23 MAY 1983

Armour Pharmaceutical Company Limited

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May 19, 1983
Ref: KWF/mb

TO ALL HAEMOPHILIA CENTRE DIRECTORS

Dear Doctor,

Re: ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS)

The Armour Pharmaceutical Company is acutely aware of the current concern of the Medical world regarding Acquired Immune Deficiency Syndrome (AIDS) and its possible implication to Haemophilia care and treatment.

Despite the fact that there is little evidence to associate plasma component therapy with the transmission of AIDS, Armour, through its affiliate organisation, Plasma Alliance, has had programmes in operation for several months, which have been designed to help prevent the utilisation of plasma obtained from members of high risk groups associated with AIDS in the production of clotting factor concentrates.

General Background

The Centres for Disease Control (CDC), an agency of the U.S. Department of Health and Human Services, has been actively engaged in investigating the incidence and epidemiology of a relatively recently encountered health problem; namely, Acquired Immune Deficiency Syndrome (AIDS). This condition, occurring in increasing frequency since first reported in 1979, involves the depression of an individual's cellular immune system, thereby enabling opportunistic organisms and/or other agents to successfully attack the victim. As defined by that Agency, AIDS is a disease at least moderately predictive of a defect in cell-mediated immunity, occurring in a person with no known cause of diminished resistance to that disease. Disease states encountered include Kaposi's sarcoma (KS), Pneumocystis carinii pneumonia (PCP), and a variety of other opportunistic infections.

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Not considered to be within the scope of the CDC definition for AIDS are patients receiving immunosuppressive therapy, patients with widely spread cancer of lymphoid or histiocytic tissue, patients under 28 days or over 60 years of age, and patients with congenital or acquired hypogammaglobulinaemia.

Data reported by CDC in May, 1983, indicate that since the initial cases were reported, approximately 1500 cases of AIDS have occurred. Of even more alarming nature is the increased rate of incidence of reporting; an accession rate of 100 patients per month appears to be current. Approximately 40% of the reported AIDS patients have died; the mortality rate is significantly higher among those patients who contracted AIDS earlier than more recent cases, indicating that mortality increases as a function of length of the disease state.

APPARENT TARGET POPULATIONS

Analysis of morbidity data by the CDC shows that several groups appear to have a higher incidence of AIDS than does the general population. Over 90% of cases reported to the CDC have occurred among homosexual or bisexual males with multiple sexual contacts, users of non-prescribed self-injected drugs, and immigrants from or visitors to Haiti. AIDS has also been reported to occur in children of drug abusers and other individuals having close contact, e.g., sexual intercourse, with AIDS victims.

The great majority of AIDS cases appears to be in the New York City, Miami, San Francisco and Los Angeles metropolitan areas, although the syndrome has been reported in at least 30 states throughout the United States as well as in several European locations.

Of additional concern to Ammour Pharmaceutical Company and to others in the health care field is the indication, from data generated by the CDC, that AIDS is being seen in recipients of blood, blood components, and blood derivatives. In a summary presentation made in May, 1983, the CDC stated that 14 haemophiliacs have apparently contracted AIDS, and that an as yet unidentified number of non-haemophilic recipients of blood and blood components also have developed the syndrome. The CDC is investigating the possible relationship between AIDS and the use of blood and blood derivatives, and is attempting to determine whether transmission of AIDS via transfusion is indeed occurring.

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EPIDEMIOLOGY AND LABORATORY TESTING APPROACHES

As pointed out earlier, the majority of those contracting AIDS are in three groups of the population - homosexual or bisexual males, drug abusers, and immigrants from or visitors to Haiti. These groups, according to the CDC, also have a very high incidence of Hepatitis B infection. This leads to the possibility that social relationships and interchanges between these groups result in the transmission of an unknown causative agent analagous to the manner in which Hepatitis B is transmitted.

The high incidence of Hepatitis B infection in each of these groups suggests that testing for laboratory markers of this virus might be of value in screening potential AIDS victims. Testing of AIDS patients for antibody to Hepatitis B core antigen (anti-HBc) shows that over 85% of them are positive for this marker. However, extrapolation of these findings to a general screening programme in order to identify potential AIDS victims or carriers may not be practical. Information developed by various organisations shows that approximately 15% of the population also tests positive for anti-HBc, indicating that this would not be a specific test for AIDS.

