Predictability of Childhood Adiposity and Insulin for Developing Insulin Resistance Syndrome (Syndrome X) in Young Adulthood

The Bogalusa Heart Study

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The occurrence of insulin resistance syndrome (syndrome X) is common in the general population. However, information is scant on the childhood predictors of syndrome X. This study examined the relative contribution of childhood adiposity and insulin to the adulthood risk of developing syndrome X in a biracial (black-white) community-based longitudinal cohort (n = 745; baseline age, 8–17 years; mean ± SD follow-up period, 11.6 ± 3.4 years). The four criterion risk variables considered were the highest quartile (specific for age, race, sex, and study year) of *1*) BMI, *2*) fasting insulin, *3*) systolic or mean arterial blood pressure, and *4*) total cholesterol to HDL cholesterol ratio or triglycerides to HDL cholesterol ratio. Clustering was defined as the combination of all four risk variables. In addition to the criterion risk variables, clustered adults had adverse levels of total cholesterol, triglycerides, LDL cholesterol, HDL cholesterol, diastolic blood pressure, and glucose compared with those who did not cluster (P < 0.001). Childhood variables, except glucose, showed adverse trends with increasing number of criterion risk variables present in adulthood (P for trend, 0.01–0.0001). The proportion of individuals who developed clustering as adults increased across childhood BMI (P for trend <0.0001) and insulin (P for trend <0.01) quartiles. The relationship to childhood BMI remained significant even after adjusting for childhood insulin. In contrast, corresponding association with childhood insulin disappeared after adjusting for childhood BMI. In a logistic regression model, childhood BMI and insulin were significant predictors of adulthood clustering, with BMI being the strongest and showing a curvilinear relationship. Using an insulin resistance index instead of insulin did not change the above findings. These results indicate that childhood obesity is a powerful predictor of development of syndrome X and underscore the importance of weight control early in life. *Diabetes* 51:204–209, 2002

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CDC, Centers for Disease Control and Prevention.

Conditions of dyslipidemia, hypertension, insulin resistance, hyperinsulinemia, and obesity, especially in constellation, are potent risk factors of coronary heart disease in adults (1–3). Furthermore, the extent of coronary atherosclerosis among adolescents and young adults has been found to increase markedly with the number of risk factors (4). Coexistence of these multiple metabolic disorders, which occur commonly in the general population (5–12), has been termed syndrome X, insulin resistance syndrome, and multiple metabolic syndrome (13–15).

Insulin resistance is thought to be the primary antecedent abnormality in syndrome X (10,13–15), although it alone does not seem to underlie all features of this syndrome (16,17). Because obesity is commonly linked to insulin resistance and the compensatory hyperinsulinemia (18,19), it may as well play a role as an initiating factor in the development of syndrome X. Of note, increases in adult morbidity and mortality from coronary heart disease are related to overweight in adolescence and its clinical consequences (20,21). In a recent cross-sectional study, we found that the degree of clustering of risk variables of syndrome X increased with age during the periods of preadolescence and adulthood, and when adjusted for adiposity, the magnitude of clustering was reduced by 50% in all age-groups and the age-related trend was no longer evident (22). Other cross-sectional and prospective studies in children and adults that examined insulin and adiposity as correlates and predictors of syndrome X have yielded mixed results (10–14,23,24). Furthermore, longitudinal information is scant on the relative contribution of childhood adiposity and insulin to the prediction of risk of developing syndrome X in adulthood.

Longitudinal data from the Bogalusa Heart Study, a long-term community-based study of cardiovascular risk variables from childhood to young adulthood (25), afford an opportunity to examine the childhood predictors of syndrome X in adulthood. Moreover, the Bogalusa cohort by its relative youth and absence of overt clinical manifestations of cardiovascular disease may aid in understanding the early natural history of the syndrome X and its predictors. In this article, we examine *1*) the metabolic and hemodynamic characteristics in childhood and adulthood by their clustering status in adulthood, *2*) the inci-

dence of clustering of the four traditional components of syndrome X in adulthood by childhood adiposity and insulin levels, and *3*) a predictive model of adulthood clustering based on childhood risk variables.

