Effect of Ethanol on Serum Cholesterol Concentration in Dog and Man

By Francisco Grande, M.D., Litle J. Hay, M.D., H. William Heupel, M.D., and Donald S. Amatuzio, M.D.

Occasional reports in the literature indicate that chronic alcoholics have a lower incidence of arteriosclerosis than non-alcoholic individuals. There is, however, no proof that alcohol exerts a protective action against arteriosclerosis, and Wilens suggested that such observations could be explained by the decreased food intake of the chronic alcoholic. On the other hand, Kimura observed marked arteriosclerosis at autopsy more frequently among men who habitually drank alcohol and smoked cigarettes than among men of the same age who indulge in neither. Other reports do not support the concept that arteriosclerosis is less frequent in the chronic alcoholic.

Little attention has been given, in the past, to the effects of alcohol on serum cholesterol concentration in man. Hobson et al. have reported that in elderly men (over 60) the average serum cholesterol concentration in heavy drinkers is lower than that of abstainers or moderate drinkers. These observations do not agree with the older data from Ducceschi and Barilari, who found higher cholesterol values in habitual drinkers of alcoholic beverages than in abstainers of a comparable age. Jankelson et al. found no difference in serum cholesterol between chronic alcoholics and non-alcoholics. Experimental work in animals has given conflicting results. Ducceschi reported an increase of serum cholesterol concentration in dogs given daily doses of alcohol for a few days, and more recently Eberhard observed that alcohol increases serum cholesterol in the rabbit. This result, however, has not been confirmed by Feller and Huff, and Morgan et al. have found that the rise in serum cholesterol of female hamsters on a cholesterol diet was greater in animals drinking water than in animals given wine. Gottlieb et al. have described a marked increase of serum cholesterol in rats fed a diet containing 1 per cent of cholesterol and 0.3 per cent of cholic acid when given ethanol and a similar result has been obtained by Nikkila and Ollila in chickens.

Our interest in studying the effect of ethanol on serum cholesterol concentration was aroused by the finding that alcoholic beverages increase the serum cholesterol level in hyperlipemic patients. The present paper reports observations concerning the effect of alcohol on serum cholesterol concentration in male dogs and in normal men under controlled dietary conditions.

Methods

Experiments on Dogs

The normal male mongrel dogs used had been in the laboratory for more than a month before the beginning of the experiments. The basic diet was a commercial dog food which by analysis had a fat content corresponding to 4 per cent of the total calorie value. The cholesterol content of the diet was measured after saponification, extraction of the unsaponifiable matter and precipitation with digitonin. The amount of digitonin precipitable, Lieberman Burchard reaction material in the basic diet was equivalent to 18 mg. of cholesterol/100 Gm. When this diet was mixed with lard to give 40 per cent of total calories from fat, the cholesterol equivalent material was 30 mg./100 Gm., and when mixed with sunflower oil, 14 mg./100 Gm. The animals were fed ad libitum and the body weight was determined weekly. Alcohol was given daily in

