AIDS vaccine experiment 'worrisome,' doctor says

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BOSTON — The death of three monkeys that had gotten an AIDS vaccine in a Boston lab suggests that a closely watched strategy intended to blunt the deadly progression of the human immunodeficiency virus may not provide total protection.

For several years, researchers have concentrated on crafting vaccines that prompt the body to mount a vigorous challenge to the AIDS virus and hold it in check.

Much of the enthusiasm for this approach comes from experiments on monkeys, which appear to survive for years with these vaccines even after they receive high doses of the monkey form of the virus.

However, at a conference yesterday, researchers from Beth Israel Deaconess Medical Center in Boston who helped develop the strategy reported that monkeys eventually appear to fall sick and die, even after showing promising resistance to the virus.

"This suggests that viral escape will prove to be a challenge," Dr. Daniel Barouch, one of the Boston researchers, said at the 10th Conference on Retroviruses in Boston.

In his experiment, three of four vaccinated monkeys got sick during three years of follow-up after their shots with an experimental vaccine created by Merck & Co.

Typically these new vaccines take a two-step approach. The first, called the prime, is AIDS virus genes that are injected into muscle, where they are taken up by cells and result in production of viral proteins. The second is the boost, often a harmless hollowed-out virus that carries in more of the genes.

Together, if all goes as planned, they induce the body to mount an attack by killer T cells that destroy infected cells. This may not prevent an infection, but it can minimize its consequences by keeping virus levels low.

Dr. David Ho, scientific director of the Aaron Diamond AIDS Research Center in New York City, said the monkey deaths are "enough to be worrisome."

In fact, Ho said the emphasis in the vaccine field seems to be shifting back toward an older strategy that many had dismissed as unworkable against the AIDS virus. Ordinarily, vaccines do their job by prompting the immune system to churn out antibodies that recognize an invading germ and kill it before it ever establishes an infection.

Even though the body readily makes antibodies against the AIDS virus they cannot penetrate a thick coat of sugar that covers the virus' surface. However, new studies suggest it is possible to concoct antibodies that actually do kill the virus, and studies are under way to find ways to trigger their production.

Several vaccines based on the prime-boost approach are already in human testing, and the Boston monkey results do not mean they are doomed. The monkeys received only the prime, not the boost, stage of the strategy, and some experts said the experiment is not a fair test of the current generation of vaccines.

Among the furthest along are vaccines from Merck that have been given to about 600 human volunteers so far.

"You shouldn't read too much into it," Dr. Emilio Emini, head of Merck's AIDS vaccine program, said of the monkey results.

He said effective vaccines using this strategy will almost certainly be more sophisticated than the one used in Boston, since they will carry in more viral genes, giving the body more targets to mount a defense.

Dr. Norman Letvin, another of the Boston researchers, said scientists assumed from the start that the vaccine would not always stop the virus completely. Unvaccinated monkeys fared even worse, so "this tells us that a T cell vaccine has the ability to slow disease progression."

At yesterday's meeting, Merck scientists presented data on another experimental vaccine that appeared to be still working well in monkeys 2½ years following infection with an especially aggressive form of the virus.

"I am encouraged," said Merck's Dr. John Shiver. "There are very obvious things we can do to improve that vaccine."

Furthest along in testing is VaxGen's AIDSVax vaccine, a more traditional approach using the outer shell of the AIDS virus. It has already been given to 7,900 volunteers in America, Europe and Thailand. Results are expected within a month or two.

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