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Serum Total Cholesterol Levels in Japanese Children

The Shimane Heart Study

(cholesterol/Japanese children)

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Serum cholesterol levels of 395 children and some of their family members were measured as a part of Shimane Heart Study, the purpose of which was to obtain information on risk factors involved in adult vascular diseases, during childhood.

Mean serum cholesterol levels ± S. D. were 149.9 ± 22.4 mg/dl, 152.0 ± 23.6 mg/dl, 140.7 ± 26.2 mg/dl, in 6, 9, and 12 − 15 year-old children, respectively. No significant differences were observed between boys and girls, and between 6 and 9 year-old children. The differences between primary school pupils and junior high school children were statistically significant ($p < 0.01$). Mean values of cholesterol reached the lowest levels during puberty (13−15 yrs).

The family study revealed that cholesterol levels showed the same tendency among siblings. Cholesterol levels in mothers of high cholesterol children were high in 2 and low in 2 cases. Cholesterol levels were normal among all fathers of the high cholesterol group, and all parents of the low cholesterol group. Interrelationships between cholesterol and hemoglobin or total protein were not statistically significant.

Vascular disorders such as hypertension, coronary heart disease and cerebral vascular accidents constitute the major causes of death in Japan, and the prevention of these disorders has been one of the most important problems in the field of preventive medicine.

Recent studies have revealed that vascular changes already begin during the first and second decades of life and are related to serum cholesterol levels (1−5).

The Shimane Heart Study was initiated in the spring of 1978 in Izumo, Shimane Prefecture. The objective was to obtain information on risk factors of adult vascular diseases which might begin during childhood.

Extensive data were collected on serum cholesterol, serum hemoglobin, serum total protein, body weight and length, skin fold thickness, blood pressure, electrocardiogram, and echocardiogram of the heart.

This paper reports the serum cholesterol levels of children and some of their family members. Other data will be reported elsewhere.

MATERIALS AND METHODS

Population

Three hundred and ninety five children of a primary school (aged 6 and 9 yrs) and a junior high school (ranging in age from 12—15 yrs) participated in the Study ; 158 aged 6 yrs, 139 aged 9 yrs and 98 aged from 12—15 yrs. All children were residents of Shimane Prefecture. Examinations were performed in the spring of 1978.

Examination

All of the eligible children were examined. Appropriate permission was obtained from one parent of each child. Anthropometric measurements and physical examination were performed before venipuncture.

Collection of Blood Specimens

Blood was drawn for serum cholesterol, hemoglobin and total protein assessments. The children were seated and antecubital venous blood was collecetd in vacutainer tubes at 11 : 30 a. m. after a 4 hrs fast. The blood was allowed to clot at room temperature for approximately 2 hrs and centrifuged at 2,500 r.p. m. for 10 min. The serum was extracted and preserved in a freezer at −20°C until tested.

Serum Cholesterol Determination

The serum total cholesterol levels were measured by a modified Zurkowski-Shibata method. This method consists of mixing the serum, sulfosalicylic acid, acetic acid and sulfuric acid, incubating the mixture at 37°C for 15 min and measuring the absorbance at 578 nm against the blank containing a similar mixture but omitting the serum.

Hemoglobin Determination

Venous blood was collected in a tube containing ammonium and potassium oxalate. The measurements were performed within 3 hr after the blood collection. Hemoglobin was determined by azide-methohemoglobin method.

Blood, sodium nitrite and sodium azide were mixed and incubated for 10 min at 37°C, and absorbance of the mixture was measured at 546 nm against the water blank.

Serum Total Protein Determination

Serum total protein was measured in a Hitachi 706 D Auto-Analyzer.

Determination of Lipid Levels

Children with high cholesterol levels were bled after an overnight fast and levels of triglycerides, phospholipids, β-lipoprotein, and free fatty acids were measured.

Family Study

The family members of 6 and 9 year-old children whose cholesterol levels were abnormal ($>$ 205 mg/dl, or $<$ 100 mg/dl) were bled and their cholesterol levels were also determined.

RESULTS

Cholesterol Levels

Mean serum cholesterol levels by age and sex are shown in Table I. The distributions of the level in each age group are shown in Fig. 1. No statistically significant differences were observed in cholesterol levels between boys and girls in either age group, and between 6 and 9 year-old children.

The differences of cholesterol levels between primary school pupils (6 and 9 yrs) and junior high school children (13—15 yrs) were statistically significant ($p < 0.01$). Mean values reached the lowest levels in those from 13—15 yrs.

