There is no longer much argument against the theory that the diet of man has a powerful effect on the concentration of cholesterol and related substances in his blood (Keys and Anderson, '54; Mann and Stare, '54; Keys et al., '55b) but this merely emphasizes the importance of the question as to the role of the several dietary elements in this effect. The first item for consideration, obviously, is the cholesterol in the diet. We have already reported briefly both survey and experimental evidence indicating that the cholesterol in ordinary human diets has substantially no effect on the concentration in the blood (Keys, '49, '52a, b; Keys and Anderson, '54).

The present paper is a report of dietary experiments on men under completely controlled conditions, as well as of both cross-sectional and longitudinal studies on men in Minnesota and on two samples of men in Sardinia. In the latter studies the men lived at home and ate as usual.

1 The results reported here were obtained from studies aided by a grant from the National Dairy Council, Chicago and, in part, by a grant (C10) from the U. S. Public Health Service, recommended by the Cardiovascular Study Section.
2 This investigation was supported (in part) by research grant H-10 from the United States Public Health Service.
3 Present address: Institute for Arthritis and Metabolic Diseases, Bethesda, Maryland.
4 Present address: Institute of Physiology, University of Naples.
SUBJECTS AND METHODS

All of the subjects were men between the ages of 20 and 60 and were pronounced to be physically healthy on the basis of medical examinations, including electrocardiography. The subjects in the prolonged controlled experiments were schizophrenic patients in a special metabolic unit in Hastings State Hospital. They, too, were similarly judged to be physically “normal.” The men in the longitudinal surveys, as well as in the detailed measurements of diets made by members of the nutrition research staff of the U. S. Department of Agriculture, were professional and business men, aged 45 to 55 in 1947, who have cooperated with this laboratory for the past 9 years. The surveys on the Island of Sardinia covered coal miners in the small mining town of Bacu Abis and moderately active men employed by the city of Cagliari (policemen and firemen) and by the University of Cagliari Medical School (attendants, mechanics, etc.).

In the Minnesota surveys, except for those done in cooperation with the U. S. Department of Agriculture, and in the experiments with the rice-fruit diet, serum total cholesterol was measured by the Liebermann-Burchard reaction applied to the Bloor extract. In all of the other surveys and experiments the method of Abell et al. ('52), as modified by us (Anderson and Keys, '55), was used. The latter method consistently yields results somewhat lower than the older (Bloor) method but there is a very close correlation between the two. Cholesterol in the beta lipoprotein fraction of the serum was measured on the materials separated by paper electrophoresis as described by Anderson and Keys ('55). All blood samples were drawn from antecubital veins in the morning, with the subjects in the basal state. All analyses were in duplicate.

Dietary cholesterol was computed from the values for foods given in table 1. It is probable that the values for meats are too high in this table. In surveys, except for those where the diets were measured by the U. S. Department of Agriculture group, the dietary intake of cholesterol-containing foods was
CHOLESTEROL IN DIET AND SERUM

estimated by individual interviews, with particular attention to the use of eggs, cream, milk, butter, cheese, ice cream, meats, fish and chicken. The individual cholesterol values thus obtained are only crude estimates, of course, but it should be noted that the consumption of cholesterol-containing foods is more accurately recollected than the rest of the diet.

On the Island of Sardinia the estimation of dietary cholesterol was particularly simple. Because of the low and relatively invariable consumption of all cholesterol-containing foods except eggs, the individual habit of eating eggs almost wholly accounted for the variation in total cholesterol intake. Among these Sardinians scarcely 10% eat butter, cream or ice cream except on rare occasions, only small portions of meat are eaten a few times a week, milk is consumed only in the morning coffee, the bread and “pasta” (spaghetti, etc.) is made without shortening and olive oil is the sole cooking fat. But the mean for the total of 187 men was 4.92 eggs per week, eaten as such, and the range of consumption was from zero to 30 eggs per week.

