Medical Aspects of Hemophilia and AIDS

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By July 1982, when the Centers for Disease Control reported the first cases of AIDS among people with hemophilia, the majority of hemophiliacs who were to become infected already had been exposed to HIV. Of the 20,000 hemophiliacs in the United States, approximately half are now HIV infected. But although the public and the media are aware of how AIDS has affected other populations, little has been said about this group of people who shoulder the burden not only of HIV infection, but also of a serious blood disorder and the stigma associated with it. This article offers a medical perspective of hemophilia and of the effects of HIV infection on people with hemophilia.

Hemophilia is a genetic disorder that leads to bleeding, primarily into joints and muscles, that can lead to crippling arthritis and disability in especially severe cases. It is a recessive trait linked to a defect in the X chromosome, a male baby receives from his mother and occurs in one in 10,000 male births. The trait causes a deficiency in the clotting proteins that prevent excessive bleeding from wounds or into joints or muscles. There are two types of hemophilia representing deficiencies in two different coagulation proteins or factors: factor VIII (Hemophilia A) and factor IX (Hemophilia B). People who have factor levels of less than 1 percent have severe hemophilia; those who have levels of 5 percent or greater have mild hemophilia.

Bleeding problems among people with hemophilia can occur spontaneously or as a result of trauma. Hemorrhages in those with moderate and mild disease are usually trauma-induced, while hemorrhages in those with severe disease are usually spontaneous and occur four or more times a month. Recurrent hemorrhages, particularly in joints, may lead to joint damage and to disability, pain, and crippling. Until recently, individuals with recurrent hemorrhages had a shorter average life span, a poorer quality of life, and were required to make numerous visits to the emergency room for treatment.

In the mid-1970s, home injection of blood products, such as clotting factors that help the blood to coagulate, revolutionized hemophilia care and allowed people with hemophilia to become much more productive, live a normal life span, and sustain a markedly better quality of life. Since the clotting factors were manufactured using donated blood, however, hemophiliacs, particularly those with the most severe disorders, were exposed to blood-borne infections such as hepatitis and, later, HIV.

Source of HIV Infection among People with Hemophilia

The clotting factors used to treat hemophilia are derived from plasma, a component of whole blood. In the past, since the blood is donated, the clotting factors sometimes contained organisms that caused disease. In 1985, a heat-treating process was introduced to eliminate infectious agents, such as HIV, in order to produce safer blood products. In recent years, other methods, including the use of detergents and affinity column purification, a process by which only factor VIII is separated from plasma, have been used to further improve product safety and purity.

Several studies, using retrospective HIV antibody testing of the stored, frozen blood samples of hemophiliacs, have detected HIV infection in blood from as early as 1978. These studies also have shown a peak in HIV seroconversion among hemophiliacs occurring in 1982 and 1983. Individuals with severe hemophilia, who routinely use hundreds of thousands of units of clotting factor each year, represent the majority of hemophiliacs who are infected. Far fewer of those with moderate or mild disease are infected. While 80 to 90 percent of those patients treated with factor VIII concentrate have seroconverted, HIV seroprevalence among those treated with factor IX is only 30 to 40 percent. Among those treated with locally-produced plasma derivatives, which require fewer donors and less blood, seroprevalence is only 10 to 15 percent.

The differences in seroconversion among hemophiliacs using different factors may be linked to the differences in the manufacture of the concentrates. Both are derived from thawed, frozen plasma; however, factor IX concentrate is made from the supernatant (the liquid component of plasma that remains after precipitation) while factor VIII concentrate is made from the plasma precipitate, which includes cellular debris that may contain HIV. Since no component of HIV or HIV antibody has been isolated in the factor concentrates, this explanation represents only a theory.

Early in the epidemic, some investigators believed that the presence of HIV antibodies among hemophiliacs might be caused by exposure to non-infectious viral proteins. But the growing number of symptomatic seropositive hemophiliacs confirms that these people were exposed to HIV-infected clotting factor concentrates.