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Table 1

<table>
<thead>
<tr>
<th>Groups</th>
<th>H 1</th>
<th>H 2</th>
<th>L 1</th>
<th>L 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of men</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>Age (years)</td>
<td>46.0</td>
<td>49.0</td>
<td>48.5</td>
<td>49.9</td>
</tr>
<tr>
<td>±1.5</td>
<td>±1.7</td>
<td>±2.2</td>
<td>±1.6</td>
<td></td>
</tr>
<tr>
<td>Weight (kg.)</td>
<td>77.1</td>
<td>59.4</td>
<td>74.9</td>
<td>82.5</td>
</tr>
<tr>
<td>±2.4</td>
<td>±3.5</td>
<td>±3.4</td>
<td>±2.4</td>
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</tr>
<tr>
<td>Relative weight (per cent)</td>
<td>106.3</td>
<td>107.7</td>
<td>105.8</td>
<td>111.1</td>
</tr>
<tr>
<td>±2.6</td>
<td>±3.8</td>
<td>±3.9</td>
<td>±2.9</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>322</td>
<td>323</td>
<td>201</td>
<td>205</td>
</tr>
<tr>
<td>±7.2</td>
<td>±6.5</td>
<td>±5.6</td>
<td>±6.3</td>
<td></td>
</tr>
<tr>
<td>Total serum cholesterol mg./100 mg.</td>
<td>323</td>
<td>314</td>
<td>210</td>
<td>221</td>
</tr>
<tr>
<td>Period 1</td>
<td>±11.5</td>
<td>±5.2</td>
<td>±5.2</td>
<td>±7.4</td>
</tr>
<tr>
<td>Period 2</td>
<td>317</td>
<td>310</td>
<td>216</td>
<td>215</td>
</tr>
<tr>
<td>±8.5</td>
<td>±6.1</td>
<td>±7.6</td>
<td>±7.5</td>
<td></td>
</tr>
<tr>
<td>Mean cholesterol, alcohol periods</td>
<td>265(±7.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean cholesterol, no alcohol periods</td>
<td>265(±7.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean difference alcohol minus no alcohol</td>
<td>-3(±2.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Cholesterol values in control are means of duplicate analysis of 2 blood samples taken with a 4-week interval, while subsisting on the usual diet. Cholesterol values in periods 1 and 2 are means of duplicate analysis on blood samples taken on 2 consecutive days at the end of each period. The duration of the experimental periods was 3 weeks. Ethanol (0.45 Gm./Kg./day) was given in period 1 to the men in groups H 1 and L 1, and in period 2 to the men in Groups H 2 and L 2. The underlined values correspond to the periods of alcohol administration.

the morning by stomach tube in the amount of 1 ml. of 55 per cent alcohol per pound of body weight, diluted with 4 parts of water. This corresponds to 1.65 Gm. of ethanol/Kg. of body weight, or approximately 16 per cent of the mean caloric intake of the animals.

A switchback or reversal experimental design was followed. The animals were divided into 2 matched groups and kept on the same diet. In the first experimental period, alcohol was given for 2 weeks to one of the groups, after which it was discontinued and given to the second group for 2 weeks. Weekly blood samples were taken from all the animals and on 2 consecutive days at the end of each experimental period.

**Human Experiments**

Sixty healthy male inmates of the Minnesota State Prison (Stillwater, Minnesota) participated in the experiment. One of the subjects was discharged at the beginning due to illness. The other 59 successfully completed the whole experiment. The mean age of the 59 men was 47.6 years (range 36 to 66). They had an average body weight of 78.7 Kg. and a mean relative body weight of 107.7 per cent.16 The men were selected from 164 volunteers on the basis of their serum cholesterol concentration. One half of the men chosen had a high serum cholesterol (over 300 mg./100 ml), while the other half had serum cholesterol around 200 mg./100 ml. Both the high- and low-cholesterol groups were further subdivided into 2 subgroups (H 1, H 2, L 1, and L 2), as shown in Table 1.

**Diet**

The institutional diet was a good varied diet of the usual American type. Its mean caloric value and fat content was computed with the help of standard tables17 from the menus served during the last 35 days of the experiment. The mean caloric value was found to be 3,100 calories per day (SE, 60) and the fat content was 132 Gm./day, or 38.3 per cent of the total calories. As a check of this computation, individual servings of the food were collected for 7 days during the last week of the experiment and kept frozen until analyzed for fat. After thawing and mixing, the food was ground, mixed again, homogenized, and Soxhlet extractions with ether of 4 samples were done. The mean fat content was found to be 121 Gm./day.

Samples of the dietary fat were saponified and the fatty acids extracted with petroleum ether after neutralization. The methyl esters of the fatty acids were prepared with diazomethane in ether and analyzed by gas phase chromatography. The composition was found to be 51.0 per cent of saturated, 40.0 per cent of monoene, 7.7 per cent of diene, and 1.3 per cent of triene, fatty acids.

