The Adult Health Consequences of Childhood Obesity

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The short-term complications of severe obesity among children—which include orthopedic complications, pseudotumor cerebri, sleep apnea, gall bladder disease, and polycystic ovary disease—have recently been reviewed (1,2). It is likely, however, that the most common consequences of childhood obesity, including coronary heart disease and the complications of type 2 diabetes mellitus, will not be apparent until adulthood. The recent secular increases in obesity among children, along with the persistence of weight status throughout life, suggest that the impact of childhood obesity on adult morbidity and premature mortality will become increasingly important.

Although overweight children are at increased risk of coronary heart disease and premature mortality, it is uncertain if the associations are independent of adult weight status and depend on the development of obesity during critical periods of growth. Additional information on the natural history and effects of childhood obesity would help guide the development of primary and secondary prevention programs.

In this chapter we will review the adult health consequences of childhood obesity. The data presented are derived largely from the Bogalusa Heart Study (Louisiana), a long-term study of the early natural history of coronary heart disease that involved seven examinations of children and young adults (ages 2 to 38 years) between 1973 and 1993 (3). The panel design of this study, which has data on coronary heart disease risk factors (anthropometry, serum lipids, insulin, blood pressure) from more than 11,500 subjects in a biracial (black/white) community, allows both cross-sectional and longitudinal analyses to be performed.

ASSESSMENT

Childhood Obesity

Childhood obesity has typically been assessed using various combinations of weight and height or by skinfold thickness measurements. Despite the inherent limitations of using weight/height indices to assess excess adipose tissue, they appear to predict various disease outcomes as well as more direct estimates of body fat.
Adolphe Quetelet, a nineteenth-century Belgian mathematician, first noted that the weight of adults was proportional to height squared, and this ratio—the body mass index (BMI, kg/m²)—is now widely used in studies of children. BMI measurements in childhood, however, vary substantially with age, with the values increasing markedly during the first year of life, slowly decreasing until about 6 years of age, and then increasing by around 40% up to 18 years (4). The correlation with age (r ranges from 0.5 to 0.6) among school-aged children can greatly complicate the interpretation of the BMI. For example, a small difference in the mean age of two groups of children could result in significantly different BMI levels, and a value of 17.6 kg/m² among girls in the United States is the 90th centile at age 5 years, the 50th centile at age 11 years, and the 10th centile at 16 years of age.

It is therefore necessary to relate a childhood BMI to values among sex- and age-matched peers, and BMI-for-age centiles have recently been developed from national data collected in the United States between 1963 and 1980 (5). It has been suggested that children with a BMI above the 95th centile of these data are considered to be overweight and that children between the 85th and 95th centiles are “at risk for overweight.” The use of these BMI centiles (and terminology) will greatly simplify comparisons across studies.

Although these centiles account for sex and age differences in BMI levels during childhood, other statistical techniques can provide similar results. For example, residuals from regression models that include sex and age (linear and higher-order terms) yield adjusted BMI values that are highly correlated (r > 0.95) with external BMI-for-age centiles. It may also be important to account for sexual maturation and ethnicity, in addition to sex and age, when interpreting BMI levels among adolescents. For example, the risk of developing type 2 diabetes among Asians begins to increase at relatively low BMI levels (6,7).

**Body Fat Distribution**

Systematic methods for describing body shape were first introduced in the 1930s. It was later suggested (8) that the distribution of body fat among adults might be important in various chronic diseases, and a relative excess of body fat in the abdomen, upper body, and trunk is predictive of total mortality, type 2 diabetes, and coronary heart disease. Although the role of intraabdominal visceral fat has often been emphasized, other fat depots may be important (9), and fat distribution has typically been assessed through the measurement of various circumferences (waist girth or waist/hip) or skinfold thicknesses (subscapular/triceps). As these indices of fat distribution are correlated with BMI, careful statistical adjustments are needed to assess the independent effect of fat distribution.

Although the importance of fat distribution in early life is less certain, associations with coronary heart disease risk factors have been observed. Skinfold and circumference measurements among 3,000 children, for example, indicated that a relative excess of abdominal or truncal fat is associated with adverse levels of triglycerides, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and insulin (10). In agreement with results that have emphasized the use of
waist circumference (alone) as a measure of visceral fat mass among children (11), waist girth has often shown more consistent associations with levels of lipids and insulin than other measures of fat distribution.

Additional studies of fat patterning among children are needed to examine its tracking into adulthood and its long-term health consequences. It is also possible that the waist circumference may provide useful information on the risk for pediatric type 2 diabetes.

Secular Trends

The prevalence of childhood obesity has increased in many countries, and trends have accelerated since 1980 (3,12–14). For example, data from 5- to 17-year-olds who were examined in the Bogalusa Heart Study (3) indicate that there were substantial increases in mean levels of weight, BMI, and triceps skinfold thickness between 1973 and 1993. These BMI changes, which varied from 1.5 to 2.0 kg/m² across ages, are shown in the top panel of Fig. 1.

