The influence of dietary protein on serum cholesterol in man and experimental animals


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1. Introduction

While studying the effect of dietary protein derived from animal sources on the structure and function of parenchymous organs in rabbits, Ignatowski (1) in 1909 discovered fortuitously that rabbits fed meat, milk and eggs developed arterial lesions. The resemblance of these lesions to human atherosclerosis was immediately recognized. Great interest was aroused by the findings of Ignatowski (1) since now an experimental model for studying human atherosclerosis was provided. Furthermore, he had demonstrated that atherosclerosis could be produced by dietary means. The changes in the vessels were initially ascribed to the injurious effects of animal protein (1). However, Stuckey (2) tested different foodstufs of animal origin and found that the feeding of egg yolk to rabbits resulted in atheromatous changes in the intima, whereas other animal products, such as milk, egg white and meat juice had no effect. These findings together with the observation that feeding egg yolk resulted in deposition of large amounts of fatty substances in the liver and aorta, prompted the hypothesis that the lipid in the egg yolk was responsible and that the protein in the diet had little to do with atherosclerosis. Further studies on rabbits fed egg yolk by Wesselin (3) provided evidence that the fatty substances deposited in the liver and aorta contained mainly cholesterol esters. This prompted the idea that in the diet the cholesterol from the egg yolk was the culprit. This early work was rounded off by Anitschkow and Chalatow (4) and Wacker and Hueck (5) who demonstrated independently that feeding to rabbits crystalline cholesterol dissolved in sunflower oil resulted in similar arterial lesions as did the feeding of egg yolk. Therefore, the view of Ignatowski (1) that the arterial lesions in rabbits fed animal products could be attributed to animal protein, was largely abandoned. From then on the inclusion of cholesterol in the diet was generally considered as a prerequisite for the production of experimental atherosclerosis in rabbits. Nevertheless, a number of investigators over the years have still adhered to the idea that dietary protein might play an important role in the etiology of atherosclerosis. Newburgh (6) observed in 1919 that high casein diets were able to produce atherosclerosis whereas the feeding of soybeans could not. Similar results were reported by Meeker and Kesten (7) in 1941 and by Lambert et al. (8) in 1958, and by Wigand in 1959 (9).

The induction of atherosclerosis in rabbits fed casein was associated with a marked increase of the concentration of cholesterol in the serum (7–10). When the rabbits were fed soy protein, the level of serum cholesterol remained low. We have obtained similar results in our studies with cholesterol-free, semipurified diets in which the protein source was the only variable (Fig. 1). When the rabbits on the casein diet were transferred to the diet containing soy protein (Fig. 1), a rapid decrease in serum cholesterol occurred. Conversely, changing the rabbits from the diet containing soy protein to the casein diet

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Figure 1: Serum cholesterol concentrations in rabbits fed cholesterol-free, semipurified diets containing either 40% (w, w) casein or 40% (w, w) soy protein. o, group receiving diet containing casein before the cross-over and soy protein after the cross-over; ●, soy protein and casein, respectively. Each point denotes the mean from 6 rabbits, aged 13 weeks at the beginning of the experiment; the vertical bars correspond to 1 SE. Reproduced from reference (11), with permission from the publishers.

resulted in a significant increase in the concentration of serum cholesterol after only one day (11).

2. The nature of dietary protein and serum cholesterol in rabbits

Carroll and Hamilton (12, 13) have reported the results of a series of feeding trials designed to test the effect of different proteins on plasma cholesterol levels. Some protein sources, such as extracted whole egg, skim milk powder and casein produced rather high concentrations of serum cholesterol, whereas other sources of protein, such as wheat gluten, peanut meal and soybean protein were able to maintain low levels of serum cholesterol (Fig. 2).

Table 1: Concentration of serum cholesterol in rabbits fed semipurified diets containing various sources of protein or amino acid mixtures (25%, w, w)

<table>
<thead>
<tr>
<th>Protein and amino acid source</th>
<th>Amino acids composition equivalent to:</th>
<th>Number of animals</th>
<th>Serum cholesterol (mmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Casein</td>
<td>Casein</td>
<td>6</td>
<td>5.72±0.98</td>
</tr>
<tr>
<td>Amino acids</td>
<td>Casein</td>
<td>9</td>
<td>5.62±1.09</td>
</tr>
<tr>
<td>Soybean protein</td>
<td>Soybean protein</td>
<td>6</td>
<td>1.78±0.36</td>
</tr>
<tr>
<td>Amino acids</td>
<td>Soybean protein</td>
<td>10</td>
<td>3.21±0.78</td>
</tr>
</tbody>
</table>

