Serum Glucose Levels and Alcohol-consumption Habits in a Large Population

Marie José Gérard, M.D., Arthur L. Klatsky, M.D., Abraham B. Siegelaub, M.S., Gary D. Friedman, M.D., and Robert Feldman, M.D., Oakland, California

SUMMARY

Using information from approximately 100,000 multiphasic check-ups performed in these facilities, we have found an association between alcohol-drinking habits and serum glucose values one hour after an oral challenge with 75 gm. of glucose. There was a positive dose-response relation between reported alcohol intake and serum glucose level over the most common range of alcohol intake. Serum glucose levels were highest in the group who consumed six to eight alcoholic drinks per day. However, among those who said they took nine or more drinks per day, mean serum glucose levels were significantly lower than in the six-to-eight-drink group. These relations persisted when the analysis was controlled for the effects of age, sex, race, adiposity, time since last food intake, time of day, previously known diabetes, and previously known liver disease. A search of the literature failed to uncover a complete explanation for these phenomena. DIABETES *26*:780-85, August, 1977.

Much has been written on the possible influence of alcohol drinking on serum glucose concentration. Many published findings are based on experimental work. Consequently, they do not cover large numbers of subjects and may not reflect the effects of habitual alcohol consumption on serum glucose levels in a free-living population. Using data collected in multiphasic check-ups given by the Kaiser-Permanente Medical Care Program, we have been able to relate self-reported drinking habits to postchallenge serum glucose levels in approximately 100,000 persons.

From the Department of Medical Methods Research and the Department of Internal Medicine, Kaiser-Permanente Medical Care Program, 280 West MacArthur Boulevard, Oakland, California 94611.

Address reprint requests to Dr. Klatsky.

Accepted for publication March 7, 1977.

METHODS

The Kaiser-Permanente Medical Care Program offers its members a general health evaluation in the form of a multiphasic health check-up, which includes a health questionnaire and a number of laboratory and clinical tests.[1] For this study we selected all check-ups performed in approximately a four-year period, from mid-1964 to mid-1968. Only the first check-up in this period for a given person was used. Serum glucose concentration was measured one hour after an oral challenge with 75 gm. of glucose in a lemon-flavored solution. Chemical analysis was done on a Technicon AutoAnalyzer by the potassium ferricyanide method. In our study, subjects were classified by alcohol-consumption habits based on responses to two questions in the self-administered health questionnaire: (1) In the past year did you drink any alcohol? (2) If yes, how many alcoholic drinks did you usually have? - total of nine a day or more; - six to eight drinks a day; - three to five drinks a day; - two or less a day.

Of the 110,507 subjects whose serum glucose was measured; 95,098 (86 per cent) answered the first question above; 8,135 answered yes to the first question but did not specify the amount of alcohol consumed (question 2). Thus 86,963 (79 per cent of the subjects whose serum glucose was measured) provided adequate information on alcohol consumption. Approximately 55 per cent of these subjects were women and 45 per cent men. The racial distribution was 80 per cent whites, 11 per cent blacks, 4 per cent yellows, and 3 per cent other races; 2 per cent were not classified in any of these categories and were considered of an unknown race.

Information was also obtained from the Multiphasic

Health Checkup data on these subjects concerning the following potentially confounding variables: age, sex, race, ponderal index (height [in.]/$\sqrt[3]{\text{weight [lb.]}}$), educational level attained, time since last food intake, time of day glucose ingested, and history of diabetes and liver disease.

The ponderal index was used to estimate adiposity; the population was divided into three groups with regard to this factor: (1) **light**: ponderal index >12.60; (2) **medium**: ponderal index 12.20-12.59; (3) **heavy**: ponderal index <12.19.

Level of education was also considered, and again the total population was divided into three groups with regard to education: (1) elementary school only; (2) high school, trade or business school, up through two years of college; (3) three or more years of college.