<table>
<thead>
<tr>
<th>TABLE 1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Approximate cholesterol contents of foods used in the dietary calculations</strong></td>
</tr>
<tr>
<td><strong>CONSTITUENT</strong></td>
</tr>
<tr>
<td>Butter</td>
</tr>
<tr>
<td>Cheese</td>
</tr>
<tr>
<td>Cream, 20% fat</td>
</tr>
<tr>
<td>Egg *</td>
</tr>
<tr>
<td>Fish *</td>
</tr>
<tr>
<td>Ice cream, 12.5% fat</td>
</tr>
<tr>
<td>Poultry</td>
</tr>
</tbody>
</table>

* Based on reports of Okey (‘45), Nataf (‘48), Pihl (‘52) and on analyses made by Okey and Strisower, cited in Dobbin et al. (‘51).

* One medium egg contains 300 mg of cholesterol.

* High-fat fish such as Atlantic herring or mackerel contain 80 mg of cholesterol.

* Contains 65% of animal fat. Vegetable oils contain no cholesterol.

* Beef, veal, pork, and lamb. Recent analyses by Del Vecchio et al. (‘55), using digitonin precipitation, give lower results than these values from the older literature.
In the surveys conducted in cooperation with the U. S. Department of Agriculture, elaborate efforts were made to obtain a complete and accurate measurement of every item of food and drink consumed by the individual men during the period of one or two weeks of study. Enthusiastic cooperation of the wives as well as of the men themselves was a condition for acceptance of the subjects in this program. Portions of food eaten at home were weighed on a gram scale or measured in 8 oz. cups or standard-sized spoons, recipes were checked and care was taken to allow for meat trimmings and other table waste. In these surveys most of the men ate their noon meals during the week in restaurants or clubs. The portions of food at these and other meals were carefully estimated or measured with a pocket rule by the men. In addition, the cooperation of these establishments was frequently enlisted so that the accuracy of the records of lunch consumption could approach that of the records made in the home by the wives of these subjects. Between-meal and evening snacks were also recorded. Every effort was made to assure that normal dietary habits of the individuals were not changed during the period of the study.

RESULTS

Six surveys in Minnesota. Simple cross-sectional surveys always raise the question as to whether the dietary variable is properly isolated. This is particularly true of dietary cholesterol which conceivably may be related, directly or inversely, to other characteristics of the diet or mode of life which, in turn, have an effect on the serum level. This possibility is much reduced when the population is homogeneous in regard to age, economic status, ethnic pattern, clinical status and occupation. The validity of the results is further increased when, as in the case of the 6 surveys to be summarized below, it is found that both absolute body size and relative obesity are not significantly related to either the diet or the serum cholesterol.
The results of 6 surveys in Minnesota are summarized in table 2. Clearly, any relationship between serum cholesterol and that consumed in the diet must be very small indeed in such men. It appears, however, that there may be a tendency for men who consume the least cholesterol to have slightly lower concentrations of cholesterol than the average while those who consume the most cholesterol have the opposite tendency, the deviations in each case being about 3% of the grand mean. Complete independence prevails over the middle range of intakes (second through 4th quintiles) including 60% of the subjects.

### TABLE 2

Serum total cholesterol in successive quintiles of cholesterol intake from lowest to highest (1 to 5) in 6 surveys of Minnesota men. For each survey the mean serum value of the middle quintile is taken as 100 and all other values are expressed as percentage of this.

<table>
<thead>
<tr>
<th>NO. OF</th>
<th>AGE RANGE</th>
<th>CHOLESTEROL INTAKE QUINTILES</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUBJECTS</td>
<td>18-25</td>
<td>20-27</td>
</tr>
<tr>
<td>160</td>
<td>105.9 ± 3.8</td>
<td>109.7 ± 3.5</td>
</tr>
<tr>
<td>86</td>
<td>92.9 ± 5.6</td>
<td>89.3 ± 3.7</td>
</tr>
<tr>
<td>236</td>
<td>95.9 ± 2.2</td>
<td>103.0 ± 2.4</td>
</tr>
<tr>
<td>214</td>
<td>98.5 ± 2.4</td>
<td>101.2 ± 2.8</td>
</tr>
<tr>
<td>208</td>
<td>95.3 ± 2.8</td>
<td>96.6 ± 3.0</td>
</tr>
<tr>
<td>168</td>
<td>93.5 ± 3.5</td>
<td>95.1 ± 2.8</td>
</tr>
</tbody>
</table>

1 The distribution of cholesterol intakes varied somewhat in the 6 series but, in general, they approximated less than 500 mg of cholesterol in the daily diet for the lowest quintile, 500 to 680 mg for the second quintile, 680 to 850 mg for the third, 850 to 980 mg for the 4th and over 980 for the highest quintile.