These secular increases, however, varied substantially across the distribution of BMI (or skinfold thickness) values, with much larger changes occurring at the upper percentiles (Fig. 1, bottom). Whereas the increase in the median BMI level between 1973 and 1993 was around 1 kg/m², the 95th centile increased by about 5 kg/m², and about 15% of the children examined in 1993 had a BMI that was above the 95th centile of the 1973 data. These BMI changes reflected large increases in weight, with the 95th centile of weight among 11-year-old boys, for example, increasing from 54 to 67 kg over the 20-year period. (About 4% of the 158 11-year-old boys examined in 1993 had a BMI of more than 30 kg/m².) National US data over the same time period also indicate that there was a large increase in the positive skewness of the BMI distribution but little change at lower centiles (12).

BMI levels show an exponential relation to several coronary heart disease risk factors, and severely overweight children are more likely to remain obese in adulthood than moderately overweight children. It is therefore possible that future increases in obesity-associated morbidities will be greater than suggested by an analysis of mean BMI levels.

HEALTH CONSEQUENCES

Social Consequences

The stigmatization of obesity begins early in life (1,2), with obese children in the United States characterized as lazy and ugly by their peers. Although obese adolescents tend to have low self-esteem, eating disorders, and a preoccupation with weight, these associations vary greatly across social and ethnic groups. In addition, it is likely that these associations will be influenced by the recent increase in the number of overweight children.

Obesity is inversely associated with socioeconomic status among women in developed countries, and some evidence indicates that obesity may be a cause as well as a
FIG. 1. The top panel shows (lowess) smoothed levels of BMI by age among children in the Bogalusa Heart Study. The bottom panel shows a centile comparison plot for the BMI distributions in 1973 and 1993. The data have been adjusted for sex and age, and the distance above the diagonal line represents the secular increase in BMI at each centile.

consequence of social status. A 7-year follow-up of 16- to 24-year-olds, for example, found that, as compared with women who were of normal weight at baseline, overweight women completed fewer years of education, had lower family incomes, and were less likely to be married (15). These differences could not be explained by family income at baseline, the educational level of the parents, or aptitude test scores. Similar findings have also been observed among overweight girls who subsequently lost weight (16).
Associations between obesity and socioeconomic status in developing and transitional countries are likely to be complex. For example, the relation of income to the prevalence of overweight (BMI 27 kg/m²) in China is positive in rural areas but negative in cities (17).

**Persistence of Obesity**

Childhood levels of BMI are predictive of levels in later life, and it has been estimated that around 40% of overweight children will be obese in adulthood (positive predictive value), whereas 15% to 20% of obese adults had been overweight as children (sensitivity) (1,2,4). These estimates, however, have varied markedly across studies, and a wide range of predictive values (26% to 63%) and sensitivities (5% to 44%) has been reported (18). Although these estimates might be expected to be influenced by the length of follow-up, childhood age, and demographic and social characteristics, they are also strongly influenced by the prevalence of obesity. This prevalence is, in turn, partly determined by the categorization of BMI levels.

The influence of these cutoff points can be seen in an analysis of 2,640 2- to 17-year-olds who participated in the Bogalusa Heart Study and who were subsequently reexamined after a mean follow-up of 17 years. Overall, 76% (143) of the 187 children whose BMI was above the 95th centile had an adult BMI ≥30 kg/m² (Table 1), and predictive values differed only slightly between boys (80%) and girls (73%). Of the 586 adults with a BMI ≥30 kg/m², 24% (sensitivity) had a childhood BMI 95th centile. It is likely that the high predictive value of childhood obesity in this cohort reflected, at least in part, the secular increase in adult obesity during the follow-up period. Of the children with a BMI ≥95th centile, one-fourth had an adult BMI 40 kg/m², emphasizing the potential consequences of recent secular trends.

These estimates, however, are markedly influenced by the categorization of BMI levels (Table 1). The positive predictive value increased with the childhood BMI cutoff point but decreased with the adult BMI cutoff point, ranging from 53% (childhood BMI ≥75th centile and adult BMI ≥30 kg/m²) to 100%. Sensitivity showed the opposite relation to the cutoff points, ranging from 3% (adults with a BMI ≥25 kg/m² who had a childhood BMI ≥99th centile) to 60%. Relative risks increased with the adult BMI cutoff but varied only slightly across childhood cutoffs. The variability of these estimates can make it difficult to compare the results of studies using different BMI cutoff points.

Simple correlation coefficients, which do not depend upon the categorization of BMI levels, provide a measure of BMI tracking that can be more easily compared across studies. Figure 2 shows the association (Spearman r = 0.61) between childhood and adult BMI levels among the 2,640 persons. The magnitude of this association varied only slightly (0.57 to 0.65) across race/sex groups but was weaker for children less than 7 years of age than among older children (r = 0.50 versus 0.64). In addition, the strength of the association was inversely associated with the length of follow-up, ranging from r = 0.76 (less than 10 years of follow-up) to r = 0.59 (20 years). In contrast, the tracking of BMI levels among children in China appears to be
substantially lower, with a correlation of 0.39 over a 6-year period among 6- to 13-year-olds (19).

Although childhood obesity is the strongest correlate of adult obesity, with multiple \( r^2 \) values (after accounting for race, sex, and age) of up to 0.40, other predictors of adult BMI include parental fatness, birth weight, the timing of sexual maturation, socioeconomic status, and physical activity (20). Children with an early adiposity rebound are also at increased risk of adult obesity, but it is possible that similar information can be obtained more easily from the BMI level at 7 years of age (21). Other anthropometric dimensions in childhood, such as height or triceps skinfold thickness, may also improve the prediction of adult BMI, and many of these characteristics can probably be examined in existing datasets.