TABLE I. *Serum Total Cholesterol Levels by Age and Sex*

Age (yr)	Number of children		Mean ± S. D. (mg/dl)	Range (mg/dl)
6	Boys	99	148.1±23.1	90—225
	Girls	59	153.0±21.0	121—219
	Total	158	149.9±22.4	90—225
9	Boys	69	154.5±24.7	95—265
	Girls	70	149.5±22.3	109—207
	Total	139	152.0±23.6	95—265
12—15	Boys	48	138.8±30.0	94—277
	Girls	50	142.6±21.8	89—207
	Total	98	140.7±26.2	89—277

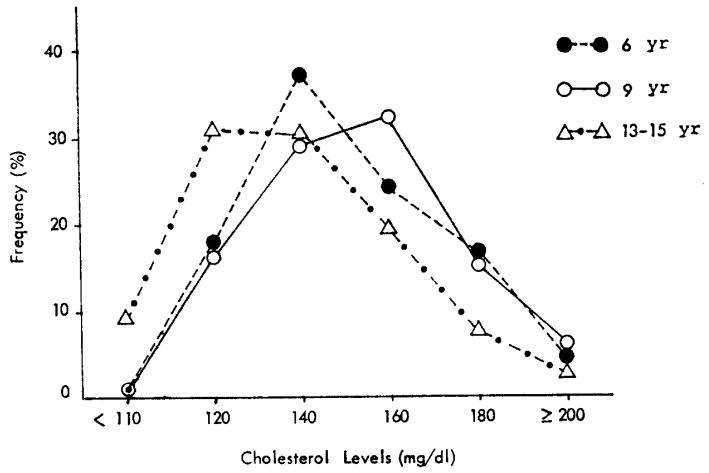

Fig. 1. Distribution of cholesterol levels in each age group.

Percentile levels for cholesterol are shown in Table II. The cumulative percent curve (Fig. 2) shows that there are more children with low cholesterol levels in the 12—15 yrs group than in other age groups.

Levels of Various Lipids in High Cholesterol Children

Table III shows the values of various lipids in 5 high cholesterol children. Free fatty acid levels were high in 3 children and triglycerides levels were high in one child. There were no abnormalities in levels of phospholipids and β-lipoprotein.

TABLE II. *Percentile for Serum Cholesterol (mg/dl) by Age and Sex*

Age (yr)	sex	Percentile		
		5th	50th	95th
6	Boys	102	148	194
	Girls	111	153	195
	Total	106	150	194
9	Boys	105	155	204
	Girls	105	150	194
	Total	105	152	199
12–15	Boys	78	139	199
	Girls	99	143	187
	Total	88	141	193

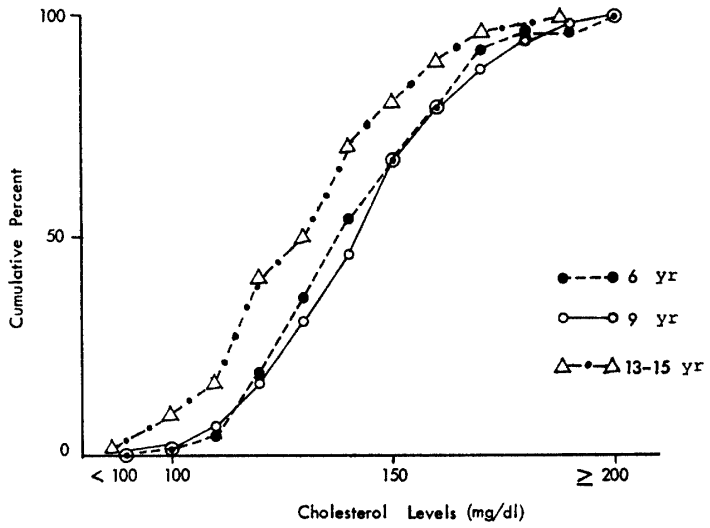

Fig. 2. Cumulative percent of cholesterol levels in each age group.

TABLE III. *Serum Lipids Levels (mg/dl) in High Cholesterol Children Aged 6–9 yrs*

Lipids	Case					
	A. S. girl	T. Y. boy	R. F. girl	K. I. boy	T. T. boy	Normal ranges
Cholesterol	207	216	219	225	265	110–200
Triglycerides	89	109	149	83	98	50–120
Phospholipids	194	235	246	151	238	190–290
Free fatty acid	585	1972	781	1251	961	400–800
β-Lipoprotein	277	335	369	185	468	150–500

Family Study

Six and nine year-old children were divided into 3 groups according to their cholesterol levels, i. e., high cholesterol group ($>$ 205 mg / dl), low cholesterol group ($<$ 100 mg/dl) and normal group. The numbers of children in each

group were 5, 4 and 288, respectively.

Fig. 3 shows cholesterol levels of family members of the children with abnormal cholesterol levels. Cholesterol levels were much the same among the siblings. Cholesterol levels in mothers of high cholesterol group were high in 2 and low in 2 cases. Cholesterol levels were normal among all fathers of the high cholesterol group, and all parents of the low cholesterol group.

