Relation between visceral fat and disease risk in children and adolescents

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ABSTRACT This review examines whether the relations and metabolic parameters necessary for the development of syndrome X are present in children and whether the metabolic complications of obesity in children are explained by excess intraabdominal adipose tissue (IAAT), or visceral fat. Despite the limited use of imaging techniques in research studies, an increasing number of studies reported on IAAT and its relation to disease risk in children and adolescents. For this article we reviewed studies that documented the early accumulation of IAAT in children and adolescents and the factors that contribute to variation in the degree of IAAT accumulation. We also reviewed studies that showed the clinical relevance of IAAT in children and adolescents through significant relations with adverse health effects including dyslipidemia and glucose intolerance in obese and nonobese children and adolescents of different ethnic groups. Am J Clin Nutr 1999;70(suppl):149S–56S.

KEY WORDS Fat distribution, visceral fat, subcutaneous fat, intraabdominal adipose tissue, subcutaneous abdominal adipose tissue, diabetes, cardiovascular disease, heart disease, dyslipidemia, obesity, development, metabolic risk, disease risk, children, adolescents, ethnicity, syndrome X

INTRODUCTION

The prevalence of obesity among US children is ~22–30% (1, 2) and has increased at an accelerated rate in the past several years (2, 3). In addition, the prevalence of obesity is >30% in some pediatric populations (3, 4). Among schoolchildren in Birmingham, Alabama (4), the prevalence of obesity (defined as body weight >120% of ideal body weight) at age 10 y was 21% in white boys and girls, 26% in African American boys, and 38% in African American girls. Although the immediate health implications of childhood obesity have not been examined extensively, obesity in childhood is associated with obesity in adulthood (5, 6), which in turn is associated with increased morbidity (7), cardiovascular disease (CVD) (8), and type 2 diabetes (9).

Epidemiologic evidence supports the theory that the relation between obesity and disease risk begins early in life. For example, in young adults who died in accidents, fatty streaks in the coronary arteries and aorta that were found at autopsy were associated with blood lipid profile, blood pressure, and obesity status obtained at one or more points antemortem (10, 11). Additional longitudinal data from the Bogalusa Heart Study indicate that the occurrence of overweight, hypertension, and dyslipidemia in young adults (aged 19–32 y) was associated with these same risk factors in childhood. More recently, data from Children’s Hospital Medical Center in Cincinnati showed that the incidence of type 2 diabetes among adolescents increased 10-fold from 1982 to 1994 and virtually all diagnosed cases of type 2 diabetes occurred in obese individuals (12). These observations are likely to reflect national trends. The group with the highest prevalence of adolescent type 2 diabetes was African American females, a group that also showed an increase in obesity (assessed by body mass index) over the study period. Thus, the evidence indicates that obesity-related disease can begin in childhood and that risk factors for disease track, or remain at a similar level, with advancing age, growth, and development.

Adipose tissue stores are heterogeneous with respect to metabolic activity and relation to disease risk. In adults, intraabdominal adipose tissue (IAAT), or visceral fat (body fat located within the abdominal cavity around the visceral organs), has emerged as the clinically relevant type of body fat independent of total body fat (13, 14). The metabolic complications and adverse health effects of increased IAAT include insulin resistance, type 2 diabetes, dyslipidemia, and CVD (14–17). The relation between obesity and disease was noted as early as 100–200 BC by Sushruta and Ayurveda, who observed the relation between glycosuria, obesity, and lifestyle (18). In 1717, Morgagni noted the android fat pattern in the corpse of a woman (19) and in 1947, Vague described the metabolic risk of android obesity as compared with the protective nature of gynoid obesity (19). With the use of imaging techniques for direct measurement of IAAT (20), Kissebah et al (15), Després et al (16, 17), Björntorp (14), and Vague et al (19) reported in the 1980s and early 1990s that...
excess IAAT explains the relation between obesity and metabolic complications in adults.