**Type 2 Diabetes Mellitus**

In addition to the severity of obesity, the duration of obesity is an independent predictor of type 2 diabetes mellitus among adults (7). At similar levels of obesity, the

<table>
<thead>
<tr>
<th>Childhood BMI</th>
<th>( \geq 25 \text{ kg/m}^2 )</th>
<th>( \geq 30 \text{ kg/m}^2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \geq 75 \text{ C} (N = 670) )</td>
<td>83% (555)</td>
<td>53% (354)</td>
</tr>
<tr>
<td>( \geq 85 \text{ C} (N = 443) )</td>
<td>88% (392)</td>
<td>62% (274)</td>
</tr>
<tr>
<td>( \geq 95 \text{ C} (N = 187) )</td>
<td>94% (175)</td>
<td>76% (143)</td>
</tr>
<tr>
<td>( \geq 99 \text{ C} (N = 32) )</td>
<td>100% (32)</td>
<td>91% (29)</td>
</tr>
</tbody>
</table>

**TABLE 1. Positive predictive values, sensitivities, and relative risks using different BMI cutoff points: the Bogalusa Heart Study**

<table>
<thead>
<tr>
<th>Childhood BMI</th>
<th>Positive predictive value( ^a )</th>
<th>Sensitivity( ^b )</th>
<th>Relative risk( ^c )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \geq 75 \text{ C} (N = 670) )</td>
<td>44%</td>
<td>60%</td>
<td></td>
</tr>
<tr>
<td>( \geq 85 \text{ C} (N = 443) )</td>
<td>31%</td>
<td>47%</td>
<td></td>
</tr>
<tr>
<td>( \geq 95 \text{ C} (N = 187) )</td>
<td>14%</td>
<td>24%</td>
<td></td>
</tr>
<tr>
<td>( \geq 99 \text{ C} (N = 32) )</td>
<td>3%</td>
<td>5%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Childhood BMI</th>
<th>Positive predictive value( ^a )</th>
<th>Sensitivity( ^b )</th>
<th>Relative risk( ^c )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \geq 75 \text{ C} (N = 670) )</td>
<td>2.3</td>
<td>4.5</td>
<td></td>
</tr>
<tr>
<td>( \geq 85 \text{ C} (N = 443) )</td>
<td>2.2</td>
<td>4.4</td>
<td></td>
</tr>
<tr>
<td>( \geq 95 \text{ C} (N = 187) )</td>
<td>2.1</td>
<td>4.2</td>
<td></td>
</tr>
<tr>
<td>( \geq 99 \text{ C} (N = 32) )</td>
<td>2.1</td>
<td>4.2</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: C, centile.

\( ^a \) The proportion of children who became overweight/obese adults; the number of true positives is shown in parentheses. For example, 555 of the 670 children with a BMI > 75th centile had an adult BMI \( \geq 25 \text{ kg/m}^2 \), yielding a positive predictive value of 83%.

\( ^b \) The proportion of overweight/obese adults whose childhood BMI was above the specified centile. Of the 1,266 adults who had a BMI \( \geq 25 \text{ kg/m}^2 \), 44% had a childhood BMI > 75th centile.

\( ^c \) The probability that a child with a BMI above the specified centile will be overweight/obese in adulthood as compared with that for a child with a lower BMI level.
FIG. 2. The relation of childhood BMI centiles (x axis) to adult BMI levels over a (mean) 17-year follow-up period among 2,640 participants in the Bogalusa Heart Study. The smoothed line was constructed using the loess procedure, with levels roughly corresponding to median BMI levels in adulthood. The horizontal line indicates the cutoff point for obesity in adulthood.

diabetes risk among Pima Indian adults is about twice as high among those who had been obese for more than 10 years than among those who had recently become obese (22). Associations with the duration of obesity have also been observed in other ethnic groups (23) and among 15- to 24-year-olds (22). The recent trends in childhood obesity will prolong its duration and probably increase the incidence of type 2 diabetes among adults.

The prevalence of type 2 diabetes among adults in the United States increased by around 40% during the 1980s (24), and an increase in incidence has also been noted. Despite the lack of national data among children, the prevalence of pediatric type 2 diabetes (estimated to be around 0.2%) also appears to be increasing (25,26). The prevalence among American Indian adolescents, for example, increased by around 50% during the 1980s (26), and comparable increases in incidence have been observed among schoolchildren in Tokyo (27). Clinic-based studies support these trends, with the annual number of newly diagnosed cases of type 2 diabetes among adolescents increasing from 2 to 20 (0.7 to 7.2 per 100,000) between 1982 and 1994 in the Cincinnati area (28).

Obesity is very common among newly diagnosed cases of pediatric type 2 diabetes, with mean BMI values ranging from 29 to 38 kg/m² in several studies (25), and the high prevalence of diabetes among American Indians, African Americans, and Hispanics may reflect their high rates of obesity. The potential effect of the recent obesity trends is highlighted by a study of Pima Indian adolescents in which a combination of birth weight, weight in childhood, and exposure to diabetes in utero accounted for most of the increase in type 2 diabetes since the 1960s (25). Secular increases in
type 2 diabetes among schoolchildren in Tokyo have also been accompanied by increases in obesity (27). As the relation of obesity to type 2 diabetes risk among adults is exponential rather than linear, the increased prevalence of very overweight children is of great concern.