RESEARCH DESIGN AND METHODS

Study population. The biracial (65% white and 35% black) population of the Bogalusa Heart Study consists of all school children aged 5–17 years and eligible young adults aged 19–38 years living in the semirural community of Bogalusa, Louisiana. Between 1978 and 1996, five cross-sectional surveys of school children and five surveys of young adults who were examined previously as children and residing in the community were conducted. The participation rate was ~80% for the children and 60% for the young adult cohort.

The study cohort was selected from 4,262 children (50% male and 65% white) and 2,324 adults (41% male and 69% white) who participated in cross-sectional studies and met the following criteria: *1*) overnight fasting; *2*) no missing data on the variables of interest; *3*) absence of reported pregnancy, diabetes, hypertension, or dyslipidemia and use of medications for conditions of diabetes, hypertension, and dyslipidemia; and *4*) participated in the surveys both as a child aged 8–17 years and as an adult aged 19 years or above. When the individuals participated in the multiple screenings as children and adults, the earliest childhood screening and most recent adulthood screening data were used to maximize the follow-up interval. Accordingly, 745 individuals (39% male and 67% white) with a mean ± SD follow-up interval of 11.6 ± 3.4 years were selected for the study.

General examinations. Identical protocols were used by trained examiners across all surveys (26). Participants were instructed to fast 12 h before the screening, and compliance regarding fasting was determined by an interview on the morning of examination.

Height and weight were measured twice to ±0.1 cm and to ±0.1 kg, respectively. As a measure of overall adiposity, the BMI (weight in kilograms divided by the square of the height in meters) was used. Systolic and diastolic (fourth phase for children and fifth phase for adults) blood pressure levels were measured in six replicates by two randomly assigned nurses on the right arm of participants in a relaxed, sitting position. Mean arterial pressure was calculated as diastolic blood pressure plus one third pulse pressure.

Laboratory analyses. From 1978 to 1986, cholesterol and triglyceride levels were measured using chemical procedures on the Technicon AutoAnalyzer II (Technicon Instrument, Tarrytown, NY) according to the Laboratory Manual of the Lipid Research Clinics Program (27). Since then, these variables have been determined by enzymatic procedures on the Abbott VP instrument (Abbott Laboratories, North Chicago, IL). Serum lipoprotein cholesterol levels were analyzed by a combination of heparin-calcium precipitation and agar-agarose gel electrophoresis procedures (28). Both chemical and enzymatic procedures met the performance requirements of the Lipid Standardization Program of the Centers for Disease Control and Prevention (CDC; Atlanta, GA). The laboratory is being monitored for precision and accuracy of lipid measurements by the agency's surveillance program. Measurements on CDC-assigned quality control samples showed no consistent bias over time within or between surveys. Intraclass correlation coefficients (a measure of reproducibility of the entire process from blood collection to data processing) between the blind duplicate values ranged from 0.93 to 0.98 for total cholesterol, 0.91 to 0.99 for triglycerides, 0.94 to 0.98 for LDL cholesterol, and 0.94 to 0.98 for HDL cholesterol. The ratio of triglycerides to HDL cholesterol or total cholesterol to HDL cholesterol was used as a measure of dyslipidemia because these ratios reflect the combination of high triglycerides or high non-HDL cholesterol and low HDL cholesterol levels characteristic of syndrome X (13).

Plasma immunoreactive insulin was measured by a commercial radioimmunoassay kit (Phadebas; Pharmacia Diagnostics, Piscataway, NJ). This insulin assay has 41% cross-reactivity with proinsulin and <0.2% cross-reactivity with C-peptide. High cross-reactivity of the insulin assay with proinsulin should not affect the insulin measurements because proinsulin is secreted in very low concentrations relative to insulin in individuals without diabetes. The detection limit of insulin level was 2.0 μU/ml. From 1978 to 1991, plasma glucose was measured by a glucose oxidase method using a Beckman glucose analyzer (Beckman Instruments, Fullerton, CA). Since then, it has been measured enzymatically as part of a multichemistry profile. Any bias between the glucose analyzers should be minimal because both used the glucose oxidase method. Furthermore, the cutoff points used for risk variables, including glucose, were study year–specific. The intraclass correlation coefficients between the blind duplicate values ranged from 0.94 to 0.98 for insulin and 0.86 to 0.98 for glucose.

