Preventing AIDS transmission: should blood donors be screened?

During the past year, evidence has accumulated to suggest that the lethal and mysterious acquired immunodeficiency syndrome (AIDS) can be spread by infusion of blood and blood products.

Initially, patients with AIDS were mostly from two groups, male homosexuals with histories of numerous sexual contacts and persons who abused intravenous (IV) drugs (*JAMA* [MEDICAL NEWS] 1982;248:1423-1431). Disease transmission among these two groups could be explained by person-to-person contact and shared needles.

A few cases were also described among native Haitians in both Haiti and the United States.

But in late 1981 and early 1982, the Centers for Disease Control (CDC), Atlanta, began to receive reports of cases of AIDS among persons with hemophilia A. Since these persons all received multiple infusions of factor VIII concentrate, the reports raised the possibility that the putative infectious agent in AIDS could be transmitted through blood products. As of mid-January 1983, there were eight confirmed cases and two more under investigation.

In December 1982, CDC officials described in *Morbidity and Mortality Weekly Report* (1982;31:652-654) three persons in whom AIDS or an AIDS-like illness had developed but who had none of the previously known risk factors for this disease. In one case, multiple infections and immunological abnormalities typical of AIDS developed in an infant 20 months old. The disease in this infant is thought to have originated from multiple transfusions of whole blood and packed RBCs given for an Rh problem after birth. The blood came from 19 different donors, in one of whom AIDS developed about eight months after the blood donation but who also had donated blood to others without incident (so far). The CDC cautioned that . . . "any interpretation of this infant's illness must be made with caution."

Two adults are also known who may have acquired AIDS through whole blood transfusions during surgery. In one case, one of the blood donors used IV drugs and shared needles with a close friend who recently died of AIDS. This donor is currently being watched for symptoms of AIDS.

An Ad Hoc Committee

In response to these findings, in early January of this year, the CDC convened an ad hoc advisory committee to discuss the extent of the apparent problem and possible ways of preventing further spread of AIDS by this route.

Opinions—and emotions—expressed at the day-long meeting were diverse. Certainly in part this reflected the variable makeup of the committee, which comprised university blood bankers, experts on hemophilia, and representatives from the CDC's task force on AIDS, the Pharmaceutical Manufacturers Association, the American National Red Cross, the American Association of Blood Banks, the National Institutes of Health, the Food and Drug Administration, the National Gay Task Force, the National Hemophilia Foundation, and many other groups.

Some persons expressed doubt that a risk exists of transmission of AIDS by transfusion of whole blood. Others were not even sure whether hemophiliacs receiving factor VIII concentrate are in danger. Many public health officials, however, were convinced that there is a risk, although its magnitude cannot yet be estimated, and that swift action must be taken.

When it came to recommending preventive measures, however, disagreement was strong. Possibilities included increasing the safety of factor VIII preparations; setting up a laboratory test, such as measurement of antibody to hepatitis core antigen, that will identify persons at high risk of having AIDS; and asking all persons in high-risk groups donating blood to identify themselves so that their plasma could be excluded from factor VIII preparations.

No recommendations were issued. But representatives of commercial plasmapheresis centers, which provide 80% or more of the plasma used to make factor VIII concentrate, revealed that they indeed are instituting a policy of asking persons in high-risk groups to identify themselves.

There was considerable discussion of whether this action was ethical or fair. Physicians from the National Gay Task Force called it "scapegoating." They also questioned whether such a course of action would be effective.

But representatives of the National Hemophilia Foundation revealed that the blood centers' action is being taken at the foundation's request. For better or worse, this policy will soon be in place at commercial plasma collection centers.

CDC officials, on the other hand, are thinking seriously of recommending institution of a laboratory test that could detect high-risk donors, at least on a trial basis.

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The Frightening Facts

AIDS is a syndrome that was virtually unknown before mid-1981. Now the number of reported cases has doubled every six months. James Curran, MD, director of CDC's AIDS task force, provided as good a hypothesis as one can at this point: "AIDS is a disease in which exposure to a transmissible agent results in suppression of the immune system and increased susceptibility to serious illnesses," he told the meeting.

The illnesses make up a frightening catalog of conditions usually seen only in patients who are immunosuppressed by disease or drug therapy: Kaposi's sarcoma and other cancers, *Pneumocystis carinii* pneumonia, and infection with *Mycobacterium avium intracellulare*, cytomegalovirus and herpesviruses, *Toxoplasma gondii*, the rare parasite *Cryptosporidium*, and various fungi. Many patients have multiple infections with these organisms.