Although there are no long-term studies of children with type 2 diabetes, newly diagnosed cases often have microalbuminuria and hypertension, along with raised levels of insulin, C-peptide, and triglycerides (25,26). If the duration of hyperglycemia and hyperinsulinemia is the primary factor in the development of adverse health outcomes, the development of diabetes in early life will probably result in complications at young ages. Poor glycemic control among those with type 2 diabetes (as in type 1 [29]) is predictive of early retinopathy, nephropathy, and vascular disease (6), and high complication rates have been observed in the short-term follow-up of children and young adults with type 2 diabetes (6,25). The poor compliance of adolescents with lifestyle modifications and medical treatment is likely to exacerbate these complications.

A better understanding of the natural history of pediatric type 2 diabetes will become increasingly important, as will assessment of the efficacy of various treatments. The possible interaction of childhood obesity with fetal undernutrition (30) in the development of type 2 diabetes should also be explored.

Atherosclerosis

Risk Factors in Childhood

Obesity among children is associated with adverse levels of several coronary heart disease risk factors, the magnitude of the correlations being typically stronger for levels of C-reactive protein, triglycerides, HDL cholesterol, blood pressure, and insulin (\(r \sim 0.15\) to 0.30) than for levels of total and LDL cholesterol. Adverse levels of these risk factors are associated with the early stages of atherosclerosis (31) and tend to track into adulthood, but serial correlations are weaker than those for BMI.

Several aspects of the associations with coronary heart disease risk factors should be considered. Many of the relations are nonlinear, with risk factor levels often increasing only at BMI levels above the 75th centile. Furthermore, although most overweight children do not have a specific coronary heart disease risk factor, such as a high plasma triglyceride concentration, most have adverse levels of at least one risk factor (32). Furthermore, children with multiple risk factors may be at particularly high risk for the early stages of atherosclerosis (31), and about three-quarters of these children are overweight.

The standard chemical analysis of lipid levels also may have resulted in underestimating the importance of childhood obesity in dyslipidemia. The major lipoprotein classes—very low density (VLDL), LDL, and HDL—are heterogeneous, with coronary heart disease risk varying by the size of the lipoprotein subclass. The risk is increased by high levels of small LDL and small HDL particles, in contrast to the protective effect of the typically measured HDL cholesterol level, and varies according to the size of VLDL particles (33). Although the relation of lipoprotein
subclass levels in childhood to atherosclerosis has not been studied, subclass levels are associated with insulin levels and obesity in childhood.

The relation of BMI and waist circumference to various lipoprotein subclasses among 916 adolescents, determined by nuclear magnetic resonance (NMR) spectroscopy (33), is shown in Table 2. Associations with childhood BMI centiles and waist circumference measurements were generally similar in magnitude, but there were large differences within each lipoprotein class. For example, BMI was related to levels of HDL cholesterol \( (r = 0.34) \), but the inverse association with large HDL was stronger \( (r = 0.50) \) and there was a positive association \( (r = 0.13) \) with levels of small HDL. BMI also showed differing associations with levels of large and small LDL (negative and positive, respectively), and was not associated with levels of small VLDL.

The relation of obesity to various risk factors also varies by race/ethnicity. For example, childhood BMI in the Bogalusa Heart Study is more strongly related to triglyceride levels among whites than among blacks (Fig. 3). Whereas levels of triglyceride among white children differed by about 40 to 60 mg/dl (0.45 to 0.67 mmol/l) across BMI centiles, differences of around 10 mg/dl (0.11 mmol/l) were seen among black girls. Furthermore, overweight black children tended to have triglyceride levels that were similar to those seen among thin white children, a finding that may reflect differences in the activity of lipoprotein lipase. These racial differences, which are also present among young adults, may partly account for the weak relation of obesity to coronary heart disease that has often been seen among black adults.

### TABLE 2. Relation of body mass index (BMI) and waist circumference to levels of lipids and lipoprotein subclasses among 916 10- to 17-year-olds: the Bogalusa Heart Study

<table>
<thead>
<tr>
<th>Lipid/Subclass</th>
<th>BMI centile</th>
<th>Waist circumference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td>0.16</td>
<td>0.14</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>0.33</td>
<td>0.35</td>
</tr>
<tr>
<td>Large VLDL</td>
<td>0.30</td>
<td>0.32</td>
</tr>
<tr>
<td>Small VLDL</td>
<td>0.02</td>
<td>0.03</td>
</tr>
<tr>
<td>VLDL size(^a)</td>
<td>0.24</td>
<td>0.25</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>0.23</td>
<td>0.22</td>
</tr>
<tr>
<td>Large LDL</td>
<td>-0.12</td>
<td>-0.13</td>
</tr>
<tr>
<td>Small LDL</td>
<td>0.15</td>
<td>0.13</td>
</tr>
<tr>
<td>LDL size(^b)</td>
<td>-0.28</td>
<td>-0.28</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>-0.34</td>
<td>-0.39</td>
</tr>
<tr>
<td>Large HDL</td>
<td>-0.50</td>
<td>-0.53</td>
</tr>
<tr>
<td>Small HDL</td>
<td>0.13</td>
<td>0.14</td>
</tr>
<tr>
<td>HDL size(^b)</td>
<td>-0.53</td>
<td>-0.55</td>
</tr>
</tbody>
</table>

**Abbreviations:** HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very-low-density lipoprotein.

\(^a\) Values are Spearman correlations that have been adjusted for race, sex, and age. With a sample size of 916, a correlation of 0.08 is statistically significant at the 0.01 level.

