19. Diem, K., and Lenter, C., editors: Scientific tables, 7Ed. Ciba-Geigy Ltd., Basle, Switzerland, 1973, pp. 107-108, 189.
20. DeCoufle, P.: Occupation. *In* Cancer epidemiology and prevention, edited by D. Schottenfeld and J. F. Fraumeni. W. B. Saunders, Philadelphia, PA, 1982, pp. 318-335.
21. Newhouse, M. L., Berry, G., Wagner, J. C., and Turok, M. E.: A study of mortality of female asbestos workers. Brit J Ind Med 29: 134-141 (1972).
22. Wignall, B. K., and Fox, A. J.: Mortality of female gas mask assemblers, Brit J Ind Med 39: 34-38 (1982).

Correlates and Predictors of Serum Total Cholesterol in Adolescents Aged 12–17 Years: the National Health Examination Survey

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Synopsis

To examine correlates and childhood predictors of serum total cholesterol in adolescence, measures of growth, development, and obesity were related to serum total cholesterol levels of youths aged 12-17 years in the National Health Examination Survey. In this sample, drawn from the U.S. population, serum total cholesterol levels were negatively correlated with indicators of growth and maturation in males aged 12-14 years and positively correlated with overweight or obesity at all ages.

All measured variables could account for less than 15 percent of cholesterol variation in males and less than 6 percent in females. In white males, indicators of levels of maturation, growth, and changes in body fatness measured 28-53 months earlier were significant predictors of serum total cholesterol in adolescence, explaining 13 percent of its variation. Despite significant associations, indicators of growth, sexual maturation, and obesity explained only a small fraction of serum cholesterol variation in adolescents.

SERUM TOTAL CHOLESTEROL concentration is a major risk factor for coronary heart disease in adults (*1*). Arteriosclerotic changes may appear in the coronary arteries as early as the second and third decades of life (*2*). Furthermore, serum total cholesterol tracking has been demonstrated in adults and over followup periods of at least 9 years in children (*3-6*). Therefore, the determinants of serum total cholesterol in childhood and adolescence are of interest both for understanding the origins of coronary risk and for coronary prevention.

National population estimates have been published of serum total cholesterol levels in adolescents as well as the associations of cholesterol with age, sex, race, region, income, and education (*7-9*). Other correlates of serum total cholesterol in youths aged 12–17 years and childhood predictors of serum total cholesterol in adolescence were examined.

Methods

The third cycle of the National Health Examination Survey (HES) was conducted on a nationwide multistage probability sample of 7,514 youths from the noninstitutionalized population of the United States, aged 12–17 years. The survey started in March 1966 and ran until March 1970. Out of the 7,514 youths selected for the sample, 6,768 (90 percent) were examined. There were 5,735 whites, 999 blacks, and 34 others.

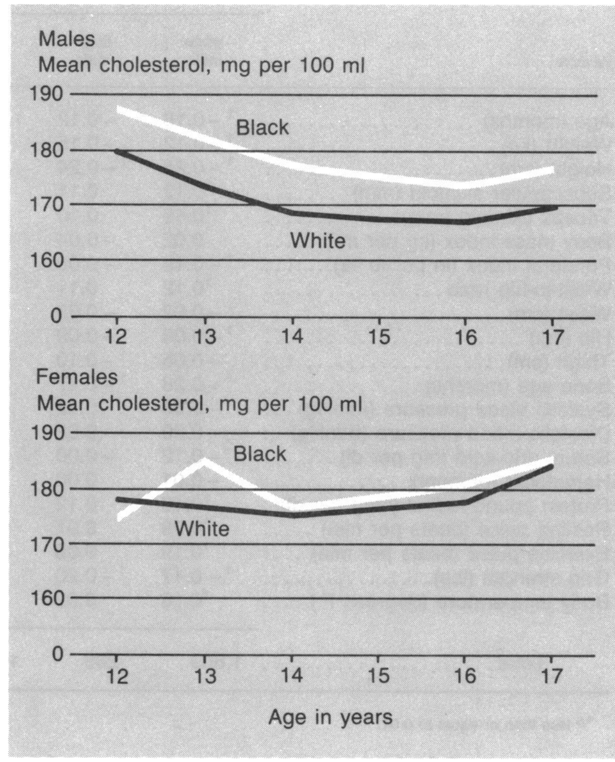
Details of the plan, sampling, response, and operation were published previously, as were procedures for informed consent and confidentiality of data (*10*). Demographic, medical history, and behavioral information was collected by household interview and self-administered questionnaires prior to the examination.

Conducted in a mobile center, the examination included a pediatrician's assessment of breast development stage in girls, male genital development stage in boys, and pubic hair stage in both sexes (*11*). A blood sample was taken with the subject in the supine position. At the discretion of the physician, a tourniquet was used to fill the vein; however, once the needle was inserted into the vein, the tourniquet was taken off the arm so that the blood flowed freely. Each tube of blood was labeled with the examinee's number and left in the test tube holding rack at room temperature for 1 hour, then placed in the laboratory refrigerator. After preliminary laboratory preparation, the serum samples were packed into specially devised styrofoam containers for shipment via air freight to the Lipid Standardization Laboratory at the Centers for Disease Control, where they were kept frozen until assay (*7*).

After being thawed, samples were divided and stored in two vials. All sample vials were then randomized over a 6-day period so that a pair of duplicate samples might have been analyzed on the same day or as many as 6 days apart. A semiautomated method based on the Abell-Kendall procedure was employed to measure total cholesterol (*7*). Determinations were carried out on an assembly line basis so that two analysts could analyze more than 120 samples in duplicate per day. If a difference greater than 9 milligrams per deciliter (mg per dl) was found in duplicate determinations, a second set of determinations was performed. An extra blood sample was drawn for replicate studies on 424 examinees, of which 98 percent were adequate. The analyses of replicates and originals were performed under identical laboratory conditions by the same technician in a true double blind manner.

