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How HIV vaccine might have increased odds of infection

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In September 2007, a phase II HIV-1 vaccine trial was abruptly halted when researchers found that the vaccine may have promoted, rather than prevented, HIV infection. A new study by a team of researchers at the Montpellier Institute of Molecular Genetics in France shows how the vaccine could have enhanced HIV infection. The study, lead by Matthieu Perreau, will be published online on November 3 of the *Journal of Experimental Medicine*.

The HIV-1 vaccine used in Merck's STEP trial relied on a weakened form of a common cold virus, Adenovirus 5 (Ad5), to carry bits of HIV into the body. Those bits would presumably trigger the immune system to fight off later infection with the virus. One worry about the Ad5 vaccine vector was that widespread immunity to adenoviruses might cause the vaccine to be ousted from the body before an anti-HIV response could develop. Yet three years after the trial began, researchers realized that more of the vaccine recipients who had prior immunity to adenoviruses had been infected with HIV than those without such immunity.

The new study shows how the presence of long-lasting Ad5-specific antibodies—generated during natural infections with adenoviruses—may have altered the immune response to the HIV vaccine. In the presence of antibodies from Ad5-immune individuals, HIV infection spread through cell cultures three times faster than without them. The antibodies tethered the Ad5-HIV vaccine to receptors on the surface of specialized immune cells, called antigen-presenting cells (APCs), thus facilitating

entry of the vaccine into the cell. Once inside, components of the vaccine then activated these cells, allowing the APCs in turn to activate T cells. Since HIV prefers to infect active T cells, the virus was thus provided with more cells to infect.

Merck's vaccine may have made it to phase II trials because primates, used in the phase 1 trials, don't naturally come in contact with human adenoviruses, and therefore the potential problem went unrecognized.

Source: Rockefeller University