\(^b\) The lipoprotein particle sizes, which represent the mass weighted average size of the VLDL, LDL, or HDL particles, are in nanometers. All other lipid measurements are concentrations.
FIG. 3. The relation of childhood BMI centiles to triglyceride levels among children in the Bogalusa Heart Study. Lowest curves were constructed separately for each race/sex group. Black children are shown with black lines, white children with gray lines, boys with solid lines, and girls with dashed lines.

Risk Factors in Adulthood

Obese children have also been found to have adverse levels of lipids, insulin, and blood pressure in adulthood. However, because of the strong tracking of BMI, these associations may reflect the importance of adult rather than childhood weight status. If the development of obesity at specific ages in childhood or adolescence were found to have an independent effect on adult risk factor levels, preventive efforts could focus on these age groups.

These associations were studied among 2,609 people who were initially examined between the ages of 2 and 17 years in the Bogalusa Heart Study and who were followed for an average of 17 years. Childhood BMI was related to adult risk factor levels, with the magnitudes of the correlations ranging from $r = 0.08$ (systolic blood pressure) to $r = 0.26$ (insulin). Mean levels of the examined risk factors in adulthood also differed among those who had a childhood BMI above the 95th centile and those whose childhood BMI was less than the 50th centile, with a 7 mg/dl (0.18 mmol/l) difference seen for levels of HDL cholesterol (Table 3). Within categories of adult BMI (<25 kg/m² and 30 kg/m²), however, risk-factor levels varied only slightly according to childhood weight status. (See the last four columns of Table 3.) Mean concentrations of HDL cholesterol among normal-weight adults, for example, were 54 mg/dl (1.40 mmol/l) for childhood BMI < 50th centile, and 55 mg/dl (1.42 mmol/l) for childhood BMI ≥95th centile, and the mean level was 42 mg/dl (1.09 mmol/l) among both subgroups of obese adults. Additional analyses (data not shown) revealed that adult risk factor levels were not influenced by the age of obesity onset (childhood, adolescence, or adulthood).
Table 3. Mean risk factor levels in adulthood by categories of adult body mass index (BMI) and childhood BMI centile (C): the Bogalusa Heart Study

<table>
<thead>
<tr>
<th></th>
<th>&lt;25 kg/m²</th>
<th>&gt;30 kg/m²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;50th C</td>
<td>95th C</td>
</tr>
<tr>
<td>N</td>
<td>1,317</td>
<td>186</td>
</tr>
<tr>
<td>Childhood BMI centile</td>
<td>24</td>
<td>97</td>
</tr>
<tr>
<td>Age (years)</td>
<td>27</td>
<td>27</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.5a</td>
<td>34.9a</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)b</td>
<td>82a</td>
<td>108a</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dl)</td>
<td>112a</td>
<td>121a</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dl)</td>
<td>52a</td>
<td>45a</td>
</tr>
<tr>
<td>Insulin (mU/L)</td>
<td>8a</td>
<td>14a</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>112a</td>
<td>117a</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>72a</td>
<td>76a</td>
</tr>
</tbody>
</table>

Abbreviations: DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure.

*p < 0.05 for difference in adult levels between persons whose childhood BMI P was < 50th centile or ≥ 95th centile.

It should be realized, however, that these results apply to risk factor levels, and childhood obesity may have a long-term cumulative effect on the development of atherosclerosis. The duration of hypercholesterolemia, for example, is strongly correlated with the extent of coronary artery calcification (34), and the duration of obesity may have a similar influence.

Assessment of Atherosclerosis

The initial stages of atherosclerosis begin in the aorta by the age of 3 years, and appear 5 to 10 years later in the coronary arteries, with some of these fatty streaks progressing to more advanced atherosclerotic lesions. Pathology studies of children and young adults who died from external causes indicate that obesity plays a role in the development of these lesions. Among decedents (ages 2 to 39 years) who had participated in the Bogalusa Heart Study (31), previously measured BMI was associated (r = 0.24 to 0.41) with both fatty streaks and fibrous plaques. Interestingly, associations with BMI were comparable in magnitude to those with LDL cholesterol levels and were stronger than those with diastolic blood pressure and HDL cholesterol. Another study (35) of young adults (ages 15 to 34 years) found that BMI at death was associated with raised lesions in the coronary arteries among men, but not women.

The role of obesity has also been assessed using noninvasive techniques, such as B-mode ultrasonography and electron beam tomography (EBT), that provide information on the extent of atherosclerosis in the carotid and coronary arteries, respectively (36). Among 384 young adults (mean age 33 years) who had been examined in
the Muscatine Heart Study (37), childhood BMI and triceps skinfold thickness were more predictive of EBT-determined coronary artery calcification than were levels of lipids and blood pressure. Somewhat similar associations have also been seen in cross-sectional studies of 28- to 40-year-olds (38), and hypercholesterolemic 11- to 23-year-olds (39).

