The Abnormal Serum Lipid Pattern in Patients with Coronary Arteriosclerosis

By Alfred Steiner, M.D., Forrest E. Kendall, Ph.D., and James A. L. Mathers, M.D.

Studies in experimental arteriosclerosis have indicated that the relative level of serum lipid phosphorus may be as significant a factor as the absolute level of serum cholesterol in the production of arterial lesions. For this reason, the serum lipid pattern of 82 patients with coronary arteriosclerosis has been compared with that of 112 healthy adults. An elevation of the serum cholesterol, serum lipid phosphorus and the serum cholesterol–lipid phosphorus molar ratio has been found in most of the patients with coronary arteriosclerosis.

Previous studies from this laboratory have demonstrated that the serum cholesterol pattern of patients with coronary arteriosclerosis differs from that of normal individuals in that the serum cholesterol levels are higher and more inconstant than those in control subjects. Recent experimental data have indicated that the ratio between serum cholesterol and serum phospholipids may be as significant as the absolute level of serum cholesterol in the production of arteriosclerosis in animals. A report from this laboratory revealed that in the production of experimental arteriosclerosis in rabbits fed cholesterol or dogs fed cholesterol plus thiouracil, the serum cholesterol levels increased disproportionately to the increase in serum phospholipid. This resulted in an abnormal cholesterol-phospholipid ratio. Kellner and his co-workers have recently shown that the intravenous injection of synthetic detergents in rabbits resulted in an elevation of the serum cholesterol and serum phospholipids. The injection of detergents in cholesterol fed rabbits partially inhibited the development of experimental arteriosclerosis. The protective effect was evident in those animals in which the elevation of serum cholesterol was accompanied by a parallel or disproportionate increase in serum phospholipids. Duff and Payne have reported that the inhibition of experimental cholesterol arteriosclerosis in rabbits with alloxan diabetes is related to a marked increase in serum neutral fat and lipid phosphorus.

It was therefore thought to be of interest to study the serum cholesterol, serum lipid phosphorus and the serum cholesterol–lipid phosphorus ratio in a group of patients with coronary arteriosclerosis to determine if further abnormal patterns of serum lipids existed in this condition. While this project was underway, a report by Gertler and his co-workers presented data and postulated that the levels of serum cholesterol and serum phospholipid are less important in coronary artery disease than is the ratio of cholesterol to phospholipids.

Methods

Two groups of individuals were studied. The first was composed of 82 patients in whom bouts of well documented coronary thrombosis had occurred. Individuals were not included in this group until at least two months had elapsed from the onset of the acute cardiac infarction. There were 20 women and 62 men whose ages varied from 32 to 72 years, the average age being 52 years. The second group consisted of 112 healthy adults varying in age from 23 to 62, the average being 41 years.

Blood was obtained in the nonfasting state. Serum cholesterol determinations were made by the method of Schoenheimer and Sperry. Serum lipid phosphorus was determined by the method of Fiske and Subbarow upon an alcohol-acetone extract of serum. The serum cholesterol–serum lipid phosphorus molar ratio was computed for each individual. The value for the serum phospholipid may be obtained by mul-
**Table 1.—Serum Cholesterol, Serum Lipid Phosphorus, and Molar Ratios in Coronary Arteriosclerosis and Control Subjects**

<table>
<thead>
<tr>
<th>Coronary Arteriosclerosis (82 patients)</th>
<th>Range</th>
<th>Mean</th>
<th>Lipid Phosphorus mg/100 cc.</th>
<th>Range</th>
<th>Mean</th>
<th>Cholesterol-Lipid Phosphorus Molar Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (112 subjects)</td>
<td>174–371</td>
<td>263 ± 44*</td>
<td>7.7–17.6</td>
<td>11.2 ± 1.9</td>
<td>1.52–2.43</td>
<td>1.88 ± 0.18</td>
</tr>
<tr>
<td></td>
<td>118–297</td>
<td>198 ± 33</td>
<td>6.5–12.7</td>
<td>9.3 ± 1.4</td>
<td>1.30–2.09</td>
<td>1.72 ± 0.17</td>
</tr>
</tbody>
</table>

* Standard deviation.

**Table 2.—Serum Cholesterol, Serum Lipid Phosphorus and Molar Ratios in Coronary Arteriosclerosis and Control Subjects**

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>20–29</td>
<td>40</td>
<td>183</td>
<td>8.66</td>
<td>1.72</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–39</td>
<td>25</td>
<td>101</td>
<td>9.40</td>
<td>1.71</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>40–49</td>
<td>30</td>
<td>215</td>
<td>10.08</td>
<td>1.71</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50–59</td>
<td>17</td>
<td>204</td>
<td>9.32</td>
<td>1.76</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>60–69</td>
<td>112</td>
<td>198</td>
<td>9.3</td>
<td>1.72</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70–79</td>
<td>82</td>
<td>263</td>
<td>11.2</td>
<td>1.885</td>
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</tbody>
</table>

**Table 3.—Individuals with Total Cholesterol Levels between 200 and 250 mg. per 100 cc.**

<table>
<thead>
<tr>
<th>Age</th>
<th>Control</th>
<th>Coronary Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>Average Total Chol.</td>
<td>Average Molar Ratio</td>
</tr>
<tr>
<td>-----</td>
<td>--------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>40–49</td>
<td>20</td>
<td>222</td>
</tr>
<tr>
<td>50–50</td>
<td>9</td>
<td>221</td>
</tr>
</tbody>
</table>

The range and the average values for the serum cholesterol, lipid phosphorus, and the serum cholesterol–lipid phosphorus molar ratio for the two groups are tabulated in table 1. The serum cholesterol values of the normal subjects varied from 118 to 297 mg. per 100 cc. with a mean of 198 mg. per 100 cc. The serum cholesterol of the patients with coronary arteriosclerosis varied from 174 to 371 mg. per 100 cc. with a mean of 263 mg. per 100 cc. Figure 1 reveals the different distribution curves for serum cholesterol of the patients and the normal subjects.

