Plasma Lipids and Proteins and their Relationship to Coronary Disease among Navajo Indians

By Irvine H. Page, M.D., Lena A. Lewis, Ph.D., and Jarvey Gilbert, M.D.

Coronary disease is rare among the Navajo Indians. Their plasma proteins and lipids differ from those of the population of Cleveland in that albumin is low normal and $\alpha$- and $\gamma$-globulin elevated; total cholesterol was much lower. Since the diet and living habits are not strikingly different from those of the control group, it is suggested that heredity, in this case, is the most likely explanation for the low incidence of coronary disease and low level of cholesterol. Neither in the control nor Navajo group did mean serum total cholesterol rise with age.

REVIEW of the records of the Navajo Medical Center General Hospital at Fort Defiance, Arizona, showed that the diagnosis of myocardial infarction was made in only 5 full-blooded Navajo Indians among 10,267 admissions over a 4-year period. Even in the 5, electrocardiographic evidence failed to confirm the diagnosis. During the same period there were 60,405 out-patient visits without a single patient showing evidence of coronary disease. For comparison, the records for the same period at St. Joseph’s Hospital in Albuquerque, New Mexico, about 150 miles from the Navajo Medical Center, were reviewed. The number of admissions of white people was 20,289; of these, 146 had myocardial infarction. The distribution of the various age groups was about the same in both hospitals.

Navajos usually eat a typically American diet, often containing high-cholesterol and high-fat foods. They eat less fruit and vegetables and fry more of their foods than we do. They are well nourished; the average weight of 100 male out-patients over 30 years of age was 159 pounds (range 102 to 275 pounds) and average height 67.4 inches. The average of females weighed 147 pounds (range 101 to 220 pounds) and the average height was 62 inches. Noniodized salt is used abundantly; food is usually highly seasoned.

This striking lack of coronary disease among the Navajo people, while consuming the average American diet, prompted us to examine their plasma proteins and lipids. It is our belief that atherosclerosis is rarely caused by one defect alone, such as hyperlipemia; rather, it is the resultant of multiple factors such as diet, elevated plasma lipids, the quality of the blood vessels and the filtration pressure. This concept has recently been summarized by one of us.3

METHODS

Lipoproteins were studied by Gofman’s ultracentrifuge technic as modified by Lewis, Green, and Page. The designation of the unit of measurement $-S_{1,0}$ represents a negative sedimentation of $1 \times 10^{-13}$ cm. per second per dyne per grams at a density of 1.21 and temperature of 26 C. The advantage of using the higher density is that it allows measurement of the $\alpha$-lipoproteins.

Cholesterol was determined by the method of Abell, Levy, Brodie, and Kendall. We are indebted to Dr. Helen Brown for these determinations. The electrophoretic analysis of serum proteins was by Longsworth’s modification of the Tiselius technic, with phosphate buffer of pH 7.8 and ionic strength of 0.16 $\mu$.

Blood samples were drawn from fasting patients hospitalized at the Navajo Medical Center, Fort Defiance, Ariz., with the variety of diseases ordinarily found in a general hospital. Those with diseases known to be associated with hyperlipemia were avoided. The serum samples were shipped by air in iced Thermos bottles to the Cleveland Clinic for analysis. All of the patients studied were full-blooded Navajos.

RESULTS

The number of examinations of the serum lipoproteins was not sufficiently great to justify
Table 1.—Serum Proteins of Navajo Indians