2 Mean and standard error.
However, even these slight trends are not necessarily indicative of any effect of dietary cholesterol itself. In the first place, the dietary cholesterol is expressed in absolute units and differences in these absolute amounts do not necessarily imply a corresponding difference in the character of the diets consumed by the different men. Two men differing in body size and physical activity and therefore consuming different total amounts of food when they are in calorie balance will, of course, consume different total amounts of cholesterol even though the composition of the diet is exactly the same. We do not have information to show that the men in different quintiles were, in fact, all at the same average level of total metabolism. However, we cannot explain more than a small part of the differences in intake as possibly being a reflection of differences in the total mass of the diet; the average cholesterol intake in the top quintile was more than three times that in the bottom quintile.

A more serious question is whether the observed variations in cholesterol intake are independent of important differences in other characteristics of the dietary composition. As a matter of fact, we find that cholesterol intake in the American diets is almost always related, to some extent, to the intake of animal protein and animal fat in the diet. For instance, in table 5, below, it will be noticed that the cholesterol intake of the men on high-fat diets average 20% more than for the men on low-fat diets.

Longitudinal studies on businessmen. Among 286 clinically healthy Minnesota business and professional men studied annually since 1947, there were 33 men whose jobs, diets and body weights were very constant over a period of 4 years and whose dietary intakes of cholesterol were consistently in the lower third of the distribution of the intakes of the entire group of 286. With these men it is possible to contrast 35 of their fellows, similarly constant in work, diet and body weight, whose average cholesterol intake was consistently in the upper third of the distribution. The summarized comparison of these men is given in table 3. It is clear that the
long-standing habit of consuming more or less dietary cholesterol produced no significant difference in the average serum cholesterol level between the two groups.

In this same population of businessmen there were 64 men who made major changes in their dietary cholesterol from one year to another but who maintained their dietary habits relatively constant otherwise and who did not change body weight by more than 5 lbs. The altered cholesterol intakes resulted from exchanging eggs, fat meats and dairy products for oleomargarine, vegetable fats, cereals and lean meats or fish in the diet. The men who increased their dietary cholesterol did so either without deliberate intent (incidental to a change in domestic status — marriage, divorce or death of the wife), or because they were abandoning a previous effort to curtail cholesterol intake; the result was at least a doubling of the previous cholesterol intake. The men who decreased their cholesterol intake did so in some cases incidental to changed domestic status but most of them had been persuaded, often by the family doctor, that cholesterol in the diet should be avoided; their cholesterol intakes decreased by 50% or more. The serum cholesterol findings on these men are summarized in table 4. When these men changed their cholesterol

<table>
<thead>
<tr>
<th>CHOLESTEROL IN DIET</th>
<th>NO. OF MEN</th>
<th>AV. AGE</th>
<th>REL. BODY WT.</th>
<th>SERUM CHOLESTEROL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>33</td>
<td>49.8</td>
<td>102.9 ± 13.9</td>
<td>248.9 ± 41.4</td>
</tr>
<tr>
<td>High</td>
<td>35</td>
<td>51.2</td>
<td>99.7 ± 11.4</td>
<td>256.2 ± 42.9</td>
</tr>
</tbody>
</table>

* The "Low" cholesterol men always received less than 600 mg daily, their average intake being 401 mg, while the "High" intake men always received more than 850 mg, their average diet providing 1010 mg daily.

* Relative body weight is the body weight expressed as a percentage of the value, for the same age, sex and height, given in the standard U.S. table of average weights, first published in Medico-actuarial Soc. America (N.Y.), Vol. 1, 1912.

