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# Mechanisms by which co-infections modify HIV-1 transmission

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Women with HIV-1 are frequently co-infected with other pathogens that may influence transmission of HIV-1. Bacterial, helminth, and viral infections are prevalent in settings with high HIV-1 prevalence and may be associated with immune activation, increased HIV-1 replication and genital shedding. Discerning the contribution of co-infections to HIV-1 transmission is difficult because co-infections are more prevalent with advanced HIV-1, a scenario in which transmission is concurrently elevated due to increased systemic HIV-1 burden.

Maternal plasma HIV-1 RNA level is a key determinant of vertical HIV-1 transmission. In addition, mucosal HIV-1 RNA levels in maternal secretions to which the infant is exposed (genital secretions and breastmilk) correlate with transmission risk, independent of plasma HIV-1 levels. Co-infections that cause local inflammation (STDs, mastitis) may increase local mucosal HIV-1 RNA and increase transmissibility of HIV-1. It is plausible that co-infections may contribute to some loss of efficacy of HAART regimens if local HIV-1 shedding occurs despite systemic suppression of virus. In a study with frequent serial sampling of women on HAART, episodic detection of breastmilk HIV-1 RNA occurred despite adherence suggesting local inflammation.

To date, published studies have noted associations between HSV-2, helminth, and TB infections and mother-to-child transmission of HIV-1. Of these, the evidence base is strongest for HSV-2, which has been associated with increased systemic and genital HIV-1 shedding and mother-to-child transmission of HIV-1. Decreased systemic and genital HIV-1 RNA has also been demonstrated following anti-HSV-2 treatment (valacyclovir). There is more limited evidence for helminth and TB infections, in which single studies for each have noted increased risk of vertical transmission among mothers with the co-infection. CMV co-infection is almost universally present in HIV-1 infected women and CMV co-infection is associated with disease progression in infant HIV-1 infection.

The mechanisms by which co-infections exert their effects on infant HIV-1 acquisition and progression are likely to differ. Sexually transmitted infections, in particular HSV-2, are likely to increase transmission via increases in genital HIV-1. Bacterial, helminth, CMV, or TB infections may increase immune activation and systemic HIV-1 replication, which in turn may increase infectivity. A comprehensive approach to maternal care, including management of co-infections will be useful to minimize HIV-1 transmission, morbidity, and progression in infants born to HIV-1 infected women.