

Lay Supplement No. 9

FACTS ON  
CIRRHOSIS OF THE LIVER  
AND OTHER LIVER  
DAMAGE IN CHRONIC  
ALCOHOLISM

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1. The Problems of Alcohol
2. The Nature of Alcoholic Beverages and the Extent of their Use
3. Alcohol and Industrial Efficiency
4. Facts on Delirium Tremens
5. Alcohol, Heredity and Germ Damage
6. Alcohol and Length of Life
7. What Happens to Alcohol in the Body
8. Alcoholic Beverages as a Food and their Relation to Nutrition
9. Facts on Cirrhosis of the Liver
10. The Drinker and the Drunkard
11. How Alcohol Affects Psychological Behavior
12. The Rehabilitation of Inebriates

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## FACTS ON CIRRHOSIS OF THE LIVER AND OTHER LIVER DAMAGE IN CHRONIC ALCOHOLISM

THE liver is one of the vital organs of the body; it is indispensable to life. The liver carries out a great many important functions which are concerned particularly with the utilization of food. In ancient times, the functions of the liver were not well known, but even then it was considered to be one of the most important organs of the body and one whose disturbances were frequent causes of ill health. Most indigestion was called "biliousness" on the presumption that the fault lay in the liver and disturbances in the nature of the bile were supposed to be the cause of a great variety of maladies ranging from a bad disposition to cancer and insanity.

Without such views it was not surprising that the ill effects of excessive use of alcohol—the hang-over—were often attributed to injury of the liver. There is mention of this in the documents of early Greek medicine; and in the sixteenth century, Vesalius, the father of modern anatomy, definitely taught that excessive drinking was the cause of many liver troubles. Later, when the disturbance known as cirrhosis of the liver was described, it was this disease which became specifically associated with alcohol. Both the doctor and the public came to believe that the almost inevitable consequence of excessive use of alcohol was cirrhosis of the liver and that, in turn, the occurrence of cirrhosis almost invariably indicated the excessive use of alcohol. Cirrhosis was the "alcohol disease."

In recent years, physicians have changed their views as to the certainty of these relations, but the popular view has not changed. Some vague rumors have reached lay publications to the effect that "alcohol has nothing to do with cirrhosis." But this is going even further than the physician. The situation in regard to alcohol and cirrhosis, as he sees it today, is this: Cirrhosis is not a common disease. It is not limited to those who use alcohol but occurs in

those who use none. It does occur more commonly, however, in those who use alcohol to excess.

Cirrhosis of the liver is present in perhaps 1 per cent of the general population and is the cause of death in about 9 per 100,000 of the total population. Nine per 100,000 is only nine thousandths of 1 per cent. In individuals whose health has been injured by long continued excessive use of alcohol—chronic alcoholics\*—the occurrence of cirrhosis of the liver and cirrhosis as a cause of death are greater than in the general population. But even among chronic alcoholics they are below any figures which could justify calling cirrhosis a common disease. About 8 per cent of chronic alcoholics develop cirrhosis of the liver (as compared to 1 per cent for the general population) and the death rate from cirrhosis among chronic alcoholics is about 650 per 100,000 or 0.65 per cent (as compared to 9 per 100,000 and 0.009 per cent in the general population. The fact that cirrhosis of the liver occurs more commonly among chronic alcoholics than among the general population indicates that there is an association between inebriety and cirrhosis of the liver, but it does not show that alcohol itself is the direct cause of the cirrhosis.

## THE LIVER

THE liver is situated in the upper right side of the abdomen. It is dark red in color—"liver colored"—and normally weighs 3 to 4 pounds. It is composed of a great number of microscopically small cells which carry out the functions of the liver. The cells are supported by connective tissue (such as tendons are composed of) and between the masses of cells there run blood vessels and bile ducts. The latter carry away the bile that is formed by the liver cells. This bile is collected in a small sac, the gall bladder, located beneath the liver and is emptied into the intestine when needed to assist in the digestion of fats.

The flow of blood reaching the liver is particularly important to its many functions. All of the blood flowing about the stomach and intestines, and carrying from them all substances which are absorbed, passes through the liver before it flows to the heart.

\*For definition, see Supplement No. 1.

