

# Cholesterol in Preteen Children of Parents with Premature Coronary Disease

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A pediatric population at high risk for the development of coronary artery disease has been identified. Using a simple and inexpensive protocol, serum cholesterol determinations were performed on 50 children 12 years old and younger. These children were taken from 28 families in which one parent had suffered a myocardial infarction before the age of 50. Eight of the 50 children were found to have significant elevation of serum cholesterol. This was an incidence of 16 percent—twice that of the general pediatric population. Subjects with both adverse genetic and metabolic backgrounds need to be identified in this simple way. Preventive and therapeutic measures in such children may alter in the future the serious morbidity and mortality of coronary artery disease.

Premature coronary artery disease is promoted by three major risk factors: high serum cholesterol, high blood pressure, and cigarette smoking.<sup>1</sup>

The atherosclerotic process is known to begin early in life and the pathological changes may be irreversible once they are established. Therefore, if the predisposing traits could be identified in childhood, early intervention would be desirable.<sup>2,3</sup>

Some authors have suggested that the general population of children should be screened for

hypercholesterolemia<sup>3,4</sup> and for hypertension;<sup>4</sup> but others are against these suggestions.<sup>5-7</sup>

An approach for the primary care physician, yet unaware of how best to proceed, can use the fact that high serum cholesterol, high blood pressure, and premature coronary disease all show familial aggregations.<sup>8-14</sup> Early prevention of premature coronary heart disease therefore can begin in those families prone to the disease.

This study suggests a simple solution to a potentially complex problem, a problem which community physicians may otherwise be tempted to leave to the lipoprotein research laboratory. Families containing a parent who had manifested coronary heart disease before the age of 50 were identified and the preteen children underwent a single serum cholesterol estimation. The presence of disease in the parent before the 50th birthday clearly establishes the early onset of the pathological process which presumably, therefore, is both

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more severe and more apt to be familial than when the disease occurs in more senior citizens.

Young children identified both as belonging to such affected families and as having an elevated serum cholesterol level would have a doubled risk factor. These children, together with their families, would be suitable for further advanced lipid studies, and would be considered suitable for dietary prophylaxis. Furthermore, those families already affected by premature coronary artery disease would be those most likely to comply with changes in household dietary habits.

The measurement of serum cholesterol alone, rather than any other single lipid fraction, and rather than total lipid analysis, was chosen for the following reasons:

1. Serum cholesterol is the universally accepted lipid risk factor in the development of atherosclerosis. The risk of coronary heart disease, both in individuals and in populations, is proportional to the level of serum cholesterol, even to the moderately elevated levels commonly found in the community. As found in the Framingham study, "any one of the lipids . . . can be used effectively for assessing vulnerability to coronary heart disease. None, however, would appear superior to the more convenient serum cholesterol determination for this purpose."<sup>15</sup>

2. Those lipid disorders in which the cholesterol is elevated are those in which a hereditary element is strong, and in which the changes in the blood are expected to be detectable in childhood. By contrast, in high triglyceride states the disease is frequently acquired, or sporadic, and hereditary factors are less well established. Furthermore, high levels of serum triglyceride do not usually become manifest before the third decade of life, so that they cannot often be detected in children.<sup>2,13</sup>

3. Serum cholesterol levels have been studied for many years and the range in health and disease is better known than that of the other lipid fractions.

4. Cholesterol sampling may be done at any time of the day without relation to meals—the variation with intake of food is three percent or less.<sup>16</sup> Population studies customarily use nonfasting serum cholesterol levels.<sup>4,9,10,15,17</sup>

5. Serum cholesterol levels for screening purposes may be obtained from any laboratory and are not expensive.

It is hoped that this study, performed on am-

bulatory patients in a family practice setting, will encourage community practitioners to engage in cholesterol screening in their young patients at risk; and that they will be reassured that neither the facilities of a lipoprotein research laboratory, nor great trouble or expense are required.

