Adolescent Overweight Is Associated With Adult Overweight and Related Multiple Cardiovascular Risk Factors: The Bogalusa Heart Study

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Overweight in adolescence is considered an important predictor of long-term morbidity and mortality. The impact of adolescent overweight on adult overweight and related multiple cardiovascular risk factors was examined in a biracial (black-white) cohort (N = 783) who participated in two cross-sectional surveys as adolescents aged 13 to 17 years and as young adults aged 27 to 31 years. The cohort was categorized as adolescent-onset adult overweight (N = 110) or lean (N = 81) according to age-, race-, and sex-specific body mass index (BMI) greater than the 75th percentile or between the 25th and 50th percentiles on both surveys. The risk for overweight adolescents to remain overweight as young adults ranged from 52% in black males to 62% in black females. As young adults, the overweight cohort showed adverse levels of body fatness measures, systolic and diastolic blood pressure, lipoprotein cholesterol, insulin, and glucose as compared with the lean cohort ($P < .01$ to $P < .0001$). The prevalence of clinically recognized hypertension and dyslipidemia increased 8.5-fold and 3.1- to 8.3-fold, respectively, in the overweight cohort versus the lean cohort ($P < .05$ to $P < .0001$). The prevalence of parental history of diabetes mellitus and hypertension increased 2.4-fold ($P < .01$) and 1.3-fold ($P < .05$), respectively, in the overweight cohort. Clustering of adverse values (> 75th percentile) for the total cholesterol to high-density lipoprotein (HDL) cholesterol ratio, insulin level, and systolic blood pressure occurred only among the overweight cohort ($P < .0001$). Thus, excess weight in adolescence persists into young adulthood, and has a strong adverse impact on multiple cardiovascular risk factors, requiring primary prevention early in life.

OVERWEIGHT in adulthood is associated with cardiovascular disease, diabetes, hypertension, dyslipidemia, certain types of cancer, and premature mortality.[1] The adverse impact of overweight and obesity on serum lipoprotein levels, blood pressure, and insulin level, the major cardiovascular disease risk factor variables, has been found in adults and children alike.[1-8] Because adult obesity is considered intractable[1] and truncal body fat is known to increase in adolescence,[9] there is a need to identify children at risk for adult obesity and its attendant metabolic and clinical manifestations.

The impact of adolescent-onset adult overweight on long-term morbidity and mortality has been investigated in several studies.[10-15] In general, these studies found tracking of obesity measures from adolescence through adulthood.[10,11] The strongest associations between morbidity and mortality from cardiovascular disease were found with adolescent overweight, not with adult overweight.[12,14] On the other hand, overweight adults who were lean as adolescents also showed adverse health effects of obesity.[15] While longitudinal studies have mainly examined the effect of childhood weight status on morbidity and mortality in an older age group, few population-based studies have assessed simultaneously the risk for overweight adolescents to become overweight young adults and related multiple cardiovascular risk factors.

The early natural history of obesity has been studied as part of the Bogalusa Heart Study, a long-term epidemiologic study of cardiovascular disease risk factors beginning in childhood.[16,17] The purpose of this study was (1) to determine the risk for overweight adolescents to remain overweight as young adults 12 to 14 years later in a biracial (black-white) cohort, and (2) to assess the association of multiple cardiovascular risk factors with adult overweight of adolescent-onset.

SUBJECTS AND METHODS

Study Population and Design

The Bogalusa Heart Study is a biracial (65% white and 35% black) community-based study of the early natural history of cardiovascular disease.[16] The population consists of all children and eligible young adults living in Ward 4 of Washington Parish, which includes Bogalusa, LA (total population, ~22,000). Participation rates ranged from over 80% for school-aged children to over 60% for the adult cohort.

Adolescents (n = 1,594) aged 13 to 17 years were examined as part of the 1976 to 1977 cross-sectional survey of school children. Subsequently, 783 of these individuals participated in the 1988 to 1991 cross-sectional survey of young adults. Individuals who participated as adolescents aged 13 to 17 years and young adults aged 25 to 31 years in both surveys were selected retrospectively as the study cohort. At the initial examination, age/race/sex distributions and body mass indices ([BMIs] weight [kilograms]/height [meters]^2) of the study cohort were similar to those of 13- to 17-year-old subjects who did not participate as young adults in the 1988 to 1991 survey (data not shown).

