Vaginal microbes, inflammation, and HIV risk in African women

Women from sub-Saharan Africa have a disproportionately higher risk of becoming infected with HIV than their male counterparts. Having bacterial vaginosis, a heterogeneous vaginal microbial dysbiosis, increases a woman's risk of acquiring HIV infection[1] and the risk of transmitting the virus to their partners[2] or their children during childbirth.[3] Although bacterial vaginosis is highly prevalent and recurrent in reproductive-aged women worldwide, the composition of organisms that constitute this condition might differ regionally and ethnically.[4,5] Therefore, it is important to understand whether particular vaginal commensals or categories of dysbiosis contribute to HIV acquisition and transmission risks.

In *The Lancet Infectious Diseases*, Scott McClelland and colleagues[6] eloquently show that presence of specific bacterial vaginosis-associated taxa predicted the risk of acquiring HIV infection in five cohorts of women, representing three distinct risk groups recruited from six sub-Saharan African countries. Using both 16S rRNA gene sequencing to explore the relative abundance of vaginal microbes associated with HIV infection, and subsequent real-time PCR to evaluate absolute concentrations of the 20 most influential bacterial species, they showed that *Parvimonas* species type 1 and *Gemella asaccharolytica* were the strongest predictors of HIV infection. Healthy lactobacillus quantities were, however, not protective in the primary analysis. Given that parvimonas and gemella are common constituents of bacterial vaginosis and their presence has previously been associated with genital inflammation in heterosexual South African women,[5,7] this study by McClelland and colleagues suggests that both the presence but also the absolute quantity of these particular organisms might be important drivers of inflammation and HIV risk in sub-Saharan African women.

Genital inflammation increases HIV infection risks either by attracting HIV target cells into the vaginal mucosa or by damaging the mucosal barrier in ways that facilitate HIV penetration.[8] Therefore, the genital inflammation that is commonly associated with bacterial vaginosis might contribute to increasing HIV acquisition risks. Many bacterial vaginosis-associated organisms, besides parvimonas and gemella, have been associated with genital inflammation.[5] Additionally, the presence of some of these organisms in the female genital tract has been further associated with impaired wound healing and decreasing the integrity of the mucosal barrier,[9] potentially through the production of sialidases that degrade protective cervical mucous that would normally trap HIV particles.[8]

By including a wide representation of high-risk women from several countries in eastern and southern Africa—including female sex workers, pregnant and post-partum women, and women in serodiscordant relationships—McClelland and colleagues[6] generalise their findings that certain bacterial vaginosis-associated bacterial genera are major drivers of HIV risk throughout this region. It is nevertheless apparent that certain species might be more influential in some groups of women than in others. For example, although high concentrations of *Mycoplasma hominis* in vaginal swabs from female sex workers had almost a seven-times increased risk of HIV infection, it was not associated with such an effect in the other groups of women. Because pregnant women have less diverse vaginal biomes,[10] it was unsurprising that McClelland and colleagues found that only *Gemella* species were associated with increased HIV acquisition risk during pregnancy. It remains to be determined whether bacterial vaginosis-associated species such as *Parvimonas* and *Gemella* are also important contributors to women-to-men or mother-to-child HIV transmission, or both.

The importance of McClelland and colleagues' study[6] is that it should directly inform future HIV risk-mitigation interventions in Africa. None of the present approaches to treat bacterial vaginosis have long-term efficacy, including the use of lactobacilli-containing probiotics and antibiotics that target anaerobic bacteria such as metronidazole. Whereas most of the probiotics that are used to promote vaginal health do not contain the most common vaginal *Lactobacillus* species, antibiotics used to treat bacterial vaginosis also kill beneficial anaerobes. Furthermore, although resistance to metronidazole is rare it can occur with gemella and parvimonas.[11] Despite the inability to effectively manage bacterial vaginosis, in the context of preventing HIV transmission, it is essential that studies direct us towards novel methods to improve the vaginal health of women.

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