Frequency and percent distributions have been published of the absolute differences between the duplicated determinations on the original specimen and also between the duplicated determinations on the replicate and original specimens (*7*). For these distributions, the coefficient of variation was less than 5 percent for determinations on original and replicate specimens and less than 2 percent for duplicated determinations on the original specimen. Serum uric acid concentration was measured by the Technicon auto-analyzer-1 method, and protein-bound iodine was measured as described (*10,12*).

Mean cholesterol levels of male and female youths 12–17 years of age by age and race: United States, 1966–70.



SOURCE: National Center for Health Statistics, reference 7.

Blood type was measured at the immunogenetics laboratory of the Johns Hopkins University (*13*).

A nurse measured blood pressure supine at the beginning and end of the physician's examination using a mercury sphygmomanometer as described (*14*). The average of the readings was used in the present analysis. In the HES, diastolic pressure was defined as the complete cessation of sounds. If sounds failed to disappear, the pressure at which muffling occurred was used. A pediatric or adult cuff was used as appropriate.

Heart rate was measured from a electrocardiogram monitor strip containing 15 to 20 clear complexes taken with the subject standing quietly prior to a 5-minute treadmill exercise test (*10*). An ECG monitor strip was recorded again at the end of the exercise test for the 5-minute exercise heart rate. The grade of the treadmill was zero degrees for the first 2 minutes, and was raised to 10 degrees for the last 3 minutes of the test. The calibrated treadmill speed was 3.5 miles per hour for the entire test. The subject was instructed to walk naturally with hips straight, head up and arms swinging. ECG measurements were made by an expert consultant. Room temperature was main-

Table 1. Correlations of serum cholesterol with other variables in youths 12–17 years of age; Health Examination Survey

	12–14 years				*15–17 years*			
Variable	*White male*	*Black male*	*White female*	*Black female*	*White male*	*Black male*	*White female*	*Black female*
Age (months)	[1]−0.18	−0.12	−0.04	−0.03	−0.01	0.03	[1]0.09	0.06
Weight (kg)	[1]−0.12	−0.15	0.01	0.01	[1]0.16	0.12	[1]0.08	0.05
Height (cm)	[1]−0.26	[1]−0.24	−0.05	−0.06	−0.04	0.00	−0.04	−0.13
Subscapular skinfold (mm)	[1]0.12	0.11	[1]0.07	0.08	[1]0.22	0.09	[1]0.11	0.10
Triceps skinfold (mm)	[1]0.19	0.10	0.05	0.09	[1]0.19	0.02	[1]0.11	0.03
Body mass index (kg per m^2)	0.02	−0.04	0.04	0.04	[1]0.21	0.16	[1]0.11	0.11
Ponderal index (in per lb ⅓)	[1]−0.12	−0.06	−0.05	−0.05	[1]−0.21	−0.15	[1]−0.12	0.14
Waist-to-hip ratio	[1]0.12	0.11	0.06	−0.03	[1]0.13	−0.03	[1]0.07	[1]0.18
Waist (cm)	−0.02	−0.03	0.04	0.01	[1]0.20	0.14	[1]0.11	[1]0.17
Hip (cm)	[1]−0.08	−0.09	0.00	0.03	[1]0.17	0.15	[1]0.09	0.09
Thigh (cm)	−0.05	−0.10	0.01	0.03	[1]0.17	0.13	[1]0.08	0.05
Bone age (months)	[1]−0.28	[1]−0.17	[1]−0.08	−0.08	0.01	−0.08	0.02	−0.00
Systolic blood pressure (mmHg)	−0.06	−0.12	0.04	0.06	[1]0.14	0.04	0.02	0.08
Diastolic blood pressure (mmHg)	−0.00	−0.02	0.05	0.08	[1]0.11	0.10	[1]0.08	−0.03
Serum uric acid (mg per dl)	[1]−0.12	−0.00	[1]0.08	−0.07	[1]0.07	−0.10	[1]0.08	−0.06
Hematocrit (percent)	−0.01	0.00	[1]0.15	[1]0.17	[1]0.13	[1]0.19	[1]0.11	−0.10
Protein bound iodine (mcg per dl)	[1]0.13	0.12	0.06	0.11	[1]0.09	0.00	[1]0.10	[1]0.33
Resting pulse (beats per min)	[1]0.09	0.07	0.05	−0.09	[1]0.09	−0.01	[1]0.11	0.08
Exercise pulse (beats per min)	[1]0.19	0.08	[1]0.10	−0.01	[1]0.11	0.07	[1]0.09	0.08
Grip strength (lbs)	[1]−0.17	[1]−0.20	−0.01	−0.02	0.03	−0.06	0.03	0.04
Body temperature (degrees F.)	[1]0.10	0.02	−0.01	−0.11	0.05	−0.06	−0.01	−0.12
Total	1,609	268	1,428	280	1,438	209	1,258	240

[1]*P* less than or equal to 0.01.

Table 2. Relationship of serum cholesterol with subscapular skinfold, waist-to-hip ratio, and serum protein bound iodine, by age of youths 12–17 years of age; Health Examination Survey

	Subscapular skinfold				*Waist-to-hip ratio*				*Protein-bound iodine*			
Age in years	*White male*	*Black male*	*White female*	*Black female*	*White male*	*Black male*	*White female*	*Black female*	*White male*	*Black male*	*White female*	*Black female*
12	0.13	0.13	0.06	−0.04	0.10	−0.04	0.11	0.08	0.11	[1]0.27	0.11	0.09
13	[1]0.13	0.17	0.10	0.06	[1]0.10	0.17	0.06	−0.10	[1]0.21	0.16	−0.03	0.19
14	[1]0.13	0.06	0.05	0.19	0.09	0.17	0.01	−0.05	−0.01	−0.04	0.09	0.05
15	[1]0.18	0.07	0.09	0.09	[1]0.11	−0.14	0.05	0.04	0.08	0.15	0.00	0.22
16	[1]0.25	0.29	[1]0.14	0.11	0.13	−0.12	0.02	0.09	−0.03	0.09	0.11	[1]0.34
17	[1]0.25	−0.00	0.10	0.08	[1]0.19	0.14	[1]0.17	[1]0.38	[1]0.15	−0.27	[1]0.19	[1]0.47

[1]*P* less than or equal to 0.01.

