Age, Sex, and Ethnic Variations in Serum Insulin Concentrations Among U.S. Youth

Findings from the National Health and Nutrition Examination Survey 1999–2002

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OBJECTIVE — Distributions of serum concentrations of insulin among adolescents and young adults are poorly understood in the U.S. The objective of this study was to describe the distribution of serum insulin across demographic characteristics of U.S. adolescents and young adults.

RESEARCH DESIGN AND METHODS — A total of 1,791 male and female subjects aged 12–19 years who participated in the National Health and Nutrition Examination Surveys for 1999–2002 were included in the analyses.

RESULTS — Among male participants, serum concentrations of insulin increased from age 12 to 14 years before decreasing. Among female participants, concentrations were highest at age 13 years before decreasing steadily through age 19 years. Among participants aged 12–17 years but not those aged 18–19 years, females had higher mean log-transformed concentrations than males (*P*, Wald, $F = 0.038$ and 0.125, respectively) after adjusting for age and ethnicity. After adjusting for age and BMI percentile, mean log-transformed concentrations were higher in African-American females aged 12–17 years than in white or Mexican-American participants. No significant ethnic differences were found among female participants aged 18–19 years or male participants aged 12–19 years. Concentrations of insulin increased strongly with increasing levels of BMI.

CONCLUSIONS — These results provide detailed information about serum concentrations of insulin in a representative sample of U.S. adolescents and young adults and may be useful to monitor future trends of this risk factor for diabetes and cardiovascular disease.

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The increase in obesity among children in the U.S. has generated great concern about their future health because of the increased risk of cardiovascular disease and diabetes associated with obesity (1,2). Obesity is associated with insulin resistance, a state characterized by the body's resistance to the actions of insulin, which results in increased insulin production by the pancreas and hyperinsulinemia. Measures of adiposity are generally strongly related to concentrations of insulin (3). In children and adolescents, elevated concentrations of circulating insulin are associated with risk factors for cardiovascular disease such as high blood pressure, dyslipidemia, inflammatory markers, endothelial dysfunction, and cardiovascular reactivity (4–12). Thus, early increases in insulin concentrations may promote early vascular changes that lead to early onset of cardiovascular disease. Furthermore, because high concentrations of insulin may serve as a surrogate marker for insulin resistance (13), a step on the road to diabetes, changes in circulating concentrations of insulin may serve as early indications of future trends in diabetes incidence and prevalence.

These considerations suggest that surveillance of circulating concentrations of insulin may be of critical importance during a time in world history when increases in the prevalence of obesity are occurring in many countries and are expected to continue (14). Such information may be useful in anticipating which particular population groups may be at increased risk for developing adverse events and may help target resources for intervention programs. In general, however, such data are not available in most countries, and even more rarely are such data available from nationally representative samples of the population of country, including the U.S. Our objective was to characterize serum concentrations of insulin for adolescents and young adults in the U.S.

RESEARCH DESIGN AND METHODS

— We examined data from National Health and Nutrition Examination Surveys (NHANES) for 1999–2002 for participants aged 12–19 years. Detailed information about the methods and procedures of this survey is available elsewhere (15,16). In brief, representative samples of the noninstitutionalized civilian U.S. population were selected through a stratified multistage design. Trained interviewers, using a computer-assisted personal interview system, interviewed participants at home. Participants were asked to attend the mobile examination center, where they completed additional questionnaires, underwent various examinations, and provided a blood sample. The study received human subjects approval from the Centers for Disease Control and Prevention.

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Abbreviations: NHANES, National Health and Nutrition Examination Survey.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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Table 1—*Unadjusted mean and geometric mean concentrations of serum insulin* in 1,791 participants aged 12–19 years, National Health and Nutrition Examination Survey 1999–2002*