The liver thus has the opportunity of dealing with any absorbed substance before it has reached the rest of the body. The liver is the great "chemical clearinghouse of the body." It converts the excess sugar coming from the intestines after meals into an animal starch known as glycogen and reconverts this into sugar as the needs arise. The liver renders harmless many poisonous substances formed in the body or absorbed from the intestines. It assists in the formation of the red coloring matter of the blood. And it plays an important, but as yet not fully understood, part in the utilization and storage of vitamins.

Although there are listed here only some of the main functions of the liver, it is clear from these few why it is indispensable to life and why disturbance of its functions may cause profound ill health. One function is particularly significant to chronic alcoholism—the utilization of vitamins. In recent years considerable support has been given to the belief that much of the ill health in chronic alcoholism is due to disturbances both in the supply and utilization of vitamins.

And there is an additional function of the liver which ties it in even closer with the use of alcohol. It has been shown that alcohol is oxidized in the liver—a feature discussed in Supplement 7, "What Happens to Alcohol in the Body."

## THE IMMEDIATE EFFECTS OF ALCOHOL ON THE LIVER

MODERATE drinking, even when long continued, has no effect upon the liver that can be observed by any tests. When, however, very large amounts of alcohol are drunk in a short time (say a pint of whisky within a few minutes) and there is severe drunkenness, some of the functions of the liver may be temporarily disturbed. The flow of bile may be increased and there may be a change in its color; the stored glycogen may be converted into sugar; and there may be some interference with the formation of the waste products from the utilization of protein. These facts, however, do not mean that the flesh of the liver has been injured. The liver may appear inflamed and swollen; the inflammation and swelling subside when sobriety returns. The swelling and the

inflammation are the only changes found in the livers of men who have died from acute intoxication.

In chronic alcoholism resulting from the prolonged drinking of excessive quantities of strong alcoholic beverages, some permanent damage to the liver may develop. The most common damage is not cirrhosis, but is so-called "fatty liver." It is estimated that the condition exists in some 75 per cent of habitual inebriates. Fat is deposited within the cells of the liver. This change in the liver is not caused by the direct action of alcohol on the liver; it results from the more fundamental disturbance in nutrition caused by excessive amounts of alcohol.

### CIRRHOSIS OF THE LIVER

THE word "cirrhosis" is from the Greek meaning "tawny yellow"; but the yellow fatty liver discussed above is not cirrhosis. What occurs in the condition which is now known as cirrhosis is an increase in the supporting connective or fibrous tissue at the expense of the liver cells. These fibrous changes crowd and finally destroy the cells essential to the functions of the liver.

There are many different types of cirrhosis of the liver. Usually the liver shrinks in size and becomes hard. Sometimes, however, it becomes enlarged. And, in one type, small lumps appear on the surface and give the name "hobnail liver."

One grave consequence of the fibrous changes in cirrhosis of the liver is the obstruction of the bile ducts and especially the blood vessels. When the latter are partially shut off, the blood is dammed back throughout the entire digestive tract. As a result, digestion is disturbed and fluid seeps from the blood vessels into the abdomen, causing dropsy. Interference with the liver functions also leads to anemia and to profound disturbances of nutrition.

Fatty liver is much more common in chronic alcoholism than is cirrhosis, but the latter is a much more serious condition and has therefore attracted more attention. When cirrhosis of the liver was first described, fatty liver was not strictly distinguished from it. In fact, the discovery of the changes in the liver made such a great impression on physicians that, for a time, most diseases of the liver were labelled as cirrhosis. Furthermore, the

belief that the sole cause of cirrhosis was excessive use of alcoholic beverages became so deeply rooted in medical opinion that, when doubts arose about it, a violent debate ensued. This debate continued as long as the question remained undecided.

Certain facts first became clear to refute older views. It was supposed that the organs, especially the liver, of the chronic alcoholic were continually bathed in alcohol. From the fact that strong alcoholic beverages cause a burning sensation in the throat when swallowed it has often been assumed that alcohol burns up and destroys internal tissues. Under this assumption, cirrhosis of the liver was easy to understand; the alcohol scarred and corroded the liver. In reality, the alcohol is diluted in the stomach and intestines before it is absorbed and in the blood after it is absorbed.\* The concentration of alcohol reaching the liver is too low to cause even slight harm by any direct action.

At first, cirrhosis of the liver was attributed solely to alcohol. But finally, first an occasional description and then many descriptions of cirrhosis in men and women who used no alcohol appeared in the medical literature. It was found to occur in small children and in the inhabitants of countries where the consumption of alcohol, for religious reasons, was small. These facts shook the belief in alcohol as the exclusive cause of cirrhosis of the liver.