<table>
<thead>
<tr>
<th>Group</th>
<th>No. and Sex of Subjects</th>
<th>Age (Mean ± S. E. of Mean)</th>
<th>Total Protein Gm./100 ml.</th>
<th>Albumin Gm./100 ml.</th>
<th>%</th>
<th>α1 and α2 Globulin Gm./100 ml.</th>
<th>%</th>
<th>β-Globulin Gm./100 ml.</th>
<th>%</th>
<th>γ-Globulin Gm./100 ml.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young</td>
<td>15 (12 M 3 F)</td>
<td>31 ± 1.7</td>
<td>6.94 ± 0.30</td>
<td>3.53 ± 0.20</td>
<td>51.0 ± 1.5</td>
<td>0.70 ± 0.05</td>
<td>10.0 ± 0.56</td>
<td>1.20 ± 0.04</td>
<td>17.3 ± 0.56</td>
<td>1.49 ± 0.06</td>
<td>21.5 ± 1.00</td>
</tr>
<tr>
<td>Older</td>
<td>21 (13 M 8 F)</td>
<td>50 ± 3.4</td>
<td>6.76 ± 0.25</td>
<td>3.28 ± 0.08</td>
<td>48.6 ± 1.0</td>
<td>0.68 ± 0.04</td>
<td>10.2 ± 0.54</td>
<td>1.24 ± 0.04</td>
<td>18.4 ± 0.54</td>
<td>1.53 ± 0.07</td>
<td>22.7 ± 1.09</td>
</tr>
<tr>
<td>Cleveland controls</td>
<td>27 (12 M 15 F)</td>
<td>29.5 ± 1.72</td>
<td>7.44 ± 0.15</td>
<td>4.74 ± 0.11</td>
<td>63.5 ± 1.09</td>
<td>0.54 ± 0.01</td>
<td>7.2 ± 0.36</td>
<td>1.11 ± 0.03</td>
<td>15.2 ± 0.40</td>
<td>1.04 ± 0.08</td>
<td>14.1 ± 0.56</td>
</tr>
</tbody>
</table>

SERUM LIPOPROTEINS AND ChOLESTEROLS OF NAVAJO INDIAN MALES AND CLEVELAND AREA WHITE MALES

<table>
<thead>
<tr>
<th>CHOLESTEROL</th>
<th>-S25-40</th>
<th>-S1-10</th>
<th>-S70-400</th>
<th>-S40-70</th>
<th>-S20-25</th>
</tr>
</thead>
<tbody>
<tr>
<td>young</td>
<td>old</td>
<td>young</td>
<td>old</td>
<td>young</td>
<td>old</td>
</tr>
<tr>
<td>mg/100 ml</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>265</td>
<td>250</td>
<td>235</td>
<td>210</td>
<td>180</td>
<td>150</td>
</tr>
<tr>
<td>240</td>
<td>225</td>
<td>200</td>
<td>175</td>
<td>150</td>
<td>120</td>
</tr>
<tr>
<td>220</td>
<td>200</td>
<td>175</td>
<td>150</td>
<td>120</td>
<td>100</td>
</tr>
<tr>
<td>200</td>
<td>180</td>
<td>150</td>
<td>120</td>
<td>100</td>
<td>80</td>
</tr>
<tr>
<td>180</td>
<td>160</td>
<td>140</td>
<td>120</td>
<td>100</td>
<td>80</td>
</tr>
<tr>
<td>160</td>
<td>140</td>
<td>120</td>
<td>100</td>
<td>80</td>
<td>60</td>
</tr>
<tr>
<td>140</td>
<td>120</td>
<td>100</td>
<td>80</td>
<td>60</td>
<td>40</td>
</tr>
<tr>
<td>120</td>
<td>100</td>
<td>80</td>
<td>60</td>
<td>40</td>
<td>20</td>
</tr>
<tr>
<td>100</td>
<td>80</td>
<td>60</td>
<td>40</td>
<td>20</td>
<td>0</td>
</tr>
</tbody>
</table>

Fig. 1. Serum cholesterol and lipoproteins determined by ultracentrifugation, d 1.21, with sodium chloride and potassium bromide, of Navajo Indian males and Cleveland area white males. Shaded area represents Mean ± the standard error of the Mean, of normal white males from Cleveland.

separate analysis by sexes. Instead, subjects were divided into younger (31 years mean age) and older (59 years mean age).

