Losing AIDS Antibodies

People who test positive for the AIDS virus may subsequently stop making detectable levels of antibody against it, according to a newly published study. The situation is rare and has occurred in only 4 of 1000 men with antibodies. Still, it adds another level of complexity to the problem of keeping the blood supply safe from HIV, the human immunodeficiency virus that causes AIDS. It also calls into question whether these men have successfully gotten over their infection.

Alfred Saah and Homayoon Farzadegan of the Johns Hopkins University School of Hygiene and Public Health in Baltimore and their colleagues report in the 1 June issue of the *Annals of Internal Medicine* that 0.4% of men, infected with HIV but without symptoms of AIDS, stopped producing antibodies that were previously detectable by three different blood tests. Two of the tests, the ELISA and Western blot assays, are used routinely by blood banks to determine if a donor is infected with HIV.

Thomas Zuck of the University of Cincinnati Medical Center wrote an accompanying editorial saying that it is futile for the public to expect "a zero-risk blood supply," but that "the blood supply is safer than at any time since AIDS has emerged." Saah concurs. "We think the impact [on blood banking] is going to be minimal," he said in an interview.

The patients in the new report are homosexual men participating in the ongoing Multicenter AIDS Cohort Study (MACS), which is based in Baltimore, Chicago, Los Angeles, and Pittsburgh. Last year, Saah and his colleagues reported that five men in the Baltimore group of the MACS study had lost detectable levels of antibodies against HIV. (Reports of the same apparent phenomenon are now being investigated at other MACS sites.) But it was not until the researchers used the polymerase chain reaction, a new test that can detect the presence of tiny amounts of DNA—in this case coded for by the AIDS virus—that they could be certain that four of the men were truly infected. This new detection technique is very sensitive but it is too cumbersome to use as a routine method for screening blood (see p. 1408).

Zuck is unsure about how to interpret the findings. "I don't know what the data mean," he says. "I also don't know if these men are infectious." Like Saah, he points out that all attempts to culture the AIDS virus from these men have failed. The ability to culture HIV from someone who is suspected of being infected is another way to document that they really are infected and may be capable of transmitting the virus.

Over a period of 6 to 18 months, tests of the four men differed in several respects. For example, three of them lost detectable levels of HIV antibodies while maintaining a positive polymerase chain reaction. One of them eventually lost reactivity on all tests. The fourth showed a reappearance of antibodies but lost reactivity on the polymerase chain reaction test.

An obvious question is whether three of the men have cleared the virus from their systems. "I am very reluctant to say that these men are controlling the virus," says Saah. He emphasizes that the appearance and then disappearance of antibodies against HIV is a very rare event in people who remain free of symptoms.

Researchers have been aware of two other time periods in which an HIV-infected person may not have detectable antibodies against the virus. One occurs soon after infection, presumably before the body has had time to make antibodies in response. The other occurs much later in the disease, when the immune system is so suppressed that AIDS patients can no longer make detectable levels of antibody. According to Saah, the phenomenon he and his co-workers report is probably more likely to occur in someone who never had a well-established infection.

No one knows precisely why the antibodies disappeared or dropped to very low levels in the four men, but Saah is fairly certain that HIV shifted from replicating at one level to replicating at a lower level. He speculates that the virus might somehow have become ineffectual in its ability to reproduce or to damage cells. Why the polymerase chain reaction became negative in one man after being positive is more difficult to explain, but it may mean that HIV is being harbored in some tissue other than peripheral blood. Then, a blood sample, which is taken to perform the test, might not reveal the presence of DNA from the AIDS virus in the genome of the host's cells.

The loss of antibodies against an infectious virus is not unprecedented. "It is a fascinating phenomenon, but by the same token it happens with other diseases," says Zuck. "With hepatitis B, for example, patients may lose detectable antibodies against proteins on the surface of the virus but retain antibodies against core proteins." Although this situation does not exactly parallel that of the four men in the present study, it does indicate that levels of antibody are known to change during the course of other diseases. ■ **DEBORAH M. BARNES**

Disappointing Brain Graft Results

Participants at the Ninth International Symposium on Parkinson's Disease, held this week in Jerusalem, heard that two Swedish patients who received implants of human fetal brain tissue 6 months ago had not shown any therapeutically useful improvement. Making the first public announcement on the progress of these patients, Olle Lindvall of the University of Lund Medical Center reported that, nevertheless, there was some improvement in neurological and neurophysiological measures that may indicate a slow recovery.

Following the disappointing outcome of the 80 or so implants of adrenal medullary tissue into the brains of Parkinson's patients in the United States, researchers and clinicians have been anxiously awaiting the results of fetal brain implants. The logic of repairing brain tissue with brain tissue and the very promising results of fetal brain implants in parkinsonian animals have encouraged high expectations.

"It is too early to draw conclusions about the final outcome," Lindvall told *Science*. "Our experimental work with human nerve implants into rat brains indicates that the time course of recovery could be slow." Lindvall cautions against making direct comparisons with the speed of response in experimental animals, because rates of growth may well be different. Pertinent here is the observation that brain implants into monkeys produced significant behavioral recovery within a couple of months.

The two Swedish patients were women in their fifties, suffering severe parkinsonian symptoms of rigidity and tremor. Both had undertaken continual monitoring of symptoms for 6 months prior to the implant, thus producing a base line for comparison. The implant—a suspension of brain cells from four fetuses—was injected into three places in the patients brains: two in the putamen, one in the head of the caudate. A key issue is survival of the graft, and although PET scanning has been unable to detect a change in dopamine activity in the patients' brains, Lindvall says that it cannot be categorically concluded that the grafts have not survived.

"In any case, we intend to continue working, slowly and scientifically," says Lindvall, "collecting as much information as we can from each patient." ■ **ROGER LEWIN**