Results are expressed as means ± SE.
The diets were fed for 28 days to rabbits aged about 10 weeks at the beginning of the experiment.
Data are taken from reference (14).
It cannot be decided from the data presented in Figure 2 whether the differing effects of dietary proteins on plasma cholesterol in rabbits are due to the proteins themselves or to other constituents of the protein preparations. Most of the preparations used in the reported experiments contained very little fat, but the protein content was often no more than 60 to 65 percent of the total. Even the purest preparations of casein and isolated soy protein contained up to 20 percent of non-protein material.

To see whether the protein itself determines the level of serum cholesterol, rabbits were fed semipurified diets containing an amino acid mixture resembling the composition of either casein or soy protein (14). It was found that the amino acid mixture equivalent in composition to casein produced concentrations of serum cholesterol similar to those obtained with casein, whereas the mixture imitating soy protein induced higher levels of serum cholesterol than the intact protein, but the levels were still lower than those seen with casein (Table 1). Thus, at least part of the differential effect of casein and soy protein on serum cholesterol appears to be related to differences in the amino acid composition of these proteins.

Kritchevsky et al. (15) suggested that the differential effects of casein and soy protein on serum cholesterol levels and atherosclerosis in rabbits are due to the different ratios in the protein of lysine to arginine (casein, 2.04; soy protein, 0.68 on a weight basis). Indeed they found that addition of lysine to soy protein increased the level of serum cholesterol, but addition of arginine to casein gave equivocal results (15). Although addition of arginine plus glycine plus alanine to casein does produce some lowering of serum cholesterol levels, no clear relation with the lysine:arginine ratio is observed (14, 16, 17). When the results of feeding trials with amino acid mixtures were combined, and the lysine:arginine ratio was plotted versus the level of plasma cholesterol, only a very scattered graph was obtained (18). Furthermore, we found that increasing the amount of casein in both diets with and without added cholesterol further increased serum cholesterol levels (19), while the lysine:arginine ratio obviously remained constant.

There is evidence that amino acids other than lysine and arginine also play a role in determining serum cholesterol levels in rabbits. Glycine, when added to a semipurified diet containing casein, counteracted the hypercholesterolemic response (16, 17). Methionine, when added in relatively large amounts to a soy protein diet, elevated serum cholesterol (12).
Table 2: Serum cholesterol and body weight of rabbits fed semipurified diets containing formaldehyde-treated proteins.

<table>
<thead>
<tr>
<th>Dietary protein (weight %)</th>
<th>Body weight (g)</th>
<th>Serum cholesterol (mmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>initial</td>
<td>final</td>
</tr>
<tr>
<td>21% casein + 21% soy</td>
<td>2204±67</td>
<td>2875±50</td>
</tr>
<tr>
<td>42% casein</td>
<td>2204±44</td>
<td>2818±69</td>
</tr>
<tr>
<td>21% casein + 24.2% F-soy</td>
<td>2200±51</td>
<td>2828±60</td>
</tr>
<tr>
<td>21% casein + 23% F-casein</td>
<td>2195±69</td>
<td>2702±50</td>
</tr>
</tbody>
</table>

Results are expressed as means ± SE for 10 animals per group. The animals, aged about 12 weeks at the beginning of the experiment, were fed the diets for 8 weeks. F = formaldehyde-treated; figures bearing a different superscript are significantly different (P<0.05).

Data from unpublished observations of C. E. West, A. C. Beynen, A. H. M., Terpstra, K. E., Scholz, J. B., Schutte, K., Deuring and L. G. M. van Gils.

It is clear that the serum cholesterol level in rabbits can be modified by the amino acid composition of the diet. However, it follows from the data in Table 1 that other factors such as the structure and digestibility of the proteins are almost certainly also involved.

The possibility that the cholesterolemic responses to casein and soy protein are effected by the structure of the proteins was tested by modifying their structure by formaldehyde-treatment. The formaldehyde-treated proteins were incorporated into semipurified diets and fed to New Zealand white rabbits. The data in Table 2 show that formaldehyde-treatment of the proteins did not significantly affect growth of the rabbits. However, the hypercholesterolemic effect of casein is markedly reduced after formaldehyde-treatment. The addition of formaldehyde (0.4%, w/w) per se to the 42% casein diet did not significantly affect the level of serum cholesterol. We conclude that the tertiary structure of casein is an important factor in determining the cholesterolemic response in rabbits to this protein.