The mean of the total plasma proteins of the Navajo Indians was only slightly lower than the average found in people from the Cleveland area; albumin was lower, 3.21–3.53 Gm. as compared with 4.74 in the Cleveland group (table 1 and figs. 1 and 2). Globulins tended to be slightly elevated, especially in the α- and
SERUM LIPOPROTEINS AND CHOLESTEROL OF NAVAJO INDIAN FEMALES AND CLEVELAND AREA WHITE FEMALES

Table 2.—Serum Cholesterol and Lipoproteins of Navajo Indians

<table>
<thead>
<tr>
<th></th>
<th>No. of Subjects</th>
<th>Age, Yr.</th>
<th>Lipoproteins mg./100 ml.</th>
<th>Cholesterol mg./100 ml.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>-S70-400</td>
<td>40-70</td>
</tr>
<tr>
<td>Navajo Indians</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Young Men</td>
<td>12</td>
<td>32 ± 1.7</td>
<td>25 ± 4.1</td>
<td>21 ± 2.8</td>
</tr>
<tr>
<td>Older Men</td>
<td>13</td>
<td>64 ± 3.3</td>
<td>15 ± 2.9</td>
<td>22 ± 3.2</td>
</tr>
<tr>
<td>Young Women</td>
<td>3</td>
<td>28†</td>
<td>37</td>
<td>42</td>
</tr>
<tr>
<td>Older Women</td>
<td>8</td>
<td>54†</td>
<td>30</td>
<td>31</td>
</tr>
<tr>
<td>Cleveland controls</td>
<td></td>
<td></td>
<td>7-96</td>
<td>14-49</td>
</tr>
</tbody>
</table>

* Mean ± standard error of mean.
† S.E. not calculated because of insufficient numbers.
\(\gamma\)-fractions; the \(\beta\)-fraction was the same as in the Cleveland control group.

The various lipoprotein components of serum of the Indians were also very similar to those of our Cleveland control group. The \(-S_{15-40}\) and \(-S_{1-10}\) fractions tended to be lower in the Indians. These fractions correspond to \(\beta_1\) and \(\alpha_1\) lipoprotein. Mean total cholesterol values were lower in the Indians by approximately 50 mg. per 100 ml. The analytic variation with the method employed was 4 mg. per 100 ml. in serum containing normal amounts of cholesterol. There was no difference between the older and younger age groups, either among the Indians or the control group (table 2 and figs. 1 and 2).

**Discussion**

There seems to be little doubt that coronary disease is uncommon among Navajo Indians. The plasma proteins of the Indians differ from those of a control group from the Cleveland area in having somewhat lower value for albumin. It would be idle to speculate on the cause because there are so many possibilities. The difference is not great enough to suspect widespread malnutrition among the Indians. The elevated \(\gamma\)-globulin may have been characteristic of the Navajo population or may have reflected some rather widespread pathologic conditions. We have no way of knowing which is correct. The association of elevated \(\gamma\)-globulin levels and low serum cholesterol is reminiscent of our findings in patients with myelomatosi.\(^6\) The only significant difference in the lipoprotein pattern is the slightly lowered \(\alpha_1\) and \(\beta_1\)-fractions. The supposedly most highly atherogenic fractions (\(-S_{40-70}\) and \(-S_{16-40}\)) did not vary from values found in the controls.

Serum total cholesterol was definitely lower in the Indians and this may be one facet of the low degree of atherogenesis among the Navajo Indians. A difference in means of 50 mg. per 100 ml. appears sufficiently great to be of importance, although ignorance must be admitted about what differences are significant in terms of atherogenesis. In neither controls nor Indians was there a difference in the level of serum cholesterol between the younger and older groups. This confirms our observation on a smaller but very critically selected group of normal white persons.\(^7\) We believe that serum cholesterol rises in some people with aging; whether as a result of disease or simply as normal accompaniment of aging is not known. Contrariwise, a rise does not occur under many other circumstances.

Since the Navajo diet as far as cholesterol intake is concerned is the same as that of most Americans, according to Gilbert,\(^1\) it is hard to explain why the serum cholesterol levels are lower than levels of the non-Indian population living in the same geographic area. The Navajo people live to ages at which coronary artery disease develops in other people.

