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Dietary Factors and Alcoholic Cirrhosis

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Mortality from cirrhosis in many countries deviates markedly from that expected for a given per capita alcohol intake. We investigated the possibility that dietary factors might explain the deviation expected and actual mortality rates in different countries. Deviations from expected cirrhosis mortality was calculated as a percentage for 17 different countries, all of whom had carrier rates for hepatitis B virus of less than 2%. The percentage of deviation was correlated with dietary intake of sautrated fat, polyunsaturated fat, cholesterol, and also with mortality from ischemic heart disease. The percentage of deviation correlated inversely with dietary cholesterol ($r = -0.86$, p 0.001) and saturated fat ($r = -0.80$, p 0.001) and positively with polyunsaturated fats ($r = -0.55$ p 0.05). This suggests that both saturated fat and cholesterol protect against alcoholic cirrhosis while polyunsaturated fats promote cirrhosis. The correlation between percentage of deviation and ischemic heart disease ($r = -0.78$, p 0.002) suggests that those factors that promote ischemic heart diease protect against alcoholic cirrhosis.

ALCOHOL ingestion is known to produce a variety of metabolic and pathologic alterations in the liver, including cirrhosis.[1] In many countries, mortality from cirrhosis deviates markedly from that expected for a given per capita alcohol intake.[2] For example, New Zealand and Belgium both had a similar per capita consumption of alcohol in 1970, yet, the mortality from cirrhosis in Belgium is about three times greater than in New Zealand. Furthermore, not all alcoholics develop cirrhosis.[3,4] Thus, other factors such as diet and type of drinking behavior have to be considered in the etiology of alcoholic cirrhosis.

Studies in experimental animals have shown that diets rich in saturated fats and low polyunsaturated fats provide resistance to the effects of alcohol.[5,6] Therefore, we investigated the possibility that differences in diet might explain the deviation from expected rates for cirrhosis in different countries.

METHODS

Previously published data[7] were obtained for per capita consumption of cholesterol, saturated fatty acids, and polyunsaturated fatty acids. All consumption data were expressed in grams/capita/day and were the average/yr for the 1954–1965 period. The 17 countries included in the present study (New Zealand, Ireland, Australia, England, Netherlands, Switzerland, Canada, Belgium, Denmark, Sweden, France, Finland, Norway, Germany FR, Austria, United States, and Japan) all had carrier rates for hepatitis B virus of less than 2%.[8] Deviations from expected mortality rates from cirrhosis for 1967 were obtained from previously published sources[2] which utilized both actual and estimated age-adjusted mortality rates. The deviation was calculated as a percentage, e.g., the actual mortality cirrhosis rate for England in 1967 was 2.8/100,000. The mortality rate estimated from the alcohol consumption per capita was 6.6/100,000. The deviation of −3.8 calculated as a percentage was −57.5%.

To determine whether dietary factors could explain the deviation from estimated rates for cirrhosis (henceforth referred to as a percentage of deviation), the dietary intake per capita of saturated fats, polyunsaturated fats, and cholesterol was correlated with percentage of deviation for all countries studied. In addition, the amount of saturated fat and polyunsaturated fat as a percentage of total calories was also correlated with percentage of deviation (Table 1).

Since the dietary factors (saturated fats, cholesterol, and polyunsaturated fats) are also the same factors implicated in the pathogenesis of atherosclerosis and ischemic (coronary) heart disease,[9] the relationship between percentage of deviation and mortality rates per 100,000 for ischemic heart disease was also studied to provide perspective. Data for age-adjusted mortality rates from ischemic heart disease for 1967 were obtained from previously published sources.[10,11] Pearson's correlation coefficient, r, was used to evaluate associations. The Student test was used to assess statistical significance.

