IN CONFIDENCE

NOTES FOR SCOTTISH HEALTH SERVICE HAEMOPHILIA CENTRE/ TRANSFUSION SERVICE DIRECTORS' MEETING

JANUARY 1983

S N B T S

JDC/SHHD/1/83/1

These notes have been produced primarily to facilitate discussion with regard to future SNBTS planning for the production of blood products associated with the management of patients with haemostatic or thrombotic manifestations. The figures given in this document refer to years ending 31st March.

FACTOR VIII CONCENTRATES

FRESH PLASMA PROCUREMENT

Progress made in the last 5 years has been maintained and consolidated. A summary of the trends over the past 5 years is given below (details in Appendix I).

Total Fresh Plasma Processed for VIII Concentrates (Kg.)

1978	1979	1980	1981	1982
19,581	20,553	25,059	28,474	35,748

ISSUES OF FACTOR VIII CONCENTRATES

The total issues for factor VIII concentrates from the Regional Transfusion Centres (cryoppt.) fell but there has been a substantial increase in issues of PFC product which largely parallels the increases in plasma procurement. These can be summarised as follows (details in Appendices II and III).

Total Cryoppt. Issued from RTCs (Donations)

1978	1979	1980	1981	1982
31,151	35,199	30,273	26,045	17,855

Total PFC Issues of Intermediate VIII (i.u. x 10^6) to RTCs

1978	1979	1980	1981	1982
1.55	1.66	1.99	3.58	4.70

COMMERCIAL FACTOR VIII PURCHASES

Recent evidence would indicate that the figures available to the SNBTS for this item may be in error (too low). It is hoped that improved precision will evolve in the near future. The figures available can be summarised as follows (details in Appendix IV).

SHS Commercial Purchases of Factor VIII (i.u. x 10^6)

1978	1979	1980	1981	1982
NK	0.85	0.98	1.37	1.4

Summary/

Summary Position (i.u. x 10^6) (Details in Appendix V)

	1978	1979	1980	1981	1982
Cryoppt.*	3.15	3.52	3.02	2.60	1.78
PFC	1.55	1.66	1.99	3.58	4.70
Commercial	(0.50)	0.85	1.00	1.37	1.40
Total	(5.2)	6.03	6.01	7.55	7.88

* Each donation is assumed to yield 100 i.u. of factor VIII.
Figures in brackets are 'guesstimates'.

NEW DEVELOPMENTS

(i) Freeze Dried Cryoprecipitate

The SNBTS would wish to put on record its thanks to colleagues in the West who undertook the successful clinical trial of the product produced at Law. Notwithstanding this work it has been decided to cease this activity in the light of closing down of the freeze dried plasma plant, the cost of meeting the demands of the Medicines Inspectorate and the recent evidence of imminent availability of a low risk factor VIII concentrate from commercial sources.

(ii) SNBTS Factor VIII Study Group

This Study Group was established in 1982 and is chaired by the NMD. The Group's activities include examination of ways by which the quality of fresh plasma fractionated at PFC can be improved. Satisfactory progress is being made and it is hoped that within the next 3 years significant benefits will accrue.

(iii) Higher purity Factor VIII concentrate

Rapid progress has been made following the last meeting of the Haemophilia/Transfusion Centre Directors during which it was requested that efforts be made at PFC to explore the possibility of producing an VIII concentrate with a low fibrinogen content. A new method has been developed and is currently subject to patent application. It is anticipated that by late 1983/early 1984 small amounts of the product will be released for limited clinical trials.

(iv) Heat treated Factor VIII concentrate

It is common knowledge that this type of product, which should have a reduced risk of transmitting hepatitis, will be commercially available in 1983 throughout/

throughout the UK. Colleagues at PFC have been working on this problem for some time and it is hoped that in 1983/84, in close association with the work referred to above (iii), that limited supplies will be available for clinical trials. The progress of this work has been slow, primarily due to a desire to minimise the deleterious effects on yield. Efforts are now being made to offset what is regarded as an inevitable yield penalty by the introduction of an additive anticoagulant programme at the RTCs. This programme will, in the fullness of time, yield a 25% increase of fresh plasma from existing donation input.