Subjects were also classified according to whether at least four hours had elapsed (as had been instructed) between last eating and ingestion of the glucose solution. To control for possible effects of time of day, subjects were divided into three groups according to the hour at which the oral glucose was administered: (1) between 1200 and 1500 hours; (2) between 1500 and 1800 hours; (3) between 1800 and 2100 hours.

Previously known diabetics were identified from answers to the question, "Has a doctor said you had diabetes?". Patients with known liver disease were identified from answers to the question, "Has a doctor said you had liver disease?". As an indicator of prevalence of possible hepatic dysfunction, we also examined mean serum glutamic oxaloacetic transaminase (SGOT) levels in relation to alcohol consumption.

To control for possible effects of age on serum glucose levels, comparisons were made within specific age subgroups, or, when over-all comparisons were made, age adjustment was used. The indirect method of age adjustment was employed, using as the standard the entire population's data from first check-ups during the same period (n=110,507).

RESULTS

Age-adjusted mean serum glucose values in relation to drinking categories for the total population studied are presented in table 1. There was an increase in mean serum glucose with increasing alcohol consumption with the exception of the highest alcohol-consumption category (nine drinks a day or more). In this last category, which was the smallest in size but still contained a reasonable number of subjects (840), we observed a substantial and statistically significant lower mean serum glucose than in the preceding category. We attempted to determine whether the relation observed could be explained by some of the large number of factors previously described[2-4] as related to alcohol-drinking habits and possibly to serum glucose levels as well.

TABLE 1

Mean one-hour postchallenge serum glucose according to alcohol-drinking categories in the entire population studied

Drinking category	Number of persons	Mean serum glucose*	S.D.	Significance/ nondrinkers†
Nondrinker	22,981	171	48.63	
≤ 2 Drinks/day	54,405	176	45.99	$p < 10^{-9}$
3-5 Drinks/day	7,372	185	49.46	$p < 10^{-9}$
6-8 Drinks/day	1,365	186	51.78	$p < 10^{-9}$
≥ 9 Drinks/day	840	178	50.13	$p < 10^{-3}$
Total	86,963			

*Age-adjusted.
†The mean value for each drinking group was compared to that of the nondrinking group on a *t*-test.

With regard to basic demographic characteristics, age and race were strongly related to the response to an oral glucose load;[5] sex was much less related. Similarly, marked differences in alcohol consumption in relation to age, sex, and race have been noted by others[2-4] and by us.[6] For these reasons the relation of alcohol-drinking habits to serum glucose was examined within each race and sex group separately and was adjusted for age. Because of the small size of some of the subgroups in other races, we present only whites and blacks. In each sex-race category (figure 1), we again found the pattern described for the total population: the more alcohol consumed, the higher the mean blood sugar level. But this relation was true only up to a certain level of drinking; beyond that limit the trend was reversed. The trend was changed within all subgroups in the nine-or-more-drinks-per-day category, except for white women, in whom the trend reversed at six to eight reported drinks per day.

Not only was adiposity related to alcohol consumption,[6] but it seemed to be also related to serum glucose levels in a variety of ways in different age-sex groups. For this reason, we computed mean glucose values within each drinking category for the "light," "medium," and "heavy" groups separately (on the ponderal index). This analysis was repeated for each race and sex subcategory. Combined results illustrating the general trend and the results for white men (the only race-sex group with substantial numbers in all categories) are presented in figure 2. Within each "adiposity" group the relation of alcohol consumption

