Summary Report on Open Meeting of PHS Committee on Opportunistic Infections in Patients with Hemophilia

I. The Meeting

On July 27, 1982, from 8:30 a.m. to 4:30 p.m. a meeting was held to consider the significance of the occurrence of opportunistic infections (OI) with Pneumocystis carinii pneumonia (PCP) in three patients with hemophilia.

Invited participants included representatives of the CDC, FDA, NIH, National Hemophilia Foundation, American National Red Cross, various blood banking organizations, National Gay Task Force, New York City Health Department, and the New York Inter-Hospital Study Group on the Acquired Immune Deficiency Syndrome (AIDS) and Kaposi's Sarcoma (KS) (Attachment 1).

The morning was spent reviewing the various contributory disciplines related to the problem: the epidemiology of AIDS/KS; immunosuppression associated with AIDS/KS; the course, complications, etc. of hemophilia; description of Factor VIII concentrate and other blood products; and a description of the three hemophilia patients with opportunistic infections.

The afternoon was spent discussing the significance of the finding and the appropriate course of action.

II. Aspects of Discussion

A. AIDS (and the sequelae of KS and OI) are occurring in several populations—homosexual men, recent Haitian entrants and I.V. drug abusers. The possibility exists that it is occurring in patients with hemophilia.

B. If the PCP observed in three patients with hemophilia represents the same process as seen in other groups with AIDS, then a possible mode of transmission is via blood products, in this case Factor VIII concentrate. This finding would strengthen the existing hypothesis that AIDS is caused by a transmissible agent.

C. Other seemingly unusual disorders among hemophilia patients were mentioned at the meeting, including cases of Burkitt's Lymphoma, unexplained thrombocytopenia, and possibly other opportunistic infections; but these have not been studied sufficiently to establish their relationship to AIDS.

D. There are 11,000 to 15,000 persons with hemophilia in the United States with varying severity of condition. The morbidity and mortality from hemophilia as well as the lifestyle of hemophilia

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patients has changed considerably over the past 10 years. These patients are treated with either a product derived from fresh frozen plasma (cryoprecipitate) or a protein concentrate prepared from these precipitates called antihemophilic factor or Factor VIII. Such therapy has allowed the development of home treatment regimens which permit patients to live a more normal life, including sharing educational and vocational opportunities and pursuits with the rest of the population. The number of days of hospitalization annually has decreased markedly for hemophilia patients on home treatment programs. Hemorrhage (spontaneous and traumatic) remains the major cause of death in hemophilia patients.

E. Almost all patients regularly receiving Factor VIII or cryoprecipitate develop hepatitis B and non-A—non-B (NANB) infections. These products have been shown to transmit these infections. Because of the freedom and reduction of suffering permitted hemophilia patients by Factor VIII concentrate, the product's benefits are perceived by patients to vastly outweigh currently known risks.

F. The Factor VIII normally present in fresh plasma is heat labile and inactivated by many types of chemical or physical treatment. For this reason, the techniques developed for the production of Factor VIII concentrate from fresh plasma are known to have little effect on hepatitis viruses. There are five commercial producers of Factor VIII concentrate. Lots of Factor VIII concentrate are prepared from plasma pooled from 1,000 - 5,000 donors. Donors come from many parts of society. Most material is pooled from paid donors in plasmaphoresis centers. Hemophilia patients use large amounts of Factor VIII (40,000 to over 65,000 factor units per year) from multiple preparations with subsequent potential exposure to material derived from thousands of donors.

G. The occurrence of PCP in three patients with hemophilia is disturbing, particularly since there is no previous evidence that this infection is common in hemophilia patients. The two patients who had immunologic studies performed demonstrated a T-cell abnormality similar to that among other patients in other high-risk groups with AIDS/KS. There is no known intrinsic immune disorder in hemophilia patients that would permit or promote such opportunistic infections.

III. Conclusions and Recommendations

There was general agreement among all participants on the following:

A. Conclusions

1. The pathologic process should be termed Acquired Immune Deficiency Syndrome (AIDS). Kaposi's Sarcoma and the various opportunistic infections are sequelae of the AIDS state.

2. AIDS has characteristics which suggest an infectious etiology.

3. There is an increased risk of AIDS for homosexual men, I.V. drug abusers, and among Haitians who have recently entered the United States. The recent occurrence of PCP in three patients with hemophilia raises the question whether the underlying immunodeficiency seen in these patients has the same etiology as among other groups with PCP. High priority should be given to obtaining information that will answer this question.

4. There is need to determine if certain blood products, particularly Factor VIII, are risk factors for AIDS.

B. To this end, we make the following recommendations:

1. An active surveillance system should be instituted at once to determine if other suspicious cases of AIDS (including OI, KS, or lymphodenopathy) are occurring in hemophilia patients. The CDC, the National Hemophilia Foundation, and the Hemophilia treatment centers volunteered to work together to establish this system and have begun its development.

2. Detailed laboratory studies are needed urgently to develop data relative to the immunologic competence of patients with hemophilia who have no symptoms of opportunistic infection. In addition, it is important to identify promptly and test any patient with hemophilia exhibiting disorders that are considered suspicious (such as thrombocytopenia, Burkitt's Lymphoma, persistent lymphodenopathy, etc.).

3. There is urgent need to determine practical techniques to decrease or eliminate the infectious risks from Factor VIII. Several experimental means of accomplishing this are currently being evaluated. A meeting of the FDA's Advisory Panel on Blood and Blood Products will be held in early September to discuss and evaluate these approaches.

4. There should continue to be broad input into these issues, including representatives from the gay community, hemophilia groups, etc.

5. Concerns were raised over the adequacy of funding to support these new activities, such as active epidemiologic surveillance and intensive laboratory studies. In addition, the existing Federal grants and contracts mechanisms are not responsive to rapid funding of urgent problems. Thus the National Cancer Institute's use of contract funds for AIDS research could not be provided to investigators for at least several months. It would be helpful if the Department could identify resources quickly to assist in these studies.

OPEN MEETING OF PHS COMMITTEE ON OPPORTUNISTIC INFECTIONS
IN PATIENTS WITH HEMOPHILIA

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