		Serum insulin (pmol/l)		
	n	Mean ± SE	Geometric mean ± SE	Range
Aged 12–19 years				
Males				
Whites	254	70.63 ± 3.11	60.75 ± 2.12	10.62–358.32
African Americans	282	75.20 ± 2.97	65.22 ± 2.43	15.60–283.38
Mexican Americans	331	83.42 ± 3.63	70.06 ± 2.39	17.76–478.32
BMI percentile				
<85th	602	55.40 ± 1.15	51.34 ± 1.04	10.62–277.02
85th–<95th	142	77.66 ± 4.01	71.06 ± 4.31	4.26–341.58
≥95th	187	133.16 ± 7.13	115.45 ± 5.79	30.90–478.32
Females				
Whites	234	70.78 ± 3.03	63.92 ± 2.64	22.38–345.84
African Americans	225	98.47 ± 4.23	83.21 ± 2.71	23.04–473.16
Mexican Americans	335	85.21 ± 2.82	74.96 ± 2.27	22.80–450.78
BMI percentile				
<85th	564	64.50 ± 2.19	59.95 ± 2.00	22.38–286.14
85th–<95th	136	85.50 ± 3.96	80.44 ± 3.32	31.92–313.14
≥95th	160	135.00 ± 6.58	118.98 ± 4.61	43.32–473.16
Aged 12–17 years				
Males	707	72.93 ± 2.53	62.41 ± 1.63	4.26–478.32
Whites	184	70.97 ± 3.56	60.92 ± 2.08	10.62–358.32
African Americans	218	76.27 ± 3.44	66.58 ± 2.72	15.60–283.38
Mexican Americans	255	83.99 ± 4.14	70.71 ± 2.94	17.76–478.32
BMI percentile				
<85th	443	55.47 ± 1.41	51.40 ± 1.31	10.62–277.02
85th–<95th	116	76.14 ± 4.16	69.74 ± 4.56	4.26–341.58
≥95th	148	135.91 ± 9.78	117.27 ± 7.85	30.90–478.32
Females	676	78.83 ± 2.74	69.23 ± 2.41	22.38–473.16
Whites	190	71.34 ± 3.57	63.76 ± 3.10	22.38–345.84
African Americans	180	100.73 ± 4.54	85.51 ± 2.75	23.04–473.16
Mexican Americans	257	85.63 ± 3.07	75.24 ± 2.27	22.80–450.78
BMI percentile				
<85th	447	65.30 ± 2.69	60.35 ± 2.49	22.38–286.14
85th–<95th	101	84.20 ± 4.63	78.64 ± 3.80	31.92–313.14
≥95th	128	142.12 ± 8.00	125.16 ± 5.84	43.32–473.16
Aged 18–19 years				
Males	224	70.92 ± 3.66	61.40 ± 2.93	21.24–395.40
Whites	70	69.73 ± 5.56	60.29 ± 4.21	21.60–243.54
African Americans	64	71.04 ± 5.31	60.22 ± 4.40	21.24–259.32
Mexican Americans	76	81.41 ± 6.07	67.78 ± 4.00	28.14–395.40
BMI percentile				
<85th	159	55.19 ± 3.01	51.15 ± 2.48	21.24–151.14
85th–<95th	26	84.42 ± 8.72	77.25 ± 8.14	22.14–294.18
≥95th	39	125.16 ± 11.45	110.30 ± 11.27	35.76–395.40
Females	184	74.38 ± 2.53	68.19 ± 2.20	26.46–443.34
Whites	44	68.34 ± 3.70	64.61 ± 3.38	32.10–129.00
African Americans	45	90.27 ± 9.87	75.40 ± 8.17	26.46–260.46
Mexican Americans	78	83.96 ± 6.99	74.16 ± 5.16	34.38–443.34
BMI percentile				
<85th	117	61.01 ± 2.60	58.25 ± 2.43	26.46–158.88
85th–<95th	35	88.74 ± 5.22	85.11 ± 4.91	46.62–190.32
≥95th	32	111.42 ± 9.11	100.60 ± 8.57	52.56–443.34

*To convert from picomoles per liter to units per milliliter, divide by 6.945.