The study cohort was categorized as adolescent-onset adult overweight or lean according to the age-, race-, and sex-specific BMI percentile of the Bogalusa population: those who remained above the 75th percentile and those who remained between the

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25th and 50th percentiles, respectively, during adolescence, as well as adulthood (see results). Although clinically the term obesity usually refers to individuals with obesity measures such as BMI greater than the 95th percentile, the present study categorized individuals in the upper 25th percentile as overweight and obese. Overweight individuals were compared with moderately lean individuals rather than with those with a BMI less than the 25th percentile, to reduce the potential bias related to choosing the leanest individuals for comparison. Although BMI does not distinguish between body fatness and lean body mass, measurements are made with good accuracy and track relatively well over time in comparison to other obesity measures such as skinfold thickness.[10,16]

General Examinations

Identical protocols were used across all surveys.[16] Subjects were instructed to fast 12 hours before venipuncture, and compliance was determined by interview on the morning of examination.

Height was measured to the nearest 0.1 cm, weight to the nearest 0.1 kg, and triceps and subscapular skinfold thicknesses to the nearest 1 mm. These measurements were obtained in triplicate, and mean values were used in analyses. Replicate blood pressure measurements were obtained in a relaxed, sitting position. Systolic and diastolic blood pressures were recorded as the first and fourth Korotkoff phases, respectively. The mean of six readings was used in analyses.

Medical histories of adult participants and their biological parents were obtained through questionnaires. Verification of parental histories was not performed.

Laboratory Measurements

Cholesterol/triglyceride levels of whole serum and the fraction containing high-density lipoprotein (HDL) were determined using enzymatic procedures[18,19] on the Abbott VP instrument (Abbott Laboratories, North Chicago, IL). Serum very–low-density lipoprotein (VLDL), low-density lipoprotein (LDL), and HDL cholesterol were analyzed by a combination of heparin-calcium precipitation and agar-agarose gel electrophoresis procedures.[20] The laboratory is monitored by the Centers for Disease Control (Atlanta, GA) surveillance program.

Plasma glucose levels were analyzed by an enzymatic method using the Beckman glucose analyzer (Beckman Instruments, Palo Alto, CA). Plasma immunoreactive insulin levels were measured by a commercial radioimmunoassay kit (Phadebas; Pharmacia Diagnostics, Piscataway, NJ). According to the manufacturer, the detection limit is less than 2 μU/mL; the antibody has 41% (by weight) cross-reactivity with proinsulin, which is disproportionately low in nondiabetics.

Measurement error, estimated from the coefficient of variation of 189 pairs of blind duplicate determinations, was 2.1% for total cholesterol, 3.9% for triglycerides, 3.6% for LDL cholesterol, 4.9% for HDL cholesterol, 13.4% for VLDL cholesterol, 9.9% for insulin, and 3.2% for glucose. Reproducibility (intraclass correlation coefficient) of measurements for these variables varied from .95 (HDL cholesterol) to 1.0 (triglycerides).

Statistical Analyses

The Statistical Analysis System was used for data analyses.[21] Distributions of study variables were examined, and proper transformations were used for certain analyses. Differences between adolescent-onset adult overweight and lean cohorts were evaluated in an analysis of covariance, adjusting for race, sex, and age. To examine the effect of adolescent weight status (overweight *v* lean) and change in BMI from adolescence to adulthood on adult cardiovascular risk factor variables, a stepwise regression was conducted in subjects who were overweight or lean as adolescents; age, race, and sex were also included as independent variables. Prevalence of risk factors or parental disease of adolescent-onset adult overweight and lean cohorts was compared using a chi-square test. Coexistence of adverse levels of risk factor variables was expressed as a relative proportion of observed frequency to expected frequency (risk ratio). Significance of the risk ratio was calculated based on a binomial distribution.