Associations with intima–media thickness, an early atherosclerotic change that is typically assessed in the carotid artery with B-mode ultrasonography, have been less consistent. Some investigators have found BMI levels to be associated with intima–media thickness among children (40) and young adults (41), the magnitude of the correlations being at least as strong as those with lipid levels. However, negative results have also been reported, and the strength of the association varies according to the site at which intima–media thickness is assessed (40).

Despite concerns about disease classification, reproducibility, and specificity (36), these noninvasive techniques would allow serial estimates of the extent of atherosclerosis to be made in representative cohorts of children. These studies could greatly advance the understanding of the risks associated with childhood obesity and other risk factors. Longitudinal analyses would be able to assess whether the effect of childhood BMI (and body fat distribution) is independent of adult BMI and whether specific ages are critical for the development of obesity.

Adult Morbidity and Mortality

Background

The relation of childhood obesity to adult mortality and morbidity has been examined in several cohort studies (42–48) that have varied in design. Whereas some children have been followed prospectively (46,48), most investigators have identified cohorts in adulthood who had baseline (historical) data previously collected by elementary schools (43,47), by colleges (42), or in preparation for military service (44,45). In addition, some studies of adults (49–51) have been able to examine the relation of BMI at 18 years of age, based on self-reported weight, to morbidity and mortality.

Participation rates in these studies have varied substantially, with around 50% of eligible subjects in some studies not being traced or reexamined (43,47). These substantial losses to follow-up, which are not unexpected over periods of several decades, could greatly increase the potential for bias. The results of the historical cohort studies, along with those that used self-reported weight at age 18 years, could also be biased if childhood obesity was related to premature mortality that occurred before the formation of the adult cohort.

Other differences among these studies include, first, the classification of normal weight and overweight (typically, the upper fourth or fifth of the BMI distribution, or a value of more than 25 kg/m^2); second, sample sizes that range from 508 (46) to more than 78,000 (45); and third, mean baseline ages that ranged from approximately 8 years (48) to 19 years (42). In addition, few of these studies have information on BMI levels in both childhood and adulthood, precluding the assessment of an independent effect of childhood BMI on adult disease. Furthermore, in the studies with
information on BMI in both adulthood and childhood (43,46) (or at age 18 years [49–51]), one BMI value was always based on self-reported weight.

**Effects of Childhood Obesity**

Despite the numerous differences in study design, overweight children have consistently been found to be at increased risk of premature mortality, with relative risks (RR) generally ranging from 1.3 to 2.0. This increased mortality is largely attributable to coronary heart disease (RR 1.7 to 2.5). Childhood obesity has also been found to increase the risk for diabetes mellitus, colon cancer, menstrual problems, gestational hypertension, gout, arthritis, and hip fractures in adulthood (2,4). Although information on potential confounders has varied across studies, associations with childhood BMI do not appear to reflect the effects of various socioeconomic characteristics (including number of siblings, education, and social class) (45,48,51), cigarette smoking (46,51), or general health status (45).

The consistency of the findings for the relation of childhood obesity to coronary heart disease and total mortality contrasts with the sometimes weak (or null) results of studies of modest overweight among adults. These differences may be attributable, in part, to the long follow-up periods in studies of childhood obesity, as well as to the lack of confounding by preclinical disease and cigarette smoking. In addition, the relation of adult obesity to mortality, typically assessed with relative risks or rate ratios, is stronger among young adults than among older persons (52), and this interaction with age may extend into adolescence.

However, some differences among these findings should be considered. The effects of modest obesity among adults have often been seen only after a long follow-up, and one study (45) found overweight adolescents to be at increased risk only after the age of 40 years. Other investigators, in contrast, have found the risk among overweight 18- to 19-year-olds to be raised after 5 years of follow-up (44) or highest before 45 years of age (42). It has been suggested that overweight in adolescence is more strongly related to adult disease among boys than to that among girls (46), but the opposite has been found as well (47). It is also possible that associations are J shaped (45,48), with the lowest risks occurring at a childhood BMI between the 25th and 49th percentiles (48). The possibility that the effects of childhood obesity may be limited to specific subgroups, such as those who are relatively tall (42) or sedentary, has received little attention.

It should be realized that the typical categorization of childhood BMI levels has resulted in very high BMI levels (e.g., 31 kg/m² at age 18 years) being assessed in only one study (44). Studies of the relatively low BMI levels seen among children in the 1920s to 1940s may underestimate the risks associated with the higher BMI levels that are currently seen among children.

**Is The Relation Independent of Adult Obesity?**

Because of the persistence of weight status throughout life, with overweight children likely to be obese adults, the observed associations could reflect the importance of adult
weight status. Although most studies do not have information on BMI levels in both childhood and adulthood, and have therefore been unable to disentangle their effects, results of the Harvard growth study support an independent effect of childhood obesity. Over 55 years of follow-up, multivariable adjustment for adult BMI only slightly reduced the relation of adolescent overweight (BMI more than 75th centile) to mortality from all causes (RR of 2.9 [unadjusted] versus 2.4 [adjusted]) and from coronary heart disease (2.6 versus 1.9) among men (46). Although the adult BMI level was based on self-reported weight at age 53 years from only 61% of the study cohort, it was related to both disease risk and childhood BMI levels (Must A, personal communication).