Experiments were then carried out on animals to see whether cirrhosis of the liver could be produced by the administration of alcohol. It could not. Practically every medical discussion of cirrhosis of the liver now mentions in its introduction that no one has succeeded in producing this condition experimentally. To some students this seemed to be definite proof that cirrhosis of the liver had nothing to do with drinking. These experiments, however, prove only that the direct contact of the liver with alcohol does not bring about cirrhosis. There still remains the possibility of an indirect causation through disturbances in the general nutrition of the excessive drinker.

Numerous theories have been advanced as to how nutritional disturbances of chronic alcoholism could lead to cirrhosis of the

\*See Supplement No. 7, "What Happens to Alcohol in the Body."

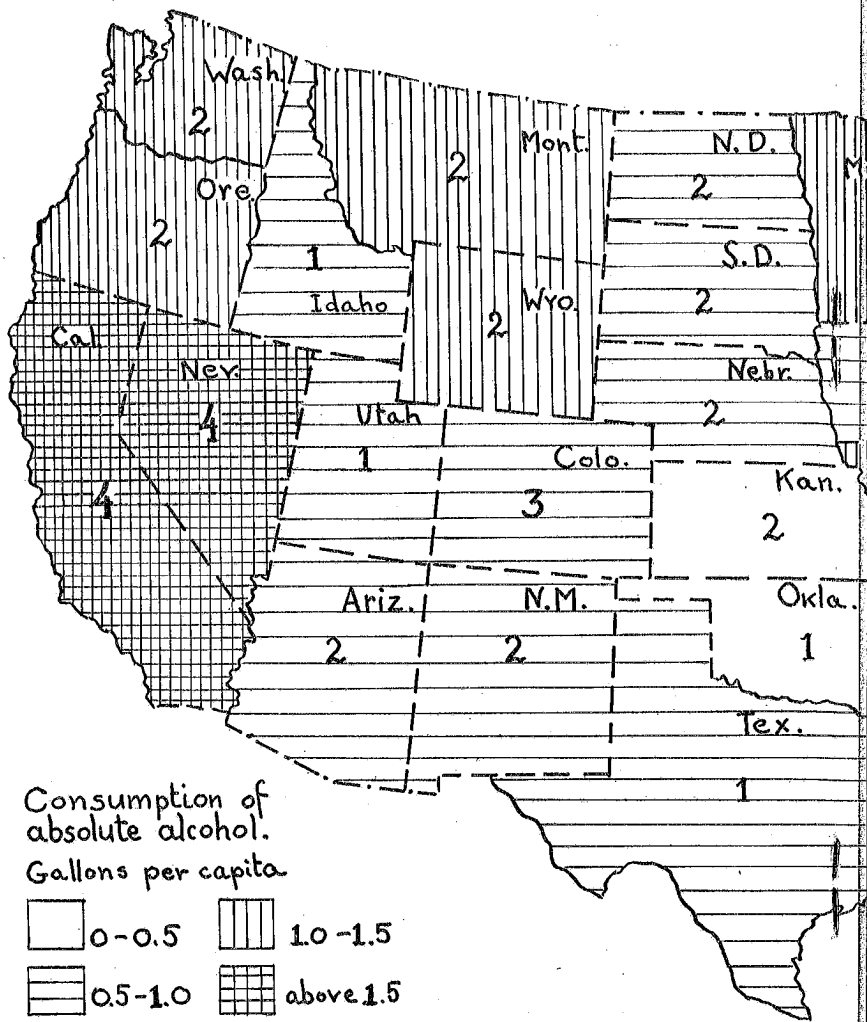
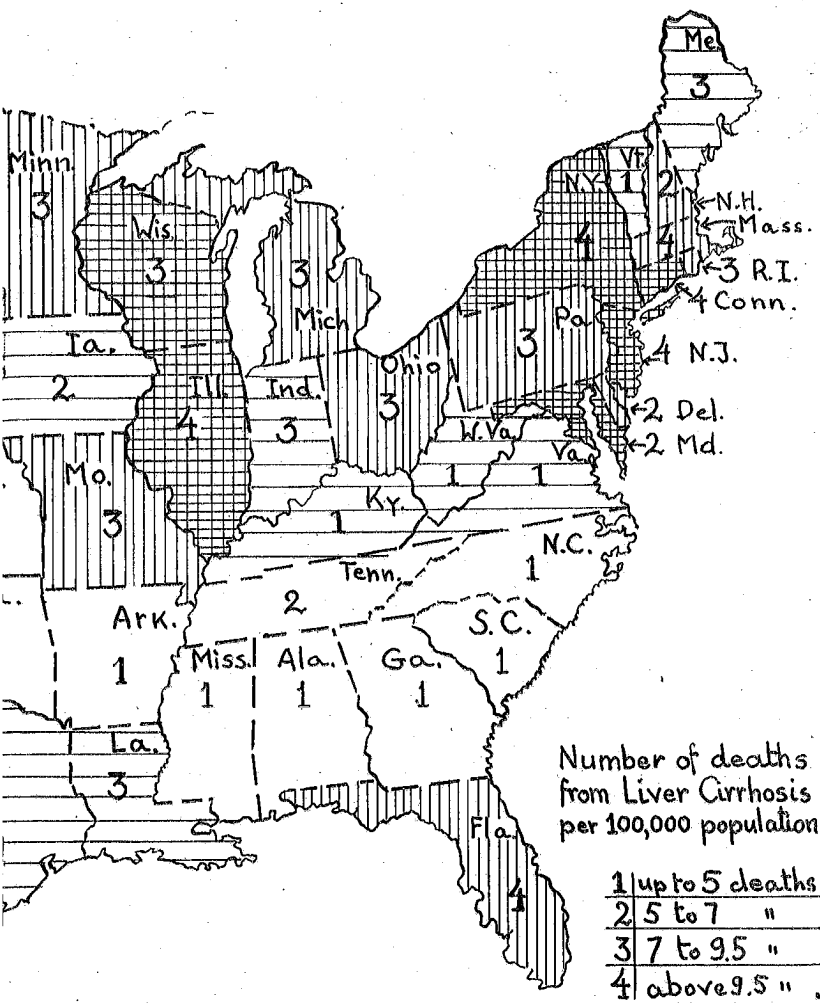


