CONCISE REPORT

Geographic Differences in Hemophilia-Associated AIDS Incidence in Pennsylvania

By The Pennsylvania AIDS Surveillance Study Group

A 1986 survey of seven hemophilia treatment centers in Pennsylvania (PA) has revealed that 22 hemophiliacs residing in PA have developed the acquired immunodeficiency syndrome (AIDS), representing 9.2% of the total 238 United States hemophilic AIDS cases. These 22 included ten (45.5%) from western PA (W-PA), eleven (50.0%) from central PA (C-PA), and one (0.5%) from eastern PA (E-PA). The HIV antibody prevalence for these three geographic groups is comparable, with 84 of 178 (47.2%) of hemophiliacs in W-PA seropositive, 102 of 182 (56.0%) in C-PA seropositive, and 105 of 177 (59.3%) in E-PA seropositive.

Blood product usage for these three areas is comparable: 47.8 x 10^4 (W-PA) vs 43.9 (C-PA) vs 53.3 (E-PA) units factor VIII concentrate per patient per year; 36.5 vs 24.5 vs 33.7 for factor IX concentrate; 8.4 vs 4.7 vs 7.7 for cryoprecipitate; and 1.3 vs 2.7 vs 1.0 for fresh frozen plasma, respectively. These data demonstrate a geographic variation in hemophilia AIDS incidence in PA, with a tenfold higher incidence in W-PA and C-PA than E-PA, which is unrelated to differences in HIV antibody prevalence, patient blood product usage, or inaccuracies in AIDS case reporting. Because of the ≥5 year median latency between HIV infection and development of AIDS, the AIDS incidence will continue to change, but other factors appear to be operative in the development of AIDS in hemophiliacs.

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THE INCIDENCE of the acquired immunodeficiency syndrome (AIDS), identified in hemophiliacs early in the AIDS epidemic, is quite high in hemophiliacs, with more than one case per 100 hemophiliacs. Surveillance figures by the Center for Disease Control (CDC), however, have suggested some geographic variation in the distribution of United States hemophilia-associated AIDS cases, with some states reporting none or only a few cases and others reporting as many as eleven or more cases per 100 based on state hemophilia populations. Presumably hemophiliacs were exposed to the human immunodeficiency virus (HIV), the etiologic agent, through infectious blood products, primarily factor concentrates, at about the same time as these products were manufactured and distributed nationally. This presumption is further corroborated by the documentation that the first HIV exposures in hemophiliacs occurred as early as 1978 and 1979 and the peak in seroconversion occurred in 1982 and 1983. Thus, although the geographic variability in AIDS incidence remains unexplained, other factors could play a role, specifically differences in HIV antibody prevalence, yearly blood product usage, age, and accuracy of AIDS case reporting. Therefore, we studied these factors by distributing a questionnaire to the seven comprehensive care hemophilia treatment centers in Pennsylvania, and reviewed each center’s state annual report for blood product usage and age.

MATERIALS AND METHODS

A questionnaire was distributed to the seven hemophilia treatment centers in Pennsylvania in September 1986, to determine the number of hemophilia AIDS cases in their center, the number tested for HIV antibody, the number HIV antibody positive, and the number and types of blood products used in that center. Only Pennsylvania residents at these centers were included. The centers included the Hemophilia Center of Western Pennsylvania (W-PA) (Pittsburgh) with 178 patients (178 tested), the Hemophilia Center of Central Pennsylvania (C-PA) (Hershey) with 182 patients (182 tested), and five centers in Eastern Pennsylvania (E-PA) with a total of 292 patients (177 tested). The latter included centers at Allentown Hospital (30 patients of which 15 were tested), Albert Einstein Medical Center (Philadelphia) (54 patients of which 27 were tested), Cardeza Foundation of Jefferson Medical College (Philadelphia) (90 patients of which 83 were tested), Children’s Hospital (Philadelphia) (88 patients of which 32 were tested), and Reading Hospital (Reading) (30 patients of which 20 were tested). Information was obtained on a total of 537 hemophiliacs.

State annual reports for each hemophilia center for the years 1978 through 1985 were reviewed, and the mean age and mean number of units of each blood product used (factor VIII concentrate, factor IX concentrate, cryoprecipitate, and fresh frozen plasma) was determined. There was very little difference in age or blood product usage for a single center from year-to-year, and thus we used 1985 figures for the purposes of this report.