* Mean and standard deviation.
intakes, either up or down, there was no significant change in the serum level. The standard error of the mean of the differences, before and after, was ± 5.86 mg % for the men who increased their cholesterol intake and ± 5.05 for those who decreased the cholesterol in the diet.

**U. S. Department of Agriculture collaborative survey.** In the Spring of 1953, and again in 1954, the nutrition research staff from the Agricultural Research Service of the U. S. Department of Agriculture carried out a very careful study on the diets consumed by 119 men in the same general group of middle-aged businessmen mentioned above. Because of the possibility that different relationships might obtain at different levels of total fat in the diet, the analysis was made separately for the 61 men whose diets provided more than 40% of the calories from fats and for the 58 men whose diets were less rich in fats. The findings in regard to dietary cholesterol, together with the serum cholesterol values, are summarized in table 5.

It will be observed that there was considerable variation in the cholesterol intakes of these men, both in absolute units and in concentration per 1000 calories, but in neither unit is there a significant correlation with the serum cholesterol concentration.

**Experiments with modified rice-fruit diets.** A simple way to demonstrate an effect of the diet on the serum cholesterol

<table>
<thead>
<tr>
<th>DIET CHANGE</th>
<th>NO. OF MEN</th>
<th>SERUM CHOLESTEROL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Before</td>
</tr>
<tr>
<td>Increase</td>
<td>23</td>
<td>245.0 ± 39.8$^1$</td>
</tr>
<tr>
<td>Decrease</td>
<td>41</td>
<td>241.5 ± 45.2</td>
</tr>
</tbody>
</table>

$^1$ The mean change in daily cholesterol intake was +350 mg for the mean in the 'Increase' group and —480 mg for those in the 'Decrease' group.

$^2$ Mean and standard deviation.
concentration is to use a rice-fruit diet but it is erroneous to credit the effects to the absence of cholesterol from that diet. Proof of this is given in table 6, which summarizes the results of completely controlled experiments on men in Hastings State Hospital. A modified rice-fruit diet was devised which included salt to improve taste and a daily allowance of 11 gm of fat, either in egg yolks (diet R3) or in the form of all-vegetable oleomargarine (diet R1), so that the daily cholesterol intake would be 500 to 600 mg or zero, respectively. The serum cholesterol was measured at the end of 4 weeks on

### Table 5

Dietary cholesterol intake and correlation coefficients between intake and serum total cholesterol in middle-aged business and professional men on high-fat (more than 40% of calories from fats) and lower-fat (less than 40%) diets.

<table>
<thead>
<tr>
<th>ITEM</th>
<th>Intake, mg/day</th>
<th>Intake, mg/1000 Cal.</th>
<th>serum vs. 1 *</th>
<th>serum vs. 2 *</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Intake, mg/day</td>
<td>825.6 ± 206.7</td>
<td>707.4 ± 240.3</td>
<td>0.176</td>
<td>0.134</td>
</tr>
<tr>
<td>2 Intake, mg/1000 Cal.</td>
<td>330.5 ± 83.5</td>
<td>287.9 ± 89.7</td>
<td>0.037</td>
<td>0.024</td>
</tr>
<tr>
<td>3 r, serum vs. 1 *</td>
<td>—</td>
<td>0.184</td>
<td>0.001</td>
<td>0.024</td>
</tr>
</tbody>
</table>

1 Mean and standard deviation.

2 To reach the 5% level of probability, with N = 61, 58, and 119, r should be 0.250, 0.257 or 0.180, respectively.

### Table 6

Mean serum total cholesterol values from 4 experiments in which men changed from the house diet (H)1 to a modified rice-fruit diet (R or R1)1 or the reverse