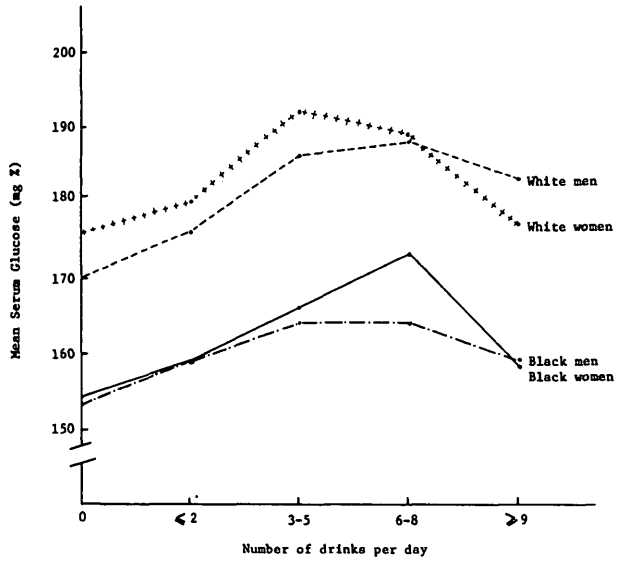

FIG. 1. Age-adjusted mean serum glucose levels by alcohol consumption, race, and sex.

to glucose level was the same as that for all adiposity groups combined (table 1 and figure 1).

Association between alcohol-drinking habits and highest educational level attained has been shown.[2-6] Table 2 suggests that serum glucose level is also related to education. Mean serum glucose levels in relation to alcohol-drinking habits were thus computed in every race-sex-education subgroup. The general trend, with all race-sex subgroups combined, and the results for white men are shown in figure 3. The previously described relation between drinking habits and glucose level was still present in each education subgroup.

TABLE 2

Mean serum glucose levels (age-adjusted) in relation to education in various race-sex groups

	Elementary	High, trade, or business school or college ≤2 yr.	College ≥3 yr.
White men	180	176	177
White women	185	176	179
Black men	161	157	160
Black women	161	156	157
Yellow men	184	179	185
Yellow women	185	181	186

We also cross-classified the analysis for elapsed time since last food intake, with the results for white men shown in table 4. The 2,574 white men who had taken food within four hours of the oral glucose challenge had substantially lower blood sugar levels than the majority, who obeyed instructions not to eat for at least four hours before the examination. This was ex-

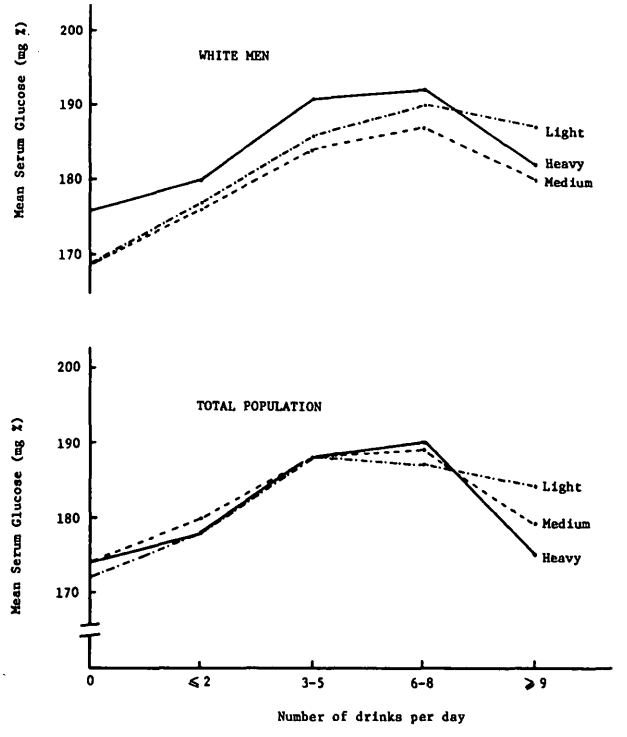

FIG. 2. Age-adjusted mean serum glucose levels by alcohol consumption and ponderal index.

