

*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*

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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<sup>3</sup>. 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<sup>3</sup>) and persistent inversion of his T-helper/T-suppressor ratio (T<sub>H</sub>/T<sub>S</sub> = 0.2). He was readmitted for the third time in early September with fever, chills and nonproductive cough. His cumulative weight loss was

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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<sup>3</sup>) and the T-helper/T-suppressor ratio was markedly reduced ( $T_H/T_S = 0.1$ ). His platelet count was 171,000/mm<sup>3</sup>. 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<sup>3</sup> with 9% lymphocytes (absolute lymphocyte number 990/mm<sup>3</sup>). 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<sup>3</sup>). 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<sup>3</sup> 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-

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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.

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**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<sup>3</sup>) 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.

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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	218	125	127	8,508	8,831	7,282
Brucellosis	1	3	3	147	163	187
Encephalitis: Primary (arthropod-borne & unspc)	38	17	20	1,347	1,393	1,113
Post-infectious	-	3	3	58	88	202
Gonorrhea: Civilian	18,795	17,956	19,839	881,075	923,108	823,923
Military	289	770	461	23,944	25,597	24,753
Hepatitis: Type A	470	518	556	20,940	23,303	28,940
Type B	431	487	340	19,870	19,050	15,066
Non A, Non B	58	N	N	2,162	N	N
Unspecified	173	230	222	8,135	9,988	9,813
Legionellosis	13	N	N	503	N	N
Leprosy	2	11	7	188	233	180
Malaria	23	21	21	965	1,278	725
Measles (rubella)	4	35	112	1,583	2,891	13,255
Meningococcal infections: Total	42	84	48	2,705	3,228	2,385
Civilian	42	63	48	2,692	3,216	2,365
Military	-	1	-	13	13	18
Mumps	111	182	243	4,855	4,266	12,833
Pertussis	95	18	34	1,808	1,135	1,568
Rubella (German measles)	13	28	89	2,189	1,966	11,304
Syphilis (Primary & Secondary): Civilian	563	598	615	30,265	28,595	23,032
Military	2	5	6	405	351	280
Tuberculosis	578	533	596	23,890	25,101	25,281
Tularaemia	6	9	4	234	260	178
Typhoid fever	3	8	12	368	530	489
Typhus fever, tick-borne (RMSF)	4	6	5	868	1,160	1,109
Rabies, animal	118	108	77	5,736	6,730	4,672

TABLE II. Notifiable diseases of low frequency, United States

Disease	Cum 1982	Cum 1982
Anthrax	-	7
Botulism (Calif. 1)	78	7
Cholera	-	113
Congenital rubella syndrome	6	-
Diphtheria	3	74
Leptospirosis	67	82
Plague	18	40
Poliomyelitis: Total	-	7
Paralytic (Ind. 1, Wash. 1)	-	7
Psittacosis	-	113
Rabies, human	-	-
Tetanus	3	74
Trichinosis (W.J. 1)	-	82
Typhus fever, flea-borne (endemic, murine) (Tex. 1)	-	40

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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 2850 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.

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At 14 months of age, the infant developed neutropenia and an autoimmune hemolytic anemia and thrombocytopenia. Immunologic studies showed elevated serum concentrations of IgG, IgA, and IgM, decreased numbers of T-lymphocytes, and impaired T-cell function in vitro. Following these studies, he was begun on systemic corticosteroid therapy for his hematologic disease. Three months later, a bone marrow sample, taken before steroid therapy began, was positive for *Mycobacterium avium-intracellulare*. Cultures of urine and gastric aspirate, taken while the infant received steroids, also grew *M. avium-intracellulare*. The infant is now receiving chemotherapy for his mycobacterial infection. He continues to have thrombocytopenia.

The parents and brother of the infant are in good health. The parents are heterosexual non-Haitians and do not have a history of intravenous drug abuse. The infant had no known personal contact with an AIDS patient.