Table 3: Concentration of cholesterol in lipoprotein fractions of rabbits fed semipurified diets containing either soy protein or casein.

<table>
<thead>
<tr>
<th>Lipoprotein fraction</th>
<th>Cholesterol concentration (mmol/l serum)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Soy protein diet</td>
</tr>
<tr>
<td>VLDL (g&lt;20&lt;1.006)</td>
<td>0.15±0.04</td>
</tr>
<tr>
<td>IDL (1.006&lt;g&lt;20&lt;1.012)</td>
<td>0.03±0.01</td>
</tr>
<tr>
<td>IDL (1.012&lt;g&lt;20&lt;1.019)</td>
<td>0.18±0.02</td>
</tr>
<tr>
<td>LDL (1.019&lt;g&lt;20&lt;1.040)</td>
<td>0.77±0.13</td>
</tr>
<tr>
<td>LDL (1.040&lt;g&lt;20&lt;1.063)</td>
<td>0.17±0.04</td>
</tr>
<tr>
<td>HDL (1.063&lt;g&lt;20&lt;1.092)</td>
<td>0.29±0.08</td>
</tr>
<tr>
<td>HDL (1.092&lt;g&lt;20&lt;1.125)</td>
<td>0.36±0.09</td>
</tr>
<tr>
<td>HDL (1.125&lt;g&lt;20&lt;1.210)</td>
<td>0.21±0.02</td>
</tr>
<tr>
<td>Serum total cholesterol (mmol/l)</td>
<td>2.27±0.32</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± SE for 9 rabbits in each dietary group. All rabbits were fed the semipurified diet containing soy protein (21%, w/w) for 4 weeks when 9 animals, aged about 14 weeks at that time, were allocated to the semipurified diet containing casein (21%, w/w). Blood samples were taken 36 days after this allocation to the dietary groups.

Significantly different (two-tailed Wilcoxon test) from the soy-fed group: a, P<0.01; b, P<0.05, c, P<0.10. Data are taken from reference (20).
3. Effects of casein and soy protein on the cholesterol concentration in serum lipoproteins of rabbits

The cholesterol concentrations in the different serum-lipoprotein fractions of rabbits fed casein and soyprotein diets are given in Table 3. The increase in serum cholesterol of the casein-fed animals was reflected in all fractions, except for the fraction with density limits 1.250<q<20<1.210 kg/l, which is the HDL<sub>3</sub> fraction. However, only the increases in the LDL<sub>1</sub> (1.006<q<20<1.019 kg/l) and LDL<sub>2</sub> (1.019<q<20<1.063 kg/l) fractions reached statistical significance.

We have studied the time course of the changes in the concentration of cholesterol in the LDL and VLDL fraction of rabbits fed casein (21). It appeared that the cholesterol concentration increased first in the LDL fraction and subsequently in the VLDL fraction. The VLDL fraction in rabbits fed casein becomes markedly enriched with apo E (21).

4. Mechanism of action of dietary protein

Feeding casein to rabbits has been shown to reduce the faecal excretion of steroids compared to that of soy protein (22), an effect paralleling, if not preceding, the elevation of serum cholesterol (23). Subsequently, the number of hepatic LDL receptors decrease (24), which aggravates the degree of hypercholesterolemia and which may further reduce biliary steroid output. Thus the accumulation of serum cholesterol in the casein-fed rabbit most likely is the result of a decreased clearance of plasma cholesterol.

Total body cholesterol synthesis in rabbits fed casein has been found to be reduced when compared to animals on a diet containing soy protein (22). The depressed synthesis of cholesterol in rabbits fed casein is most likely the result of feed-back inhibition effected by the increased level of serum cholesterol (25). This regulatory device, however, only protects the animals against further development of the hypercholesterolemia. The depressed synthesis of cholesterol and the diminished faecal excretion of steroids in casein-fed rabbits results in a reduced turnover of cholesterol when compared with rabbits fed soy protein.