Table 3. Correlations of serum cholesterol with stage of sexual maturation and skeletal age in youths 12–17 years of age; Health Examination Survey

	12–14 years				*15–17 years*			
Variable	*White male*	*Black male*	*White female*	*Black female*	*White male*	*Black male*	*White female*	*Black female*
Bone age	[1]−0.19	[1]−0.12	[1]−0.06	−0.06	0.02	−0.07	−0.00	0.01
Pubic hair	[1]−0.21	[1]−0.17	−0.03	0.01	0.00	−0.03	0.02	[1]0.13
Male genital	[1]−0.20	[1]−0.13	...	...	−0.00	−0.06	...	...
Right breast	...	...	[1]−0.06	0.01	...	...	[1]0.09	0.12
Left breast	...	...	[1]−0.06	−0.01	...	...	[1]0.09	[1]0.14

[1]*P* less than or equal to 0.01.

Table 4. Correlations of serum cholesterol with stage of sexual maturation and skeletal age, by age in youths 12–17 years; Health Examination Survey

	Bone age				*Pubic hair*				*Male genital*		*Breast*	
Age in years	*White male*	*Black male*	*White female*	*Black female*	*White male*	*Black male*	*White female*	*Black female*	*White male*	*Black male*	*White female*	*Black female*
12	[1]−0.14	−0.12	−0.07	−0.12	[1]−0.20	−0.19	−0.05	−0.07	[1]−0.19	−0.16	−0.06	−0.08
13	[1]−0.16	−0.10	−0.04	−0.04	[1]−0.17	−0.12	−0.04	0.09	[1]−0.18	−0.09	−0.04	−0.02
14	[1]−0.14	−0.02	[1]−0.08	−0.06	[1]−0.12	−0.07	0.01	−0.01	[1]−0.12	−0.03	−0.05	0.03
15	−0.04	−0.15	−0.03	0.07	−0.04	−0.12	0.05	0.15	−0.04	−0.19	0.09	0.12
16	−0.00	−0.17	−0.04	−0.04	0.00	−0.08	−0.05	0.12	0.03	−0.01	0.03	0.12
17	0.08	0.00	0.01	0.03	0.05	0.10	0.03	0.14	−0.00	0.12	[1]0.15	0.18

[1] *P* less than or equal to 0.01.

tained at 70–74 degrees F. and relative humidity was maintained at 50–60 percent during the exercise test.

Technicians took an X-ray of the hand and wrist for assessment of bone age (*10*). Weight was measured to the nearest pound, standing height to the nearest centimeter, and waist and hip girth, subscapular skinfold, and tricep skinfold thickness to the nearest millimeter (*15*). Prior to examination, body temperature was measured to the nearest 0.1 degree F. with an oral thermometer. Any examinee with a temperature of 100 degrees or more could be sent home and rescheduled for another date at the physician's discretion.

The Health Examination Survey Cycle III of youth was based on the same sample design as the previous survey of children aged 6–11 years (*16*). Since the same sampling areas and households were used, nearly one-third of the youths examined in Cycle III had been examined in the earlier Cycle II survey of children. Cycle II was conducted in the period 1963–65. The time lapse between the two examinations of the same sample person ranged from 28 months to 5 years. In longitudinal analyses, only subjects with followup times of 28–53 months were included.

Methods used in the earlier examination were similar to those described above. No blood samples were taken. Resting heart rate was measured from a 10-lead electrocardiogram with the child supine. A nurse took two blood pressure readings in the right arm with the child supine with a mercury sphygmomanometer as described in detail (*17*). The average of these was used in the present analysis.

Technicians measured height to the nearest millimeter, weight to the nearest half pound, and a series of body measurements, including waist and hip girth, and subscapular and triceps skinfold thickness, to the nearest millimeter (*18*). An X-ray film of the right hand and wrist was taken for determination of skeletal age as described (*19*).

Population estimates for most of the variables have been published by the National Center for Health Statistics in the form of Series 11 reports. Data in this paper were not weighted to give precise estimates for the U.S. population. However, the sample was large and quite like the population in most demographic characteristics. Furthermore, the subsample examined two times resembled the overall sample for most characteristics.

All descriptive statistics were computed by standard methods using unweighted data. Pearson product moment correlation was used to assess the association of serum cholesterol with other continuous variables. Kendall's nonparametric rank correlation was used to assess the association of serum cholesterol with ordinal variables (*20*). Because of the large number of correlation coefficients computed, only those with an associated *P* value of 0.01 or less were considered significant. Stepwise forward linear multiple regression analysis was used to assess the independent relationship of multiple variables to serum cholesterol level in Cycle III data (*21*).

Models for predicting serum cholesterol level at Cycle III from variables measured at Cycle II were developed for white males only using the maximum R^2 technique for forward stepwise linear regression with pair switching (*21*). Age in months was forced to enter each model as the first variable. After age, only variables with statistically significant bivariate correlation coefficients were eligible to enter the model. Change variables were expressed as the logarithm of the ratio of the followup to the baseline value.

