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The Australia (hepatitis-associated) antigen amongst heroin addicts attending a London addiction clinic

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SUMMARY

Thirty-three of 72 heroin addicts attending a recognized clinic for drug addition had a history of jaundice, but in only five was the serum positive for hepatitis-associated antigen (HAA) when examined by immunodiffusion, immunoelectro-osmophoresis and complement fixation. Two of these were repeatedly positive over an 8–12 month follow-up period and liver biopsy showed chronic persistent hepatitis. A third later developed acute hepatitis. A study of the injection habits suggested that the present low incidence of HAA and the decrease in number of cases with jaundice was probably related to the provision of free disposable syringes by the clinic since it was opened in 1968.

INTRODUCTION

Since the first report by Steigmann, Hyman & Goldbloom (1950) of an outbreak of hepatitis amongst narcotic addicts, there have been numerous reports suggesting that the infection is acquired through the communal use of syringes and needles (reviewed by Zuckerman, 1970). Although serum hepatitis is now known to be specifically associated with the presence of Australia (hepatitis-associated) antigen (HAA) in the blood, the sensitivity of the currently available techniques for its detection does not provide an absolute index of infection (*Bulletin of the World Health Organization*, 1970). It is uncertain whether the antigen represents incomplete virus particles, an aggregate of protein subunits, excess production of unstable virus-like particles or a specific protein produced by cells infected with the serum hepatitis agent. Nevertheless, the availability of tests for this antigen has provided the means for studying and re-evaluating the epidemiology of serum hepatitis. In this paper we report a survey of 72 heroin addicts attending one of the recognized centres for drug addition (the St Giles' Clinic, Camberwell), with particular reference to the incidence of HAA, the occurrence of hepatitis and the injection habits of the addicts.

PATIENTS AND METHODS

The 49 male and 23 female addicts seen had been addicted for periods of 1–15 years. All had taken heroin regularly, although some had recently been weaned to physeptone or methadone. The addicts were questioned specifically for a history of jaundice and about their injection habits. Liver function tests were performed whenever sufficient blood could be obtained, and when abnormal, a complete physical examination was performed.

Serum was examined for HAA by immunodiffusion (Zuckerman & Taylor, 1969), by immunoelectro-osmophoresis (Zuckerman & Taylor, 1970) and by a micro-titre complement-fixation test (Taylor, 1970). The laboratory reference antigen gave a reaction of immunological identity with other known Australia (hepatitis-associated) antigens (*Bulletin of the World Health Organisation*, 1970).

RESULTS

None of the 72 addicts were jaundiced at the time of the survey, although 33 (46%) gave a history of jaundice in the past. An analysis of the years in which these attacks of jaundice had occurred showed a peak incidence in 1967, and since 1968 when the clinic was started the frequency has declined (Fig. 1). This may have

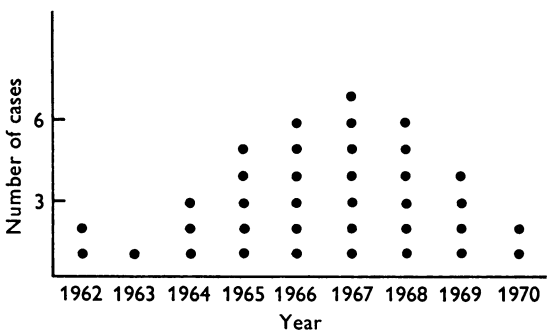

Fig. 1. The number of cases with jaundice each year.

been related to the provision in the clinic of free disposable syringes, ampoules of sterile water and advice on syringe hygiene, for the incidence of previous jaundice was significantly higher in those who admitted sharing syringes with other addicts (Table 1). It was also higher in those who used water from the lavatory pan to make up injections rather than tap or sterile water and in those who did not cleanse the skin before injection, although in neither instance did the difference reach statistical significance.

Liver function tests were carried out in 53 addicts which included 28 of the 33 with a past history of jaundice. None had a raised serum bilirubin level, but four had an elevated serum alkaline phosphatase and in 17 (32%) the serum aspartate aminotransferase (SGOT) was moderately raised with values up to 122 mU./ml. The serum gamma globulin was greater than 1·3 g/100 ml., the upper limit of

normal, in 34 (83%) of the 41 patients in whom it was estimated. The highest gamma globulin level encountered was 3·1 g/100 ml., in a patient who had previously been jaundiced but whose serum aspartate aminotransferase was only 25 mU./ml. No relationship could be detected between these abnormalities in liver function tests and a previous history of jaundice.