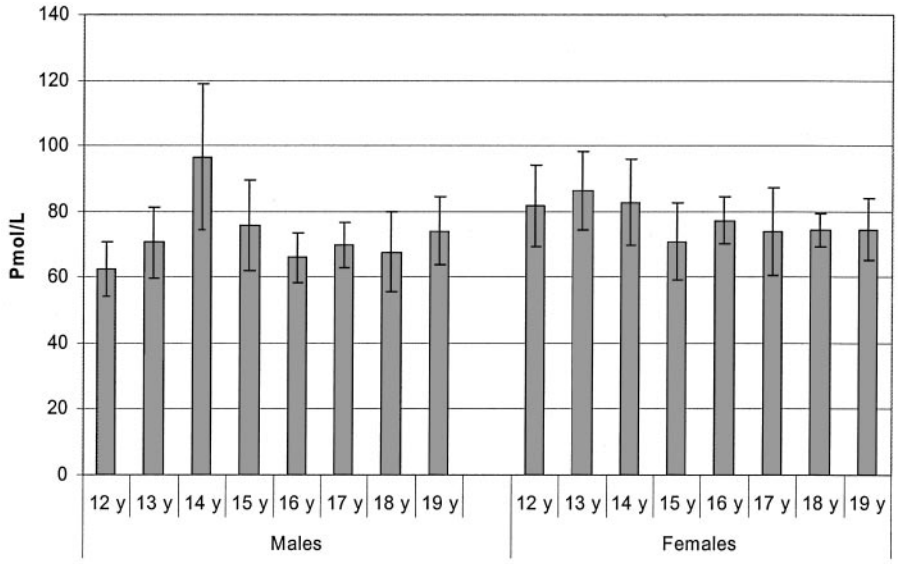

Figure 1—*Unadjusted geometric mean concentrations (95% CI) of serum insulin among 1,791 youth aged 12–19 years by sex and age, NHANES 1999–2002.*

All insulin assays for NHANES 1999–2002 were performed in the same laboratory at the University of Missouri, Columbia, using the same method. Serum specimens were frozen at <−70°C, shipped on dry ice, and stored at <−70°C until analysis. The serum insulin concentration was measured using a radioimmunoassay kit (Pharmacia Diagnostics, Uppsala, Sweden). Quality control procedures following modified Westgard rules were used; these included both within- and between-assay quality control measures as well as monitoring of trend. The coefficient of variation of the method was 5.0–6.9% during the 4 years of the study.

We included participants aged 12–19 years who attended the morning examination and who had fasted at least 8 h. We excluded females who were pregnant, and participants with diabetes. We included age, sex, ethnicity, and BMI percentiles as covariates. We categorized age into two groups: 12–17 years and 18–19 years. This categorization was done for several reasons. First, the gap in terms of maturation between a 12 year-old and a 19 year-old is substantial. Second, the division was based on sociocultural reasons. Third, using a cut point of 18 years may facilitate comparisons of the results from the present analyses with those of other studies. Finally, having adequate sample size for analyses also played a role in determining how many age categories were feasible. For analyses stratified by ethnicity, we only included whites, African Americans, and Mexican Americans because the sample sizes for other participants were relatively small. We present means and geometric means with SEM or 95% CIs. For regression analyses, concentrations of insulin were log-transformed to improve the distribution of this variable. To account for the complex sampling design, SUDAAN version 9.0 software was used to calculate means and to perform linear regression analyses. Percentiles were calculated with SAS version

Table 2—*Selected percentiles of serum concentrations of insulin* among 1,791 participants aged 12–19 years, National Health and Nutrition Examination Survey 1999–2002*

		Percentiles of serum insulin (pmol/l)								
	n	15	20	25	40	50	60	75	80	85
Males										
Age (years)										
12–13	249	33.90	40.86	42.30	50.82	56.40	64.86	81.72	89.76	98.94
14–15	199	43.74	45.60	48.66	59.40	63.00	71.94	92.88	96.66	120.30
16–17	259	38.22	40.86	47.16	54.12	59.58	65.46	78.54	84.60	88.62
18–19	224	37.08	38.82	41.34	51.36	56.58	62.40	84.72	99.30	108.90
Females										
Age (years)										
12–13	253	47.22	51.24	52.92	61.50	69.96	78.84	102.48	108.90	118.20
14–15	214	43.02	46.38	49.80	60.54	65.34	74.28	90.00	101.88	114.42
16–17	209	43.20	47.16	49.26	58.50	64.56	73.02	82.56	88.74	98.46
18–19	184	46.74	50.34	51.42	58.86	63.00	70.62	86.46	92.70	105.30
Race or ethnicity										
Males										
White	254	37.62	40.86	44.76	53.28	57.78	63.00	78.66	88.20	98.22
African American	282	40.02	42.90	46.32	55.38	62.58	71.64	88.74	98.28	108.60
Mexican American	331	40.74	43.14	46.92	57.78	65.64	74.22	95.28	108.48	126.24
Females										
White	234	42.54	46.44	49.02	57.96	62.40	69.54	84.00	87.72	101.64
African American	225	47.04	52.02	55.14	67.74	79.44	90.48	120.72	132.36	156.66
Mexican American	335	48.30	51.06	54.42	63.06	70.98	79.68	100.02	109.08	120.84

*To convert from picomoles per liter to units per milliliter, divide by 6.945.

