

EPIDEMIC HEPATITIS B WITH DELTA-ANTIGENAEMIA AMONG DUBLIN DRUG-ABUSERS

A. G. Shattock

M. G. Kelly, J. Fielding and Yvonne Arthurs

*Department of Medical Microbiology, University College, Dublin 2, and
The Charitable Infirmary, Dublin*

Summary

ONE hundred and fifty-eight cases of hepatitis B have been detected among Dublin drug-abusers from January to August 1981 during an epidemic which originated in 1980 and still continues. The mean age was 21 years and the male/female susceptibility to hepatitis B was the same. An unusually high proportion (29%) of a sample of 50 tested had the hepatitis B associated delta antigen in their serum and confirms that the delta agent is probably common in drug addicts and not confined to Italy.

Introduction

It is now well documented that hepatitis B is frequent among drug addicts, since those who use drugs intravenously regularly share syringes and needles (Grady *et al*, 1972; Sutnick *et al*, 1971; Alter, 1958; Altshul *et al*, 1952; Steigman *et al*, 1950; Blanck *et al*, 1979). In two studies (Sutnick *et al*, 1971; Cherubin and Hargrove, 1970) asymptomatic heroin users had an increased incidence of HB_sAg antigenaemia and in a study of U.S. soldiers returning from Vietnam there was a significant increase in HB_sAg positivity in those abusing heroin by any method compared with non-drug-taking controls. There was also a significant increase in anti-HB_s positivity among those using heroin intravenously compared with those using heroin by smoking and sniffing (Blanck *et al*, 1979).

Hepatitis B markers among drug-abusers have been monitored by the Virus Reference Laboratory, University College Dublin, since 1970. Up to the beginning of 1980 the incidence of hepatitis B surface antigen (HB_sAg) among drug-abusers has been low but increasing from an average of two cases per year between 1970-1974 to 10 cases per year between 1975 and 1979, in proportion to a general increase in drug abuse. This paper reports an alarming increase in hepatitis B among drug-abusers in Dublin during 1981.

We also report the unusual finding of delta antigen in the serum of a significant number of abusers in this epidemic. The delta antigen, found in the liver of some patients with hepatitis B infection, has been shown to be associated with a transmissible agent (the delta agent) which co-infects with, and may be dependent on, hepatitis B virus (Editorial, *Lancet*, 1982).

Patients and Methods

Patients

The patients in this report were principally those attending the Drug Advisory and Treatment Centre, or as in-patients with hepatitis, at The Charitable Infirmary, Dublin, during 1980 and up to August 31st 1981. Drug-abusers with hepatitis admitted to other hospitals are also included. Two other groups of drug-abusers, one negative for all hepatitis B virus (HBV) markers and the other with antibody to the hepatitis B core antigen (anti-HBc) only were used as controls, totalling 105.

Serological tests for HBV markers

Screening tests for HB_sAg were carried out by radio-immunoassay (RIA, Abbott) using overnight incubation at 45°C, and for antibody to HB_sAg (Anti-HB_s) by immunodiffusion (ID) on concentrated sera (Shattock, 1974).

Patients positive for HB_sAg were also tested for the hepatitis B 'e' antigen

TABLE

	No.	Male	Female	Ratio	Mean age	Duration of IV Drug-abuse (yrs.)	Range (yrs.)
HBsAg Positive	140	110	30	3.7:1	21.4	2.9	0.1 - 17
Anti-HBs Positive	18	15	3	5:1	22.0	4.0	1 - 12
TOTALS	158	125	33	3.8:1	21.7	3.5	0.1 - 17

Outline data on 158 cases of HBV infection in drug-abusers detected from January to August 1981.

(HBeAg) and antibody to it (Anti-HBe) by a semimicro ID in 0.7% agarose in barbitone buffer at Ph 8.6, with double filling of wells with serum samples concentrated a minimum of four-fold with polyacrylamide gel ("lyphogel", Hawksley Ltd).

Tests for anti-HBc IgG were carried out by RIA (Abbot 'Corab') or enzyme immunoassay (EIA, Abbott 'Corezyme') according to the manufacturers' instructions.

For the purposes of this study drug-abusers were classified as having 'acute' HBV infection if they cleared their HBsAg within 4 months, had clinical and biochemical findings consistent with acute hepatitis and cleared HBeAg within 2 weeks of onset, and/or sero-converted to anti-HBe positivity.

Tests for delta antigen and antibody were kindly carried out by Dr. M. Rizzetto (Ospedale Maggiore, Turin) using an RIA technique developed by him, on serum samples pre-treated with the non-ionic detergent Nonidet P40 (Rizzetto *et al*, 1975).

