A Long-Time Study of the Blood Lipids of Two Students of Atherosclerosis

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

SUMMARY

A study of serum cholesterol and lipoproteins covering periods of 28 years in a male physician and 17 years in a female research worker showed relative constancy for the cholesterol levels and greater variability for the lipoproteins. Cholesterol was reduced sharply and temporarily just after each influenzal infection. In the male, the level of cholesterol was slightly above 300 mg/100 ml for more than 13 years. An extremely low cholesterol and high carbohydrate diet proved unacceptable. A more liberal, relatively low-saturated fat, low-cholesterol, and high polyunsaturated fatty acid diet with about 30% of the calories from fat, maintained the cholesterol level between 230 and 270 mg and has been followed with relish for a number of years. A myocardial infarction occurred 27 years after the study began. Clofibrate since then has reduced the cholesterol level further.

The female subject is in good health and maintains cholesterol levels slightly below 300 mg on a usual American diet. She is 10 years younger than the male. Her - S 40-70 lipoproteins have usually been well below the male subject's. Weight gain and lack of exercise seemed regular to increase both levels.

The data are presented because we believe them to be accurate; their interpretation is for the reader. We hope he must wait for some time for the outcome of the study.

Additional Indexing Words: Coronary disease Diet Anticholesterol drugs

Occasionally self-revelation, if it does not consist of recounting dreams, has significance. For many years we have regularly measured our own blood lipids. One of us (I. H. P., aged 68, 5'10", 149 lb) has tried many, and often odd, dietary experiments on himself, beginning in 1940, while the other (L. A. L., aged 58, 5'8", 145 lb) has followed a much more customary and perhaps sensible food pattern. One of us (I. H. P.) had a myocardial infarction in June 1967, while the other is well.

Care has been taken in the drawing of blood samples to avoid stasis from long application of a tourniquet, because cholesterol content rises surprisingly quickly. The methods used for analysis were not always the same over the years, but all were controlled by determining the limits of error through double-blind analysis.

The technical error is small enough that the cholesterol and lipoprotein level can be assigned to a given sample with considerable confidence.

Technical error = \sqrt{d^2/2K} where K is the number of duplicates and d is the difference between duplicates (table 1).

The above confidence values were determined over a 3-year period and are representative of the study as a whole (fig. 1).

Before 1951, the values on I. H. P. are not charted because they were done repeatedly but sporadically in connection with experiments on several varieties of low-cholesterol diets, in which high-cholesterol-containing foods were specifically excluded and the loss of fat was replaced by the noncholesterol-containing varieties. None caused significant

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change in the level of blood cholesterol which remained quite consistently about or slightly above 300 mg/100 ml. During an earlier and quite exceptional period of 9 months in 1943, both fat and cholesterol were sharply curtailed, and carbohydrate was greatly increased. The kinds of carbohydrate were not accurately controlled but, because of the war, contained less sugar than customary. A fall to a level averaging 210 mg occurred. The experiment was also associated with an unenviable contraction in his circle of friends. Again in 1953, a low-fat diet was instituted, restrictive at first and much more relaxed after

### Table 1

<table>
<thead>
<tr>
<th>Lipoprotein Category</th>
<th>Mean (mg/100 ml)</th>
<th>Technical Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-S 25-40 (i.e. S&lt;sub&gt;f&lt;/sub&gt; 0-12)</td>
<td>185</td>
<td>3.5</td>
</tr>
<tr>
<td>-S 40-70 (i.e. S&lt;sub&gt;f&lt;/sub&gt; 12-20)</td>
<td>320</td>
<td>29.0</td>
</tr>
<tr>
<td>-S 70-400 (i.e. S&lt;sub&gt;f&lt;/sub&gt; 20-100)</td>
<td>40</td>
<td>5.0</td>
</tr>
<tr>
<td>-S 0-10 (not floated at d 1.063, equivalent to α-lipoprotein)</td>
<td>255</td>
<td>19.5</td>
</tr>
</tbody>
</table>

### Figure 1

*Comparison of lipoprotein and cholesterol blood levels in a female and a male over a period of 18 years exhibiting the effects of diet, exercise, virus infections, myocardial infarction, and to a much lesser extent clofibrate.*

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a year or two. In 1966, an increase (not measured) of polyunsaturated fatty acids was made. This diet contained less cholesterol than is usual in the ordinary American diet. It resembles that used in the National Diet-Heart Study. This has been maintained to the present.