Table 1. *The frequency of a history of jaundice in the 72 addicts related to injection habits*

Injection habits		Percentage of total number of addicts	Percentage of addicts in each group with a history of jaundice
Sharing of syringes	Yes	71	52
	No	29	26
Source of injection water	Lavatory pan on occasion	45	62
	Always tap or sterile	55	47
Cleansing of skin before injection	No	83	50
	Yes	17	30

Table 2. *Clinical details of the five addicts with HAA in their sera*

Case	Syringe sharing	Previous jaundice	Serum aspartate aminotransferase (mU./ml.)	Persistence of HAA	Liver biopsy
5	Yes	No	24	8 months	Chronic persistent hepatitis
19	Yes	Yes (1967)	55	12 months	
31	Yes	No	85	4 months	Acute hepatitis (3 months later)
35	Yes	Yes (1966)	20	—	—
44	No	No	24	—	—

Australia (hepatitis-associated) antigen

This was found in the sera of five patients. In three the positive result was obtained in the immunodiffusion test, but in the fourth patient HAA was detected by immunoelectro-osmophoresis, and in the fifth by complement fixation alone. The presence of HAA was confirmed in all five patients by electron microscopy.

Of the five patients, two gave a history of previous attacks of jaundice (Table 2). One of these (Case 19) had recently given up drugs and remained clinically well during the subsequent follow-up period of 12 months, although his serum remained consistently positive for HAA. Liver function tests were virtually normal, but a liver biopsy showed the histological appearances of chronic persistent hepatitis. These were also seen in the liver biopsy of Case 5 who, unlike the previous patient, was not aware of jaundice in the past. His liver function tests were normal at the time of survey and remained so until his death eight months later from an overdose, his serum during this time being repeatedly positive for HAA. Another patient

(Case 31) had no previous history of jaundice and had normal liver function tests when his serum was first found to be positive for HAA in February 1970. Three months later he developed acute hepatitis with jaundice and the characteristic histological changes on liver biopsy. From this, he appeared to make a complete recovery and HAA disappeared from the blood.

DISCUSSION

Nearly half of these addicts had had jaundice, but in only five (7%) was HAA detected in the serum. This cannot be attributed to use of relatively insensitive techniques, since we employed in parallel immunodiffusion, immunoelectro-osmophoresis and the complement-fixation test, which in our hands is very sensitive. Some of our patients may have become immune to hepatitis as a result of previous exposure. Immunity to second attacks of hepatitis has been reported in human volunteer experiments by MacCallum (1953) and Giles, McCollum, Berendtson & Krugman (1969). In none of the present patients were we able to detect antibody to HAA in the serum by the immunodiffusion technique. Immunity may, however, depend on cell-mediated mechanisms. In fact, three of our patients claim to have had more than one attack of jaundice. Although it has been suggested that the drugs and other ingredients used for dissolving them may have a direct hepatotoxic effect (Marks & Chapple, 1967), this view is not supported by epidemiological evidence in outbreaks of hepatitis (Bewley, Ben-Arie & Marks, 1968), or by experimental data (Brooks *et al.*, 1963; Gorodetzky, Sapira, Jasinski & Martin, 1968). There was a significant association in our patients between a history of jaundice and the sharing of syringes. It appears likely that the sterile syringes supplied by the clinic since it opened in 1968, together with instruction concerning hygiene, have resulted in a lower rate of transmission of serum hepatitis.

Nevertheless, in two of the five patients found to have HAA at the time of the survey, the antigen persisted over long periods of time. This was associated with histological changes of chronic persistent hepatitis. Norris & Potter (1965) found similar histological changes with infiltration of lymphocytes in the portal tracts in 27 of 36 addicts examined, but this unfortunately was before tests for HAA were generally available. To what extent chronic persistent hepatitis is the result of persistence of HAA is uncertain at present. Becker, Scheuer, Baptista & Sherlock (1970) have suggested that the prognosis of chronic persistent hepatitis is good. Their patients, however, were not addicts. Recently, Tamburro, Rajan & Leevy (1971) have reported a follow-up study of 104 patients including 63 addicts, with non-epidemic hepatitis. Four addicts developed cirrhosis and ten fibrosis. In six of these the serum was positive for HAA. Cirrhosis was seen to follow hepatitis in addicts in whom HAA was not detected, and malnutrition and alcoholism as well as persistent antigenaemia with repeated re-inoculation are probably all important factors contributing to its development. One-third of the patients in the present series had raised serum aspartate aminotransferase levels, and in over two-thirds the serum gamma globulin was elevated. Bewley, Ben-Arie & Marks (1968) reported a similar frequency of abnormal liver function tests in a series of 254 non-jaundiced

addicts. Histological abnormalities in the liver might well be apparent in these patients if liver biopsies were performed.

Serum hepatitis can be transmitted not only parenterally, but also by the oral route (Krugman, Giles & Hammond, 1967; Krugman & Giles, 1970) and persisting infection in the addict can be spread to family contacts. One of our patients was potentially infectious for at least 3 months before the onset of clinical hepatitis, and the two with chronic persistent hepatitis had HAA in their sera for 8 and 12 months respectively. Although the incidence of HAA in the clinic as a whole is low, it would seem worth while to screen all drug addicts when they register initially and thereafter at regular intervals.

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