

Changes in Incidence of Hepatitis B in Ireland from 1970 - 1987

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Summary

This paper analyses data on 2,226 cases of Hepatitis B virus (HBV) infection detected during the years 1970 to 1987. Of those where information on risk-group was available (1,301), infection among intravenous drug-abusers accounted for the largest proportion (49%). Most became infected during and since an outbreak of hepatitis B and Delta hepatitis which originated in this group in 1980. A comparison of the data before and after the start of the outbreak among drug-abusers shows a marked increase in the number of HBV infections in non drug users, including haemophiliacs, homosexuals and health-care staff, and a dramatic decrease in hepatitis B following blood transfusion. A larger group (165 cases), many of whom are long-term healthy hepatitis B surface antigen carriers, were patients in institutions for the mentally handicapped (IMH). Most were detected recently during pre-vaccination sampling programmes. Others affected included visitors to and from high-incidence areas, tattooed persons, dialysis patients, persons born to infected mothers, and members of the security forces dealing with drug-abusers.

In all, 8.4% of the hepatitis B cases detected were found to be carriers and 67% of these remained carriers in 1987. The mean duration of carriage was 3.25 years. Intravenous drug-abusers and IMH patients constituted the two largest groups of carriers.

The running-three-yearly mean incidence of new cases of hepatitis B has levelled off below the peak of 1981. Although the number of cases among drug-abusers has apparently decreased, the number of cases among non drug-abusing groups has increased by 50%. The use of recently introduced vaccines in some risk groups should help to reverse this upward trend.

Introduction

Routine tests for hepatitis B became available in Ireland in 1970. Five of the first¹⁶ hepatitis B surface antigen (HBsAg) positive cases and two of Five anti-HBs positive cases detected up to August 1972 occurred in persons who had received blood; only three HBsAg positives were drug-abusers¹. Among intravenous drug-abusers a very large increase in hepatitis B cases occurred in 1980 due to the increased availability and use of heroin by injection². At the same time the Hepatitis D virus (HDV, Delta agent) was introduced and caused coinfection in up to 36% of cases^{2,3}. By 1983, there was evidence that the increase in incidence of hepatitis B among drug-abusers was also causing an increase in cases among their contacts⁴.

This paper details the epidemiology of all hepatitis B cases detected at the Virus Reference Laboratory since 1970, notes the changes in incidence of HBsAg in various risk-groups during this time and identifies those risk-groups which are most affected in Ireland at present.

Patients and Methods

Specimens included in this study were sent to the Virus Reference Laboratory (VRL) at this Department, for hepatitis serology by clinicians in hospitals and general practice, in sexually transmitted disease (STD) clinics and in institutions for the mentally handicapped (IMH), from 1970 to 1987 inclusive. The blood transfusion services referred samples to us for confirmation from donors found initially positive or possibly positive for hepatitis B surface antigen by screening tests.

A total of 64,897 specimens have been tested for hepatitis by us since 1970. Lack of clinical and sociological information made it impossible to classify fully 638 of the 2,226 hepatitis B cases detected. These are referred to as “unknown” in Tables I and V. Patients with markers of past hepatitis B infection are not included in this study.

Hepatitis B surface antigen (HBsAg) was originally assayed by a semi-microimmunodiffusion (ID) test on concentrated sera, supplemented from 1974 with a haemagglutination test (Hepatest, Wellcome). These were replaced in March 1979 by radioimmunoassay (RIA) (Abbott, Ausria II) and from July 1985 by enzyme-immunoassay (EIA, Abbott, Roche and Wellcome). HBsAg positives are always confirmed by neutralising assay, or by repeat testing and by serology for other hepatitis B markers, i.e.: Hepatitis Be antigen (HBeAg), anti-HBe, and antibody to hepatitis B core (anti-HBc) IgG and IgM by in-house EIA's⁵. An HBsAg carrier is defined as a case where HBsAg is detected in the blood at approximately the same level for six months or more. Healthy carriers are characteristically negative for HBeAg and anti-HBc IgM

Statistical analyses were carried out using Students t tests.