The mechanism or mechanisms underlying the relations among obesity, IAAT, insulin action, and dyslipidemia are unknown. In 1988, Reaven (21) characterized the interrelations of insulin resistance, dyslipidemia, and hypertension as syndrome X; this description was later expanded to include excess IAAT (22). However, the specific effects of excess IAAT have not yet been identified and it is also unknown whether insulin resistance precedes and causes dyslipidemia or vice versa. It was postulated that because IAAT is more sensitive to lipolytic stimuli than is adipose tissue stored at other sites, turnover of triacylglycerols and release of fatty acids into the portal circulation are increased. Increased hepatic release of fatty acids leads to excess hepatic exposure to fatty acids, which may increase hepatic gluconeogenesis and secretion of LDLs and inhibit hepatic clearance of insulin, leading to hyperinsulinemia and peripheral insulin resistance (14). In prospective studies, fasting hyperinsulinemia was a risk factor for future metabolic abnormalities (23) and for ischemic heart disease in men, independent of altered lipid levels (24). On the other hand, some research suggested that inherent abnormalities in fat oxidation in the obese state cause changes in insulin sensitivity (25). According to the Randle hypothesis (26), an increase in fat oxidation reduces the need for glucose oxidation leading to reduced glucose uptake and insulin resistance. However, there is controversy concerning the existence of an inherent abnormality in fat oxidation in the obese state. Some studies support the theory that there is an alteration in fat oxidation due to obesity (27, 28) whereas others do not (29–31).

REVIEW OF THE LITERATURE

Measurement of intraabdominal adipose tissue

Because IAAT lies within the abdominal cavity it can only be directly quantified with imaging techniques. Both computed tomography (CT) and magnetic resonance imaging (MRI) have been used in children and adolescents for this purpose (32–35). With these approaches, adipose tissue is measured in terms of cross-sectional area (cm²) or volume (cm³). Because these techniques are expensive and CT involves radiation exposure, IAAT is often measured in a single, cross-sectional slice at an anatomic landmark, usually the level of the umbilicus or the L3–L4 disk space. The major advantages of these imaging techniques are the high resolution of the images and the capability to identify small deposits of IAAT. In addition, subcutaneous abdominal adipose tissue (SAAT) is also accurately quantified at the same time. Some investigators have used multiple-slice CT to measure adipose tissue in multiple slices of the abdominal area or across the whole body (36) to determine adipose tissue volume. There is some concern that a single slice of the abdomen may not reflect total IAAT content (37), and further studies in children and adolescents are needed to explore this issue. Indirect measures of IAAT include dual energy X-ray absorptiometry (DXA) to measure fat mass in the trunk region and anthropometric measures (circumferences and skinfold thicknesses). The relations between IAAT and these indirect measures are reviewed in greater detail later in this article.

Factors that influence intraabdominal adipose tissue

It is currently unclear whether the amount of IAAT accumulation seen in children is appropriate for their body size, and whether the observed extremes are related to extremes of general body fatness. For example, some studies suggest that IAAT in children increases in proportion to overall fatness (34) as measured in adults (38), whereas other studies showed that obese children tend to accumulate subcutaneous fat and not IAAT (33).

In healthy young children (aged 6.4 ± 1.2 y; 24.8 ± 5.4 kg), mean IAAT at the level of the umbilicus was 8.3 ± 5.8 cm² and mean SAAT was 65.3 ± 44.8 cm³ as measured by CT scanning (34). In 101 African American and white obese and nonobese children (aged 7.5 ± 1.7 y; 33.0 ± 12.2 kg body weight; 30 ± 11% body fat), IAAT averaged 30.0 ± 23.0 cm² and varied greatly from 6 to 102 cm² (35). SAAT averaged 101 ± 95 cm³ and also varied greatly (range: 8–372 cm³). When MRI was used in healthy 11- and 13-y-old girls, IAAT at the level of the umbilicus was 24.1 ± 4.1 and 25.7 ± 4.1 cm², respectively (39). In a study of 11-y-olds, IAAT was 17.8 ± 10.0 and 24.8 ± 8.8 cm² in boys and girls, respectively (33). These values in children and adolescents compare with typical values of 100–120 cm² of IAAT in healthy nonobese adults (38), although it is difficult to compare absolute amounts because of differences in body size.

