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TITLE Acquired Immunodeficiency Syndrome (AIDS) in Hemophilia

AUTHORS James J. Goedert, M.D., M. Elaine Eyster, M.D.*,
Deborah M. Winn, Ph.D., Douglas M. Strong, Ph.D.**,
and Dean L. Mann, M.D.

ADDRESSES Environmental Epidemiology Branch
National Cancer Institute
National Institutes of Health
Bethesda, Maryland 20205

Milton S. Hershey Medical Center*
Pennsylvania State University
Hershey, Pennsylvania 17033

Naval Medical Research Institute**
Uniformed Services University
of the Health Sciences
Bethesda, Maryland 20814

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FOR MORE INFORMATION
Lorraine M. Kershner
(301) 496-6641

FOR RELEASE AT TIME
OF PRESENTATION

An immunologic imbalance in T-lymphocytes similar to that seen in patients with acquired immunodeficiency syndrome (AIDS) was found in a group of otherwise healthy hemophiliacs who were patients at one of the nation's 10 comprehensive regional hemophilia centers. The imbalance was most severe in those hemophiliacs who received the largest numbers of doses of the blood plasma derivative, Factor VIII concentrate, according to Dr. James J. Goedert, a National Cancer Institute (NCI) epidemiologist. He reported these findings today at the American Society of Clinical Oncology annual meeting in San Diego, California.

"Now that these initial studies have been done, we plan to follow these hemophiliacs to see if the imbalance might be an early indicator of AIDS," the NCI physician said.

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Dr. Goedert worked with physicians at the Pennsylvania State University Regional Hemophilia Center in Hershey to study blood samples and medical records of 44 patients who routinely receive a pooled blood product to replace their missing serum clotting factor. Dr. Goedert reviewed the cases of the 12 hemophiliacs who are on record with the Centers for Disease Control as documented AIDS cases. Two of these patients were treated at the Pennsylvania center.

In AIDS, the immune system shuts down, making patients susceptible to life-threatening infections with rare opportunistic agents, such as Pneumocystis carinii and cytomegalovirus. Some patients also get Kaposi's sarcoma, a rare cancer. The syndrome was not seen before 1979. Now there are more than 1,400 cases on record with the Centers for Disease Control. So far AIDS has occurred among four groups: homosexual men (71 percent of cases), intravenous heroin or cocaine users (17 percent of cases), Haitian immigrants (5 percent of cases) and hemophiliacs (1 percent of cases). Although the groups seem unrelated, they share two things in common--a high risk of hepatitis B and repeated exposure to foreign antigens from infectious diseases or blood products. Many scientists are working to identify the cause(s) of AIDS and to find ways to treat the disease, which now appears to be almost invariably fatal.

A hallmark of AIDS is an imbalance in the relative numbers of helper and suppressor T-lymphocytes--white blood cells that mediate immune reactions. Helper cells interact with other cells to activate an immune response, whereas suppressor cells interact with cells to inhibit the immune response. A balance between the two types of cells appears to be critical. Normal individuals have twice as many helper as suppressor cells, an H/S ratio of 2. In AIDS patients the helper T-cell population is severely depleted. Their H/S ratio

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is often as low as 0.20; they have as many as five times more suppressor than helper cells. In addition, the few helper cells they have appear to be defective and nonfunctional.

Since January, several published studies have documented a low H/S ratio in healthy hemophiliacs. The defect was more common among patients with the classic hemophilia A who were treated with Factor VIII concentrates. But the defect differed from that seen in AIDS patients. Although the hemophiliacs had a depressed H/S ratio--as low as 0.86 in some cases--their imbalance was primarily due to a relative increase in the number of suppressor T-cells rather than to the sharp decrease in helper cells seen in AIDS patients. It is not yet known whether low H/S ratios in hemophiliacs are an early sign of AIDS.

"Our study was designed to test the hypothesis that the low H/S ratio was related to Factor VIII concentrate therapy," Dr. Goedert said. He and his colleagues computerized the treatment records of 34 hemophilia A and 10 hemophilia B patients at the Hershey hemophilia center.

About 85 percent of the 25,000 hemophiliacs in the United States have the A form of this inherited disease that occurs only in males. They are unable to make sufficient amounts of Factor VIII, a serum factor necessary for the production of the clotting protein thrombin. The disease varies in severity. Some patients require Factor VIII supplements as often as three times a week, others only for sporadic bleeding problems. In hemophilia B, the defect is in the gene coding for serum Factor IX, which is also involved in thrombin formation.

Because these serum factors occur in minute amounts in the plasma of a single donor, a hemophiliac would need an extraordinary volume of blood for replacement therapy. Blood bank specialists have found a way to prepare

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concentrates by pooling plasma from thousands of donors. Factor VIII and Factor IX are concentrated from different portions of the pooled plasma.

"Thirty of the hemophilia A patients we examined were regular Factor VIII concentrate users, and seven hemophilia B patients were regular Factor IX concentrate users," Dr. Goedert said. "Although the groups did not differ by age, the Factor VIII recipients had significantly lower H/S ratios. Nine of them had ratios between 0.6 and 0.98," he said.

In a more refined analysis, the NCI scientists determined that there was a statistically significant correlation between the amount of concentrate a patient received and his immune status. "This analysis told us that the most important factor predicting a low H/S ratio was the number of vials of Factor VIII concentrate a patient received," reported Dr. Goedert. "Those patients who received more than 556 vials of Factor VIII during the course of the study had the lowest H/S ratios." Although the relationship with Factor VIII dose was clear, the investigators could only account for about one-third of the risk of low H/S ratios. "There are clearly other unknown factors involved," Dr. Goedert said.

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