FACTOR IX CONCENTRATES

SUPPLY

(a) DEFIX

The supply position, with regard to DEFIX remains strong and the issues from PFC to RTCs reasonably stable. The position over the last 5 years can be summarised as follows:-

DEFIX Issues from PFC to RTCs (i.u. of IX x 10^6)

1978	1979	1980	1981	1982
1.1	0.86	1.0	0.89	0.91

(b) PPSB

The demand for a factor VII containing factor IX concentrate remains, albeit low. The position over the last 5 years can be summarised as follows:-

PPSB Issues from PFC to RTCs (i.u. of IX)

1978	1979	1980	1981	1982
130,000	70,000	45,000	66,000	30,000

DEVELOPMENTS

(i) Supernine (SIX)

This product, a more purified form of DEFIX and believed to have a reduced hepatitis transmission risk, has now almost completed those clinical studies from which data will be generated for submission for a product licence. This work has been organised by Dr Frank Boulton, but thanks are due to colleagues in the Haemophilia Centres of Edinburgh and Glasgow. The results, to date, look excellent.

(ii)/

(ii) Future Status of DEFIX

It had been anticipated that the introduction of SIX to routine clinical practice would permit the withdrawal of DEFIX from PFC's product range. Recent exploration of the feasibility of producing an activated IX concentrate for the management of haemophilia A patients with inhibitors has led us to reconsider the desirability of abandoning DEFIX prematurely. This decision has been fortified by the recent information following contact with colleagues in the US who have intimated that the 'proplex'/'autoplex' clinical trial has revealed no significant difference. Accordingly, a more detailed analysis of the constituents of PPSB, DEFIX and SIX is currently underway, as are studies with colleagues in NIBSC in the general area of new products for the management of haemophilia A with inhibitors.

(iii) Heat treated Factor IX concentrate

Heat treatment studies, to reduce the hepatitis risk, are currently underway, using SIX. It is probable that the rate of progress with this product will be slower than factor VIII because it will be necessary to submit the heated IX concentrate to intensive animal studies prior to administration to patients, in order to confirm that the heat reatment has not resulted in the evolution of a thrombogenic product.

It should be noted that the forthcoming arrival of a hepatitis 'safe' factor IX concentrate will raise the clinical demand for a prothrombin complex concentrate. The current inhibition to its use in patients with liver disease and oral anti-coagulants will be removed. This increased demand might necessitate a production target (vials on shelf) as much as 50% of existing programme.

FACTOR VII CONCENTRATE

There is a view, strongly held by some (including the author) that a small number of patients with acquired severe forms of prothrombin complex deficiency require factor VII to arrest bleeding. At the present time the SNBTS makes PPSB available for this use. PPSB is an unsatisfactory product from a manufacturing point of view (requires EDTA plasma) and PFC has now made significant progress towards the production of a VII concentrate. This product should be animal tested (thrombogenicity) in 1983 and be available for clinical evaluation in 1983/84. Dr John Davidson has kindly agreed to collaborate with the NMD on this project.

ANTITHROMBIN III CONCENTRATE

It is hoped that by the end of 1983 PFC will have reduced to practice (into production) their successful development programme designed to make available a heat treated antithrombin III (AT-III) concentrate.

The demands for this product are now under serious review. There seems little doubt that it will be of benefit to those patients, which are increasingly being recognised, who have a congenital deficiency associated with recurrent thrombotic problems. The biggest potential demand may arise from acquired deficiencies. However, the data available at the present time leads the author to conclude that considerable caution is required and that the SNBTS should endeavour to promote clinical research in this area within the SHS and, at the same time, maintain contact with colleagues overseas.

It is hoped that preliminary clinical evaluation (in congenitally deficient patients) of the SNBTS product will be initiated in 1983/84. In preparation for this work the SNBTS gratefully acknowledge the efforts of clinical colleagues throughout Scotland who have already agreed to participate.

MISCELLANEOUS

ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS)

The attention of the Haemophilia Directors is drawn to this problem (Appendix VI). It is noted that in the US the National Haemophilia Foundation and CDC are already conducting a survey and intend to establish a permanent surveillance programme. The information contained in Appendix VI has been sent to Professor A L Bloom, Chairman of the UK Haemophilia Centre Directors' meeting.

