Acute inhibition of hepatic lipase and increase in plasma lipoproteins after alcohol intake

Charles S. Goldberg,[1] Alan R. Tall,[2] and Steven Krumholz

Gastrointestinal Division, Department of Medicine, Columbia University College of Physicians and Surgeons, 630 West 168th Street, New York, NY 10032

Abstract Chronic alcohol intake is associated with an increase in fasting plasma high density lipoproteins (HDL). To study alcohol's acute effects on plasma lipoproteins, we measured plasma lipoprotein concentrations and activities of postheparin plasma lipases in nine normolipemic males after ingestion of 40 g of ethanol (as whiskey). After alcohol there was no change in lipoprotein lipase activity but hepatic lipase was decreased to 67% of baseline at 6 hr. There were associated increases in HDL phospholipids (12 mg/dl) and cholesterol (10 mg/dl) resulting in prominence of larger, lipid-enriched HDL particles. Changes were most pronounced in the HDL_3 and HDL_{2a} subclasses. Very low density lipoprotein (VLDL) phospholipids and cholesterol were also increased by 13 and 9 mg/dl, respectively, with no significant change in triglycerides. Changes in lipoproteins and lipase were largely reversed 10 hr after alcohol intake. The transient increases in VLDL and HDL lipids after alcohol may result in part from acute inhibition of hepatic lipase activity. The results suggest a role of hepatic lipase in the catabolism of phospholipids of VLDL and possibly HDL.—**Goldberg, C. S., A. R. Tall, and S. Krumholz.** Acute inhibition of hepatic lipase and increase in plasma lipoproteins after alcohol intake. *J. Lipid Res.* 1984. **25:** 714–720.

Supplementary key words high density lipoprotein • very low density lipoprotein • lipoprotein lipase • phospholipid • cholesterol

There is substantial evidence that moderate alcohol ingestion is associated with decreased morbidity and mortality from atherosclerotic cardiovascular disease (1–3). In epidemiological studies, alcohol ingestion has been strongly linked to increased levels of fasting plasma high density lipoprotein (HDL) cholesterol (4). Since increases in HDL are associated with a decreased incidence of atherosclerotic cardiovascular disease (5), it has been postulated that the apparent protective effect of alcohol is mediated by increases in HDL (1, 4).

There is a relative paucity of metabolic studies examining the effects of alcohol on the plasma lipoproteins. Alcoholics presenting to a detoxification center had greatly increased HDL levels, which returned to normal with abstinence (6). Normal subjects fed alcohol in doses of 75 g/day developed increased levels of HDL (7). The increase in fasting HDL developed only after 2 weeks of daily alcohol intake (7, 8). These increases were associated with increased activity of lipoprotein lipase (7), a triglyceride hydrolase situated on the capillary endothelium of adipose, skeletal muscle, and other tissues. In other populations there has also been a positive correlation between lipoprotein lipase activity and HDL levels (9). By contrast, some studies have found an inverse relationship between HDL levels and the activity of hepatic lipase (10), an enzyme with both triglyceride hydrolase and phospholipase activities, located on the endothelial cells of the hepatic sinusoids.

The present study was undertaken to examine the acute effects of alcohol intake on plasma lipoproteins and on the activities of lipoprotein and hepatic lipases. We hypothesized that alcohol metabolism might result in inhibition of hepatic lipase, leading to accumulation of plasma lipoprotein components normally catabolized by this enzyme.

METHODS

Subjects

The study group comprised nine healthy, ambulatory, adult males aged 21 to 35. All subjects had normal plasma cholesterol (range 115 to 232 mg/dl) and triglycerides (range 47 to 69 mg/dl). Their weights ranged from 67 to 83 kg. No subject was suffering from obesity, diabetes hypothyroidism, or other significant illness. Their habitual alcohol intake varied from 15 to 150 g/week.