RESULTS

The risk of overweight adolescents (BMI, > 75th percentile) to remain so as young adults 12 to 14 years later was examined in the study cohort by race and sex (Fig 1). Corresponding data for lean adolescents (BMI, 25th to 50th percentile) were included for comparison. Overall, of 191 adolescents originally identified as overweight, 110 (58%, the predictive value) remained overweight as adults 12 to 14 years later, with the remainder classified as lean (n = 17) or between the 50th and 75th percentiles (n = 64, data not shown). Among the four race-sex groups, the predictive value of overweight status was lowest in black males (52%) and highest in black females (62%). With respect to lean adolescents (n = 199), 41% (the predictive value) retained this status as adults, with the remainder shifted to the overweight category (n = 19) or other percentiles (< 25th percentile or 50th to 75th percentile, data not shown). The predictive value of lean status was lowest in black males (28%) and highest in white males (52%). Of 192 overweight adults, 110 were overweight as adolescents, for a sensitivity of 57%. Likewise, 81 (41%) of lean adults had been initially classified as lean adolescents.

Adulthood characteristics of the cohort who remained overweight (n = 110) or lean (n = 81) as adolescents and adults over the 12- to 14-year follow-up period were then examined (Table 1). With respect to race-sex distributions, the overweight cohort contained 33% white males, 35% white females, 13% black males, and 19% black females; corresponding values for the lean cohort were 41%, 32%, 10%, and 17%. Due to small sample size, data are not presented separately by race and sex. Unlike body weight and BMI, age and height did not differ significantly between

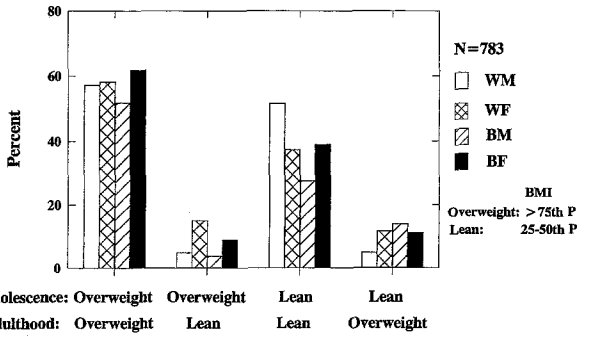

Fig 1. Persistence of adolescent overweight and lean status over 12 to 14 years in the study cohort. Bars depicting percentage of follow-up overweight status do not add up to 100% within adolescent overweight or lean groups due to shifts of subjects into other percentiles in adulthood. WM, white males; WF, white females; BM, black males; BF, black females.

Table 1. Follow-up Characteristics of Adolescent-Onset Overweight Versus Lean Young Adult Cohort: The Bogalusa Heart Study

Variable	Overweight (n = 110)	Lean (n = 81)
Age (yr)	28.0 ± 1.5	28.0 ± 1.5
Height (m)	1.7 ± 0.1	1.7 ± 0.1
Weight (kg)	97.3 ± 17.7‡	67.2 ± 9.5
BMI (kg/m²)	33.9 ± 5.1‡	22.9 ± 1.5
Triceps (T) skinfold (mm)	24 ± 8‡	15 ± 7
Subscapular (S) skinfold (mm)	31 ± 10‡	14 ± 5
Skinfold ratio (S/T)	1.4 ± 0.7‡	1.1 ± 0.6
Systolic blood pressure (mm Hg)	117 ± 13‡	109 ± 9
Diastolic blood pressure (mm Hg)	77 ± 11‡	71 ± 8
Total cholesterol (mg/dL)	200 ± 35†	177 ± 36
Triglycerides (mg/dL)	157 ± 132*	100 ± 112
VLDL cholesterol (mg/dL)	22 ± 18†	12 ± 14
LDL cholesterol (mg/dL)	132 ± 30‡	111 ± 28
HDL cholesterol (mg/dL)	46 ± 13†	54 ± 16
Insulin (μU/mL)	17 ± 12†	8 ± 3
Glucose (mg/dL)	91 ± 32*	80 ± 8

NOTE. Values are the unadjusted mean ± SD.