Total fat mass is an important determinant of IAAT (38). It is currently unclear whether increasing adiposity in children and adolescents is related to increasing deposition of IAAT. Fox et al (33) found that differences in adiposity between obese and nonobese children are predominately found in SAAT; in obese as compared with control adolescents, the majority of excess abdominal adipose tissue was subcutaneous (353 ± 94 and 79 ± 61 cm², respectively), although IAAT was still greater in the obese than the control children (49 ± 21 and 22 ± 11 cm², respectively). It is clear that a portion of the variance in IAAT is explained by total fat mass, although interpretation of findings is complicated by strong multicollinearity among IAAT, SAAT, and total body fat (36). In 101 prepubertal children, the correlation between IAAT and total fat was 0.81 (36), similar to that seen in 206 adult women (40). However, the relation between IAAT and total body fat is not significant after adjusting for SAAT and there is no relation between IAAT and percentage body fat (35). Thus, the relation between IAAT and body fat may be explained by multicollinearity, and a major portion of the variance in IAAT is independent of total body fat.

Ethnicity is known to affect fat distribution. Results from previous studies that used anthropometric measures suggested that African Americans, Mexican Americans, and Mohawk Indians have more central fat than whites (41, 42). Because prior studies of ethnic differences in fat distribution have been limited to skinfold thickness data, it is not known whether the findings represent differences in SAAT or IAAT. More recent data based on direct measurement of IAAT in women (37) and prepubertal children (43, 35) suggest, however, that African Americans have less IAAT and that this is apparent early in life. However, the important issue in terms of health risk is whether ethnicity influences the strength or magnitude of the relations between IAAT and the subsequent development of disease risk factors as discussed later in this article.

The hormonal environment plays a key role in determining body fat distribution (44). Because sex hormones are known to affect regional fat deposition (45), the changing hormonal environment during puberty may contribute to the development of sex differences and large individual changes in fat distribution (32, 46). To date, no studies have used imaging to track or compare children at different stages of maturation and relate differences in
fat distribution to hormone concentrations. However, cross-sectional studies that used DXA showed that during growth, white girls store more fat in the trunk than girls of other ethnic backgrounds as adiposity increases (47). Also, when comparing girls of different Tanner pubertal stages (48), it was shown that puberty was associated with greater gains in fat than lean tissue and the accumulation of fat was greatest in the trunk region.

The earlier onset of puberty in the United States (49) implies that the development of an adult body-fat pattern will occur at an accelerated pace and that this in turn may lead to earlier onset of diseases of adulthood.

The influence of dietary factors on IAAT accumulation has not been extensively studied. One study of healthy, white, nonobese men examined the relations between CT measures of IAAT and SAAT and dietary factors (50). Fat intake explained only 2% of the variance in general adiposity after adjusting for fat-free mass, age, sex, physical activity, and intake of energy from nutrients other than fat. Dietary fat accounted for only 1.4% of the variance in SAAT (and this effect disappeared after adjusting for age, sex, and physical activity) and none of the variance in IAAT before or after adjustment (50). Thus, in agreement with other studies reviewed by Lissner and Heitmann (51), dietary fat appears to play a minor role in determining general adiposity and is not related to IAAT when measured in cross-sectional studies (50). We are not aware of any studies of the link between diet and regional adiposity in children and adolescents based on direct measures of IAAT.

Finally, physical activity is an important determinant of IAAT. In adults, physical inactivity is associated with elevated IAAT (13, 52, 53) and IAAT is selectively reduced after aerobic (54) and strength-training exercise (55). In adults, the effect of physical inactivity on CVD risk factors is mediated in part by the effects of inactivity on IAAT (56). To our knowledge, only 2 studies of children or adolescents examined the interrelations among physical activity, IAAT, and increased risk of disease by using sophisticated measurement techniques. In an intervention study in obese girls, strength training (3 times/wk for 5 mo) had no effect on IAAT despite significant increases in body weight, total body fat, and SAAT (57). In another study in 7–11-y-old obese children there was no significant change in IAAT but a significant loss of SAAT after a 4-mo aerobic training program, whereas there were significant increases in both IAAT and SAAT in a control group that received no exercise intervention (B Gutin, unpublished observations, 1998). Thus, both strength training and aerobic exercise appear to slow the time-related increase in IAAT in obese children.