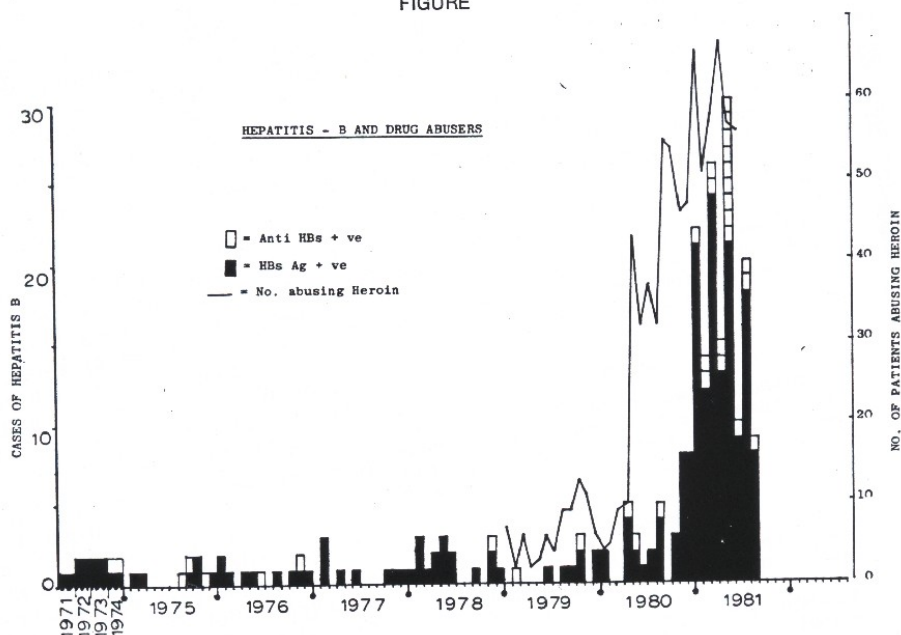
Results

The figure shows the incidence of HBsAg and anti-HB_s positives among drug-abusers tested since 1970. From January to August 31st, 1981, 158 cases of HBV infection among drug-abusers have been detected compared with 37 for the whole of 1980. The Table shows the data for age, sex ratio and mean duration of intravenous drug abuse. The male to female ratio was nearly four to one which exactly reflects the male/ female ratio among the drug-abuser population as a whole in Dublin. The average age was approximately 21 years, ranging from 14-34 years. Again this did not differ from the average age of the abuser group as a whole. The duration of intravenous drug abuse varied from one month to 17 years. However, in many cases the duration of intravenous drug abuse was not disclosed or not asked. Those with anti-HBs were, on average, using heroin intravenously longer but not significantly so. Six females and one male included in this study denied intravenous drug abuse but had sexual contact with intravenous drug-abusers and are fully reported elsewhere (Kelly *et al*, 1982).

A control group of 105 HBsAg and anti-HBs negative drug-abusers were examined for anti-HBc to determine the proportion in previous contact with hepatitis B. Forty-six per cent were positive.

Fifty HBsAg positive drug-abusers from this epidemic have been tested for the delta antigen and antibody. Surprisingly, 14 (29%) of these had serum delta antigen. One had anti-delta and one had both delta antigen and antibody. Four anti-HBs positive drug-abusers were also tested and one had delta

FIGURE



antigenaemia. This patient had acute hepatitis which was serologically negative for hepatitis A IgM antibody and his anti-HBs titre remained unchanged before and after the acute episode. Delta antigen and antibody were not found in any of 19 HBsAg positive non-drug-abusing patients with acute hepatitis tested.

Discussion

The epidemic appears to have originated during the Summer of 1980, the first sharp rise in hepatitis cases occurring in November, approximately 6 months following the increase in numbers using heroin by smoking, snorting and sniffing.

Many of these changed to intravenous use of heroin approximately 3 months before the rise. The reason for the unexpected rise and fall of incidence of hepatitis B in consecutive months in the Figure is not known but suggests periodic transfer of hepatitis B from one group of abusers to the next. Although there has been no diminution in the numbers of new heroin users the epidemic is showing signs of declining or levelling off (October 1981). It appears that new groups are not intermixing with previous groups.

The incidence of hepatitis B among males and females was the same as the male to female drug-abuser ratio and strongly suggests that male/female susceptibility to HBV infection is the same among drug-abusers.

The abusers who denied intravenous use of drugs admitted intimate association with intravenous drug-abusers; these are regarded as secondary cases occurring as a result of transmission by close sexual contact or by other inapparent parenteral routes (Frosner *et al*, 1975; Heingst, 1973 and Heathcote and Sherlock, 1973). Follow-up has revealed further cases of hepatitis B occurring among non-drug-abusing contacts of drug-abusers arising from this epidemic (Kelly *et al*, 1982).

The reasons for this dramatic increase in hepatitis B in Dublin drug-abusers are thought to be principally the increased availability of heroin and the increased use of this drug intravenously by a relatively large number of young adults a few months before the onset of the epidemic. Also anti-HBc tests on current and past attenders at the clinic showed that 54% of abusers had not encountered hepatitis B previously, indicating a large non-immune reservoir. However, increased referral of patients with hepatitis to the Clinic, including self-referral among the abuser groups, coupled with increased surveillance, have probably contributed to the numbers of hepatitis B cases detected.

The delta antigen has been found in the liver of some patients with HBV infection in the south of Italy. Chronic carriers of HBsAg with intrahepatic delta antigen have high titres of anti-delta but the presence of serum delta antigen has been rarely reported. To date delta antigen or antibody has not been reported in the absence of evidence of HBV infection so that it appears that the delta agent may be dependent on HBV (Rizzetto, Purcell *et al*, 1980). Anti-delta has been reported more common in haemophiliacs, drug-abusers and other groups with multiple parenteral exposure (Pera *et al*, 1981 and Rizzetto, Purcell *et al*, 1980).

Our finding of 29% of 50 HBsAg positive drug-abusers with delta antigenaemia is unusually and unexpected since delta antigenaemia was shown to be very transient in chimpanzee transmission experiments (Rizzetto, Canese *et al*, 1980). It also confirms that the delta agent is not confined to localities such as Italy (Raimondo *et al*, 1982). Our case of delta antigenaemia in the anti-HBs positive abuser with acute hepatitis is of great interest since it suggests independent delta infection. These and other cases are part of an ongoing study to see if the presence of delta is modifying the short and long-term outcome of HBV infection and are the subject of a separate report (Shattock *et al*, 1982). The existence of underlying chronic liver disease attributable to non-A, non-B hepatitis in a number of patients from this epidemic has also become evident and is reported elsewhere (Shattock *et al*, 1981; Shattock, 1982).

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FOOTNOTE

Since August 1981 the numbers of hepatitis B cases among drug-abusers has remained at a high level, averaging between 10 and 15 new cases per month.

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