

## THE EFFECT OF DIET ON THE SEVERITY OF LIVER DAMAGE IN ACUTE ALCOHOLIC HEPATITIS\*

By W. P. Fung, K. K. Tan and C. Y. Tye

### SYNOPSIS

The effect of diet on the severity of liver damage was assessed in 50 cases of acute alcoholic hepatitis. Comparison of the liver function tests of 35 patients on a poor diet with 15 patients taking a fair diet, showed no significant difference. Comparison of the liver histology of these 2 dietary groups showed no significant difference in triaditis, liver cell necrosis, Mallory bodies, fatty change and bile stasis. The patients on a poor diet, however, had significantly more severe periportal fibrosis and cirrhosis than those on a fair diet.

### INTRODUCTION

In the past dietary deficiency was thought to be the cause of liver damage in alcoholics (Mallory, 1960; Best *et al*, 1935; Best *et al*, 1949; Himsworth, 1950; Gyorgy and Goldblatt, 1939; Klat-skin *et al*, 1954). Alcohol has now been shown to have a direct effect on the liver cell, causing hepatic damage even when the diet was adequate (Lieber *et al*, 1965; Lieber, 1965). Of the patients in the present series, some had a poor diet, while others had a fair or adequate diet. This study is an attempt to determine what effect the diet had over the severity of the liver disease, in these 50 cases of acute alcoholic hepatitis.

### METHOD

A prospective clinicopathological study of acute alcoholic hepatitis in Singapore was initiated in 1966. In a 3-year period, 50 cases of acute alcoholic hepatitis were found. The diagnosis was confirmed by liver histology in every case. The

clinical, hematological, biochemical, and histological features of these 50 cases have been reported (Fung, 1972).

A dietary history was obtained from each patient and the diet was graded fair or poor. The staple diet in the population in Singapore is rice, and 92% of cases, in the present study, took rice daily. In addition, the patients may take vegetables, meat and fish. A diet was assessed as "fair" if the patient took meat or fish daily in addition to the staple diet of rice. A diet was considered "poor" if the patient did not take meat or fish at all, or only once or twice a week, in addition to rice. Vegetables were taken by every case, and was not used as a criterion for differentiating between "fair" or "poor" diet. The intake of protein in the form of meat or fish was thus used as the main criterion in differentiating between "fair" and "poor" diet. The majority (35 cases) was found to be taking a "poor" diet, while the remaining 15 cases were considered to be on a "fair" diet. The liver function tests and the hepatic histological changes of these 2 groups were compared, to determine if the type of diet had any effect on the severity of liver damage. In the liver function tests, the most abnormal value of serial readings, in each case, was used. The mean of these was used for comparison by statistical analysis using the standard *t*-Test. In the liver histology, each change was graded in severity from 0 (absent) to 1 (mild), 2 (moderate) and 3 (severe). The means of these were analysed for any significant difference.

### RESULT

The results of the statistical comparison between the group on a poor diet (35 cases) and the group on a fair diet (15 cases) are shown in Table I.

\*This paper incorporates part of a dissertation submitted by the author (W. P. FUNG) for the M.D. (University of Singapore).

Requests for Reprints should be addressed to:

Dr. W. P. FUNG, Department of Medicine (Medical Unit II), University of Singapore, Singapore 3.

Department of Medicine (Medical Unit II), Faculty of Medicine, University of Singapore.

W. P. FUNG, M.D., F.R.A.C.P., Senior Lecturer and Consultant Physician.

Outram Road General Hospital, Singapore.

K. K. TAN, M.B., D.C.P., M.R.C.Path., M.C.P.A., F.C.A.P., Former Senior Pathologist.

Department of Social Medicine and Public Health, University of Singapore.

C. Y. TYE, B.A., Senior Lecturer (Statistics).

TABLE I

Statistical comparison between patients with acute alcoholic hepatitis taking a poor diet (35 cases) and those taking a fair diet (15 cases). In the liver function tests, the mean values were taken from the most abnormal value of serial readings, in every case. In the liver histology, each change was graded as follows:

0 = absent, 1 = mild, 2 = moderate, and 3 = severe. NS = no significant difference.

Liver Function Test	Mean		P
	Poor Diet	Fair Diet	
S. Bilirubin	7.21	6.45	NS
S. Alkaline Phosphatase	17.14	14.73	NS
S. Albumin	2.94	3.37	NS
S. Globulin	4.01	3.83	NS
S.G.P.T.	293.40	282.10	NS
Liver Histology*			
Triaditis	1.94	1.80	NS
Necrosis	1.97	1.87	NS
Mallory Body	0.46	0.47	NS
Fat	2.17	2.20	NS
Bile Stasis	0.77	0.60	NS
Peri-Portal Fibrosis	2.20	1.47	<0.01
Cirrhosis	1.51	0.80	<0.05

Comparison of the liver function tests of patients with acute alcoholic hepatitis and taking a poor diet with that of patients taking a fair diet, showed no significant difference between the 2 groups. Comparison of the liver histology of the 2 groups showed no significant difference in triaditis, liver cell necrosis, Mallory body, fatty change and bile stasis. The patients on a poor diet, however, had significantly more severe periportal fibrosis ( $p < 0.05$ ) and cirrhosis ( $p < 0.05$ ) than those on a fair diet.