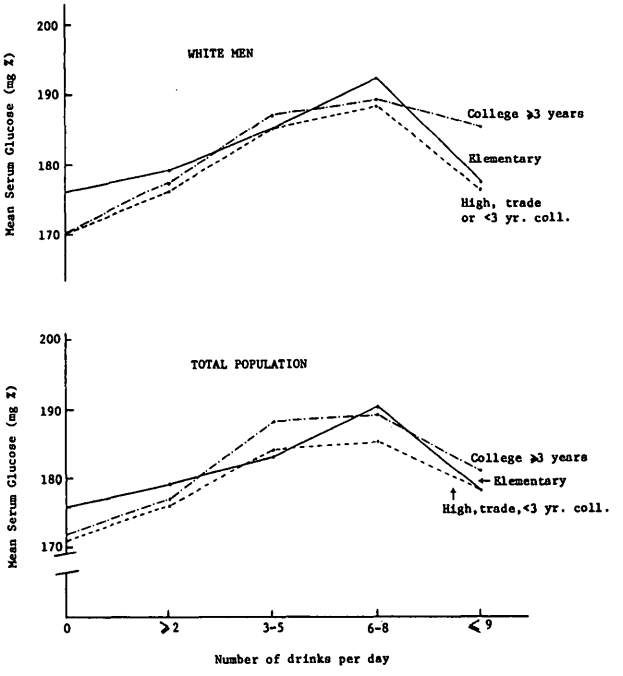

FIG. 3. Age-adjusted mean serum glucose levels by alcohol consumption and educational status.

TABLE 3

Mean serum glucose levels (age-adjusted) in relation to ponderal index in race-sex groups

	Ponderal index group		
	Light	Medium	Heavy
White men	177	176	181
White women	180	179	181
Black men	156	157	163
Black women	155	157	160
Yellow men	182	180	189
Yellow women	182	182	185

pected, representing the long-known "Staub-Traugott phenomenon" (also called the "Hamman-Hirshman effect" and "Allen's paradox"). However, the relation of blood sugar level to alcohol consumption was similar to the general trend in this subgroup. Furthermore, the proportions of white men with various alcohol habits who had taken food less than four hours before the test were similar (9.0 per cent of nondrinkers, 7.7 per cent of ≤2 per day drinkers, 7.8 per cent of 3+ per day drinkers). It thus appears probable that the various groups (categorized by usual alcohol consumption) were tested at approximately the same mean interval between the last meal and the glucose challenge. Data are not available about diet in the days preceding the test. It seems probable that substantial differences exist in usual dietary habits between nondrinkers and regular users of 3-5, 6-8, or 9+ drinks per day. We cannot assess the role of usual diet (other than alcohol) in our results.

During the study period the examinations were administered between 1200 and 2100 hours, and the glucose challenge was given shortly after the examinees began the procedure. Subclassification of white men into roughly three equal groups according to the time of glucose ingestion (table 4) showed (1) no substantial differences in mean blood sugar between the time subgroups and (2) independence of the alcohol use—mean glucose relation from this variable. There were no substantial differences in the proportions of persons in the various alcohol-consumption categories who took the examination early or late in the day. We conclude that time of day is not a significant confounding factor. It is possible that we would have found more relation of time of day to blood sugar levels if testing were begun earlier in the day. Table 4 also presents data showing mean glucose values for white men who answered either "yes" or "no" to the question about known liver disease. The 155 white men who answered "yes" do not show a consistent trend, but the mean glucose values in this small subgroup show no statistically significant differences (drinkers vs. nondrinkers). Of the 155 white men with known liver disease, 31 were nondrinkers, and 63, 20, 14, and 27 consumed ≤2, 3-5, 6-8, or 9+ drinks per day, respectively. As a possible additional indicator of prevalence of active liver disease, we present (table 5) data showing mean SGOT values in white and black men and women with various alcohol habits. The data show little difference in mean SGOT between nondrinkers and ≤2 per day drinkers. (White men and women who drink ≤2 drinks per day have slightly lower mean serum SGOT than nondrinkers.) Persons who take 3-5, 6-8, or 9+ drinks per day had, as expected, progressively higher mean serum SGOT. If, as seems plausible, this represents evidence of liver disease in some persons, such disease clearly could be a factor in the relative glucose intolerance of persons who have 3-5 and 6-8 drinks per day. But the evidence does not support a higher hypothetic

TABLE 4

Mean serum glucose levels (age-adjusted) as they relate to time since last food taken, time of day,* and known liver disease† in white men with various alcohol-intake habits

	Number of drinks per day				
	None	≤2	3-5	6-8	9+
Interval since last food					
<4 hours	147.2	150.7	158.2	174.6	157.9
>4 hours	172.7	178.7	187.8	189.9	185.3
Time of day (hr.)*					
1200 to 1500	176.0	178.9	190.3	191.8	180.4
1500 to 1800	173.0	178.8	187.5	189.8	178.7
1800 to 2100	174.2	177.8	187.8	187.2	177.4
Known liver disease†					
Yes	172.0	173.3	157.3‡	175.3‡	189.9‡
No	170.4	176.5	185.8	188.9	182.2

*Time oral glucose load administered.

