Vaginal microbicide research finally coming of age

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Presently, the only device with proven efficacy in decreasing sexual HIV transmission of HIV is the male condom. However, condom use is at the discretion of males, and many women are unable to enforce condom use, even when fearing they might expose themselves to HIV infection.

According to UNAIDS, more than 75% of all HIV infections in the world are due to heterosexual intercourse. In addition, the epidemic affects more and more women, who account for almost 9.1 million of the total 20.1 million people living with HIV now. Thus, there is a need for methods that women can use to protect themselves against HIV infection and STD without necessitating the cooperation of their sexual partners. The development of the female condom appears to be a first step in this direction, but it is hard to imagine how it can be used if the male partner does not consent to its use. A vaginally administered microbicidal preparation with activity against HIV and other STD is thus high on the wish list. Candidate ingredients include spermicides, disinfectants, polyanion sulphates (which inhibit interaction between HIV or HIV-infected cells and target cells) and reverse transcriptase inhibitors.

Recently the development of vaginal microbicides received more attention. After female health activists, such as Lori Heise, Zena Stein and Chris Elias drummed up enough support to get the field moving, the WHO organized a meeting advocating the development of vaginal microbicides, which led to collaboration of major public agencies in the International Working Group on Vaginal Microbicides. In 1996 in the USA, a presidential advisory panel earmarked vaginal microbicide development as a priority research area, and had its recommendations publicly endorsed by the vice-president, and in the UK, the Medical Research Council hit headlines with news that British scientists were to develop a chemical condom.

Given the ready availability of spermicides in the market, their evaluation for efficacy against HIV infection is clearly the top priority in vaginal microbicide development. This is indeed a controversial issue: two studies and a meta-analysis of the effect of spermicides on transmission of STD pathogens have suggested that spermicides might protect against HIV transmission, but this was not confirmed in a randomized controlled trial among female sex workers in Nairobi, in which a sponge with a very high dose (1 gram) of nonoxynol-9 was used. The controversy on spermicides can probably be explained by their narrow therapeutic margin: as they are detergents, they are not only active against HIV, but also toxic to human tissues. Their use was thus associated with a dose-dependent incidence of genital lesions, that could conceivably increase HIV transmission.

Several groups are now investigating nonoxynol-9 containing products with low doses of the active product, such as C-film or COL-1492, which contain 72 mg and 52.5 mg of nonoxynol-9 per dose, respectively. These products appeared much less toxic, and are now in phase III trials.

Data on the efficacy of C-film from a study by Family Health International in Cameroon might be available as soon as June 1996, if the study is stopped after the next interim analysis. A final analysis of this study is expected in December 1996. UNAIDS announced the launch of phase III study with COL-1492, in May 1996, and the same product is studied in Kenya by the University of Washington.

Thanks to the increasing support for vaginal microbicide development, a number of other spermicidal (e.g. C31G, benzalkonium chloride) and non-spermicidal products, such as dextrin sulphate, beta-lactoglobulin, polyanionic polymers, and gramicidin are now in different stages of pre-clinical or clinical development. Preferences of potential users for different formulations of microbicides are being assessed, and, lastly, the potential utility of microbicides to decrease HIV transmission through rectal intercourse will be addressed in a NIH-funded pilot study in the USA.

In spite of the progress being made in microbicide development, it should also be recognized that this field is
fraught with many problems. The most important problem is lack of resources and commitment to fund the research. Indeed, in the public sector and in academia interest in microbicides was until recently very limited, because of a pessimistic assessment of the ability to be successful in or get scientific credit out of the development of a crude chemical to prevent a tricky disease such as HIV infection. In the private sector interest in the development of these products is even more limited, because spermicides are already on the market, and are considered a low-profit category of products. In addition, the market for spermicides is decreasing, which is perceived as arguing against investments in their development for additional indications, such as HIV transmission or STD prevention. As long as research on the efficacy on nonoxynol-9 is not conclusive, there is also little interest in the development of non-spermicidal vaginal microbicides, the market of which is perceived to be located almost exclusively in developing countries, that would have extremely limited ability to pay for them. Lastly, the regulatory requirements for vaginal microbicides are unclear in all major pharmaceutical markets, so that even the investments needed to bring a vaginal microbicide to the market cannot be budgeted easily. This would now be partly resolved: the International Working Group on Vaginal Microbicides now endorse precise recommendations for microbicide development (70), which will also be presented at the next International Conference on AIDS in Vancouver.

It is anticipated that at that conference more data on vaginal microbicides will be presented. On July 9, Chris Elias from the Population Council will have a plenary address on "Female-controlled methods to Prevent Sexual transmission of HIV", and on July 10 there will be an Abstract Session on "Microbicide Development" from 17h30 to 18h30 in room A2. On July 8, there will be a NIH-UNAIDS co-sponsored satellite meeting on "Topical Microbicides" in Wall Centre Garden Hotel Ballrooms C&D from 7-10 p.m. These sessions should be a gathering point for those interested in new technology to prevent HIV transmission, and it is hoped that the data presented will amplify the advocacy of those who are campaigning for further microbicide development.

References:

5. Rosenberg MJ, Callah RL. Methods women can use that may prevent sexually transmitted disease, including HIV. Am J Public Health 1992, 82, 1473-8.

Current members of the International Working Group on Vaginal Microbicides include:

1. Center for Disease Control and Prevention (CDC), Atlanta, GA, USA (represented by the Division of Reproductive Health)
2. CONRAD Program, Arlington, VA, USA
3. Family Health International (FHI), Research Triangle Park, NC, USA
4. Food & Drug Administration (FDA), Rockville, MD, USA (represented by the Division of Antiviral Drug Products)
5. Joint United Nations co-sponsored programme on HIV/AIDS (UNAIDS), Geneva, Switzerland
6. Medical Research Council, London, UK
7. National Institute of Health (NIH), Bethesda, MD, USA; represented by the National Institute of Allergy & Infectious Diseases (NIAID) and the National Institute of Child Health and Human Development (NICHD)
8. The Population Council, New York, USA
9. Society for Women and AIDS in Africa (SWAA), Freetown, Sierra Leone
10. Women Health Activists for Microbicides, New York, USA
11. World Health Organization, Geneva, Switzerland

(Represented by the Special Programme for Research, Development and Training in Human Reproduction).