5. The rabbit and other laboratory animals as experimental model to study the effects of dietary protein on serum cholesterol levels

It has to be stressed that the concept of casein as a hypercholesterolemic protein in rabbits has several limitations. The hypercholesterolemic response of rabbits to a cholesterol-free, casein containing diet, depends on several other components of the diet, such as carbohydrates, fiber (12), fats (26) and possibly salts (27). Furthermore, the hypercholesterolemic effect of casein in a cholesterol-free diet was only observed in young growing rabbits and not in their mature counterparts (28). When 0.25% (w/w) cholesterol was added to the semipurified diet, the differential effect of casein and soy protein was also seen in mature rabbits (29). In rats (30), mice (31), guinea pigs (32), chickens (33) and calves (34) fed cholesterol-free diets, casein did not significantly affect serum cholesterol levels when compared with soy protein. However, when cholesterol was added to the diets, a hypercholesterolemic effect of casein was observed in female lean Zucker rats, but not in the males (35) or chickens (36). In chickens (36), we have observed that increasing the level of protein, irrespective of whether it was casein or soy protein, decreased the concentration of cholesterol in serum.

The lack of hypercholesterolemic effect of casein versus soy protein in essentially cholesterol-free diets with mature rabbits (29), rats (30), mice (31), guinea pigs (32), chickens (33) and calves (34), may be due to the composition of the diets used with respect to components other than protein. In rats, Néjat et al. (37) have found that the
Table 4: Serum cholesterol concentration (mmol/l) of male Wistar rats fed cholesterol-free, semi-purified diets containing either casein or soybean protein.

<table>
<thead>
<tr>
<th></th>
<th>Initial</th>
<th>day - 29</th>
<th>day - 15</th>
<th>day - 14</th>
<th>day + 28</th>
<th>day + 33</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soy-casein group</td>
<td>2.13±0.11</td>
<td>1.91±0.09</td>
<td>2.02±0.09</td>
<td>2.19±0.04</td>
<td>2.87±0.24</td>
<td>2.67±0.29</td>
</tr>
<tr>
<td>Casein-soy group</td>
<td>2.16±0.03</td>
<td>2.48±0.10a</td>
<td>2.70±0.15a</td>
<td>2.73±0.15b</td>
<td>2.32±0.12a</td>
<td>2.24±0.12a</td>
</tr>
</tbody>
</table>

Rats, aged about 6 weeks and raised on a commercial rat diet, were fed the semi-purified diet containing soybean protein for 23 days until day -43 of the experiment. Then, one group was allocated to the casein diet (casein-soy group) and the other group remained on the soybean-protein diet (soy-casein group) until the cross-over (day 0), when the diets were changed. The initial serum-cholesterol value refers to day -49 of the experiment. Results are expressed as means ± SE for 6 or 7 animals in each group. a, statistically different P<0.01 from the soy-casein group; b, P<0.05. The diets contained 21% (w, w) casein or soybean protein and 1% (w, w) corn oil as fat source. Data taken from unpublished observations of A. C. Beynen, A. H. M. Terpstra, C. E. West and G. van Tintelen.

amount of fat in the cholesterol-free diet must be as low as 1% (w, w) in order to demonstrate a hypercholesterolemia effect of casein. We have recently reproduced this observation in male Wistar rats (Table 4).

We have also studied the effects of dietary casein and soybean protein on the concentration of serum cholesterol in rhesus monkeys. Ten mature female rhesus monkeys were alternately fed semi-purified diets containing either casein or soybean protein. The diets contained 26 energy % protein, 13 energy % fat and 300 mg cholesterol per 4.18 MJ (1000 kcal). In addition, a restricted amount of fruit and vegetables were fed, providing 2.2 g protein per day. All together, the animals received a diet containing 21–24 energy % protein of which 92–95% was provided by the test protein. The results in Table 5 show that the feeding of diets containing casein produced a marked elevation of serum cholesterol levels, whereas the replacement of casein by soybean protein had the opposite effect. The initial increase in serum cholesterol level observed when the animals were transferred from the commercial diet to the semi-purified diet can be explained by the increased concentration of cholesterol in the latter diet. The results of this study suggest that the hypercholesterolemia effect of casein in comparison with soybean protein is not merely a phenomenon observed in experimental animals such as rabbits and rats, but is a more general phenomenon also observed in species more akin to man.

6. Dietary protein and serum cholesterol in man

The ultimate aim of the studies with experimental animals is to provide further insight into practical means of decreasing the level of serum cholesterol in humans by means of

Table 5: Concentration of serum cholesterol in rhesus monkeys fed alternately semi-purified diets containing casein or soybean protein.