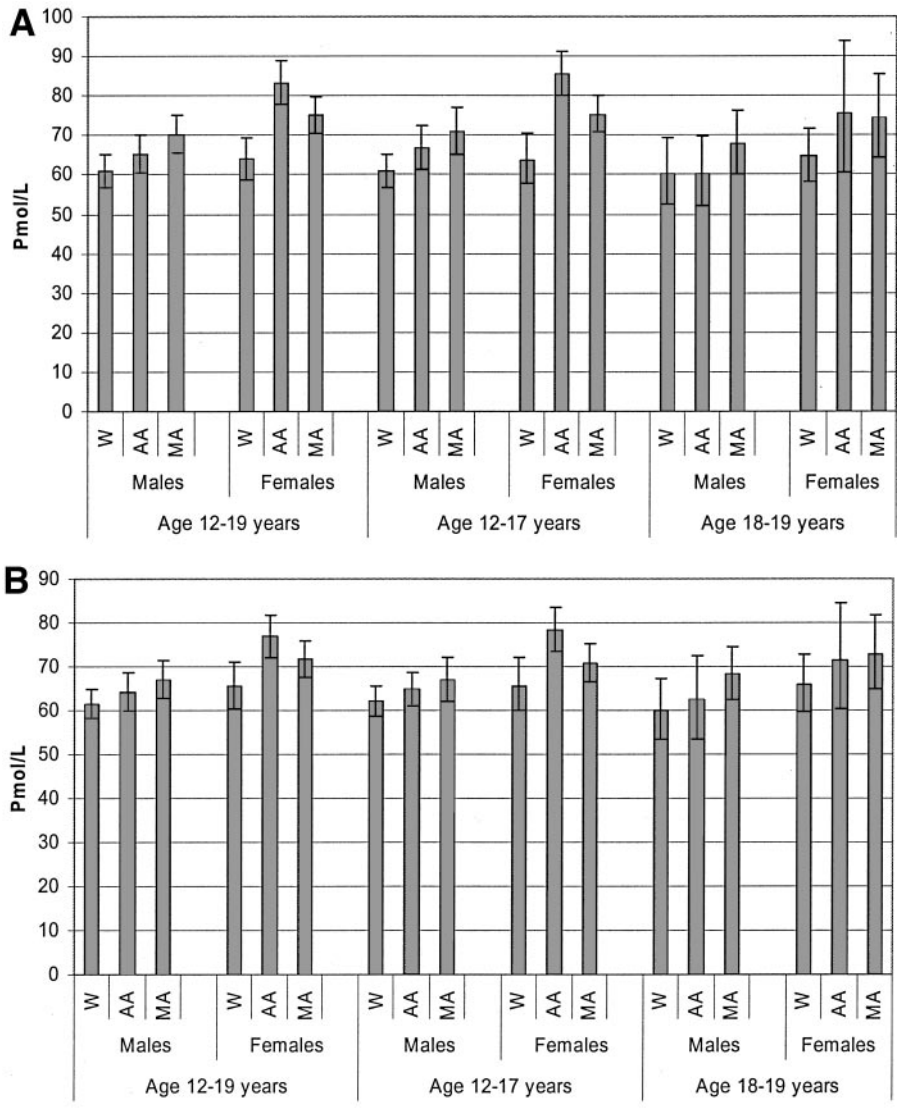

Figure 2—*Geometric mean (95% CI) concentrations of insulin among 1,791 participants aged 12–19 years, by age, sex, and ethnicity, NHANES 1999–2002. A: Unadjusted results. B: Adjusted for age and BMI percentile. W, whites; AA, African Americans; MA, Mexican Americans.*

8.2. Sampling weights were used to calculate measures of central tendency, percentiles, and regression estimates.

RESULTS — A total of 1,791 participants aged 12–19 years who attended the morning examination had a value for insulin. These included 931 male and 860 female subjects, 488 whites, 507 African Americans, 666 Mexican Americans, and 130 other participants.

