

---

## Seropositivity for HIV in U.K. Haemophiliacs

Aids Group of the United Haemophilia Centre

*Phil. Trans. R. Soc. Lond. B* 1989 **325**, 179-183

doi: 10.1098/rstb.1989.0083

---

### Email alerting service

Receive free email alerts when new articles cite this article - sign up in the box at the top right-hand corner of the article or click [here](#)

---

To subscribe to *Phil. Trans. R. Soc. Lond. B* go to: <http://rstb.royalsocietypublishing.org/subscriptions>

---

## SEROPOSITIVITY FOR HIV IN U.K. HAEMOPHILIACS

AIDS GROUP OF THE UNITED KINGDOM HAEMOPHILIA CENTRE DIRECTORS  
WITH THE COOPERATION OF THE U.K. HAEMOPHILIA CENTRE DIRECTORS†

The results of a third seroprevalence survey of antibody to HIV in U.K. haemophiliacs, done in 1987, are presented. Out of 3028 men with haemophilia A living in the U.K. during the period 1980–1987 who had been tested for HIV antibody, 39% were positive, and out of 517 men tested with haemophilia B, 5% were positive. For both haemophilia types the proportion of seropositive men is greater among patients with a severe coagulation defect. No new seroconversions are known to have taken place after November 1986.

### 1. INTRODUCTION

Two surveys of the prevalence of antibody to HIV in U.K. haemophiliacs, carried out in 1985 and 1986, have been published (AIDS Group of the United Kingdom Haemophilia Centre Directors 1986, 1988). This paper gives results of a third seroprevalence survey, done in 1987. In addition to updating the information from earlier reports, the 1987 survey collected extra information about the date of the last seronegative test in patients for whom there was a subsequent seropositive test, thus enabling a more detailed investigation of the likely dates of the more recent seroconversions than was possible previously. The information from the 1987 survey, together with data from other surveys, has also enabled the cumulative incidence of AIDS in this group to be estimated. It was found that the rate of progression to AIDS was strongly dependent on age. The cumulative incidence amongst those aged less than 25 at their first seropositive test was 4% after 5 years, whereas for age groups 25–44 and 45+, 6% and 19% of patients respectively had developed AIDS. There was little evidence that the type or severity of haemophilia or the type of Factor VIII or IX that had caused HIV infection affected the rate of progression to AIDS. Details are published elsewhere (Darby *et al.* 1989).

### 2. PATIENTS AND METHODS

As in previous seroprevalence surveys, each of the 109 haemophilia centres in the U.K. was sent a computer printout showing the name, date of birth, and the National Haemophilia Registry number of patients with haemophilia A, B, or von Willebrand's disease who were known to have attended the centre during the period 1980–1987. The centres were asked to indicate on the printout those patients who had been tested for HIV antibody, the most recent test result and the date of the test. If the test was positive, the haemophilia centres were invited

† Report prepared by S. C. Darby, R. Doll, F.R.S., (Imperial Cancer Research Fund Cancer Epidemiology and Clinical Trials Unit, University of Oxford, Gibson Laboratories, Radcliffe Infirmary, Oxford OX2 5HE, U.K.), C. R. Rizza and R. J. D. Spooner (Oxford Haemophilia Centre, Churchill Hospital, Headington, Oxford OX3 7LJ, U.K.).

to supply the date of the first positive test and the date of the last negative test, if known. Information was requested for patients known to have died during this period as well as for those who were still alive. After the data from the 1987 survey was collated, a search was made of the results of the earlier surveys for any seropositive patients who were not included in the 1987 survey; information on these patients has been included in the present report.

All information received by August 1988 has been included, but patients known to be normally resident outside the U.K., one female patient, and one patient known to be homosexual have been excluded from the analysis.

### 3. RESULTS

#### 3.1. Prevalence of antibody to HIV

Ninety-four of the 109 haemophilia centres in the U.K. took part in the 1987 survey and a further six centres took part only in previous surveys. Out of a total of 4401 registered haemophiliacs who received blood products in the period 1980–1987, 3545 (81%) are known to have been tested (table 1), but among patients with a severe coagulation defect (factor VIII or IX level less than 2% of average normal) the proportion tested was appreciably higher (1931 out of 2170 or 89%). Altogether 1179 seropositive patients with haemophilia A and 27 patients with haemophilia B were identified. Among haemophilia A patients, 39% of those tested were seropositive, whereas for those with a severe coagulation defect the proportion was 58%. Among patients with haemophilia B the corresponding figures were 5% and 9% respectively. For five patients with haemophilia A who were reported to be seropositive in the 1987 survey, the date of their first positive test was not available. These have been included in table 1, but excluded from all further tables. The dates of earliest seropositivity ranged from December 1979 to November 1987 for haemophilia A patients and from February 1984 to September 1987 for haemophilia B patients (table 2). Explicit dates of the last negative test were available for 329 (28%) of the seropositive patients with haemophilia A, and 12 (44%)

