apart and were comparable to the correlation observed in twins reared together ( $0.66$  to  $0.74$ ). Although the authors concluded that the childhood environment has little or no influence on BMI, these findings offer limited insight into the heritability of obesity. As stated previously, BMI is an indirect measure of body fatness. Therefore, similarities in members of a nonobese population may reflect that the

size of the body frame rather than obesity is inherited. Moreover, this study was limited to Scandinavia, where similar lifestyles may have minimized the environmental contribution to fatness in twins reared apart.

Recently, Bouchard and coworkers overfed 6 pairs of MZ twins for 100 days to elucidate the role of the genetic component on the storage of energy.<sup>18</sup> Although weight gain and body fat distribution were more similar within twin pairs than between twins, the intrapair correlation coefficient was approximately 0.5. This indicated that a significant portion of the variance in weight gain and fat distribution was unexplained by genetics. Since TEE was not measured, it is unclear whether the energy cost of fat accretion differed more between than within twin pairs. Some twin pairs apparently were more energy efficient and unmeasured differences in  $E_A$  may have contributed to the variability.

We conclude that the relative contributions of genetic and environmental factors to the energy imbalance that produces childhood obesity are as yet unclear. Obesity is clearly related to genetic factors, but published studies have been confounded by environmental factors and failure to distinguish frame size from fatness. Lack of differences in energy expenditure between obese and nonobese adolescents does not exclude the possibility that before becoming obese, the obese child had a reduced energy requirement. The next major challenge for research in obesity is to demonstrate to what extent reductions in BMR, TEF, activity, and/or daily energy expenditure are genetically mediated and, therefore, increase the susceptibility to obesity.

### **Growth**

Clinically obese children tend to be taller and to demonstrate

greater maturational advancement than their nonobese counterparts. Fatter children are both larger in body size and advanced in skeletal maturation, as reported in a review of the literature by Garn et al in 1973.<sup>26</sup> Lean (<15th percentile for triceps skin-fold measurements) and obese (>15th percentile) children were separated out of a group, and their heights were analyzed. The obese children were significantly taller (by as much as 6 cm or more) than the lean children. The lean boys and girls averaged -0.21 Z scores or 0.2 SD below stature expectancy while the obese children averaged 0.48 Z scores or 0.48 SD above height expectancy, as calculated on the basis of the total 4,888 children studied. By the ages of 11 and 12 years, the lean children were nearly 0.4 SD below the median and the obese children were nearly 0.6 SD above the median, with a difference of nearly 1 SD between the groups. The lean boys and girls were below the median at all ages considered, and the obese children were above the median at all ages. Appropriately, the authors did not conclude whether obesity was prone to produce accelerated growth or whether children with accelerated growth were more prone to be obese.

Forbes<sup>27</sup> reported that obese children who became obese during infancy tended on average to have a greater relative height than those who became obese in childhood. Subsequently, using data collected in a longitudinal growth study, Forbes reported that children who developed obesity during childhood reveal a distinct tendency for height to accelerate coincident with or after the onset of excessive weight gain.

The magnitude of the relative height increment is related to

the degree of overweight. "Overnutrition accelerates growth just as undernutrition retards it."<sup>27</sup>

Recently, Vignolo et al reported a study on growth and development in obesity in 303 subjects.<sup>29</sup> Obesity was defined as a weight >20% than that expected for height and sex. Adiposity strongly correlated with BMI and skin-fold measurements. Twenty-five percent of boys and 29% of girls were above the 90th percentile for height when first seen. As they approached adolescence, they moved closer to, and then below, average stature.

Thus, although prepubertal children who are obese are taller than their peers, the data are conflicting as to whether these children remain taller by adolescence.

Growth velocities (GVs) decrease during weight reduction. We demonstrated that even mildly restrictive diets may be associated with a reduction in linear growth velocity.<sup>28</sup> In 19 children studied, the mean SD score for GV was  $2.3 \pm 2.4$  prior to weight reduction, which is in accord with the relationship between obesity and increased height. For the 11 patients with GVs >2 Z scores above the mean, the mean Z score decreased significantly to  $0.62 \pm 2.37$  on a restrictive diet. The data did little to identify the cause of the reduction in GV, and further research in this field is very much indicated. Regardless, the data emphasize the need for careful monitoring of GV's of obese children during weight reduction.

The hormonal and nutritional biochemistry that produces a correlation of increased growth and maturation in obesity remains to be unraveled, but offers a fertile field for investigation.

*References available upon request.*