Study design

The experimental protocol was approved by the Institutional Review Board of Columbia University College of Physicians and Surgeons. Subjects were asked to abstain from alcohol for 5 days prior to the study. At 9 AM, after a 14-hr overnight fast, the subjects consumed 100 ml of blended whiskey (containing 40 g of ethanol). Blood sam-

Abbreviations: HDL, high density lipoprotein; VLDL, very low density lipoprotein; LCAT, lecithin:cholesterol acyltransferase.

[1] Present address: Department of Medicine, Mountainside Hospital, Montclair, NJ 07042.

[2] To whom correspondence should be addressed.

ples were collected at 0, 4, 6, 8, and 10 hr time points in tubes containing Na_2EDTA, 1 mg/ml. After the 10 hr time point, the subjects received 60 I.U. heparin/kg body weight. Fifteen minutes later another blood sample was obtained and used for estimation of postheparin plasma lipase values. It was necessary to obtain the lipase values of each time point on separate days (separated by an interval of 1 week) since in preliminary studies we found that postheparin lipase values obtained on the same day at 4-hr intervals showed a progressive fall with serial sampling. In five of the study subjects we determined the effects of continued fasting on plasma lipoproteins by obtaining samples 14 hr and 20 hr after the last meal. Also, to determine possible effects of fasting on hepatic lipase activity, postheparin plasma was obtained from these subjects after a 14-hr fast (9 AM, 0 hr time point) and then a week later after a 20-hr fast (3 PM, 6 hr time point).

Lipoprotein preparation and analysis

Lipoproteins were separated by preparative ultracentrifugation in a Beckman Ti 50.3 rotor by standard techniques. Protein and lipid were determined as described previously (11). Apoprotein composition was assessed by electrophoresis in 4/27% SDS polyacrylamide gradient gels, stained with Coomassie Blue and scanned in a Transidyne densitometer. The triglyceride content of lipoprotein fractions was determined by an enzymatic method using the kit of Worthington Diagnostics. VLDL was sized by negative stain electron microscopy (11) and by chromatography on a 100 × 1.5 cm column of 2% agarose (BioGel A-50 m). HDL subclasses were separated by electrophoresis in non-denaturing 4/30% polyacrylamide gradient gels and sized by comparison of their R_f values with those of protein standards, as described previously (12).

Lipase assays

Lipoprotein and hepatic lipase values were measured in postheparin plasma by the method of Boberg et al. (13). In this method hepatic lipase activity is measured under conditions of high salt concentration, where lipoprotein lipase activity is abolished. Lipoprotein lipase activity is also measured under optimized conditions, but under these conditions there is some contribution from hepatic lipase (14). Thus, lipoprotein lipase was also measured by the method of Baginsky and Brown (15), where hepatic lipase activity is abolished by the addition of sodium dodecylsulfate.

Statistics

Unless otherwise indicated, mean ± SEM values are given. The data were tested for overall differences over time by analysis of variance (16). Also, the significance of the difference of means was assessed by the paired t test.

RESULTS

Lipase activities

Alcohol ingestion was followed by a decrease in hepatic lipase activity (**Fig. 1**). Expressed as a percent, the activity at 6 hr had decreased to 67% of the fasting hepatic lipase activity ($P < 0.001$). The absolute hepatic lipase values showed a decrease from 9.1 ± 1.0 μmol free fatty acid released per ml plasma per hr (fasting) to 6.1 ± 1.1 (6 hr) ($P < 0.01$). Ten hours after alcohol intake, hepatic lipase activity had returned to the baseline value. By contrast, lipoprotein lipase activity showed no significant change after alcohol. Expressed as a percent of the mean fasting value, the lipoprotein lipase activities were 97 ± 2 (4 hr), 90 ± 6 (6 hr), 100 ± 9 (8 hr), and 98 ± 3 (10 hr); the absolute values at 0 and 6 hr were 8.0 and 7.2 μmol free fatty acid per ml per hr, respectively. Measurement of lipoprotein lipase activity using conditions that completely abolish hepatic lipase activity (15), showed that the 6 hr value was 108 ± 15% of the 0 hr value (difference not significant). The absolute values of lipoprotein lipase activity (3.16 ± 0.4 (0 hr) and 3.42 ± 0.5 (6 hr) μmol free fatty acid per ml per hr) were similar to those obtained when hepatic lipase was inhibited by immunochemical means (14).

