Biochemical studies on hepatic involvement in infectious mononucleosis

D. N. BARON, JOYCE L. BELL, AND W. N. DUNNET¹

*From the Departments of Chemical Pathology and Infectious Diseases,
Royal Free Hospital, London*

SYNOPSIS Eighty cases of infectious mononucleosis have been investigated by serum enzyme studies and other liver function tests.

Maximum abnormalities occurred between the second and fourth weeks of illness and all tests were usually normal by the sixth week. Serum isocitric dehydrogenase activity was increased in 93% of cases and serum glutamic-oxaloacetic transaminase in 74%. Conventional liver function tests were less sensitive. Serum bilirubin was above normal in 40% of cases; in 17% of cases the increase was sufficient to show as clinical jaundice.

No patient has developed chronic hepatitis.

The incidence of jaundice and of liver damage in infectious mononucleosis is undecided. Leibowitz (1953), reviewing 3,000 published cases from 1923-51, found 144 cases of jaundice, with an incidence in individual reports of 1.4% to 25%. With the advent of enzyme tests as sensitive indicators of hepatocellular damage (Baron, 1963) it was considered timely to re-examine the problem.

MATERIAL

Eighty consecutive unselected cases of infectious mononucleosis admitted to the infectious diseases department of the Royal Free Hospital between August 1959 and November 1962 have been studied. The clinical, haematological, and immunological findings and criteria for diagnosis have been described in detail elsewhere (Dunnet, 1963). Blood was taken for biochemical examination approximately twice weekly while the patient was in hospital (in certain instances more frequently), and at less frequent intervals after discharge until repeated tests were normal. Some patients were visitors and students from abroad, consequently routine follow-up examination after discharge in every case was impracticable. This paper is confined in the main to an investigation of the acute phase of the disease.

METHODS

During the period of this survey the following methods, with modifications, were employed for analysis of serum.

¹Present address: Epidemiological Section, Ministry of Health, London.

Received for publication 25 June 1964.

Glutamic-oxaloacetic transaminase (G.O.T.) (Reitman and Frankel, 1957); isocitric dehydrogenase (I.C.D.) (Bell and Baron, 1960); total and differential proteins (Wolfson, Cohn, Calvary, and Ichiba, 1948); total and conjugated bilirubin (Malloy and Evelyn, 1937); alkaline phosphatase (King and Armstrong, 1934); thymol turbidity, thymol flocculation, and colloidal gold flocculation (MacLagan, 1944); zinc sulphate turbidity (Kunkel, 1947). This work was done before the introduction of the new terminology and international units for enzymes.

RESULTS

Maximum abnormality of all biochemical findings occurred between the second and fourth weeks of illness, this period being about a week later than that of maximum clinical involvement. By the sixth week these abnormalities had usually returned to normal, except that the serum I.C.D. was often raised for a further week.

Enzyme tests were abnormal in a higher proportion of cases than were conventional 'liver function tests'. Isocitric dehydrogenase was elevated in 74 cases (93%) and G.O.T. in 58 cases (74%). Of conventional liver function tests, the most sensitive tests appeared to be thymol turbidity, abnormal in 42 out of 68 cases tested (62%), though thymol flocculation was only abnormal in 41%; alkaline phosphatase, abnormal in 37 out of 67 cases tested (55%) and above 30 units in nine cases (13%); and colloidal gold, abnormal in 28 out of 54 cases tested (52%). Zinc sulphate turbidity was abnormal in only 16 out of 66 cases tested (24%). Serum

evidence from liver biopsy (Nelson and Darragh, 1956) and by serum transaminase estimations (Rosalki *et al.*, 1960). In this series many patients showed biochemical abnormalities into the sixth week and by the most sensitive test of liver cell damage (serum I.C.D.) into the seventh week. Very careful history taking in this series has often elicited vague complaints of malaise and general weariness which may precede even by a week the acute symptoms such as sore throat and fever by which the patients usually tend to date the beginning of their illness.

It has been suggested that hepatitis in infectious mononucleosis may become chronic (Bennett, Frankel, Bedinger, and Baker, 1950) or lead to cirrhosis (Leibowitz and Brody, 1950). In the present series in one case serum I.C.D. was minimally raised and colloidal gold still abnormal seven months after the onset of the illness, after which time contact with the patient was lost. In three years since the beginning of this study no cases of chronic hepatitis were observed in the 40 patients who were followed.

Much of the material in this article was included in the thesis by W.N.D. accepted for the degree of M.D. (Aberdeen). We wish to thank Dr. W. Gunn and Dr.

A. M. Ramsay for access to patients under their care and for much advice, and Dr. Roger Williams for valuable criticism.

REFERENCES

- Baron, D. N. (1963). *Proc. roy. Soc. Med.*, **56**, 173.
 Bell, J. L., and Baron, D. N. (1960). *Clin. chim. Acta*, **5**, 740.
 Bennett, H. D., Frankel, J. J., Bedinger, P., and Baker, L. A. (1950). *Arch. intern. Med.*, **86**, 391.
 Berk, J. E., Shay, H., Ritter, J. A., and Siplet, H. (1948). *Gastroenterology*, **11**, 658.
 Dunnet, W. N. (1963). *Brit. med. J.*, **1**, 1187.
 Gelb, D., West, M., and Zimmerman, H. J. (1962). *Amer. J. Med.*, **33**, 249.
 Kalk, H., Schmidt, E., Schmidt, F. W., and Wildhirt, E. (1960). *Klin. Wschr.*, **38**, 421.
 King, E. J., and Armstrong, A. R. (1934). *Canad. med. Ass. J.*, **31**, 376.
 Kunkel, H. G. (1947). *Proc. Soc. exp. Biol. (N.Y.)*, **66**, 217.
 Leibowitz, S. (1953). *Infectious Mononucleosis*. Grune and Stratton, New York.
 —, and Brody, H. (1950). *Amer. J. Med.*, **8**, 675.
 MacLagan, N. F. (1944). *Brit. J. exp. Path.*, **25**, 234.
 Malloy, H. T., and Evelyn, K. A. (1937). *J. biol. Chem.*, **119**, 481.
 Mason, W. R. Jr., and Adams, E. K. (1958). *Amer. J. med. Sci.*, **236**, 447.
 Nelson, R. S., and Darragh, J. H. (1956). *Amer. J. Med.*, **21**, 26.
 Reitman, S., and Frankel, S. (1957). *Amer. J. clin. Path.*, **28**, 56.
 Rosalki, S. B., Jones, T. G., and Verney, A. F. (1960). *Brit. med. J.*, **1**, 929.
 Schultz, A. L., and Hall, W. H. (1952). *Ann. intern. Med.*, **36**, 1498.
 Sullivan, B. H. Jr., Irely, N. S., Pileggi, V. J., Crone, R. I., and Gibson, J. R. (1957). *Amer. J. dig. Dis.*, **2**, 210.
 Wadsworth, R. C., and Keil, P. G. (1952). *Amer. J. Path.*, **28**, 1003.
 Wechsler, H. F., Rosenblum, A. H., and Sills, C. T. (1946). *Ann. intern. Med.*, **25**, 113.
 Wolfson, W. Q., Cohn, C., Calvary, E., and Ichiba, F. (1948). *Amer. J. clin. Path.*, **18**, 723.