

## Reversal of Changes in Lipoprotein A and Lipoprotein B Cholesterol during and for a Year after a Detoxication Treatment Program in Chronic Alcoholism

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We studied the individual and occasional changes in lipid metabolism induced by chronic alcohol abuse. In addition, the influence of a detoxication treatment program on the evolutionary changes in some serum lipidic components was studied for a one-year period. Before this program, total cholesterol was above normal, with high values for LP-A cholesterol, whereas for some patients LP-B cholesterol was increased. After the program, there was an increase in total cholesterol, LP-B cholesterol, and apolipoprotein B, with a decrease in LP-A cholesterol. These evolutionary changes continued during the one-year period after the end of the inpatient program.

For many years, the prognostic value of measuring different cholesterol-containing fractions in plasma of patients with atherosclerosis, cardiovascular diseases, and alterations in lipid metabolism has been recognized (for review, see 1). More recently, the changes in the distribution of cholesterol among the different plasma lipoprotein fractions in cases of chronic alcohol abuse have been studied (2-17). Thus, excessive chronic alcohol consumption, besides influencing triglyceride metabolism (3, 16), involves an increase in the cholesterol fraction associated either with the  $\alpha$ -lipoproteins (5, 11, 12) or with the high-density lipoprotein fractions (4, 6-10, 13, 14). The aim of the present work was to study not only the occasional and individual changes in plasma cholesterol fractions during chronic alcoholism, but also especially the evolutionary changes in this distribution before and just after an inpatient detoxication treatment program and for a year after the end of this program—each patient thus serving as his/her own reference.

### Materials and Methods

#### Patients

We studied all of the various patients (115 men and three women, 28-65 years old, mean 38 years) voluntarily entering a detoxication treatment program lasting for four weeks, as inpatients in a specialized department for the treatment of nutritional diseases. These patients were free of cardiovascular diseases, hepatic deficiency, renal diseases, neuritis, psychiatric diseases, epilepsy, and diabetes mellitus. Moreover, there were no clinical or histological data for objectifying any hepatic diseases. Their favorite drinks were mainly red or white wine, beer, and anised alcohols—rarely liquors or distilled spirits. In this department, the patients follow up the detoxication program with a daily dose of their favorite drink accompanied by a dose of disulfiram. Our

investigation preceded and followed the inpatient detoxication treatment program at the hospital, continuing for one year after the end of the treatment, as outpatients. During this one-year period, the patients were taking a weekly dose of disulfiram.

#### Methodology

The investigation included measurement of body weight with use of a ponderal index, actual body weight/theoretical body weight [the theoretical body weight being determined according to Lorentz's formula:  $[\text{height} - 100 - (\text{height} - 150/2)] + 0.1 \times \text{age}$ , and assay for triglyceride, total cholesterol, LP-A and LP-B cholesterol (cholesterol-associated apolipoprotein A, cholesterol-associated apolipoprotein B), and apolipoprotein B in serum collected from patients who had fasted overnight. Triglyceride was measured according to a method involving saponification and enzymatic assay of released glycerol (18), with Boehringer reagents. Total cholesterol was assayed by use of ferrous chloride (19).

Cholesterol associated with LP-A and LP-B fractions was assayed by an enzymatic method combining release of cholesterol with cholesterol esterase (EC 3.1.1.13) and oxidation of cholesterol catalyzed by cholesterol oxidase (EC 1.1.3.6) associated with Trinder's reaction (Boehringer reagents).

Lipoprotein fractions LP-A and LP-B were separated by selective precipitation of apolipoprotein B with concanavalin A (20). In this procedure, the serum specimen is initially treated with the reagent containing concanavalin A for 15 min at 20 °C, then centrifuged at  $3000 \times g$  for 10 min. The supernatant fluid is assayed for LP-A cholesterol. The pellet is solubilized and, after centrifugation, a fraction of the supernate is collected for assay of LP-B cholesterol (Fournier reagents).

Apolipoprotein B concentration was measured by radial immunodiffusion (21), with Behring reagents.

For comparing the obtained results, Student's *t*-test was applied to the mean values for the measured components.

### Results

Before participating in the program, most patients showed a normal body weight (17% of the study population had a body weight exceeding 110% of the theoretical body weight according to Lorentz's formula) as well as normal values for triglyceride. In contrast, total cholesterol was increased, with a high value for LP-A cholesterol (Table 1). After the program, an increase in body weight was generally observed with a non-significant increase in triglyceride, an increase in total cholesterol ( $p < .05$ ) with a decrease in LP-A cholesterol and an increase in LP-B cholesterol ( $p < .01$ ). In addition, the concentration of apolipoprotein B increased between the beginning and the end of the program ( $p < .10$ ). Finally, for some patients, we were able to follow the evolution of LP-A and LP-B cholesterol after the end of the program, for one year. These observations are presented in Figure 1.

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**Table 1. Evolutionary Changes in Mean Values of Body Weight and of Biological Components between the Beginning and the End of the Detoxication Treatment Program, for Men**

Statistical parameters	Biological components	Body weight, % of theoretical weight	Triglyceride	Total cholesterol	LP-A cholesterol	LP-B cholesterol	Apolipoprotein B, g/L
			mmol/L				
Reference values		90-110	0.8-2	4.5-6	≥0.9	≤4.8	0.8-1.2
Beginning of treatment	<i>n</i>	115	111	114	21	21	19
	Mean	95.6	1.67	6.09	1.58	4.35	1.07
End of treatment	<i>n</i>	94	71	71	15	15	11
	Mean	102	1.88	6.83	1.22	5.66	1.32

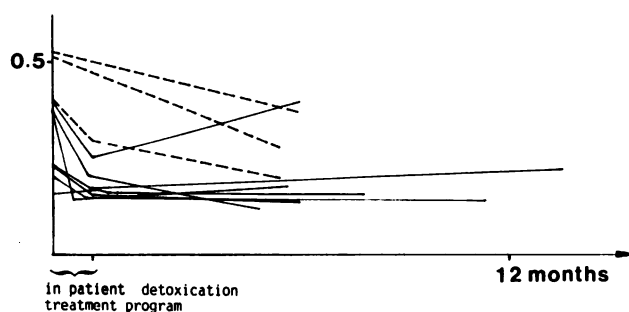


Fig. 1. Evolutionary changes in LPA cholesterol during the inpatient detoxication treatment program and a subsequent year. Results are expressed as a fraction of the values for total-cholesterol (— men; --- women).

## Discussion

Among the patients entering the program, triglyceride was not increased, in contrast with other reports (3, 16). This observation is in harmony with the hypothesis that triglyceride export by hepatocytes was altered and dependent on the degree of alcohol abuse (2). Moreover, a high value was generally observed for LP-A cholesterol. At the end of the program, lipid metabolism was generally seen to be altered. This significant evolution was verified after the end of the inpatient program, and during a one-year period. It appeared that restriction or withdrawal of alcohol consumption involved an increased move of apolipoprotein B into the circulation by the hepatocytes. The increase in LP-B cholesterol could occur as a result of the increase of total cholesterol. The evolution of the lipid metabolism that we studied may have three causes: restriction or withdrawal of alcohol consumption, a change in nutritional habits and in physical activity, and the treatment with disulfiram, with its concomitant risk of atherosclerosis (22). We conclude from our data that determination of the LP-A/LP-B ratio could be not only an accurate and persistent proof of alcoholism (4, 7, 12) but also of an adaptation of lipid metabolism dependent upon the hepatic production of apolipoproteins as an unknown pathophysiological process.

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