To determine possible effects of diurnal variation or prolonged fasting, postheparin lipase activities were measured in five fasting subjects not given alcohol. In these

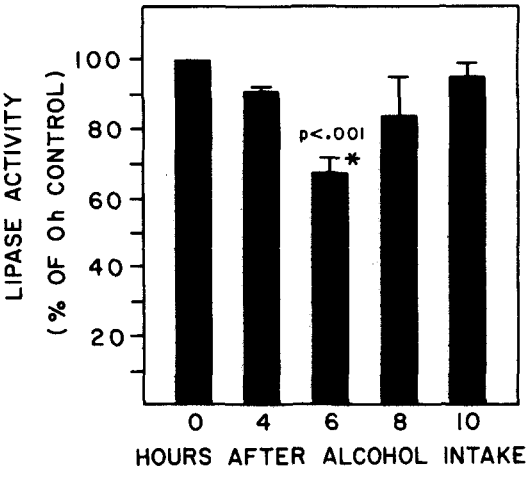

Fig. 1. Inhibition of hepatic lipase after alcohol. Activity was measured in postheparin plasma at time points indicated. Each point represents the % mean ± SEM in nine normolipemic male volunteers. Analysis of variance showed significant ($P < 0.02$) differences of hepatic lipase over time (16). The P value is given for a comparison of the 6-hr and 0-hr values by the paired t test.

subjects the 6 hr hepatic lipase activity was 100.3 ± 2.8% of the 0 hr value, while the lipoprotein lipase activity, was 102.3 ± 5.5% of the 0 hr value, indicating no significant effect of prolonged fasting on lipase activities. When alcohol in concentrations of 100 mg/dl was added to postheparin plasma, there was no effect on lipoprotein or hepatic lipase activity. To determine if the reduced activity of hepatic lipase was due to the presence of an inhibitor in plasma, fasting postheparin plasma was mixed with 6 hr postheparin plasma and hepatic lipase was assayed. Using different ratios of 0 hr and 6 hr plasma, total measured hepatic lipase was found to be the sum of the individual 0 hr and 6 hr values. These results are inconsistent with the presence of an inhibitor.

Very low density lipoproteins (VLDL)

Decreases in hepatic lipase activity were associated with reciprocal alterations in VLDL. Surprisingly, the major increase was in the VLDL phospholipids, which at 6 hr were increased 2.5-fold compared to fasting levels (**Fig. 2**). There were smaller but significant increases in VLDL cholesterol, cholesteryl esters, and protein. By contrast, there was no significant alteration in the mass of the major VLDL component, triglyceride. Although the mean triglyceride value was increased, this was due to a marked increase in VLDL triglycerides displayed by two subjects. The enrichment in VLDL phospholipids was highlighted by calculation of the percentage compositions (**Table 1**) which showed an increase from 13.8% in fasting plasma to 20.2% (6 hr, $P < 0.005$). In four subjects the apoprotein composition of VLDL was assessed by SDS polyacrylamide gradient gel electrophoresis. Compared to fasting VLDL, the 6 hr VLDL showed an increase in the content of apoC relative to apoE and apoB. Gel scanning showed the following percent chromogenicity: 0 hr, apoB (52 ± 4.3%); apoE (8.8 ± 2.4%); apoC (39.4 ± 5.6%); 6 hr, apoB (42.1 ± 3.2%); apoE (10.1 ± 3.0%); apoC (47.5 ± 5.3%). Although these changes suggest that the increased protein mass in VLDL at 6 hr was largely due to an increased content of apoC, none of the alterations in apoprotein composition was statistically significant.