Manifestation of HIV Infection

Although people with hemophilia currently constitute fewer than 1 percent of the total number of AIDS cases, the incidence of diagnosed AIDS cases among hemophiliacs is more than 4 percent. Of the more than 800 cases reported so far, nearly 90 percent have hemophilia A; 8 percent have hemophilia B. More than 50 percent of the total were diagnosed initially with Pneumocystis carinii pneumonia, and the remainder with esophageal candidiasis, cryptococcosis, wasting syndrome, crypticoccal

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meningitis, or neurologic complications (encephalopathy and dementia). HIV-related malignancies are rare among people with hemophilia, unlike gay men, occurring in fewer than 5 percent of those with AIDS. Most commonly these malignancies are B-cell lymphomas; Kaposi’s sarcoma is seen rarely.

AIDS is now the chief cause of death among people with hemophilia, surpassing hemorrhage and liver disease, previously the leading causes of death in this population. More than 50 percent of the deaths occurring among hemophiliacs since 1984 have been HIV-related.

In general, hemophiliacs, like those without hemophilia experience HIV infection and its treatments in similar ways. Among the complications caused by HIV that are peculiar to people with hemophilia are septic arthritis, loss of antibodies to factor VIII, and potential for bleeding caused by immune thrombocytopenia (ITP). Septic arthritis is caused by the bacterial infection of a joint already damaged by chronic hemorrhages. It may appear as a typical joint hemorrhage that does not improve after normal measures, such as blood product infusion and splinting.

Loss of antibodies to factor VIII has been reported occasionally in patients with AIDS or severe ARC. Ten to 15 percent of patients with hemophilia develop antibodies to infused factor VIII blood products. A higher dose of infused blood product may be required to “overcome” these antibodies, making it difficult to treat bleeding episodes and sometimes precluding surgical procedures. As a result of HIV infection, there may be a dysfunction of antibody-producing B-lymphocytes, lowering production of these factor VIII antibodies and allowing use of factor VIII to resume. This development, an advantage to the patient, may facilitate procedures necessary for those who are HIV-infected, such as spinal tap.

The third complication is the potential for excessive bleeding, especially central nervous system bleeding, in patients who have two coagulation defects, specifically, hemophilia and ITP, a low platelet count associated with HIV disease. Unlike gay men with HIV-associated ITP, who rarely bleed, hemophiliacs with ITP may require treatment to maintain a higher platelet count and to minimize their risk of increased bleeding.

Heterosexual HIV Transmission

Heterosexual transmission of HIV accounts for the majority of AIDS cases worldwide, but only 4 percent of AIDS cases in the United States. Among female partners of HIV-infected men with hemophilia, between 10 and 20 percent are seropositive. It is unclear why some female partners of hemophiliacs become infected and others do not, often despite unsafe sex practices. In studies to date, HIV transmission among hemophiliacs appears not to correlate to number of sexual partners, frequency of exposure, or practice of anal intercourse.

Some researchers have suggested that as an HIV-infected person’s immunodeficiency worsens—marked by a decreased T-cell count and progression to AIDS—the chances of HIV transmission to a sexual partner may increase. However, there are clear examples of HIV transmission to heterosexual partners from asymptomatic HIV-infected hemophiliacs, whose T-cell counts were normal and whose immunodeficiency was minimal. In these cases, transmission has occurred close to the time of the hemophiliac partner’s initial exposure to HIV.

Other researchers have suggested that women who remain seronegative, despite multiple, unprotected sexual exposures to infected hemophiliac partners, may be “immunologically protected” and have antibodies to their partners’ infected lymphocytes. These theories remain speculative and the subject of ongoing research studies.

Despite tremendous efforts by hemophilia center staff to educate and counsel couples about HIV transmission, the use of condoms, and the use of HIV-killing spermicides that contain nonoxynol-9, fewer than 30 to 40 percent of these couples practice “safe sex.” This may be related to stress and to denial of HIV infection, and warrants closer investigation.

Hemophiliacs as a Study Group

Studying HIV infection among people with hemophilia is different from studying it in other “high-risk groups.” For example, unlike gay men or intravenous drug users, hemophiliacs form a well-characterized group, typically subject to close and frequent medical evaluation through local hemophilia centers. Among hemophiliacs, sexually-transmitted diseases and herpes virus infections are rare, and monogamous heterosexual behavior is the norm. In addition, further HIV exposure is expected to decline or cease altogether because of the development of safer blood products devoid of contaminating protein and viruses.