Unadjusted mean and geometric mean concentrations of serum insulin are shown in Table 1. The pattern of geometric mean concentrations of insulin by age differed somewhat according to sex (Fig. 1). Among male participants, concentrations increased from age 12 to 14 years before decreasing somewhat. Among female participants, concentrations were highest at age 13 years before decreasing steadily through age 19 years. Selected percentiles of concentrations of insulin are shown in Table 2. Among participants aged 12–17 years but not among those aged 18–19 years, females had higher log-transformed concentrations of insulin than males (*P*, Wald, $F = 0.038$ and 0.125, respectively) after adjusting for age and ethnicity.

In unadjusted analyses of participants aged 12–17 years, ethnic variation was present among both males (*P*, Wald, $F = 0.006$) and females (*P*, Wald, $F < 0.001$). No significant ethnic variation occurred among male or female participants aged 18–19 years. Among participants aged 12–17 years, mean log-transformed concentrations did not vary significantly by ethnicity among males (*P*, Wald, $F = 0.199$) but did so among females (*P*, Wald, $F = 0.021$) after adjusting for age and BMI percentile in linear regression analysis (Fig. 2). African-American females had higher concentrations of insulin than white or Mexican-American females. Among participants aged 18–19 years, no significant ethnic differences were present among male and female participants. BMI was strongly associated with concentrations of insulin among both male and female participants (Fig. 3).

CONCLUSIONS — These data represent the first nationally representative information about the distributions of fasting insulin concentrations among youth in the U.S., and they show significant demographic variation. Concentrations were higher among females than males. Significant ethnic variation was present among female participants aged 12–17 years but not among those aged 18–19 years.

In many studies conducted in the U.S., African-American children and adolescents were found to have higher concentrations of insulin than white children (4,6,17–26). Among 2,996 Bogalusa Study participants aged 5–17 years, the difference in median concentrations of insulin between whites and African Americans was larger among females than males (3). However, in one study, the ethnic difference was eliminated after adjustment for fat mass quantified using dual energy X-ray absorptiometry (26). Factors that may account for the difference between African-American and white children and adolescents include lower insulin clearance, lower insulin sensitivity, and higher insulin secretion (24–28). Given the high prevalence of diabetes among African Americans and Mexican Americans compared with whites in the U.S. and the high mortality rates from coronary heart disease among African Americans compared with whites, the high concentrations of insulin among these groups, especially females, underscore the fact that the roots for these diseases can often be traced back to childhood. Our findings also underscore the wisdom of trying to prevent the development of disease and risk factors at an early age.

Fewer studies have compared concentrations of insulin among Hispanic

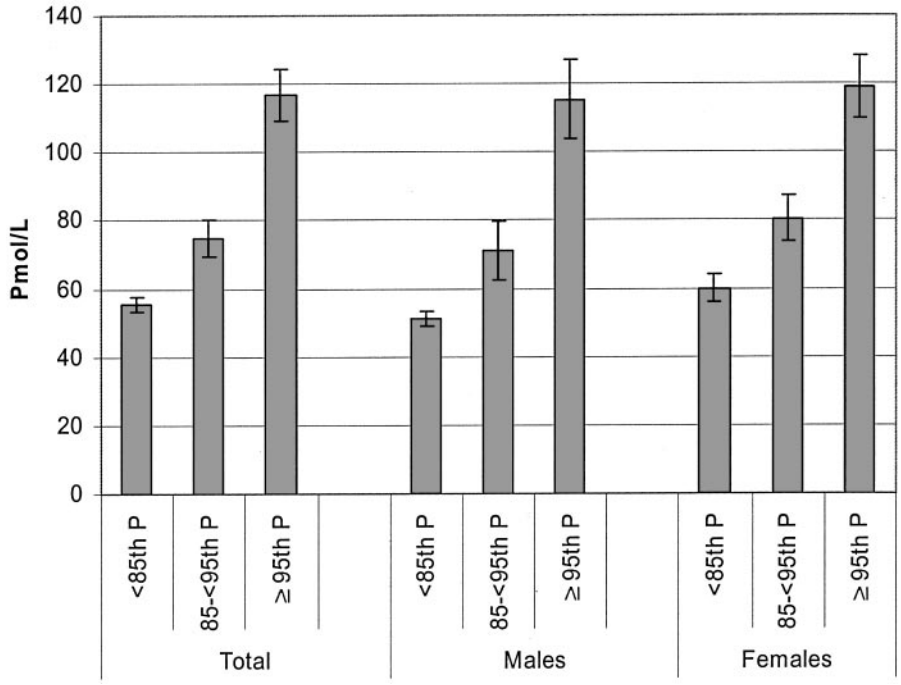

Figure 3—*Unadjusted geometric mean (95% CI) concentrations of insulin among 1,791 participants aged 12–19 years by percentiles of BMI, NHANES 1999–2002.*