†According to response to question "Has a doctor said you had liver disease?".

‡Data based on fewer than 30 persons.

TABLE 5

Mean SGOT levels (age-adjusted) in relation to alcohol consumption in white and black men and women

	Number of drinks per day				
	None	≤2	3-5	6-8	9+
White men	21.5	21.2	22.1	25.5¶	25.7§
White women	17.7	17.4†	18.9†	21.4†	23.5†
Black men	22.2	22.5	25.5‡	27.5†	27.6†
Black women	18.2	18.9*	21.6†	23.7	24.8‡

Significance level, compared with nondrinkers: *0.05 > p>0.001, †0.01 > p>0.001, ‡0.001 > p>0.0001, §0.0001 > p>0.00001, ¶ p<0.000001.

prevalence of liver disease in ≤2 per day drinkers (vs. nondrinkers). Furthermore, there is no reversal of the SGOT trend at 9+ drinks per day. It is possible that these heaviest drinkers have different types of hepatic disease from those found in 3-5 or 6-8 per day drinkers. For example, persons with chronic fibrotic disease might have less elevation of SGOT than those with active hepatocellular disease due to alcohol. Finally, a previous diagnosis of diabetes was taken into account. In the "nondiabetic" group, the previously described relation between serum glucose and alcohol consumption was unchanged. No meaningful data could be derived from the diabetic group, which was heterogeneous with regard to medication and diet and most of whom did not take the glucose challenge (only 85 white and 22 black diabetics took the glucose challenge).

Chronic pancreatitis is another condition that could be related to our findings, as prevalence of this condition is related to use of alcohol. Unfortunately, we had no information from the multiphasic examination about either a history or diagnosis of pancreatitis or exocrine pancreatic function.

DISCUSSION

Although we have not been able to find in the literature any comparable large-scale epidemiologic study, there is considerable evidence[8-14] that "alcoholic" patients diagnosed variously as having fatty liver, liver disease, or cirrhosis of the liver commonly have decreased glucose tolerance, hyperglycemia, and diabetes. To confirm these findings, experimental studies have been done with acute administration of alcohol to "alcoholic" or "nonalcoholic" subjects.[15,16] A moderate rise in blood glucose following alcohol ingestion and a higher-than-normal response to glucose challenge was documented.

It has been speculated that the relation described was possibly due to a direct effect of alcohol on the hepatic glycogenolysis as well as on peripheral utilization of glucose and/or as an indirect effect of alcohol and its metabolites, especially acetaldehyde[17,18] on stimulation of the sympathetic nervous system.[19,20] Modification in insulin response can also account for decreased glucose tolerance in such patients, either if chronic pancreatitis occurs or if resistance to insulin develops.[11,12,21,22]

However, this apparent positive relation between blood glucose level and alcohol consumption in "alcoholics" has not been confirmed by two recent experiments[23,24] and one community study[25] in which a relation between serum glucose levels and moderate alcohol intake was examined. In both experiments, a group of "nonalcoholic" persons were given moderate amounts of alcohol for several days. Neither their fasting glucose level nor their glucose tolerance appeared to be affected. The community study (much closer to ours in its design) recorded alcohol-drinking habits in a sample of 202 healthy men in Tecumseh, Mich. Fasting blood glucose and glucose tolerance tests were then performed. No clear relation of these variables to alcohol-drinking habits was documented. The apparent differences between these findings and ours are not easy to explain. Possible reasons might include different methods of selection of the study population, a much smaller sample size, the requirement of a fasting state for all subjects in Tecumseh, or differences in definition of drinking categories between the two studies.

