After microbicide failures, hope that antiviral approach will gel

AIDS experts have had high hopes that vaginal microbicides—gels and creams designed to prevent HIV infection—could empower women to protect themselves against the virus when their partners refuse to use condoms. But a string of disappointing results from clinical trials is prompting researchers to shift their focus away from earlier, basic microbicides, which do not block the virus from replicating, toward new drug options.

Many of these first-generation microbicides aimed to prevent infection by physically blocking HIV from reaching its target cells. The latest blow to this approach came on 18 February, when researchers announced that the microbicide Carraguard did not significantly reduce infection risk in a study that followed more than 6,000 women in South Africa. Scientists had thought that the seaweed extract in Carraguard would protect against HIV by coating the virus and thereby preventing it from binding to cells. One year earlier, scientists halted trials on Ushercell, a cotton-based microbicide designed to similarly block HIV, after clinical trial results suggested that the product might actually increase the risk of infection.

Trials involving two other microbicides, Pro 2000 and BufferGel, are currently underway in the US and southern Africa, with results expected next year. Researchers hope these will prevent HIV transmission by either blocking viral entry into cells or maintaining acidity in the vaginal tract, respectively.

However, at the international Microbicides 2008 conference held in New Delhi in late February, scientists seemed eager to move toward microbicides that instead contain antiretroviral drugs. These drugs already serve as the mainstay of treatment of infected people. The hope is that the antiretroviral drugs—which typically interfere with HIV replication—can double as preventive agents in the genital and anal tracts.

Magee-Womens Research Institute/University of Pittsburgh

Delivery options: Microbicides come in many forms.

Of the microbicides containing antiretroviral drugs, "the farthest in the line is tenofovir gel," says Sharon Hillier, principal investigator for the Pittsburgh-based Microbicide Trials Network, set up in 2006 by the US National Institutes of Health to coordinate trials.

At the New Delhi conference, experts reported that preliminary results from a phase 2 trial involving 200 women suggest that a gel containing the antiretroviral medication tenofovir is safe for daily use. Seven additional trials involving the tenofovir gel are planned or in progress, including a study scheduled to start in October 2008 that will compare the pill and vaginal-gel forms of tenofovir in 4,200 women.

In the past, women in microbicide trials have received piston-like devices to apply the microbicide gels shortly before intercourse. Now, however, some scientists have started to favor the idea of blocking transmission using rings coated with anti-HIV drugs, which can be left in the vagina for a month and slowly diffuse the antiretroviral medication. The International Partnership for Microbicides, a nonprofit partnership headquartered in Silver Spring, Maryland, plans to start trials in South Africa by the end of 2008 on an antiretroviral called dapivirine given orally and through an intravaginal ring.

John Mellors, chief of the infectious diseases unit at the University of Pittsburgh, warns that the antiretroviral approach carries the risk of promoting HIV drug resistance. The potential leakage of antiviral drugs into the bloodstream and their possible toxic effects also concern experts. Others continue to worry that objections from husbands or male partners will prevent the microbicide approach from taking off.

"Even if we have the first successful microbicide, our journey has just begun," says Hillier. "We need products that are simple to use, cheap and easily available, whether in a shop in Delhi or in Pittsburgh."

T V Padma, New Delhi

Gates Foundation looks to fund unconventional health solutions

On 3 March the Bill & Melinda Gates Foundation detailed its plans to invest $100 million over the next five years to fund bold solutions to public health problems. The best part: no preliminary results are necessary, and applications need to be just two pages.

Through its Grand Challenges in Global Health initiative, the foundation has already poured more than $430 million into 43 grants for projects aimed at developing new and inexpensive tools—such as heat-stable vaccines and hand-held diagnostic devices—for developing-world diseases.

The new scheme, dubbed Explorations, has similar aims. Applications should propose ways to understand and protect against infectious diseases, including HIV/AIDS and tuberculosis, and to combat drug resistance. But unlike proposals for the more ambitious Grand Challenge grants, these need not map out the entire solution—only a way to test the initial concept.

"This [scheme] allows researchers to put forward riskier ideas," says Steve Buchsbaum, senior program officer for the foundation.

REUTERS/Jeff Christensen

Idea seekers: Bill and Melinda Gates

In a bid to attract unorthodox approaches, the foundation is reaching out to scientists in disciplines other than medicine, including physics, chemistry and mathematics, and to those from countries such as China and India.

Initial grants will each top off at $100,000 for one year, but if a project is successful, the foundation will provide another $1 million over two years. In theory, a successful project would then become eligible for the more traditional grants from the foundation. "We are likely to continue funding until we solve that grand challenge or until the barrier that it creates is no longer relevant," says Buchsbaum.

Apoorva Mandavilli, New York