Results

Mean levels of serum total cholesterol by age, sex, and race as previously published are shown in the chart. Because serum total cholesterol values of

Table 5. Relationship of serum total cholesterol levels to relative skeletal maturity (bone age minus chronologic age in years), with standard error (SE)

Age in years	Less than −2 Mean	SE	−2 to less than −1 Mean	SE	−1 to 1 Mean	SE	More than 1 to 2 Mean	SE	More than 2 Mean	SE
12–14 years:										
White males	188.5	2.0	183.1	2.0	170.9	1.0	166.6	1.9	170.0	4.1
Black males	186.2	4.5	187.9	4.9	183.7	2.8	174.9	5.8	...	...
White females	...		...		182.9	2.0	176.1	1.3	176.1	1.1
Black females	...		...		185.8	6.4	181.5	3.7	177.7	2.3
15–17 years:										
White males	172.7	2.8	167.0	2.1	167.7	1.0	169.0	2.0	181.1	6.4
Black males	184.9	7.7	172.2	3.6	175.3	2.4	164.6	5.0	...	
White females	182.1	2.6	180.7	5.6	180.7	1.5	176.9	1.4	175.8	2.1
Black females	187.5	5.9	...		184.8	3.7	178.9	4.0	180.7	3.9

NOTE: No mean was tabulated when the number of persons in a category was less than 15.

Table 6. Serum total cholesterol in youths aged 12–17 years by sex, race, and stage of breast development (females), or genital development (males)

Stage	Females Mean	SE	Number	Males Mean	SE	Number
12–14 years						
Whites:						
1	183.80	4.20	30	188.77	2.18	207
2	180.17	2.25	144	182.40	1.55	422
3	180.85	1.57	332	174.81	1.53	337
4	173.92	1.27	502	166.85	1.47	356
5	176.18	1.53	420	164.36	1.60	283
Blacks:						
1	...			190.95	6.06	28
2	...			190.19	4.14	60
3	182.51	4.69	47	186.30	4.29	60
4	177.18	3.05	98	173.27	4.53	52
5	179.15	2.81	117	177.90	3.71	67
15–17 years						
Whites:						
1	...			...		
2	...			181.00	7.67	17
3	174.92	3.81	63	176.38	5.27	38
4	174.49	1.46	409	166.38	2.03	240
5	181.65	1.12	773	168.27	0.86	1,137
Blacks:						
1	...			...		
2	...			...		
3	...			...		
4	175.39	3.63	55	175.34	4.90	28
5	185.59	2.62	175	174.52	2.22	168

NOTE: No mean was tabulated when number of persons was less than 15.

350 mg per dl or greater may indicate familial hypercholesterolemia, two male and three female subjects with such levels were excluded from the present analyses. Also excluded were youths of races other than black or white.

Table 1 shows correlations of serum total cholesterol with other continuous variables by age, sex, and race. The correlations of serum cholesterol with age in months were consistent with the differing patterns by age shown in the chart in early *versus* late adolescence. The negative association with age in early adolescence was reflected in the negative associations with other maturity indicators, such as height, bone age, weight, and ponderal index. In contrast to these correlations, skinfold thickness was positively correlated with serum cholesterol in both early and late adolescence. This relationship seemed strongest in white males. The ratio of waist to hip girth was a significant correlate of serum cholesterol level in white males and older females. Serum uric acid showed weak but significant associations in most groups, while hematocrit showed the strongest associations in younger females and older males. Protein-bound iodine concentration was significantly correlated with serum cholesterol in several groups. To assess the effect of residual confounding by age, all correlations were repeated within 1-year age groups.

The results for selected variables are shown in table 2. In younger white males, the correlations of serum cholesterol with age in months and weight were diminished, and no longer significant except for that with age in months in 12-year-olds. Height and bone age remained significantly correlated with serum cholesterol, as did subscapular skinfold and triceps skinfold, and the ratio of waist to hip girth, exercise pulse, and grip strength. Protein-bound iodine concentration was significantly correlated with serum cholesterol only at ages 12 and 13 in white males. In younger females, the significant correlation of cholesterol with hematocrit persisted.

In older males, the correlation of serum cholesterol with weight, skinfolds, body mass index, ponderal index, waist-to-hip ratio, waist girth, hip girth, blood pressure, and exercise pulse were little diminished within one-year age groups. The correlations of hematocrit and protein bound iodine with serum cholesterol were significant only in 17-year-olds. In older females, correlations of serum cholesterol with weight, skinfold, body mass index, ponderal index, uric acid, and hematocrit were significant only in 16-year-olds, and that of waist-to-hip ratio only in 17-year-olds. The correlation of serum cholesterol with diastolic blood pressure was significant only in 15-year-olds, and that with protein-bound iodine concentration only at age 17.

Within 1-year age groups with sufficient numbers of current smokers, mean serum cholesterol was lower in smokers at ages 14, 15, and 16 years, but not at age 17, in white males; and at 14 and 16, but not at 15 and 17 in white females. For ages 15–17 years combined, serum cholesterol was lower in smokers than non-smokers in black males.

The association of serum total cholesterol with indicators of sexual maturation was assessed in detail. Table 3 shows rank-order correlations of serum cholesterol with stage of sexual maturation in youths. Correlations with bone age are shown for comparison. Stage 5 indicates full sexual maturity, while stage 1 indicates immaturity. Serum cholesterol was negatively correlated with stage of sexual development in boys aged 12–14 years. Correlations were smaller and less consistent among females. Surprisingly, larger positive correlations were observed for females aged 15–17 years. Most females have reached sexual maturity by age 15. Further, these results seem inconsistent with lack of correlation with bone age in older females.

Table 4 shows correlations of serum cholesterol with stage of sexual maturation within 1-year age groups. The same general pattern is revealed.

The difference between bone age and chronologic age is an expression of relative progress of biologic maturity. Table 5 shows that relatively advanced bone age was most clearly associated with lower serum total cholesterol only in younger males, the results being less consistent for other groups.

Table 6 shows that mean serum cholesterol was 7.6 mg per dl lower in the most mature, compared to the least mature, 12–14-year-old white females. At ages 15–17 years, cholesterol was 6 mg per dl higher in the most mature, compared to those at stage 3. In white males 12–14 years of age, mean serum cholesterol was 24 mg per dl lower in the most mature compared to the least mature. At age 15–17 no consistent differences were observed.