TABLE 1
Baseline characteristics of selected versus not selected individuals from the original study participants

	Selected	Not selected
n	745	3,517
Age (years)	12.7 ± 0.09§	11.1 ± 0.04
BMI (kg/m^2)*	18.7 ± 0.14†	19.1 ± 0.06
Systolic BP (mmHg)*	103.6 ± 0.33†	102.5 ± 0.15
Mean arterial pressure (mmHg)*	76.5 ± 0.28‡	75.5 ± 0.12
Insulin (μU/ml)*	9.6 ± 0.65	10.5 ± 0.29
Total cholesterol/HDL cholesterol*	3.1 ± 0.25	3.4 ± 0.11
Triglycerides/HDL cholesterol*	1.1 ± 0.92	1.1 ± 0.42

Data are means ± SE. *Adjusted for age, race, and sex; †$P < 0.01$; ‡$P < 0.001$; §$P < 0.0001$.

Statistical analyses. All analyses were performed using SAS software (version 8.0). The percentile (75th) used as cutoff point to define adverse level was age-, race-, sex-, and study year–specific. The four metabolic and hemodynamic variables considered as components of syndrome X were the highest quartile of *1*) BMI, *2*) fasting insulin, *3*) systolic or mean arterial blood pressure, and *4*) total cholesterol to HDL cholesterol ratio or triglycerides to HDL cholesterol ratio. Clustering was defined as coexistence of all four criterion risk variables.

Analysis of variance methods and exact binomial methods were used to assess differences between clustered and nonclustered participants. Trend analysis was used to assess whether childhood risk variable levels differed as a function of the number of adulthood risk criterion risk variables (0–4), after adjustment for age at baseline, sex, and race. Orthogonal polynomial coding was used in logistic regression to determine whether the childhood status (quartiles) of BMI or insulin was significantly associated with the incidence of clustering (as already defined) in adulthood. Only participants who were free of clustering in childhood ($n = 718$) were included in this analysis.

Childhood variables were standardized using the formula $(x_i - x_{mean})/s$, where x_i is the risk variable level, x_{mean} is the mean, and s is the SD. Means and SD were sex-, race-, age-, and study-specific. Each resulting score can be interpreted as an SD from the mean, with a score of 0 equal to the mean for that of sex, race, age, and study. These standardized scores were used as predictors of adulthood clustering in a stepwise logistic regression model. Only those covariates that improved the model significantly ($P < 0.05$) were allowed to enter the model, and all interactions were available for entry as appropriate. The fit of the final model was assessed using the Hosmer-Lemeshow goodness-of-fit statistic, and the final model did fit well ($P \approx 0.87$).

RESULTS

Baseline characteristics of selected cohort. Baseline age and levels of criterion risk variables of syndrome X for selected versus not selected individuals from the original study participants are given in Table 1. Children who were selected for the study were older and had lower BMI and higher systolic blood pressure and mean arterial pressure than those who were not selected. However, these differences, although significant, were small. The values for insulin, total cholesterol to HDL cholesterol ratio, and triglycerides to HDL cholesterol ratio were not significantly different between the groups.

Risk variables by clustering status. As in our previous cross-sectional findings from the Bogalusa population (22), the magnitude of clustering of adverse levels of criterion risk variables of syndrome X in the study cohort was significantly higher in adulthood than in childhood (6.4 vs. 3.6%; $P < 0.01$).

In the study cohort, clustered and not clustered adults were, on average, 12.8 and 12.7 years old at baseline and 25.1 and 24.3 years old at follow-up, with no significant age difference between the groups at baseline or follow-up. Furthermore, 4, 25, 65, and 6% of subjects had, respec-