A number of good reviews[15,26-31] have been published recently that deal with the general area of metabolic effects of ethyl alcohol. Our data, which relate to habitual use of alcohol, are in agreement with those of others who have noted that alcohol consumption results in an increased serum glucose level in response to a glucose challenge. These data also demonstrate a positive relation between the amount of alcohol usually consumed and the mean response to an oral glucose tolerance test. However, this relation did not persist in the highest-alcohol-consumption group of our study population. In that group the mean response to the oral load of glucose decreased to below that of the preceding group. The meaning of this apparent paradox, however, is unclear. This group (9+ drinks a day) might differ from the other groups in a number of ways not explored in our study, such as duration of alcohol drinking, type of alcohol used, diet, prevalence of specific types of liver disease, or other illness. Thus, we plan studies in the future to attempt to determine the role that liver disease and other pertinent health characteristics might play in the relationship of alcohol consumption to serum glucose level.

ACKNOWLEDGMENTS

This study was supported by a grant from the United States Brewers Association and by the Kaiser Foundation Research Institute. Dr. Gérard expresses her gratitude to Drs. Prosper Loustalot and Claude Laplanche of Ciba-Geigy, who made possible her visit to the United States for further training in epidemiology. She is also grateful to Dr. Loring Dales for assis-

tance in English composition. Betsy Zavela did the computer programing, and Agnes Lewis, May Kuwatani, Patricia Crump, and Della Mundy provided technical assistance.

REFERENCES

[1]Collen, M. F., and Davis, L. F.: The multitest laboratory in health care. J. Occup. Med. *11*:355-60, 1969.

[2]Cahalan, D., Cisin, I. H., and Crossley, H. M.: American drinking practices: A national study of drinking behavior and attitudes. New Haven, College and University Press, 1969.

[3]United States Department of Health, Education and Welfare: Alcohol and health. New knowledge. Second special report to the United States Congress. (DHEW Pub. ADM 74-124) Washington, GPO, 1974.

[4]DeLint, J., and Schmidt, W.: The epidemiology of alcoholism. *In* Biological Basis of Alcoholism, chap. XV. Isral, Y., and Mardones, J., Eds. New York, Wiley Interscience, 1971, pp. 423-41.

[5]Dales, L. G., Siegelaub, A. B., Feldman, R., Friedman, G. D., Seltzer, C. G., and Collen, M. F.: Racial differences in serum and urine glucose after glucose challenge. Diabetes *23*:327-32, 1974.

[6]Klatsky, A. L., Friedman, G. D., Siegelaub, A. B., and Gérard, M. J.: Alcohol consumption among white, black and yellow men and women: Kaiser Permanente multiphasic health examination data. Am. J. Epidemiol. Accepted for publication, 1977.

[7]Danowsky, T. S.: Diabetes Mellitus, With Special Emphasis on Children and Young Adults. Baltimore, Williams and Wilkins, 1957, p. 145.

[8]Voegtlin, W. L., O'Hollaren, P., and O'Hollaren, N.: The glucose tolerance of alcohol addicts—a study of 303 cases. Q. J. Stud. Alcohol *4*:163-82, 1943.

[9]Leevy, C. M., Fineberg, J. C., and White, T. J.: Hyperglycemia and glucosuria in the chronic alcoholic with hepatic insufficiency. Am. J. Med. Sci. *223*:88-95, 1952.

[10]Leevy, C. M.: A study of 270 patients with biopsy proven fatty liver and a review of the literature. Medicine (Baltimore) *41*:249-76, 1962.

[11]Samaan, N. A., Stone, D. B., and Eckhardt, R. D.: Serum glucose, insulin, growth hormone in chronic hepatic cirrhosis. Arch. Intern. Med. *124*:149-52, 1969.

