FACT SHEET

Microbicides for Pregnant and Breastfeeding Women

Fast Facts

- Nearly 16 million women around the world are living with HIV, close to half of all people who are infected. Most of these women acquired HIV from unprotected vaginal sex.

- Many women remain sexually active while pregnant and breastfeeding, putting them at continued risk for HIV infection.

- HIV prevention may be most critical during pregnancy – a woman’s risk of becoming infected by a sexual partner may be twice as high when she is pregnant. In addition, women who become newly infected with HIV during pregnancy are much more likely to pass HIV to their newborns than women who were already infected when they became pregnant.

- Vaginal microbicides are products designed to prevent or reduce the risk of HIV infection or other sexually transmitted infections in women. Tenofovir gel, the only vaginal microbicide shown in a clinical trial to reduce the risk of HIV, may be the first product approved for preventing HIV infection in women.

- Although microbicides for pregnant and breastfeeding women are only beginning to be studied, data from the first-ever study of microbicides in pregnancy found that a single dose of tenofovir gel given to pregnant women hours before giving birth by scheduled Cesarean delivery was safe for both mother and infant.

Overview

Microbicides, which could take the form of either a gel, cream or dissolving film, can contain an active ingredient that blocks HIV directly or that acts as a physical barrier in the lining of the vagina or rectum. Newer generation products are based on antiretroviral (ARV) drugs, commonly used to treat people with HIV, that prevent the virus from making copies of itself once inside a cell. Examples include tenofovir gel, MIV-150 and dapivirine. Of these products, tenofovir gel has been evaluated the most in clinical studies, and researchers are hopeful it may be the first microbicide approved for HIV prevention in women.

The majority of microbicide research has focused on products to prevent HIV in women of reproductive age who are sexually-active – the very women who are most likely to become pregnant. Yet, there is very little information about whether these products can be safely used by women who are pregnant or breastfeeding. Can exposure to a product, especially early in pregnancy, pose risks to the developing fetus? Can pregnancy affect how a particular microbicide might work? When a woman breastfeeds, how much, if any, of the product is likely to be transferred to her baby through breast milk? Researchers at the Microbicide Trials Network (MTN) seek to answer these questions as part of a comprehensive research program designed to take incremental steps toward determining whether tenofovir gel can safely and effectively protect women against HIV when they are pregnant or breastfeeding.
Why Do We Need Microbicides for Pregnant and Nursing Women?

Nearly 16 million women around the world are living with HIV, which represents almost half of all people who are infected. Most of these women acquired HIV from unprotected vaginal sex. Many women remain sexually active during pregnancy and breastfeeding, putting them at continued risk for HIV. In fact, some studies suggest that women may be particularly susceptible to HIV during pregnancy due to heightened immune responses or hormonal changes that affect the mucosal lining of the vagina. Because women often continue to use medications during pregnancy, knowing whether microbicides are safe to use in this population before they become readily available also is vitally important.

There are no vaginal microbicides approved or available for widespread use, but recent developments are promising — a clinical trial called CAPRISA 004 found that tenofovir gel reduced the risk of HIV by 39 percent in women who used it before and after sex compared to women who used a placebo, or in-active, gel. The MTN is conducting a major large-scale trial called VOICE – Vaginal and Oral Interventions to Control the Epidemic – that is testing whether daily use of tenofovir gel, or an ARV tablet, can reduce women’s risk for HIV among 5,000 women in southern Africa. The U.S. Food and Drug Administration (FDA) has indicated it will consider approving tenofovir gel as an HIV prevention method for women based primarily on its review of the results of CAPRISA 004 and VOICE, which are expected in 2013. Results from studies on the safety of tenofovir gel during pregnancy and lactation also will be essential to the FDA’s decision whether to approve the gel.