Since AIDS results in a disruption of the cellular immune system, it is not surprising that patients demonstrate unusual findings in some aspects or components of this system. Over 85% of AIDS patients demonstrate significantly reduced ratios (±1.0) of T-helper (T_H) to T-suppressor (T_S) cells, but this finding is of limited value in predicting the likelihood of someone without signs or symptoms of AIDS being a potential victim or carrier. Recent information developed at the University of New Mexico shows that a large number of acute infections resemble AIDS by decreasing the number of T_H cells, thereby causing an inversion of the T_H/T_S ratio. The CDC agrees that such alterations are not specific for AIDS.

Thus, until the causative agent responsible for transmission of AIDS is identified and isolated, it is highly unlikely that a suitable laboratory tool will be available for implementation of any general testing programmes. The absence of any specific and sensitive test to identify potential AIDS victims and carriers has resulted in activities and programmes to be described in subsequent portions of this summary statement.

PLASMA COLLECTION AND UTILISATION BY ARMOUR PHARMACEUTICAL COMPANY U.S.A.

Armour Pharmaceutical Company U.S.A., through its subsidiary, Plasma Alliance, operates 16 centres located in the Midwest and Southeast portions of the United States. None of these centres are located in the AIDS high incidence areas of the country (New York City, Miami, San Francisco, Los Angeles) mentioned earlier, nor is plasma used in the manufacture of clotting factor products obtained

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from facilities located in these areas. Furthermore, no plasma is obtained from collection facilities located outside of the United States. Nevertheless, the AIDS issue cannot be treated solely on the basis of geography, since incidence of the syndrome is scattered over a wide area.

Taking the first of several steps designed to avoid collecting plasma from members of groups shown to be at high risk for contracting AIDS, informational posters were displayed at our centres in December, 1982. These posters advised potential donors about AIDS and its possible impact on the treatment of haemophilia, and requested donors in any of these groups to defer themselves from plasma donation.

In February, 1983, a more aggressive programme was initiated, following discussions with organisations such as the U.S. Food and Drug Administration Office of Biologics, the National Haemophilia Foundation, the Centres For Disease Control, and other commercial manufacturers of clotting factor concentrates. This programme included direct communication with each donor in the form of written and oral information and questions, designed to defer from the donor population individuals at risk for contracting AIDS. Each donor is presented a fact sheet describing the high risk groups thus far identified with AIDS, the seriousness of the syndrome, and the possible link to the treatment of haemophilia. Furthermore, all donors are questioned by trained processors as to their being members of high risk groups and as to the presence of any signs (night sweats, diarrhoea, chills, etc.) that might be indicative of AIDS. Donors are required to affirm in writing that they are not members of any of the several high risk groups involved, without having to reveal any facet of their personal and private lives. Periodic physical examinations performed by plasma centre attending physicians also include evaluations for possible signs and symptoms of AIDS.

We will continue to move forward, in co-operation with other responsible segments of the health care team, both governmental and non-governmental, to implement additional plasma collection activities and programmes deemed to be effective and appropriate.

SUMMARY AND ADDITIONAL ACTIONS

The plasma collection actions described earlier in this statement are designed to prevent the use of plasma obtained from individuals in one or more of several high risk groups in the production of clotting factor concentrates. They are predicated on the possibility that AIDS may be transmitted through blood and certain blood derivatives, although it must be re-emphasised that no

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agent responsible for transmission has yet been identified. However, one must consider that an infectious organism may be involved, and that the appearance of AIDS is prevalent in groups with high incidence of Hepatitis.

Armour Pharmaceutical Company U.S.A. has provided information to the U.S. Food and Drug Administration Office of Biologics, regarding a revised manufacturing process that includes heat treatment. The process is designed to reduce the Hepatitis risk associated with the use of clotting factor concentrates, and approval of the process change is anticipated within the near future. The effectiveness of such procedures in preventing the possible transmission of AIDS cannot be directly determined at this time, since appropriate challenge studies cannot yet be designed. However, it should be pointed out that the occurrence of AIDS has not been noted with administration of products such as Normal Serum Albumin, which also undergo heat treatment during their manufacture.

The Revlon Health Care Group, of which Armour Pharmaceutical Company is a member, is firmly committed to providing safe and effective products to the medical community, and will continue to devote considerable time and attention to the problems associated with AIDS and haemophilia treatment, and to efforts undertaken to resolve them. We believe that, given the level of today's knowledge regarding AIDS and its transmission, the programmes in place at our plasma collection centres provide an effective way to reduce the potential for use of plasma obtained from high risk groups. Activities involving increasing the safety of clotting factor concentrates relative to their Hepatitis risk may also prove to be of benefit in the AIDS situation as well.

Yours faithfully,

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K.W. Fitch,
Chairman and Managing Director