Enemy at the Gate

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Researchers have spent 20 years and hundreds of millions of dollars trying to figure out how to undo HIV once it's in the body. But as virology and reproductive biology expert David Phillips, PhD, and his peers labor to prove the anti-HIV power of microbicides, a key mystery persists: How does the virus get into the body in the first place?

Theories of infection abound. Phillips believes that most acts of unprotected sexual intercourse with an HIV-infected partner won't result in transmission without certain mechanisms to facilitate viral entry. "It's like if a bunch of people drink contaminated water," he says. "Some will get sick. Others won't." The ideas about transmission vary, but ultimately any could be true -- or not. "There's so much we still don't know," Phillips says bluntly.

Most experts assume that semen carries the virus into the cervix, vagina or rectum, allowing it to invade other cells, which then circulate it bodywide. One leading theory holds that the fatal carriers are dendritic cells -- the ones that signal the immune system to produce antibodies. According to this view, dendritic cells pick up the virus and take it back to the lymph nodes, contaminating them.

Another top hypothesis links HIV infiltration to epithelial cells, which line the vagina, intestines and interior of the lungs. Even though these cells are designed precisely to protect these sensitive organs from infection, for some reason they are vulnerable to viral violation, especially in the rectum.

With a number of theories in play, the ideal microbicide would cover as many bases as possible, making the virus unsavory to dendritic cells and preventing the virus from binding to epithelial cells. But even if a microbicide trial is successful, it will be very difficult, if not impossible, to isolate which infection mechanisms were blocked. "It's my job to worry about them all," Phillips says. Clearly, the mystery of infection is fertile ground for future research.

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