RESULTS

The relationship between dietary cholesterol and percentage of deviation from estimated cirrhosis mortality is shown in Fig. 1*A* (r −0.86, p 0.001). The relationship between dietary saturated fatty acid and intake and percentage of deviation is shown in Fig. 1*B* (r −0.80, p 0.001). Fig. 1*C* shows the correlation between polyunsaturated

Table 1. Liver Cirrhosis Mortality Rate and Alcohol Consumption in the Countries Studied

	Liver cirrhosis deaths/100,000 (1967)			Per capita consumption of absolute alcohol
	Actual	Estimated	Deviation	
				liters
New Zealand	2.7	12.2	−9.5 (−77.8%)	6.7
Ireland	2.6	8.1	−5.5 (−67.9%)	5.0
Australia	5.1	13.9	−8.8 (−63.2%)	7.4
England	2.8	6.6	−3.8 (−57.5%)	4.3
Netherlands	3.5	6.1	−2.6 (−42.3%)	4.1
United States	9.3	14.1	−4.8 (−34.0%)	5.5
Switzerland	14.0	19.3	−5.3 (−27.6%)	9.7
Canada	7.2	9.5	−2.3 (−24.5%)	5.6
Belgium	9.9	12.1	−2.2 (−18.5%)	6.6
Denmark	7.6	8.7	−1.1 (−12.8%)	5.2
Sweden	7.4	7.8	−0.4 (−5.5%)	4.8
France	35.7	37.0	−1.3 (−3.6%)	17.1
Finland	3.2	3.0	0.2 (+5.5%)	2.9
Norway	3.8	3.3	0.5 (+13.7%)	3.0
Germany FR	22.6	19.8	2.8(+14.1)	9.9
Austria	28.0	20.5	7.5 (+36.4)	10.1
Japan	10.4	6.4	4.0 (+62.0)	4.3

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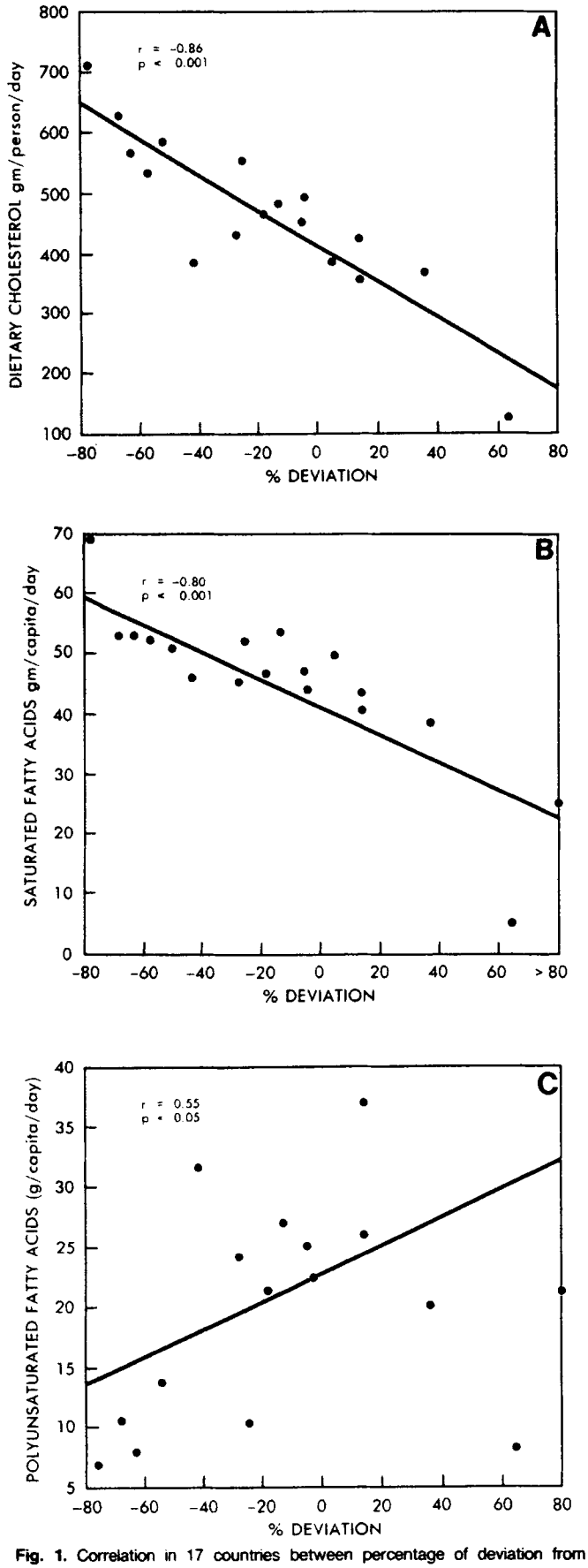

Fig. 1. Correlation in 17 countries between percentage of deviation from estimated cirrhosis mortality and dietary cholesterol (*A*), dietary saturated fatty acids (*B*), and dietary polyunsaturated fatty acids (*C*). All dietary intake data are expressed in grams/capita/day.

fatty acid consumption and percentage of deviation (r 0.55, p 0.55). When the percentage contribution of saturated fatty acids and polyunsaturated fatty acids to total calories was considered, a significant correlation was obtained only with saturated fatty acids ($r = -0.64$, p 0.01). The correlation with percentage of polyunsaturated fatty acids was $r = 0.30$, p = NS. The relationship between ischemic heart disease mortality and percentage of deviation is shown in Fig. 2 ($r = 0.78$, p 0.002).