RESULTS

As shown in Table 1, HIV antibody prevalence in hemophiliacs from the three geographic areas of Pennsylvania was similar with between 47% and 59% of those tested HIV antibody positive. The proportion tested for HIV antibody in these centers included a total of 100% of the W-PA, 100% of the C-PA, and 61% of the E-PA hemophilia population. The seropositive included between 76% and 90% receiving factor VIII concentrate, between 31% and 52% receiving factor IX concentrate, between 0% and 11% of cryoprecipitate treated, and 0% (for all areas) receiving fresh frozen plasma. The 22 reported cases of hemophilia-associated AIDS in Pennsylvania included ten in W-PA, 11 in C-PA, and one in E-PA, representing 5.6%, 6.0%, and 0.3% of the hemophilia population in these areas, respectively, and 11.9%, 10.8%, and 1.0% of the HIV antibody positive hemophiliacs in these three geographic areas, respectively.

Blood product usage, based on 1985 figures, in units x 10^4 per patient per year (U/p/yr) revealed 94 U/p/yr in W-PA, 76 U/p/yr in C-PA, and 96 U/p/yr in E-PA, with between 44 and 53 U/p/yr for factor VIII concentrate, between 25 and 37 U/p/yr for factor IX concentrate, between 5 and 8

From the Pennsylvania AIDS Surveillance Study Group. Participating members are listed in the Appendix.

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U/p/yr for cryoprecipitate, and between 1 and 3 U/p/yr for fresh frozen plasma (Table 1).

The three geographic areas were not significantly different by age, based on 1985 figures with 42% of the hemophiliacs <20 years of age (range, 37% to 51%), 40% between 21 and 40 years of age (range, 36% to 42%), and 18% >40 years of age (range, 14% to 23%).

**DISCUSSION**

The results of this study demonstrate for the first time that geographic differences in hemophilia-associated AIDS incidence are unrelated to differences in HIV antibody prevalence. Specifically, the data from this survey of the seven Pennsylvania hemophilia treatment centers indicate that in Pennsylvania, where a total of 22 hemophilia-associated AIDS cases have been reported as of September 1986, there is a tenfold difference between the incidence of AIDS cases in the eastern part of the state and the central or western parts of the state, despite similarities in HIV antibody prevalence, blood product usage (per patient), or age distribution of hemophilia population in these geographic areas.

In view of the median 5 to 7 years incubation period between exposure and development of AIDS, and with the peak years of seroconversion in hemophiliacs occurring in 1982 and 1983, increasing numbers of AIDS cases will be seen over the next few years in areas of low AIDS incidence currently. However, it is puzzling that such wide discrepancies in AIDS incidence exist in areas of similar HIV seroprevalence. A recent collaborative CDC study by Jason et al and a large number of hemophilia treatment centers across the country have shown that hemophiliacs exposed to "recalled" lots of factor concentrate (donor known to have subsequently developed AIDS) do not differ in HIV seroprevalence or T helper number from hemophiliacs exposed to nonrecalled lots of concentrate. These data would argue against a "bad lot" theory, that is, that some hemophiliacs or some hemophilia centers may have been exposed to a particularly infectious lot. Further, although a given hemophiliac may be exposed to a given lot of concentrate for several weeks to several months, and should this lot be a particularly "infectious" lot, there has been no evidence to support that he would be more likely to develop AIDS. On the contrary, review of lots of concentrate used by Pennsylvania hemophiliacs who subsequently developed AIDS has revealed no single common "bad" lot(s) exposure (Eyster ME, unpublished observation). Further, hemophilia brother pairs who received similar amounts of the same lots of concentrate over a several year period resulted in the development of AIDS or ARC in one but not the other brother of the pair (Ragni MV, unpublished observation). Whether the total dosage or frequency of exposure to a certain lot of concentrate plays a role in the development of AIDS is unknown.

Other possible explanations include the possibility that protective antibody or immunity to HIV may develop in some hemophiliacs rendering them "protected" from AIDS or that some hemophiliacs are exposed to less virulent strains of HIV and thus protected.

In conclusion, geographic differences in AIDS incidence in hemophiliacs in Pennsylvania appear to be unrelated to any geographic differences in HIV seroprevalence or blood product usage. These findings suggest that other factors are involved in the development of AIDS in hemophiliacs. Continued prospective surveillance of HIV infected hemophiliacs will be necessary to determine the risk factors associated with the development of AIDS in these individuals.

**APPENDIX**

The following organizations and members participated in this Pennsylvania AIDS Surveillance Study Group report: Hemophilia Center of Western Pennsylvania, Central Blood Bank and School of Public Health, University of Pittsburgh: Margaret V. Ragni, MD, Lawrence A. Kingsley, Dr P.H., Joel A. Spero, MD, Jessica H. Lewis, MD, Toni Gorenc; Hemophilia Treatment Center, Allentown...
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REFERENCES

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