AIDS Virus Creates Lab Risk

Two cases of HIV infection in lab workers have made laboratory personnel understandably nervous and prompted officials to strengthen their safety programs

THE National Institutes of Health is expanding its biosafety program after the recent discovery that two laboratory workers are infected with HIV, the human immunodeficiency virus that causes AIDS. The two cases, which came to public attention last fall, do not mean that laboratory-acquired infection is common. But they do mean that infection is possible and people working with the virus are very concerned.

The first worker is clearly infected with a laboratory strain of HIV, which makes it virtually certain that the infection resulted from occupational exposure to HIV. The worker can recall no specific incident that may account for the infection, however. In contrast, no one is certain that the second worker is infected with a laboratory strain of the AIDS virus. But he* remembers a laboratory accident that could have exposed him to HIV at a high concentration. Both cases were discovered during scientific surveys designed to assess occupational risk.

The most controversial aspect of the second case is that the worker was not informed for 16 months that he had been infected. This unreasonable delay, which NIH officials characterize as a monumental blunder, provoked an investigation that resulted in a reprimand for the scientist in charge of the study.

Until now NIH has not had a general surveillance program for either workers in clinical settings or those in research laboratories who are exposed to HIV. But as a result of the HIV infections in the two laboratory workers, a campus-wide medical surveillance program is scheduled to begin in mid-February under the direction of Robert McKinney, director of safety at NIH.

The two recent cases have important factors in common. Both workers handle large volumes of the AIDS virus in so-called high containment laboratories that are under contract with NIH; neither is an NIH employee. Both perform techniques to concentrate the virus as part of commercial processes and follow biosafety guidelines. Both deny having any risk factors for acquiring HIV other than their work in the laboratory.

In the absence of any gross breach of good laboratory practices, especially in the first case, safety officials can only surmise what might have caused the infections. W. Emmett Barkley, the former director of the division of safety at NIH, states in a report that, "the two infections can be attributed to human error and failure to recognize and prevent opportunities for worker exposure to contaminated materials."

"The two cases clearly demonstrate that there is a finite risk among laboratory workers who handle the AIDS virus."

The first worker was part of an epidemiological survey conducted between 1985 and 1987, the results of which appeared in *Science* (1 January, p. 68). "The study was designed to include workers who handle high concentrations of the virus, because previous studies had indicated that the overall risk of infection in lab workers is very low," says Stanley Weiss of New Jersey Medical School in Newark. The study included 265 study participants, 225 of whom had laboratory exposure to HIV.

"We collected samples from different groups of lab workers," says William Blattner of the National Cancer Institute (NCI). "These were sent as a batch to be screened. If anyone had a positive result, clear or borderline, we sent the same serum sample to separate facilities for Western blot and radioimmunoprecipitation analyses." Both tests are used to confirm the presence of specific antibodies to the AIDS virus. Clearly positive results are interpreted to mean that the person is infected with HIV.

No one knows how the first lab worker became infected with HIV. "There were no events that the worker recalled that suggested direct exposure to the AIDS virus," says Barkley. "But in discussions with the worker, there were a number of situations that might have involved exposure, including frequent spills of contaminated material." Barkely also cited instances in which the worker had some small cuts on his arm, but said that the worker always wore gloves. In addition, he noted that workers in high-production commercial laboratories may be under inappropriate pressures to salvage contaminated biological material, which could increase their risk of exposure.

This lab worker was the only one in the Weiss and Blattner study who was ultimately confirmed as being infected with HIV, and he was notified of his test results about 6 weeks after the study began. But a full year elapsed between that time and the scientific confirmation that he was infected with a laboratory strain of the AIDS virus.

"We spent 6 months just trying to talk to this individual," says Blattner. "The person didn't want to talk to us. We did not know his name. The contact physician had interviewed the individual and had not identified any risk factors other than possible laboratory exposure to HIV." When the worker did talk to two additional researchers in the Blattner group, he again denied any other means of exposure to HIV. At this point, Blattner notified Barkley.

From then on, the researchers focused on determining the source of HIV that had infected the worker. Some were convinced that he had acquired the infection through a sexual contact or perhaps intravenous drug use; Weiss says he thought that lab infection was likely. Proving the source of viral infection turned out to be much more difficult than anticipated, however.

The single biggest problem was that, at first, no one could get HIV from the lab worker to grow in tissue culture. Culturing was necessary in order to do the molecular analyses that could determine what strain the virus was. Six different laboratories made nine or ten unsuccessful attempts to grow the worker's virus. Then, after a conversation with Howard Stryker of NCI, Weiss turned turned to researchers in Robert Gallo's laboratory at NCI to see if the virus could be isolated from macrophages.

Finally, Mika Popovic and Suzanne

*For simplicity, both workers are referred to as "he" in this story. Their identities are being kept confidential.

Gartner of NCI successfully cultured the virus from the lab worker's macrophages. These scavenger cells in the blood engulf many kinds of foreign particles, including viruses. "The reason the other laboratories failed was that they were using traditional methods of culturing HIV with T cells only," says Gartner. This lab worker was recently infected and was still free of any symptoms of AIDS. Gartner had observed that with other healthy HIV-positive people, the virus could only be cultured from monocytes and macrophages, so this case did not surprise her.

At about the same time, David Waters of Program Resources, Inc., in Frederick, Maryland, also successfully cultured the virus. While Popovic did his own molecular analysis of the virus, Waters sent batches of DNA from his HIV-infected cells to George Shaw of the University of Alabama in Birmingham for further study.