Results

Since 1970, 2,226 patients have been found to be HBsAg positive, one of which was retrospectively detected from 1969. Of those where information on the risk group was known, 872 (49%) were drug-abusers. It can be seen from Fig. 1 and Table I that the incidence of hepatitis B in drug-abusers first exceeded that in non drug-abusers in 1980 and peaked between 1981 and 1983 (67-75% of total cases). After 1983, the incidence of hepatitis B in drug-abusers appeared to fall, while that in non-abusers rose. However, extensive enquiries during 1981-84 about the then “unknown” cases showed that many were in fact drug-abusers; figures in the “Unknown” group from 1984 to 1987 in Table I therefore almost certainly contain a significant but unknown number of drug-abusers. Overall, there has been a 15-fold increase in the number of hepatitis B cases among drug-abusers since 1980. The number of cases among non drug-abusers over the same period has increased by 50% (Table II). The running-three-yearly mean incidence of hepatitis B has remained at a level somewhat below that of the peak in 1981 (Fig. 1).

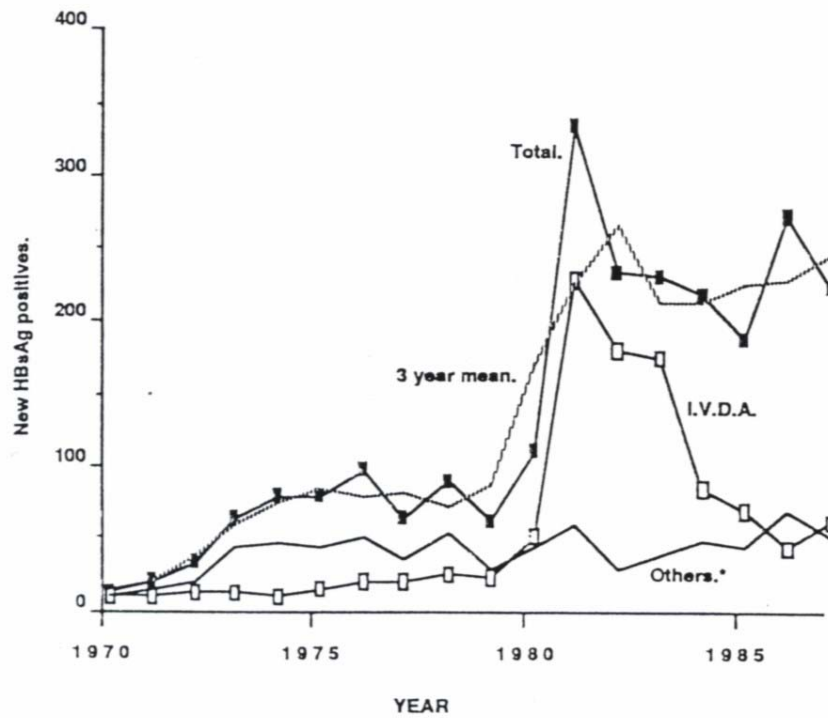


Fig. 1-Incidence of HBsAg positives in intravenous drug-abusers (IVDA) and other groups
*excluding patients in institutions for the mentally handicapped.

TABLE I
New HBsAG positives detected per year.

Year	Unknown	IVDA	IMH	Donors	PTHB	HMX/STD	Haem/iac	Visitors	HCS	Misc.	Total
1969	0	0	1	nt	0	0	0	0	0	0	1
1970	1	0	0	nt	0	0	0	0	0	1	2
1971	4	1	0	nt	2	0	1	0	1	0	9
1972	7	3	2	4	2	1	1	2	0	0	22
1973	12	2	6	13	4	0	1	0	4	11	53
1974	30	1	1	26	2	0	2	0	2	4	68
1975	26	6	3	20	4	0	3	3	3	1	69
1976	36	9	1	30	3	0	0	0	5	2	86
1977	16	11	1	17	1	0	2	0	3	2	53
1978	18	16	2	24	3	1	0	4	4	7	79
1979	20	14	1	12	1	1	0	0	1	2	52
1980	25	42	1	29	0	0	0	1	3	0	101
1981	54	217	3	24	2	5	1	5	6	6	323
1982	36	168	1	8	0	2	3	5	1	0	224
1983	27	165	0	11	0	2	6	2	3	4	220
1984	90x	75	3	18	0	4	7	6	7	1	211
1985	77x	58	8	16	0	5	1	2	4	5	176
1986	87x	34	81	21	0	14	5	11	6	5	264
1987	72x	50	50	8	0	16	3	9	4	1	213
Totals	638	872	165	281	24	51	36	50	57	52	2226

Unknown = Insufficient or no information supplied or status unconfirmed; the 'x' indicates the inclusion of a significant but unknown number of intravenous drug-abusers (IVDA), see text. IMH = patients from institutions for the mentally handicapped. PTHB = post-transfusion hepatitis B, HMX/STD = homosexuals and attenders at sexually transmitted disease clinics. Haem/iac = haemophiliacs. HCS = health-care staff. Visitors = visitors to or natives from high-incidence areas, nt = none tested. Misc. as listed in Table IV.