The compositional changes show that there was an increase in the relative mass of surface components of the VLDL particles (phospholipids and cholesterol) with a corresponding decrease in the major core lipid, triglycerides. The ratio of surface components (proteins + phospholipids + cholesterol) to core components (cholesteryl esters + triglycerides) was increased from 0.30 (0 hr) to 0.43 (6 hr) ($P < 0.02$). To determine if these changes reflected a decrease in the size of VLDL (17), or the admixture of phospholipid- and cholesterol-rich particles, such as vesicles or disks (18), VLDL were examined by negative stain electron microscopy. In four subjects the VLDL consisted of a uniform population of

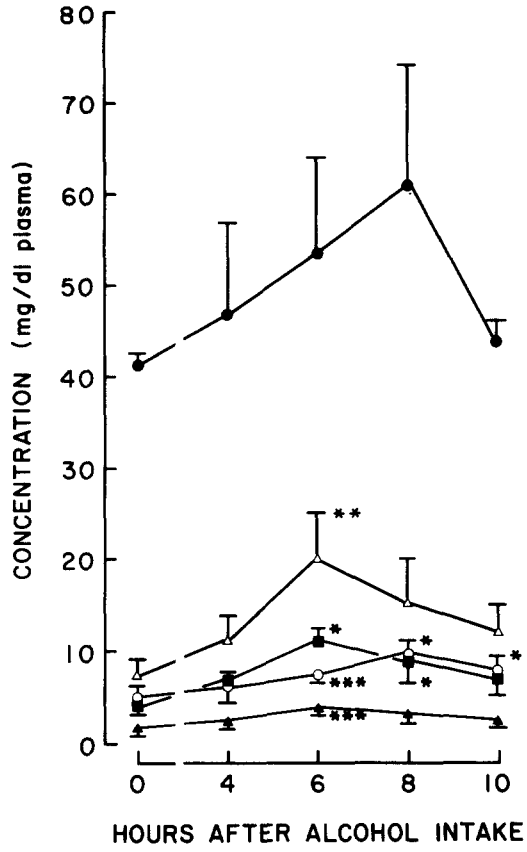

Fig. 2. Changes in VLDL composition after alcohol. Significant increases in VLDL phospholipids (△), cholesteryl ester (■), protein (○), and free cholesterol (▲) were observed at points indicated. VLDL triglyceride (●) increase was not significant and was entirely due to increase displayed by a single subject. *$P < 0.005$; **$P < 0.02$; ***$P < 0.01$ as assessed by paired t test. Analysis of variance showed significant differences over time for phospholipids ($P < 0.01$), protein ($P < 0.05$), cholesteryl esters ($P < 0.02$), and cholesterol ($P < 0.05$).

spherical particles both in fasting plasma and after alcohol ingestion. There was no significant size change of VLDL in any subject, despite the compositional alterations. For example, in one subject the diameter of VLDL in fasting plasma was 31 ± 7.0 nm (mean ± SD, n = 150) and 6 hr after alcohol it was 31 ± 6.8 nm. The lack of a size change of VLDL was confirmed in further studies where the elution volume of VLDL on 2% agarose was identical, comparing fasting VLDL to VLDL obtained 6 hr after alcohol (n = 3).

To determine if the changes in VLDL after alcohol could be due to effects of prolonged fasting, VLDL composition was determined in five subjects at 0 hr and after 6 hr of further fasting. The values (mg/dl) obtained were (0 hr, 6 hr): protein, 13.0 ± 1.3, 13.5 ± 1.8; phospholipids, 8.7 ± 2.1, 8.2 ± 2.1; cholesterol, 1.9 ± 0.5, 1.7 ± 0.5; cholesteryl esters, 6.5 ± 1.7, 5.8 ± 1.8; and triglycerides, 49.6 ± 16.4, 62.0 ± 12. None of the changes was statistically significant. These results show that the changes

TABLE 1. Percentage composition of very low density lipoprotein after alcohol intake