In contrast to these findings, other results have emphasized the greater importance of adult weight status. For example, although overweight (>20% above average weight) children in Washington County (43) had high adult rates of vascular disease, a cross classification of child and adult weight categories indicated that the risks were highest for thin children who became overweight in adulthood. In addition, multivariable analyses in the Nurses’ Health Study indicated that the relation of BMI at age 18 years (based on self-reported weight) to diabetes mellitus (49) and coronary heart disease (50) was attributable to the persistence of obesity. With adjustment for adult BMI, RRs for the upper BMI category at age 18 years decreased from 6.1 to 0.8 (diabetes) and from 1.8 to 1.0 (coronary heart disease). The Harvard Growth Study (46) also found that the relation of adolescent overweight to diabetes in adulthood was mediated by adult weight status.

The possible effects of BMI misclassification in these results, owing to the use of self-reported weight at age 53 years (46) or at 18 years (49–51), should be considered. Although self-reports of previous weights are highly correlated with measured weights ($r > 0.75$), obese adults (particularly women) tend to underestimate earlier weight status by an average of 5 to 8 kg (53). This systemic underreporting by obese persons, along with any nondifferential misclassification, could reduce the strength of the association between BMI and disease. In these studies, the BMI that was calculated from measured weight—whether in childhood (46) or in adulthood (49,50)—has been found to be more strongly related to disease risk than the BMI estimated from self-reported weight.

**Weight Gain**

Adults with lifelong obesity may have a more favorable distribution of body fat than obese adults who had been normal-weight children (54), and some results suggest that weight gain after childhood is an important predictor of disease. Among overweight adults, those who had been thin in childhood have higher rates of hypertensive vascular disease (43) and diabetes mellitus (55) than those who had been overweight children. It is possible that weight gain after the cessation of growth, which would largely reflect accumulated fat mass, may be more pathologic than weight gain during growth and development (4).

Although it can be difficult to separate the effects of weight gain from attained weight status, other findings have also emphasized the importance of adult weight
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gain. In the Rancho Bernardo Study (55), the proportional change in weight from age 18 years was a strong predictor of type 2 diabetes. Diabetes risk has also been related to weight gain after puberty among overweight children (56), after age 18 years among women in the Nurses’ Health Study (49), and after age 30 to 35 years among Pima Indian men (57). Adult weight gain has also been related to the development of coronary heart disease (50,58), with each 10% increase in weight after age 20 years increasing the risk by 17% (58). Although it has also been reported that adult weight gain is not associated with total mortality (51), its effect on coronary heart disease risk may be largely mediated through an association with diabetes, and with levels of cholesterol, blood pressure, and physical activity.

It should be realized, however, that many of these findings are based on self-reported weight in childhood or at age 18 years (49,50,55,58), and a systematic under-reporting of previous weight by obese adults would spuriously increase the magnitudes of the observed associations. In contrast, the importance of weight gain would be underestimated if the confounding effects of cigarette smoking (including its cessation) are not adequately controlled (51,58).

SUMMARY

Overweight children are at increased risk for coronary heart disease and premature mortality in adulthood, and with the recent secular increase in childhood obesity, these long-term consequences will become increasingly evident. It is not certain, however, if these associations reflect the effect of childhood obesity itself, or the persistence of obesity throughout life, with adult weight status being the important factor. Because of the many difficulties involved in following cohorts of children for periods of over 50 years, it would be useful to examine these interrelations using noninvasive techniques, such as ultrasound or electron beam tomography, to quantify the extent of atherosclerosis.

Noninvasive techniques would also be very valuable in assessing the effects of weight gain in adulthood on subsequent coronary heart disease. These cross-sectional and short-term cohort studies would be particularly valuable if recorded information on childhood weights and heights were available. Analyses could then examine the independent effects of childhood and adult weight status, and assess whether the development of obesity at specific ages is particularly detrimental.

It is likely, however, that the first consequence of the recent trends in obesity will be an increase in the incidence of pediatric type 2 diabetes, and a better understanding of its natural history is needed. The difficulties in preventing and reversing obesity, along with the frequent nonadherence of adolescents to lifestyle changes and medical treatment, will complicate treatment and prevention efforts. However, as the long-term complications of diabetes are related to the duration of hyperglycemia, the implications of large numbers of children with type 2 diabetes will be substantial.

REFERENCES

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DISCUSSION

Dr. Dietz: In response to earlier questions about the predictive validity of the BMI, we can say that these data now represent the second dataset showing that a BMI above the 95th centile is of substantial predictive value for persistence of obesity, the other being the Whitaker dataset (1). With Dr. Freedman’s earlier paper on the association of cardiovascular disease risk factors with a BMI over the 95th centile—at least in the US population (2)—these data should allow us to argue that there is some clinical validity using these cutoff points.

Dr. Freedman: One thing to note, though, is that these are continuous variables and where exactly to make the cutoff point can be debated. If the cutoff point was the 94th or the 96th centile, much the same associations will be seen. So although it is true that there is a strong association between childhood obesity and adult obesity, it is not exactly clear where to make the cutoff.

Dr. Endres: You described “pediatric diabetes” starting in the third decade. Isn’t that rather out of the frame of pediatrics?

