MEDICAL RESEARCH COUNCIL
HIV PREVENTION RESEARCH UNIT

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FOR THE FIRST TIME A MICROBICIDE GEL SHOWS PROMISE FOR HIV PREVENTION

A clinical trial involving more than 3,000 women in southern Africa and the United States has demonstrated for the first time the promise of a vaginal microbicide gel for preventing HIV infection in women. The HIV Prevention Research Unit of the South African Medical Research Council conducted the trial in South Africa, which showed that the microbicide PRO 2000 (0.5%) was partially effective for preventing HIV infection among women. The results of the study, known as HPTN 035, were presented today at an international meeting, the Conference on Retroviruses and Opportunistic Infections, in Montreal, Canada. Although further clinical research is needed to more definitively determine the gel's effectiveness, this is the first human clinical study to suggest that a microbicide gel may prevent male-to-female sexual transmission of HIV infection.

"For the first time in the history of microbicide research, the concept of microbicides as an HIV prevention tool for women seems to be a reality" says Professor Gita Ramjee, who is Director of the Unit and the Principal Investigator of HPTN 035 at the South African sites in Durban and Hlabisa. "After working for over a decade in microbicide research, we are seeing a glimmer of hope of finding a safe and effective microbicide which could protect women and substantially reduce new HIV infections here in South Africa and globally. Although we need additional evidence to determine with greater certainty whether PRO 2000 is effective for preventing HIV, the results of this study represent a significant step forward for HIV prevention research," adds Ramjee.

Microbicides are gels, foams or creams intended to prevent the sexual transmission of HIV and other sexually transmitted infections when applied topically inside the vagina or rectum.

Currently, women comprise half of all people worldwide living with HIV. In sub-Saharan Africa, women represent nearly 60 percent of adults living with HIV, and in several southern African countries young women are at least three times more likely to be HIV-positive than young men.

In most cases, women become infected with HIV through sexual intercourse with an infected male partner. Although no microbicides are approved or available for use, an effective product could provide women with an HIV prevention method they initiate. This would be particularly helpful in situations where it is difficult or impossible for women to negotiate condom use with their male partners to prevent HIV transmission. Previous microbicide clinical trials have yielded disappointing results or were stopped prematurely.

HPTN 035 was conducted between February 2005 and September 2008 and enrolled 3,099 women at 7 sites in 5 countries. In addition to the Durban and Hlabisa sites in South Africa, they were located in Harare (Zimbabwe), Blantyre and Lilongwe (Malawi), and Lusaka (Zambia) in Africa, and in Philadelphia in the United States. Of the total 3099 women enrolled in the study, the MRC sites enrolled a 1 054 women - 350 from Hlabisa and 704 from Durban. HIV prevalence at both sites was high at the start of the study; 22% of the 1435 women who were screened for enrollment into the study in Durban and 28% of the 616 women who were screened in Hlabisa were found to be HIV positive. The prevalence of HIV at the South African sites was the highest of all the sites in the study. Women in Hlabisa and Durban also had a high prevalence of sexually transmitted infections (STIs) prior to enrollment in the trial.

The clinical trial tested two microbicide gels for safety and their ability to prevent HIV infection: PRO 2000 (0.5% dose), developed by Indevus Pharmaceuticals, Inc., in Lexington, Massachusetts, U.S.A., and BufferGel, developed by ReProtect Inc., in Baltimore, Maryland, U.S.A. In earlier laboratory and animal testing, PRO 2000 demonstrated a protective effect against HIV and other sexually transmitted infections by inhibiting HIV cell entry. BufferGel was known to boost the natural acidity of the vagina in the presence of seminal fluid, which can help to inactivate HIV and other pathogens.