TABLE 2
Adulthood levels of risk variables by clustering status*

Risk variables	Means SD		% Participants in top quartile	
	Clustered†	Not clustered	Clustered‡	Not clustered
n	48	697	48	697
BMI (kg/m^2)	38.5 ± 6.3	25.6 ± 5.9	100.0	19.1
Insulin (μU/ml)	29.0 ± 16.2	11.4 ± 8.8	100.0	16.6
Glucose (mg/dl)	87.6 ± 14.4	79.0 ± 12.8	56.3	21.7
Systolic blood pressure (mmHg)	122.8 ± 8.5	109.0 ± 9.2	87.5	19.5
Diastolic blood pressure (mmHg)	81.1 ± 8.2	70.5 ± 7.4	75.0	20.2
Mean arterial pressure (mmHg)	95.0 ± 7.5	83.3 ± 7.3	81.3	20.3
Cholesterol (mg/dl)				
Total	204.8 ± 45.4	179.3 ± 35.1	43.8	23.0
LDL	133.8 ± 33.7	112.8 ± 30.6	37.5	21.4
HDL	39.6 ± 8.3	51.0 ± 12.7	50.0	17.1
Triglycerides (mg/dl)	193.0 ± 142.6	96.2 ± 58.7	81.3	20.2
Total cholesterol/HDL cholesterol	5.5 ± 2.7	3.7 ± 1.2	83.3	20.1
Triglycerides/HDL cholesterol	5.2 ± 4.0	2.1 ± 1.8	83.3	20.2

Data are means ± SD. *Clustering of adverse levels (≥75th percentile specific for age, race, sex, and survey year) of insulin, BMI, systolic blood pressure or mean arterial pressure, and total cholesterol/HDL cholesterol or triglycerides/HDL cholesterol. The latest adult measurements were used; †clustered > not clustered, all $P < 0.0001$; ‡more than expected by chance alone, all $P < 0.01$.

tively, <6 years, 6–10 years, 11–15 years, and >15 years of follow-up from childhood to adulthood, with no significant difference between clustered and not clustered groups in this regard. Also, there was no evidence of race and sex differences in the frequency of clustering, suggesting that the degree of clustering was similar in blacks and whites and in males and females. Therefore, additional analyses were performed on the total sample to improve statistical power.

As adults, the participants who displayed clustering had significantly higher mean levels of all variables listed in Table 2 compared with those who showed no such clustering, as one would expect. Furthermore, significantly higher percentage of clustered (versus not clustered) participants were located in the top quartile of glucose (56.3 vs. 21.7%), total cholesterol (43.8 vs. 23.0%), triglycerides (81.3 vs. 20.2%), LDL cholesterol (37.5 vs. 21.4%), HDL cholesterol (50.0 vs. 17.1%), and diastolic blood pressure (75.0 vs. 20.2%), although levels of these variables per se were not included as the criterion risk variables in the definition of clustering.

Mean levels of variables in childhood by number of criterion variables present in adulthood are given in Table 3. Childhood levels showed significant positive trends in BMI, insulin, systolic and diastolic blood pressures, mean arterial pressure, total cholesterol, LDL cholesterol, triglycerides, total cholesterol to HDL cholesterol ratio, and triglycerides to HDL cholesterol ratio and a negative trend in HDL cholesterol with increasing number of criterion risk variables in adulthood. However, levels of glucose in childhood showed no such significant trend.

Incidence of clustering in adulthood. The effect of childhood BMI and insulin status (quartiles) on the development of clustering in adulthood is shown in Fig. 1. There were no significant interactions by race or sex in the above relationships. Significant positive trends were noted be-

TABLE 3
Mean levels of risk variables in childhood by number of criterion risk variables present in adulthood*

Childhood risk variable†	Number of criterion risk in adulthood‡					*P* (trend)
	0	1	2	3	4	
n	310	208	112	67	48	
BMI (kg/m^2)	18.3	19.0	21.0	23.0	23.6	0.0001
Insulin (μU/ml)	8.4	8.2	10.9	14.1	13.6	0.0001
Glucose (mg/dl)	82.0	82.2	82.8	83.1	83.0	NS
Systolic blood pressure (mmHg)	104.6	106.6	107.2	109.4	110.2	0.0001
Diastolic blood pressure (mmHg)	64.7	65.0	65.4	66.7	68.3	0.01
Mean arterial pressure (mmHg)	78.0	78.9	79.3	80.9	82.2	0.0001
Cholesterol (mg/dl)						
Total	156.2	159.8	161.3	163.8	162.6	0.01
LDL	86.1	93.1	98.3	99.7	102.3	0.0001
HDL	62.7	58.5	58.8	52.0	50.4	0.0001
Triglycerides (mg/dl)	61.0	64.9	69.9	78.7	73.9	0.0001
Total cholesterol/HDL cholesterol	2.7	3.2	3.7	4.6	3.9	0.0001
Triglycerides/HDL cholesterol	1.2	1.6	1.9	2.7	2.0	0.0001

