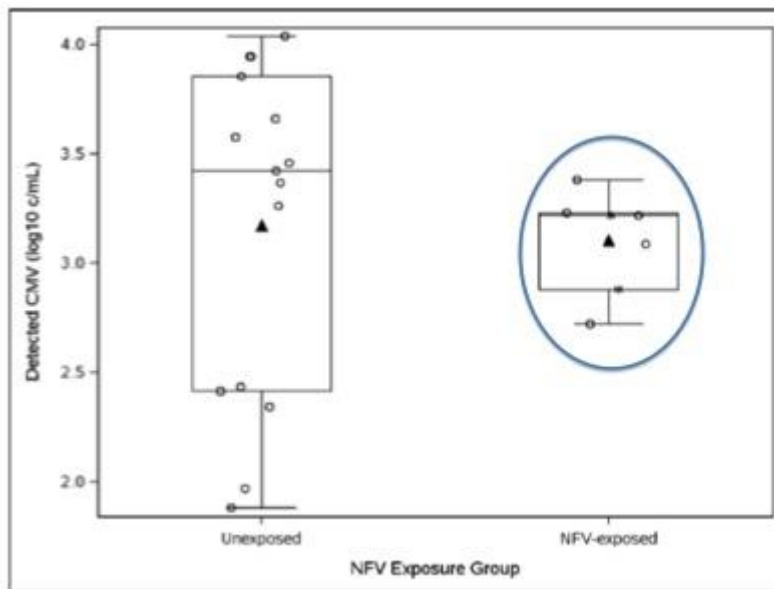


Congenital CMV prevention strategy: still missing

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CMV viral load in NFV-unexposed (left) versus exposed (right) infants.

Image modified from the article.

Although cytomegalovirus (CMV), or human herpesvirus 5, does not represent a threat for immunocompetent adults, congenital CMV infection is the most common cause of birth defects and occurs in 1 out of every 150 infants born (0.6%) in the US. The rate of CMV transmission is higher when the mother is HIV-infected, likely due to poor immune control of CMV replication. Although there are pharmacological treatments available for CMV infection, they have carcinogenic, teratogenic and gonadotoxic effects that preclude their use during pregnancy. Interestingly, nelfinavir (NFV), a protease inhibitor used for prevention of mother-to-child transmission of HIV (PMTCT), was shown to have an *in vitro* inhibitory effect on CMV replication by Dr. Soren Gantt, an Affiliate Investigator at the Vaccine and Infectious Disease Division at Fred Hutchinson. This discovery, together with the proven safety of NFV administration during pregnancy, led Dr. Soren Gantt, Dr Keith Jerome, and other investigators from US and Canadian research institutions to evaluate the effects of NFV treatment on prevention of mother-to-child transmission of CMV. The results of this study are published in the *Journal of Medical Virology*.

The study analyzed specimens from children of 1,255 women enrolled in two prospective cohort studies coordinated by the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network. The studies were designed to assess the efficacy and safety of NFV and other

antiretroviral drugs for PMTCT. In both studies, NFV was prescribed to some women as part of clinical care and not part of a randomized regimen. A total of 314 infants were identified to have samples available and whose mothers received NFV for at least four weeks during pregnancy. Among them, 22% initiated NFV before pregnancy, 11% during the first trimester, 52% during the second and 15% during the third. Another 941 infants of women who did not receive NFV were included as controls. Mothers that did not receive NFV were more likely to know their HIV status before pregnancy and have a higher CD4+ count. All of the infants were HIV-uninfected. Approximately 2% of the infants had congenital CMV infection, a result comparable with previous studies during the era of combination antiretroviral therapy (cART). Infants with congenital CMV were born earlier and weighed less at birth than uninfected infants.

NFV treatment was not shown to have a protective effect: comparable percentages of CMV-infected newborns were identified in the two groups (2.5% in the NFV versus 2.0% in the control group). Moreover, CMV viral load was not statistically different in the two groups (see Figure). This lack of association might be partially due to suboptimal timing of NFV use, a potential confounding factor in the analyses. However, mothers with a CD4+ T cell count lower than 200 cells/mm³ were more likely to have infants with CMV infection. Thus, although NFV was not found to have a direct effect on CMV infection, the results of the study provide further evidence that cART indirectly prevents congenital CMV infection by improving maternal immunity. According to Dr. Gantt, "this study underscores the importance of maintaining high CD4+ T cell counts to reduce congenital CMV infection in HIV-exposed infants, but also that unfortunately better preventive strategies are still needed."

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[Gantt S, Leister E, Jacobson DL, Boucoiran I, Huang M-L, Jerome KR, Jourdain G, Ngo-Giang-Huong N, Burchett S, Frenkel L.](#) 2015. Risk of congenital cytomegalovirus infection among HIV-exposed uninfected infants is not decreased by maternal nelfinavir use during pregnancy. *J Med Virol*. doi: 10.1002/jmv.24420. [Epub ahead of print.]