For these reasons, hemophiliacs are an ideal population in which to study the natural history of HIV infection and to gather prospective data on risk factors. In addition, since the sexual partners of hemophiliacs often visit hemophilia centers, they too may be valuable in adding to an understanding of the risks and cofactors associated with heterosexual HIV transmission.

It is frustrating to researchers that members of such an ideal study population have been reluctant to enroll in antiviral treatment studies. This reluctance is due to stress, denial and fears about openly acknowledging HIV infection. The first National Institute of Allergy and Infectious Diseases protocol, developed to study AZT in asymptomatic hemophiliacs, is now approaching the end of year one, but has enrolled only 150 of an expected 560 patients. Hemophiliacs have long and successfully used denial to cope with hemophilia. Combined with their ability to treat themselves at home, this denial has enabled people with hemophilia to get on with their lives, obtain jobs, start families and to avoid dealing with their chronic disease.

Although this “denial” has been an effective mechanism for dealing with hemophilia, it is not useful in coping with AIDS. Denial hinders people with hemophilia from dealing adequately with the reality of HIV infection. For instance, people who cannot admit and discuss HIV infection are unlikely to agree to participate in a research study or protocol, to seek treatment or to protect their sexual partners from transmission.

Another aspect of this dilemma is the stress and denial of staff who care for these patients, who have followed them for years, and who are now watching them succumb to HIV infection. These staff members may feel guilty about having prescribed blood products that turned out to be HIV-infected. They also may feel stressed by the change from caring for healthy hemophiliacs to caring for those confronting a life-threatening disease.

Resolution of these difficult issues may result from the identification and discussion of the key issues for patients and staff, particularly with the support of mental health practitioners. In addition, it may be easier to enroll subjects in protocols for people with AIDS or ARC because these patients have already acknowledged their illness.

Conclusion

For people with hemophilia, the medical aspects of their condition influence their view of the world and their psychological response to HIV infection. A medical understanding of hemophilia is crucial for physicians, mental health professionals and policy makers in order for them to offer support to hemophiliacs with HIV infection and to develop approaches to the particular problems of this population.

In addition, to effectively address the medical, scientific and psychosocial issues of HIV infection among hemophiliacs, providers and patients alike must be encouraged to confront their frustrations, denial, stress and fears regarding AIDS so the issue can be approached directly, but with compassion.

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Diagnosis/Treatment/Prevention

Counseling Issues for People with Hemophilia and HIV Infection

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The discovery of clotting factor concentrates and the emergence of a hemophilia treatment network has enabled people with hemophilia to treat themselves at home and to achieve independence, a sense of control and reduced suffering. HIV infection altered dramatically these positive adjustments, confronting people with hemophilia with a whole range of psychological challenges. Health care professionals who deal with hemophiliacs and their partners must be aware of these issues and of the importance of providing appropriate counseling.

Perhaps the most dramatic change in the psychological condition of people with hemophilia has been a loss of faith, not only in the blood products—despite the fact that the concentrates have been heat-treated, and virtually virus-free, since 1985—but also in the medical and scientific community in general. In addition to this new stress, HIV infection has also made more difficult the adjustment of people with hemophilia to the complications of being hemophiliac, causing isolation, dependency on the family, anger at the medical system, and fear of disclosure of hemophilia and HIV infection.

Pediatric and Adolescent Issues

Since children with hemophilia often lack the perspective and the access to information they need to answer questions about HIV infection, their attitudes about AIDS are most influenced by their parents’ reactions. For example, some parents have responded to the fear that blood products may still be HIV-infected by trying to limit their children’s activities and thus avoid the possibility of a bleed. This reinforces the sense that these children are different or vulnerable, and may lead them to believe they are not well, even if they are uninfected.

Parents themselves may feel responsible for their children’s HIV infection. Mothers, in particular, may feel renewed guilt because they passed on the clotting gene that caused the hemophilia. In many cases, parents who infused HIV-infected clotting factor also feel guilt.

Adolescents with hemophilia, like all adolescents, must reconcile an emerging sexuality with the sense that they may endanger a sexual partner. They must consider disclosing to potential partners, not only their hemophilia but also their HIV infection. Among adolescents, the sense of immortality, as well as peer pressure to conform, make it difficult to comply with safer sex techniques. At a time when peer acceptance is crucial, HIV infection reinforces the feelings of some adolescents with hemophilia that they are different.