PFC REFIT

The PFC is currently in the throes of the initial stages of a major refit, in order to bring it up to the standards required by Medicines Division (DHSS). There can be no doubt that despite the efforts of PFC staff there will be periods over the next 3 years during which all or part of production will cease for short periods of time. This will inevitably have some consequences on supply of products and Haemophilia Directors are strongly advised to maintain close liaison with their Regional Transfusion Directors with regard to the availability of factor VIII concentrate, in particular. In the meantime, regional/

regional allocations of intermediate factor VIII are being somewhat restricted so that sufficient national stocks can be acquired to cover any 'close-down' periods.

OXFORD RETURNS

The SNBTS would wish to record its thanks and appreciation to Dr Charles Rizza and his staff at the Oxford Haemophilia Centre for providing a complete breakdown of the UK Haemophilia Centre Directors' Annual Returns, with respect to Scotland.

Dr Ludlam may wish to comment on certain matters of detail but the following information of interest to both Haemophilia and Transfusion Centre Directors has been extracted:-

Use of All factor VIII (1.u. x 10^6)

	1980*			1981		
	Total Use	Use/ 10^6 pop.	% Commercial	Total Use	Use/ 10^6 pop.	% Commercial
E/W & NI	52.29	1.05	67	60.05	1.20	54
Scotland	5.38	1.08	20	5.65	1.01	22

* Calendar years

SNBTS FRESH PLASMA PROCUREMENT FOR FACTOR VIII CONCENTRATE PRODUCTION (Kg.)

		1978		1979		1980		1981		1982	
		Kg.	Kg/ 10^6 pop	Kg.	Kg/ 10^6 pop	Kg.	Kg/ 10^6 pop	Kg.	Kg/ 10^6 pop	Kg.	Kg/ 10^6 pop
ABERDEEN	Cryoppt.	257		220		449		333		200	
	To PFC	654		1,188		1,831		1,587		2,221	
	Total	911	1,833	1,308	2,632	2,280	4,588	1,920	3,863	2,421	4,871
DUNDEE	Cryoppt.	200		123		57		120		125	
	To PFC	864		1,006		1,572		1,423		2,429	
	Total	1,064	2,269	1,129	4,838	1,629	3,473	1,543	3,290	2,554	5,446
EDINBURGH	Cryoppt.	1,994		2,720		3,183		3,694		1,946	
	To PFC	4,985		3,982		3,786		3,821		6,256	
	Total	6,979	6,187	5,602	4,966	6,969	6,178	7,515	6,263	8,202	6,835
GLASGOW	Cryoppt.	3,765		3,678		2,785		1,341		1,068	
	To PFC	5,573		7,322		9,574		14,200		18,965	
	Total	9,338	3,264	11,000	3,845	12,359	4,320	15,541	5,359	20,033	6,908
INVERNESS	Cryoppt.	Nil		11		3		10		2	
	To PFC	1,289		1,503		1,819		1,945		2,536	
	Total	1,289	5,729	1,514	6,729	1,822	8,098	1,955	8,689	2,538	11,280
GRAND TOTALS		19,581	3,856	20,553	4,602	25,059	5,314	28,474	5,476	35,748	6,875

Note: Volume of plasma calculated for cryoppt. by multiplying by 0.2 total donations.

APPENDIX I

SNB.013.7609

SNBTS: RTC ISSUES OF CRYOPPT. (DONATIONS)

	1978	1979	1980	1981	1982
Aberdeen	1,228	1,320	1,987	1,585	1,014
Dundee	922	603	343	551	555
Edinburgh	11,069	13,329	15,375	17,358	9,221
Glasgow	17,932	19,922	12,568	6,551	7,065
Inverness	Nil	25	Nil	Nil	Nil
TOTALS	31,151	35,199	30,273	26,045	17,855

APPENDIX II

SNB.013.7610

PFC ISSUES OF FACTOR VIII TO RTCs (i.u. x 10^6)