*The earliest childhood and latest adulthood measurements with a mean ± SD follow-up period of 11.6 ± 3.4 years were used; †adjusted for age at baseline, race, and sex; ‡number of any criterion risk variables (BMI, insulin, systolic blood pressure or mean arterial pressure, and total cholesterol/HDL cholesterol or triglycerides/HDL cholesterol) ≥75th percentile specific for age, race, sex, and survey year. NS, not significant.

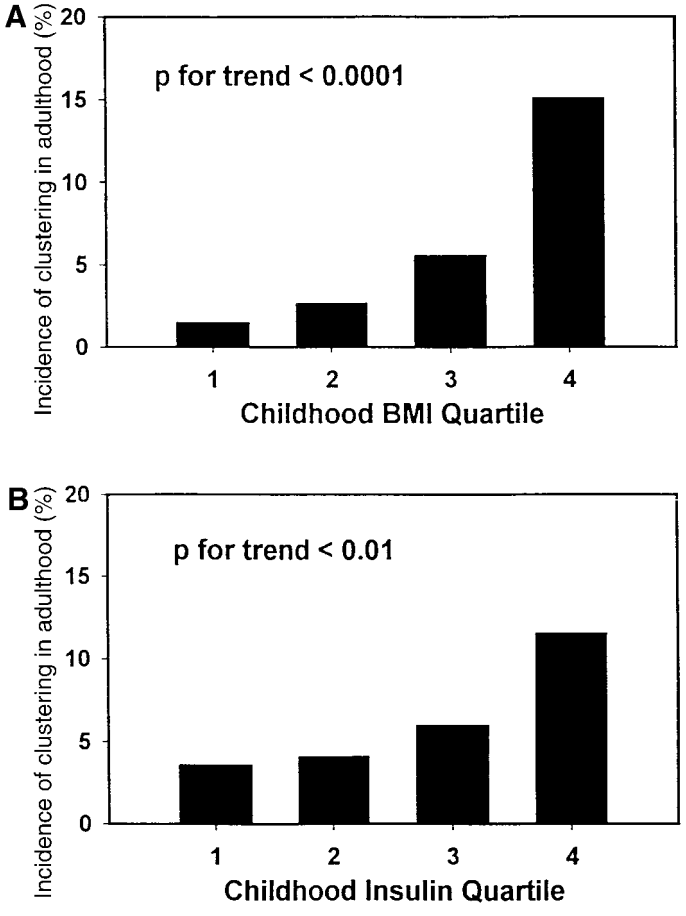

FIG. 1. Incidence of clustering of risk variables of syndrome X in adulthood by childhood BMI (*A*) and insulin (*B*) quartiles. The earliest childhood and latest adulthood measurements with a mean ± SD follow-up period of 11.6 ± 3.4 years were used. Only those without clustering in childhood (n = 718) were included in the analysis.

tween childhood BMI as well as insulin quartiles and the incidence of clustering. Children in the top quartile of BMI and insulin versus those in the bottom quartile were 11.7 and 3.6 times more likely to develop clustering, respectively, as adults (Table 4). Even after adjusting for childhood insulin levels, a high BMI in childhood was significantly associated with the incidence of clustering in adulthood. In contrast, adjustment for childhood BMI

TABLE 4
Odds ratio of developing clustering of risk variables of syndrome X in adulthood based on childhood levels of BMI and insulin*

Childhood quartiles† 4 vs. 1	Odds ratio‡	95% CI	*P*
BMI			
Unadjusted	11.7	3.4–39.7	0.0001
Adjusted for insulin§	10.0	2.8–35.5	0.001
Insulin			
Unadjusted	3.6	1.5–8.7	0.01
Adjusted for BMI§	1.8	0.7–4.7	NS

*The earliest childhood and latest adulthood measurements with a mean ± SD follow-up period of 11.6 ± 3.4 years were used; †specific for age, race, sex, and survey year (only those without clustering at baseline [n = 718] were included); ‡for developing clustering (defined as in Table 1) in adulthood; §childhood values.