TABLE 1. NUMBERS OF PATIENTS WITH HAEMOPHILIA A OR B REGISTERED IN U.K. WHO RECEIVED BLOOD PRODUCTS DURING 1980–1987, AND NUMBERS OF PATIENTS REPORTED AS TESTED AND FOUND TO BE SEROPOSITIVE IN THE THREE PREVALENCE SURVEYS, BY FACTOR VIII OR IX LEVEL

(Figures shown are totals for all three surveys. Patients known to have died since 1980 are included and patients who usually live overseas are excluded, as is one female patient and one known homosexual.)

	factor VIII or IX level (% of average normal)				total
	< 2	2–10	> 10	unknown	
haemophilia A:					
number registered	1890	1125	612	84	3711
number reported tested	1688	894	430	16	3028
number reported positive	972	164	39	4	1179
haemophilia B:					
number registered	280	279	107	24	690
number reported tested	243	209	57	8	517
number reported positive	21	5	1	0	27
all patients:					
number registered	2170	1404	719	108	4401
number reported tested	1931	1103	487	24	3545
number reported positive	993	169	40	4	1206

## HIV IN U.K. HAEMOPHILIACS

181

TABLE 2. CALENDAR DISTRIBUTION OF REPORTED DATES OF EARLIEST SEROPOSITIVE TESTS FOR PATIENTS WITH HAEMOPHILIA A OR B

(Many patients may well have seroconverted substantially before their first seropositive test.)

	haemophilia A patients	haemophilia B patients	all patients
1979 Jly-Dec.	1	—	1
1980 Jan.-Jun.	6	—	6
July-Dec.	12	—	12
1981 Jan.-Jun.	9	—	9
Jly-Dec.	13	—	13
1982 Jan.-Jun.	20	—	20
Jly-Dec.	29	—	29
1983 Jan.-Jun.	26	—	26
Jly-Dec.	56	—	56
1984 Jan.-Jun.	71	2	73
Jly-Dec.	205	6	211
1985 Jan.-Jun.	454	9	463
Jly-Dec.	187	5	192
1986 Jan.-Jun.	41	2	43
Jly-Dec.	31	1	32
1987 Jan.-Jun.	9	0	9
Jly-Dec.	4	2	6
total	1174	27	1201

TABLE 3. CALENDAR DISTRIBUTION OF REPORTED DATES OF LAST SERONEGATIVE TEST FOR PATIENTS WITH HAEMOPHILIA A OR B FOR WHOM A SUBSEQUENT SEROPOSITIVE TEST WAS AVAILABLE

	haemophilia A patients	haemophilia B patients	all patients
1979 Jan.-Jun.	4	—	4
Jly-Dec.	19	—	19
1980 Jan.-Jun.	27	—	27
Jly-Dec.	33	—	33
1981 Jan.-Jun.	16	1	17
Jly-Dec.	21	1	22
1982 Jan.-Jun.	21	—	21
Jly-Dec.	39	1	40
1983 Jan.-Jun.	11	3	14
Jly-Dec.	29	—	29
1984 Jan.-Jun.	25	1	26
Jly-Dec.	29	2	31
1985 Jan.-Jun.	45	3	48
Jly-Dec.	6	—	6
1986 Jan.-Jun.	2	—	2
Jly-Dec.	2	—	2
total	329	12	341

of those with haemophilia B. The calendar distribution of dates of the last seronegative test in patients for whom a subsequent seropositive test was available is given in table 3. For 10 patients, all with haemophilia A, a seronegative test was obtained on blood taken in or after July 1985, and a later test was seropositive, so that seroconversion apparently took place in or after July 1985. Details of these patients are given in table 4. Investigation revealed that 9 of the 10

TABLE 4. DETAILS OF 10 PATIENTS WITH HAEMOPHILIA A WITH LAST NEGATIVE TEST IN JULY 1985 OR LATER WHO HAD A SUBSEQUENT POSITIVE TEST

patient number	date of birth	date of last negative test	date of first positive test	factor VIII level (% of average normal)
1	10/39	11/07/85	31/07/85	0
2	12/46	—/08/85	—/08/86	0
3	09/79	24/09/85	08/11/85	0
4	01/75	—/10/85	—/03/86	0
5	01/76	—/10/85	02/05/86	2
6	08/65	—/11/85	24/10/86	0
7	03/62	07/03/86	29/09/86	0
8	12/74	07/05/86	16/06/86	5
9	05/80	28/09/86	19/11/86	0
10	05/78	03/10/86	25/10/86	0

patients were exposed to commercial material from a company whose licence was withdrawn in November 1986 because of known seroconversion after their product. Two of the 9 (patients 3 and 8) had received only this material; the remaining 7 had received it along with other commercial preparations or with National Health Service (NHS) material. One patient (number 4), who had received material from another company as well as NHS material, converted some time between October 1985 and March 1986.