	1978	1979	1980	1981	1982
Aberdeen	0.09 (0.18)	0.12 (0.24)	0.10 (0.18)	0.16 (0.33)	0.37 (0.74)
Dundee	0.09 (0.20)	0.10 (0.22)	0.14 (0.32)	0.16 (0.33)	0.37 (0.79)
Edinburgh	0.21 (0.18)	0.31 (0.26)	0.28 (0.23)	1.01 (0.84)	0.87 (0.73)
Glasgow	0.90 (0.31)	0.95 (0.33)	1.33 (0.46)	1.92 (0.66)	2.62 (0.90)
Inverness	0.14 (0.64)	0.18 (0.80)	0.13 (0.61)	0.25 (1.00)	0.47 (2.1)
TOTALS	1.55 (0.30)	1.66 (0.32)	1.99 (0.38)	3.58 (0.69)	4.70 (0.90)

Figures in brackets per 10^6 population

APPENDIX III

SNB.013.7611

SHS PURCHASE OF COMMERCIAL FACTOR VIII CONCENTRATES (i.u. x 10^6)*

	1978	1979	1980	1981	1982
Aberdeen	Nil	0.01	Nil	Nil	Nil
Dundee	Nil	Nil	Nil	Nil	Nil
Edinburgh	Nil	Nil	Nil	0.46	0.73
Glasgow	(0.50)	0.85	0.98	0.91	0.67
Inverness	Nil	Nil	Nil	Nil	Nil
TOTALS	(0.50)	0.86	0.98	1.37	1.40

* Information obtained by SNBTS Directors from Haemophilia Directors/Pharmacists

Figures in brackets - guesstimate

APPENDIX IV

SNB.013.7612

SHS: TOTAL "USE" OF FACTOR VIII CONCENTRATES (i.u. x $10^6/10^6$ POPULATION*

	1978	1979	1980	1981	1982
Aberdeen	0.42	0.52	0.60	0.64	0.95
Dundee	0.41	0.34	0.36	0.45	0.90
Edinburgh	1.10	1.42	1.52	2.66	2.10
Glasgow	0.71	1.32	1.23	1.2	1.38
Inverness	0.64	0.80	0.61	1.00	2.10
TOTALS	0.66	0.88	0.86	1.19	1.49

* The word "use" is not strictly accurate. The figures are derived from RTC issues of cryoppt., PFC issues of intermediate VIII and commercial purchases of VIII concentrate in each year.

APPENDIX V

SNB.013.7613

Alcohol-Related Fatalities – Continued

addition, the Department will be involved in the "National Drunk and Drugged Driving Awareness Week," December 12-18, 1982.

5. Communication has been established with the World Health Organization to develop a collaborative relationship on the issue.
6. Studies to examine the medical and developmental consequences of youth alcohol consumption are being undertaken.

Selected Bibliography

1 Malin HJ, Graves C, Harford TC, Kaelber CT. Alcohol-related traffic fatalities: findings from the Fatal Accident Reporting System (FARS) (in press).
2. Malin HJ, Munch NE, Archer LD. A National surveillance system for alcoholism and alcohol abuse. In: Proceedings of the 32nd International Congress on Alcoholism and Drug Dependence. Congress held Warsaw, Poland, 1978.

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Epidemiologic Notes and Reports

Update on Acquired Immune Deficiency Syndrome (AIDS) among Patients with Hemophilia A

In July 1982, three heterosexual hemophilia A patients, who had developed *Pneumocystis carinii* pneumonia and other opportunistic infections, were reported (*1*). Each had in vitro evidence of lymphopenia and two patients who were specifically tested had evidence of T-lymphocyte abnormalities. All three have since died. In the intervening 4 months, four additional heterosexual hemophilia A patients have developed one or more opportunistic infections accompanied by in-vitro evidence of cellular immune deficiency; these four AIDS cases and one highly suspect case are presented below. Data from inquiries about the patients' sexual activities, drug usage, travel, and residence provide no suggestion that disease could have been acquired through contact with each other, with homosexuals, with illicit drug abusers, or with Haitian immigrants—groups at increased risk for AIDS compared with the general U.S. population. All these patients have received Factor VIII concentrates, and all but one have also received other blood components.