The results revealed that the serum lipid phosphorus levels of the normal subjects varied from 6.5 to 12.7 mg. per 100 cc. with a mean of 9.3 mg. per 100 cc. for the group. The lipid phosphorus for the patients with coronary arteriosclerosis varied...
from 7.7 to 17.6 mg. per 100 cc. with a mean of 11.2 mg. per 100 cc. The difference between the mean of the normal subjects and the patients was 1.9 mg. per 100 cc. (fig. 2).

Serum cholesterol–lipid phosphorus molar ratios were computed for each individual. In the normal group the ratio fell between 1.30 and 2.09, with the mean of 1.72. In the coronary series the ratios fell between 1.52 and 2.43, with a mean of 1.88. Figure 3 reveals the difference in distribution of the molar ratios of the normal subjects and the patients with coronary arteriosclerosis.

The above results have been analyzed statistically and it has been found that the differences between the means of the serum cholesterol, serum lipid and the serum cholesterol–lipid phosphorus molar ratio of the patients with coronary arteriosclerosis and the control subjects are significant.

When the two groups are divided into age decades (table 2) it is seen that no significant difference in the average values for serum cholesterol, serum lipid phosphorus, or molar ratio is evident among the groups of the coronary series. However, in the control series a significant increase in the average serum cholesterol and average serum lipid phosphorus occurs in the age groups 30 to 39 and 40 to 49 years as compared with the 20 to 29 year group. This finding is in agreement with the recent report of Keys, who found increases in serum cholesterol with advancing years. There was no change in the molar ratios in the age groups 30 to 39 and 40 to 49, indicating that the increase in cholesterol in the normals was accompanied by a comparable increase in lipid phosphorus.

In table 3, the individuals in both groups with serum cholesterol levels falling between 200 and 250 mg. per 100 cc. have been compared. The average serum cholesterol and average molar ratios were computed. It can be seen that with fairly similar serum cholesterol levels the molar ratio for the coronary group is higher than the molar ratio in the control series. Thus in the patients with coronary artery disease with normal serum cholesterol levels, the molar ratio is frequently elevated.

**Discussion**

The above results confirm previous reports that the serum cholesterol levels of patients with coronary arteriosclerosis are generally higher than in control subjects. In addition, it has been shown that the average serum lipid phosphorus level tends to be higher in patients with coronary arteriosclerosis. However, the increase in lipid phosphorus is not proportional to the increase in serum cholesterol, resulting in an elevation of the serum cholesterol–lipid phosphorus molar ratio. Ahrens and Kunkel have shown that the phospholipids are naturally occurring emulsifying agents which maintain the lipids of the serum in solution. If the serum cholesterol–lipid phosphorus molar ratio is elevated, there is, theoretically, an insufficient amount of lipid phosphorus to maintain all of the cholesterol in solution. It is possible that this abnormal state of cholesterol is one of the factors responsible for its deposition in the arteries, rather than the absolute level of serum cholesterol. Certainly there are many patients with arteriosclerosis in whom an elevation of serum cholesterol has not been recorded. Such was the case in 25 of the 82 patients with coronary arteriosclerosis in this series. Many of these individuals had elevated serum cholesterol–serum lipid phosphorus ratios with normal serum cholesterol values.

The average serum cholesterol level of 260 mg. per 100 cc. for the patients with coronary arteriosclerosis requires approximately 13 mg. per 100 cc. of lipid phosphorus to keep the molar ratio at the average level which has been found in healthy adults. However, the average lipid phosphorus for the group of patients with coronary arteriosclerosis was 11.2 mg. per 100 cc.

The serum lipid pattern of patients with coronary arteriosclerosis differs from normal in a number of respects in addition to the abnormalities in serum cholesterol and serum lipid phosphorus. In preliminary studies from our laboratory it has been shown that the serum neutral fats and the total serum lipid are also elevated abnormally in patients with coronary arteriosclerosis. It is possible that these chem-
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ical abnormalities are related to the findings by Gofman and his co-workers who by physical means have demonstrated the presence of giant-size molecules in the serum in high concentrations in patients with coronary arteriosclerosis. Certainly for investigative purposes it will no longer be sufficient to determine a single lipid of the blood but rather it will be necessary to quantitate all of the lipid components. As more information becomes available it has become increasingly apparent that coronary arteriosclerosis is associated with complex abnormalities of the serum lipid pattern.

CONCLUSION

1. A group of individuals with proved coronary artery disease has been compared with a control group of apparently healthy adults with respect to certain lipid components of the serum. The following observations were made:

(a) The serum cholesterol and serum lipid phosphorus values were elevated in the patients with coronary arteriosclerosis as compared with the control group.

(b) The increase in serum lipid phosphorus was not proportional to the increase in serum cholesterol resulting in an increase in the serum cholesterol–lipid phosphorus molar ratio.

2. The possible significance of an abnormal serum cholesterol–serum lipid phosphorus molar ratio in the pathogenesis of arteriosclerosis has been pointed out.
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ALFRED STEINER, FÖRREST E. KENDALL and JAMES A. L. MATHERS

Circulation. 1952;5:605-608
doi: 10.1161/01.CIR.5.4.605
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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