*$P < .01$, †$P < .001$, ‡$P < .0001$: overweight *v* lean (adjusted for race, sex, and age).

the two groups. Triceps (peripheral fat) and subscapular (truncal fat) skinfold thicknesses, which have been generally used as indirect measures of body fat pattern,[22-25] were also markedly elevated in the overweight versus the lean cohort ($P < .0001$). Further, the ratio of subscapular skinfold thickness to triceps skinfold thickness, a measure of truncal fat distribution,[24,26] was higher in the overweight cohort ($P < .0001$). In terms of other cardiovascular risk factor variables, the overweight cohort, as compared with the lean cohort, had increased systolic and diastolic blood pressure and total cholesterol, triglycerides, VLDL cholesterol, LDL cholesterol, insulin, and glucose levels and decreased HDL cholesterol levels ($P < .01$ to $P < .0001$).

Adult weight status reflects adolescent weight status, as well as weight gain from adolescence to adulthood. A stepwise regression analysis was therefore performed in subjects who were overweight (n = 191) or lean (n = 199) as adolescents to assess the independent effects of adolescent overweight and weight gain on adult risk factor variables. Both adolescent overweight and weight gain from adolescence to adulthood had independent adverse effects on adult risk factor variables (Table 2).

The impact of adolescent-onset adult overweight on the prevalence of cardiovascular risk factors, determined according to clinically recognized high-risk limits,[27-29] and parental histories of cardiovascular disease are presented in Table 3. The prevalence of hypertension increased 8.5-fold in the overweight versus the lean cohort ($P < .0001$). Within the overweight cohort, the prevalence of hypertension tended to be 2.7-fold higher in blacks than in whites (data not shown). With respect to serum LDL cholesterol, HDL cholesterol, and triglycerides, the overweight cohort had a 3.1- to 8.3-fold higher prevalence of high-risk values than their lean counterparts ($P < .05$ to $P < .01$). The adverse lipoprotein pattern tended to be 1.3- to 3.5-fold more prevalent in whites, especially white males, than in blacks

Table 2. Effect of Adolescent Weight Status and Change in BMI on Adult Cardiovascular Risk Factor Variables: The Bogalusa Heart Study

Adult Risk Factor Variable	Adolescent Weight Status	Change in BMI	Black *v* White	Female *v* Male
Systolic BP (mm Hg)	4.1§	0.8§	2.7*	−7.0§
Diastolic BP (mm Hg)	2.7‡	0.5§		−4.5§
Cholesterol (mg/dL)				
Total	14.3‡	2.2§		
VLDL	5.1†	0.8‡	−6.1‡	−3.9*
LDL	12.4‡	2.3§	−8.2*	
HDL	−3.4*	−0.8§	7.9§	3.4*
Triglycerides (mg/dL)	37.5‡	5.4‡	−29.3*	−23.3*
Insulin (μU/mL)	5.1§	1.0§		
Glucose (mg/dL)	5.3*	0.8†		−5.7*

NOTE. Values are regression coefficients.

Abbreviation: BP, blood pressure.

*$P < .05$, †$P < .01$, ‡$P < .001$, §$P \leq .0001$: overweight (n = 191) *v* lean (n = 199).

(data not shown). Although not statistically significant, high-risk plasma glucose levels occurred only among the overweight cohort. These individuals were found to be diabetic black males. Whereas the prevalence of parental history of heart attack was similar in both groups, parental history of diabetes mellitus and hypertension increased 2.4-fold ($P < .01$) and 1.3-fold ($P < .05$), respectively, in the overweight cohort.

The relation of adolescent-onset adult overweight to the clustering or coexistence of increased values (> 75th percentile) for the serum total cholesterol to HDL cholesterol ratio, plasma insulin level, and systolic blood pressure is given in Table 4. A markedly increased frequency of association of two or three of these adverse conditions resulting in an elevated risk ratio was noted only among the overweight cohort ($P < .0001$). If there was no association between these conditions, one would expect 6.3% fre-

Table 3. Impact of Adolescent-Onset Adult Overweight on the Prevalence of Cardiovascular Risk Factors and Parental Diseases: The Bogalusa Heart Study

Prevalence (%)†	Overweight Cohort (n = 110)	Lean Cohort (n = 81)
Cardiovascular risk factors		
Hypertension*	21.3‖	2.5
Total cholesterol > 240 mg/dL	14.6	5.8
LDL cholesterol > 160 mg/dL	18.0‡	5.8
HDL cholesterol < 35 mg/dL	15.7§	2.9
Triglycerides > 250 mg/dL	12.4§	1.5
Glucose > 115 mg/dL	2.4	0
Parental history		
Heart attack	27.1	26.7
Diabetes mellitus	30.9§	12.7
Hypertension	69.0‡	52.1

*Systolic blood pressure > 140 mm Hg, diastolic blood pressure > 90 mm Hg, or on medication for hypertension.