## DISCUSSION

The role of the diet in the pathogenesis of alcoholic fatty liver has been a subject of debate for a long time. In 1960, Mallory thought that the fatty liver of alcoholics was related to dietary insufficiency and to the lack of lipotropic substances in their diet (Mallory, 1960). This view was supported by the work of Best *et al* (1935, 1949); Himsworth (1950); Gyorgy *et al* (1939) and Klat-skin *et al* (1954). It is malnutrition and not anutrition that causes fatty liver, since starvation does not result in fatty liver (Galambos, 1969). It has been shown, in the rat, that dietary choline deficiency induces centrilobular fatty change, while

dietary deficiency of amino acid induces periportal fatty change, which is not correctable by choline (Shils and Stewart, 1954). Protein malnutrition with high carbohydrate intake leads to fatty liver (kwashiokor), which responds to dietary protein and does not lead to nutritional cirrhosis (Waterlow and Bras, 1957). It was thought that alcohol induces fatty liver only with concomitant dietary protein deficiency, and further, that a high protein diet or choline may protect the liver (Galambos, 1969). Recent evidence (Lieber *et al*, 1965) has disproved this concept. Furthermore, it has been shown that intake of about a pint of whisky daily for 3 days or more may be expected to induce fatty change in the liver in spite of a good diet (Lieber and Rubin, 1968; Rubin and Lieber, 1968). The results of the present study agree with these recent findings, since no significant difference was found between cases on a poor diet and those on a fair diet, in both the liver function tests and in the acute histological changes of triaditis, liver cell necrosis, Mallory body, fat, and bile stasis. In chronic changes like fibrosis and cirrhosis, however, cases on a poor diet were more severely affected than those on a fair diet ( $p < 0.05$ ) (Table I). It would thus appear that dietary fac-

tors are not entirely unimportant in acute alcoholic hepatitis, since those on a poor diet may be expected to have more chronic sequelae like fibrosis and cirrhosis. This would be important in the prognosis of a case, since the acute changes of alcoholic hepatitis are reversible, while cirrhosis, once established, becomes irreversible.

## REFERENCES

1. Best, C.H., Huntsman, M.E. and Ridout, J.H.: "The 'lipotropic' effect of protein." *Nature (London)*, 135, 821, 1935.
  2. Best, C.H., Hartroft, W.S., Lucas, C.C. and Ridout, J.H.: "Liver damage produced by feeding alcohol or sugar and its prevention by choline." *Brit. Med. J.*, 2, 1001, 1949.
  3. Fung, W.P.: "Acute Alcoholic Hepatitis: a prospective clinicopathological study of 50 cases." M.D. dissertation, University of Singapore, Singapore, 1972.
  4. Galambos, J.T.: "Alcohol and Liver Disease." *Amer. J. Dig. Dis.*, 14, 477, 1969.
  5. Gyorgy, P. and Goldblatt, H.: "Hepatic injury on a nutritional basis in rats." *J. Exp. Med.*, 70, 185, 1939.
  6. Himsworth, H.P.: "The liver and its diseases." Harvard Univ. Press, Cambridge, Mass., 1950.
  7. Klatskin, G., Krehl, W.A. and Conn, H.O.: "The effect of alcohol on the choline requirement. I. Changes in the rat's liver following prolonged ingestion of alcohol." *J. Exp. Med.*, 100, 605, 1954.
  8. Lieber, C.S., Jones, D.P. and DeCarli, L.M.: "Effects of prolonged ethanol intake: Production of fatty liver despite adequate diets." *J. Clin. Invest.*, 44, 1009, 1965.
  9. Lieber, C.S.: "Alcohol and the liver, in 'Progress in Liver Diseases'." Ed. H. Popper and F. Schaffner, London, W. Heinemann, p. 134-154, 1965.
  10. Lieber, C.S. and Rubin, E.: "Alcoholic fatty liver in man on a high protein and low fat diet." *Amer. J. Med.*, 44, 200, 1968.
  11. Mallory, G.K.: "Liver disease associated with chronic alcoholism." *Lab. Invest.*, 9, 132, 1960.
  12. Rubin, E. and Lieber, C.S.: "Alcohol-induced hepatic injury in non-alcoholic volunteers." *New Engl. J. Med.*, 278, 869, 1968.
  13. Shils, M.E. and Stewart, W.B.: "Preventive influence of certain aminoacids on experimental fatty liver of portal types." *Proc. Soc. Exp. Biol. Med.*, 87, 629, 1954.
  14. Waterlow, J.C. and Bras, G.: "Nutritional liver damage in man." *Brit. Med. Bull.*, 13, 107, 1957.
-