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Table 2

Subjects of Experiment 2

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of men</th>
<th>Age (years)</th>
<th>Weight (Kg.)</th>
<th>Relative weight per cent</th>
<th>Cholesterol mg./100 ml.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7</td>
<td>47.0</td>
<td>77.6</td>
<td>±3.5</td>
<td>110.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>±2.5</td>
<td>±24.4</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>47.3</td>
<td>75.8</td>
<td>±3.2</td>
<td>102.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>±4.8</td>
<td>±25.4</td>
</tr>
</tbody>
</table>

*Values are Means and SEM.
†Cholesterol values as in table 1.

The effect of a high-fat diet of ethanol on serum cholesterol concentrations in the dog (8 dogs). Cholesterol values (mg./100 ml.) at 0 time correspond to the low-fat diet (4 per cent of fat calories). At this point, all the animals are placed on the high-fat diet (40 per cent of fat calories from lard). One week later, 4 of the dogs (group I) are given 1.65 Gm. of ethanol per Kg. per day, for 2 weeks. At the end of this period (week 3), ethanol is discontinued to this group and given to the other 4 dogs (group II) for another 2 weeks. Values are means of the 4 dogs in each group.

Experimental Design

The experiment was conducted in 2 periods of 3 weeks. During the first period, alcohol was given to half of the men (half high-cholesterol and half low-cholesterol), while the other half received a supplement of syrup of the same caloric value as the alcohol supplement. During the second period, the supplements were reversed. The alcohol supplement consisted of 3 oz./day of 100 proof whisky. This corresponds approximately to 0.45 Gm. ethanol/Kg. of body weight per day, equivalent to 245 calories/day, or 7.9 per cent of the caloric value of the diet (alcohol not included). Both whisky and syrup were taken after dinner under the surveillance of the prison personnel.

Blood samples were taken weekly and twice on 2 consecutive days, at the end of each experimental period. Total serum cholesterol was estimated by the method of Abell et al. Total esterified fatty acids were measured by the method of Bauer and Hirsch. Cholesterol distribution among lipoproteins were studied, using paper electrophoresis according to Anderson and Keys. The body weight was determined weekly.

A second experiment was done with a group of 14 men receiving 9 oz. of 100 proof whisky/day (or 1.35 Gm. ethanol/Kg./day) for 3 weeks. This amount of ethanol represents approximately 24 per cent of the total caloric value of the diet as served (alcohol not included). Nine ounces of syrup providing the same amount of calories as the ethanol were given to subjects not having the alcohol supplement. The experimental design was the same as in the previous experiment. The supplements were given in divided portions of 2, 3, and 4 oz. after lunch, dinner, and at bed time, respectively. Blood samples were taken as in the previous experiment and body weight was measured every week. The data of the subjects are given in table 2.

Results

Effect of Ethanol (1.65 Gm./Kg./day) on Serum Cholesterol Concentration in the Dog

The effect of administration of alcohol to dogs subsisting on a diet low in fat (4 per cent of total calories from fat) was studied in 8 dogs. The total cholesterol values at the end of the 2-week periods are given in table 3. Each dog had an increase of the serum cholesterol while receiving alcohol that promptly decreased upon discontinuing the alcohol. The mean cholesterol difference (ethanol minus no ethanol) was 52 mg./100 ml. (SE, 8.2). This difference was highly significant (p = 0.0004).