AIDS patients do show abnormalities of the immunologic system, but they have no known underlying cause of immunosuppression. In addition, the epidemiologic pattern of the outbreak suggests an infectious agent that may be transmitted by sexual contact. These features give rise to the hypothesis that Curran expressed.

In addition, the disease has a latent period as long as one year or more. (The infant described earlier received blood transfusions at birth, but did not show clear signs of AIDS until after 1 year of age.) Thus, the few cases seen so far associated with blood transfusion and factor VIII concentrate administration may indicate that many more cases are incubating.

'What, Me Worry?'

Among those at the ad hoc committee meeting questioning the existence of a risk was Aaron Kellner, MD, of the New York Blood Center. "Don't overstate the facts," he said. "There are, at most, three cases of AIDS from blood donation, and the evidence in two of these cases is very soft. And there are only a handful of cases among hemophiliacs."

Joseph Bove, MD, director of the blood bank at Yale University Hospitals, New Haven, Conn, stressed the limited evidence for AIDS transmission from whole blood transfusion. "We are contemplating all these wide-ranging measures because one baby got AIDS after transfusion from a person who later came down with AIDS and there may be a few other cases."

But those persons who have seen AIDS develop from a few isolated cases to an epidemic during the last 18 months had a different attitude.

Jeffrey Koplan, MD, assistant director of public health practice for the CDC and chair of the meeting, told Bove, "To bury our heads in the sand and say, 'Let's wait for more cases' is not an adequate public health measure."

Said Donald Armstrong, MD, of Memorial Sloan-Kettering Cancer Center, New York City, who has treated many AIDS victims, "I have absolutely no doubt that AIDS is transmitted by sex and blood products." David Sencer, MD, of the New York City Health Department, agreed: "Does anyone doubt that we are dealing with an infectious agent that is transmitted by blood and sexual contacts?"

CDC officials indicated that they strongly feel the need to take some preventive action. Donald Francis, MD, who directed the CDC's hepatitis vaccine trials, stressed the danger posed by AIDS' long latent period. "We can't constantly be reacting and be constantly behind the eight ball," he asserted.

The New York Blood Center's Kellner had another question: whether AIDS is truly new in hemophiliacs.

In response, Bruce Evatt, MD, of the CDC's AIDS task force, stressed that "AIDS just didn't occur in hemophiliacs prior to 1982." He cited a recent CDC survey of the health status of more than 4,000 hemophiliacs that showed that AIDS was the second leading cause of death among hemophiliacs in 1982 and that 37 living hemophiliacs currently have an AIDS-like illness. "Before 1982, there were no deaths that were even suspicious as AIDS on the basis of history," said Evatt.

Oscar D. Ratnoff, MD, professor of hematology at Case Western University Medical School, Cleveland, and an expert on hemophilia, corroborated Evatt's statement with results of a survey done in Northern Ohio among 100 hemophiliacs receiving home therapy. In 1982, there were six deaths, he said. Two were from *P carinii* pneumonia and one from Burkitt's lymphoma. In addition, three patients are alive with severe thrombocytopenia, which is a prodrome of many AIDS cases. "That makes almost a 10% morbidity and mortality in one year," said Ratnoff. "This kind of finding didn't exist before December 1981."

If AIDS can be transmitted through blood and blood products, how likely is it that an infectious agent will get into the blood and plasma pool? Selma Dritz, MD, of San Francisco, summarized some of the information obtained from questioning San Francisco patients in whom AIDS has developed in the last two years. "Of about 140 people, 10 or 11 had donated whole blood in the previous few years," she said. "We don't know how many others sold their blood or plasma at commercial centers."

Furthermore, each pool of factor VIII concentrate goes to about 100 patients. Thus, for the ten hemophiliacs who have confirmed or possible AIDS, there are approximately 990 more who received the same lots of factor VIII concentrate. Unfortunately, since each hemophilia patient receives many lots of factor VIII concentrate over the course of a few years, it is not possible to identify the infectious lots.

What to Do?