†Young adults.

‡$P < .05$.

§$P < .01$.

‖$P < .0001$.

Table 4. Relation of Adolescent-Onset Adult Overweight to the Clustering of Cardiovascular Risk Factors: The Bogalusa Heart Study

	Coexisting Conditions (> 75th percentile)†		
Total cholesterol/HDL cholesterol	+		+
Insulin	+	+	+
Systolic blood pressure*		+	+
Overweight cohort (n = 110)			
Frequency (%)	36	34	19
Risk ratio‡	5.8§	5.4§	3.0§
Lean cohort (n = 81)			
Frequency (%)	9	3	3
Risk ratio†	1.4	0.5	0.5

*Includes those on medication for hypertension.
†Young adults.
‡Observed frequency/expected frequency.
§$P < .0001$.

quency for two associations and 1.6% frequency for three associations by chance alone.

DISCUSSION

The present study demonstrates that adolescent overweight persists over a period of 12 to 14 years into young adulthood, especially in black females, and adversely impacts multiple cardiovascular risk factors. These observations are based on a community-based study that has examined multiple cardiovascular risk factor variables in subjects as children and as adults. Since age/race/sex distributions and BMIs of the study cohort at initial examination remained essentially similar to those of subjects who did not participate as young adults in subsequent surveys, it is unlikely that selection bias could have distorted the current findings.

The present observations regarding the persistence of adolescent overweight extend our earlier reports[30,31] and agree with other studies.[13,14,32-35] In general, it has been found that the risk of becoming an overweight adult was greater among children who were overweight at or around puberty and among those who were at extremely high percentiles of the distribution.[35] Although the 75th rather than a higher percentile of BMI was used to define overweight or obesity in the present study, 52% to 62% of overweight adolescents remained so as adults 12 to 14 years later. This percentile reflects the upper limit of recommended weights for young adults.[14] As previously reported,[31,36,37] the persistence of overweight in the study cohort was strongest in black females.

Although adolescent overweight persists into young adulthood, many overweight young adults in the present study were lean as adolescents. Since adolescent weight status, as well as weight gain from adolescence to adulthood, had an independent adverse effect on adult cardiovascular risk factor variables in the study cohort, weight gain during the transition to adulthood may be important in this regard. It has been reported that increased cardiovascular disease and diabetes occur among overweight adults who were lean as adolescents.[15,38] The present study did not address this issue, due to limitations of sample size.

Although BMI does not reflect body fatness exclusively, the overweight study cohort also displayed increased skinfold thicknesses and ratios of subscapular to triceps skinfold thickness, measures of body fat pattern and truncal fat distribution. This may reflect the central deposition of fat that occurs in adolescence.[9,39] The adverse impact of obesity, especially central body fatness, on cardiovascular risk factor variables is well known.[23-26] Consistent with this relationship, the overweight study cohort showed an adverse serum lipoprotein level, blood pressure, and plasma insulin and glucose levels. This is noteworthy, because in the current study overweight individuals were compared with moderately lean individuals rather than with those in the lowest quartile of BMI.

From the clinical viewpoint, a markedly higher prevalence of hypertension (especially among black subjects) and dyslipoproteinemia (especially among white males) was noted in the overweight cohort versus the lean cohort. Of particular interest is that the prevalence of parental history of diabetes mellitus and hypertension was also significantly higher in the overweight cohort. Parental history may be a surrogate measure of future risk of morbidity in this relatively younger adult cohort, given the familial aggregation or resemblance of obesity.[40,41] Although not statistically significant, 2.4% of the overweight cohort expressed frank diabetes mellitus, versus none in the lean group. There was no increase in the prevalence of heart attack in parents of the overweight cohort. The reason for this is not clear. The multifactorial nature of coronary artery disease[42] might have obscured the association.