Time	Protein	Phospholipid	Free Cholesterol	Cholesteryl Ester	Triglyceride
hr					
0	7.0 ± 1.8	13.8 ± 2.1	2.5 ± 0.3	7.5 ± 0.9	69.6 ± 3.3
4	7.2 ± 2.2	15.0 ± 0.8	3.2 ± 0.3	9.7 ± 0.8	64.9 ± 2.9
6	6.4 ± 1.6	20.2 ± 1.7[a]	3.6 ± 0.4[b]	11.3 ± 1.4[b]	58.4 ± 3.0[b]
8	8.6 ± 2.3	13.3 ± 1.7	2.9 ± 0.4	8.9 ± 1.1	66.2 ± 1.6
10	8.4 ± 2.0	15.3 ± 2.7	3.4 ± 0.5	10.3 ± 1.6	62.6 ± 4.9

[a] Significantly different from 0-hr value, $P < 0.005$.
[b] $P < 0.01$.

in VLDL after alcohol (Fig. 1) were not due to prolonged fasting.

Intermediate (IDL) and low density (LDL) lipoprotein

After alcohol intake there were no significant changes in mass of IDL or LDL (**Table 2**). Sizing of LDL on 2–16% polyacrylamide gradient gels failed to show any size change of the major LDL band or any alteration in LDL subclass distribution.

TABLE 2. Mass of plasma intermediate and low density lipoproteins after alcohol intake

	LDL (d 1.019–1.063 g/ml)	IDL (d 1.006–1.019 g/ml)
	mg/dl ± SEM	
0 Hr		
Pro	46.2 ± 4.8	4.1 ± 1.8
PL	50.3 ± 7.4	8.4 ± 3.3
FC	24.2 ± 2.2	3.3 ± 1.6
CE	59.2 ± 6.0	11.5 ± 5.9
TG	3.4 ± 0	5.1 ± 7
4 Hr		
Pro	46.0 ± 5.4	3.7 ± 1.4
PL	49.9 ± 7.2	5.2 ± 1.7
FC	26.8 ± 1.9	2.9 ± 1.0
CE	67.1 ± 7.6	7.8 ± 3.8
TG	3.4 ± 0.1	5.0 ± 0.5
6 Hr		
Pro	48.7 ± 5.9	3.7 ± 1.5
PL	49.6 ± 7.1	7.0 ± 2.9
FC	23.5 ± 2.0	2.6 ± 1.3
CE	63.4 ± 5.4	9.3 ± 4.7
TG	3.5 ± 0	5.9 ± 0.1
8 Hr		
Pro	49.2 ± 5.8	6.1 ± 2.6
PL	46.3 ± 3.8	10.2 ± 4.4
FC	19.8 ± 1.9	4.6 ± 2.5
CE	59.6 ± 5.7	19.0 ± 7.5
TG	3.1 ± 0.3	7.4 ± 1.7
10 Hr		
Pro	53.0 ± 6.2	5.5 ± 2.2
PL	54.0 ± 9.1	10.5 ± 4.1
FC	23.7 ± 3.2	5.0 ± 2.7
CE	64.0 ± 8.7	16.9 ± 9.0
TG	3.1 ± 0	6.2 ± 1.0

Abbreviations: Pro, protein; PL, phospholipid; FC, free cholesterol; CE, cholesteryl ester; TG, triglyceride.

High density lipoproteins (HDL)

Alcohol intake was followed by significant increases in HDL phospholipids and cholesteryl esters, peaking at 6 hr, and returning to baseline at 8 to 10 hr (**Fig. 3**). At 6 hr the increase in HDL cholesterol (cholesterol ± cholesteryl esters) was 10 mg/dl ($P < 0.05$) and in HDL phospholipids it was 12 mg/dl ($P < 0.01$). By contrast, HDL protein and triglycerides showed no significant alterations.

Analysis of HDL subclasses showed that the most pronounced changes occurred in HDL_3 and HDL_{2a}, (**Table 3, Fig. 4**). Significant changes in mass were observed at 6 hr for phospholipids in all HDL subclasses and for cholesteryl esters in HDL_3. In the five subjects who were studied during continued fasting, at 6 hr there was no significant change in mass for any HDL constituent in