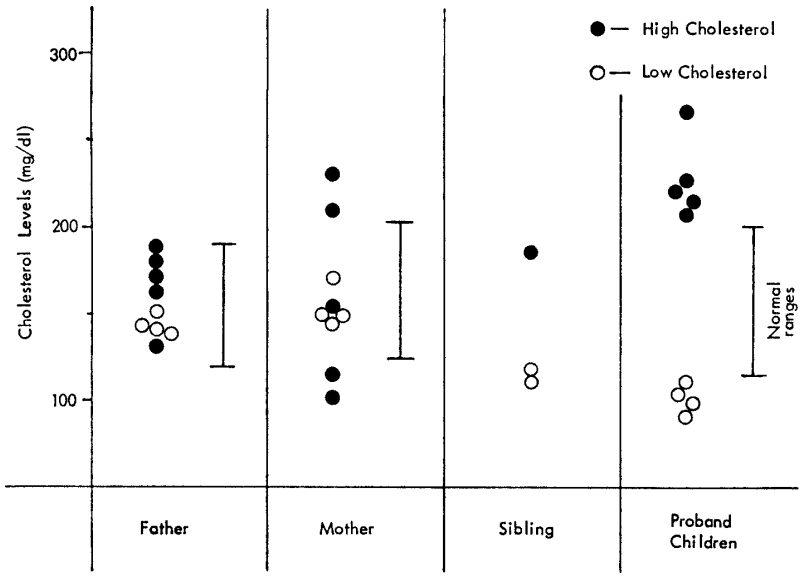

Fig. 3. Cholesterol levels of family members of the children with abnormal cholesterol levels.

Interrelationships between Cholesterol and Hemoglobin or Total Protein

Interrelationships between these values representing the nutritional status of the individual child were not statistically significant.

DISCUSSION

An increase in blood cholesterol levels is considered to be one of the most important factors in the pathogenesis of atherosclerotic diseases and their sequelae (5—8). Efforts to prevent the progress of atherosclerosis should be begun during childhood, since necropsy studies of children have shown that vascular changes may occur years before symptoms develop (9).

The Shimane Heart Study was initiated in order to investigate the risk factors for adult vascular diseases during childhood before development of the symptoms. It was postulated that cholesterol levels in childhood were one of the risk factors for adult vascular diseases.

As a part of the Study, cholesterol levels of about 400 children were determined to establish the normal ranges of cholesterol in Japanese children.

Our mean levels of cholesterol were 150 mg/dl in 7 and 10 year-old children, and 140 mg/dl in 12—15 year-old children. These values are lower by 10—30 mg/dl than levels reported in American children (10—15).

Why there are differences among the races in the levels of serum cholesterol is not clearly known, however, genetic and dietary factors do influence cholesterol metabolism in children (16). The differences in cholesterol levels between Japanese children (the present study) and American children might be due to genetic and dietary differences.

In the present study, cholesterol levels were lowest in 12—15 year-old children, especially in boys. A similar tendency toward decrease in cholesterol levels around puberty has been observed in both cross-sectional and longitudinal studies (10, 14, 15, 17—23). Changes in endocrine functions (thyroid and pituitary) during puberty may influence the cholesterol levels.

In the Shimane Heart Study, cholesterol levels higher than 200 mg/dl were considered to be one of the risk factors for atherosclerotic vascular diseases. Among 395 children tested, 7 revealed levels over 200 mg/dl. We measured the cholesterol levels of 5 parents and one sibling in the high cholesterol group. Among them, 2 mothers and one sibling showed higher levels of cholesterol (Fig. 3).

This finding suggests that cholesterol levels do have a similar familial pattern. The same tendency was observed by Deutcher *et al.*(24).

Because levels of other lipids in high cholesterol children were normal as shown in Table III, precise etiologies of the hypercholesterolemia could not be established in these children.

Siblings of low cholesterol children showed cholesterol levels below normal limits. Thus, the low cholesterol levels in siblings in the same family may be due to low cholesterol contents in their diet.

A close relationship between serum cholesterol and diets high in cholesterol was observed by some investigators. The vegetarians were found to have lower levels of cholesterol (25). McGandy *et al.* (26) observed that serum cholesterol levels were decreased by the low cholesterol diet.

Family studies of low cholesterol children will be continued as a part of the Shimane Heart Study.

We thank the staff of the schools for kind cooperation during examinations.