The plant sterol suspension (Cytellin, Lilly) was tried but did little more than blunt the appetite, being itself so unappetizing. A variety of drugs, purporting to reduce cholesterol but not including triparanol, were tried intermittently for a period of 2 years with no significant effect except to remind the experimenter of the nuisance of taking large numbers of pills four times a day. A viral infection in 1963 was associated with a sharp fall in cholesterol but a concurrent rise in the \(-S\) 40-70 (that is, S, 12-20) lipoprotein. On June 11, 1967, an anterior myocardial infarct occurred while the cholesterol level was about 210 to 230 mg. A week later the cholesterol level had risen to 280 mg, and the level of very low density lipoprotein, from 30 mg to nearly 100 mg; a sharp fall in both followed shortly. This rise occurred during a period when almost no food was being taken and little fluid as well; hence dehydration may have played a part, despite fall in body weight. After 6 weeks, use of clofibrate was started and has been continued for 2 years. Serum cholesterol has stayed at levels of about 180 to 210 mg, and very low density lipoprotein, at levels of 60 to 70 mg/100 ml of serum.

Triglycerides have been measured only since 1966. They were variable before the heart attack, rose directly following it, and have since been quite stable at levels of 80 to 100 mg.

At about the same time as the regular and detailed description of the blood lipids of the male subject was undertaken, the female investigator joined the study (L. A. L.).

During the period of 18 years the greatest decrease in serum cholesterol and lipoprotein concentrations of L. A. L. occurred during a bout of viral pneumonia, and the largest short-time increase, during some vacations when "gourmet" eating rather than exercise was the pastime; weight gain of about 5 pounds occurred. She ate the usual American diet. With return to work, exercise, and normal food habits the cholesterol level decreased. After other vacations when no weight gain occurred and a large amount of exercise was taken, no change in levels was noted. As in the female population studies, increase in serum cholesterol level occurred during the menopause.

The cholesterol values for both subjects were quite stable and the level of \(-S\) 40-70 lipoproteins of the female for several years was clearly much lower than that of the male. The variability of the lipoproteins over the 15-year period would have made their predictive value precarious in contrast to that of the cholesterol.

The very low density, \(-S\) 70-400, lipoprotein levels of Lewis were consistently within the average normal range throughout the study (average normal, 25 mg/100 ml). In contrast, the levels of Page varied greatly, from a low of 12 mg to a high of 390 mg/100 ml (average normal, 60 mg/100 ml), which did not correlate with the relatively minor weight changes. Blood sugar levels have been normal, but glucose tolerance was not measured. The alpha-lipoprotein level of Lewis was in the normal range for females—it increased slightly during the study—18% higher (average level of all determinations) during the second 9 years than during the first 9 years. I. H. P.'s alpha-lipoprotein level increased significantly during the study, the average level for the first 9 years being 157 mg, a low normal level, while during the second 9 years it was 235 mg (normal, 180 mg/100 ml). The low density beta-lipoprotein (\(-S\) 25-40) levels of both subjects were in the high normal range throughout the 18 years.

Discussion

The analytical problems in ultracentrifugal determinations are such that small changes in levels may be misleading. Larger changes, such as those observed in L. A. L. following "gourmet" eating, are certainly real. The slight increase in alpha-lipoprotein level of Lewis (average normal, 249 mg/100 ml) and the
more marked increase in Page are changes
similar to those reported in population studies
by Chirkin and Makhocheeva6 who found it
increased in women after the age of 45 to 49
and in men past the age of 50 to 54. Increase
in alpha-lipoprotein also occurs as a result of
exercise.7 Somewhat more consistent exercise
in the form of "walking the dog" has been
taken by L. A. L. during the later part of
the study, while I. H. P. had consistently taken
moderate exercise regularly. In hyperlipemic
patients treated with cholesterol-lowering
diets for 1 to 10 years, no consistent change in
alpha-lipoprotein levels has been noted.8
Whether the relatively high alpha-lipoprotein
levels of I. H. P. during the second half of
the study had any delaying effect on the occur-
rence of his myocardial infarction is specula-
tive. Certainly the 50 to 60-year age group of
men is very vulnerable, but Page got through
that decade without an infarct despite a
strong taint of cardiovascular disease from his
father's side.

As in the female population studies, a slight
increase in serum cholesterol level during
menopause is suggested in 1965-1966. The
levels in 1967-1968, however, do not continue
the upward trend.

Extremely low cholesterol diets with chole-
sterol-containing fats replaced by the non-
cholesterol-containing varieties and with
correspondingly high carbohydrate content
neither reduced cholesterol nor proved socially
pleasant. But the relatively low-saturated fat,
high-polyunsaturated fatty acid food pattern
was wholly acceptable to Page; about 30% of
calories are taken as fat. It lowered his
cholesterol level significantly and clofibrate
lowered it even further. Virus infections in
both subjects were extremely effective agents
but are not to be recommended.

The plant sterol anticholesterol preparation
was too unpalatable for regular consumption.
It should not be forgotten that anything taken
as a requirement four times a day is likely to
be discontinued unless it causes minimum
gustatory annoyance. Clofibrate seems to be
such a drug.

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