



## Spotlight

### Capping infection

*Can the diaphragm help lower women's risk of HIV infection?*

On a recent afternoon at a health clinic in Epworth, a densely-populated suburb of Harare, Zimbabwe, a dozen or so women arrived for their final visit of a year-long study to see if a small, round disc of latex known as a diaphragm can protect them from sexually contracting HIV. Researchers from the University of California at San Francisco (UCSF), University of Zimbabwe, and Ibis Reproductive Health have enrolled 2503 women aged 19-49 for a randomized, controlled trial. If the diaphragm is found effective the researchers hope that this old-fashioned birth control method could soon make a comeback as a woman-controlled HIV prevention method.

"Biologically, it's very plausible that it will work," says Nancy Padian, a researcher at UCSF and principal investigator of the study. Contraceptive diaphragms are designed to cover a woman's cervix, the lower opening of the uterus, and prevent access to the upper genital tract. Both of these sites, the cervix and the uterus, are thought to be important target tissues for the sexual transmission of HIV.

One reason for this is that the tissues of the cervix are much thinner than those that line the vagina. Observational studies suggest that other sexually-transmitted pathogens, including those causing gonorrhea and chlamydia, preferen-

tially infect cervical as opposed to vaginal cells. Diaphragms have been shown to prevent the transmission of some sexually-transmitted infections (STIs), when used along with contraceptive spermicidal gels. The cervix also contains some of the same target cells for HIV that are found within the foreskin of the penis; a recent prospective study in South Africa showed that male circumcision, which involves removing the foreskin, may significantly reduce a man's chances of acquiring HIV.

Together, these findings suggest that shielding the cervix with a diaphragm might lower the risk of a woman contracting the virus. It is unlikely that this simple female-controlled device will offer complete protection since other studies have shown that even women who have undergone hysterectomies (where the cervix and uterus are removed) can still become HIV infected. But even if diaphragms offer only partial protection against HIV, Padian is hopeful that they can have a powerful effect on the epidemic. "None of the methods we are looking at are 100% effective," she says. "Even though it's not perfect, it's better than nothing, especially when women can't negotiate male condom use."

#### Current methods fall short

With effective AIDS vaccines and microbicides still years away from practical use, male and female condoms remain the most reliable method for HIV prevention. Yet condom use remains extremely low. Female condoms, comparable in efficacy to the male condom in preventing STIs other than HIV and on the market for more than a decade, have been

inadequately supplied and adopted—in 2005, only 14 million female condoms were available worldwide, compared with 6 to 9 billion male condoms.

Male circumcision is showing some promise in trials as a way for men to reduce their risk of HIV infection. But female-initiated HIV prevention methods are still urgently needed. Young married women are the fastest-growing group of new HIV infections in many countries and they often have difficulty negotiating condom use. The diaphragm, which can be inserted by a woman and used without her partner's knowledge, is also already an approved device. If the current ongoing Bill & Melinda Gates Foundation-funded trials in Zimbabwe and in Durban and Johannesburg, South Africa show that the diaphragm is effective at protecting women against HIV infection, the approach could be implemented nearly immediately. This makes it particularly attractive to prevention researchers.

Diaphragm use as a birth-control method has mostly fallen out of favor in countries like the US where oral hormonal contraceptives are affordable and widely available, and researchers wondered if this device would be accepted by women as an HIV prevention method in developing countries. So before starting the HIV prevention studies Padian launched a six-month diaphragm acceptability study in Zimbabwe. She found that nearly all of

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the 186 participants reported trying the diaphragm during the study period.

In the ongoing diaphragm trials in Zimbabwe and South Africa, women are randomized into two groups or arms; both are given condoms and HIV education but only one group receives the diaphragm. At the conclusion of the trial all women are offered a diaphragm. "Most women are accepting it," says Project Director Agnes Chidanyika. "They look forward to using it, especially those in the condom arm who haven't used it."

In the Zimbabwe study Chidanyika says the diaphragms were acceptable among the male partners of most women, who were happy to let their female partners use a potential HIV prevention method that their partners were responsible for and they could not feel. However, this sentiment was not universal, she says. "The problem we did have with some women is the partner would say if she can use it without me knowing, then she can be unfaithful."