<table>
<thead>
<tr>
<th>EXP. NO. AND OF DIET MEN</th>
<th>SERUM TOTAL CHOLESTEROL</th>
<th>EXP. NO. AND OF DIET MEN</th>
<th>SERUM TOTAL CHOLESTEROL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SE, A</td>
<td></td>
<td>Mean ± SE, A</td>
</tr>
<tr>
<td>50 A</td>
<td>217.2 ± 11.0</td>
<td>50 B</td>
<td>211.7 ± 11.0</td>
</tr>
<tr>
<td>H</td>
<td>183.5 ± 11.0</td>
<td>H</td>
<td>170.7 ± 11.0</td>
</tr>
<tr>
<td>H</td>
<td>181.8 ± 11.0</td>
<td>H</td>
<td>178.8 ± 11.0</td>
</tr>
<tr>
<td>50 C</td>
<td>228.6 ± 7.2</td>
<td>50 D</td>
<td>256.1 ± 7.2</td>
</tr>
</tbody>
</table>

1 House diet.

Rice-fruit diet R1 contained zero cholesterol.

Rice-fruit diet R3 provided 500 to 600 mg of cholesterol daily.
diet R₃ or R₄ and the control values were obtained from blood samples drawn either before or a month after the dietary restriction had been removed. Calorie balance was maintained throughout.

Table 6 shows that the change from the ‘‘house’’ diet to the modified rice-fruit diet for 4 weeks produced a marked drop, averaging 15 to 20%, in the blood serum cholesterol, and this was not significantly affected by the presence or absence of cholesterol. Further, change from the rice-fruit diet back to an ordinary diet produced even greater increases, averaging 20 to 30%, and this rise was at least as great when

```
<table>
<thead>
<tr>
<th>SUBJECT</th>
<th>DIET R₃ Weeks 3 and 4</th>
<th>DIET R₁ Weeks 1</th>
<th>Weeks 2</th>
<th>Weeks 3</th>
<th>Weeks 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Br</td>
<td>150</td>
<td>146</td>
<td>150</td>
<td>139</td>
<td>145</td>
</tr>
<tr>
<td>Er</td>
<td>181</td>
<td>200</td>
<td>188</td>
<td>184</td>
<td>188</td>
</tr>
<tr>
<td>Hi</td>
<td>209</td>
<td>208</td>
<td>204</td>
<td>158</td>
<td>228</td>
</tr>
<tr>
<td>Pr</td>
<td>247</td>
<td>251</td>
<td>255</td>
<td>233</td>
<td>239</td>
</tr>
<tr>
<td>Tw</td>
<td>162</td>
<td>168</td>
<td>159</td>
<td>139</td>
<td>150</td>
</tr>
</tbody>
</table>

Mean 190 195 191 171 191
```

the previous diet provided a good deal of cholesterol, i.e. diet R₃, as when it provided none (R₁).

A more direct comparison was provided by an experiment on 5 men who, after 4 weeks of subsistence on diet R₃, were changed to diet R₁ and continued for another 4 weeks. The findings are given in table 7. Obviously, the removal of the 500 to 600 mg of cholesterol from the daily diet was without effect.

**Experiments with a mixed diet.** Critical experiments with mixed diets of ordinary food require that all conditions, including all nutrients in the diet and all factors, such as exercise, that influence the metabolism, are constant except for the single experimental variable of the dietary cholesterol.
In order to assure this, schizophrenic men were selected for their ability to cooperate and they were housed and fed in a separate unit at the Hastings State Hospital. A series of rotating menus was developed so that the daily nutrient intake varied little though the diet was not particularly monotonous. An average level of 400 to 450 mg of cholesterol daily was aimed at and special cookies were provided which could add to this about 1000 mg daily of pure cholesterol when desired. The mode of life of the subjects was carefully standardized in regard to exercise, recreation, and so on, and this standard was maintained 24 hours a day by a special staff of aides.

After a month of standardization in the metabolic unit, subsisting on measured portions of the regular hospital diet, the men subsisted on the experimental diet for 8 weeks during which time all items of food were measured as served and each man’s rejections or extra servings were also recorded. Careful attention was given to maintain the food consumption at the calorie balance point.

In experiment 54 A, 13 men consumed 374 mg of cholesterol daily for the first 4 weeks and then received an average of 1369 mg daily for the final 4 weeks. In experiment 54 B, 14 men went through the reverse order of change in cholesterol intake. The average values for dietary items of interest and for the serum total cholesterol at the end of each 4-week period are given for both experiments in table 8. There are suggestions of a trivial response of the serum cholesterol to the diet but in neither experiment is this statistically significant.