The effect of ethanol on serum cholesterol on 8 dogs kept on a high-fat diet (40 per cent of total calories from fat by adding lard to the diet) was first studied. The results of this experiment are shown in figure 1. All of the dogs were first maintained on the low-fat diet,

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Effect of Ethanol (1.65 Gm./Kg./day) on Total Serum Cholesterol in Dogs Fed Diets of Different Fat Content

<table>
<thead>
<tr>
<th>Diet</th>
<th>No. of dogs</th>
<th>Total serum cholesterol mg./100 ml.</th>
<th>Alcohol</th>
<th>No alcohol</th>
<th>Difference</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-fat (4 per cent fat calories)</td>
<td>8</td>
<td>188 ±14.8</td>
<td>136 ±11.7</td>
<td>52 ±8.2</td>
<td>36 ±11.5</td>
<td>0.0004</td>
</tr>
<tr>
<td>High-fat (40 per cent fat calories from lard)</td>
<td>24</td>
<td>275 ±10.8</td>
<td>200 ±9.5</td>
<td>75 ±6.6</td>
<td>75 ±6.6</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

*Values are means and standard errors of duplicate analysis on blood samples taken on 2 consecutive days at the end of the 2-week experimental periods.

and then placed on the high-fat diet. The change from the low- to the high-fat diet produced an elevation of serum cholesterol concentration which increased further when ethanol (1.65 Gm./Kg./day) was given. As in the previous experiment, the cholesterol concentration decreased after discontinuing the administration of ethanol. The same effect was found in 4 different experiments on 24 dogs. The results of these experiments are summarized in Table 3. Every animal showed an increase in serum cholesterol concentration within 2 weeks after the administration of ethanol. The mean serum cholesterol value at the end of the high-fat no-alcohol periods for the 24 dogs was 200 mg./100 ml. (SE ± 9.5), and at the end of the high-fat plus alcohol periods it was 275 (SE ± 10.8). The mean difference (75, SE = ± 6.6) was highly significant (p = 0.0001). No significant changes of body weight occurred throughout these experiments and the animals did not show any abnormal manifestation, with the exception of the expected effects of alcohol intoxication for a few hours after the administration of the ethanol. No apparent relation was observed between the magnitude of the cholesterol concentration increase produced by the ethanol and the initial cholesterol level in the dogs on the high-fat diet.

Administration of alcohol for a second period with the same diet produced a cholesterol response very similar to that observed after the first administration. The mean cholesterol increase observed in 5 dogs on high-fat diet after 2 weeks of alcohol was 7 mg./100 ml. (SE, 11.0); when the experiment was repeated with the same 5 dogs on the same diet one month later, the increase produced by the alcohol after 2 weeks was 71 mg. (SE, 8.8). The serum cholesterol concentration remained elevated with continuous daily administration of ethanol as shown in figure 2, which gives the mean values for 3 dogs observed for 17 weeks. Two of these dogs continued to have high cholesterol values after 24 weeks of daily ethanol (1.65 Gm./Kg./day) administration. Their mean values for the whole 24-week period were 302 mg./100 ml. (SE, 7.6) and 325 (SE, 8.1) as compared with 161 (SE, 6.6) and 224 (SE, 5.8) for 3 weeks on the high-fat diet without alcohol. One dog has been kept in the laboratory for 10 months on the high-fat diet and daily administration of ethanol. The serum cholesterol after this period was 312 mg./100 ml., as compared to the initial value of 170 while on the high-fat diet and no alcohol.

The effect of ethanol was studied when given either in a single or in divided doses to 4 dogs. These animals received the usual amount of ethanol (1.65 Gm./Kg./day) for 2 weeks while consuming the high-fat (lard) diet. Two dogs received the alcohol as a single dose, while the other 2 received the same amount of alcohol divided into 3 equal portions at 4-hour intervals. After 2 weeks, the manner of administration was reversed. The mean cholesterol increase was 65 mg./100 ml. (SE, ± 18.5), when the ethanol was given as a single daily
The mean cholesterol increase was greater while on the sunflower oil diet than on the lard diet (89 mg./100 ml. SE, 6.0, and 66, SE, 8.8, respectively). The mean difference (23 SE, 9.3) was not significant (p = 0.055—table 4).

