

Linking the microbial and immune environment in semen to HIV viral load and transmission

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While HIV is found in many body fluids, sexual transmission through semen is the most common route of infection. Consequently, the amount of virus in semen (the semen viral load) affects the likelihood of HIV transmission. Besides sperm, semen also contains immune factors and communities of bacteria, an environment that could influence the viral load. Research published on July 24th in *PLOS Pathogens* reports that HIV infection re-shapes the relationship between semen bacteria and immune factors which in turn affects viral load, suggesting that the semen microbiome plays a role in sexual transmission of HIV.

Researchers led by Lance Price, from the Translational Genomics Research Institute, USA, and Rupert Kaul, from the University of Toronto, Canada, studied the relationship of semen bacteria with HIV infection by analyzing semen samples from 49 men who have sex with men (MSM). They focused on MSM because of the high risk of sexual HIV transmission in this population. 27 of the men were HIV infected, and provided samples both before they started anti-retroviral therapy (ART) and one and six months after. Samples from 22 MSM not infected with HIV served as controls.

In HIV-infected men not on ART, overall numbers of bacteria in the samples—the semen bacterial load—was correlated with HIV viral load. Analyzing the bacterial DNA in the samples, the researchers detected a total of 248 unique types of bacteria in semen from the controls, on



average 71 different ones per sample. In samples from HIV-infected untreated men, semen microbiome diversity was markedly reduced, and the relative abundance of the more common bacterial groups differed. ART for six months reduced semen viral load to undetectable levels, and restored bacterial diversity and composition to a situation similar to the controls.

There was no correlation in uninfected controls between levels of immune factors and semen bacterial load. In contrast, in HIV-infected men, several factors, and most strongly one called interleukin-1beta (IL-1b), a mediator of inflammation, showed a correlation with both semen bacterial load and semen viral load.

"While delineating the directionality and causality of the complex relationships they observed will require further studies", the researchers say, their data "suggest an interaction between semen microbiome, local immunology, and semen viral load. Higher bacterial load in semen could lead to higher IL-1b levels, which in turn could induce viral shedding, thereby increasing viral load." They conclude that the results "support the hypothesis that <u>semen</u> bacteria play a role in local inflammation and HIV shedding, and that they are a possible target for reducing HIV transmission."

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