No data on oral contraceptive use were available. White girls 12–14 years who reported that their menstrual periods had started had lower mean serum cholesterol levels than girls whose periods had not started (age 12, 174.5 *versus* 180.1 mg per dl; age 13, 176.6 *versus* 181.3; and age 14, 175.5 *versus* 179.5). There were similar differences in black girls. After age 14, there were too few girls whose periods had not started to obtain meaningful analysis.

Stepwise forward multiple linear regression analyses were performed for each of eight age, sex, and race groups. Serum total cholesterol level was the dependent variable. Age in months was forced to enter each model. Based on the results of correlation analyses, the following variables could be selected to enter the model: subscapular skinfold thickness, waist-to-hip ratio, bone age, protein-bound iodine concentration, exercise heart rate, breast development stage (females), male genital development stage (males), family income (1 = $10,000 or more per year; zero = less than $10,000 per year), education of parent (1 = high school or greater; zero = less than high school), ABO blood groups (1 = group A1; zero = other), region (1 =

Table 7. Stepwise multiple regression of selected variables on serum cholesterol concentration in males

Variables	*Coefficient*[1]	*Standard error*[1]	R^2
12–14 years			
White males:			
Age (months)	0.565	0.146	0.035
Age times bone age	−0.003	0.000	0.080
Subscapular skinfold	0.809	0.151	0.120
Blood group A1	6.00	1.705	0.130
Exercise pulse	0.151	0.053	0.136
Parental education	4.173	1.623	0.141
Region	4.358	1.827	0.144
PBI	0.137	0.064	0.147
Black males:			
Age (months)	0.237	0.288	0.014
Age *times* subscapular skinfold	0.014	0.004	0.047
Bone age	−0.464	0.132	0.103
15–17 years			
White males:			
Age (months)	−0.398	0.127	0.001
Age *times* subscapular skinfold	0.004	0.001	0.044
Family income	7.018	1.884	0.055
Age *times* PBI	0.001	0.000	0.064
Region	6.738	2.061	0.071
Season	4.454	1.789	0.076
Age *times* waist-to-hip ratio	0.282	0.117	0.081
Black males:			
Age (months)	0.063	0.180	0.001
Waist-to-hip ratio	−99.816	41.682	0.039

[1]Coefficient and standard error with all significant (*P* less than 0.05) variables in model. Variables are listed in the order of entry. Age was forced to enter first regardless of significance.

NOTE: R^2 is the percent of variation explained by the variables in the model (the multiple correlation coefficient squared).

Table 8. Stepwise multiple regression of selected variables on serum cholesterol concentration in females

Variable	Coefficient[1]	Standard error[1]	R^2
12–14 years			
White females:			
Age (months)	0.491	0.181	0.002
Age *times* bone age	−0.002	0.000	0.011
Exercise pulse	0.178	0.064	0.024
Blood group AI	6.157	1.800	0.033
Region	6.147	1.995	0.041
Parental education	4.135	1.715	0.045
Age *times* subscapular skinfold	0.002	0.001	0.049
Age *times* PBI	0.001	0.000	0.054
Black females[2]	...		
15–17 years			
White females:			
Age (months)	0.270	0.109	0.010
Age *times* subscapular skinfold	0.003	0.001	0.031
Region	7.706	2.461	0.042
Bone age	−0.241	0.112	0.047
Age *times* PBI	0.001	0.000	0.052
Black females:			
Age (months)	0.111	0.254	0.001
PBI	0.412	0.139	0.058

[1] Coefficient and standard error with all significant (*P* less than 0.05) variables in model. Variables are listed in order of entry. Age was forced to enter first regardless of significance. [2]No significant variables.

NOTE: R^2 is percent of variation explained by the variables in the model (the multiple correlation coefficient squared).

North East; zero = other), season (1 = October-March; zero = other), smoking (1 = current smoker; zero = other), plus interaction terms for age in months with each of the above variables.

The results of these analyses are shown in tables 7 and 8. All variables whose regression coefficients were significant (*P* less than 0.05) are shown in the order of entry into the model. The cummulative R^2 after entry of each variable is shown in the last column. The coefficient and standard error in columns 2 and 3 were computed with all significant variables in the model. In males, variables related to body fat have significant independent associations with serum cholesterol in both age groups and both races. Maturity variables were important only among younger males.

Overall, less than 15 percent of the variation in serum cholesterol was explained for younger males and less than 9 percent for older males. Less of the variation was explained among blacks, compared to whites. The positive regression coefficients for age among 12–14-year-old white males and among white females when bone age or age times bone age was in the model (tables 7 and 8) indicate that at a given bone age, mean serum cholesterol increases slightly with increasing chronologic age. The finding was confirmed by examination of mean cholesterol levels by age within 12-month strata of bone age in whites. In 12–14-year-olds, serum cholesterol decreased with increasing bone age. However, the difference between bone age and chronologic age at Cycle II was not significantly correlated with serum cholesterol at Cycle III in children examined at both times, noted subsequently.

Rank correlations among the differences between bone age and chronologic age at the two examinations ranged from 0.3 to 0.4 (*P* less than 0.01). In females, less than 6 percent of the variation in serum cholesterol was explained for any age, or race group. Thus, the variables measured in the Health Examination Survey explained little of the variation in serum total cholesterol.

Table 9 shows the correlations of serum total cholesterol at age 12–17 years with other variables measured 28–53 months earlier. With few exceptions, variables from the earlier examination were significantly correlated with serum cholesterol at the second examination only for white males. The average followup interval was 42 months in white males, 42 months in white females, 43 months in black males, and 43 months in black females. Significantly correlated variables were those indicating level of maturation, growth, and changes in body fatness. None of the correlations was large. These relationships resided chiefly among the majority of subjects who were aged 12–14 years at the second examination (table 10).