Case 1: A 55-year-old severe hemophiliac from Alabama developed anorexia and progressive weight loss beginning in September 1981. He had developed adult-onset diabetes mellitus in 1973, which had required insulin therapy since 1978. He had had acute hepatitis (type unknown) in 1975. In March 1982, he was hospitalized for herpes zoster and a 17-kg weight loss. Hepatosplenomegaly was noted. The absolute lymphocyte count was 450/mm^3. Liver enzymes were elevated; antibodies to hepatitis B core and surface antigens were present. A liver biopsy showed changes consistent with persistent hepatitis. Evaluation for an occult malignancy was negative. The zoster resolved following 5 days of adenosine arabinoside therapy.

In early June, he was readmitted with fever and respiratory symptoms. Chest x-ray showed bibasilar infiltrates. No causative organism was identified, but clinical improvement occurred coincident with administration of broad spectrum antibiotics. Laboratory studies as an outpatient documented transient thrombocytopenia (63,000/mm^3) and persistent inversion of his T-helper/T-suppressor ratio (T_H/T_S =0.2). He was readmitted for the third time in early September with fever, chills and nonproductive cough. His cumulative weight loss was

Acquired Immune Deficiency Syndrome – Continued

now 47 kg. Chest x-ray demonstrated bilateral pneumonia, and open lung biopsy showed infection with *P. carinii*. He responded to sulfamethoxazole/trimethoprim (SMZ/TMP). His T-cell defects persist.

Case 2: A 10-year-old severe hemophiliac from Pennsylvania had been treated with Factor VIII concentrate on a home care program. He had never required blood transfusion. He had been remarkably healthy until September 1982 when he experienced intermittent episodes of fever and vomiting. Approximately 2 weeks later, he also developed persistent anorexia, fatigue, sore throat, and nonproductive cough. On October 20, he was admitted to a hospital with a temperature of 38.4 C (101.2 F) and a respiratory rate of 60/min. Physical examination revealed cervical adenopathy but no splenomegaly. The absolute number of circulating lymphocytes was low (580/mm^3) and the T-helper/T-suppressor ratio was markedly reduced (T_H/T_S = 0.1). His platelet count was 171,000/mm^3. Serum levels of IgG, IgA, and IgM were markedly elevated. Chest x-rays showed bilateral pneumonia and an open lung biopsy revealed massive infiltration with *P. carinii* and *Cryptococcus neoformans*. Intravenous SMZ/TMP and amphotericin B have led to marked clinical improvement, but the T-cell abnormalities persist.

Case 3: A 49-year-old patient from Ohio with mild hemophilia had been treated relatively infrequently with Factor VIII concentrate. During the summer of 1982, he noted dysphagia and a weight loss of approximately 7 kg. In October, he was treated for cellulitis of the right hand. Two weeks later, he was observed by a close relative to be dyspneic. He was admitted in November with progressive dyspnea and diaphoresis. Chest x-rays suggested diffuse pneumonitis. His WBC count was 11,000/mm^3 with 9% lymphocytes (absolute lymphocyte number 990/mm^3). The T_H/T_S ratio was 0.25. Open lung biopsy revealed *P. carinii*. The patient was treated with SMZ/TMP for 6 days with no improvement, and pentamidine isethionate was added. Virus cultures of sputum and chest tube drainage revealed herpes simplex virus. He died on November 22.

Case 4: A 52-year-old severe hemophiliac from Missouri was admitted to a hospital in April 1982 with fever, lymphadenopathy, and abdominal pain. Persistently low numbers of circulating lymphocytes were noted (480/mm^3). Granulomata were seen on histopathologic examination of a bone marrow aspirate. Cultures were positive for *Histoplasma capsulatum*. The patient improved after therapy with amphotericin B. During the following summer and early fall, he developed fever, increased weight loss, and difficulty thinking. On readmission in early November, he had esophageal candidiasis. Laboratory tests showed profound leukopenia and lymphopenia. A brain scan showed a left frontal mass, which was found to be an organizing hematoma at the time of craniotomy. A chest x-ray showed "fluffy" pulmonary infiltrates. Therapy with SMZ/TMP was begun. Exploratory laparotomy revealed no malignancy. A splenectomy was performed. Biopsies of liver, spleen, and lymph node tissues were negative for *H capsulatum* granulomata. The lymphoid tissue including the spleen showed an absence of lymphocytes. His total WBC declined to 400/mm^3 and the T_H/T_S cell ratio was 0.1. He died shortly thereafter.

