The Effect of Vegetable Fat Ingestion on Human Serum Cholesterol Concentration

By E. A. Hildreth, M.D., S. M. Mellinkoff, M.D., G. W. Blair, M.D., and D. M. Hildreth, B.S.

In 3 healthy male physicians a reduction of dietary fat produced a significant fall in the serum cholesterol concentration. Subsequently, when a diet containing normal quantities of fat but very low in cholesterol was taken, a rise in serum cholesterol concentration occurred in all 3 subjects.

While controversy has long prevailed concerning the possibility of lowering serum cholesterol by regulation of the diet, there is now ample evidence that in most individuals the serum cholesterol concentration will fall if the intake of fat is sufficiently restricted. Some investigators believe that the chief reason for this chemical alterations is that a low-fat diet automatically restricts the ingestion of cholesterol. However, animal experiments suggest that the dietary fat level, per se, is more important than is the dietary cholesterol level in changing the serum cholesterol concentration. Our experiments were designed to discover whether human serum cholesterol concentration can be affected by a diet low in cholesterol but of normal fat content. Since there is evidence that vegetable fats contain no cholesterol whatsoever and since sterols found in plants are not absorbed or converted into cholesterol in significant amounts by animals, it seemed worthwhile to investigate the effect of vegetable fat on serum cholesterol concentration.

Evaluation of the effect of diet on serum cholesterol concentration requires studies over a considerable period of time. In view of the difficulties of conducting prolonged studies on patients, three of the authors served as subjects.

One of the authors (subject 2) constantly had a level of serum cholesterol which exceeded the normal. The other 2 subjects had much lower values and were always within the normal range of serum cholesterol concentration. One of the authors, a trained dietitian, designed and supervised the diets.

Therefore 3 of the authors subjected themselves to strict diets for three to eight months. Each was studied; first on his customary diet, second when both fat and cholesterol were greatly restricted, and third, when through a diet containing vegetable fats, cholesterol was restricted but fats were normal in amount. The serum cholesterol was estimated on samples taken twice weekly during these periods by a method previously described. The normal range of values for this method agrees with those recently reported by Keys.

The results showed that the serum cholesterol concentration was always decreased by dietary restriction of both fat and cholesterol, but that it again approached the control level when fat without cholesterol was added.

Plan of Study

The subjects kept a list of the kinds and amount of food ingested. Liquids were measured exactly in

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This work was done while one of us (E.A.H.) was a Postdoctorate Research Fellow of the United States Public Health Service, and another (S.M.M.) was a Smith, Kline and French Fellow in Gastroenterology.
cc., vegetables as cupsful, and more solid food as servings. At the start of the investigation, the subjects and the dietitian discussed the menus, so that the more indefinite of these measurements could be roughly standardized. Only subject 3 was placed on a weighed diet, and he only for a part of the experiment. For the experimental periods the dietitian designed the diets and supplied each person with a diet list adjusted to his taste.

The estimated composition of these diets is given in table 1. During the control period, 2 subjects ate what they were accustomed to have. The third (subject 2), who had a high serum cholesterol level, had been limiting his fat intake for a year and continued so to do.

During the first test period, total fat was greatly reduced below the control level, but protein was kept unchanged, and the total calories maintained by increasing carbohydrate. The protein intake was kept as constant as possible because there are theoretic reasons for suspecting that dietary protein might also influence the serum cholesterol level. Had the caloric intake been altered, a confusing variable would have been present, because semi-starvation short of ketosis will lower serum cholesterol concentration. The body weights of these subjects were recorded daily and did not fluctuate more than 2 lbs. during the entire experiment.

Results

Since each subject presented a somewhat different problem, the three sets of data will be considered separately.

Subject 1 was a white male physician, 26 years of age. There was no history of any close relative's dying or suffering from a disease attributed to atherosclerosis except in old age. Calculation showed that he selected a diet providing approximately 2500 calories and 100 Gm. of fat daily. During the 37 days on this diet (the control period) the serum cholesterol concentration averaged 217 mg. per cent (fig. 1), and fluctuated little. His diet was then changed to one containing 9 mg. per cent. The serum cholesterol concentration diminished by 47 mg. per cent within five days and remained at approximately this level for 18 days, the average for this period being 170 mg. per cent. At this point 86 Gm. of vegetable fat were added to the diet while the caloric value was kept constant. The serum cholesterol concentration began to rise promptly and after 14 days approximated the original level (fig. 1). For the last 20 days of the high vegetable fat diet the control level was maintained, averaging 200 mg. per cent. However, the average value during the whole 34 days of the diet was only 192 mg. per cent, since this includes the transition figures as well as the final level attained.

