Sciencexpress News of the Week

HIV/AIDS

At Last, Vaginal Gel Scores Victory Against HIV

Jon Cohen
Contributing correspondent, *Science*

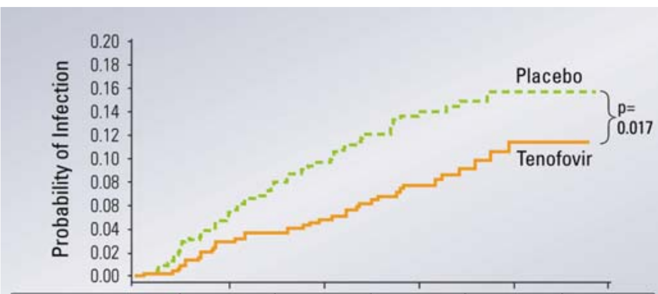
Goooooal! While South Africa was in the spotlight for hosting the World Cup games, its AIDS researchers were quietly preparing for an announcement of a major milestone in their field: For the first time ever, a vaginal gel has unequivocally blocked the transmission of HIV.

In a trial that involved nearly 900 South African women, those who received a vaginal gel that contains an anti-HIV drug had a 39% lower chance of becoming infected by the virus than those who received a placebo. "It is the first time any biological intervention against HIV-1 transmission has ever shown convincing efficacy in a large trial," says John Moore, who studies similar vaginal microbicides at the Weill Cornell Medical College in New York City. "It's a clear-cut result with obvious protection at a meaningful level."

More than 30 randomized controlled studies of microbicides, vaccines, and drugs to date have failed to thwart sexual transmission of HIV or have yielded such marginal success that researchers wound up hotly debating the data for years after the trials were complete. But there's no ambiguity about the data from this new microbicide study reported today online in *Science* and in a presentation at the 18th International AIDS Conference in Vienna: Of the 444 women who received a placebo gel, 60 became infected with HIV versus 38 infections in the 445 women who received the microbicide. The result was statistically significant, and no serious side effects occurred. "It's a moment we've been waiting for 2 decades," says epidemiologist Quarraisha Abdool Karim, who, with her husband, Salim Abdool Karim, headed the study, known as CAPRISA 004.

The study began in May 2007 and enrolled sexually active women between the ages of 18 and 40 who attended clinics in KwaZulu-Natal, South Africa, an area that has an extremely high rate of new HIV infections in young females. Researchers randomly assigned the women to receive either an inert gel or the gel mixed with the anti-HIV drug tenofovir for 30 months. Participants were asked to insert the gel within 12 hours before and after having sex. They were also provided with condoms and HIV-prevention counseling.

Teamwork. Salim and Quarraisha Abdool Karim headed the successful trial of a gel that reduced the risk of HIV infection.



Months of follow-up	6	12	18	24	30
HIV incidence rates (Tenofovirus vs Placebo)	6.0 vs 11.2	5.2 vs 10.5	5.3 vs 10.2	5.6 vs 10.2	5.6 vs 9.1
Effectiveness (p-value)	**47%** (0.064)	**50%** (0.007)	**47%** (0.004)	**40%** (0.013)	**39%** (0.017)

Diminishing returns. Effectiveness declined late in the trial, perhaps because adherence to the protocol dropped off.

The women reported their sexual activity each month, and the researchers also collected used gel applicators—181,340 to be exact—to monitor adherence. On average, women used the gel as advised nearly three-fourths of the time. Subset analyses showed, as expected, that the women who used the gel most frequently had the most protection: In a group of 336 "high adherers" who used the gel as advised more than 80% of the time, the reduction in risk of infection over 30 months jumped from the 39% found in the entire group to 54%. In the group that used the gel less than half the time, the risk reduction plummeted to 28%. The study also found that adherence dropped over time; among the entire group, the gel reduced the risk of infection by 50% over the first 12 months versus 39% over 30 months. "Task number one is better adherence," says Salim Abdool Karim, also an epidemiologist and the head of the Durban, South Africa–based CAPRISA, which stands for Centre for the AIDS Programme of Research in South Africa.

Both the CAPRISA investigators and other researchers who were not involved with the study stress that these results do not mean that a tenofovir microbicide gel is ready for market. “It’s a really exciting first step,” says Sharon Hillier, a reproductive specialist at the University of Pittsburgh in Pennsylvania who heads the Microbicide Trials Network sponsored by the U.S. National Institutes of Health. Earlier microbicide studies had all used compounds that attacked HIV nonspecifically, using surfactants and the like, she notes. “We got a proof of concept: Topically applied antiretrovirals can interrupt HIV in women. Is it good enough? Absolutely not. We want to see something more effective.” Hillier and others also say they would like to see the CAPRISA 004 results confirmed in a second study.

Hillier is heading just such a trial. Called Vaginal and Oral Interventions to Control the Epidemic (VOICE), the study is comparing two types of pre-exposure prophylaxis: daily vaginal application of a tenofovir gel and oral administration of an anti-HIV drug. (It is testing both tenofovir and a sister compound, Truvada.) VOICE, begun in September 2009, is expected to run for 4 years and enroll 5000 women in South Africa (the Abdool Karims are collaborators) and three other countries in southern Africa. “It’s going to be important to have data from more than that very high incidence single site, and it’s important to see if we can do better with more frequent dosing of the gel,” says Hillier. Other microbicide researchers are exploring what they believe are more potent anti-HIV drugs than tenofovir and simpler delivery methods like vaginal rings that periodically secrete the compounds.

Even if oral pre-exposure prophylaxis works, many researchers believe a microbicide gel could have many benefits for women. For one, only minimal amounts of the drug make it to the blood system, reducing the risk of side effects. Salim Abdool Karim further stresses that prevention strategies, just like contraception options, are not one-size-fits-all.

The next step for the CAPRISA researchers is to analyze why some women who received the tenofovir gel still became infected. “What undermined tenofovir’s ability to protect some of those women?” asks Salim Abdool Karim. “We need to go back into the lab and understand why we didn’t see a better effect to find potential avenues to try and do better.”

Published online 19 July 2009; 10.1126/science.329.5990.374
Include this information when citing this article.