There have been increases in incidence of hepatitis B cases among most risk groups: fifty-one cases were seen among homosexuals and those attending sexually transmitted disease (STD) clinics. Forty-eight of these cases occurred after 1980, which was a 20-fold increase in incidence before 1980. The male to female ratio was 25 : 1 and the mean age was 33 years (range 20-50 years).

Significant increases were also seen among haemophiliacs (three-fold), health-care staff (almost two-fold) and among visitors to and those native from high-incidence areas (five-fold). A total of 57 cases of hepatitis B were detected among health-care staff (Table III). Twenty-three cases (40%) were detected among nurses, 26% among doctors and surgeons and 19% in laboratory staff. This data includes cases occurring among missionaries involved in health care returning from high incidence areas.

Among the miscellaneous group (Table IV), three clusters of cases occurred among persons who had been tattooed approximately three months earlier. These occurred in 1978 (three cases), 1981 (four cases) and 1983 (three cases). A total of 15 cases in the miscellaneous group were spouses of family contacts of acute cases of carriers. Of these, five were children born to infected mothers and all five became carriers (Table V). Thirteen cases were referred as part of an outbreak of 37 cases of hepatitis B which occurred in a tuberculosis unit and have been reported previously⁶. One of the three priests in Table IV was involved in social work with drug-abusers; the source of infection of the other two is unknown but many of those included in Table I, as visitors to foreign areas of high-incidence, were also priests.

Although testing for HBsAg or anti-HBs is not routinely necessary prior to vaccination, we have carried out tests on samples from residents in a number of institutions for the mentally handicapped (IMH) to confirm the expected high incidence, as seen elsewhere⁷. HBV infection was confirmed in 115 residents (12.5%). The mean age of those infected was 35 years and the ratio of males to females was 1.5 : 1. The

TABLE II

Incidence of Hepatitis B before and after the outbreak among Drug-abusers.

HBsAg positives in:	Pre-outbreak		Post-outbreak
	1970-79	1980-87*	p**
Drug abusers	63	809	<0.001
Homosexuals and STD clinic attenders	3	48	<0.001
Visitors to and natives from high-incidence areas	9	41	<0.05
Haemophiliacs		1020	<0.05
Health-care staff	23	34	<0.05
Miscellaneous	30	22	not done
Blood donors	146	135	N.S.
Post-transfusion	22	2	<0.01
Total of non-drug-abusers	243	302	

* Note that this period is two years shorter than the pre-1980 period.

** by Student's t test. N.S. = No significant difference

TABLE III
Hepatitis B among Health-Care Staff before and since 1980.

	Pre-outbreak 1970-79	Post-outbreak 1980-87	Total
Nurses	7	9	16 (28%)
Nurses (IMH)*	3	4	7 (12%)
Lab. Staff	4	7	11 (19%)
Doctors	5	7	12 (21%)
Surgeons	0	3	3 (5%)
Others and Unspecified 4	4	4	8 (14%)
Totals 23	23	34	57

* Nurses working in institutions for the mentally handicapped.

serological pattern indicated that most were long-term healthy carriers of HBsAg although some had HBeAg and IgM anti-HBc, indicating infectivity. As discussed below, IMH patients are excluded from Figure 1 because many of those detected in 1986 and 1987 were long-term carriers.

The HbsAg positivity rate among donors in Ireland has been found to be only one per 10,000 (0.01%), which is one of the lowest rates in the world (Dr. T. Walsh, Blood Transfusion Service, Dublin, personal communication). Specimens from a total of 281 donors were referred to us by the Blood Transfusion Service for confirmation tests and there has been a small decline in the number of positives detected annually but the decrease is not statistically significant. However the number of post-

TABLE IV
Miscellaneous Hepatitis B cases.

Category	No.
Tuberculosis unit patients	13 (25%)
Recently tattooed*	10 (19%)
Dialysis patients	8 (15%)
Spouses of HBsAg positives	7
Other family contacts, Including babies	8 (29%)
Priests	3 (5.7%)
Police	1 (2%)
Prison Staff	1 (2%)
Diabetic	1 (2%)
Total	52

* Associated with three clusters, see text.

transfusion hepatitis B cases has decreased significantly since 1980, with no cases detected since 1981.