The most likely explanation for both the reduced levels of serum cholesterol and the low incidence of coronary disease seems to us to be heredity. As Gilbert puts it, “Navajos almost never become bald. They have practically no hair on the chest or the sides of the face. They are different outwardly, probably because of heredity, and probably are also different inwardly.”

The importance of heredity in determining the serum cholesterol and lipoprotein pattern has been emphasized by studies on 2 strains of dwarf pigs, a long-lean and a short-fat type. The concentration of serum cholesterol and lower density (i.e. \(-S_{70-400}\), \(-S_{62-70}\) and \(-S_{15-40}\) lipoproteins was significantly higher in the short-fat than the lean animals.\(^8\)

Chavez\(^2\) has shown that essential hypertension is rare among the poor Mexican and Indian population (2.6 per cent) and rises (37 per cent) among the pure white and those with little Indian blood. Angina pectoris, coronary thrombosis, and coronary atherosclerosis were also infrequent in the former group. Chavez writes me that the diet of the Indian population in Mexico is mostly carbohydrate; fat and protein intake is very low. The fat intake amounts to 12 to 14 per cent of the total caloric intake and protein to 10 to 12 per cent. It is interesting to compare these Indians with the Navajos in whom a diet high in fat apparently failed to increase the incidence of atherosclerosis. While such evidence as this is not conclusive, nevertheless it suggests caution in the accept-
ance of radical changes in diet calculated to prevent coronary atherosclerosis. On the other hand it should not engender a fatalistic attitude to close the door to human dietary experimentation.

ACKNOWLEDGMENT

We wish to express our deep appreciation to Dr. Marion Sumner for his help in collecting the blood samples. The technical assistance of Mrs. Laverne Fisher is gratefully acknowledged.

SUMMARY

1. The serum cholesterol, proteins and lipoproteins have been measured in a group of pure-blooded Navajo Indians because of the observations that coronary artery disease among them is rare.

2. Comparison with plasma of a non-Indian population in the Cleveland area shows albumin to be low normal and α and γ-globulin elevated in the Indians. Alpha₁ and β₁-lipoproteins were low but the remainder of the lipoproteins did not differ from the controls. Mean total cholesterol was lower than that in the control group by a degree well outside the analytic error.

3. Since diet and living habits of the Navajos were not strikingly different from those of the control group, heredity seems the most likely explanation for both the low incidence of coronary disease and the low level of serum cholesterol. Probably contributing to the low incidence of coronary disease were the low plasma cholesterol levels.

4. In neither the control nor Navajo groups did mean serum total cholesterol rise with age.

SUMARIO IN INTERLINGUA

1. Le cholesterol, proteinas, e lipoproteinas del sero eseva mesurate in un gruppo de indianos navajo de sanguine pur, proque il habeva esite observeate que morbo de arteria coronari es rar in iste populuo.

2. Le comparation con studios de plasma ab subjectos non-indian in le area de Cleveland monstava que in le indianas le nivello de albumina es basse-normal durante que le globulinas α e γ ha nivelllos elevate. Lipoproteinas α e β₁ monstava nivelllos basse, sed le altere lipoproteinas non differa ab le valores del gruppo de controlo. Le valores median del cholesterol total eseva plus basse que in le gruppo de controlo. Le differentia excedeva le margine de error analytic.

3. Proque le dieta e le habitudes del viver inter le navajos non differa frappantemente ab illos del gruppo de controlo, hereditate pare offerer le plus satisface explication del basse frequentia de morbo coronari e del basse nivello de cholesterol seral. Il es probable que le basse nivelllos de cholesterol plasmatic contribueva a reducir le frequentia de morbo coronari.

4. Le nivello median de cholesterol total del sero non se augmentava con le etate del subjectos in o le gruppo de controlo o le gruppo del navajos.

REFERENCES

Plasma Lipids and Proteins and their Relationship to Coronary Disease among Navajo Indians

IRVINE H. PAGE, LENA A. LEWIS and JARVEY GILBERT

Circulation. 1956;13:675-679
doi: 10.1161/01.CIR.13.5.675

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/13/5/675

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/