Relation between IAAT and anthropometric indexes

CT and MRI are accurate imaging techniques for assessing body fat distribution, but their disadvantages are cost, radiation exposure (for CT), and limited availability outside of research settings. Thus, based on the relation between IAAT and anthropometric measures, other indirect indicators of body fat distribution were used. For example, in adults the waist-to-hip ratio and waist circumference are often used as markers of IAAT (58, 59). However, in children (34) and adolescents (33, 39) the correlation between these markers and IAAT as measured by imaging techniques is not strong. To identify an accurate alternative index, it is important to study the relations between IAAT and both anthropometry and body composition.

In young children (34) waist-to-hip ratio is not significantly correlated with IAAT, whereas individual trunk skinfold thicknesses and the ratio of trunk-to-extremity skinfold thicknesses explain 62% of the variation in IAAT. In adolescent girls, there were no significant correlations between IAAT area as measured by MRI and either waist circumference, waist-to-hip ratio, or trunk-to-extremity skinfold thickness ratio (39). Similarly, in 11-y-old boys and girls, waist-to-hip ratio was not significantly correlated with IAAT (33). In these studies of adolescents, anthropometric indexes explained only 25–50% of the variation in IAAT (33, 39).

In 101 prepubertal white and African American children the strongest anthropometric correlates of IAAT were abdominal skinfold thickness (r = 0.88), subscapular skinfold thickness (r = 0.85), suprailiac skinfold thickness (r = 0.85), and waist circumference (r = 0.84); the strongest correlates of SAAT were waist circumference (r = 0.93), triceps skinfold thickness (r = 0.92), abdominal skinfold thickness (r = 0.91), suprailiac skinfold thickness (r = 0.91), and axillary skinfold thickness (r = 0.84) (36). There were much lower correlations between IAAT or SAAT and the traditional indexes of central fat distribution, such as trunk-to-extremity skinfold thickness ratio (r = 0.49 for IAAT; r = 0.50 for SAAT) and waist-to-hip ratio (r = 0.32 for IAAT; r = 0.40 for SAAT). In forward multiple regression analysis, abdominal skinfold thickness, ethnicity, and subscapular skinfold thickness explained 82% of the variance in IAAT whereas waist circumference, subscapular skinfold thickness, height, and abdominal skinfold thickness explained 92% of the variance in SAAT. Based on this information, prediction equations were developed that estimated accurately IAAT and SAAT as measured by CT in an independent sample of 12 children (36).

DXA measurements of total abdominal fat do not distinguish SAAT from IAAT. IAAT has been estimated in adults with reasonable accuracy by combining measures of total abdominal fat by DXA with skinfold thickness and anthropometric data (as an index of subcutaneous fat) (40, 60). In 101 prepubertal children, the combination of trunk and total fat by DXA and abdominal skinfold thickness predicted IAAT as measured with CT scanning (model R², 0.85; SEE, ±9 cm²) (36). However, this approach only marginally improved the prediction power of the anthropometric equation that included abdominal skinfold thickness, ethnicity (white compared with African American), and subscapular skinfold thickness (model R², 0.82; SEE, ±6 cm²).

Thus, combinations of skinfold thicknesses and circumferences can be modeled to yield relatively accurate estimates of IAAT and SAAT in the absence of direct measurement by imaging techniques. The addition of regional measures of trunk fat by DXA only marginally improves the prediction of IAAT.

Regional adiposity and insulin action in children and adolescents

In general, obesity in children and adolescents is related to differences in insulin action. Although relatively few studies have examined fat distribution in children, epidemiologic data from the Bogalusa Heart Study provide evidence of a link between central body fat (measured by skinfold thicknesses) and fasting insulin level (61). Research with predominantly obese white adolescents indicated that IAAT is associated with both insulin secretion and insulin sensitivity. Among 21 obese children and adolescents (62), IAAT assessed with MRI (t ± SD: 49 ± 21 cm²) tended to be associated with insulin area-under-the-curve (AUC) during an oral glucose tolerance test (OGTT) (t = 0.44, P = 0.07). In contrast, SAAT was not associated with insulin AUC (t = 0.04, P = 0.88). Neither index of central adiposity
TABLE 1
Summary of studies that examined relations between adiposity and metabolic risk factors by using direct measures of IAA T and SA A T in children and adolescents