DISCUSSION

The above relationships indicate that an association may be present in that a diet high in cholesterol and saturated fat protects against the development of alcoholic cirrhosis while polyunsaturated fats promote cirrhosis. The relationships are further strengthened by the fact that the percentage of deviation also correlates significantly with mortality from ischemic heart disease lending further evidence to the hypothesis that those dietary risk factors (cholesterol and saturated fats) that promote atherosclerosis[9] also protect against the development of cirrhosis.

Our observations are in keeping with experimental findings regarding the pathogenesis of alcoholic cirrhosis. Although the mechanisms responsible for the production of cirrhosis are not understood, evidence has accumulated that lipid peroxidation may be responsible for ethanol-associated hepatoxicity.[12,13] Studies showing that an increase in the proportion of polyunsaturated to saturated fatty acids in the diet enhances lipid peroxidation[14] is in keeping with our observations.

Another factor implicated in the tolerance of experimental animals to the effect of ethanol is the lipid composition of cell membrane.[15] Increasing the cholesterol content of membrane lipid makes the cell membrane

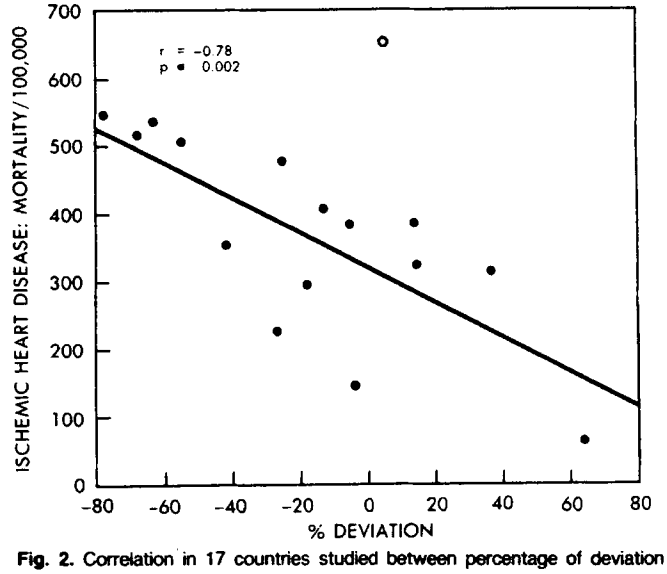

Fig. 2. Correlation in 17 countries studied between percentage of deviation from estimated cirrhosis mortality and mortality rates for ischemic heart disease per 100,000 population.

relatively resistent to the effect of ethanol.[16] Diets rich in saturated fats and low in polyunsaturated fats also have a similar stabilizing effect.[17]

The observation that factors which promote atherosclerosis and ischemic heart disease must also somehow protect against cirrhosis is borne out by the fact that the two conditions are not commonly seen together in autopsy series.[18,19] One explanation for this occurrence is the fact that alcohol protects against coronary artery disease. This, however, is highly controversial.[19,20] We suggest that the converse also be considered in the factors that promote atherosclerosis also protect against the development of cirrhosis.

We must also consider the possibility that the relationship between dietary cholesterol, saturated fat, and cirrhosis is fortuitous and that the relationship between them merely reflects the risk of developing cirrhosis and an unknown dietary or environmental factor associated with conditions of cholesterol and saturated fat intake. The strength of correlations combined with the fact that a relationship exists between two disease processes (ischemic heart disease and cirrhosis) makes a spurious relationship less likely. Also, our choice of countries with carrier rates for hepatitis B virus of less than 2% excludes the possibility that part of the deviation from expected cirrhosis can be explained as being due to hepatitis. Our hypothesis that fat and/or factors linked to fat might be casual in cirrhosis deserves further study.

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