### A look to the future

At the Epworth study site, women arriving for their quarterly visit fill out computer surveys and meet with counselors and clinicians. In a counseling room at the clinic, a young woman in the diaphragm arm of the study demonstrated its use on a plastic pelvic model. She grasped the latex, cup-shaped diaphragm by its firm, springy lip, squeezed it in half, and inserted it easily into the model. This young woman said she found her own diaphragm comfortable and had used it throughout the study period except when she tried to get pregnant. As with all barrier methods, the importance of child-bearing in many societies may be an obstacle to widespread adoption of the diaphragm as an HIV prevention method.

Completing this large study in Zimbabwe has taken an immense commitment from both the study volunteers and the research staff. The country is currently experiencing epic inflation and unemployment. The Epworth study site sits just a few feet away from the rubble of countless shanties destroyed by order of the Zimbabwean government in the summer of 2005 in a campaign called Operation Murambatsvina or "Drive out Trash." According to a UN-Habitat study, an estimated 700,000 people lost their homes or businesses in

the campaign. Over a quarter of the trial participants in Zimbabwe were displaced by Operation Murambatsvina.

Yet researchers managed to retain a stunning 99% of the participants by visiting homes, villages, and displaced persons camps, reaching out to alternative contacts, and launching a radio and poster campaign. Chidanyika says the high retention rate also reflects the enthusiasm of the diaphragm study participants. "The participants themselves, they were very interested in participating in the study and coming back," she says.

Results from the study across sites in Zimbabwe and South Africa are not expected until 2007 but if diaphragms prove effective at lowering HIV transmission then those wishing to promote wide-scale adoption of the method will need to contend with several difficulties. The major fear is that diaphragms could potentially lead to lower condom usage. "I don't think anyone thinks diaphragms will be more effective than condoms," acknowledges Padian, "but we're doing the study in the situation where many women cannot use condoms." There is also a fear that behavioral disinhibition will encourage women to engage in riskier behavior because they wrongly believe they can stop worrying about contracting HIV if they are using a diaphragm.

Perhaps the most serious obstacle to future use of diaphragms is the possibility that they will be less acceptable in real settings than they are in the research environment. Over-optimism about the prospects of the female condom, another woman-controlled contraceptive and HIV prevention method, is a cautionary case. While evidence suggests that the female condom is effective and easy to use, it has taken a long time to increase its uptake. But the diaphragm does offer an economic advantage over the female condom; a single diaphragm, though initially more expensive than a female condom, may be used for several years.

The main problem with traditional diaphragms is the cumbersome way they are fitted. Standard diaphragms come in nine different sizes and women must be properly fitted before they can begin using one. In Padian's ongoing study all women start with one size of diaphragm and then try other sizes as necessary

after an examination. Even this simpler method, however, requires a visit to a health clinic, a potentially costly prospect if implemented broadly in developing countries. It may also make women vulnerable to stigma.

This limitation has led developers to pioneer alternate forms of cervical barriers. Maggie Kilbourne-Brook, program officer with the Program for Appropriate Technology in Health (PATH), says a one-size-fits-all device would be a major improvement. Researchers have also identified several other modifications that would make diaphragms much more acceptable. "What we need to be able to achieve is to make a device that is easier to insert and remove than standard products, and easier to use and learn to use than the currently available product," says Kilbourne-Brook. "It needs to be comfortable for both partners."

The PATH researchers used this information to develop an improved diaphragm, known as SILCS, which is a single-sized silicone diaphragm that fits most women. The researchers expect to begin testing the product for contraceptive effectiveness in late 2006.

A number of other cervical barriers are also in the process of being developed and approved. The single-sized Lea's Shield is a silicone cervical barrier contraceptive already approved by the US Food and Drug Administration for up to 48 hours of continuous use. Another product being tested, the BufferGel Duet, is a disposable, one-size diaphragm pre-filled with the candidate microbicide and contraceptive BufferGel.

Indeed, if both microbicides and diaphragms prove to be partially effective at preventing HIV transmission then combining them could well offer higher protection. "We're interested in evaluating whether the use of a physical barrier like a diaphragm could advance the effectiveness of a microbicide," says Sharon Hillier, a microbicides researcher at the University of Pennsylvania. If the ongoing study indicates that traditional diaphragms are protective against HIV transmission, Padian believes there will be ways to extend the results to the new forms of cervical barriers that are being developed without doing large, time-consuming, and costly trials to prove their efficacy. "We'll be able to generalize somewhat," she says.