<table>
<thead>
<tr>
<th>Study</th>
<th>Subject characteristics</th>
<th>Major findings</th>
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<tbody>
<tr>
<td>Brambilla et al (62)^2,3</td>
<td>21 white obese children and adolescents (aged 10–15 y)</td>
<td>IAA T but not SA A T was associated with insulin AUC (P = 0.07); IAA T and SA A T were not correlated with fasting insulin concentration, and IAA T but not SA A T was related to blood lipid concentrations.</td>
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<tr>
<td>Caprio et al (63, 67)^2,4</td>
<td>13 obese and 9 nonobese adolescent girls</td>
<td>In obese subjects, IAA T correlated with fasting insulin concentration, insulin secretion, and insulin sensitivity; IAA T was related to triacylglycerol (+) and HDL cholesterol (−) concentrations; and SA A T was related to LDL cholesterol concentration (−). In nonobese subjects, IAA T was not related to any index of insulin action and SA A T was related to insulin-stimulated glucose metabolism.</td>
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<tr>
<td>Yanovski et al (43)^2,5,5</td>
<td>40 normal-weight white and African American 7–10-y-old girls</td>
<td>In African Americans, SA A T but not IAA T was related to basal and 2-h insulin concentrations. In whites, SA A T and IAA T were not related to insulin action.</td>
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<tr>
<td>Gower et al (64)^1,3,6</td>
<td>74 obese and nonobese white and African American prepubertal boys and girls</td>
<td>IAA T, SA A T, and total fat were all correlated with all parameters of insulin action; total fat was related to fasting insulin concentration independent of IAA T and SA A T; SA A T was related to insulin AUC independent of total fat and IAA T; and IAA T was related to 30-min insulin concentration independent of SA A T and total fat (only in whites). Ethnicity effects: Fasting and 30-min insulin concentrations and insulin AUC were higher in African Americans independent of any adiposity index.</td>
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1 IAA T, intraabdominal adipose tissue; SA A T, subcutaneous abdominal adipose tissue; MRI, magnetic resonance imaging; CT, computed tomography; DXA, dual energy X-ray absorptiometry; OGTT, oral glucose tolerance test; AUC, area-under-the-curve.

2–6 Study methods included measurement of: ^1 IAA T and SA A T by MRI, ^2insulin action by OGTT, ^3insulin action by hyperglycemic and euglycemic clamps, ^4total fat by DXA, and ^5IA A T and SA A T by CT.

was associated with fasting insulin. Among 13 obese adolescents, IAA T assessed with MRI (± SEM for total volume = 160 ± 16 cm³), but not SA A T, was highly and significantly correlated with fasting insulin (r = 0.89), stimulated insulin secretion (r = 0.61), and insulin sensitivity as assessed with a euglycemic clamp (r = −0.63) (63). Nonobese adolescents in this study (n = 9) showed no association between IAA T volume and indexes of glucose metabolism. However, among nonobese adolescents, SA A T was significantly correlated with insulin-stimulated glucose metabolism (r = −0.60). These data suggest that the contribution of IAA T and SA A T to the metabolic profile may differ in lean compared with obese children.

In a heterogeneous sample of 74 obese and nonobese, prepubertal, white and African American children (aged 5–10 y; 11–47% body fat; 7.0–114.4 cm² IAA T), we examined several indexes of insulin secretion and action in data obtained from a 3-h OGTT (64). Total fat, IAA T, and SA A T were all significantly correlated with fasting insulin, incremental 30-min insulin, and incremental insulin AUC in both white and African American children (r ranged from 0.40 to 0.81). After multiple regression analysis, total fat remained independently related to fasting insulin after adjusting for IAA T and SA A T. This finding supports the general notion that simple obesity is commonly associated with fasting hyperinsulinemia, even in individuals without visceral obesity (22). In multiple regression analysis, SA A T was independently related to incremental insulin AUC in the group as a whole (P < 0.05) after adjusting for other indexes of adiposity (64). This finding suggests that subcutaneous upper-body fat, rather than IAA T, may be the primary determinant of insulin resistance in children. In adults, SA A T has greater lipolytic responsiveness than does peripheral adipose tissue (65, 66) and thus shares some of the metabolic features of IAA T. Therefore, in subjects with relatively low amounts of IAA T (such as children), SA A T may have a greater effect on insulin resistance.

