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# Vaginal microbicides may prevent more infections in men than women

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Vaginal microbicides currently in clinical trials may be the only weapon that will protect women against infection from HIV. Yet, under likely circumstances, these microbicides may be of more benefit to men than women, according to a new UCLA AIDS Institute study.

The study, which used novel mathematical models to simulate clinical trials and population-level transmission of HIV, appears July 7 in the online issue of *Proceedings of the National Academy of Sciences.*

"At the moment, there is absolutely nothing that women can do to protect themselves from HIV —condoms are not in women's control," said senior study author Sally Blower, professor of psychiatry and biobehavioral sciences at the Semel Institute for Neuroscience and Human Behavior at UCLA and a member of the UCLA AIDS Institute. "Drug companies are developing vaginal microbicides to provide direct protection to women and basically empower them so women have some preventive measure that's under their control."

Microbicides are compounds that can be applied inside the vagina to protect against HIV and other sexually transmitted diseases. Pharmaceutical companies are currently conducting trials of second-generation microbicides that are based on antiretroviral, or ARV, drugs, Blower noted.

The UCLA study raises concerns that microbicides could lead to drug resistance if they are used by HIV-positive women and that this risk may

be masked under current clinical trial designs — necessitating significant caution if the microbicides are licensed for use by the general public.

The researchers developed the mathematical models to determine if ARV-based microbicides that could cause moderate to high levels of drug resistance might pass clinical trials. They used epidemiological, clinical and behavioral data to construct models for both clinical trials and heterosexual transmission of HIV.

The models were based on the Phase 3 clinical trial for second-generation microbicides now under way in South Africa, Tanzania, Rwanda and Belgium. This trial is a 12-month, placebo-controlled study involving 10,000 participants.

The researchers developed simulations for two scenarios: one for high-risk microbicides, in which there is a high probability that the vagina will absorb dapivirine, the ARV drug in the microbicide; the other for low-risk microbicides, with a low probability of absorption. The team created the two scenarios because it is not currently known if ARV-based microbicides will be low- or high-risk.

The researchers found that men would likely benefit more than women if the microbicides' efficacy for women was less than 50 percent and if adherence was less than 60 percent. This would occur if HIV-positive women used microbicides and developed drug-resistant strains of HIV that are then less likely to be transmitted to men.

In the high-risk scenario, for instance, the microbicide could prevent infection in up to 21 percent of women and up to 27 percent of men. In the low-risk scenario, the microbicide would be of less benefit, preventing infection in up to 17 percent of women and 18 percent of men.

"The antiretroviral drugs within these microbicides are the same as those used to treat people who are infected with HIV, so there is great expectation that these microbicides will be very effective," said first author Dr. David Wilson, of the National Centre in HIV Epidemiology and Clinical Research at Australia's University of New South Wales.

"But the concern is that these microbicides are going to lead to drug resistance," he said.

The concern about drug resistance arises from the fact that women in the current clinical trial are being tested once a month for HIV infection and those found to be infected are dropped from the trial, according to researchers.

"Since monthly testing will take place in the dapivirine trial, we predict that few, if any, cases of acquired resistance will arise during the trial, even if the drug is readily absorbed (i.e., the microbicide is high risk)," the researchers write. "Therefore our analyses have shown that high-risk microbicides could pass Phase III trials, as their potential to cause resistance will be masked by frequent testing."

Source: University of California - Los Angeles