## Normal Cholesterol Levels in Children

The general pattern of serum cholesterol levels from birth through adulthood has been studied in the United States<sup>7,17,18</sup> and in Australia.<sup>9</sup> The value in the neonate is approximately 65 mg/100 ml, from which it rises to a mean value of 165 mg/100 ml by the age of two. From this point some authors<sup>9,17,18</sup> find a slight upward gradient until mean levels are reached at adolescence of 185 mg/100 ml. Lauer et al,<sup>4</sup> beginning at the child's age of six, find no increase with age and other workers are indefinite.<sup>2,10</sup> In the late teens a further rise in cholesterol begins, continuing on until the mature adult levels are attained. There is debate on the acceptable upper limit of "normal" in the adult not considered here. In fact, there is no fixed upper limit in children or adults, but most workers<sup>2,6,7,9,11</sup> suggest that for children an arbitrary level of 200 mg of cholesterol per 100 ml of serum be considered to be that above which therapeutic intervention should be considered.

Different "normal" values for cholesterol in different reported studies may be due to alternative methods of chemical estimation and to the effects of age, diet, and socioeconomic factors in the study of populations.

## Method

Community family physicians were asked to refer families in which a parent had premature coronary heart disease before the age of 50. Twenty-eight families were referred with 97 total offspring, 50 of whom were children aged 12 and under. Twenty-six of the affected parents were males and two were females. The average age of onset of the disease had been 40 years (range of age of onset was 29 to 45 years). Six parents had died of their disease at the time of the study. The other 22 had had myocardial infarcts documented at the time of hospitalization.

From each of the 50 preteen children, a single random blood specimen was drawn. It was tested for serum cholesterol on a Technicon SMA-12:60



multichannel analyser. No blood was taken from controls since it was felt that the distribution of normal and abnormal cholesterol levels in American children, as for other hematological and biochemical tests, are sufficiently well established.

There was no attempt to conduct total lipid analyses in the children or to document detailed family histories.

The sole purpose of the study was to identify a group of young children with potential double jeopardy for the onset of premature coronary artery disease: adverse family history and elevated serum cholesterol levels.

## Results

The result of serum cholesterol testing in the 50 children is shown in Figure 1.

There was some increase in serum cholesterol with age compatible with that found in previous population studies.<sup>9,17,18</sup> Age two to seven years (11 subjects), mean cholesterol 166 mg/100 ml. Age 7 to 12 years (39 subjects), mean cholesterol 181 mg/100 ml.

For all ages combined the median figure for serum cholesterol was 171 mg/100 ml. The median figure is that above and below which the numbers of children were the same: 25 above and 25 below.

The mean, or average, serum cholesterol was 178 mg/100 ml (range 112 to 365 mg/100 ml). Twenty-nine readings were below this mean and 21 were above it.

Half of the 50 children were boys and half were girls. There was no difference in mean serum cholesterol level between the two sexes.

Eight children (age range 8 to 12 years) had cholesterol levels above 200 mg/100 ml (16 percent). There were four boys and four girls. Of these eight children, four had readings over 240 mg/100 ml (eight percent).

Table 1 shows an outline of the percentage of children found to be over various arbitrary limits in former population studies and in the present work.

## Discussion

Several population studies<sup>7,10,11,17,19</sup> have found that the distribution curve of cholesterol values in children has a "skew to the right." In this present study too, using the simple reasoning of Friedman and Goldberg<sup>17</sup> and Thomas,<sup>19</sup> the chart in Figure 1

can be seen to be skewed to the right. The median is less than the mean; that is, more of the population of children are below the mean than above it (29:21). In the literature this finding is taken to suggest that the population of children is not homogeneous but contains two distinct populations; a larger group having normal serum cholesterol levels and a smaller group with higher, abnormal levels.<sup>7,11,19</sup> The existence of these two populations is suggestive evidence that the inheritance of hypercholesterolemia is largely by a single dominant gene.<sup>13,14,19,20</sup> If one parent is affected half of his/her offspring will be also, the abnormality being detectable in early childhood.