Subject 2 was a white male physician, aged 30 years. Coronary artery disease and hypercholesterolemia were prevalent in his immediate family. This subject had voluntarily restricted his fat intake for the year preceding this study to the amount of 58 Gm. daily. He continued this diet for the first 20 days of this study and his serum cholesterol concentration averaged 290 mg. per cent (fig. 1), but fluctuated within a wide range. In order to test the possibility that the restricted diet taken during the year preceding the study had not lowered his cholesterol concentration, his fat intake was then raised to 114 Gm. per day. During 56 days on this diet containing a normal quantity of fat, there was no significant change in the serum cholesterol concentration, so that it is proper to condense these two periods into a single control period. In this prolonged control period...
there was an average serum cholesterol level of 287 mg. per cent.

The dietary fat was then reduced to 10 Gm. per day. The serum cholesterol concentration dropped significantly, the average for this period being 241 mg. per cent, but the fluctuations in the serum cholesterol continued to be great on this low fat diet. After 37 days the diet was changed to one high in vegetable fat. This he continued for 39 days, during which 105 Gm. of vegetable fat were consumed daily. On this diet containing little cholesterol and approximately 110 Gm. of total fat this subject’s serum cholesterol concentration rose to its original level.

Subject 3 (fig. 1) was a white male physician, 26 years of age, with a family history of coronary artery disease. Three members of his family, however, failed to show hypercholesterolemia when tested.

During the control period of 20 days, this subject ingested an average of 138 Gm. of fat per day (table 1) and maintained an average serum cholesterol of 221 mg. per cent (fig. 1). At the end of this period, the dietary fat was reduced to 62 Gm. for a period of 45 days. On this low fat diet the serum cholesterol level became stabilized at approximately 60 mg. per cent lower than it had been during the control diet, a highly significant difference. Finally, 70 Gm. of vegetable fat a day were added for five and one-half months. After four and one-half months on this diet, his serum cholesterol concentration did not differ significantly from the control level. While the subject was on a high vegetable fat diet the serum cholesterol rose, the average changing from 162 mg. per cent (diet II) to 206 mg. per cent (diet III).

Finding that in subject 3 the high fat, low cholesterol diet resulted in a delayed return of serum cholesterol to the control level, additional studies were made on him. First this period was continued for many months. Also, to assure ourselves that the composition of the diet was exactly known, he was placed on a constant weighed diet, eating the same foods every day. No conspicuous change in the serum cholesterol resulted, although a slow increase in serum cholesterol level is obvious in this part of the experiment (fig. 1).

Finally, to see if the control cholesterol level might have changed, a distinct possibility because of the long duration of the experiment, a final control period of 64 days was undertaken. In this the average serum cholesterol level was 213 mg. per cent.

In setting up the data for statistical analysis (table 2) there was one important consideration. Inspecting figure 1 shows that when the diet was changed the serum cholesterol level did not always respond immediately. Thus there was usually a period which in five instances lasted less than 18 days, but on one occasion continued as long as four and one-half months, until the new level was attained.

<table>
<thead>
<tr>
<th>Subject and diet</th>
<th>Protein (Gm.)</th>
<th>Fat (Gm.)</th>
<th>Carbohydrate (Gm.)</th>
<th>Calories</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Animal</td>
<td>Veg.</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>1 Diet I</td>
<td>68</td>
<td>60</td>
<td>37</td>
<td>97</td>
</tr>
<tr>
<td>II</td>
<td>66</td>
<td>5</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>III</td>
<td>65</td>
<td>5</td>
<td>90</td>
<td>95</td>
</tr>
<tr>
<td>2 Diet I (A)</td>
<td>62</td>
<td>38</td>
<td>20</td>
<td>58</td>
</tr>
<tr>
<td>I (B)</td>
<td>71</td>
<td>100</td>
<td>14</td>
<td>114</td>
</tr>
<tr>
<td>II</td>
<td>64</td>
<td>6</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>III</td>
<td>66</td>
<td>6</td>
<td>105</td>
<td>111</td>
</tr>
<tr>
<td>3 Diet I</td>
<td>83</td>
<td>60</td>
<td>78</td>
<td>138</td>
</tr>
<tr>
<td>II</td>
<td>84</td>
<td>46</td>
<td>16</td>
<td>62</td>
</tr>
<tr>
<td>III</td>
<td>84</td>
<td>46</td>
<td>92</td>
<td>138</td>
</tr>
<tr>
<td>(A &amp; B)</td>
<td>80</td>
<td>60</td>
<td>80</td>
<td>140</td>
</tr>
</tbody>
</table>

We had little interest in this transition period, and sought to compare the new level of the cholesterol concentration with the corresponding levels existing before and afterward. The decision as to when the transition period ended was usually easy. In table 2, therefore, the data have been set up in two ways. In the first method all the data obtained during each dietary period have been averaged, so that the transition period and the final level were combined, a method which has the advantage of avoiding a decision which might be regarded as arbitrary. We place more weight, however, on the statistics secured when the transition period was omitted. But indeed, except in one
instance, the changes between cholesterol levels on diets used were all significantly different by both methods. The one instance in which the difference was not significant when values of the transition period were included in the calculations was highly significant when the transition values were omitted. Therefore, we have confidence in the reality of the changes we describe.  