and white children and adolescents. In a study of 403 third graders in Corpus Christi, Texus, median concentrations were higher in Mexican Americans than in whites (29). Among children from the Los Angeles area, concentrations of insulin were higher among 28 Hispanic children than 14 among Caucasian children (25). In a study of 491 Hispanic children aged 2–3 years from New York City, concentrations of insulin were higher in girls than in boys (11). In the San Diego Study of Children's Activity and Nutrition, concentrations of insulin were higher in 54 Mexican American children than in 29 white children at age 11 years (30). Although the median concentration of insulin was still higher in Mexican American children than in white children, 6 years later the difference was not significant.

Most studies conducted in U.S. youth have also shown that concentrations of insulin are higher in females than in males (31). Among 90 Pima Indian children aged 5 and 10 years, concentrations of insulin were similar in boys and girls aged 5 years but were higher in girls than in boys at the age of 10 years (32). In addition, many studies conducted in other countries have also reported higher circulating concentrations of insulin in females than in males (33–38). However, in some studies no sex differences were found (38,39).

Our results showing a large increase in fasting concentrations of insulin in those who were overweight compared with those who were not reiterate some of the negative physiological consequences of excess weight. In addition, the significant increase in concentrations of insulin among those who were at risk for being overweight shows that even this degree of excess weight produces unfavorable physiological changes.

A limitation of our study is the lack of data on pubertal status and serum androgens, estrogens, or growth hormone. Such information would be helpful to describe the difference in distribution of insulin concentrations among teens at different pubertal stages, when elevated values may reflect either a normal physiological state or a pathological one. For now, our results suggest that fasting serum insulin concentrations peak earlier in girls than in boys. The lack of insulin values for subjects <12 years of age, when some youth, mostly girls, may enter early pubertal development, precludes our ability to comment on the distribution of insulin among preadolescent children. Previous NHANES surveys did not collect serum insulin on adolescents, so comparisons to a group of U.S. teens that were less overweight than this sample are not possible.

Although the relative merit of surrogate markers for insulin resistance continues to be researched, fasting concentrations of insulin correlate about as well with measures of insulin resistance determined by gold standard methods as other surrogate markers. In four studies, correlation coefficients between fasting concentrations of insulin and measures of insulin sensitivity/resistance determined by gold standard methods ranged from 0.4 to 0.91 (28,40–42). In three of these studies, the correlation coefficients ranged from 0.8 to 0.91 (28,41,42).

In our analysis, we examined fasting serum concentrations of insulin, one facet of a complex physiological picture. Glucose loading or meals elicit a greater insulin response in African Americans than in whites (17,43). Unfortunately, measures of stimulated insulin response were not available in the NHANES data set.

In summary, fasting concentrations of insulin showed significant demographic differences. Geometric mean concentrations were higher in females than in males and peaked at age 14 years in males and 13 years in females. The only ethnic or racial differences occurred in females aged 12–17 years among whom geometric mean concentrations were higher in African Americans than in whites or Mexican Americans. The increases in obesity among U.S. youth, the strong links between obesity and hyperinsulinemia and insulin resistance, and the effects of hyperinsulinemia and insulin resistance on cardiovascular disease and diabetes suggest that surveillance of concentrations of insulin in the population, particularly in children and adolescents, may be useful to assess early effects of obesity on health and to allow international comparisons. For example, a report on the distribution of serum insulin in Canadian youth collected in 1999 showed median values of plasma insulin to be lower than those in comparable groups of U.S youth (35). The values reported for 13-year-old boys were lower than those for the 12- to 13-year-old boys in this study (41.9 vs. 56.4 pmol/l), and values for the 16-year-old boys were lower than those for the 16- to 17-year-old boys (38.7 vs. 59.58 pmol/l). These differences may be attributable to differences in race or ethnicity or distribution of obesity. Assay variability may be a significant reason for these differences, highlighting the need for achieving standardization in insulin measurements among laboratories (44) to facilitate surveillance.

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