Figure 1. The Distribution of Per Capita Consumption Rates by States in the United





es of Alcohol and Death Rates from Cirrhosis of the Liver,  
 ed States, 1940 Data.

liver. One of the most widely held is that the poor food habits of the inebriate play the important part. Vitamin deficiency has been suspected as contributing to cirrhosis and also some poisonous substances of undetermined origin formed in the body or even present in the alcoholic beverages. Cirrhosis of the liver has been induced in animals with certain poisons, such as phosphorus, but no similar poisons have been found in alcoholic beverages.

### HOW CIRRHOSIS OF THE LIVER IS PRODUCED

WE have already mentioned the condition of fatty liver and have said that it occurred frequently in chronic alcoholics. For a long time it had been denied that the fatty liver could develop into a cirrhotic liver. In the past few years, however, opinion on this matter has greatly changed; one of America's foremost authorities on cirrhosis of the liver has demonstrated, by careful experimental work, that a transition from a fatty liver to cirrhosis of the liver is not only possible but actually occurs. The frequency of fatty liver in chronic alcoholics is therefore a predisposing factor for the development of cirrhosis. Since fatty liver occurs in about 75 per cent of excessive drinkers, and cirrhosis of the liver in only about 8 per cent, there must be some other special factor which causes the transition from fatty liver to cirrhosis. This factor is probably a nutritional one, but it has not yet been determined.

### STATISTICAL FACTS

THE controversies over the causes of cirrhosis of the liver have led to the accumulation of many statistics—some good and some bad. When the statistics are handled critically, they yield important information. But in this critical handling, more than the mere figures must be taken into consideration—the way in which they were obtained, the kind of material from which they originated and the logic with which they are organized. The most reliable information is derived from autopsies of chronic alcoholics and nonalcoholic men and women.

Mortality statistics in different occupations have been frequently used but must be viewed with great caution. The mortality rates for cirrhosis of the liver in the general population may be utilized to some advantage, but these statistics do not permit

us to distinguish between nonalcoholics and chronic alcoholics who died from cirrhosis of the liver. Those who use statistics from nations of the Mohammedan religion are also on insecure ground since the nonuse of alcohol is only assumed and particularly since the cirrhosis found in Oriental countries is largely of an entirely different variety from that of Europe and America, being mainly due to parasites of the liver.