Surveys in Sardinia. On the Island of Sardinia the dietary pattern of the general population is very uniform in most respects and the consumption of cholesterol in the diet is relatively trivial except for that provided by eggs which are eaten in widely varying amounts. Hence, in dietary surveys it is readily possible to separate population samples into relatively low and high cholesterol intakes with the rest of their diets being substantially the same.
Table 9 summarizes the results of two surveys in Sardinia in 1955, one on moderately active municipal employees in Cagliari and one on poor coal miners in the small mining town of Bacu Abis. It will be observed that a two-fold difference in cholesterol intake was not associated with a significant difference in the serum of the men of Cagliari. In the men of Bacu Abis the intake difference was almost three-fold yet the serum levels were not statistically different.
DISCUSSION

The foregoing evidence is definitive, we think, in showing that variations in the intake of cholesterol over the whole range of natural diets do not influence the serum level of physically normal adult men so long as other elements in the diet are constant. The results of experiments on 5 normal subjects reported by Mayer et al. ('54) are in agreement for the limited range of cholesterol intakes tried. The findings, too, of Kinsell et al. ('52) and of Ahrens et al. ('55) on hospital patients are confirmatory though the formula diets used in these experiments are radically different from any natural diets and are not, therefore, fully comparable.

According to the results of the carefully controlled experiments of Heymann and Rack ('43), the same rule applies to infants and children. In regard to women, Moses ('52) and Moses et al. ('52) found that the addition of 2 gm of cholesterol to the daily diet of pregnant women did not increase the normal trend to hypercholesterolemia in pregnancy.

The findings in two series of experiments reported in the literature may seem to be in disagreement but on closer scrutiny the results cannot be cited as showing an effect on dietary cholesterol. Okey and Stewart ('33) obtained a small positive response in young women when the yolks of two eggs were added to the daily diet but the fact that this involved a daily addition of about 100 Cal. of fats was not controlled. Similarly, in a prolonged experiment on 60 volunteers (Groen et al., '52), the dietary cholesterol changes were accompanied by substantial changes of the diet in other respects. For example, the “high” cholesterol diet (940 mg daily), provided 100 gm of proteins, 128 gm of fats and 2618 Cal., while for the “standard average” diet the subjects consumed an average of 75 gm of proteins, 99 gm of fats and 2391 Cal. Gillum et al. ('55) reporting on a survey on men and women aged 50 to over 80 years found that the dietary and serum cholesterol values were correlated with a coefficient value of $r = +0.12$. This value may be statistically significant because of the large number (53) of subjects,
but it is obviously biologically trivial even if the dubious proposition is accepted that the cholesterol was the only effective variable in the diets of their subjects. Wilkinson et al. ('50) and Gertler et al. ('50) were unable to find any correlation between cholesterol intake and that in the blood in similar surveys.

It is probable that when cholesterol is artificially added to the diet in increasingly large amounts a point will be reached where there will be a positive effect on the serum level in man. We have shown that the intake of a single meal containing more than 10 gm of cholesterol tends to result in a slight increase in the serum cholesterol for a few hours but the effect is so small that relatively large numbers of experiments are required to prove it statistically (Keys et al., '55b). With intakes of 30 gm of cholesterol per day, for 29 days, Messinger et al. ('50) produced serum elevations in 4 out of 5 subjects but the serum increases were very small; when these huge cholesterol doses were given with large amounts of cream or egg yolk fat the serum rose sharply by averages of 10 to 20%. Kinsell et al. ('52) had negative results with equally large amounts of cholesterol given by mouth to patients with metabolic disorders but these results may not be comparable because of the highly abnormal character of the diet in other respects.

When different populations with divergent dietary patterns are compared it is easy to point out an apparent relationship between cholesterol intake and the concentration in the blood. In general, whenever the population pattern of diet involves a low cholesterol intake, the serum level is also low but this seems to be readily explicable in terms of other peculiarities of the diets that are correlated with their average cholesterol content (Keys et al., '54; Keys et al., '55a, b).