[12]Samols, E., and Holdsworth, D.: Disturbances in carbohydrate metabolism; liver disease. *In* Carbohydrate Metabolism and Its Disorders, vol. 2. Dickens, F., Randle, P. J., and Whelan, W. J., Eds. New York, Academic Press, 1968, pp. 289-336.

[13]Collins, J. R., and Crofford, O. B.: Glucose intolerance and insulin resistance in patients with liver disease. Arch. Intern. Med. *124*:142-48, 1969.

[14]Megyesi, C., Samols, E., and Marks, V.: Glucose tolerance and diabetes in chronic liver disease. Lancet *2*:1051-56, 1967.

[15]Arky, R. A.: The effect of alcohol on carbohydrate metabolism: carbohydrate metabolism in alcoholics. *In* The Biology of Alcoholism, Vol. I: Biochemistry. Kissin, B., and Begleiter, H., Eds. New York, Plenum Press, 1971, pp. 197-228.

[16]Dornhorst, A., and Ouyang, A.: Effect of alcohol on glucose tolerance. Lancet *2*:957-59, 1971.

[17]Truit, E. B., and Duritz, G.: The role of acetaldehyde in the actions of ethanol. *In* Biochemical Factors in Alcoholism. Maickel, R. P., Ed. New York, Pergamon Press, 1967, pp. 61-69.

[18]Kohei, H: Effects of acetaldehyde on carbohydrate metabolism—studies on the mechanism of acetaldehyde induced hyperglycemia. Med. J. Shinshu Univ. *12*:1-9, 11-15, 1967.

[19]Lieber, C. S.: Metabolic effects produced by alcohol in the liver and other tissues. Adv. Intern. Med. *14*:151-99, 1968.

[20]Perman, E. S.: The effect of ethyl alcohol on the secretion from the adrenal medulla in man. Acta Physiol. Scand. *44*:241-47, 1958.

[21]Metz, R., Berger, S., and Mako, M.: Potentiation of the plasma insulin response to glucose by prior administration of alcohol. Diabetes *18*:517-22, 1969.

[22]Danowski, T. S., Gillespie, H. K., Fergus, E. B., et al.: Significance of blood sugar and serum electrolyte changes in cirrhosis following glucose, insulin, glucagon, or epinephrine. Yale J. Biol. Med. *29*:361-75, 1956.

[23]Carey, M. A., Jones, J. D., and Gastineau, C. F.: Effects of moderate alcohol intake on blood chemistry values. J.A.M.A. *216*:1766-69, 1971.

[24]Ginsberg, H., Olefsky, J., Farquhar, J., and Reaven, G.: Moderate ethanol ingestion and glucose triglyceride levels. Ann. Intern. Med. *80*:143-49, 1974.

[25]Ostrander, L., Lamphiear, D., Block, W., Johnson, B., Ravenscroft, C., and Epstein, F.: Relationship of serum lipid concentrations to alcohol consumption. Arch. Intern. Med. *134*:451-56, 1974.

[26]Salaspuro, M. P.: Influence of ethanol on the metabolism of the pathological liver. *In* Biological Basis of Alcoholism. Mardones, Israel, Ed. New York, Wiley Interscience, 1971, pp. 163-82.

[27]Becker, C. E., Roe, R. L., and Scott, R. A.: Alcohol as a Drug. Curriculum on Pharmacology, Neurology, Toxicology. New York, Medcom Press, 1974.

[28]Kissin, B., and Begleiter, H.: The Biology of Alcoholism. Vol. 1: Biochemistry. New York, Plenum Press, 1971.

[29]Kissin, B., and Begleiter, H.: The Biology of Alcoholism. Vol. 3: Clinical Pathology. New York, Plenum Press, 1974, pp. 53-107.

[30]Lundquist, F.: Metabolic consequences of ethanol metabolism. *In* Biological Basis of Alcoholism. Mardones, Israel, Ed. New York, Wiley-Interscience, 1971, pp. 32-38.

[31]Wallgren, H., and Barry, H.: Actions of Alcohol. Vol. 1: Biochemical, Physiological, Psychological Aspects. New York, Elsevier, 1970, pp. 104-53.