

Imperfect AIDS Vaccine Still Useful

Researchers Say 50% Effective Drug Could Change Course of African Epidemic

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PHILADELPHIA, Sept. 8 -- A vaccine that is not even 50 percent effective could nevertheless change the course of the AIDS epidemic in Africa under certain circumstances, according to predictions made here at the conclusion of a scientific conference.

A poor AIDS vaccine would have to be used by nearly an entire population to have any benefit. However, even with less-than-complete coverage, such a vaccine could prove useful if already-infected people had access to antiviral drugs, which reduce a person's likelihood of transmitting the virus to someone else.

On the other hand, if people were to greet the arrival of a modestly effective vaccine by increasing their risky sexual behavior even a little, all benefit would disappear.

"We don't need a perfect vaccine to have a public health impact. Even one that is only moderately protective could control the epidemic," said Ronald H. Gray, of the Bloomberg School of Public Health at Johns Hopkins University, who created a mathematical model that tested the effects an AIDS vaccine would have on Uganda, one of the worst-hit nations in Africa.

In the Rakai district of Uganda, about one in every 900 acts of heterosexual intercourse results in a new infection with human immunodeficiency virus (HIV). As in the rest of Africa, this is the main mode of virus transmission.

Each infected person in Rakai infects an average of 1.34 other people before he or she dies. That is called the "reproductive number" of the epidemic, and if it can be reduced to less than 1, disease transmission will abate and, theoretically at least, eventually burn out.

Gray and his colleagues calculated that a 50 percent effective vaccine would have to be taken by everyone in Rakai to tip the reproductive number below 1. A 75 percent effective vaccine used by half the population would do the same thing.

Even a 25 percent effective vaccine used by three-quarters of the population would drive the number below 1 if already-infected people received antiviral treatment at the stage of disease recommended by guidelines from the Department of Health and Human Services, Gray calculated.

Such treatment does not exist in Africa now. But with deeply cut drug prices and the United Nations' recent decision to create a global fund to buy AIDS drugs for the developing world, the possibility is not entirely out of the question.

In Rakai, 25 percent of men, and 4 percent of women, have extramarital intercourse each year. If that behavior doubled after the widespread introduction of a 50 percent effective vaccine, the epidemic would actually worsen.

"It will completely wipe out the benefit of the vaccine," said Gray, who produced the model with the help of researchers at Columbia University and Uganda's Makerere University.

There are two large-scale AIDS vaccine trials underway. The bigger and longer running involves 5,100 gay men and 300 women recruited at 61 sites in the United States, Canada and the Netherlands.

All are at high risk of acquiring HIV because of their sexual practices. Two-thirds received a vaccine containing a protein called gp120 taken from HIV's envelope, or outer covering. The remaining one-third were injected with a placebo.

The researchers conducting the trial estimate that about 1.5 percent of participants will become infected each year (assuming those getting the vaccine are not protected by it). The Food and Drug Administration has suggested it would consider approving an AIDS vaccine if a trial shows with a high degree of certainty that the substance reduces the rate of HIV infection by at least 30 percent.

The trial, which is costing about \$200 million, is scheduled to last three years, ending in late 2002. However, an independent monitoring panel will secretly review the data in November to determine whether the vaccine is unusually effective. If it is -- and it would have to cut infections by more than 60 percent -- the study would be stopped ahead of schedule. People who received the placebo would then be offered the vaccine.

"I think it's a high hurdle to achieve," said Donald P. Francis, president of VaxGen, the California biotechnology company that makes the vaccine. "I would be surprised if it were stopped."

Interviews with people in the trial suggest for the most part that possible access to a vaccine is not causing an increase in risky behavior. At the start of the study, 60 percent of the gay men reported having unprotected anal sex in the previous six months. One year into the trial, 46 percent reported they had.

The women, many of whom are users of crack cocaine who have traded sex for drugs, also reported a lower rate of unprotected intercourse a year into the study. Curiously, though, the women who felt strongly they had received placebo injections reported higher rates of risky behavior than at the start.

"They have difficulty understanding the concept of placebo," said Bradford Bartholow, one of the researchers. "Many women believe the placebo is the vaccine."

The designers of the second trial, which is testing a vaccine in 2,500 drug users in Bangkok are addressing that problem in a highly unusual way.

As part of the process of giving "informed consent," volunteers must take a test to determine whether they understand the purposes, procedures, risks and benefits of the vaccine trial. Each person must take the test twice, more than 24 hours apart, and pass it with an 80 percent score. Furthermore, a person must correctly answer all of a core group of questions the researchers believe are essential for understanding what a volunteer is getting into.

That trial, which is also testing the VaxGen gp120 vaccine, will run about two more years.

An issue in vaccine trials, especially those in developing countries, is how to treat people who become HIV-infected during the study.

In the Bangkok trial (in which about 300 people are expected to acquire the virus, assuming the vaccine doesn't work), VaxGen bought local health insurance policies for all the participants, at a cost of about \$2.50 a person. People who become infected will be treated under the national guidelines set by the Thai government's health ministry. Starting next month, those guidelines ensure that all HIV-infected people will get three-drug combination therapy (without a drug from the expensive protease-inhibitor family).

The U.S. Army hopes to start another AIDS vaccine trial in Thailand next year, which would enroll about 16,000 non-drug users. The Defense Department will "support . . . drug availability" for people who become infected in that study, Col. Deborah L. Birx said.

There is no guarantee that every person in a developing country who becomes infected during a vaccine trial will receive triple-drug therapy for life provided by a study's sponsors. But UNAIDS, the AIDS organization run by the United Nations and World Bank, has said it expects that people who become infected during vaccine trials will be provided medical care that is at least somewhat better than what is available for the general population of the country where the study is held. Precisely what that consists of will be negotiated by the parties involved.

Malegapuru Makgoba, a physician who heads South Africa's Medical Research Council (the equivalent of this country's National Institutes of Health), said he is confident that equitable arrangements can be made. Early plans are underway for a vaccine trial in his country sponsored, in part, by those two research entities.

"All the institutions have reputations to protect. They have integrity to deal with. Their necks are on the line," he said.

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