Traditionally, pregnant and breastfeeding women have been excluded from participating in biomedical research. Many regulatory organizations, including the FDA, are now recognizing that lack of knowledge about how certain medications or drugs might affect women when they are pregnant or nursing can do more harm than good. Questions have been raised about whether it is ethical to prevent pregnant women from entering HIV prevention studies since, given the global impact of HIV, women need safe and effective prevention products they can use throughout their lives. Similarly, despite intensive counseling on family planning and use of condoms, a large percentage of women enrolled in biomedical HIV prevention trials become pregnant. Since little information is available about whether these products are safe, women who become pregnant are taken off study products, which can have an impact on the validity of a study’s outcomes or results.

What Will it Take to Discover a Safe and Effective Microbicide to Use During Pregnancy and Nursing?

HIV prevention trials with pregnant and breastfeeding women are being undertaken in a cautious and step-wise manner to ensure the safety of both mothers and their infants. These and other biomedical trials are carried out in several phases under the oversight of regulatory authorities and according to strict ethical and scientific guidelines. Phase I trials are designed to evaluate safety in a small number of people who are exposed to study products for short periods, say, one to two weeks. If results of a Phase I study suggest the product is safe, investigation progresses to a Phase II trial, in which researchers continue to track safety over more extended periods of time. Phase IIb and III trials are performed to determine how effective a product may be and are conducted with large numbers of participants, typically at multiple clinical centers. These trials are usually designed to compare a product with a placebo or another active product. Data from Phase IIb and Phase III trials are often used by regulatory agencies to determine if a product should be approved for widespread use.

Studies of microbicides for pregnant and breastfeeding women are only beginning to be studied in Phase I clinical trials. If particular products are determined to be safe by Phase I studies, they will progress to later phases of study. To date, there has been only one Phase I study of a microbicide and pregnant women. That study, MTN-002, showed that a single dose of tenofovir gel given to pregnant women hours before scheduled Cesarean delivery resulted in only trace amounts of active drug in the mother’s bloodstream, and in the amniotic fluid and umbilical cord blood. Based on these reassuring findings, a follow-up Phase I study now underway, MTN-008, is assessing whether using tenofovir gel daily for one week is safe for women late in pregnancy and while breastfeeding.
Current and Planned Clinical Trials for Microbicides in Pregnant and Breastfeeding Women

- **MTN-002** – A Phase I study of the safety of a single-dose of tenofovir gel applied to 16 pregnant HIV-negative women hours before scheduled Cesarean delivery. The study results, reported in May 2010, found that only trace amounts of the active drug passed to the fetus. Conducted by the MTN.

- **MTN-008** – A Phase I follow-up study to MTN-002 focusing on the safety of tenofovir gel in pregnant and breastfeeding women. Conducted by the MTN, the study is currently enrolling 90 women in their third trimester of pregnancy and 15 women who are breastfeeding.

- **EMBRACE (MTN-016)** – An observational study and registry of women enrolled in any MTN study who become pregnant and are subsequently taken off study products, or who participated in a safety study of microbicides during pregnancy or lactation. Conducted by the MTN, EMBRACE is following women and their babies to determine whether exposure to the study products affects pregnancy outcomes or the baby’s growth and development.

- **MTN-019** – A Phase II extended safety study of tenofovir gel used daily in the second and third trimesters of pregnancy. The study, which is being developed, will enroll approximately 360 women who will use study product for 28 days or until delivery, whichever occurs first. It will be conducted by the MTN at sites in both the U.S. and Africa.

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More information about microbicides and other HIV prevention approaches can be found at [AVAC: Global Advocacy for HIV Prevention](http://www.avac.org) and the [Global Campaign for Microbicides](http://www.campaignformicrobicides.org).

The **Microbicide Trials Network** (MTN) is an HIV/AIDS clinical trials network established in 2006 by the National Institute of Allergy and Infectious Diseases with co-funding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the National Institute of Mental Health, all components of the U.S. National Institutes of Health. Based at Magee-Womens Research Institute and the University of Pittsburgh, the MTN brings together international investigators and community and industry partners who are devoted to reducing the sexual transmission of HIV through the development and evaluation of products applied topically to mucosal surfaces or administered orally. More information about the MTN is available at [www.mtnstopshiv.org](http://www.mtnstopshiv.org).

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