Failed HIV Vaccine May Have Increased Vulnerability to Infection

8 November 2007 (Reuters Health [Megan Rauscher])—It is possible that the delivery vehicle for a recently discontinued investigational HIV vaccine increased susceptibility to HIV infection among the volunteers who received the vaccine, the researchers said at a press conference in Seattle, Washington.

Healthy volunteers who received the shelved V520 HIV vaccine—a mixture of 3 synthetically produced HIV genes (gag, pol, and nef) within an attenuated adenovirus type 5—were more likely to contract HIV than those who received placebo.

Moreover, according to the latest data from the vaccine trial, known as the STEP study, individuals who entered the study with higher levels of background immunity to adenovirus type 5 appeared to be most susceptible to HIV infection.

“There were more infections in vaccinees than in placebo recipients, and this trend was more pronounced in participants with high baseline Ad-5 titers,” said Dr. Keith Gottetsdiener, vice president of Clinical Research for Merck and Co.

Briefly, the STEP study was a multicenter, randomized, double-blind, placebo-controlled phase II “test of concept” trial cosponsored by Merck and the HIV Vaccine Trials Network, which is funded by the National Institute of Allergy and Infectious Diseases.

The STEP study was designed to determine whether V520 prevented HIV infection and reduced the amount of virus in individuals who developed infection. Trial investigators enrolled 3000 HIV-negative adult volunteers from diverse backgrounds who were at high risk for HIV infection.

The trial was halted in September, when a planned interim efficacy analysis in roughly 1500 participants showed that the vaccine did not prevent infection or reduce serum HIV RNA levels in those who became infected. At the time the study was discontinued, there were more cases of HIV infection in the vaccine arm than in the placebo arm (24 vs. 21).

At the press conference, Dr. Gottesdiener said the latest data from post-hoc analyses are consistent with the interim analysis. As of 17 October, in the overall study population, there were 49 cases of HIV infection in the vaccine group, compared with 33 cases in the placebo group, he reported.

Among the subpopulation with high levels of pre-existing immunity to adenovirus type 5, there were 21 HIV infections among those who received vaccine, compared with 9 among those who received placebo.

Presently, it’s not clear why the vaccine group had a higher number of HIV infections, and investigations are underway to try to uncover the reasons for this finding. Differential risk behaviors over time in the 2 groups may or may not explain the findings, Dr. Gottesdiener said, adding that “that analysis is just beginning.”

“Of course, the differences could also be due to the vaccine,” he said, noting that trial investigators had an “extensive discussion” focused on trying to understand hypotheses about why that could occur and figure out next steps.

One theory is that the adenovirus delivery vehicle could have activated the immune system of vaccine recipients, making them more vulnerable to HIV infection when exposed to the virus.

South Africa AIDS Activist Urges New TB Plan

5 November 2007 (Reuters [Wendell Roelf])—African nations are failing to control tuberculosis (TB) and could be overwhelmed by drug-resistant strains of the infectious lung disease, with dire implications for the war on AIDS, a leading AIDS activist said.

“Tuberculosis is now a major threat to South Africa’s fight against HIV,” said Zackie Achmat, the head of South Africa’s Treatment Action Campaign (TAC), told Reuters in an interview in Cape Town. “We need new TB vaccines, new TB testing, and we need new TB medicines.”

Spread through close personal contact, TB has long been a problem in Africa, where hundreds of millions of people are latently infected. But its growing relationship with HIV has made treating both diseases more difficult in vulnerable populations.

The emergence of extensively drug-resistant TB (XDR-TB), a strain virtually immune to traditional and modern antibiotics, has raised alarm bells since surfacing in South Africa’s KwaZulu-Natal Province and neighbouring Lesotho in 2006, where it killed up to 85% of those infected.

The majority of those who died also had HIV.

The strain has since spread to other parts of Africa, as well as to the industrialized world.

The prospect of a more virulent TB epidemic sweeping through Africa—where crowded shantytowns and fragile health systems help spread the infection—is a more serious threat, because the 2 diseases are so prevalent and interlinked in the region.

A third of the estimated 40 million HIV-positive people worldwide are believed to be coinfected with TB and HIV. In South Africa, 61% of the roughly 250,000 people diagnosed with TB each year have HIV.

“If XDR-TB becomes widespread and endemic it’s going to cost the health system a phenomenal amount, never mind the fact that it will lead to phenomonal loss of life,” said Achmat, who added that richer, industrialized nations were also not doing enough to fight TB.

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Editorial comment. The increase of spread of XDR-TB throughout Africa has major implications for the industrialized nations because of the potential for more spread outside of Africa. Treatment for these infections is poorly effective, even in developed countries.

HIV Status Often Unknown for Tuberculosis Patients in the U.S.

25 October 2007 (Reuters Health)—In 2005, HIV infection was identified in 9% of patients with tuberculosis (TB), but the rate may be higher, because 31% of TB patients have an unknown HIV status, according to findings in the Morbidity and Mortality Weekly Report.

As the authors note, knowing the HIV status of TB patients is essential for optimal patient management.

“Improvements in HIV testing and reporting are needed,” researchers from the Centers for Disease Control and Prevention (CDC) comment in the report. “All TB patients should be offered HIV testing where feasible, especially injection-drug users (IDUs), noninjection-drug users, homeless persons, non-Hispanic blacks, correctional-facility inmates, and alcohol abusers.”

In the study, CDC investigators analyzed data from the US National TB Surveillance System for the period from 1993 to 2005.

In addition to the overall HIV infection rate and the prevalence of unknown HIV status among TB patients, other key findings of the analysis were:

- The percentage of TB patients reporting their HIV status rose from 35% in 1993 to 68% in 2003. In recent years, however, little change in reporting rates has occurred
- As alluded to, IDUs, noninjection-drug users, homeless persons, non-Hispanic blacks, correctional-facility inmates, and alcohol abusers were at elevated risk for HIV infection. Each of these groups had HIV infection rates significantly higher than the overall 9% infection rate.

The investigators also found that roughly half of the TB patients with an unknown HIV status in 2005 were not offered testing. This represents a missed opportunity for detecting HIV infection and optimizing patient care, the report emphasizes.

“Implementation of the 2006 updated CDC HIV-testing recommendations, calling for routine HIV testing of all TB patients, and increased use of rapid HIV tests that can provide results in <20 minutes might increase acceptance of HIV testing,” the report states.

“These improvements might increase the proportion of TB patients in the United States whose HIV status is known and who can thereby benefit from optimal care.”


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