<table>
<thead>
<tr>
<th>Diet</th>
<th>Weeks on diet</th>
<th>Serum cholesterol (mmol/l)</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Final</td>
<td>Change</td>
</tr>
<tr>
<td>1. Commercial</td>
<td>13</td>
<td>3.92±0.24</td>
<td>+0.51±0.24a</td>
</tr>
<tr>
<td>2. Soybean protein</td>
<td>15</td>
<td>4.44±0.28</td>
<td>+1.38±0.32a</td>
</tr>
<tr>
<td>3. Casein</td>
<td>15</td>
<td>5.81±0.45</td>
<td>-1.63±0.37a</td>
</tr>
<tr>
<td>4. Soybean protein</td>
<td>17</td>
<td>4.18±0.31</td>
<td>+1.28±0.37a</td>
</tr>
<tr>
<td>5. Casein</td>
<td>17</td>
<td>5.46±0.50</td>
<td></td>
</tr>
</tbody>
</table>

Results are expressed as means ± SE for 10 animals. Change significantly different from zero: a, P<0.01; b, P<0.05. Data taken from unpublished studies of A. H. M. Terpstra, C. E. West, J. T. C. M. Fennis, J. A. Schouten and E. A. van der Veen.
Table 6: Effects of casein and soybean protein on serum cholesterol concentration in healthy human subjects.

<table>
<thead>
<tr>
<th>Age of subjects</th>
<th>Number</th>
<th>Dietary protein</th>
<th>Composition of diets</th>
<th>Serum cholesterol (mmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Protein (energy %)</td>
<td>Fat (energy %)</td>
</tr>
<tr>
<td>Exp. 1 18–28 yr</td>
<td>25</td>
<td>casein</td>
<td>13</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>soybean protein isolate</td>
<td>13</td>
<td>37</td>
</tr>
<tr>
<td>Exp. 2 29–60 yr</td>
<td>17</td>
<td>casein</td>
<td>16</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>soybean protein isolate</td>
<td>16</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>soybean protein concentrate</td>
<td>16</td>
<td>35</td>
</tr>
</tbody>
</table>

The initial values in Exp. 1 were measured after a control period of 10 days during which all the subjects received a diet containing a 2:1 mixture of casein and soybean protein. In Exp. 2 the control period lasted 17 days during which all the subjects received the casein diet. The data are taken from references (45) and (46).
dietary alterations. A decrease in the level of serum cholesterol would probably lead to a
decrease in the incidence of atherosclerotic diseases.

It was shown by Hodges et al. (38) that the substitution of vegetable proteins (mainly
soybean protein) for animal proteins in the diet of hypercholesterolemic subjects markedly
lowered plasma cholesterol levels. Further studies have also shown a reduction (by
10–25%) in the concentration of plasma cholesterol in individuals with varying degrees of
hypercholesterolemia (39–41). However, in all these studies the transfer of the subjects
from their habitual, mixed protein diet to the diet containing predominantly soybean
protein, involved a marked increase in the ratio of dietary polyunsaturated fatty acids to
saturated fatty acids (P/S ratio) and/or a decrease in cholesterol intake. The soybean
protein diets were most likely also relatively rich in complex carbohydrates and dietary
fiber. In one study (38) a tremendous increase in the intake of the plant sterol, β-sitosterol,
was found to be associated with the diet containing soybean proteins. These changes in
the diet, namely an increased P/S ratio, a decreased content of cholesterol and an
increased content of β-sitosterol are all known to lower plasma cholesterol levels. Thus it
is likely that changes in these dietary factors and not the soybean protein component had
caused the reported (39–41) lowering of plasma cholesterol. This is substantiated by the
work of investigators who used two experimental diets with a relatively high P/S ratio and
low cholesterol content, which differed only in their protein constituents. It was then found
that both diets, when compared to the habitual diet, lowered plasma cholesterol in
hypercholesterolemic individuals and that the responses were identical, irrespective of
whether animal protein or soybean protein was the main protein source (42, 43). Goldberg
et al. (44), who used a similar experimental design, reported that soybean protein, when
compared to animal protein, resulted in an additional reduction in the plasma concentra-
tions of total cholesterol by 3.5±5.5% (n = 12).

