The Great AIDS Race: Testing the Test

The discovery of the putative AIDS agent last April kicked off a race for a quick, easy and inexpensive blood test, with the goal of eliminating transfusion-related cases of AIDS. Food and Drug Administration (FDA) approval for one or more testing kits being developed by five companies is expected any day now. The race is nearly over.

When Robert Gallo nine months ago announced HTLV-III as the U.S. candidate for the AIDS-causing virus (SN: 4/28/84, p. 260), Health and Human Services Secretary Margaret M. Heckler stood by his side. She followed his announcement with one of her own: A "100 percent certain" blood test to safeguard the nation's blood supply would be available within six months.

Her timing was a bit off, and the test being worked on will never attain 100 percent accuracy. Three reports in recent weeks point out the strengths, weaknesses and ethical problems of the test as blood banks gear up to use it on each of the millions of pints of blood transfused in the United States each year.

While a blood test will limit the number of transfusion-related AIDS cases, it will not put a stop to the as-yet-incurable disease. Transfusions of blood products represent only 2 percent of the 7,788 (as of last week) U.S. AIDS cases, and with the long incubation period for the virus it could take years for the beneficial effects of a blood test to be seen.

In the Jan. 11 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION (JAMA), Gallo and Stanley Weiss of the National Cancer Institute in Bethesda, Md., and researchers from several other government agencies evaluated an ELISA test (for enzyme-linked immunosorbent assay) that identifies an antibody to AIDS in blood serum. All five companies working toward FDA approval are thought to be developing ELISA tests.

In the JAMA study, blood samples from 72 of 88 people with AIDS were positive — an 82 percent accuracy rate, with another 16 percent borderline. Among 297 donors at no known risk of AIDS, 1 percent were positive and 6 percent were borderline. The results, the authors note, demonstrate "that this ELISA for HTLV-III antibodies is highly specific and sensitive for AIDS — excluding borderline results, 98.6 percent and 97.3 percent respectively."

But the test shows only that a person has encountered AIDS virus, not that he or she still harbors it or would necessarily pass it on. The 1 percent false positive rate presents a problem: Should the person, whose risk of AIDS is not known, be told? The authors recommend the development and use of a second assay for positive cases, "to minimize the psychic trauma to donors who are determined to have been categorized incorrectly as positive."

The JAMA report followed a report in the Dec. 22 LANCET that pointed out another weakness of the ELISA test — the possibility of missing the virus when it is there. Gallo, Jerome E. Groopman of Harvard Medical School and others found that among 96 people, all of whom were in a high risk group or had AIDS, four had the virus in their blood but came up negative with the ELISA assay. They had no antibodies to the AIDS virus, though they had other antibodies. (Three of the four, curiously enough, had no symptoms.) Since the virus itself is believed to be the problem causer, a test that misses people with virus may be missing carriers.

"The major question," says Groopman, "is how many people are there like that?"

The ultimate best test, he says, would be for a viral antigen — a piece of the virus. "If you had a test for antigen you could encompass antibody-positive and antibody-negative people," he says.

Nevertheless, the test will ferret out most contaminated blood, says Howard Streicher of Gallo's lab. "Based on these findings," he says, "the test would eliminate 19 out of every 20 potentially infected donors."

False negatives don't mean an FDA refusal. "Our scientists feel that's not going to slow down test kits," an FDA spokesperson said last week. "High risk people will pull themselves out of the pool."

Nor does Lawrence Sherman, assistant director of the St. Louis region of the American Red Cross, see the antibody-free virus carriers as an insurmountable problem. "This is a high risk population group," he says. With the prescreening done by the Red Cross and other blood agencies, he notes, most of these people are eliminated as donors. "What remains to be seen is what percentage of people — and I assume that it's a fraction of a percent — in seemingly low risk groups would have comparable results.

"The dilemma is for people in the high risk groups positive for the antibody," Sherman says. "They'll want to know — does the antibody indicate I'm protected, I'm a carrier, or I'm coming down with this horrible disease?"

As yet, there is no answer, leaving blood bankers with the potential problem of deciding whether or not to tell a person he or she has antibody to AIDS. To deal with the ethical issue, the Centers for Disease Control in its Jan. 11 MORBIDITY AND MORTALITY WEEKLY REPORT (MMWR) published a list of guidelines for administering the test. Sherman expects that the Red Cross and other agencies will follow these guidelines.

They recommend that people with a positive ELISA be told that their prognosis is not known, that they will probably remain infected and that they can infect others. They suggest these people be told to refrain from donating blood, plasma, body tissue and sperm. While a positive ELISA in the absence of AIDS symptoms is not a death sentence, it's not a clean bill of health either. "There is a risk of infecting others by sexual intercourse, sharing of needles and, possibly, exposure of others to saliva through oral-genital contact or intimate kissing," the MMWR notes. And pregnant carriers are at risk of bearing children with AIDS.

While a lead time between exposure and illness that can reach a few years or more clouds the AIDS picture, the MMWR guidelines note that "the majority of infected adults will not acquire clinically apparent AIDS in the first few years after infection." They cite reports of AIDS occurring in anywhere from 5 to 19 percent of homosexual men two to five years after antibodies show up in the blood. "The long-term prognosis for most persons infected with AIDS is unknown," according to the guidelines.

Blood collecting facilities should let a potential donor know if an initial check tests out positive on reexamination; the donor should be assured this "may not represent true infection," according to the guidelines. Confidentiality is crucial, and facilities "should consider developing contingency plans in the event that disclosure is sought through legal processes."

Meanwhile, work goes on in other laboratories. At Chiron Research Laboratories in Emeryville, Calif., a test for the presence of viral DNA is in the developmental stage, but is still a long way off. The problem, says Dino Dina, a member of the Chiron team that recently reported cloning the AIDS virus (SN: 1/5/85, p. 7), is that the AIDS virus is sometimes present in concentrations that strain the sensitivity of the technique. "They [DNA probes] have definite potential but as far as I know no one has been able to make it practical," Dina says.

Thomas Merigan, an infectious disease expert at Stanford University, says, "It's the obvious next step but whether it is successful depends on whether the virus grows and persists. But we don't know about that."

Because of the virus's long incubation period, even a perfect blood test won't eliminate transfusion-caused AIDS soon. Notes Merigan, "It could be two to three years before the benefits of the test are seen. We need to start as soon as we can, because we don't want to put that impact further out." — *J. Silberner*

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