It was of interest to determine whether the administration of acetate at a dose corresponding to the amount of alcohol used in these experiments produced any change of cholesterol concentration in the dog. Accordingly, 2 dogs were given 2.94 Gm. of sodium acetate/Kg./day for 2 weeks by stomach tube while kept on the high-fat (lard) diet. No significant change of serum cholesterol concentration was detected in these animals, as shown in table 5. The body weight of the dogs remained constant and the animals showed no abnormal responses to the administration of acetate, except for some vomiting after the first 2 doses.

Effect of Ethanol on Total Esterified Fatty Acids

Total esterified fatty acids were measured in 8 of the dogs on high-fat diet in table 3. All the values reported are means of duplicates on each of 2 blood samples taken at the end of the corresponding periods. The mean concentration at the end of the alcohol periods was 13.0 mEq./L. (SE, 0.76) and at the end of the nonalcohol periods 10.0 (SE, 0.46). The mean difference of 3.0 (SE, 1.12) when analyzed by the test for paired variates proved to be significant at the level of p = 0.03.

Changes in Cholesterol Distribution

The distribution of total cholesterol between the alpha and beta lipoproteins fractions separated by paper electrophoresis was studied in 4 dogs. The 4 animals showing the greatest cholesterol changes were used. The results are given in table 6. The increase of total cholesterol is distributed nearly equally between the 2 lipoprotein fractions.

Effect of Ethanol on Serum Cholesterol Concentration in Man

The effect of the administration of ethanol at the dose of 0.45 Gm./Kg./day for 3 weeks was studied on 59 inmates of Stillwater prison.
Table 4

<table>
<thead>
<tr>
<th>Comparison</th>
<th>No. of dogs</th>
<th>Mean cholesterol increase mg./100 ml.</th>
<th>Mean difference mg./100 ml.</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Single dose versus divided dose</td>
<td>4</td>
<td>Single dose 65±18.5</td>
<td>9±20 0.7</td>
</tr>
<tr>
<td>B. Low-fat diet versus high-fat diet</td>
<td>5</td>
<td>Low-fat diet 74±20.3</td>
<td>9±20 0.7</td>
</tr>
<tr>
<td>C. Unsaturated fat versus saturated fat</td>
<td>6</td>
<td>Sunflower oil 65±18.3</td>
<td>33±22.3 0.18</td>
</tr>
<tr>
<td>Unsat. fat</td>
<td>5</td>
<td>Sunflower oil 65±18.3</td>
<td>33±22.3 0.18</td>
</tr>
</tbody>
</table>

*Each comparison was made with the same animal on the 2 experimental conditions.

(Experiment 1). The results are summarized in Table 1. No significant change of the serum cholesterol was found after 3 weeks of ethanol administration. The effect of 1.35 Gm. of ethanol/Kg./day on total serum cholesterol was examined in 14 men (Experiment 2). An increase of cholesterol concentration was observed at the end of the first week of the second period. The mean increase (Table 7) was 18 mg./100 ml. (SE 5.0) the difference being significant (p = 0.004). When the comparison was made at the end of the 3 week periods the cholesterol difference was only 10 (SE 4.4) which is significant at the 0.04 level.

It was observed in this experiment that the men with higher cholesterol tended to have a greater increase in serum cholesterol after alcohol than those with lower cholesterol. A significant correlation exists between the cholesterol increase produced by ethanol and the control cholesterol level (r = + 0.67, p < 0.01) of the 14 men receiving 1.35 Gm. ethanol/Kg./day.

Body Weight Changes

In experiment 1, the mean body weight was 79 Kg, both at the end of period 1 and of period 2, which compares with 78.7 Kg. at the end of the control period. No important individual changes were noticed. In experiment 2, there was a mean increase of 0.6 Kg. in the mean weight of the 14 men at the end of period 2, as compared with the end of period 1. This increase is mainly accounted for by the weight gain of 3 men (Ca., McD, and Sh. in Table 7), who gained more than 2 Kg. each. These 3 men had a rise of cholesterol concentration when receiving syrup.