#### 4. DISCUSSION

The estimated prevalence of antibody to HIV among patients with haemophilia A or B from this survey is very similar to that found in the earlier surveys on these patients. The earlier findings of an increased prevalence among those with a severe coagulation defect and among patients with haemophilia A as compared with haemophilia B are also confirmed. The probable reason for the different prevalences between patients with haemophilia A and haemophilia B is that, until heat treatment was introduced in the U.K. fractionation centres, most factor IX (the principal material received by patients with haemophilia B) that was used in the U.K. was derived from volunteer donor plasma collected in this country. Any commercial factor IX concentrates used, that would have been based on paid donor plasma from the U.S.A. were heat treated. In an earlier survey the prevalence of anti-HIV in patients with haemophilia B was roughly the same as that in haemophilia A patients who had received only NHS factor VIII concentrates (AIDS Group of the U.K. Haemophilia Centre Directors 1986). Heat treated commercial factor VIII concentrate was introduced into the U.K. in December 1984 and over the subsequent few weeks unheated concentrates were withdrawn. With regard to the NHS concentrates, heat-treated factor VIII became available from the Scottish National Blood Transfusion Service in December 1984 and from Blood Products Laboratory (BPL) Elstree in February 1985. By July 1985 only heat-treated factor VIII was being supplied by BPL. Heat-treated factor IX concentrate became available in August–September 1985, and by early October issues of unheated factor IX from BPL were discontinued. The period between HIV exposure and seroconversion is usually less than 14 weeks (Simmonds *et al.* 1988) but in rare cases it may exceed 6 months (Ranki *et al.* 1987). Thus the one patient who apparently seroconverted after all concentrate was heat-treated but who had not received material from the company whose licence was later withdrawn may have been

infected by one of the last few batches of unheated factor VIII. Individual donor testing was in place for all concentrates by November 1986, and no seroconversions are known to have taken place in or after November 1986. This accords with the results of a recent review of the safety of products used for treating haemophilia patients carried out at the U.S.A. Centers for Disease Control that concluded that cases of HIV seroconversion associated with the use of heat-treated products are now rare (Centers for Disease Control 1988).

We gratefully acknowledge the help of Mrs Irene Stratton, Mrs Valerie Weare, and Mrs Patricia Wallace in assembling the data, Sir David Cox for helpful discussions, and Mrs Cathy Harwood for typing the manuscript.

## REFERENCES

- AIDS Group of the U.K. Haemophilia Centre Directors 1986 Prevalence of antibody to HTLV III in haemophiliacs in the United Kingdom. A survey carried out by the AIDS Group of the United Kingdom Haemophilia Centre Directors with the co-operation of the United Kingdom Haemophilia Centre Directors. *Br. med. J.* **293**, 175–176.
- AIDS Group of the U.K. Haemophilia Centre Directors 1988 Prevalence of antibody to HIV in haemophiliacs in the United Kingdom: A second survey. *Clin. Lab. Haemat.* **10**, 187–191.
- Centres for Disease Control 1988 Safety of therapeutic products used for haemophilia patients. *Morbidity mortality wkly. Rep.* **37**, 441–450.
- Darby, S. C., Rizza, C. R., Doll, R., Spooner, R. J. D., Stratton, I. M. & Thakrar, B. 1989 Incidence of AIDS and excess of HIV associated mortality in U.K. haemophiliacs: report on behalf of the directors of haemophilia centres in the U.K. *Br. med. J.* **298**, 1064–1068.
- Ranki, A., Valle, S.-L., Krohn, M., Anttonen, J., Allain, J.-P., Leuther, M., Franchini, G. & Krohn, K. 1987 Long latency precedes overt sero-conversion in sexually transmitted human-immunodeficiency-virus infection. *Lancet* **ii**, 589–593.
- Simmonds, P., Lainson, F. A., Cuthbert, R., Sted, C. M., Peutherer, J. F. & Ludlam, C. A. 1988 HIV antigen and antibody detection: variable responses to infection in the Edinburgh haemophiliac cohort. *Br. med. J.* **296**, 593–598.