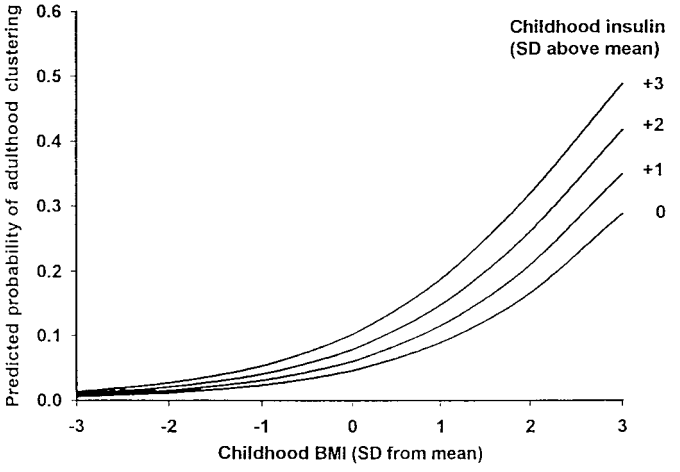

FIG. 2. The predicted probability of adulthood clustering of risk variables of syndrome X with increasing childhood BMI according to childhood insulin status. The earliest childhood and latest adulthood measurements with a mean ± SD follow-up period of 11.6 ± 3.6 years were used.

eliminated the influence of childhood insulin on the incidence of clustering in adulthood.

Predictor variables. The best childhood risk variables (listed in Table 3) that could be used to predict clustering in adulthood were examined by a stepwise logistic regression model. The best-fitting model for the prediction of clustering in adulthood from the standardized (z score) childhood risk variables included only BMI and insulin: log odds = $-3.03 + 0.71^* z$BMI $+ 0.29^* z$ insulin.

For someone at the race-, sex-, age-, and study year–specific mean levels of BMI and insulin (zBMI = 0 and z insulin = 0) in childhood, the predicted log odds and probability of adulthood clustering were −3.03 and 0.05, respectively. With respect to increases in childhood BMI at constant insulin levels, each SD unit increase from the mean resulted in a 0.71-unit increase in the predicted log odds of clustering in adulthood; the predicted probability increased in a nonlinear manner, as illustrated in Fig. 2. A corresponding increase in childhood insulin at constant BMI increased the predicted log odds of clustering by only 0.29 units, with the predicted probability far less than that noted for BMI (data not shown).

In terms of odds ratios, children with BMI 1 SD above the mean versus those with the mean value were 2.03 times more likely to develop clustering as adults. In comparison, the odds of developing clustering in adulthood for corresponding increase in insulin was 1.33.

DISCUSSION

In this community-based study, childhood adiposity, unlike insulin, was associated with the incidence of clustering of all four traditional components of syndrome X in adulthood. In addition, childhood adiposity remained as the strongest predictor of this clustering in adulthood, independent of the contributing effect of childhood insulin. This relationship was similar in males and females and in blacks and whites. To our knowledge, no comparable data on the relative contribution of childhood adiposity versus insulin to the risk of developing clustering of all four components of syndrome X in young adulthood are

available as part of the early natural history of the syndrome X in the general population.

In this study, childhood levels of adiposity, along with insulin, blood pressure, and lipoprotein variables, showed significant adverse changes with increasing number of syndrome X risk factors in adulthood. This is consistent with previous reports, including our own showing persistence of clustering of risk variables over time (9,29), with persistence of clustering from childhood to adulthood increasing progressively with childhood adiposity (9). Furthermore, it has been reported that overweight during childhood and adolescence is a determinant of risk variables of syndrome X in adulthood (30,31).