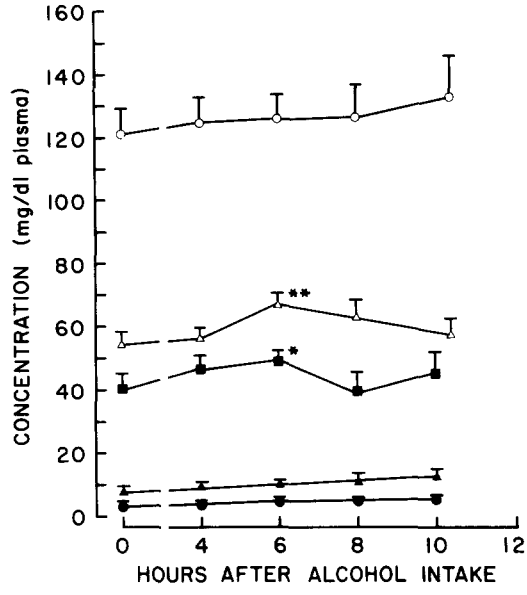

Fig. 3. Increase in HDL lipids after alcohol. Significant increases in HDL phospholipids (△) and cholesteryl ester (■) were observed 6 hr after alcohol intake. There were no significant increases in HDL protein (○), free cholesterol (▲), or triglyceride (●). *$P < 0.01$; **$P < 0.001$. Analysis of variance showed significant differences over time for phospholipids ($P < 0.02$) and cholesterol ($P < 0.05$).

TABLE 3. Mass of plasma high density lipoprotein subfractions after alcohol intake

	HDL_{2b} d 1.07–1.10 g/ml	HDL_{2a} d 1.10–1.13 g/ml	HDL_3 d 1.13–1.21 g/ml
		mg/dl ± SEM	
0 hr			
Pro	12.5 ± 1.2	40.9 ± 3.0	67.2 ± 6.1
PL	7.6 ± 1.0	20.4 ± 1.6	27.1 ± 1.8
C	1.5 ± 0.3	3.1 ± 0.4	3.4 ± 0.6
CE	6.4 ± 0.6	15.4 ± 2.0	19.2 ± 2.2
TG	0.7 ± 0.1	1.5 ± 0.2	1.5 ± 0.2
4 Hr			
Pro	12.4 ± 1.4	40.8 ± 3.5	70.2 ± 6.8
PL	6.8 ± 0.9	22.1 ± 1.9	26.6 ± 2.3
C	1.4 ± 0.2	3.5 ± 0.6	3.7 ± 0.7
CE	6.4 ± 0.5	17.8 ± 2.0	22.7 ± 3.1
TG	0.6 ± 0.1	2.4 ± 0.5	1.5 ± 0.2
6 Hr			
Pro	13.4 ± 1.2	42.8 ± 3.0	62.3 ± 6.5
PL	8.9 ± 0.7[a]	23.8 ± 1.5[a]	32.0 ± 2.3[b]
C	1.6 ± 0.3	3.5 ± 0.5	4.2 ± 0.9
CE	7.3 ± 0.6	17.7 ± 1.7	23.1 ± 2.8[a]
TG	0.7 ± 0.1	1.7 ± 0.3	1.6 ± 0.2
8 Hr			
Pro	16.0 ± 1.5	9.5 ± 3.8	70.6 ± 8.4
PL	8.0 ± 0.9	22.6 ± 1.5	32.0 ± 4.8
C	1.9 ± 0.3	4.4 ± 1.0	4.3 ± 1.2
CE	8.0 ± 0.5	12.4 ± 2.6	21.2 ± 2.7
TG	0.7 ± 0.1	1.7 ± 0.3	1.7 ± 0.3
10 Hr			
Pro	14.8 ± 1.8	42.7 ± 4.6	75.2 ± 10.2
PL	7.4 ± 1.3	20.5 ± 1.5	28.9 ± 3.7
CC	1.9 ± 0.4	4.4 ± 0.9	5.5 ± 1.6
CE	6.2 ± 1.1	16.3 ± 3.0	24.8 ± 4.9
TG	1.2 ± 0	2.0 ± 0.5	2.2 ± 0.3

HDL subclasses were isolated by preparative ultracentrifugation.
[a] $P < 0.05$.
[b] $P < 0.01$.

