Researchers Look Ahead to AIDS Meeting

There is growing optimism about vaccine prospects, but no startling developments are expected in San Francisco

As the Sixth International AIDS Conference approaches, the possibility that the meeting will be disrupted by activists is capturing the lion's share of attention (see box, p. 1181). But what about the science, you may ask. The conference will, after all, feature some 2500 talks and posters detailing the results of research on all aspects of AIDS. Although AIDS experts don't expect any startling developments in San Francisco, they do expect to see a continuation of the steady incremental progress toward understanding HIV, the virus that causes AIDS, and toward developing effective AIDS vaccines and therapies.

The past year has, for example, seen a marked upturn in optimism about the feasibility of an AIDS vaccine, a switch from the previous pessimism that had been fueled by several experimental failures, as well as by knowledge of the insidious way that HIV invades and destroys key immune cells.

But last year researchers began getting positive results in monkeys for the first time. Experiments, conducted independently by the teams of Ronald Desrosiers at the New England Regional Primate Center in Southborough, Massachusetts, Michael Murphy-Corb of the Delta Regional Primate Center in New Orleans, and Murray Gardner at the University of California at Davis, showed that rhesus macaques could be protected against the AIDS-like disease caused by simian immunodeficiency virus (SIV), an HIV relative, if they were first immunized with whole killed SIV.

Although promising, these results led some researchers to suspect that effective protection could be achieved only with whole killed virus, a vaccination method considered by many to be too risky. The concern is that whole virus preparations might be incompletely inactivated or the genetic material that they contain might recombine with the genes of another virus to generate a disease-causing hybrid.

But recent findings suggest that something less than a whole virus might work, says Dani Bolognesi, an AIDS vaccine researcher at Duke University School of Medicine. Preliminary results from a number of groups indicate that animals might be successfully immunized with viral proteins or protein fragments. One such report has come from Marc Girard of the Pasteur Institute in Paris. At an AIDS meeting held in April in Keystone, Colorado, he presented the results of experiments in which chimpanzees were protected from HIV infection with a cocktail of HIV proteins. And Genentech, Inc., of South San Francisco announced last week that two chimpanzees had been protected from HIV infection by vaccination with a viral coat protein. More reports of successful immunization with proteins or peptides are expected at the San Francisco conference, Bolognesi says.

June Armstrong

Protecting monkeys against SIV. *Ronald Desrosiers leads one of the groups working with animal AIDS models.*

He points out that some big obstacles still lie ahead, however. "What is being done now are the most simple experiments you can do," he says. In the successful experiments so far, vaccinated animals have been challenged by injecting them intravenously with the same viral strains used for their immunization. But that laboratory situation does not reflect the real-life transmission of the AIDS virus.

For one, the virus is extremely variable and to be effective a vaccine must protect against any strain a person might encounter. There are hints that immunization with one strain might protect against another, most notably in experiments by Erling Norrby of the Karolinska Institute and Gunnel Biberfeld of the National Bacterial Laboratory in Stockholm. These researchers vaccinated three cynomolgus macaques with HIV-2, a close relative of SIV, and subsequently challenged the animals with SIV. They did not come down with disease. "This means we can obtain broad-spectrum protection within a type," Norrby told *Science*.

The Swedish workers used live HIV-2 for the vaccination, however, an option no one wants to attempt with the dangerous AIDS virus. In the next round of experiments, they will try vaccinating with killed HIV-2.

But even if cross-protection against multiple AIDS virus strains can be achieved, other hurdles will remain, such as the problem of producing immunity against cell-associated virus, something that has been traditionally possible only with live attenuated viruses. These, like whole, killed vaccines, carry the potential risk of regenerating a virulent virus strain.

One strategy Gardner, Murphy-Corb, and others are considering is developing local forms of vaccination that would raise antibodies in the mucosal membranes of the rectum or reproductive tract, through which the virus must pass during sexual transmission, to nab the virus before it can enter the bloodstream and gain refuge in blood cells. But that still doesn't address the problem of virus that enters the bloodstream already in cell-associated form.

So while AIDS experts are more hopeful than before about an AIDS vaccine, they do not expect one soon. Moreover, some 5 million people worldwide may have already been infected and will eventually develop AIDS. So the need for effective AIDS therapies will continue to increase for the foreseeable future.

Here the principal message from the past year is that less may be more. The anti-AIDS drugs furthest along in the clinical pipeline are AZT, already approved by the U.S. Food and Drug Administration, and two newer and still experimental drugs called ddI and ddC. They all work by inhibiting reverse transcriptase, an enzyme needed for the virus to reproduce itself, and the use of

Danforth Reapproached

Washington University chancellor William H. Danforth has been approached by Health and Human Services Secretary Louis Sullivan to be director of NIH, *Science* has learned. Danforth, who declined to be considered last year when a White House aide asked him his views on abortion, is the only candidate Sullivan is known to have called. ■ **B.J.C.**