Resistant HIV quickly hides in infants' cells

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New evidence shows that drug-resistant virus passed from mother-to-child can quickly establish itself in infants' CD4+ T cells where it can hide for years, likely limiting their options for future treatment. The study is published in the May 15 issue of *The Journal of Infectious Diseases*, now available online.

Mother-to-child transmission of HIV is an important factor in the AIDS pandemic, although important strides have been made in limiting transmission with antiviral drug therapies before, during, and following birth. In the last few decades the rate of mother-to-child transmission of HIV in the United States has been reduced from 25 percent to its current rate of less than 2 percent. However, the transmission of drug-resistant strains of HIV from mother to child is still a problem, and much is unknown concerning how such transmission affects the responses of infants to various drug treatments.

The study, conducted by Deborah Persaud, MD, of Johns Hopkins University School of Medicine and colleagues working throughout the United States, analyzed HIV-infected infants less than six months of age enrolled in a large, multi-center clinical trial covering 10 states.

Their results showed that five of 21 HIV-positive infants were infected with drug-resistant HIV transmitted from their mothers—a surprisingly high figure. Of those five, four were resistant to non-nucleoside reverse transcriptase inhibitors (NNRTIs), a common class of antiretroviral drug used to treat HIV infection and to prevent mother-to-child transmission. All had uncommon drug-resistance mutations that some resistance tests

would miss.

Earlier studies looking at infants treated with antiretrovirals in an unsuccessful attempt to prevent mother-to-child transmission found the virus quickly developed resistance, but levels of resistant virus declined over time to undetectable levels. In the current study, however, researchers found these resistant viruses quickly took up residence in inactive T cells, from where they could later launch an attack that NNRTIs could not stop. The news was not all bad: a different class of antiretroviral drugs, protease inhibitors (PIs), was effective in controlling HIV viral load and NNRTI-resistant virus strains for all infants studied.

These findings have important implications when it comes to choosing among available treatments. As Persaud summarized, "The initial transmitted drug-resistant virus will likely never be cleared from that infant with currently available treatments. However, it is important to point out that because PIs are the first-line drugs used to treat HIV infection in infants in the United States, PI-containing treatment was still effective in controlling the NNRTI-resistant virus in the infants in this study. As long as you do not use NNRTI-based treatment in these infants, you avoid applying pressure that allows drug-resistant HIV to flourish."

The study concluded that it is important to consider drug-resistance testing as a part of the initial evaluation of newly HIV-infected infants so that appropriate choices can be made when considering possible treatments, especially since PIs are not used worldwide as first-line therapy. Such testing must be paired with further studies on available and new therapies. As Persaud remarked, "It is important to fully understand the extent to which the persistent drug-resistant virus affects whether those drugs can be reused within the child's lifetime.… This is a critical question and an area of intense investigation, especially in light of the high rates of antiretroviral drug resistance occurring in infants in

low-income countries who received a single dose of an NNRTI for prevention of mother-to-child transmission, and for whom treatment options are few."

In an accompanying editorial, Paul A. Krogstad, MD, of the David Geffen School of Medicine at UCLA, noted that global elimination of pediatric AIDS will require not only prevention of mother-to-child transmission but also development of new antiretroviral agents for pediatric use, particularly against highly resistant infection. "There is also a need for new and widely accessible methods for detecting HIV infection in infants, whether resistant or not," he pointed out, "since transplacental transfer of maternal antibodies precludes the use of antibody detection methods." Affordable techniques also are necessary to reliably detect resistant HIV in less affluent areas of the world.

"FAST FACTS":

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-- These drug-resistant strains in quickly took up residence in inactive T cells, from where they could later launch an attack that NNRTIs could not stop. Protease inhibitors were still effective, however.
-- These results suggest that drug resistance testing of viruses from HIV infected infants before treatment should be implemented wherever feasible.

Source: Infectious Diseases Society of America