Studies that used direct measures of IAA T and SA A T to explore their relations with insulin action in children and adolescents are summarized in Table 1. Collectively, the results of these studies show that central fat is associated with indexes of insulin resistance in children and adolescents, as in adults. However, the precise depot associated with insulin resistance differs with obesity status; in lean children it is subcutaneous whereas in obese children it is intraabdominal. Further research will be required to determine whether cause-and-effect relations exist between IAA T or SA A T and insulin action in obese and nonobese adolescents, respectively.

Regional adiposity, lipids, and insulin action

Several studies have used circumferences and skinfold thicknesses to determine whether fat distribution is related to CVD risk factors in children (68–74). However, most of these studies were cross-sectional and in those studies that showed a link between body fat and cardiovascular risk, the correlations were weak (r values of 0.1–0.3). The weak correlations may have been due to the fact that body fat and fat distribution were usually estimated from crude anthropometric indexes (33, 39).

In the Bogalusa Heart Study, among children and adolescents aged 6–18 y, those with high LDL- and VLDL-cholesterol concentrations had more trunk fat and less thigh fat (after adjusting for total adiposity) than those with low concentrations of these lipids (75). In early pubertal white girls (aged 10 ± 0.1 y, Tanner stage 1 or 2), waist-to-hip ratio was positively associated with total cholesterol, LDL cholesterol, and apolipoprotein B and inversely associated with the apolipoprotein A-I to apolipoprotein B ratio after adjusting for the sum of 4 skinfold thicknesses (76). In contrast, regional subcutaneous adiposity as assessed with skinfold thicknesses (adjusted for total adiposity) was not associated with the lipid profile. These data support the hypothesis that deposition of relatively greater amounts of IAA T...
adversely affects circulating lipid and lipoprotein concentrations in young females. The data did not indicate that regional adiposity influences the lipid profile in early pubertal males. Another study of early pubertal and prepubertal children showed that waist-to-hip ratio was not a useful index of metabolic dysfunction (77). As discussed earlier, lack of agreement among studies is likely due to the poor correlations between some of the frequently used anthropometric indexes and IAA T in children.

Two studies have used direct measures of IAA T and SAA T to examine relations between regional adiposity and blood lipids. In obese, predominantly white adolescent girls, fat distribution was measured with MRI and the results showed that: 1) IAA T was positively correlated with triacylglycerol and basal insulin concentrations and inversely correlated with HDL-cholesterol concentrations, 2) SAA T was inversely correlated with LDL-cholesterol concentrations, and 3) femoral adipose tissue was inversely correlated with triacylglycerol and LDL-cholesterol concentrations (67). The inverse association between femoral adipose tissue and lipid risk factors has been observed in adults (78, 79) and may suggest that deposition of lipid in this low-flux depot actually protects against CVD. In obese boys and girls aged 10–15 y, IAAT as determined by MRI was positively associated with total-and LDL-cholesterol and triacylglycerol concentrations but SAAT was not associated with any lipid or lipoprotein index (62). Taken together, the results of these 2 studies suggest that, at least among obese adolescents, IAAT is the only adipose tissue depot associated with lipid risk factors; SAAT and femoral fat appear to have either no effect or a protective effect.