Suspect Case: Described below is an additional highly suspect case that does not meet the strict criteria defining AIDS. A 7-year-old severe hemophiliac from Los Angeles had mild mediastinal adenopathy on chest x-ray in September 1981. In March 1982, he developed a spontaneous subdural hematoma requiring surgical evacuation. In July, he developed parotitis. In August, he developed pharyngitis and an associated anterior and posterior cervical adenopathy, which has not resolved. In late September, he developed herpes zoster over the right thigh and buttock, and oral candidiasis. Chest x-rays revealed an increase of the mediastinal adenopathy and the appearance of new perihilar infiltrates. In late October, enlarge-

APPENDIX VI

SNB.013.7614

Acquired Immune Deficiency Syndrome – Continued

ment of the cervical nodes led to a lymph node biopsy. Architectural features of the node were grossly altered, with depletion of lymphocytes. Heterophile tests were negative. IgG, IgA, and IgM levels were all elevated. He has a marked reduction in T-helper cells and a T_H/T_S ratio equal to 0.4. Recent progressive adenoid enlargement has caused significant upper airway obstruction and resultant sleep apnea.

Reported by M-C Poon, MD, A Landay, PhD, University of Alabama Medical Center, J Alexander, MD, Jefferson County Health Dept, W Birch, MD, State Epidemiologist, Alabama Dept of Health; ME Eyster, MD, H Al-Mondhiry, MD, JO Ballard, MD, Hershey Medical Center, E Witte, VMD, Div of Epidemiology, C Hayes, MD, State Epidemiologist, Pennsylvania State Dept of Health; LO Pass, MD, JP Myers, MD, J Politis, MD, R Goldberg MD, M Bhatti, MD, M Arnold, MD, J York, MD, Youngstown Hospital Association, T Halpin, MD, State Epidemiologist, Ohio Dept of Health; L Herwaldt, MD, Washington University Medical Center, A Spivack, MD, Jewish Hospital, St Louis, HD Donnell MD, State Epidemiologist, Missouri Dept of Health; D Powars, MD, Los Angeles County-University of Southern California Medical Center, SL Fannin, MD, Los Angeles County Dept of Health Svcs, J Chin, MD, State Epidemiologist, California State Dept of Health; AIDS Activity, Div of Host Factors, Div of Viral Diseases, Center for Infectious Diseases, Field Svcs Div, Epidemiology Program Office, CDC.

Editorial Note: These additional cases of AIDS among hemophilia A patients share several features with the three previously reported cases. All but one are severe hemophiliacs, requiring large amounts of Factor VIII concentrate. None had experienced prior opportunistic infections. All have been profoundly lymphopenic (< 1000 lymphocytes/mm^3) and have had irreversible deficiencies in T-lymphocytes. Clinical improvement of opportunistic infections with medical therapy has been short lived. Two of the five have died.

(Continued on page 652)

TABLE I. Summary—cases of specified notifiable diseases, United States.

Disease	48th Week Ending			Cumulative, First 48 Weeks		
	December 4, 1982	December 5, 1981	Median 1977-1981	December 4, 1982	December 5, 1981	Median 1977-1981
Aseptic meningitis	216	125	127	8,506	8,931	7,262
Brucellosis	1	3	3	147	163	187
Encephalitis Primary (arthropod-borne & unspec.)	38	17	20	1,347	1,393	1,113
Post-infectious		3	3	56	86	202
Gonorrhea Civilian	16,795	17,956	19,839	881,075	923,109	923,923
Military	289	770	461	23,944	25,597	24,753
Hepatitis Type A	470	518	556	20,940	23,303	26,940
Type B	431	487	340	19,870	19,050	15,066
Non A, Non B	56	N	N	2,162	N	N
Unspecified	173	230	222	8,135	9,988	9,613
Legionellosis	13	N	N	503	N	N
Leprosy	2	11	7	186	233	160
Malaria	23	21	21	965	1,279	725
Measles (rubeola)	4	35	112	1,583	2,891	13,255
Meningococcal infections Total	42	64	49	2,705	3,239	2,385
Civilian	42	63	49	2,692	3,216	2,365
Military	-	1	-	13	13	18
Mumps	111	182	243	4,855	4,266	12,833
Pertussis	55	19	34	1,608	1,135	1,568
Rubella (German measles)	19	29	89	2,189	1,966	11,304
Syphilis (Primary & Secondary) Civilian	563	598	515	30,265	28,595	23,032
Military	2	5	6	405	351	290
Tuberculosis	578	533	596	23,690	25,101	25,261
Tularemia	4	9	4	234	260	178
Typhoid fever	3	8	12	368	530	489
Typhus fever, tick-borne (RMSF)	4	5	6	966	1,160	1,109
Rabies, animal	116	108	77	5,736	6,730	4,672