The present study demonstrates that adverse serum lipoprotein levels, plasma insulin level, and systolic blood pressure cluster strongly in the overweight cohort. The clinically evident ubiquitous association of hyperinsulinemia/insulin resistance, hypertension, and dyslipidemia seen among obese middle-aged adults has been termed syndrome X,[43] the deadly quartet,[44] and the insulin resistance syndrome.[45] Insulin resistance is considered to play a pathogenic role in this multiple metabolic disorder.[43-45] The link between obesity and insulin resistance and the attendant hyperinsulinemia is well known.[24,46] In terms of dyslipidemia, increased VLDL synthesis in the presence of hyperinsulinemia/insulin resistance has been attributed to increased transport of glucose and free fatty acids, substrates that promote hepatic triglyceride synthesis,[47,48] or alternatively, reduced adipose tissue lipoprotein lipase activity and the attendant inhibition of VLDL clearance from the circulation.[49] Regarding hypertension, hyperinsulinemia/insulin resistance could elevate blood pressure in different ways, ie, (1) by increasing renal sodium retention,[50] (2) by disturbing cell membrane cation transport,[51] (3) by stimulating the sympathetic nervous system,[52] and (4) by increasing proliferation of smooth muscle cells.[53]

Earlier, we noted that "healthy" young adults with elevated VLDL cholesterol levels displayed clustering of adverse insulin level, subscapular skinfold thickness, and systolic blood pressure.[54] These individuals as a group also had increased subscapular skinfold thicknesses, postglucose plasma insulin level, and fasting and postglucose plasma free fatty acid levels in childhood. However, a

considerable proportion of these individuals displayed increased insulin levels, but did not show a concomitant increase in subscapular skinfold thickness. Further, in a related study, we found that clustering, measured in terms of risk ratio, was markedly reduced but remained significant after adjusting for subscapular skinfold thickness.[55] These observations suggest that insulin resistance, as well as truncal obesity, may underlie the clustering early in life.

Because adolescent overweight is associated with adult overweight and related multiple cardiovascular risk factors in young adults, there is a need for prevention in early life. Further, an upward secular trend for being overweight during childhood underscores the need for early prevention.[10,56] Therefore, universal adoption of a healthy lifestyle such as eating a prudent diet and exercising, if undertaken early in life, may have a long-term salutary effect in preventing adult obesity and related morbidity and mortality.

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REFERENCES

1. National Institutes of Health Consensus Development Conference: Health implications of obesity. Ann Intern Med 103:981-1077, 1985

2. Garrison RJ, Wilson PW, Castelli WP, et al: Obesity and lipoprotein cholesterol in the Framingham Offspring Study. Metabolism 29:1053-1060, 1980

3. Stamler R, Stamler J, Reidlinger WF, et al: Weight and blood pressure: Findings in hypertensive screening of one million Americans. JAMA 240:1607-1610, 1978

4. Aristimuno GG, Foster TA, Voors AW, et al: Influence of persistent obesity in children on cardiovascular risk factors: The Bogalusa Heart Study. Circulation 69:895-904, 1984

5. Lauer RM, Burns TL, Clarke WR, et al: Childhood predictors of future blood pressure. Hypertension 18:174-181, 1991 (suppl 3)

6. Wattigney WA, Harsha DW, Srinivasan SR, et al: Increasing impact of obesity on serum lipids and lipoproteins in young adults. The Bogalusa Heart Study. Arch Intern Med 151:2017-2022, 1991

7. Freedman DS, Srinivasan SR, Burke GL, et al: Relation of body fat distribution to hyperinsulinemia in children and adolescents: The Bogalusa Heart Study. Am J Clin Nutr 46:403-410, 1987

8. Laskarzewski P, Morrison JA, Mellies MJ, et al: Relationships of measurements of body mass to plasma lipoproteins in school children and adults. Am J Epidemiol 111:395-406, 1980

9. Deutsch MI, Mueller WH, Malina RM: Androgyny in fat patterning is associated with obesity in adolescents and young adults. Ann Hum Biol 12:275-286, 1985