Owing to the age ranges for eligibility in the two surveys, few subjects were 15–17 years of age at the second examination. In a stepwise multiple regression analysis, with serum cholesterol at second examination as the dependent variable, and the baseline variables with significant correlation coefficients in table 9 as independent variables, only 13 percent of the variation of serum cholesterol among white males aged 12–14 years was explained with all 10 variables in the model. All of the variables with significant correlation coefficients in table 9 had significant regression coefficients, except for change in subscapular skinfold thickness and change in weight. The best three-variable model included only age, change in height, and height at baseline, and explained 9 percent of the variance in followup serum cholesterol.

Discussion

Data from more than 6,000 youths aged 12–17 years in the National Health Examination Survey revealed that serum total cholesterol levels were negatively correlated with indicators of growth and maturation in younger male adolescents. Correlations with measures of obesity were positive and significant at all ages, although small in magnitude.

All measured variables could account for less than 15 percent of variation in males and less than 6 percent in females. Although significantly correlated with serum cholesterol levels, sexual maturation added little to the explanation of variation. Genetic variables other than race and blood group probably account for some of the unexplained variation. Other environmental factors, such as diet, probably would add little to the explanation of variance in this cross-sectional study, given the difficulty in measuring inter-individual variation in fat and cholesterol intake within populations (*1*).

The mechanism of the striking decline in serum total cholesterol in early adolescence is unknown. Decreases in both beta and alpha lipoprotein cholesterol contribute to the decrease (*22,23*). About 40 percent of serum total cholesterol is in the alpha lipoprotein fraction in white and 45 percent in black adolescents. This fraction decreases between ages 12 and 17 only in white males (*22*).

The much stronger correlations of serum cholesterol with sexual maturation in boys compared to girls in this and other studies suggest a role for testosterone in determining serum cholesterol levels and changes during adolescence (*23–25*).

The fall in serum cholesterol also coincides with the adolescent growth spurt (*23*). It is of interest to note that the level of the ratio of waist to hip girth declines between the ages of 12 and 17 (*26*). Waist-to-hip girth ratio increases during the third decade similar to serum cholesterol. However, the decline in the ratio begins earlier than that in serum cholesterol in cross-sectional data beginning at least by age 6.

Some of the decrease in serum cholesterol with age is consistent with the increasing prevalence of cigarette smoking, which is associated with a lower level of alpha, or high density lipoprotein cholesterol (*27*).

The slight increase in total cholesterol in late adolescence in girls could be related to increasing use of oral contraceptives (*23*).

The positive association of serum total cholesterol with protein-bound iodine concentration was unexpected, since thyroxin administration and hyperthyroidism are associated with lowered serum cholesterol and thyroid hormone deficiency with elevated serum cholesterol (*28*). Thyroid hormones enhance cholesterol synthesis and degradation with a predominant effect on degradation. However, within normal limits, thyroxin might have predominantly anabolic effects (*28*). Since thyroxin and T3 levels are stable between ages 12 and 17 years, they are not likely to explain changes in serum cholesterol during adolescence. The results are generally similar to those reported by other cross-sectional sudies of serum cholesterol in adolescents (*22–31*).

The Bogalusa Heart Study found similar relationships of total serum cholesterol to measures of obesity and sexual maturation (*24,29*). Similar results were reported from an English study (*23,30*). Longitudinal studies have focused on tracking of serum lipid levels (*2–6*). One study revealed that serum total cholesterol at age 12 was well correlated with levels 9 years later (r = 0.52) (*6*). In Bogalusa, LA, significant positive correlations were found between changes in triceps skinfold, percentage body fat and ponderal index, and changes in serum total cholesterol levels over a 5-year follow-up of children initially aged 5 to 12 years (*32*).

Earlier analyses of the HES data showed high rank-order correlations of skinfold thickness in childhood with that in adolescence (*33*). Although dietary intakes of saturated fat and cholesterol may be important in cross-cultural and within-individual

Table 9. Correlations of serum cholesterol at age 12–17 years with other variables measured 28–53 months earlier; Health Examination Survey

1963–65 variable	*White male*	*Black male*	*White female*	*Black female*
Age (months)	[1]−0.15	−0.18	−0.04	−0.03
Body mass index	−0.00	−0.03	0.06	−0.02
Subscapular skinfold	0.04	0.01	0.06	−0.00
Waist-to-hip ratio	−0.01	0.04	0.05	0.02
Bone age	[1]−0.17	[1]−0.24	−0.08	−0.09
Ponderal index	−0.07	−0.06	−0.08	0.01
Systolic blood pressure	−0.01	0.13	0.08	−0.18
Diastolic blood pressure	−0.00	0.15	0.02	−0.00
Resting heart rate	−0.07	0.01	0.04	−0.16
Height	[1]−0.18	−0.20	−0.03	−0.04
Weight	[1]−0.09	−0.15	0.03	−0.01
Change in age	−0.07	0.05	0.00	0.10
Change in height	[1]−0.20	−0.02	−0.02	−0.03
Change in weight	[1]−0.12	0.04	−0.01	0.10
Change in subscapular skinfold	[1]0.11	0.20	−0.00	0.11
Change in body mass index	0.00	0.07	0.00	0.16
Change in ponderal index	−0.07	−0.07	−0.02	−0.15
Change in waist-to-hip ratio	[1]0.11	0.02	0.01	−0.03
Change in bone age	[1]−0.15	0.07	0.04	0.12
Change in systolic blood pressure	−0.05	−0.17	0.02	[1]0.28
Change in diastolic blood pressure	−0.01	−0.00	0.06	0.11
Total	1001	129	892	141

[1] *P* less than or equal to 0.01.