Women in the study were randomly assigned in approximately equal numbers to one of four groups: those who used BufferGel prior to engaging in sexual acts; those who used PRO 2000 before each sexual act; those who used placebo gel (with no active ingredient) before each sexual act; and those who used no gel. Women in the no gel group were counseled on the use of condoms to prevent HIV infection. All women were provided with a comprehensive HIV prevention package including free condoms, safe sex counseling, and treatment of curable sexually transmitted infections (STIs) throughout the study. Women took part in the study for an average of 20 months from February 2005 to September 2008 and were evaluated monthly. All participants underwent a comprehension test to assess their understanding of the trial prior to enrollment and throughout the study. They received detailed information about the possible risks and benefits of trial participation prior to enrollment and were monitored closely throughout the study. Relatively few left the study before it was completed; 94% of the women enrolled in the study were retained. Hlabisa site had the highest retention rate in the study of 96.4%.

Based on the studies final results, of the 3099 HIV negative women enrolled, a total of 194 new infections occurred in the study as a whole over the course of the study period (2005 – 2008). Of this total, 36 infections occurred among participants who used PRO 2000, 54 infections occurred among participants who used BufferGel, 51 infections occurred among participants who used placebo gel, and 53 infections occurred among participants who used no gel. Using these data as a basis for determining the effectiveness of the two candidate microbicides, the researchers found that BufferGel had no effect on preventing HIV infection, but PRO 2000 had a 30 percent level of effectiveness against HIV. Both PRO 2000 and BufferGel were found to be safe for long term use.

“I feel great and very happy with the results. Results are fruitful and encouraging and enlightened us about what was researched. I expect more research to increase the 30% upwards for PRO2000” commented Mrs. S M Hlabisa member of the Community Working Group in Hlabisa.

All women in the study who became HIV positive were provided counseling and were referred for ongoing psychosocial care. Women were also requested to remain in contact with sites for long term care and monitoring of their HIV infections, and referrals were made to local health service providers for sustainability of care.

Participants who were assigned to the three gel groups used the gels about 80% of the time. The majority, over 90% of the women, said that they liked using the gel; nearly all (99%) said they would use the products if approved for HIV prevention. Condom use was also reportedly high in the study. Women in the gel groups used condoms 72% of the time during sex. Women who were not receiving any gel reportedly used condoms 81% of the time.

“The dedication and commitment of the women who took part in the study made possible the study’s important contribution to the fight against HIV,” says Dr. Roshini Govinden, project manager for HPTN 035 at the South African site.

Trial communities and study participants are currently being informed of the study results and counseled on safe sex practices to curb the high rates of new infections seen among young women.

The South African Medical Research Council and Prof. Ramjee’s HIV Prevention Research Unit is participating in a separate Phase III clinical study sponsored by the Medical Research Council (MRC UK) and the Department for International Development of the United Kingdom which is testing PRO 2000 (0.5% dose) for preventing HIV infection . The trial, known as MDP 301, has completed enrollment of 9,395 women at sites in South Africa**,** Tanzania**,** Uganda**,** and Zambia and is expected to report results by the end of 2009.

Global management of the HPTN-035 study was coordinated by American researchers working in the Microbicide Trials Network (MTN). The MTN is a clinical trials network established and funded in 2006 by the U.S. National Institute of Allergy and Infectious Diseases (NIAID) with co-funding by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development and the National Institute of Mental Health, all components of the National Institutes of Health. Prior to the establishment of the MTN in 2006, the study was led by the NIAID-funded HIV Prevention Trials Network (HPTN), from which the study gets its name. The study protocol was led by Professor Salim S. Abdool Karim, MBChB, Ph.D., from the University of KwaZulu-Natal in Durban.

The HPTN 035 study was funded by NIAID. Indevus Pharmaceuticals, Inc. provided PRO 2000 and ReProtect, Inc. provided BufferGel. The U.S. Agency for International Development (USAID) provided funding to manufacture BufferGel for the study.

For more information about the HPTN 035 clinical study, see http://www3.niaid.nih.gov/news/newsreleases/2009/HPTN_035_gel.htm or http://www.mtnstopshiv.org/news/studies/17 .

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