

All About Rectal Microbicides

Who needs rectal microbicides?

Heterosexual men and women, gay men, and males who have sex with males practice anal intercourse (AI) for pleasure. Heterosexuals may also practice AI to avoid risk of pregnancy or to maintain “virginity.” In U.S. surveys, 35% of heterosexual women reported having had AI at some time in their lives and 6.7% of heterosexual couples practice AI at least once a month.^{1 2} Among a cohort of U.S. women recruited because of other HIV-related risk, 32% reported having had AI in the past six months. The few international studies available show that AI is also practiced in various populations all over the world.³

During an act of unprotected anal intercourse, HIV is 10-100 times more easily transmitted to a receptive partner (male or female) than during vaginal intercourse. Condoms provide an effective barrier against HIV infection and some other sexually transmitted infections, such as gonorrhea and syphilis, which may facilitate HIV transmission. However, millions of receptive sex partners find it very difficult or impossible to ensure condom use every time.

Currently in development, a microbicide is a cream or gel that could be used to reduce a person’s risk of HIV infection vaginally and rectally. Rectal microbicides could offer both primary protection in the absence of condoms and back-up protection if a condom breaks or slips off during AI. For those unable or unwilling to use condoms, rectal microbicides could be a safe and effective alternative means of reducing risk, especially if they were unobtrusive and/or enhanced sexual pleasure enough to motivate consistent use. Such alternatives are essential if we are to address the full spectrum of prevalent sexual practices and the basic human need for accessible, user-controlled HIV and STD prevention tools.

What’s the difference between vaginal and rectal microbicides?

More than a dozen potential vaginal microbicides are currently in human trials, but it is not clear whether any of them will be suitable for rectal use. The rectum and the vagina have very different structures and natural ecologies. The vagina, for example, is a closed pouch while the rectum is part of an open-ended cavity. A greater quantity of the microbicidal product is likely to be required for adequate rectal coverage than for effective vaginal use. More immune cells with CD4 receptors and more CD4 receptors per cell also make rectal mucosa particularly vulnerable to HIV infection. The rectal lining is one cell layer thick and rather fragile compared to most of the vaginal lining, which is 40 cell layers thick. These factors further enhance rectal vulnerability to irritation, tearing and infection during sex.



What do we need to know?

Researchers are now seeking answers to questions about:

- How does HIV infection occur in the rectum?
- How do we design tests that will give us this essential information?
- What happens to the microbicide once it is inside the rectum?
- What kind of application method are people willing to use?
- What happens if someone inserts a vaginal microbicide (once available) rectally?
- Is it possible to design a safe and effective rectal microbicide?
- What concentration provides the most protection without causing damage to rectal tissue?

What is going on with rectal microbicide research?

Although most microbicide research focuses on vaginal use, research and development (R&D) of rectal microbicides is a growing segment in the field. Rectal microbicide R&D includes several types of research that are underway to find answers to some of these questions. For additional research updates, visit www.lifelube.org.

- **Phase 0 trials, or baseline studies**, are underway to measure the baseline levels of injury and inflammation that occur in the rectum during typical AI. In 2005, researchers at the University of California Los Angeles (UCLA) completed

¹ US National Survey of Family Growth - Mosher WD, Chandra A, Jones J. Sexual behavior and selected health measures: Men and women 1544 years of age, United States, 2002 . Advance data from vital and health statistics; no 362. Hyattsville, MD: National Center for Health Statistics. 2005.

² Kelly, Brian. 2001. Letter to the Editor: On Encompassing Sexuality. *American Journal of Public Health* 91:11.

³ Smith, Gary. 2001. Heterosexual and homosexual anal intercourse: an international perspective. *Venerology* 14:28-37.

a study looking at the physical changes that occurred in the rectal tissue of 16 men who were having anal intercourse. Dr. McGowan's data contributes substantially to the development of a baseline picture of the regular "wear and tear" that anal intercourse causes in the body.

- **Distribution studies** look at how a microbicide might travel and be distributed during and after sex. Researchers at Johns Hopkins University conducted a study to look at how far an artificial semen substance and a "microbicide-like substitute" could travel up the colon. These initial results suggest that four hours after sex, both the "semen" and "microbicide" may have traveled 60 centimeters (approximately two feet) up the colon, nearly to the spleen.
- **A Phase 1 clinical trial** is set to begin in fall 2006 at UCLA. This study tests the safety and applicability of UC-781 for rectal use, using the vaginal microbicide gel formulation. UCLA is also planning pre-clinical and formulation work for a rectal-specific microbicide with the aim of starting another Phase 1 trial as well.
- **"Male Tolerance" trials** are studying whether potential microbicides may cause irritation to the penis or within the male urethra. This information is vital to the successful introduction of both vaginal and rectal microbicides, since a product that is irritating to the insertive partner would clearly be unacceptable.
- **Acceptability or behavioral studies** to begin to learn what kinds of products people might be willing and able to use. Researchers at Fenway Community Health in Boston and Columbia University in New York are gathering information on user reactions to inserting varying amounts of neutral lubricants rectally (how much is "too much"?) and on user preferences regarding use of suppositories versus gels.

What about using vaginal microbicides for anal intercourse?

It is essential that all vaginal microbicides candidates in late stage clinical testing be tested for rectal safety, because it is likely that some people will try to use them rectally in the hope of gaining some protection. A product may be very safe for vaginal use while unsafe for rectal use – in which case people who use it rectally may actually increase their risk of infection. Rectal safety testing of vaginal products is essential so that any such products that are NOT safe for rectal use can be labeled in a way that specifically indicates what the consequences of using them rectally may be.

What do we know now?

We now know that Nonoxynol-9 IS NOT an effective microbicide! Manufacturers started adding N-9 (a spermicide commonly used in over-the-counter birth control products) to condoms and sexual lubricants when it was shown to kill HIV in a test tube. Now we know conclusively that N-9 can irritate both rectal and vaginal tissues, possibly making it easier for HIV to reach and infect susceptible cells. In one study, lubricants containing N-9 were shown to strip surface cells off of the rectal lining, potentially enhancing its vulnerability to infection. The World Health Organization and numerous other health authorities strongly advise against the rectal use of products containing N-9, including condoms coated with N-9 (often labeled "spermicidally lubricated"). For more information, see the Global Campaign *Factsheet #9 on Nonoxynol 9* (www.global-campaign.org/download.htm)

What is the advocacy message?

Men and women demand safe and effective rectal microbicides. The time to develop them is now!

There are significant biological, sociocultural, and political barriers to the research and development of safe and effective rectal microbicides. But we must not delay efforts to develop these urgently needed products. The escalating numbers of new HIV and STD infections resulting from unprotected AI testify to the fact that having one prevention tool, condoms, just isn't enough. It is time for receptive partners of both genders to have prevention methods they can control. It is time for rectal microbicides.

How can you get involved in advocating for rectal microbicides?

Convened by AIDS Foundation of Chicago, the Canadian AIDS Society, and CHAMP, the **International Rectal Microbicide Working Group** is a coalition of over 250 advocates, policymakers and scientists from 29 countries on 5 continents working to advance a robust rectal microbicide research and development agenda. To get involved, join the listserv, or to learn more, visit www.lifelube.org or contact Jim Pickett at jpickett@aidschicago.org.

The Global Campaign for Microbicides is a broad based, international coalition of organizations working to accelerate access to new HIV prevention options. Visit our website: www.global-campaign.org or contact us:

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