One suggestion was to increase the safety of blood products. Said Clyde McAuley, MD, medical director of Alpha Therapeutic Corporation of Los Angeles, a major supplier of commercial plasma products: "We are currently working on a heat-pasteurization process for factor VIII. We hope to make a product that will be free of hepatitis and hopefully free of AIDS." And National Hemophilia Foundation advisor Louis Aledort, MD, of Mount Sinai Medical Center in New York, told *JAMA* MEDICAL NEWS that all major suppliers currently have licenses pending with the FDA to market new preparation methods that may result in lowered infectivity, such as heat-treated Factor VIII concentrate products.

But Ratnoff asked, "What criteria will be used to judge improvement in risk? Will you 'test' it in patients? It's a long way before you can rid lyophilized donor pools of [a possible AIDS] agent."

Concluded Sencer, "I don't think that trying to make the product safer will solve this problem."

Excluding High-Risk Plasma . . . or Trying To

Of the two possible immediate responses to the problem, one already is being mandated at commercial plasma collection centers. Said Alpha Therapeutic's McAuley, "We are excluding plasma from homosexuals, drug addicts, and Haitians from the pool used to make factor VIII because frankly we don't have anything else to offer at this time."

The company has sent information about AIDS and its possible transmission through blood and blood products to all medical directors of its blood collection centers and to those centers who supply it with additional plasma. Each center also has received a letter to be given to each person who comes in to sell plasma. The letter says in part:

> In past years you have helped us help others through your plasma donations. We are now faced with a situation in which only you can help us ensure a safe product to those whose lives depend on it. Because of our shared goal of producing a continuous and safe supply of plasma products for use worldwide, Alpha has committed its resources to reducing the possibility that this disease might be transmitted through our products. We are now asking for your commitment also.

The letter goes on to ask anyone in a "high-risk" group to identify himself or herself to the medical receptionist. The person is offered further information if he or she requests it.

Alpha Therapeutic is not alone in this move. Said Michael Rodell, MD, of the Pharmaceutical Manufacturers Association, "The rest of the plasmapheresis industry is in various stages of instituting a program like Alpha's. Our goal is to make a cogent presentation of what the AIDS risk is to [blood donors] and to recipients and to ask them to identify themselves in private questioning."

In addition, Leon Hoyer, MD, chief of hematology at the University of Connecticut Health Center, Farmington, and chair of the Medical and Scientific Advisory Council of the National Hemophilia Foundation, told *JAMA* MEDICAL NEWS that the foundation sent a letter to all factor VIII suppliers in late 1982 asking them to exclude from production of factor VIII concentrate any plasma donations from IV drug abusers, homosexuals, and Haitians.

At least some community blood centers are putting the same policy into effect. Said Mary Leaman Morrison, scientific director of the Dayton, Ohio, Community Blood Center, "Exclusion of gays is already being done in a lot of smaller blood centers throughout the country. There's a lot of panic. People from the local hemophilia societies are demanding that something be done."

But the representatives from the National Gay Task Force felt that excluding people in risk groups from donating was the wrong course. Said Bruce Voeller, MD: "So-called 'fast-lane' gays are causing the problem, and they are just a minority of male homosexuals. You'll stigmatize at the time of a major civil rights movement a whole group, only a tiny fraction of whom qualify as the problem we are here to address."

Voeller gave additional reasons why he believes the policy would not be effective. "To identify gays as those across-the-board that you exclude will not eliminate AIDS from blood products," he asserted. "For one thing, it ignores the fact that 20% to 25% of the at-risk population is not gay. Also, many gays don't self-identify as such and won't respond to the questionnaire."

Voeller was not alone in condemning this policy. Said Armstrong of Sloan-Kettering, "I don't think anyone should be screened for donating blood on the basis of sexual preference. I think that is wrong."

But Aledort told *JAMA* MEDICAL NEWS, "I feel the industry's response is appropriate. I disagree vehemently with the National Gay Task Force. They may want to protect their rights, but what about the hemophiliacs' right to life?"

Despite the protests, it looks as though the policy will be put in place, at least at commercial plasma collection centers. Whether members of risk groups will identify themselves remains to be seen.

And even if the policy works for plasma collection, it still leaves open the question of what to do to ensure safety of voluntary whole blood donations.

Surrogate Marker Screening

Since there currently is no test to detect persons with AIDS or its prodromal illness, another approach is to see whether any test will detect a person at

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increased risk of having AIDS.