Effect of Ethanol on Total Serum Esterified Fatty Acids in Man

No measurements were made in the first experiment on men. In the second experiment, the mean concentration before the beginning of the experiment for the 14 men was 10.4 mEq./L. (SE 0.84). The mean value for the alcohol periods was 10.8 (SE 1.22) and for the nonalcohol periods, 10.9 (SE 0.97).

Discussion

Animal Experiments

It is evident that administration of ethanol produces a marked increase of serum cholesterol concentration in the dog. The cholesterol rise occurs within a few days, and reaches its maximum between the second and third weeks while on ethanol. If the administration of ethanol is continued, the cholesterol concentration is maintained at this high level or rises even further at a slower rate. The cholesterol concentration decreases rapidly on discontinuing the administration of ethanol, and approaches the prealcohol level in 2 to 3 weeks. There is no significant difference between the cholesterol response of animals on either a high- or low-fat diet, although our data indicate that the effects of dietary fat and of alcohol on serum cholesterol are at least additive. The nature of the dietary fat with ethanol administration did not influence significantly...
Effect of Acetate on Serum Cholesterol Concentration in the Dog

<table>
<thead>
<tr>
<th>Dog</th>
<th>Before acetate</th>
<th>1 week</th>
<th>2 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>136</td>
<td>125</td>
<td>126</td>
</tr>
<tr>
<td>2</td>
<td>100</td>
<td>100</td>
<td>106</td>
</tr>
</tbody>
</table>

*(2.94 Gm. sodium acetate/Kg./day.) Cholesterol values (mg./100 ml.) are means of duplicate estimations on 2 blood samples taken on 2 consecutive days at the end of the different experiment periods. The animals were on high-fat (lard) diet.

Table 6

Distribution of Total Serum Cholesterol in 1 dogs on Alcohol and No Alcohol

<table>
<thead>
<tr>
<th>Cholesterol mg./100 ml.</th>
<th>Per cent of total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alpha</td>
</tr>
<tr>
<td>Total</td>
<td>Alpha</td>
</tr>
<tr>
<td>Alcohol</td>
<td>299</td>
</tr>
<tr>
<td>±6.5 ±11.7 ±11.9</td>
<td></td>
</tr>
<tr>
<td>No alcohol</td>
<td>197</td>
</tr>
<tr>
<td>±9.5 ±7.8 ±3.2</td>
<td></td>
</tr>
<tr>
<td>Difference</td>
<td>102</td>
</tr>
<tr>
<td>alcohol minus no alcohol</td>
<td></td>
</tr>
</tbody>
</table>

*Values are means and standard errors of the mean.

the cholesterol response when either lard or sunflower seed oil were used.

These results confirm and extend the old observations by Duccechi and are in general agreement with other reports about the effects of ethanol on serum cholesterol in rabbits, rats and chickens. It should be noted that the amount of alcohol given by Gottlieb et al. to rats was, on body weight basis, 7 to 8 times greater than in the present experiments. On a caloric basis, however, the proportion of alcohol calories to dietary calories was approximately the same. These authors obtained very large elevations of serum cholesterol in rats fed a diet containing 1 per cent of cholesterol and bile acids. In the animals consuming cholesterol and bile acid-free diets the mean serum cholesterol increase that they observed was only 25 per cent above the nonalcohol level, while in our dogs (see table 3), the mean increase was 37 per cent above the nonalcohol value. The diets used in our experiments were of low-cholesterol content, and the small difference of cholesterol content between the lard and the sunflower diets failed to affect the cholesterol response to ethanol (table 4).

In 1915, Duccechi expressed the opinion that the effect of ethanol on serum cholesterol is related to the narcotic effect of the alcohol. Our experiments do not lend support to this concept, since the same cholesterol responses were obtained when the same daily amount of alcohol was given, either as a single dose or in equally divided portions; this did not produce a narcotic effect (table 4).