**COMMENT**

In all three cases a reduction in fat consumption was followed by a lowering of the serum cholesterol concentration. The change is very striking and statistical analysis confirms the impression that the average level on the low fat diet is significantly lower than that of the control period in all three subjects. It is worthy of note that in one subject (subject 2) a 10 Gm. fat diet lowered the serum cholesterol concentration, whereas a 58 Gm. fat diet did not. On the other hand, in subject 3, there was a significant reduction in the serum cholesterol concentration on a 62 Gm. fat diet. These findings are in agreement with our impression gained in treating a variety of patients with low fat diets, that there is considerable variation from person to person in the degree of fat restriction necessary to lower the serum cholesterol concentration. A similar impression is gained from the variable effects upon the serum cholesterol concentration in patients on the Kemner rice diet.  

Also, experience with patients has led us to conclude that the rate of decrease of serum cholesterol concentration is dependent on the degree to which fat ingestion is restricted. Figure 1 clearly shows that there was a slow fall of the serum cholesterol level when the diet re

<table>
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<th>Table 2.—Serum Cholesterol Levels under Different Diets</th>
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<tr>
<td><strong>Subject</strong></td>
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<tr>
<td>-------------</td>
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<tr>
<td></td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>Including Transition Levels</td>
</tr>
<tr>
<td>Omitting Transition Levels</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>Fat 68 Gm.</td>
</tr>
<tr>
<td>Including Transition Levels</td>
</tr>
<tr>
<td>Fat 114 Gm.</td>
</tr>
<tr>
<td>Omitting Transition Levels</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>Including Transition Levels</td>
</tr>
<tr>
<td>Omitting Transition Levels</td>
</tr>
</tbody>
</table>

* The difference from the preceding mean is significant for p = 0.05.
not rise when his dietary fat was raised from 58 to 114 Gm., so evidently the 58 Gm. fat diet had not been adequate to lower his serum cholesterol value. Similarly, Turner was unable to raise serum cholesterol levels above the normal or control average by markedly increasing the fat ingestion of his patients.29

A diet measured by household measurements is practicable for most patients, while a weighed diet is not. Although we at first questioned the dependability of the rough measurements, it appears that this method suffices for the production of significant changes in serum cholesterol levels. As a further test of the adequacy of this method, one subject (subject 2) was placed on a weighed constant diet, giving the same fat, protein, and carbohydrate values which the rough measurements were supposed to supply. The more exact measurement was accompanied by no noteworthy change in the serum cholesterol values. This is as one might have expected from the work of O'Key and Boyden,16, 24 who demonstrated that small day to day variations in the diet had little influence on serum cholesterol.

That the reduction in the serum cholesterol was not due to the elimination of dietary cholesterol is clear in subjects 1 and 2. Restoration of the fat in the diet without restoring the cholesterol is followed by a prompt return to the control levels. This has also been noted by Keyes in one patient.6

The results in subject 3 were much more gradual. When fat was restored to the diet, without cholesterol, the blood level rose significantly, finally attaining values insignificantly lower than in the control periods. Also a resumption of the control diet led to no significant change. We believe the end results secured in this subject are similar to those encountered in the other cases. Apparently in this case, as well as in subjects 1 and 2, reduction of serum cholesterol concentration on the low fat diet was not due to the elimination of exogenous cholesterol.

It seemed in these experiments that the total fat content of the diet was a more important factor in determining the serum cholesterol level than is the amount of cholesterol ingested. This hypothesis is consistent with other experiments on cholesterol metabolism. It is known that the body synthesizes cholesterol from acetate, which is made available mainly by breakdown of fat.9, 10, 13 However, carbohydrate, and to some extent protein, can give rise to two carbon fragments which are used by the body in synthesizing cholesterol. A portion of the cholesterol so formed is excreted into the intestines.23 Its subsequent reabsorption, together with the absorption of ingested cholesterol, appears to depend upon the simultaneous absorption of fatty acids.12, 26 It may well be that this fatty acid–cholesterol absorption relationship, as well as cholesterol synthesized from acetate, shares in the regulation of the serum cholesterol concentration. Lowering of the fat content of the intestine may thus decrease the amount of cholesterol absorbed and also the amount of acetate available for cholesterol synthesis in the body. These may be the methods by which a low fat diet decreases the serum cholesterol concentration.

**SUMMARY**

The following results were obtained in a study designed to show the effect on serum cholesterol when vegetable fat containing no cholesterol was added to a diet in which total fat had been restricted previously.

1. In three healthy male physicians a reduction in the dietary fat produced a significant fall in the serum cholesterol concentration.

2. In two of the individuals, addition of vegetable fat to the diet was associated with a rapid significant rise in the serum cholesterol, to the levels observed before fat restriction. In the third, the serum cholesterol rose much more gradually, but also attained the control values.

3. Therefore, it would seem that in these three subjects the restriction of total fat and not of cholesterol alone was probably the decisive factor in lowering the serum cholesterol concentration.

**ACKNOWLEDGMENTS**

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