Table 10. Correlations of serum cholesterol at age 12–17 years with variables measured 28–53 months earlier, by age; Health Examination Survey

	1966–1970 age			
	12–14 years old		15–17 years old	
1963–1965 variable	White male	White female	White male	White female
Age (months)	[1]−0.15	−0.03	0.01	−0.15
Height	[1]−0.19	−0.01	−0.06	−0.11
Weight	[1]−0.10	−0.03	0.05	0.07
Subscapular skinfold	0.04	0.05	0.09	0.13
Waist-to-hip ratio	−0.02	0.03	−0.02	0.11
Body mass index	−0.01	0.05	0.10	0.15
Ponderal index	−0.06	−0.06	−0.13	−0.21
Bone age	[1]−0.18	−0.06	0.00	−0.22
Systolic blood pressure	−0.00	0.08	−0.01	0.07
Diastolic blood pressure	0.02	0.02	−0.13	0.03
Resting heart rate	0.06	0.03	0.13	0.08
Change in age	0.08	−0.01	−0.06	0.15
Change in height	[1]−0.21	−0.04	−0.05	0.00
Change in weight	[1]−0.15	−0.03	0.06	0.03
Change in skinfold	[1]0.09	0.00	0.15	−0.02
Change in body mass index	−0.02	0.00	0.10	0.03
Change in ponderal index	−0.07	−0.02	−0.12	−0.04
Change in waist-to-hip ratio	[1]0.10	0.01	0.15	0.02
Change in systolic blood pressure	−0.07	0.00	0.15	0.17
Change in diastolic blood pressure	−0.03	0.05	[1]0.23	0.13
Change in bone age	[1]−0.16	0.01	−0.03	[1]0.27
Total	854	771	147	121

[1] P less than or equal to 0.01.

differences in serum cholesterol, they are inconsistently related to within-population differences in cross-sectional studies (*1*).

Genetic variables may be important in explaining inter-individual differences within populations (*29,30*). The role of genetics in explaining the timing and magnitude of changes in serum cholesterol in adolescence remains to be explored.

The limitations of the present study were several. Although no major sources of bias were likely to exist, the fact that only total serum cholesterol was measured makes interpretation of associations difficult. This is because a given variable may have opposite associations with low density lipoprotein and high density lipoprotein cholesterol, the latter comprising about 40 percent of serum total cholesterol in children (*23–31*).

No data were available on two important confounders, alcohol intake and oral contraceptive usage. Alcohol may raise and oral contraceptives may lower high density lipoprotein cholesterol concentrations (*23–31*). Both of these variables were most likely to have had an effect in the 15–17-year-old age group. Thus, correlations in the younger group were unlikely to have been seriously affected.

The large study sample size ensured high statistical power, especially for whites. The use of the criterion of P less than or equal to 0.01 for statistical significance of correlation coefficients minimized the likelihood of conclusions being based on chance alone. Furthermore, the data were presented in detail, so that the consistency and strength of associations among various age, sex, and race groups could be evaluated. However, some between-group differences in associations could be due to chance or to differences in average age of puberty. Even so, the generally low strength of the associations and the cross-sectional nature of the study design make causal conclusions impossible.

Unlike blood pressure (*34–36*), serum cholesterol was not measured in Cycle II, weakening longitudinal analyses in the sub-group examined twice. Due to the use of a large nationwide sample with a 90 percent response rate, the results are more likely to be widely generalizable than those from smaller local studies with lower response rates.

In conclusion, serum total cholesterol levels were significantly related to variables indicating level of growth, sexual maturation, and obesity. However, all measured variables explained only a small fraction of cholesterol variation.

Longitudinal studies with repeated measures of indices of growth, sexual maturation, obesity, multiple confounder variables, and serum lipoprotein levels are needed for the explanation of levels and changes in levels of serum lipids during adolescence. The role of sex hormones, thyroid hormones, and dietary factors should be examined. Also to be examined where possible are genetic variables, such as parental or sibling serum lipoprotein levels, and family history of premature coronary heart disease or familial hyperlipoproteinemia.

References

1. Blackburn, H., and Gillum, R. F.: Heart disease. *In:* Public health and preventive medicine, ed. 11, edited by J. M. Last. Appleton Century Croft, New York, NY, 1980, pp. 1168–1201.
2. Berenson, G. S. et al.: Cardiovascular risk factors in children. The early natural history of atherosclerosis and essential hypertension. Oxford University Press, New York, NY, 1980, pp. 3–18.
3. Clarke, W. R. et al.: Tracking of blood lipids and blood pressure in school age children: The Muscatine Study. Circulation 58: 626–634, October 1978.
4. Webber, L. S. et al.: Tracking of cardiovascular disease risk factor variables in school-age children. J Chronic Dis 36: 647–660, September 1983.
5. Laskarzewski, P. et al.: Lipid and lipoprotein tracking in

