Blood Products Advisory Committee
July 19, 1983

Summary Minutes - Meeting 8

1. The meeting opened at 8:30 a.m., July 19, 1983, at the Lister Hill Auditorium, National Library of Medicine, National Institutes of Health (NIH), Bethesda, Maryland, with Dr. William V. Miller as the acting chairman. The entire meeting was held in open session.

2. Dr. John Petricciani, Director of the Office of Biologics, National Center for Drugs and Biologics (NCDB), described the general problems associated with the Acquired Immunodeficiency Syndrome (AIDS) and its relationship to the safety of plasma derivatives. An important objective for the committee was to define working principles for FDA and the plasma derivative manufacturers, particularly for antihemophilic factor (AHF) derived from plasma which is pooled from thousands of donors. A particular lot could theoretically contain plasma obtained from a donor who subsequently developed AIDS or some signs and symptoms of AIDS. For the immediate future, decisions must be made on the disposition of such material in the absence of a solid data base.
Dr. Petricciani pointed out that voluntary recall is the quickest and most reliable method for removing a potentially dangerous product from the market, but that in the case of blood derivatives a number of variables needed to be considered which may affect a decision on recall such as the accuracy of the diagnosis of AIDS, the occurrence of symptoms in relation to the time of donation, and the impact of a recall on the supply. He also recounted the programs instituted at donation centers to exclude persons at increased risk of AIDS.

3. Dr. Bruce Evatt of the Centers for Disease Control (CDC) summarized the epidemiology of AIDS especially as it pertains to patients with hemophilia and in specific patients who have received blood or blood components. The CDC uses the following criteria for defining AIDS:

a. Kaposi's sarcoma in patients less than 60 years of age, or

b. Opportunistic infection (e.g., Pneumocystis carinii pneumonia) in previously healthy people.

Using these criteria, male homosexuals with multiple partners, intravenous drug abusers, Haitian immigrants, and patients with hemophilia have been found to be at increased risk.

Dr. Evatt said that the majority of cases fall in the 30-40 year old age group. Most of the AIDS cases occur in New York, San Francisco, and Los Angeles, although the disease has been found in 39 states. The available epidemiological evidence suggests that AIDS is a transmissible disease. Since the first hemophilia cases in 1982, 17 cases from the U.S. have been reported to CDC. Almost all of the cases develop Pneumocystis carinii pneumonia, but none have Kaposi's sarcoma. The helper-suppressor ratio of the T-cells in

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patients is very low, usually less than 0.5. While it has not yet been definitively established that AIDS is transmitted by blood and blood products, it has been suggested as a possibility because of the fact that the epidemiologic pattern of AIDS is similar to that of hepatitis B virus infection.

4. Dr. Henry Masur of the NIH presented the clinical criteria used in the diagnosis of AIDS. In the late 1970's patients in California and New York began to appear with infections that had never previously been recognized in healthy individuals, (e.g., Pneumocystis pneumonia, Candida esophagitis, Mycobacterium avium intracellulare, and/or an unusual tumor, Kaposi's sarcoma). The patients had abnormal T-cell functions. Dr. Masur stated he believes that AIDS is a new disease because Kaposi's sarcoma has not commonly occurred in previously healthy individuals younger than 60 years of age, and there is little evidence of Pneumocystis infection occurring in previously healthy individuals who are not immunosuppressed as a result of treatment for an underlying disease. AIDS patients have T-lymphocyte defects, but particularly depletion of T_4 cells. The B cells are activated and secrete large amounts of immunoglobulin including IgG, IgM and IgA.

A considerable number of patients will live for two to three years after their initial diagnosis of Kaposi's sarcoma, but once an opportunistic infection develops very few survive longer than 18 months.

Dr. Masur noted that clinicians in California and New York have reported seeing a large number of males in groups at increased risk for AIDS with lymphadenopathy that is present in more than two extrainguinal sites. Some are severely debilitated by fever, fatigue, and weight loss. However, only a very small percentage of patients who have such lymphadenopathy for more than six months develop AIDS. At present there is no way of predicting which of these patients will develop AIDS.

Dr. Masur concluded by saying that the development of a serologic test which is specific for AIDS is critically needed.