Among all HBsAg positives detected, 170 (8.3%) were found to be HBsAg carriers and, of those tested in 1987, 67% remained carriers. The largest groups of carriers were drug-abusers

(29%) and IMH patients (26%). Only five donors are listed as carriers, a figure which is likely to be an underestimate for reasons discussed below. The minimum mean duration of carriage was 3.25 years, with one being followed up for 17 years. All cases of vertical transmission detected in this study have become carriers.

Discussion

Our data show that the mean annual incidence of hepatitis B has quadrupled since 1980, compared with the ten years before 1980. Although some of this increase may be due to greater awareness resulting in more testing, most is a result of the 15-fold increase in hepatitis B infections in an expanded population of intravenous drug-abusers. Prior to 1980 only 20% of HBsAg positives were intravenous drug-abusers, whereas since 1980, 72% of HBsAg positives were associated with intravenous drug-abuse and, additionally, 36% were also infected with hepatitis D³. Although there has been a reduction in the number of hepatitis B cases detected among drug-abusers since 1983, it may not reflect the true incidence, because of the probability that many cases in the “unknown” risk group may also be drug-associated.

We have also seen increases in hepatitis B cases in many non drug-abusing groups: the largest increase in incidence of hepatitis B has been among homosexuals and attenders at STD clinics, although the total number of positives (51) is not large compared with the number of cases among drug-abusers. However, the early figures may not be truly representative because the national STD service was not as well developed prior to 1980, or as freely used as in recent times, and there has since been a greater awareness of the possibilities of spread of hepatitis B by sexual contact.

Hepatitis has been recognised as a problem in institutions for the mentally handicapped since the identification of two types of hepatitis in patients at the Willowbrook State School by Krugman in the 1960's⁸. Occasional cases of acute hepatitis B have been detected in residents of such institutions in the

TABLE V

HBsAG Carriers in each Group.

Group	No.	Male/Fem.	Mean 1987 Age (range)	Mean duration of Carriage (range) mts.	No. known still positive in 1987 (%)
Drug-abuser	50	46/4	29.2 (21-39)	35 (6-108)	17 (34%)
IMH	44	32/12	38.3 (13-80)	20(6-180)	36 (89%)
Donors	5	4/1	insf. ages	55 (9-108)	1 (20%)
PTHB	2	1/1	53.0 (46, 60)	52 (7-96)	0
Hmx/STD	7	7/0	38.3 (24-61)	21 (6-72)	4 (57%)
Haemophiliac	8	8/0	28.0 (7-48)	31 (17-38)	5 (62%)
Visitors	3	3/0	41.6(30-61)	63 (10-132)	0
HCS	6	4/2	44.6 (30-66)	26 (9-48)	4 (67%)
Peri./vert.	5	3/2	8.4(2-18)	62 (10-204)	5(100%)
Misc.	7	4/3	30.3 (7-43)	33 (6-108)	3 (43%)
Unknown	33	23/10	46.7 (7-80)	32(6-120)	14 (42%)
Total	170	135/35	35.8 (2-80) yrs.	39 (6-204) months	88 (67%)

Peri./vert = perinatal or other vertical transmission. Other abbreviations as in Table I.

Republic and follow-up of immediate contacts of these cases at the time revealed other sub-clinical cases or carriers (Table I). Because of the recent introduction of hepatitis B vaccines a number of institutions were screened for hepatitis B markers in 1986 and 1987, preparatory to the use of vaccine. This revealed many more positives, with follow-up serology indicating that the majority were carriers. Some of these also had HBeAg and IgM anti-HBc, indicating infectivity and they constitute a considerable reservoir of infection in such institutions. Screening has revealed positive cases, mostly carriers, in all but one of 15 institutions sampled but there is no evidence to suggest that there has been any change in incidence in these institutions. The numbers of positives in institutions for the mentally handicapped in Table I, for 1986 and 1987, are relatively high because of the recent screenings and are therefore excluded from Figure 1 so as not to raise the real trend in population incidence. We have also found an increased incidence of hepatitis B infection among visitors to high-incidence areas of hepatitis B and among natives of such areas residing in Ireland. This increase may have been caused partly by increased foreign travel. Furthermore, many of these cases were missionaries visiting high-incidence areas, such as Africa, and some of them have also been involved in health-care in these areas. It is therefore difficult to be certain if their hepatitis B was acquired solely by health-care exposure. In such high-incidence areas, the risk of exposure to HBV in any one parenteral accident is increased, compared with such accidents in low-incidence areas.

