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New study finds HIV drug can persist in mothers' milk, increasing risk to them and their babies

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A drug commonly used in the developing world to prevent transmission of HIV from mother to child persists in the breast milk and blood of the mothers, putting them and their babies at risk for developing drug-resistant strains of the virus, according to researchers at the Stanford University School of Medicine.

The researchers found that the drug, nevirapine, stays in the blood and breast milk of the infected mothers for at least two weeks. During that time, the virus has ample opportunity to transform itself into drug-resistant strains of HIV, the human immunodeficiency virus that causes AIDS, which can be very difficult to treat.

"In the short term, nevirapine is better than nothing," said David Katzenstein, MD, professor of infectious diseases and principal investigator of the study. "But in the long term, I'm concerned about conferring resistance. If you're talking about resistance on a broad scale, it could jeopardize future treatment for mothers and infants."

Seble Kassaye, MD, instructor in infectious diseases and first author of the study, will present the results Aug. 5 at the International AIDS Conference in Mexico City.

Last year, 420,000 babies were born HIV-positive, the large majority of them to HIV-infected mothers in sub-Saharan Africa, according to

figures from the United Nations Joint Programme on HIV/AIDS. The centerpiece of public health programs in the developing world to stop mother-to-child transmission of HIV are both zidovudine (AZT) and nevirapine, which have been used as preventive tools in nearly 900,000 women and infants worldwide. The drugs are relatively inexpensive and easy to administer, and nevirapine is typically given as a single pill as the mother goes into labor and as a liquid to the baby just after birth. Use of the drug reduces the chance of HIV transmission by half, to about 13 percent. However, not all HIV-infected women have access to one or both of these drugs, especially in sub-Saharan Africa.

In addition, nevirapine has proven to be problematic. Previous studies have found that as many as 69 percent of HIV-positive mothers and as many as 80 percent of babies born infected, even after being given a single-dose of nevirapine without AZT, may develop nevirapine-resistant strains of the virus.

In the latest study, the Stanford scientists set out to better understand this problem.

They looked at a group of 32 HIV-positive pregnant women in Zimbabwe, where Katzenstein and his colleagues have had ongoing research and clinical programs in HIV/AIDS for more than a decade. The sub-Saharan African country has been hard hit by the virus, with an estimated 17 to 18 percent of young adults estimated to be infected. Among pregnant women, some 20 percent are thought to carry the virus.

In recent years, Zimbabwe has begun offering antiretroviral drugs to a limited number of infected patients, but at the time of the study, none of the women had been treated for their HIV. The only drug they received was the single dose of nevirapine when they went into labor, largely for the sake of their babies.

The researchers found that the drug persisted in the body for weeks, with more than half of the women having detectable levels in their blood within two weeks after delivery. Two-thirds had measurable levels in their breast milk at two weeks, the researchers found.

The longer the drug remains in the system, the more likely it is to promote development of mutations in the virus. Although none of the HIV-infected women carried drug-resistant strains of the virus at the outset of the study, at two months after birth RNA tests showed a third of them had drug-resistant virus in their blood. Sixty-five percent had drug-resistant strains in their breast milk as well, with the potential to pass this on to their babies through breastfeeding, a common mode of viral transmission.

The mothers who were most likely to develop resistant virus were those whose disease was more advanced as indicated by lower CD4 cell counts, the immune cells targeted by HIV, Kassaye said. With advanced HIV infection, these women are likely have more replicating virus, so they may be more prone to developing mutations that make the virus resistant to treatment, she said.

If these women had access to better, combination antiretroviral treatment to optimally suppress virus replication, they might be less likely to develop these hard-to-treat strains later, she said.

"It reinforces the need to treat these women with combination therapy, thereby providing better prevention for the infant, while providing better treatment for the mother," Kassaye said. "Public health efforts should continue to expand combination therapy so that mothers and babies aren't left vulnerable to drug resistance."

Combination therapy is a mix of drugs that is more expensive - and thus less accessible - in the developing world. In the United States, HIV-

positive women receive a highly effective form of combination therapy that has reduced transmission of HIV from mother to infants to less than 2 percent.

Source: Stanford University