But not alone must the source of information be considered. The terms in which the statistics are presented are also important. Unfortunately the usual method in the literature is to state the number of cases of cirrhosis of the liver found at autopsy and to say that a certain percentage of these occurred respectively in individuals who were chronic alcoholics and in nonalcoholics. This is an entirely meaningless procedure. If the findings are taken from a hospital where a large number of alcoholics are admitted, a large percentage of the cirrhosis will be found in the chronic alcoholics. If, however, they are from a hospital in which alcoholic patients are received only occasionally, the percentage figures will be reversed. There is only one direct way to determine statistically the association or nonassociation between chronic alcoholism and cirrhosis of the liver, and that is to state what percentage of the alcoholic patients and also what percentage of the nonalcoholic patients autopsied had cirrhosis of the liver. We shall now examine some relevant statistics of the latter type. These are given in Table I.

TABLE I

*The Occurrence of Cirrhosis of the Liver at Death among  
Chronic Alcoholics and Temperate Drinkers and Abstainers  
(Combined Autopsy Records of Many Hospitals)*

	<i>Chronic Alcoholics</i>		<i>Temperate Drinkers and Abstainers</i>	
	<i>Number</i>	<i>Per Cent</i>	<i>Number</i>	<i>Per Cent</i>
Cirrhosis of the liver present	177	8.7	1,046	1.0
Cirrhosis of the liver absent	1,868	91.3	103,266	99.0
Totals	2,045	100.0	104,312	100.0

These autopsy statistics are rather consistent. On the whole it may be stated that cirrhosis of the liver occurs in about 8 to 9 per cent of chronic alcoholics autopsied. This may be compared with 1 per cent found in the autopsies of more than 100,000 nonalcoholic patients.

The fact that there is only 8 to 9 per cent—the figure usually quoted is actually about 5 per cent—of cirrhosis of the liver in alcoholics has been misinterpreted and has led to the suggestion that it is not related to chronic alcoholism. But inasmuch as it occurs so much more frequently in excessive drinkers than in the general population, the association between excessive drinking and cirrhosis of the liver cannot be disregarded. The majority of investigators hold the opinion, at present, that while alcohol, by itself, does not cause cirrhosis of the liver, the habit of excessive indulgence in alcoholic beverages does bring about conditions which favor the development of this disease.

#### DEATH FROM CIRRHOSIS OF THE LIVER

THE fact that the cirrheses of the liver cited in the above statistics were found at autopsy does not imply that all the autopsied patients had died from this disease. As a matter of fact, only a small number had died from cirrhosis of the liver. For instance, according to a report of 217 autopsied patients, all of whom had cirrhosis of the liver, 33 per cent had died from pneumonia, 20 per cent from gastrointestinal diseases, 39 per cent from various other diseases and only 8 per cent from cirrhosis of the liver. Since about 8 per cent of chronic alcoholics develop cirrhosis of the liver and since, of these, about 8 per cent die of cirrhosis, it can be computed that some 0.65 per cent of all chronic alcoholics die of cirrhosis.

That cirrhosis of the liver is not a common cause of death can be seen from recent mortality statistics of the United States. In the last few years, from 8 to 9 deaths in each 100,000 of the population of the United States have been reported as due to cirrhosis of the liver. In the more familiar terms of percentages, this means that 0.008 to 0.009 per cent of the population of the United States die annually from this cause. Of late, cirrhosis of

the liver has represented about 0.75 per cent of all deaths in the United States.

In the statistics of death from cirrhosis of the liver, further support is found for the theory of an association between inebriety and cirrhosis. In Figure 1 we present a map of the United States in which each state is marked according to the death rate from cirrhosis of the liver and the per capita consumption of alcohol in the year 1940. The shading of the states denotes, as the legends of Figure 1 indicate, whether the per capita consumption of absolute alcohol from all beverages combined amounted to  $\frac{1}{2}$ ;  $\frac{1}{2}$  to 1; 1 to  $1\frac{1}{2}$ ; or over  $1\frac{1}{2}$  gallons during the year. The numbers given to the various states denote whether the death rate per hundred thousand of the state's population during the year was (a) up to 5; (b) 5 to 7; (c) 7 to  $9\frac{1}{2}$ ; or (d) above  $9\frac{1}{2}$ . It will be seen that, generally, the numbers are distributed in relation to the amount of alcohol drunk. There are, naturally, exceptions, but the majority fall within this relationship. From this it is evident that where higher consumption of alcohol exists, people are more likely to die from cirrhosis of the liver. Great caution must be exercised in interpreting death rates of cirrhosis as indicating inebriety, especially in the case of those states having small populations. For, on the whole, cirrhosis of the liver belongs among the less frequent causes of death and thus very small changes in actual numbers can bring about great swings in the percentage of occurrence. This fact may be illustrated as follows.