Since alcohol is oxidized in the body to acetic acid and acetic acid is known to be a precursor of cholesterol, it is possible that the effect of the alcohol could be due to an increased synthesis of cholesterol induced by the accumulation of acetate in the body. Such a possibility is not supported by our experiments, since acetate administration had no effect on the blood cholesterol (table 5). No explanation for the effect of ethanol on serum cholesterol concentration in the dog can be offered at the present.

Human Experiments

The present experiments clearly show that the response of serum cholesterol concentration to the administration of ethanol in man is much smaller than that observed in the dog. Even with high doses of alcohol (1.35 Gm. ethanol/Kg./day) the response is less marked than in the dog. It appears that there is a significant specific difference between dog and man with respect to the cholesterol response to alcohol. However, large daily amounts of alcohol produced a small but significant increase of serum cholesterol in man.

In the human experiments, it should be considered that the intake of a high dose of alcohol will produce a change in the proportion of fat calories in the diet. Since our men, with a few exceptions, did not gain weight, it is to be assumed that they did decrease their food consumption by an equivalent amount of cal-
ETHANOL AND SERUM CHOLESTEROL

ories, both when taking alcohol and when taking syrup. Assuming that the decrease in food consumption affected all the components of the diet to the same extent, the proportion of fat calories decreased from 38 to 29 per cent of the total caloric intake. The analysis of the diet showed that about 50 per cent of the dietary fat was saturated and this change in the dietary intake per se will produce a decrease of serum cholesterol of some 10 mg./100 ml. Accordingly, the net elevation of serum cholesterol, produced by the administration of ethanol would be approximately 28 mg./100 ml. It was found that the cholesterol increase observed at the end of the second experimental period in experiment 2 was smaller than that observed at the end of the first week of this period. This is probably due to significant increase of body weight of 3 men who made the change from alcohol to syrup. It is known that weight gain results in cholesterol increase, and the 3 men had higher serum cholesterol values while on syrup than on alcohol. These 3 men should be expected to have a lower serum cholesterol while on syrup, had they not increased their body weight; on removing the 3 men from the series, the mean cholesterol difference, alcohol minus no alcohol, for the remaining 11 men becomes 14.5 mg./100 ml. (SE, 5.2) which is significant at p = 0.02. It appears, then, that high doses of alcohol have a small but significant cholesterol increasing effect in man, and this agrees with the observations reported by Ducceschi and Bailari but does not agree with the results reported by Hobson et al. in older men. The cholesterol increases in man are certainly small, but it is clear that alcohol can not be considered as a cholesterol decreasing agent. It is likely that alcohol may be partially responsible for the high-serum cholesterol levels in some individuals eating a high calorie high-fat diet and indulging in alcohol beverages, and that the removal of the alcohol should produce a decrease of serum cholesterol in such individuals.

The fact that the serum cholesterol increase produced by ethanol is related to the "intrinsic" cholesterol level of the individual is of some interest. Amatuzio and Hay have shown that ethanol significantly increases serum cholesterol concentration in hyperlipemic individuals, and the present data indicate that an increase is also to be expected with high doses of alcohol in individuals with high cholesterol level but not considered as hyperlipemic. In view of these findings, it may be justified to discourage habitual drinking of alcohol, in addition to the usual dietary restrictions, in subjects with high-serum cholesterol levels, if a lowering of the serum cholesterol concentration is desired.

### Summary

The effect of ethanol on serum cholesterol concentration has been studied in normal male
dogs subsisting on diets of low cholesterol content. Daily administration of 1.65 Gm. ethanol/Kg. of body weight produced significant increases of serum cholesterol in dogs when fed either a low-fat diet (4 per cent of fat calories) or a high-fat (40 per cent) diet. The mean cholesterol increase after 2 weeks of ethanol administration was 52 mg./100 ml. (SE, 8.2) for 8 dogs on the low-fat diet, and 75 (SE, 6.6) for 24 dogs on the high-fat (lard) diet. No significant difference was found between the mean increases of serum cholesterol produced by ethanol administration, using either the high-fat diet of saturated fat (lard) or that of unsaturated fat (sunflower oil). Serum cholesterol concentration decreases rapidly after discontinuing the administration of ethanol, reaching the prealcohol levels in 2 to 3 weeks. The higher levels of serum cholesterol are maintained as long as the administration of ethanol continues. Sodium acetate, when given at the same molar quantity as ethanol, failed to produce any change of serum cholesterol concentration in the dog.