Issues for Adults

There is no typical “hemophilic response” to HIV infection or AIDS. Responses depend on the individual’s defense mechanisms, support system, style of coping, opportunities for ongoing education and counseling, and the socio-political climate. The most common responses are similar to those of other people with HIV infection: mild to moderate depression, preoccupation with physical symptoms and social withdrawal. In addition, many hide their hemophilia to avoid the perception that they might be HIV-infected and in this way increase their sense of helplessness and shame. People with hemophilia may limit physical activity to avoid bleeds, delay treating bleeds and delay reporting unresolved bleeds to physicians in order to preserve autonomy from medical providers, autonomy gained through home treatment and already sacrificed by required visits to deal with HIV infection.

Single adults with hemophilia struggle with fears about maintaining intimacy and forming new relationships. A significant number have chosen to stop dating because of concerns about transmitting the virus and fears of rejection. The married adult and his spouse struggle to change what may be long-standing sexual practices and to reevaluate plans to have children. The limits imposed by HIV infection, particularly recommendations regarding the use of condoms and deferral of pregnancy, have evoked anger among many adults with hemophilia.

A person with hemophilia may resist safer sex because of his unresolved grief and anger about being infected, his sexual partner’s resistance to using condoms, or his assumption that a long-standing sexual partner must be infected already. Counseling involves helping partners grieve the loss of old behaviors, resolve underlying anger, and understand the consequences of not practicing safer sex.

Many adults with hemophilia, married or single, are choosing abstinence to prevent transmission. Others describe a marked decrease in sexual desire, frequency of activity, and ability to derive sexual pleasure. This may reflect discomfort in using condoms, a depressed mood, or a skepticism among people disappointed already by the failure of medical technology to protect them or their sexual partners from HIV infection.

It is helpful to examine the ways in which individuals adjust to hemophilia for clues as to how they may cope with AIDS.

Hemophilia providers have discussed in detail the low patient enrollment in the AZT research protocol for hemophiliacs, and many have interpreted this to be the result of patient denial. But there may be other factors in this decision. Some people with hemophilia may resist involvement in any experiment because of the breach of their trust in medicine, described earlier, and because of feeling over-researched “for the benefit of medical science.” Also, for many hemophiliacs who have low T-cell counts, AZT is available outside of an experimental protocol. Some providers, who struggle with ethical questions about enrolling patients in a placebo study, may encourage them to consider AZT treatment rather than participation in the protocol.

Coping with HIV Infection

In 1989, seven years after the first people with hemophilia were diagnosed with AIDS, most hemophiliacs with HIV are beyond the stage of denial, and are dealing with the reality of a lifelong, life-threatening infection. They cope with HIV infection in ways similar to their original adjustment to hemophilia.

It is helpful to examine the ways in which individuals adjust to hemophilia for clues as to how they may cope successfully with HIV infection. For example, those who have become more active in their hemophilia care and more informed about hemophilia in general are likely to respond in similar ways to AIDS. Others, who may deal with hemophilia only when they have a bleed or who may wait for their doctors to provide information, probably will be less involved. Ultimately, the active involvement of the individual reinforces the philosophy of hemophilia care: the patient is his own primary care taker and an integral member of his medical team.

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REFERENCES


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Recent Reports

Attitudes of Dutch Hemophiliacs Towards HIV Infection. Hemophiliacs in the Netherlands who responded to a nationwide survey expressed high levels of anxiety about AIDS, but were reluctant to use condoms and other measures to prevent transmission of HIV. They also reported potentially detrimental changes in their hemophilia treatment as a result of their fears of contagion, according to researchers from the University Hospital and the Clinical Genetics Center in Leiden, the Dutch Hemophilia Society, and the State University in Groningen (Haemostasis 1988; 18: 73-82).

The researchers received, by January 1, 1986, 935 usable responses to a survey of 1,162 hemophiliacs registered with treatment centers of the Dutch Hemophilia Society. They collected data on seropositivity rates, attitudes of people with hemophilia toward antibody testing, data on changes in hemophilia therapy and compliance with measures to prevent HIV transmission.

Although patients with severe hemophilia were more likely to have anxiety about AIDS, 65 percent of all subjects mentioned preoccupation with AIDS, 44 percent noted a sense of lost future perspective, 31 percent noted feelings of depression, 21 percent noted feelings of tension, 12 percent reported insomnia and 11 percent reported hypochondria.

