Semen Counteracts Effectiveness of HIV Microbicides

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An element of semen both lowers the effectiveness of many HIV microbicides and enhances the virus's infectiousness, possibly explaining why real-world trials of microbicides have fared so poorly. Publishing their findings in Science Translational Medicine, researchers tested various microbicides' ability to prevent infection in cells that had either been exposed just to HIV or to both HIV and semen.

Among all the microbicides tested, the cells exposed to semen had about a tenfold higher rate of HIV infection than normal. Plus, the microbicides were about 20 times less effective at blocking infection in the semen-exposed cells than in the cells that were not exposed to semen.

Semen contains protein aggregates known as amyloid fibrils that enhance HIV's infectiousness. The virus binds to the fibrils in clusters, which increases the virus's ability to latch onto cells.

"We think this may be one of the factors explaining why so many drugs that efficiently blocked HIV infection in laboratory experiments did not work in a real world setting," co-first author Nadia Roan, PhD, a visiting scientist at the Gladstone Institutes and an assistant professor-in-residence in the department of urology at the University of California, San Francisco, said in a press release. "We've shown previously that semen enhances HIV infection, but this is the first time we've shown that this activity markedly reduces the antiviral efficacy of microbicides."

The researchers next repeated their experiments with semen taken from men with a disorder called ejaculatory duct obstruction, which means semen is not ejaculated and therefore does not increase HIV's infectiousness. In these experiments, the semen did not decrease the microbicides' effectiveness.

An exception to the findings that normal semen counteracted the effectiveness of microbicides was when the active agent of the microbicide was Selzentry (maraviroc). In this case, the microbicide's effectiveness was the same regardless of the presence of semen. The reason for this is likely because, unlike most microbicides, which work by targeting the virus itself, Selzentry blocks HIV's ability to attach onto the receptors of immune cells.

"There are important potential clinical implications for this study," Warner Greene, MD, PhD, director of the Gladstone Institute of Virology and Immunology and a senior author on the paper,

said in the same press release. “Microbicides were originally developed as a way to empower and protect women in sub-Saharan Africa who often don’t have a way to negotiate safe sex or condom use. However, the first generation of microbicides were largely ineffective or worse, some even leading to increased transmission of the virus. This study sheds light on why these microbicides did not work, and it provides us with a way to fix this problem by creating a new compound drug combining antivirals and amyloid inhibitors.”

To read the press release, click here.

To read the study abstract, click here.

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http://beta.docker.poz.com/article/microbicides-semen-26487-3023