TABLE II. Notifiable diseases of low frequency, United States

	Cum 1982		Cum 1982
Anthrax	-	Poliomyelitis: Total	7
Botulism (Calif. 1)	76	Paralytic (Ind 1, Wash 1)	7
Cholera	-	Psittacosis	113
Congenital rubella syndrome	6	Rabies, human	-
Diphtheria	3	Tetanus	74
Leptospirosis	67	Trichinosis (N J 1)	82
Plague	18	Typhus fever, flea-borne (endemic, murine) (Tex 1)	40

Acquired Immune Deficiency Syndrome – Continued

In most instances, these patients have been the first AIDS cases in their cities, states, or regions. They have had no known common medications, occupations, habits, types of pets, or any uniform antecedent history of personal or family illnesses with immunological relevance.

Although complete information is not available on brands and lot numbers for the Factor VIII concentrate used by these additional five patients during the past few years, efforts to collect and compare these data with information obtained from the earlier three cases are under way. No common lot number has been found among the lots of Factor VIII given to the five patients from whom such information is currently available.

These additional cases provide important perspectives on AIDS in U.S. hemophiliacs. Two of the patients described here are 10 years of age or less, and children with hemophilia must now be considered at risk for the disease. In addition, the number of cases continues to increase, and the illness may pose a significant risk for patients with hemophilia.

The National Hemophilia Foundation and CDC are now conducting a national survey of hemophilia treatment centers to estimate the prevalence of AIDS-associated diseases during the past 5 years and to provide active surveillance of AIDS among patients with hemophilia.

Physicians are encouraged to continue to report AIDS-suspect diseases among hemophilia patients to the CDC through local and state health departments.

Reference

1. CDC. *Pneumocystis carinii* pneumonia among persons with hemophilia A. MMWR 1982; 31:365-7.

Possible Transfusion-Associated Acquired Immune Deficiency Syndrome (AIDS) — California

CDC has received a report of a 20-month old infant from the San Francisco area who developed unexplained cellular immunodeficiency and opportunistic infection. This occurred after multiple transfusions, including a transfusion of platelets derived from the blood of a male subsequently found to have the acquired immune deficiency syndrome (AIDS).

The infant, a white male, was delivered by caesarian section on March 3, 1981. The estimated duration of pregnancy was 33 weeks; and the infant weighed 2650 g. The mother was known to have developed Rh sensitization during her first pregnancy, and amniocentesis done during this, her second, pregnancy showed the fetus had erythroblastosis fetalis. The infant had asphyxia at birth and required endotracheal intubation. Because of hyperbilirubinemia, six double-volume exchange transfusions were given over a 4-day period. During the 1-month hospitalization following birth, the infant received blood products, including whole blood, packed red blood cells, and platelets from 19 donors. All blood products were irradiated.

After discharge in April 1981, the infant appeared well, although hepatosplenomegaly was noted at age 4 months. At 7 months, he was hospitalized for treatment of severe otitis media. Oral candidiasis developed following antibiotic therapy and persisted. At 9 months of age, he developed anorexia, vomiting, and then jaundice. Transaminase levels were elevated, and serologic tests for hepatitis A and B viruses and cytomegalovirus were negative; non-A non-B hepatitis was diagnosed.