REFERENCES

1) Strong, J. P. and McGill, H. C. (1969) The pediatric aspects of atherosclerosis. *J. Atheroscler. Res.* **9**, 251—265
2) Kannel, W. B. and Dawber, T. R. (1972) Atherosclerosis as a pediatric problem. *J. Pediatr.* **80**, 544—554
3) Drash, A. (1972) Atherosclerosis, cholesterol, and the pediatrician. *J. Pediatr.* **80**, 693—696
4) Blumenthal, S. (1973) Prevention of atherosclerosis. *Am. J. Cardiol.* **31**, 591—594
5) Kannel, W. B., Castelli, W. P., Gordon, T. and McNamara, P. M. (1971) Serum Cholesterol, lipoproteins, and the risk of coronary heart disease. The Framingham Study. *Ann. Intern. Med.* **74**, 1—12
6) Stamler, J. (1973) Epidemiology of coronary heart disease. *Med. Clin. North Am.* **57**, 5—46

7) Tyroler, H. A., Heyden S., Cornoni J. C., Hames C. G., and Kleinbaum D. (1971) Blood pressure and cholesterol as coronary heart disease risk factors. *Arch. Intern. Med.* **128**, 907–914
8) Truett, J., Cornfield, J. and Kannel, W. (1967) A multivariate analysis of the risk of coronary heart disease in Framingham. *J. Chronic Dis.* **20**, 511–524
9) Holman, R. L., McGill, H. C., Strong J. P. and Geer, J. C. (1958) The natural history of atherosclerosis : the early aortic lesions as seen in New Orleans in the middle of the 20th century. *Am. J. Pathol.* **34**, 209–235
10) Johnson, B. C., Epstein, F. H. and Kjelsberg, M. O. (1965) Distributions and familial studies of blood pressure and serum cholesterol levels in a total community, –Tecumseh, Michigan. *J. Chronic Dis.* **18**, 147–160
11) Baker, H., Frank, O., Feingold, S., Christakis, G. and Ziffer, H. (1967) Vitamins, total cholesterol and triglycerides in 642 New York City school children. *Am. J. Clin. Nutr.* **20**, 850–857
12) Friedman, G. and Goldberg, S. J. (1973) Normal serum cholesterol values, percentile ranking in a middle-class pediatric population. *JAMA* **225**, 610–612
13) Lauer, R. M., Conner W. E., Leaverton P. E., Reiter, M. A. and Clarke, W. R. (1975) Coronary heart disease risk factors in school children. The Muscatine study. *J. Pediatr.* **86**, 697–706
14) Hennekens, C. H., Jesse, M. L., Klein, B. E., Gourley, J. E. and Blumenthal, S. (1976) Cholesterol among children of men with myocardial infarction. *Pediatrics* **58**, 211–217
15) Frerichs, R. R., Srinivasan, S. R., Webber, L. S. and Berenson, G. S. (1976) Serum cholesterol and triglyceride levels in 3,446 children from a biracial community. The Bogalusa Heart Study. *Circulation* **54**, 302–309
16) Glueck, C. J., Tsang, R., Balistreli, W. and Fallat, R. (1972) Plasma and dietary cholesterol in infancy : Effects of early low or moderate dietary cholesterol intake on subsequent response to increased dietary cholesterol. *Metabolism* **21**, 1181–1192
17) Adlersberg, D., Schaefer, L. E., Steinberg, A. G. and Wang, C. I. (1956) Age, sex, serum lipids and coronary atherosclerosis. *JAMA* **162**, 619–622
18) Milligan, C. A., Wilcox, E. B. and Galloway, L. S. (1966) Serum cholesterol and physical characteristics of pre-adolescents and adolescents. *J. Am. Diet. Assoc.* **49**, 303–308
19) Lee, V. A. (1967) Individual trends in t he total serum cholesterol of children and adolescents over a ten-year period. *Am. J. Clin. Nutr.* **20**, 5–12
20) Lopez, S. A., Krehl, W. A. and Hodges, R. E. (1967) Relationship between total cholesterol and cholesterol esters with age in human blood plasma. *Am. J. Clin. Nutr.* **20**, 808–815
21) McGandy, R. B. (1971) Adolescence and the onset of atherosclerosis. *Bull. N. Y. Acad. Med.* **47**, 590–600
22) Starr, P. (1971) Hypercholesterolemia in school children : A preliminary report. *Am. J. Clin. Pathol.* **56**. 515–522
23) Savage, P. J., Hamman, R. F., Bartha, G., Dippe, S. E., Miller, M. and Bennett, P. H. (1976) Serum cholesterol levels in American (Pima) Indian children and adolescents. *Pediatrics* **58**, 274–282
24) Deutscher, S., Epstein F. H. and Kjelsberg, M. O. (1966) Familial aggregation of factors associated with coronary heart disease. *Circulation* **33**, 911–924
25) Sacks, F. M., Castelli, W. P., Donner, A and Kassa, E. H. (1975) Plasma lipids and lipoproteins in vegetarians and controls. *N. Engl. J. Med.* **292**, 1148–1151
26) McGandy, R. B., Hall, B. and Ford, C. (1972) Dietary regulation of blood cholesterol in adolescent males : A pilot study. *Am. J. Clin. Nutr.* **25**, 61–66