Let us assume that in State A, which has 100,000 inhabitants, 3 deaths from cirrhosis of the liver have occurred up to December 1935. It would make a difference of 33.3 per cent in the death rate from cirrhosis of that year if a fourth person were to die on December 31, 1935 instead of on January 1, 1936. If, now, in State B, having 12,000,000 inhabitants, that is, 120 units of 100,000 each, there is also a death rate from cirrhosis of 3 per hundred thousand, only the death of 120 additional people could increase this rate by 33.3 per cent. In a broad meaning of the word, it is pure chance if this 1 man in State A dies on December 31 instead of on January 1. On the other hand, the coincidence of 120 inhabitants of State B dying of that disease on December 31 instead of any time during the following year is

something that could not be brought about by chance. This imaginary example has been presented to indicate that mere chance happenings may bring about extraordinary fluctuations in the death rate from a fairly rare cause of death when a small population is involved. From such fluctuations, wholly erroneous conclusions as to the increase or decrease in inebriety can, and have, been made.

In Table 2 we present death rates from cirrhosis of the liver per hundred thousand population of the two most populous and the two least populous states of the Union for the years 1934, 1935 and 1936.

TABLE 2  
*Death Rates from Cirrhosis of the Liver in the Two Most Populous and the Two Least Populous States of the Union during the Years 1934, 1935 and 1936*

<i>State and Population</i>	<i>Deaths from Cirrhosis of the Liver per 100,000 Population</i>				
	<i>1934</i>	<i>1935</i>	<i>Percentage Change 1934-1935</i>	<i>1936</i>	<i>Percentage Change 1935-1936</i>
New York 13,479,142	10.2	10.6	+3.9	10.4	-1.9
Pennsylvania 9,900,180	8.9	8.7	-2.2	8.8	+1.1
Wyoming 250,742	4.3	9.9	+137.2	6.9	-30.3
Nevada 110,247	14.3	11.1	-22.4	17.0	+53.6

This table gives evidence that, in small populations, most anything may happen to rates from fairly rare causes of death. Nevertheless, when such enormous but haphazard changes occur in a small state, many people are tempted to use these changes as "proofs" of one theory or another.

And still another fact must be borne in mind; most individuals with cirrhosis of the liver are not excessive users of alcohol.

Cirrhosis is more common in chronic alcoholics but there is a far greater number of nonalcoholics in the population. Thus the greater tendency for alcoholics to develop cirrhosis is far more than compensated by the greater number of nonalcoholics.

#### SELECTED READING

1. Connor, C. L. *Cirrhosis of the liver*. Quarterly Journal of Studies on Alcohol, Vol. 1, pp. 95-103, 1940.
2. Haggard, H. W. and Jellinek, E. M. *Alcohol Explored*. New York, Doubleday, Doran & Co., 1942.
3. Jolliffe, N. and Jellinek, E. M. *Cirrhosis of the liver*. In: *Effects of Alcohol on the Individual*, Vol. I, *Alcohol Addiction and Chronic Alcoholism* (Jellinek, E. M., ed.). New Haven. Yale University Press, 1942.
4. Moon, V. H. *Experimental cirrhosis in relation to human cirrhosis*. Archives of Pathology, Vol. 18, pp. 381-424, 1934.
5. Klatskin, G. and Yesner, R. *Factors in the treatment of Laennec's cirrhosis*. Journal of Clinical Investigation, Vol. 28, pp. 723-735, 1949.
6. Post, J. and Rose, J. V. *Clinical, functional and histologic studies in Laennec's cirrhosis of the liver*. American Journal of Medicine, Vol. 8, pp. 300-313, 1950.
7. *Alcohol, Science and Society. Twenty-nine Lectures with Discussions as Given at the Yale Summer School of Alcohol Studies*. New Haven. Quarterly Journal of Studies on Alcohol, 1945.