Strictly controlled studies in our laboratory with young healthy volunteers (45) and also
with middle-aged volunteers (46) have demonstrated that soybean protein, when
compared to the animal protein casein has little or no effect on the serum level of
cholesterol (Table 6). In these two studies, diets were used in which 60 or 65% of the
protein in the diet consisted of either soybean protein or of casein. The similarity achieved
in other components of the diets such as in cholesterol and fat content and in P/S ratio of
the fat was optimal. Although it was not possible to demonstrate a difference in the level of
total cholesterol in plasma between the diets containing soybean protein and casein, the
soybean protein diet produced a shift in the cholesterol from the low density lipoproteins
(LDL) to the high density lipoproteins (HDL). Such an effect is generally regarded as being
favourable in the prevention of coronary heart disease. No effect on the level of cholesterol
and other components in serum was also found by Lembke et al. (47) when soybean
protein was compared with casein in a controlled experiment with adult volunteers.

Walker et al. (48) did demonstrate that a mixed vegetable protein diet did give lower
plasma cholesterol values in normocholesterolemic women than a diet containing animal
protein. In this study (48) the animal protein diet contained meat, cheese and milk as
opposed to cereals, rice, beans and legumes in the vegetable protein diet. Thus the
animal protein diet must have contained more cholesterol than the vegetable protein diet.
Carroll et al. (49) found that replacement of animal protein by soybean protein significantly
lowers (by 5%) plasma cholesterol in healthy young women. In order to balance the
experimental diets for their cholesterol content, Carroll et al. (49) added crystalline
cholesterol to the diet containing soybean protein. Since pure cholesterol is not always
absorbed as well as cholesterol in animal foodstuffs, the soybean protein diet may have
contained effectively less cholesterol, which may explain the somewhat lower plasma
cholesterol levels observed on this diet. Thus the specific effect of soybean protein versus
casein on the concentration of total cholesterol of serum in healthy humans, if any, cannot be very great.

Why does the type of dietary protein affect the plasma concentration of total cholesterol in laboratory animals, including rhesus monkeys, but not in humans? There are several ways to explain this difference. First of all, in the animal experiments diets are formulated especially so as to maximize the hypercholesterolemic response to casein. Casein is much less effective if it is part of a normal mixed animal feed. Secondly, in the human being it could be a matter of a species-dependent resistance to the dietary protein source. Furthermore, in most animal experiments young animals are used which are fed the test diets during a considerable part of their life span, whereas the above mentioned trials with humans lasted 2–6 weeks. Possibly, long-term experiments starting at an early age will show an effect of dietary protein on the level of plasma cholesterol in man. This would be compatible with the observation that the hypercholesterolemic effect of casein was only observed in young growing rabbits and not in their mature counterparts (28).

An important difference between the experiments with humans and animals relates to the amount of test protein in the diets. With animals the diets contained relatively high proportions of protein. In our experiments with humans only about 60% of the dietary protein could be replaced by either casein or soy protein; further replacement would only have been possible by the use of liquid-formula diets, analogous to semi-purified diets in animals. Possibly, with a higher degree of replacement of proteins and/or higher amounts of protein in the diets of humans, the type of protein does affect the level of serum cholesterol. In any case, the striking effects on serum cholesterol concentrations of dietary casein and soy protein per se seen in laboratory animals have until now not been observed in man.

7. References

(7) Meeker, D. R., Kenten, H. D.: Arch. Path. 31 147–162 (1941)
8. Summary


14 Proteins (metabolism, cholesterol)

Studies in experimental animals have shown that the nature of dietary protein can influence the concentration of cholesterol in serum. The replacement of soy protein in semipurified diets of rabbits and rats by casein results in higher levels of serum cholesterol. The effect appears to be associated not only with the amino acid composition, but also with the structure of the proteins although the precise mechanisms involved are not clearly understood. The hypercholesterolemic effect of dietary casein when compared with soy protein has also been found in rhesus monkeys. Thus the effect is not merely a phenomenon observed in experimental animals such as rabbits and rats but is more general as it is also observed in species more akin to man. Much attention has been directed towards the role of dietary protein in determining serum cholesterol levels in man because a decrease in the level of serum cholesterol would probably lead to a decrease in the incidence of atherosclerotic disease. Strictly controlled studies in our laboratory with healthy young volunteers and also with middle-aged volunteers have demonstrated that soybean protein, when compared to casein has little or no effect on the level of total cholesterol in serum. Several studies have demonstrated an apparent effect but often the effects can be attributed to other functions such as differences in the P/S ratio of the dietary fat and the cholesterol content of the test diets and not to the nature of the dietary protein. Thus the striking effects on serum cholesterol concentrations of dietary casein and soy protein per se seen in laboratory animals have not up until now been observed in man.
14 Proteine (Stoffwechsel, Cholesterin)


14 Protéines (métabolisme, cholestérol)