It is also apparent from the present study that the proportion of individuals who developed clustering as adults increased significantly with childhood adiposity (measured as BMI) as well as insulin levels. However, although a high childhood BMI was significantly associated with the incidence of clustering in adulthood even after adjusting for childhood insulin, a corresponding association with childhood insulin disappeared after adjusting for childhood BMI. Earlier longitudinal studies regarding the natural history of syndrome X showed only insulin (10,32) or both insulin and adiposity (12,24) as the antecedent factor(s). Most of these studies involved a relatively older adult population in whom the metabolic sequelae might already have been well-established in clinical terms. The present study's demonstration of the dependence of fasting insulin on body fatness underscores the pathogenic importance of childhood obesity in developing syndrome X.

Although insulin resistance is considered to play a pathogenic role in syndrome X (10,13–15) and the link between obesity and insulin resistance is well known (18–19), the question pertinent to the current study is whether obesity precedes or follows insulin resistance and the compensatory hyperinsulinemia. Conceptually, potential mechanisms have been proposed to explain the causality either way (33,34). With respect to children, studies in Pima Indian children found hyperinsulinemia to be a predictor of obesity (35). However, observations in this ethnic group with a strong genetic predisposition to hyperinsulinemia, insulin resistance, obesity, and type 2 diabetes may not be applicable to the general population. Relevant to this current study is our recent observations showing a temporal association between the degree of baseline adiposity and the incidence of hyperinsulinemia in children, adolescents, and young adults alike, independent of baseline insulin level (36).

In this study, the best-fitting model for predicting the probability of clustering in adulthood from childhood variables retained only adiposity and insulin. However, the predicted probability of adulthood clustering from childhood adiposity versus insulin was markedly stronger, with a curvilinear relationship. It is likely that childhood obesity and the attendant insulin resistance and hyperinsulinemia together may be integral to the prediction of clustering in adulthood.

Although the current longitudinal study cannot establish causality, several putative mechanisms link obesity and the attendant insulin resistance and hyperinsulinemia to other components of syndrome X. Excess body fat, especially visceral fat, mobilizes free fatty acids in the portal circulation, which in turn reduces hepatic clearance of insulin, causing peripheral hyperinsulinemia (19,37,38). Utilization of excess free fatty acids by muscle at the expense of glucose may contribute to the peripheral insulin resistance and compensatory hyperinsulinemia (39,40). Furthermore, increases in adipocyte-derived tumor necrosis factor-α and leptin in obesity have been invoked as a cause of insulin resistance (41,42). Under these conditions triglyceride (VLDL) levels rise as a result of excess hepatic triglyceride synthesis and/or reduced clearance from the circulation (43). In turn, decreases in HDL cholesterol levels ensue as a result of increases in the translocation of cholesteryl ester from HDL to VLDL in exchange for triglyceride and/or the rate of apolipoprotein A-I degradation (44).

With respect to blood pressure, hyperinsulinemia could raise the levels in different ways by *1*) increasing renal sodium retention, *2*) stimulating the sympathetic nervous system, *3*) disturbing cell membrane cation transport, and *4*) increasing the smooth muscle proliferation (13,14). Alternatively, obesity per se could raise blood pressure by adversely altering *1*) cardiac output, *2*) cardiac systolic and diastolic function, and *3*) renal-pressure natriuresis (45).

The present study has certain limitations. The adiposity was measured in terms of BMI, although it does not reflect body fatness exclusively. However, in this population, the trend in BMI was more closely paralleled by changes in the skinfold thicknesses and the ratio of subscapular to triceps skinfold thickness, measures of fat mass and fat distribution (30,46). Furthermore, it has been reported that the BMI was as good a predictor of risk variables such as blood pressure and glucose as was any other measure of body fat (47). Another limitation of this study is the use of fasting insulin as an indicator of hyperinsulinemia as well as insulin resistance, although these two variables are distinct metabolic entities that have a differential impact on syndrome X risk variables and their clustering (24,48). Furthermore, a measure of caution should be used in assessing the incidence of clustering of the four risk variables at follow-up because each of these variables is measured with varying degrees of precision.

In summary, childhood obesity is a powerful predictor of risk of developing a constellation of metabolic and hemodynamic disorders of syndrome X. Overnutrition in combination with a sedentary lifestyle, leading to obesity, are considered to play a major role in this process (13–14). Therefore, as a public health issue, our results when viewed in the context of the upward secular trend in the U.S. for being obese during childhood (46,49) underscore the importance of prevention and intervention of excessive weight gain early in life in the general population.

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