AIDS Vaccine Meeting: International Trials Soon

Sites are being selected as major organizations try to hurry vaccine efficacy trials; 1995 may be the earliest date

Marco Island, Florida—THE CENTRAL QUESTION in the AIDS vaccine search is no longer "Can we make a vaccine that works?" A vaccine is going to come. As Wayne Koff, head of the AIDS vaccine branch of the National Institute of Allergy and Infectious Diseases (NIAID), puts it, the question today is: "How do we speed it up?"

The message 400 AIDS vaccine researchers and policy-makers heard after journeying to this northern tip of the Everglades for a 5-day retreat covering the latest in basic and applied research was that the time was coming for real-life vaccine trials, in which promising experimental preparations are tested in populations that are at daily risk of infection. Until recently, such trials had been considered premature, but the news of the 15-19 October International Conference on Advances in AIDS Vaccine Development—sponsored by NIAID's Division of AIDS (DAIDS)—was that such trials are close to becoming a reality.

At least three major organizations have announced that they have chosen or are choosing sites for vaccine efficacy trials. The World Health Organization (WHO) boycotted the Florida meeting to protest the U.S. immigration policy preventing people infected with HIV from entering the country. But members of the WHO AIDS vaccine steering committee did attend—and revealed that their group has picked four countries for trials: Rwanda, Uganda, Brazil, and Thailand. Thailand is also a favored choice of the U.S. Army's medical research division, which is gearing up to test AIDS vaccines there (possibly in conjunction with WHO).

NIAID has selected Zaire, where NIH is working on Project SIDA with the Centers for Disease Control (CDC), though recent political turmoil in the African country has gummed up the plans. NIAID is planning to establish other overseas sites next year through American universities that are already conducting research in developing countries. NIAID is looking at the United States, too—focusing on populations such as young gay men, intravenous drug users, and people who frequent sexually transmitted disease clinics.

When the trials begin, they will draw on some of the nine prototype HIV vaccines that already have been tested in uninfected people—along with others now in the research pipeline. The studies done so far, however, have focused on the safety of the vaccines and their capacity to evoke an immune response; none has been a real-time test of effectiveness. But several factors—especially the rapid spread of the disease—are propelling the research community toward efficacy tests. WHO estimates that 8 million people were infected with HIV worldwide in 1990 and predicts the number will skyrocket to 40 million by 2000. As CDC AIDS chief James Curran said repeatedly during his presentation at the conference's opening session, "The virus is winning."

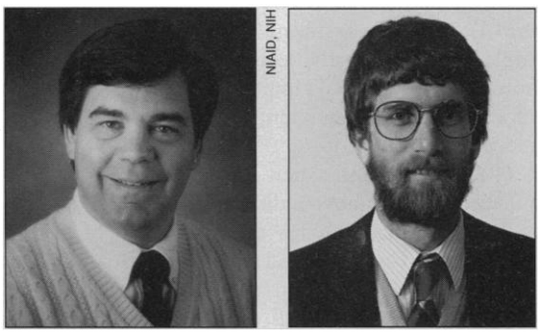
It is this gloomy fact that changed the minds of researchers who had wanted to wait for a sure bet to be developed. "Perhaps you don't need a bloody perfect vaccine," said Gordon Ada, an immunologist at Australia's John Curtin School of Medical Research. "There's a long row to hoe to get a vaccine to do everything we want it to do." Ada and others hope a less than perfect first-generation vaccine would be replaced when a better one is developed.

Another cause of the sea change has been the flood of successful vaccine experiments in monkeys and chimpanzees. Conducted at more than a dozen labs in the United States and Europe, these show that several different types of experimental vaccines can protect animals from challenges with live virus—although the experiments were done under idealized lab conditions. By far the greatest success has come with vaccines made from the whole, killed simian immunodeficiency virus—a close cousin of HIV; such preparations have protected more than 150 monkeys in challenge experiments. A few genetically engineered vaccines based on subunits of the whole virus have also worked, and many researchers favor this approach because they argue that it poses far less risk than whole, killed virus preparations.

In spite of the new enthusiasm for efficacy trials, none will begin tomorrow—selecting sites is merely the beginning of the process. Epidemiologists will have to ascertain how quickly the virus is spreading in the uninfected population, since lowering that "seroincidence" rate will be the goal of the vaccine test. And researchers must identify the prevalent types of the virus at the site, because an AIDS vaccine made from one HIV isolate may protect against only a limited range of strains.

There is also the delicate question of which vaccines are to be tested, a decision that committees will make for each site. "Right now, there is no ideal vaccine," said Daniel Hoth, head of DAIDS. "The general strategy is that there will be multiple vaccines tested at multiple sites."

So what's the prognosis? Dale Lawrence, head of international trials at DAIDS, estimates that sites could begin gathering seroincidence data by this time next year. He then predicts that each candidate vaccine will first be tested in small pilot studies in the targeted population to make sure it is safe and elicits an immune response, even if such studies have already been completed elsewhere. Add to that, says Lawrence, the inevitable unforeseen delays. "We begin our rapid progress toward efficacy trials with a timetable that is initially two-and-a-half to three years away," said Lawrence. "And what's going to happen is there's going to be slippage, which means three to four years from now is when it's really a key time."



Vaccine veterans. *Dan Hoth and Wayne Koff.*

Col. Donald Burke, director of the U.S. Army's AIDS program, ventured a similar timetable. "Even if we were to decide today and go," said Burke, "it would be no earlier than 1995 before we might have some statements about efficacy."

And that is none too soon, since as Wayne Koff pointed out in his talk, HIV is currently "beating the crap out of us." Koff concluded his talk at the meeting's closing session with the ominous warning to his colleagues that they should begin making tough choices about vaccine trials now, since if researchers can't speed things up, "we aren't going to have any choice at all." ■ JON COHEN

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