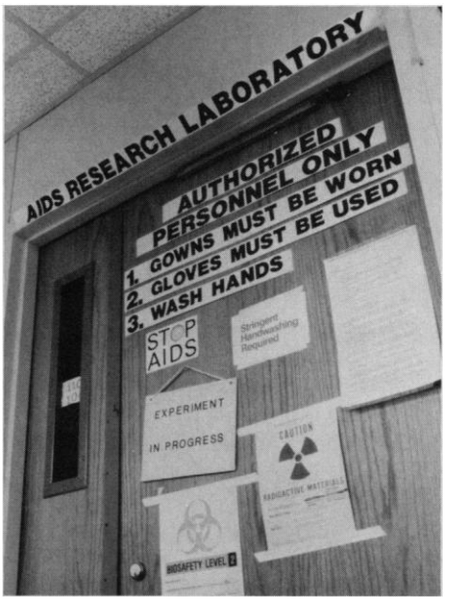
Popovic and Shaw cut the infected macrophage DNA into pieces using restriction enzymes and compared the fragments to those of known strains of HIV. They reached the same conclusion. The pieces matched the III_B isolate of HIV, a viral strain that had been grown for several years in a line of transformed T cells.

This finding in itself presents a scientific puzzle that has yet to be resolved. "The amazing thing, from my standpoint, is that the virus we're talking about is III_B," says Gartner. "In the lab it grows in T cells. But when that virus went back in vivo it infected the worker's macrophages."

Gallo, too, was surprised at the result. "Our first thought was that this can't be a laboratory infection, because the lab virus is raised in T cells." But the molecular analyses by his colleagues and by Shaw's group indicated otherwise. "I am now sure to the 99% level that this is the laboratory III_B strain. And what do you know? That's the strain the guy was working with."

How did a laboratory-bred T cell strain of HIV manage to infect a living person's macrophages, and not his T cells, at least to a detectable extent? No one as yet has definitive data, but Gallo has a theory. He proposes that within any given HIV isolate, including the III_B lab strain, there are probably different populations of viruses that vary to minor degrees. Some of those molecular differences will make a biological difference. And in the case of the lab worker, a slight molecular change apparently altered the cell types the virus could infect. "It looks as if a very small difference in amino acid sequence can make a very big biological difference," says Gallo.

The case of the second worker has angered many research personnel at NIH because of the way the information was handled. Blood drawn 4 to 6 months before his laboratory accident showed no signs of infection with HIV, but a second sample taken 6 to 9 months after the incident tested positive. The researcher responsible for informing the worker of his test result did not do so until 16 months later, however.



Biohazard warnings. *The door to an NIH laboratory cautions workers about handling the AIDS virus.*

This blatant error provoked a formal reprimand. "The researcher received a memo from his supervisor that indicated a massive breach of his responsibilities," says William Raub, deputy director of NIH. "Beyond that, NIH is moving to change the way this researcher is supervised. Otherwise, he has an excellent record of work performance." NIH officials have refused to disclose the identity of the researcher because they fear that linking his name to the case could lead to the identity of the infected worker.

It was not until after the worker was finally notified that he was infected with HIV that he recalled having a laboratory accident. He said he had cut his gloved finger with a blunt stainless steel needle while cleaning a piece of contaminated equipment. Biosafety officials Barkley and McKinney refer to the accident as the "probable cause" of infection, although they do not know for certain that the accident actually caused the infection. No one knows whether the worker is infected with a laboratory strain of HIV, however, because he has not participated in studies that could determine this information.

The two cases illustrate one overriding point, according to Barkley. "They clearly demonstrate that there is a finite risk among laboratory workers who handle the AIDS virus," he says.

This knowledge has understandably induced a great deal of anxiety among researchers working with HIV. According to one, who asked not to be identified, members of his laboratory began testing themselves for exposure to the virus. Another researcher said that at least one worker in his laboratory had resigned because of fear of infection and that the spouse of a different worker had called to express grave concern.

The two cases also prompted recommendations for increasing biosafety efforts, the primary focus of which is the workers themselves. "The thing that needs to be changed is the attitude of the workers—an increased awareness of what they are doing," says McKinney. He and Barkley both stress that existing biosafety measures are adequate, but that workers need to adhere to them more strictly.

But some issues concerning safety measures remain to be addressed. For example, NIH laboratories are typically overcrowded, which increases risk. The quality of protective clothing worn by lab workers, including latex gloves, varies widely. McKinney urges that workers double-glove with surgical gloves.

Another question concerns the AIDS virus itself. Although safety officials point to high concentrations of virus as posing an increased risk, they acknowledge that many other factors are also involved. Gartner points out, for instance, that biological differences among isolates of HIV make some strains much more infectious and therefore dangerous to handle than others.

A frequent concern is whether an aerosol form of the virus can cause infection. Barkley says that it is possible but not probable, and that no evidence suggests that it occurs. Nevertheless, he acknowledges that no studies have been done to determine whether aerosolized virus is infectious. McKinney says that such tests are being planned.

In order to determine who should be screened in their new general medical surveillance program, safety officials at NIH are urging lab personnel who work with HIV to complete a pathogen registration form. At present, no one has an exact count of the number of laboratory workers at NIH who handle the AIDS virus. McKinney says that more than 90 NIH laboratories are currently working with HIV.

Adhering to good safety practices is not enough, say Barkley and McKinney, unless lab workers are constantly aware of working with a human pathogen. To that end, NIH has revised an existing training course and oriented it toward the handling of HIV. ■

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