10. Harlan WR: Epidemiology of childhood obesity. A national perspective. Ann NY Acad Sci 699:1-5, 1993

11. Mossberg HO: 40-year follow-up of overweight children. Lancet 2:491-493, 1989

12. Hoffmans MDAF, Kromhout D, deLezenne Coulander C: The impact of body mass index of 78,612 18-year-old Dutch men on 32-year mortality from all causes. J Clin Epidemiol 41:749-756, 1988

13. Nieto FJ, Szklo M, Comstock GW: Childhood weight and growth rate as predictors of adult mortality. Am J Epidemiol 136:201-213, 1992

14. Must AP, Jacques PF, Dallal GE, et al: Long-term morbidity and mortality of overweight adolescents: A follow-up of the Harvard Growth Study of 1922 to 1935. N Engl J Med 327:1350-1355, 1992

15. Abraham S, Collins G, Nordsieck M: Relationship of childhood weight status to morbidity in adults. HSMHA Health Rep 86:273-284, 1971

16. Berenson GS, McMahan CA, Voors AW, et al: Cardiovascular Risk Factors in Children—The Early Natural History of Atherosclerosis and Essential Hypertension. New York, NY, Oxford University Press, 1980, pp 1-453

17. Berenson GS (ed): Causation of Cardiovascular Risk Factors in Children: Perspectives on Cardiovascular Risk in Early Life. New York, NY, Raven, 1986, pp 11-408

18. Allain CC, Poon LS, Chan CSG, et al: Enzymatic determination of total serum cholesterol. Clin Chem 20:470-475, 1974

19. Bucolo G, David H: Quantitative determination of serum triglycerides by the use of enzymes. Clin Chem 19:476-482, 1973

20. Srinivasan SR, Berenson GS: Serum lipoproteins in children and methods for study, in Lewis LA (ed): CRC Handbook of Electrophoresis, vol 3. Lipoprotein Methodology and Human Studies. Boca Raton, FL, CRC, 1983, pp 185-204

21. SAS Institute: SAS/STAT User's Guide, version 6 (ed 4). Cary, NC, SAS Institute, 1989

22. Ramirez ME, Mueller WH: The development of obesity and fat patterning in Tokelan children. Hum Biol 52:675-687, 1980

23. Després JP, Allard C, Tremblay A, et al: Evidence for a regional component of body fatness in the association with serum lipids in men and women. Metabolism 34:967-973, 1985

24. Peiris AN, Sothmann MS, Hennes M, et al: Relative contribution of obesity and body fat distribution to alterations in glucose insulin homeostasis: Predictive values of selected indices in premenopausal women. Am J Clin Nutr 49:758-764, 1989

25. Freedman DS, Srinivasan SR, Harsha DW, et al: Relation of body fat patterning to lipid and lipoprotein concentrations in children and adolescents: The Bogalusa Heart Study. Am J Clin Nutr 50:930-939, 1989

26. Haffner SM, Stern MP, Hazuda HP, et al: Do upper-body and centralized adiposity measure different aspects of regional body-fat distribution? Relationship to noninsulin-dependent diabetes mellitus, lipids, and lipoprotein. Diabetes 36:43-51, 1987

27. National Cholesterol Education Program: Report of the National Cholesterol Education Program Expert Panel in detection, evaluation and treatment of high blood cholesterol in adults. Arch Intern Med 148:36-69, 1988

28. National High Blood Pressure Education Program Working Group: Report on primary prevention of hypertension. Arch Intern Med 153:186-208, 1993

29. National Diabetes Data Group: Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. Diabetes 28:1039-1057, 1979

30. Freedman DS, Shear CL, Burke GL, et al: Persistence of juvenile-onset obesity over eight years: The Bogalusa Heart Study. Am J Public Health 77:588-592, 1987

31. Berenson GS, Srinivasan SR, Wattigney WA, et al: Obesity and cardiovascular risk in children. Ann NY Acad Sci 699:93-103, 1993

32. Lauer RM, Lee J, Clark WR: Factors affecting the relation-

ship between childhood and adult cholesterol levels. The Muscatine Study. Pediatrics 82:309-318, 1988

33. Rolland-Cachera MF, Bellisle F, Sempe M: The prediction in boys and girls of the weight/height index and various skinfold measurements in adults: A two-decade follow-up study. Int J Obes 13:305-311, 1989