108 children over a four-year period. Pediatrics 64: 584-591, November 1979.
6. Orchard, T. J. et al.: Cholesterol screening in childhood: Does it predict adult hypercholesterolemia? The Beaver County experience. J. Pediatr 103: 687-691, November 1983.
7. Levy, P. S., Hamill, P. V. V., Heald, F., and Rowland, M.: Total serum cholesterol values of youths 12-17 years, United States. Vital Health Stat [11] 156. DHEW Publication No. (HRA) 76-1638. U.S. Government Printing Office, Washington, DC, May 1976.
8. Abraham, S., Johnson, C. L., and Carroll, M. D.: Total serum cholesterol levels of children 4-17 years, United States, 1971-74. Vital Health Stat [11] 207. DHEW Publication No. (PHS) 78-1655, Public Health Service, U.S. Government Printing Office, Washington, DC, 1978.
9. Fulwood, R., Abraham, S., and Johnson, C. L.: Serum cholesterol levels of persons 4-74 years of age, by socioeconomic characteristics, United States, 1971-74. Vital Health Stat [11] 217. DHEW Publication No. (PHS) 80-1667. Public Health Service. U.S. Government Printing Office, Washington, DC, March 1980.
10. National Center for Health Statistics: Plan and operation of a health examination survey of U.S. youths 12-17 years of age. Vital Health Stat [1] 8. PHS Publication No. 1000. U.S. Government Printing Office, Washington, DC, September 1969.
11. Tanner, J.: Growth in adolescence. Blackwell Scientific Publications, Oxford, 1955.
12. Levy, P. S., Hamill, P. V. V., Heald, F., and Rowland, M.: Serum uric acid values of youths 12-17 years, United States. Vital Health Stat [11] 152. DHEW Publication No. (HRA) 76-1634. U.S. Government Printing Office, Washington, DC, August 1975.
13. Cohen, B. H., Bias, W. B., Hamill, P. V. V., and Drizd, T. A.: Selected genetic markers of blood and secretions for youths 12-17 years of age, United States. Vital Health Stat [11] 168. DHEW Publication No. (PHS) 80-1664. U.S. Government Printing Office, Washington, DC, February 1980.
14. Roberts, J., and Maurer, K.: Blood pressure of youths 12-17 years, United States. Vital Health Stat [11] 163. DHEW Publication No. (HRA) 77-1645. U.S. Government Printing Office, Washington, DC, March 1977.
15. Johnston, F. E., Hamill, P. V. V., and Lemeshow, S.: Skinfold thickness of youths 12-17 years, United States. Vital Health Stat [11] 132. DHEW Publication No. (HRA) 74-1614. U.S. Government Printing Office, Washington, DC, January 1974.
16. National Center for Health Statistics: Plan, operation, and response results of a program of children's examinations. Vital Health Stat [1] 5. PHS Publication No. 1000. U.S. Government Printing Office, Washington, DC, October 1967.
17. Weiss, N. S., Hamill, P. V. V., and Drizd, T.: Blood pressure levels of children 6-11 years, relationship to age, sex, race, and socioeconomic status, United States. Vital Health Stat [11] 135. DHEW Publication No. (HRA) 74-1617. U.S. Government Printing Office, Washington, DC, December 1974.
18. Malina, R. M., Hamill, P. V. V., and Lemeshow, S.: Body dimensions and proportions, white and negro children 6-11 years, United States. Vital Health Stat [11] 143. DHEW Publication No. (HRA) 75-1625. U.S. Government Printing Office, Washington, DC, December 1974.
19. Roche, A. F., Roberts, J., and Hamill, P. V. V.: Skeletal maturity of children 6-11 years, United States. VitalHealth Stat [11] 140. DHEW Publication No. (HRA) 75-1622. U.S. Government Printing Office, Washington, DC, November 1974.
20. Armitage, P.: Statistical methods in medical research. John Wiley and Sons, New York, NY, 1971, pp. 403-406.
21. SAS User's Guide: Statistics, 1982 Ed., edited by A. A. Ray, SAS Institute Inc., Cary, NC, 1982, pp. 101-110.
22. Berenson, G. S. et al.: Dynamic changes of serum lipoproteins in children during adolescence and sexual maturation. Amer J. Epidemiol 113: 157-170, February 1981.
23. Orchard, T. J., Rodgers, M., Hedley, A. J., and Mitchell, J. R. A.: Changes in blood lipids and blood pressure during adolescence. Brit Med J 1: 1563-1567, June 28, 1980.
24. Frerichs, R. R., Webber, L. S., Srinivasin, S. R., and Berenson, G. S.: Relation of serum lipids and lipoproteins to obesity and sexual maturity in white and black children. Amer J. Epidemiol 108: 486-496, December 1978.
25. Laskarzewski, P. M. et al.: Longitudinal relationships among endogenous testosterone, estradiol and quetelet index with high and low density lipoprotein cholesterols in adolescent boys. Pediatr Res 17: 689-698, August 1983.
26. Gillum, R. F.: The association of the ratio of waist to hip girth with blood pressure, serum cholesterol, and serum uric acid in children and youths aged 6-17 years. J Chron Dis 40: 413-420, May 1987.
27. Glueck, G. J. et al.: Alcohol intake, cigarette smoking and plasma lipids and lipoproteins in 12-19-year-old children, The Collaborative Lipid Research Clinics Prevalence Study. Circulation 64 (Sup. III): II, 48-56, September 1981.
28. Ingbar, S. H., and Woeber, K. A.: The thyroid gland. *In* Textbook of Endocrinology, 6 Ed, edited by R. H. Williams. W. B. Saunders Co., Philadelphia, Pa. 1981, pp. 142-406.
29. Berenson, G. S. et al.: Biochemical and anthropometric determinants of serum beta- and pre-beta-lipoproteins in children. The Bogalusa Heart Study. Arteriosclerosis 2: 325-334, July-August 1982.
30. Orchard, T. J., Rodgers, M., Hedley, A. J., and Mitchell, J. M.: Serum lipids in a teenage population: geographic, seasonal and familial factors. Int J. Epidemiol 10: 161-170, February 1981.
31. Kwiterovich, P. O., Jr.: Biochemical, clinical, epidemiologic, genetic, and pathologic data in the pediatric age group relevant to the cholesterol hypothesis. Pediatrics 78: 349-362, August 1986.
32. Freedman, D. S. et al: Relationship of changes in obesity to serum lipid and lipoprotein changes in childhood and adolescence. JAMA 254: 515-520, July 26, 1985.
33. Zack, P. M., Harlan, W. R., Leaverton, P. E., and Cornoni-Huntley, J.: A longitudinal study of body fatness in childhood and adolescence. J Pediatrics 95: 126-130, July 1979.
34. Cornoni-Huntley, J., Harlan, W. R., and Leaverton, P. E.: Blood pressure in adolescence. The United States Health Examination Survey. Hypertension 1: 566-571, November-December 1979.
35. Harlan, W. R., Cornoni-Huntley, J., Leaverton, P.: Blood pressure in childhood. The National Health Examination Survey. Hypertension 1: 559-565, November-December 1979.
36. Lauer, R. M., Anderson, A. R., Beaglehole, R., and Burns, T. L.: Factors related to tracking of blood pressure in children. National Center for Health Statistics Health Examination Surveys, Cycles II and III. Hypertension 6: 307-314, May-June 1984.