In several of the studies reported here (the surveys in Sardinia, the U.S.D.A. survey of 1954, and the experiments with a mixed diet) measurements were made of the cholesterol in the beta lipoprotein fraction of the serum in addition to the total. This major fraction of the total serum cholesterol
also appeared to be independent of the cholesterol intake in the diet. For example, in the Cagliari survey the mean percentage of the total serum cholesterol represented by that in the beta lipoprotein fraction, and its standard error, proved to be 75.93 ± 0.86 and 75.67 ± 1.04 in the low- and in the high-cholesterol-intake groups, respectively.

Finally, it may be asked why the human serum concentration of cholesterol is so remarkably independent of the amount of cholesterol supplied in the diet. After all, a daily intake of 1 gm of cholesterol, which characterizes some high-cholesterol diets, is something like a daily supply equal to 10% of the total amount of cholesterol in the entire blood volume. A very considerable proportion of this is absorbed from the intestine. But much more than this exogenous supply may be provided in the bile poured into the intestine and it would seem that this endogenous supply, synthesized by the liver, is easily regulated to adjust to the exogenous variations. A very different state of affairs prevails in the rabbit and the chick, of course, but it seems that most carnivores resemble man in this respect.

SUMMARY

1. Two cross sectional surveys in Minnesota on young men and 4 on older men showed no relationship between dietary cholesterol and the total serum cholesterol concentration over most of the ordinary intake range characteristic of American diets.

2. Two surveys on the Island of Sardinia failed to show any difference in the serum cholesterol concentrations of men of the same age, physical activity, relative body weight and general dietary pattern but differing markedly in cholesterol intake.

3. Careful study during 4 years of 33 men whose diets were consistently very low in cholesterol showed that their serum values did not differ from 35 men of the same age and economic status whose diets were very high in cholesterol.
4. Comparisons made of 23 men before and after they had voluntarily doubled their cholesterol intakes and of 41 men who halved theirs failed to show any response in the serum cholesterol level in 4 to 12 months while the rest of the diet was more or less constant.

5. A detailed study of the complete dietary intakes of 119 Minnesota businessmen failed to show any significant increase of serum cholesterol with increasing dietary cholesterol intake.

6. In 4 completely controlled experiments on men the addition to or removal from the diet of 500 to 600 mg of cholesterol daily had no effect on the serum cholesterol fall produced by a rice-fruit diet or on the rise in changing from a rice-fruit diet to an ordinary American diet.

7. In a completely controlled experiment on 5 physically healthy men the change from a rice-fruit diet containing 500 mg of cholesterol daily to the same diet devoid of cholesterol had no effect on the serum level.

8. In a similar experiment with 13 men receiving 66 gm of fat daily there was no significant effect in changing from a cholesterol intake of 374 mg/day to one of 1369 mg/day. In another 12 men the reverse change was likewise without effect on the blood serum.

9. It is concluded that in adult men the serum cholesterol level is essentially independent of the cholesterol intake over the whole range of natural human diets. It is probable that infants, children and women are similar.

ACKNOWLEDGMENTS

We are grateful to the Staff of the Hastings State Hospital and Dr. Ralph Rossen, its Director until recently, for the provision of subjects and facilities at the Hospital, to the Church of the Brethren and the volunteer aides from the Church who supervised the subjects at the hospital, and to Mrs. Helen Williams, Dietitian, who helped plan, serve and measure the diets there. Professor Mario Aresu made it
possible to carry out the work in Sardinia and in this operation we were greatly aided by Doctor Franco, Dr. Alfonso del Vecchio, and Dr. Henry L. Taylor and Mrs. Margaret Haney Keys. Most of the serum cholesterol measurements were made by Miss Erma V. O. Miller, Miss Laura Werner and Miss Nunzia Corrao. Mrs. Nedra Foster helped to plan the diets and analyze the food consumption records from Hastings, and helped analyze the blood serums. Mr. Norris Schulz aided in some of the statistical work.

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