Changes in lipid and lipoprotein concentrations may result from insulin resistance and the accompanying hyperinsulinemia. In a group of obese adolescents of mixed sex and ethnicity, both insulin sensitivity and percentage body fat showed simple correlations with the lipid profile, but only insulin sensitivity predicted LDL-cholesterol, HDL-cholesterol, and triacylglycerol concentrations in a stepwise multiple regression analysis (80). In a large sample of Finnish children and adolescents, fasting insulin at baseline was higher in those who subsequently showed a clustering of high triacylglycerol and low HDL-cholesterol concentrations and high systolic blood pressure at a 6-y follow-up examination (81). In addition, fasting insulin was independently related with the development of hypertriglyceridemia after adjusting for either baseline obesity or the change in obesity status. In a different study of white children and adolescents, insulin sensitivity was associated with triacylglycerol, VLDL concentrations, and diastolic blood pressure, and basal insulin was associated with triacylglycerol and VLDL concentrations (82). Although no measure of fat distribution was available, percentage body fat was strongly correlated with insulin sensitivity ($r = -0.82$). In a longitudinal study of obese Japanese children (boys and girls aged 7–15 y at baseline), fasting insulin was independently related to the development of lipid abnormalities and hypertension after adjusting for body mass index (in kg/m$^2$) and waist-to-hip ratio (83).

Thus, the picture that is beginning to emerge shows that central adiposity, insulin, and lipids are interrelated in children and adolescents. However, few studies have examined children before the onset of puberty, a phase of development in which normal changes in metabolism and body fat distribution may confound the interpretation of results. In addition, only a few studies have examined childhood markers of metabolic health in conjunction with IAA T in African Americans, a population with a disproportionately high rate of type 2 diabetes (84) and for which CVD is the leading cause of death (85). These studies are reviewed in more detail below.

**Ethnic differences in the association between central adiposity and disease risk**

A number of studies found that African Americans differ from whites with respect to the regulation of several metabolic risk factors. Healthy, nonobese African Americans were found to have higher fasting and postchallenge insulin concentrations, lower insulin sensitivity, and lower hepatic insulin extraction when compared with whites of similar body mass index and waist-to-hip ratio (86). In contrast, fasting glucose concentrations (37) and glucose AUC (87) were lower, HDL-cholesterol concentrations were higher (37, 87, 88), and triacylglycerol concentrations were lower (37, 89) in African Americans. The health implications of these differences in risk factors for African Americans are not clear.

The basis of some of the ethnic differences in risk factors may be differences in visceral adiposity. Recent studies in women have shown that, at any given degree of adiposity, African Americans may have less IAAT (37, 87). No ethnic differences were found in the slopes of the regressions between IAAT and glucose AUC, insulin AUC, insulin sensitivity, triacylglycerol concentration, and HDL-cholesterol concentration (87, 89). However, SAAT was significantly correlated with insulin sensitivity in African American but not white women (89). Thus, a given amount of IAAT appears to confer the same risks for both white and African American women, but for any given amount of total body fat, African American women have less IAAT. Although this observation may explain the lower triacylglycerol and higher HDL cholesterol concentrations observed in African Americans, the greater degree of hyperinsulinemia and insulin resistance seen in this group remains unexplained. Possible ethnic differences in the relation of SAAT to insulin, particularly among women, deserve further attention.

Few studies have addressed ethnic differences in the metabolic correlates of obesity or central obesity in children. Yanovski et al (43) found that, among normal-weight African American girls aged 7–10 y, SAAT but not IAAT as assessed with MRI was related to basal and 2-h insulin during an OGTT. In contrast, neither measure of adiposity was related to these insulin values in white girls matched for age, bone age, body mass index, and body weight. No relations between serum lipids or blood pressure and IAAT or SAAT were found in either group of girls. Gutin et al (77) found that percentage body fat, but not fat distribution as assessed with waist-to-hip ratio, was correlated with fasting insulin and triacylglycerol concentrations and the atherogenic index in a group of 7–11-y-old African American and white children. No effects of sex or ethnicity on the relations between adiposity and these risk factors were detected in multiple regression analysis. However, African American children had higher fasting insulin than white children, before and after adjusting for total adiposity. Likewise, in the Bogalusa Heart Study, African American children (mean age =12 y) had higher 30-min insulin concentrations than white children during an OGTT (61). In this study, central fat as assessed with skinfold thickness measurements was related to postchallenge insulin concentrations in both whites and African Americans. From these limited observations, it is difficult to draw any conclusions regarding the influence of ethnicity on the relation between central adiposity and metabolism in children, although it appears that basal insulin is significantly higher in African American children.
By using data from an OGTT, we found that fasting, 30-min (unadjusted and incremental), and 90-min insulin concentrations and incremental insulin AUC were higher and fasting glucose was lower in African American than white children (35). Both multiple regression analysis and analysis of covariance indicated that these ethnic differences in insulin were independent of total body fat, IAAT, and SAAT. Nonetheless, adiposity was more closely related to insulin secretion in white children. The slope of the regression line between total body fat and incremental 30-min insulin (1.24 and 0.57 in whites and African Americans, respectively; \( P < 0.01 \)) and the amount of variance explained by total body fat (66% and 33%, respectively) were both greater in white children. Thus, although postchallenge insulin concentration was greater in African Americans, it was more closely related to adiposity in whites.

