An overview; microbicides vital in HIV prevention

Empowering women with new HIV prevention technologies to tackle the epidemic

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Why microbicides?

- HIV/AIDS is the leading cause of death globally in women ages 15-44, and young women in sub-Saharan Africa are up to five times as likely to be infected with HIV as young men.
- Many women are unable to negotiate condom use with their male partners and abstinence is not an option for women who are married, who want children or who are at risk of sexual violence .
- Heterosexual sex is the primary mode by which HIV spreads in developing countries . Women are more at risk than men.
- This is why women urgently need new HIV prevention strategies like microbicides that they can use themselves.

What are microbicides?

- Microbicides are medical products being developed to protect healthy people from becoming infected with HIV during sex.
- Most microbicides contain antiretroviral (ARV) drugs that attack the virus at one of a number of points in the HIV life cycle.
- ARV medicines have extended and saved millions of lives across the globe — and these drugs are now being adapted to protect healthy adults from becoming infected with HIV.
- Multiple clinical trials have shown that ARVs can prevent infection when they are used consistently .

What are microbicides?.....

- Some microbicides are being designed for women as vaginal products, and others in earlier development would be rectal products that both men and women could use.
- Microbicides for women could come in many forms, such as vaginal rings, tablets or films. The International Partnership for Microbicides (IPM) is focused on developing microbicides to protect women from HIV during sex with a male partner.
- Safe and effective microbicides could have a profound impact on the epidemic as part of a comprehensive prevention strategy that includes condoms, oral ARV pills (known as pre-exposure prophylaxis or PrEP) and, one day, a vaccine.

How are close are we to having a vaginal microbicide?

- A range of microbicides containing different ARVs are now in preclinical development and clinical trials.
- One microbicide is in late-stage clinical trials: the monthly dapivirine vaginal ring, developed by IPM.
- The dapivirine ring, which women insert and leave in place for one month, is the first long-acting microbicide to be tested in large-scale safety and efficacy trials for HIV prevention.
- Because the ring is designed to deliver sustained-release of an ARV, it has the potential to help address the challenge of adherence and help ensure effectiveness.

How are close are we to having a vaginal microbicide?

- Two Phase III studies in Africa are currently evaluating whether the ring is effective and safe for long-term use.
- Launched in 2012, these two pivotal "sister studies" are The Ring Study, which is being led by IPM, and ASPIRE, which is being led by IPM's clinical trial partner, the US National Institutes of Health-funded Microbicide Trials Network, among more than 4,500 women. Efficacy results for both studies are expected by early 2016.

Findings from previous microbicide studies

- Previous studies of early generation microbicides that were not based on ARVs demonstrated no protective effect against HIV. However, in 2010, the CAPRISA 004 study showed that tenofovir gel reduced women's risk of HIV infection by 39 percent when used before and after sex.
- Subsequent studies did not confirm these results.
- In 2013, the VOICE trial did not find the gel effective when used on a daily basis, likely due to low adherence.
- More recently, the FACTS 001 trial (2015) found the gel, when used before and after sex, also was not effective for the same reason.

Findings from previous microbicide studies

- Results underscore the challenge of developing and delivering products that women, especially young women, can and will use consistently.

How do microbicides fit into the HIV prevention landscape?

- Because there will be no single solution to stopping HIV, having multiple prevention options is not simply a best-case scenario, it is the only scenario that can end the epidemic.
- This is especially true for women, who bear the brunt of the epidemic. Stopping HIV will require a variety of effective options from TasP to PrEP to rings, and one day, a vaccine.
- Condom use can be difficult for many women to negotiate
- New self-initiated prevention tools are needed that match women's individual needs and fit within the context of their lives.

How do microbicides fit into the HIV prevention landscape? .....

- Microbicides can be used discreetly, giving women who may not be able to discuss HIV prevention options with their partners the ability to protect their own health.
- In addition to the long-acting dapivirine ring now in Phase III trials, other promising approaches in earlier phase testing include long-acting injectable ARVs, new vaginal and rectal products including those with multiple ARVs, and vaccines
- Microbicides would expand the HIV prevention toolkit with products that can work for and meet the needs of different women at different times in their lives.

Testing microbicides for safety and effectiveness

- All microbicide candidate products must go through a rigorous program of laboratory screening and testing to ensure that they have an adequate safety profile before being tested in humans.
- Once a microbicide candidate satisfactorily passes these tests and additional safety tests in animals, it can be advanced through a series of human clinical trials.
- Clinical trials are carried out sequentially, first to determine the safety of the product (no significant side effects occurred) and then to test its efficacy (the ability of the product to prevent HIV infection).

Testing microbicides for safety and effectiveness

- Initial safety trials involve small numbers of women who participate under carefully controlled clinical conditions.
- Efficacy trials are then performed to test the ability of the microbicide to prevent HIV infection.
- These trials involve large numbers (hundreds to thousands) of women, and need to be conducted in locations where new HIV infections are occurring at a high rate.
- This allows researchers to better assess the difference in infection rates between those women who use the active microbicide and those who use a placebo .

Testing microbicides for safety and effectiveness

- If significantly fewer women become infected in the group that used the microbicide, then researchers know that the microbicide helps to prevent HIV infection.

What ethical standards guide clinical trials?

- All clinical trials, including microbicide trials, must be conducted according to international and national regulatory and ethics guidelines to protect trial participants' well-being, and guarantee the ethical and scientific integrity of the results.
- Informed consent is the cornerstone of ethical trial conduct .
- Clinical research teams must ensure that all participants in microbicide trials have freely given their informed consent based on a clear understanding of the trial, including the risks and benefits of trial participation.

What ethical standards guide clinical trials?

- The informed consent process must be consistent with International Conference on Harmonization Good Clinical Practice and local country guidelines. e.g. NHSRC in Malawi
- Informed consent is an ongoing process that requires periodic and ongoing discussions with participants to ensure their continued understanding of the trial.
- Participants are also referred for support, care and treatment in the event that they become infected with HIV or require medical attention for any other condition .

How are local communities involved?

- Information about microbicides and clinical trials is provided in local languages not only to trial participants but also to key stakeholders, including local officials, women's groups, medical professionals, the media, traditional leaders, ministries of health and others.
- Ongoing training and support for those involved in the clinical testing process — clinical investigators, research scientists, nurses, counselors, community health workers and project management staff — is also provided.

How will women's access to microbicides be ensured?

- Global progress against HIV/AIDS has been possible through the hard work of communities, governments, donors and researchers.
- These joint efforts must continue to ensure that once found effective and approved for use, microbicides are made available and affordable to the women who urgently need them.
- IPM is committed to this goal and is engaging partners to plan for expedited roll-out, introduction and scale-up of an effective future product.

Conclusion

- Microbicides will be critical to any comprehensive response to HIV/AIDS — one that takes into account the disproportionate impact of the epidemic on women — and a much needed tool in promoting women's sexual and reproductive health and well-being.
- Science has shown that ARVs can prevent HIV infection and save lives. Realizing that potential requires continued financial resources and political will to deliver promising innovations to the women who need them.
- Offering safe and effective microbicides for women in developing countries promises to be one of the great public health accomplishments of our generation.