CDC immunologist Thomas Spira, MD, described the results of evaluating several such "surrogate" tests in persons with AIDS or its prodromal illness. The most successful was measurement of antibody to hepatitis B core antigen. The reason: Hepatitis B is prevalent in the same populations that are at high risk for AIDS. Antibody to core antigen remains elevated even after recovery from acute hepatitis B, so it identifies all persons who have had hepatitis.

This test yielded positive results in 90% to 100% of AIDS patients in various groups (homosexuals, IV drug abusers, Haitians). Results also were positive in 80% of persons with lymphadenopathy, a prodrome of AIDS. In contrast, among first-time contributors to a voluntary blood bank, results were positive in 5%.

Spira said the assay could be introduced into routine laboratory testing. There is only one manufacturer of commercial kits, however, and some people wondered whether the supply of reagents could be increased rapidly. Others thought this would not be a major problem.

Cost would be a problem, though. Although no one had a firm figure, amounts between $5 and $100 million were mentioned. But Sencer pointed out that both cost and benefit had to be factored: "How much does it cost to care for one AIDS patient?" he asked. In addition, he suggested that it could be introduced in place of the VDRL, which is being phased out.

But other problems remain. Said the FDA's Dennis Donohue, MD, "Based on past experience, I do not think it will be possible to provide a mechanism for doing this test rapidly and efficiently in all the blood banks in this country."

And Gerald Sandler, MD, of the American National Red Cross, raised another difficulty. "I have had ten years of explaining tests to people. I want to know how you will deal with those 5% of the normal population who will be positive for anti-HBc. A recent headline in *The Washington Post* said of AIDS, 'Lethal Disease Kills Victims.' How can you convince people that their blood is no good, but they're healthy?"

Future Recommendations?

Faced with these conflicts, CDC officials retired to their offices to try to devise recommendations. Said Koplan, "I'm not surprised that there was no consensus. We had various aspects of the problem illuminated from various people's perspectives, which is what we were looking for."

Of the two major alternatives discussed at the meeting, Koplan currently favors surrogate screening. He believes the hepatitis B screening test "is worth exploring and implementing quickly to some extent and for at least a short period of time [but] we need better data on costs."

In the meantime, what of the risk from whole blood donation? Said Dritz, "It's a hell of a mess. We're still getting calls from doctors about the risk of blood transfusions and we don't know what to tell them. We can't even tell them if there is less risk from a single donor than from a multiple-donor pool."

But after sitting through the meeting, one observer said, "I know what I'd do if I were going to have elective surgery. I'd get all my friends and relatives to donate blood for me."—by WILLIAM A. CHECK

Advanced medicine goes micro-chip

Biomedical engineering virtually took over a part of Philadelphia one week last fall, with four different conferences on state-of-the-art developments in that field and in engineering and computing as they relate to medicine.

Starting out the week was the Fourth Annual IEEE Engineering in Medicine and Biology Society conference, which was split into Frontiers of Engineering in Health Care and Frontiers of Computers in Medicine (COMPMED). Then came the 35th Annual Conference on Engineering in Medicine and Biology and finally the First IEEE Computer Society International Conference on Medical Computer Science/Computational Medicine (MEDCOMP).

A recurring theme at the first meeting was that without recent advances in miniaturization and computing speed, many of the latest achievements would have been impossible. This was clear, for example, in a report by Nitish Thakor, PhD, and Robert Kuhn, PhD, both assistant professors of electrical engineering in computer science at Northwestern University, Evanston, Ill. The investigators described plans for a pacemaker that can be programmed in any mode after implantation. The pulse width and amplitude can be modified, the sensing threshold changed, and the battery tested, and the pacemaker also can be programmed to treat tachyarrhythmias and fibrillation by delivering cardioverting or defibrillating shocks.

Special techniques must be used to manufacture such an "intelligent" pacemaker. Most microprocessors on the market today are constructed from integrated circuit chips composed of hundreds of gates (individual units) per cm^2. It is possible, however, to create a chip with thousands of gates per cm^2 (or hundreds of thousands of transistors per chip). This technology, called very large scale integration (VLSI), is believed to be the miniaturization breakthrough needed to make "intelligent" implantable devices practical (Kline J: Impact of VLSI on Medicine, in Einspruch M (ed): *VLSI Electronics Microstructure Science.* New York, Academic Press Inc, 1981, vol 2).