any HDL subclass. The values (mg/dl) were (0 hr, 6 hr): HDL_{2b} phospholipids 6.5 ± 2.3, 6.6 ± 2.1; cholesterol 9.3 ± 4.7, 9.6 ± 4.6; protein 12.1 ± 5.7, 12.0 ± 5.6; HDL_{2a} phospholipids 23.0 ± 4.4, 22.2 ± 3.6; cholesterol 23.3 ± 2.0, 25.0 ± 1.7; protein 40.1 ± 7.0, 43.3 ± 5.3; HDL_3 phospholipids 27.5 ± 1.7, 29.7 ± 4.1; cholesterol 16.0 ± 4.7, 18.1 ± 4.8.

Particle size of HDL was assessed by polyacrylamide gradient gel electrophoresis. Alcohol intake was associated with a pronounced increase in particles in the clear space usually separating HDL_{2b} and HDL_3 (Fig. 4), indicating accumulation of particles of diameters 9–10.5 nm, corresponding to larger HDL_3 and HDL_{2a} (13). As assessed by gel scanning, the peak intensity of staining of the major band of HDL showed a shift in mean particle size from 9.2 ± .1 (0 hr) to 9.6 ± .1 (6 hr, $P < 0.02$) to 9.3 ± .2 nm (10 hr). By contrast, the larger HDL_{2b} showed no significant changes. The size change at 6 hr is consistent with the increase in HDL_{2a} and HDL_3 shown by the compositional analysis (Table 3).

DISCUSSION

Nine normal subjects showed a transient decrease in the activity of hepatic lipase after alcohol intake. Since similar changes were not observed in a control group of five subjects who fasted without ingesting alcohol, these changes cannot be attributed to effects of prolonged fasting, diurnal variation, or week to week metabolic changes. In vitro studies showed no direct effect of alcohol on hepatic lipase activity and no evidence for an inhibitor of hepatic lipase in plasma. Thus, it is likely that changes in hepatic lipase measured in postheparin plasma reflect alterations in the tissue activity of the enzyme. The inhibition of hepatic lipase was probably a result of hepatic alcohol metabolism. However, since alcohol was taken as whiskey, we cannot exclude the possibility that the observed changes were due to effects of the nonalcohol moiety of this beverage. The effect was observed 6 hr after alcohol, at which time a 40-g dose of alcohol is completely metabolized in normal subjects (19). The inhibition might be secondary to the decrease in hepatic fatty acid oxidation that follows alcohol intake (19). An inverse relationship between availability of fatty acids in the liver and hepatic lipase activity is suggested by studies in rats showing reciprocal changes in plasma free fatty acid levels and lipase levels (20).

Decreases in the activity of hepatic lipase were associated with increases in the plasma lipoproteins, most pronounced in the VLDL. Interestingly, there were 1.3- to 2.5-fold increases in VLDL phospholipid, cholesterol, and protein moieties with no significant change in VLDL triglycerides. These changes indicated an increased ratio of surface to core components in VLDL. Although such an

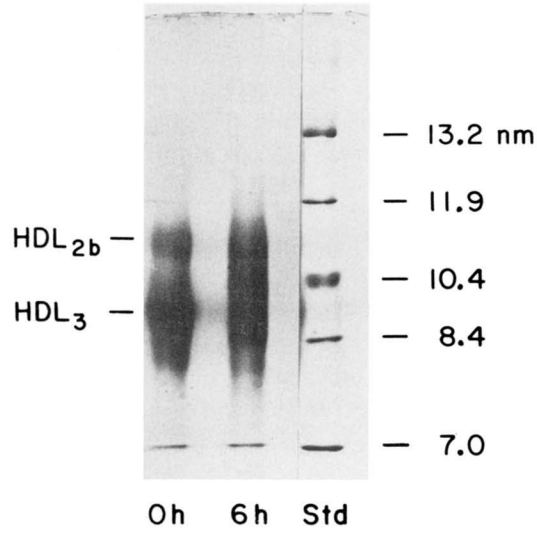

Fig. 4. Change in size of HDL subclasses after alcohol as demonstrated by nondenaturing polyacrylamide gradient gel electrophoresis.

alteration generally indicates the presence of smaller VLDL particles (16), there was, in fact, no appreciable size change in our study. Thus, the VLDL particle has the capacity to accommodate additional phospholipid and cholesterol molecules in its surface, much as HDL does (11, 18).

