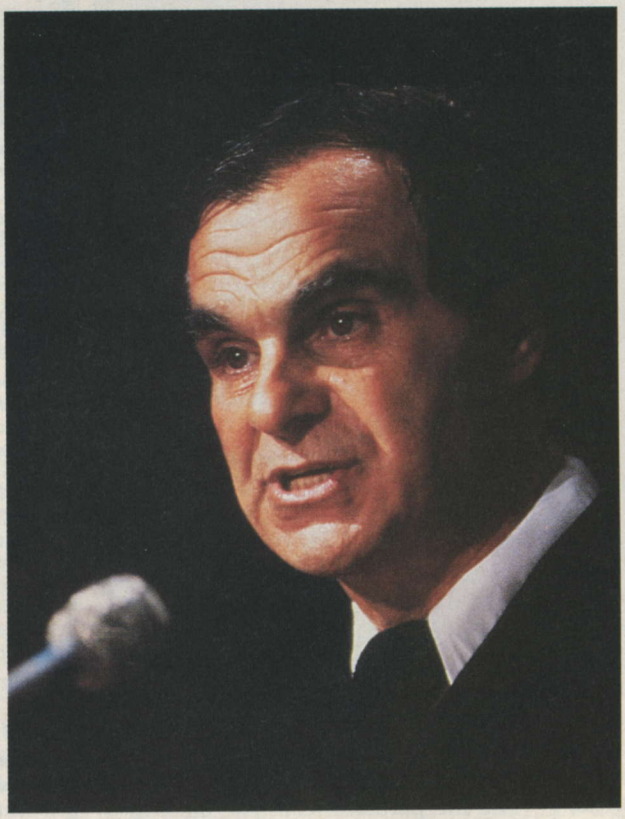
ONE SMALL STEP TOWARD A VACCINE

When French immunologist Daniel Zagury wrote a letter to *Nature* in March 1987 to report that he had inoculated himself and several volunteers with an experimental AIDS vaccine, many of his colleagues thought him foolhardy. After all, the vaccine — consisting of cowpox virus with a gene from the AIDS virus, HIV, spliced onto it — could have unforeseen side effects. Some also pronounced the effort premature; HIV is notoriously elusive, continually changing its chemical identity, thus slipping past the immune system and potential vaccines. More basic research was needed, they said.

But a year and a month after his first report, Zagury's brashness may have paid off. In the April 21, 1988, *Nature*, he reported that the vaccine, when followed by additional booster shots, produced the best immune response yet seen to HIV. Zagury summed up the preliminary results in a few dramatic words: "Our results show for the first time that an immune state against HIV can be obtained in man."



Daniel Zagury's self-inoculation has paid off.

Adding weight to his findings is the concurrence of coauthor Robert Gallo, the leading virologist in AIDS research at the National Institutes of Health. Gallo scrupulously analyzed the condition of Zagury's immune system. When Gallo presented the study at a symposium at the National Academy of Sciences a week after publication, the tentative conclusion was that Zagury's work may point the way to the first practical vaccine to protect against HIV.

Normally, when a virus strikes, distinctive chemical markers on its protein coat — called antigens — allow the immune system to recognize the virus as an intruder and attack it. A vaccine, in effect, forewarns the body of a potential invader by behaving like a harmless, small-scale infection. By exposing the immune system to a fragment of a virus's surface, or to a whole virus that's been killed or weakened, the vaccine stimulates the immune system to create antibodies to the virus and arms it against a future, actual infection.

The problem with HIV, however, is that the virus has many different strains, all marked by different combinations of antigens; antibodies against one strain might not protect against all. As soon as the body manufactures antibodies that bind to a particular HIV antigen, variants of the virus disguised in other antigens emerge and escape antibody detection. Further compounding matters, HIV infects or kills some of the immune system's most powerful weapons — T cells and macrophages — which work together to destroy pathogens. Therefore, says Gallo, to protect against AIDS, a vaccine must "block infection early on and completely."

There are encouraging signs that just such strong defenses may be rallied by the vaccine-and-booster routine Zagury and his colleagues developed at the Pierre and Marie Curie University in Paris. Their vaccine consists of the harmless cowpox virus (which is also used in the smallpox vaccine), linked by genetic engineering techniques to an HIV gene that codes for the antigen gp160. This antigen is thought to be shared by most AIDS strains, and so it's a potential chink in the virus's armor.

Studies show that a single injection of the vaccine doesn't prompt an impressive immune response in humans. But Zagury gave himself three additional booster shots, consisting of his own blood cells reinfected in the test tube with the recombinant virus used in the vaccine. Reinfection "reminded" these blood cells of the intruding HIV antigen, so that when the cells were injected back into Zagury they apparently called his immune system into combat. Later, yet another type of booster — purified gp160 antigen — was injected to bolster the waning effect of the first round of boosters.

About a year after the initial vaccination, Zagury showed no side effects and exhibited high levels of antibodies to gp160. In the test tube these antibodies disabled three very different strains of HIV. Studies also revealed that Zagury's white blood cells were extremely effective in destroying HIV. A standard skin test using the gp160 protein gave further proof of a strong immune response. With all these important immune signals present, Zagury "looks immune ready," says Gallo. "But of course," he adds with a laugh, "he could not be talked into being challenged by HIV." Ultimately, such a challenge is the only way of assessing the vaccine's effectiveness.

For now, Zagury's team plans to test the vaccine-booster protocol in chimpanzees, taking the additional step of infecting the animals with HIV.

— Margie Patlak

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