Dr. Freedman: I did show a slide of the development of diabetes before the age of 30, but I used that because there are no cohort studies of pediatric type 2 diabetes. When I was referring to “pediatric” type 2 diabetes, I really meant before the age of 18. Some of the secular trends referred to in the Pima Indians involve 10- to 19-year-olds, and I think that would be accepted as pediatric type 2 diabetes.

Dr. Dulloo: On the issue of ethnicity and the relation of BMI to percentage body fat, I have a question about the Mauritian data, as I originally came from Mauritius. The data you presented from the Dowse study (3,4) were in Mauritian Chinese, in whom for a particular BMI the prevalence of diabetes was increased. However, I’m sure the investigators must also have obtained data from Indian Mauritians, who are also classified as Asians, and from the Africans who inhabit the island. How do they compare with the ethnic Chinese?

Dr. Freedman: In a study by Deurenberg (5) I think the Chinese in Mauritius came fairly close to the median for the Asian populations. Although I hate to admit it, the situation is much more complicated than I presented. For example, different results are found among Chinese in Singapore versus Chinese in Beijing in terms of the relation of BMI to percent body fat. With regard to BMI and diabetes in Mauritian Indians and Africans, I’m afraid I do not recall the findings of the Dowse study.

Dr. Gortmaker: It’s a small point, but you say that the data from the nurses’ and health professionals’ studies imply there is no independent effect of obesity in adolescence on the onset
of diabetes in adulthood. However, if obesity in adolescence is seen as a cause of obesity in adulthood, then you could say that there is this very strong indirect pathway whereby adolescent obesity does in fact cause diabetes in adult life. At least that’s the way I interpret it. Can you comment?

Dr. Freedman: That’s true. The question is whether you consider it to be a confounding factor or an intervening factor. If childhood obesity is a cause of adult obesity, which it is, then there is an effect of childhood obesity on adult diabetes, but it’s mediated through its association with adult obesity. One can interpret the data, at least in the Nurses’ Health Study, to imply that a nonoverweight child who becomes an obese adult will have the same risk of developing diabetes in adulthood as a person who had been obese for their entire life.

Dr. Dulloo: I would like to return to one of your graphs illustrating the tracking of obesity, where you had adult BMI versus childhood BMI. There was a large scatter and a very slow rising curve between the 5th and the 75th centiles, which only became exponential between the 75th and the 95th centiles. Your overall r value was 0.6. If you were to eliminate that last bit of the graph between the 75th and 95th centiles, would you still see a correlation?

Dr. Freedman: One should be very careful about interpreting graphs showing BMI centiles. They can be very useful because you don’t have to worry about controlling for age and sex in the analysis, but in terms of centiles, a change from, say, the 90th to the 95th centile represents a large change in BMI units, whereas a different 5 percent change, say from the 50th to the 55th centile, represents only a very small change in BMI units. If you were to apply BMI in childhood versus BMI in adulthood and at the same time control for age and sex, you would find it much more linear than on that chart.

Dr. Dulloo: But if we just look at the centiles between 0 and 75, I won’t expect any relation between childhood and adult BMI.

Dr. Freedman: To some extent, that is true, but the reason for it is that the change going from the 75th centile of BMI up to the 100th centile is probably much larger than the change going from zero to the 75th centile in terms of actual BMI units. That’s in large part the reason for the curvilinearity and why the relation would be much weaker if you were to eliminate the upper 25 percent. But you are right in terms of that chart—the association would be much weaker if you eliminated the top 5 or 10 percent of BMI.

Dr. Cole: The point that you are just making is that it would actually be better to work on a scale of BMI z score rather than BMI centiles. If you used BMI z score as your x axis on that graph, you would avoid the problem of squashing together the high centiles and the low centiles, and you would be working on a scale that is closer to BMI itself.

Dr. Freeman: Thank you. Other people have suggested that to me, and I looked at that. Surprisingly, it was almost exactly the same—it was curvilinear in the same way as the BMI centiles.

Dr. Cole: I’m glad it was the same, but as a general point it is not a good idea to do calculations on the centile scale because it is nonlinear and bounded at the upper and lower ends, unlike the z score scale.

Dr. Endres: I know you tried to simplify your analysis of the relation between obesity and disease in later adulthood by limiting the amount of data, but do you have information on correlations between obesity in childhood and other factors related to cardiovascular disease, such as cholesterol, uric acid, or homocysteine? Are such data worthless?

Dr. Freedman: No, they are not worthless at all. There are many strong associations with risk factors for coronary heart disease such as HDL cholesterol, LDL cholesterol and so on, and these have been reported in many cross-sectional studies. What I think is the most interesting now is that people are measuring lipoprotein subclasses, and sometimes there are
different associations within each subclass (6,7). For example, childhood obesity is related to the small, dense LDL, but there is really no association with the larger LDL particles. There are some differences as well in the HDL and VLDL subclasses. I should also mention that in these cross-sectional associations there are often ethnic differences in outcomes. For example, there appears to be a weaker association between childhood obesity and triglyceride levels among black children than among white children (8,9).

Dr. Jacob: Have you seen any consequences of childhood obesity on eating disorders in adults?

Dr. Freedman: I'm afraid I'm not familiar with that literature.

REFERENCES