Despite a much better awareness of the dangers of parenteral exposure and the adoption of general safety precautions by health-care staff when handling blood, the incidence among health-care staff has increased by 43% since 1980. However the potential exposure rate has increased about four-fold in this time due to the quadrupling of numbers of cases. Although a 43% increase in incidence compared with a four-fold increase in potential exposure is actually a decreased infection rate, it is far from satisfactory and serves to emphasize the real need for hepatitis B vaccination in health-care staff. A high incidence of hepatitis cases in Irish laboratories during the period 1975 to 1985 was also noted in the results of a recent questionnaire which included non-A, non-B hepatitis cases but no hepatitis B serology⁹.

There has also been a three-fold increase in the numbers of hepatitis B cases among haemophiliacs. Prior to 1980 nearly all blood products administered to haemophiliacs in the Irish Republic were prepared from native blood (I. Temperley, personal communication). Imported factor VIII concentrates are thought to have been responsible for some of the increase in numbers of hepatitis B cases, including at least two cases caused by a batch of imported concentrate which was subsequently found to be HBsAg positive.

Parenteral spread of hepatitis B, other than by IV drug-abuse or blood product usage, was well illustrated by the three clusters of cases occurring among persons with recent tattoos, indicating lack of sterilisation of tattooing needles as being the likely cause of these cases. It is worth emphasising that hepatitis B was only seen in tattooed persons where the tattooing was recent and not in cases where old tattoos were present. The presence of an old tattoo per se does not therefore constitute a requirement for testing.

Although eight cases have been associated with renal dialysis patients, some of whom have been visitors to Ireland, dialysis units in the Republic are being maintained with rigorous precautions, including a regular HBsAg screening programme, and are fortunately 'clean' by comparison with units in many countries.

Heterosexual transmission is believed to have occurred in 10 of 15 family contact cases, where one spouse either had clinical hepatitis within the previous six months or was known to be a carrier. The remaining five were all born to HBsAg positive mothers. Vertical transmission is frequently associated with subsequent carriage, and this was confirmed in all five cases.

We have not detected any HBsAg positive cases among dentists, although they have been shown elsewhere to be at increased risk of acquiring hepatitis B¹⁰. Prior to 1973, clinical hepatitis B was more frequently seen in the general population after the transfusion of infected blood and less often in intravenous drug-abusers'. Notwithstanding this, Ireland has one of the lowest rates of HBsAg positivity among blood donors in the world (0.01%). As expected, mass-screening of donated blood for HBsAg by the blood transfusion centres since 1973 has resulted in a dramatic reduction in post-transfusion hepatitis B. Indeed, no such cases have been detected since 1981. Although the number of positives referred to us by the blood transfusion services has decreased a little since 1980, the change is not statistically significant. This may seem a somewhat surprising finding, since spread from the drug-abusing group to the general population is an often mooted explanation for the increase in hepatitis B seen in non drug-abusing groups. Therefore one would expect to see an increase in the numbers of positive donors, but this did not occur. Direct evidence to clarify this could be gained by determining if there has been an increase in the proportion of non drug-abusers with the "ay" HBsAg subtype, which was predominant in drug-abusers, while non drug-abusers were mainly of the "ad" subtype¹¹, but this has not been carried out. It is not known what proportion of positive donors are followed up by their GP's and hence their source of infection is unknown to us. Since repeated testing is required to determine carrier status, if any, it is also unknown what proportion of HBsAg positive donors are carriers. Hence only five donors appear as "carriers" in Table V. However, tests have shown an absence of IgM anti-HBc and the presence of anti-HBe in many HBsAg positive donors (data not shown), suggesting that many of the HBsAg positive donors listed in Tables I and II are in fact healthy carriers.

Our data clearly shows that, in the Irish Republic, as elsewhere, hepatitis B is almost entirely acquired as a result of parenteral exposure (IV drug-abuse, accidentally or in institutions for the mentally handicapped) or by sexual contact or vertically and that the risk of acquiring hepatitis B post-transfusion is now minimal. Haemophiliacs have been at risk from imported concentrates; health-care staff, especially nurses and doctors have become infected from all risk-groups and members of the prison service and police force have also become infected by parenteral contact with drug-abusers. Hepatitis B vaccines now provide the means of eliminating the risk of acquiring hepatitis B occupationally or by social habits and are therefore being used in many at-risk groups in Ireland. In the future, therefore, we expect to see reductions in the incidence of hepatitis B in those groups in whom the vaccines are used.

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