The temporal correlation of the changes in VLDL and HDL with inhibition of hepatic lipase activity suggests that the lipoprotein alterations resulted from decreased lipase activity. There is evidence that hepatic lipase is normally involved in VLDL catabolism. Antibody-mediated inhibition of hepatic lipase activity in monkeys (21) and rats (22) resulted in accumulation of VLDL in the plasma. Also, patients with congenital absence of hepatic lipase have increases in VLDL and IDL (23). Thus, in our study, alcohol-induced inhibition of hepatic lipase activity may have resulted in impaired catabolism of VLDL. The accumulation of specific components of VLDL may provide a clue to the normal functions of hepatic lipase. The VLDL after alcohol was greatly enriched in phospholipids, implying an important role for hepatic lipase in the normal removal of VLDL phospholipids.

The increase in HDL lipids after alcohol might also be the result of decreased degradation by hepatic lipase. In rats, antibody-mediated inhibition of hepatic lipase was followed by an increase in HDL phospholipids and cholesterol, suggesting decreased hydrolysis of HDL phospholipids by hepatic lipase (22). Hepatic lipase promotes hydrolysis of HDL phospholipids in vitro (24). The phospholipase activity of hepatic lipase accounts for its ability to stimulate uptake of HDL cholesterol by cultured hepatoma cells (25). Inhibition of hepatic lipase might lead to decreased degradation of HDL phospholipid and cholesterol, and as a result of LCAT action, cholesteryl ester accumulation. However, there is an alternative explanation for the increase in HDL lipids. A variety of evidence (11, 26–29) indicates that during lipolysis of the triglyceride-transporting particles, chylomicrons and VLDL, there is transfer of surface components (phospholipids and soluble apoproteins) from the triglyceride-carrying particles into HDL. The transfer results in transformation of HDL into larger less dense particles, somewhat analogous to those observed in the present study (11). Thus, it is possible that the observed increases in HDL phospholipids and cholesterol are secondary to changes in VLDL metabolism. For example, after alcohol intake VLDL phospholipids normally catabolized by hepatic lipase might be transferred into HDL. The influx of phospholipid into HDL would be followed by cholesterol derived from other lipoproteins and tissues (30). The cholesterol would subsequently be esterified with fatty acid derived from the phospholipid as a result of the action of plasma lecithin:cholesterol acyltransferase (31).

The transient increase in HDL cholesterol (10 mg/dl) occurring after a single dose of 40 g of ethanol is similar in magnitude to the increment in fasting plasma HDL cholesterol (7 mg/dl) in subjects habitually consuming 40 g of alcohol each day (4). Thus, acute changes in HDL after alcohol intake could be as metabolically important as chronic alterations in fasting HDL levels. Although there is debate (32), it is possible that HDL protects against cardiovascular disease by promoting the transport of cholesterol from peripheral tissues to the liver (18). The major compositional changes after alcohol were increases in the phospholipid content of VLDL and HDL. Similar increases in VLDL and HDL phospholipids occur upon incubation of phospholipid vesicles with isolated lipoproteins or plasma (33). In vitro the increase in HDL phospholipids is followed by influx of cholesterol (30). The infusion of phospholipids into experimental animals enhances reversal of atherosclerosis (34–36), possibly by promoting cholesterol efflux from tissues into the plasma lipoproteins, especially into HDL. It is conceivable that the transient increases in lipoprotein phospholipids occurring after alcohol intake might have a similar beneficial effect in humans.

A.R.T. is an Established Investigator of the American Heart Association. This research was supported by Research Grants HL-22682, HL-21006, and T32-AM-07330 from the National Institutes of Health.

Manuscript received 26 October 1983.

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