The effect of ethanol administration on serum cholesterol concentration in man was tested in 2 switchback experiments, comparing the effects of alcohol and those of a supplement of syrup of equal calorie value while the men were eating a normal diet containing 38 per cent of fat calories. When 0.45 Gm. ethanol/Kg./day were given to 59 normal men for 3 weeks, no significant difference of serum cholesterol concentration was observed between the values on syrup and on alcohol. However, the administration of 1.35 Gm./Kg./day to 14 men produced a mean increase of serum cholesterol concentration of 18 mg./100 ml. (SE, 5.0) within 1 week. The individual increases of serum cholesterol are correlated with the intrinsic cholesterol levels of the subjects ($r = +0.67, p < 0.01$). It is concluded that ethanol increases serum cholesterol concentration in the dog and man. The response in the dog is much greater than that observed in the human subjects.

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Summario in Interlingua
Le effecto de ethanol super le concentration serai de cholesterol esseva studiate in normal canes mascule mantenite con dietas a basso contento de choles-terol. Le administration diurne de 1,65 g de ethanol per kg de peso corporee produceva significative augmentos del cholesterol serai in canes, tanto quando illos recipieran un dieta a basso contento de grassia (4 pro cento del calorias) como etiam quando lor dieta esseva ric in grassia (40 pro cento del calorias). Le augmento medie del concentration de cholesterol post 2 septimanas del curso de ethanol esseva 52 nig per 100 ml, con un error standard de 8,2, sub le conditiones de un dieta a basso contento de grassia (8 canes) e 75 mg per 100 ml, con un error standard de 6,6, sub le conditiones do un dieta a alte contento de grassia (24 canes). Nulle significative differentias esseva constatate inter le augmentos medic del cholesterol serai producito per le administration de ethanol quando (1) le alte contento dietari de grassia esseva constitute per grassia satu-rate (lardo) e quando (2) le grassia esseva non-saturate (oleo de heliantho). Le concentration del cholesterol serai decresco rapidemente post le sus-pension del administration de ethanol. Illo re-attinge le nivcllos de base intra 2 a 3 septimanas. Le elevate nivcllos de cholesterol se mantenite si longemente como le administration de ethanol es continuate. Acetato de natrium, administrate in le mesme doses molar como ethanol, non produceva ulle alteration del concentration de cholesterol serai in canes.

Le effecto del administration de ethanol super le concentration de cholesterol serai in humanos esseva testate in 2 experimentos (ambes del typo cruciate) pro comparar le effecto de ethanol o illo de un supple-mento equicaloric de sirop durante quo le subjectos recipieran un dieta normal con 38 pro cento del calorias ab grassia. Quando (1) 0,45 g/kg/die de ethanol esseva administrate a 59 normal masculos durante 3 septimanas, nulle significative differentias esseva const-tate inter le concentration de cholesterol serai post sirop e post ethanol. Sed quando (2) 1,35 g/kg/die de ethanol esseva administrate a 14 normal masculos, un augmento del concentration de cholesterol serai amontante a 18 nig per 100 ml con un error standard de 5,0 esseva producite intra un septimana. Le aug-mentos individual del cholesterol serai es correlationalle.
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con gli livelli intrinseci di colesterolo in le sottostanti, mostrando $r = + 0.67$ e $p<0.01$. E concluso che l'alcool aumenta la concentrazione di colesterolo serum in cani e in umani. La risposta in cani è molto più forte che illo osservate in umani.

References

Effect of Ethanol on Serum Cholesterol Concentration in Dog and Man
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