More than a third of subjects with severe hemophilia had been tested for HIV antibody, compared to only 23 percent of those with moderately severe disease and 11 percent of those with mild disease. Seropositive patients had the highest anxiety scores; there was no significant difference between scores of seronegative patients and patients who had not been tested.

Sixty-three percent of the 207 patients who changed their hemophilia treatment schedules as a result of concerns about AIDS made ill-advised changes: waiting longer before treating bleeding, using smaller doses of blood products, or abandoning treatment altogether. A minority of patients complied with recommended measures to prevent HIV transmission. Most patients, including seropositives, who were married or who had steady sexual partners did not use condoms.

Comparison of Progression to AIDS between Gay Men and Hemophiliacs. Data from a study of San Francisco gay men and Pennsylvania hemophiliacs do not support the assumption that there are differences in the cumulative incidence of AIDS among gay men and hemophiliacs, according to researchers from the U.S. Centers for Disease Control, the University of Pittsburgh and the San Francisco Department of Public Health (Journal of the American Medical Association, February 3, 1989).

The study compared incidence of AIDS between a group of 117 gay and bisexual seropositive men and 79 seropositive men with hemophilia. Despite differences in patterns of seroconversion, the overall incidence of AIDS for the two groups did not significantly differ: 27 percent for the gay men and 21 percent for the men with hemophilia.

Data from recent studies show that AIDS incidence among people with hemophilia is 4 percent, while the incidence among gay men ranges from 8 percent to 30 percent. Researchers speculating about the apparent differences in rates of progression to AIDS have concluded that members of high-risk groups may differ in terms of medical cofactors, strain of infecting HIV, and exposure characteristics (route, frequency and concentration). This study, however, examined the progression to an AIDS diagnosis as a function of the year of HIV infection. Despite limitations to the authors' abilities to generalize their results, they state that the study supports the conclusion that the relative duration of HIV infection, and not the factors mentioned above, is important in predicting progression to AIDS.

HIV Transmission to Sexual Partners of People with Hemophilia. Three studies published in 1988 conclude that there is a low frequency of heterosexual transmission of HIV from seropositive people with hemophilia to their long-term sexual partners and that the reasons for this are unclear.

Researchers from Worcester, Massachusetts (Archives of Internal Medicine, June 1988) investigated the intimate household contacts of 68 seropositive hemophiliacs, including 36 sexual partners, and found all to be seronegative, including six partners of people with hemophilia from whom the virus itself was isolated, and six partners of hemophiliacs with AIDS. The low transmission rate may be related to the lower incidence of sexually-transmitted diseases among hemophiliacs and their partners than among I.V. drug users or gay men.

Researchers from the University of Pittsburgh (Public Health Reports, January-February 1988) found that four (19 percent) of the female partners of 21 seropositive men with hemophilia were seropositive. None admitted other risks for HIV infection or prior incidence of sexually-transmitted diseases. HIV itself was isolated from the lymphocytes of only one hemophiliac and one female partner. Seropositive female partners were younger, had younger hemophiliac partners, and were more likely to engage in oral sex and to have had more than one sexual partner in the previous five years. The low incidence of HIV infection may be due to the low rate of HIV isolation and infectivity among the hemophiliacs.

In support of this conclusion, a New Jersey study (American Journal of Medicine October 1988) found only one out of 14 wives of seropositive hemophiliacs was HIV-infected, and that her husband had been reactive for HIV antigen for 26 months.

Next Month

There is a common belief that the spread of HIV infection in prisons is a serious problem. Public policy makers have responded by focusing primarily on the mandatory testing of prisoners and the segregation of HIV-infected inmates from others. In the April issue of FOCUS, Judy Greenspan, of the ACLU National Prison Project, provides an overview of HIV in prisons. She details the organization of the prison system and the status of prisoners, the incidence of HIV infection in jails, testing policies throughout the country, housing and medical care for HIV-infected prisoners and the role of educational programs in stopping the spread of HIV in correctional facilities.

Also in the April issue, David Gilbert and Juan Rivera, two New York state prisoners who have been involved in prison-based AIDS education programs, discuss prison conditions for people with HIV infection and the concerns of prisoners dealing with the epidemic on the inside. They also offer advice for those counseling and educating prisoners about HIV.

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