34. Stark O, Atkins E, Wolff OH, et al: Longitudinal study of obesity in the National Survey of Health and Development. Br Med J 283:13-17, 1981

35. Serdula MK, Ivery D, Coates RJ, et al: Do obese children become obese adults? A review of the literature. Prev Med 22:167-177, 1993

36. Kumanyika S: Ethnicity and obesity development in children. Ann NY Acad Sci 699:81-92, 1993

37. National Center for Health Statistics: Anthropometric Reference Data and Prevalence of Overweight, United States, 1976-80. Rockville, MD, US Department of Health and Human Services, Publication No. (PHS) 017-023-01023-2, 1986

38. Holbrook TL, Barrett-Connor E, Wingard DL: The association of lifetime weight and weight control patterns with diabetes among men and women in the adult community. Int J Obes 13:723-729, 1989

39. Baumgartner RN, Roche AF, Guo S, et al: Adipose tissue distribution: The stability of principal components by sex, ethnicity, and maturation stage. Hum Biol 58:719-736, 1986

40. Garn SM, Bailey SM, Solomon MA, et al: Effects of remaining family members on fatness prediction. Am J Clin Nutr 34:148-153, 1981

41. Price RA, Stunkard AJ, Ness R, et al: Childhood onset (age <10) obesity has high familial risk. Int J Obes 14:185-195, 1990

42. Castelli WP: Epidemiology of coronary heart disease: The Framingham Study. Am J Med 76:4-12, 1984

43. Reaven GM: Role of insulin resistance in human disease. Banting Lecture 1988. Diabetes 37:1595-1607, 1988

44. Kaplan NM: The deadly quartet: Upper-body obesity, glucose intolerance, hypertriglyceridemia, and hypertension. Arch Intern Med 149:1514-1520, 1989

45. Haffner SM, Valdez RA, Hazuda HP, et al: Prospective analysis of the insulin-resistance syndrome (syndrome X). Diabetes 41:716-722, 1992

46. Olefsky JM, Kolterman OG, Scarlett JA: Insulin action and resistance in obesity and noninsulin-dependent type II diabetes mellitus. Am J Physiol 243:E15-E30, 1982

47. Kissebah AH, Adams PW, Wynn V: Interrelationship between insulin secretion and plasma free fatty acid and triglyceride transport kinetics in maturity onset diabetes and the effect of phenethylbignanide (Phenformin). Diabetologia 10:119-130, 1974

48. Nikkilä EA: Regulation of hepatic production of plasma triglycerides by glucose and insulin, in Lundquist F, Tygstrup N (eds): Regulation of Hepatic Metabolism. Copenhagen, Denmark, Munksgaard, 1974, pp 360-387

49. Pykälisto OJ, Smith PH, Brunzell JD: Determinants of human adipose tissue lipoprotein lipase: Effect of diabetes and obesity on basal diet induced activity. J Clin Invest 56:1108-1117, 1975

50. DeFronzo RA: The effect of insulin on renal sodium metabolism—A review with clinical implications. Diabetologia 21:165-171, 1981

51. Resnick LM: Ionic basis of hypertension, insulin resistance, vascular disease, and related disorders. The mechanism of "syndrome X." Am J Hypertens 6:1235-1345, 1993

52. Landsberg L, Krieger D: Obesity, metabolism, and the sympathetic nervous system. Am J Hypertens 2:1255-1325, 1989

53. Stout RW, Bierman EL, Ross R: Effect of insulin on the proliferation of cultured primate arterial smooth muscle cells. Circ Res 36:319-327, 1975

54. Srinivasan SR, Bao W, Berenson GS: Coexistence of increased levels of adiposity, insulin, and blood pressure in a young adult cohort with elevated very–low-density lipoprotein cholesterol: The Bogalusa Heart Study. Metabolism 42:170-176, 1993

55. Smoak CG, Burke GL, Webber LS, et al: Relation of obesity to clustering of cardiovascular disease risk factors in children and young adults: Bogalusa Heart Study. Am J Epidemiol 125:364-372, 1987

56. Shear CL, Freedman DS, Burke GL, et al: Secular trends of obesity in early life: The Bogalusa Heart Study. Am J Public Health 78:75-77, 1988