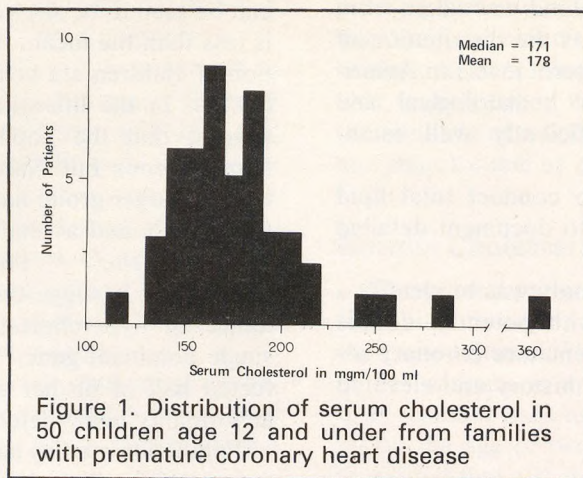
Population studies have also shown the characteristic of familial clumping of those individuals with elevated serum cholesterol values.<sup>9,11,13</sup> In this study four out of the eight children with levels of serum cholesterol over the arbitrary 200 mg/100 ml limit come from two of the 28 families.

The literature contains three papers dealing with lipid studies in offspring of parents with premature coronary artery disease, performed by research laboratories in university centers, with complete lipid and lipoprotein analyses. Some of the offspring in these three studies were adolescents and some were adults. Each study used a different standard for defining abnormal lipid levels but comparable results were obtained; elevated cholesterol levels were found in 20 percent,<sup>21</sup> 21 percent,<sup>22</sup> and 16 percent<sup>23</sup> of the offspring of affected parents.

In this study, for simplicity and economy without loss of efficiency, serum cholesterol alone was tested, rather than any other lipid. Elevated serum cholesterol levels were found in 16 percent of the preteen children from the families affected by premature coronary artery disease. This is twice the incidence that has been found in the general pediatric population (Table 1) and agrees well with the more complex studies in affected families cited above.<sup>21-23</sup>

The patient with a single random elevated serum cholesterol, once identified, must be evaluated to confirm the diagnosis of hypercholesterolemia and to exclude secondary causes such as diabetes mellitus, thyroid, renal or hepatic disease, or the use of birth control pills in older girls. With the diagnosis confirmed the whole family should be investigated. However, such testing was beyond the intent of this study.





A high-yield group of children to whom it is easy to gain access has been identified. Preteen children are not difficult to bring in for investigation and the normal serum cholesterol levels in children are well known. Families affected by premature coronary artery disease readily accept screening and advice about habits and diets. Information on lipid lowering diets is available from the National Institute of Health<sup>24</sup> and a practical diet for young children has recently been published.<sup>25</sup>

Intervention is controversial. No long-term studies are available, Glueck, Fallat, and Tsang<sup>3</sup> have reviewed the current status of the hoped-for benefits of therapy against the possible risks; decisions have to be made on the basis of incomplete evidence.

The Atherosclerosis Study Group<sup>1</sup> concluded that the existing evidence was sufficient to justify beginning a national program of dietary modification for all children while the Committee on Nutrition of the American Academy of Pediatrics<sup>26</sup> opposed dietary changes for all children but agreed that intervention should be tested where there was high risk of familial coronary heart disease.

It would appear reasonable to say that if there is to be prophylaxis of coronary heart disease, then it may begin in these easily identified preteen children with both an adverse family history and an elevated serum cholesterol level. Such children may be found among the patients of every family physician.

If atherosclerosis begins as a pediatric disease, as it is thought to do, then it is beginning in these children.

That is our challenge!

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Table 1. Percentages of Children with Serum Cholesterol Levels Greater than Certain Arbitrary Levels		
Cholesterol Level (mg/100 ml serum)	Percentage of Children Over this Level	Reference
200	9.0	7
200	9.0	11
220	9.0	4
220	6.6	10
220	3.3	11
235	2.0	7
238	2.5	9
240	3.0	4
200	16.0	This study
240	8.0	This study

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