The cause of hyperinsulinemia that is independent of adiposity in African American children is not clear. It could result from greater pancreatic responsiveness, insulin resistance, or reduced insulin clearance. Likewise, the physiologic implications of hyperinsulinemia in this population of African American children are not known. However, in general, insulin is an anabolic hormone that stimulates lipid deposition, skeletal muscle growth, and bone accrual. It is possible that ethnic differences in body composition (43), prevalence of obesity (4), rate of sexual maturation (49), and incidence of type 2 diabetes (12) between whites and African Americans are due to the greater circulating insulin concentrations in the latter.

In agreement with other studies, we found that triacylglycerol concentrations were significantly greater in white children than in African American children [0.67 ± 0.30 mmol/L (59 ± 27 mg/dL) and 0.50 ± 0.21 mmol/L (44 ± 19 mg/dL), respectively], whereas total-, HDL-, and LDL-cholesterol concentrations and fatty acid concentrations did not differ based on ethnicity.

SUMMARY AND CONCLUSIONS

IAAT, or visceral fat, begins to accumulate in early childhood. IAAT can be quantified directly only with imaging techniques, although various anthropometric indexes are highly correlated and therefore may provide indirect measures. Even before puberty there is tremendous variation in the amount of IAAT in children. Some of the interindividual variation is explained by multicollinearity with other adipose tissue stores, but a portion of the variance in IAAT appears to be completely independent of these stores. Ethnic differences in IAAT exist; in African American, prepubertal children, relatively less adipose tissue is deposited within the abdominal cavity and relatively more is deposited subcutaneously. Sex differences in IAAT begin to emerge during pubertal development, with boys having more IAAT than girls. Some studies suggested that the rate of IAAT accumulation can be slowed in children by using exercise interventions.

Significant findings regarding the relation between obesity indexes and metabolic risk factors, based on direct measures of IAAT and SAAT, are summarized in Table 1. A positive correlation between IAAT and insulin resistance has been observed in obese (but not nonobese) adolescents and in prepubertal children with a range of body fat values. In the latter, IAAT was not independently associated with insulin AUC after adjusting for total body fat and SAAT. SAAT was associated with insulin resistance in children (an independent association) and in nonobese adolescents (a simple correlation). Thus, obesity status may affect relations between regional adiposity and disease risk such that SAAT may have more of an effect on metabolic health in nonobese children, in whom IAAT deposits are quite low. Further research will be required to determine whether cause-and-effect relations exist between IAAT or SAAT and insulin action in obese or nonobese adolescents.

Data suggest that the visceral adiposity and insulin resistance syndrome may have its origins in childhood. Among predominantly obese, white adolescents, IAAT is the only adipose tissue depot associated with lipid risk factors; SAAT and femoral fat appear to have either no effect or a protective effect. In children and adolescents, insulin sensitivity and hyperinsulinemia are independently related to circulating lipids after adjusting for adiposity. Thus, the relations necessary for the development of syndrome X are apparent at an early age and may be exacerbated by accumulation of IAAT.

In children, ethnic differences in aspects of insulin metabolism parallel those observed in adults. As in adults, SAAT is related to insulin in African American but not white girls. Also as in adults, higher insulin concentrations in African American children are independent of total and regional adiposity. The adiposity-independent hyperinsulinemia or insulin resistance among African Americans could be genetically based or could be secondary to lifestyle factors such as diet and physical activity.

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REFERENCES