Investigation of the blood products received by the infant during his first month of life has revealed that one of the 19 donors was subsequently reported to have AIDS. The donor, a 48-year-old white male resident of San Francisco, was in apparently good health when he donated blood on March 10, 1981. Platelets derived from this blood were given to the infant on March 11. Eight months later, the donor complained of fatigue and decreased appetite. On examination, he had right axillary lymphadenopathy, and cotton-wool spots were seen in the retina of the left eye. During the next month, December 1981, he developed fever and severe tachypnea and was hospitalized with biopsy-proven *Pneumocystis carinii* pneumonia.

Although he improved on antimicrobial therapy and was discharged after a 1-month hospitalization, immunologic studies done in March 1982 showed severe cellular immune dysfunction typical of AIDS. In April 1982, he developed fever and oral candidiasis, and began to lose weight. A second hospitalization, beginning in June 1982, was complicated by *Salmonella* sepsis, perianal herpes simplex virus infection, encephalitis of unknown etiology, and disseminated cytomegalovirus infection. He died in August 1982.

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**Editorial Note:** The etiology of AIDS remains unknown, but its reported occurrence among homosexual men, intravenous drug abusers, and persons with hemophilia A (1) suggests it may be caused by an infectious agent transmitted sexually or through exposure to blood or blood products. If the infant's illness described in this report is AIDS, its occurrence following receipt of blood products from a known AIDS case adds support to the infectious-agent hypothesis.

Several features of the infant's illness resemble those seen among adults with AIDS. Hypergammaglobulinemia with T-cell depletion and dysfunction are not typical of any of the well-characterized congenital immunodeficiency syndromes (2), but are similar to abnormalities described in AIDS (3). Disseminated *M. avium-intracellulare* infection, seen in this infant, is a reported manifestation of AIDS (4). Autoimmune thrombocytopenia, also seen in this infant, has been described among several homosexual men with immune dysfunction typical of AIDS (5). Nonetheless, since there is no definitive laboratory test for AIDS, any interpretation of this infant's illness must be made with caution.

If the platelet transfusion contained an etiologic agent for AIDS, one must assume that the agent can be present in the blood of a donor before onset of symptomatic illness and that the incubation period for such illness can be relatively long. This model for AIDS transmission is

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consistent with findings described in an investigation of a cluster of sexually related AIDS cases among homosexual men in southern California (6).

Of the 788 definite AIDS cases among adults reported thus far to CDC, 42 (5.3%) belong to no known risk group (i.e., they are not known to be homosexually active men, intravenous drug abusers, Haitians, or hemophiliacs). Two cases received blood products within 2 years of the onset of their illnesses and are currently under investigation.

This report and continuing reports of AIDS among persons with hemophilia A (7) raise serious questions about the possible transmission of AIDS through blood and blood products. The Assistant Secretary for Health is convening an advisory committee to address these questions.

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3. Gottlieb MS, Schroff R, Schanker HM, et al. *Pneumocystis carinii* pneumonia and mucosal candidiasis in previously healthy homosexual men: evidence of a new acquired cellular immunodeficiency. N Engl J Med 1981;305:1425-31.
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6. CDC. A cluster of Kaposi's sarcoma and *Pneumocystis carinii* pneumonia among homosexual male residents of Los Angeles and Orange Counties, California. MMWR 1982;31:305-7.
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**Update: Influenza Virus A(H3N2) Isolations — United States**

Three additional states, Pennsylvania, Tennessee, and Washington, as well as upstate New York, have reported influenza virus type A(H3N2) isolations. The isolates were collected from patients who had onset of influenza from mid to late November in Pittsburgh, Pennsylvania (1 case), Nashville, Tennessee (2 cases), and Skagit County, Washington (2 cases). The isolate from upstate New York was obtained from a 16-year-old female who had visited in Ottawa, Canada, for approximately 2 days, when she had onset of influenza on November 19. She returned to her home in Rochester, New York, on November 21, and a specimen was collected for virus testing on November 22.

Isolations of H3N2 influenza virus had earlier been reported from Alaska, New York City, Oregon, and Virginia (1). Alaska has widespread outbreaks of influenza, and 33 isolates of influenza virus, all H3N2, have now been identified. Isolates from other locations have been associated with sporadic cases of influenza rather than outbreaks.

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