5. Dr. Gerald Quinnan (NCDB) reviewed current research concerning the etiology, the host factors which might be involved, and the development of tests which might be used in assisting in the diagnosis of AIDS. Dr. Quinnan suggested that AIDS is new in homosexual males, drug abusers, and other populations, but may not be caused by a new agent. It has been suggested that AIDS may be caused by infection with a virus. Among the viruses considered have been human T-cell leukemia virus, parvoviruses, papovaviruses, as well as agents such as cytomegalovirus (CMV) and Epstein-Barr virus (EBV). Dr. Quinnan stated that EBV and CMV have been found frequently associated with AIDS and should be considered epidemiologic risk factors. Screening sera for the presence of antibodies to EBV-early antigen, a test for EBV reactivation, might provide a potential screening test for individuals at increased risk of AIDS.

6. Dr. Michael Rodell represented the four member companies of the Pharmaceutical Manufacturers Association (PMA) involved in the manufacturing

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of Antihemophilic Factor (AHF) -- Alpha Therapeutic Corporation, Armour Pharmaceutical Company, Miles-Cutter Laboratories, and Hyland Therapeutics. Dr. Rodell outlined the donor education and screening program initiated by each of the companies in early 1983 to reduce the number of donors from the high risk groups. Approximately four to four and one-half million liters of source plasma are fractionated on an annual basis which result in 800 million AHF units. Primary plasma pool sizes range from 1,000 to 10,000 liters with the result that a given pool could produce between 0.5 million to 5 million AHF units and treat an estimated 12 to 125 patients per year (or 500 to 5,000 individual treatments). Because the industry estimates that the average frequent plasma donor makes between 40 and 60 donations a year, a single donor could easily be represented in as many as 50 plasma pools in one year. Were this donor subsequently found to have AIDS and a decision made to recall all units collected in a time period of one year prior to that, 25 to 250 million AHF activity units could be affected, all in various stages of pooling, production, and distribution. Given the PMA estimate of 800 million AHF activity units produced annually by the fractionation industry, the potential for serious disruption of AHF supply described by Dr. Rodell seems quite real.

7. Dr. Steven J. Ojala (Miles-Cutter Laboratories) presented the PMA recommendation against automatic recall. Automatic recall could lead to serious product shortages. PMA recommends that manufacturers continue current screening and policies of discarding plasma from suspect donors. Dr. Ojala stated that recall decisions should be made following each company's policy in close consultation with the FDA and should be considered on a case-by-case basis in light of current knowledge of AIDS. One lot of final product has been voluntarily withdrawn from the market and suspect units of plasma are routinely discarded by plasma derivative manufacturers.

8. Dr. Louis Aledort presented the National Hemophilia Foundation (NHF) recommendation that any product concentrate be recalled if it includes material from an individual that has later been identified as having AIDS, or from an individual that in the best medical judgment of the manufacturer has characteristics strongly suggestive of AIDS. He noted, however, that the NHF did not have access to the PMA data when the statement was formulated, and that there was great concern about the continued supply of AHF.

9. Summary

It was very clear that confronted with this complex problem the Committee felt that a balance must be struck between theoretical risk of the product to recipients against the need for an uninterrupted supply of a life-sustaining therapy. As several members of the panel stressed, it would be undesirable to distribute and use a lot of product which incorporated plasma from a donor with a definite diagnosis of AIDS. However, signs and symptoms suggestive of AIDS (e.g., persistent lymphadenopathy, night sweats, etc.) would not be persuasive enough to dictate a recall of product. Enough concern was expressed about the question of supply that the Committee was unwilling to advise the agency to take an unalterable regulatory position calling for an automatic recall which would likely jeopardize product availability. Adding

to the uncertainty with regard to the decision of whether to quarantine or recall a product lot, several Committee members and other participants expressed the opinion that the risk of AIDS from transfusion of plasma derivatives or use of AHF concentrate has not been definitely established. They cited the fact that nearly all the hemophiliacs with AIDS had used material from different lots, and that many other hemophiliacs receiving these same lots had not developed AIDS. They stressed the need for studies to followup recipients of blood products derived from AIDS patients. The consensus of the Committee was that the action to be taken for each incident of inclusion of plasma from a donor who might have AIDS into a product pool should be decided on a case-by-case basis.