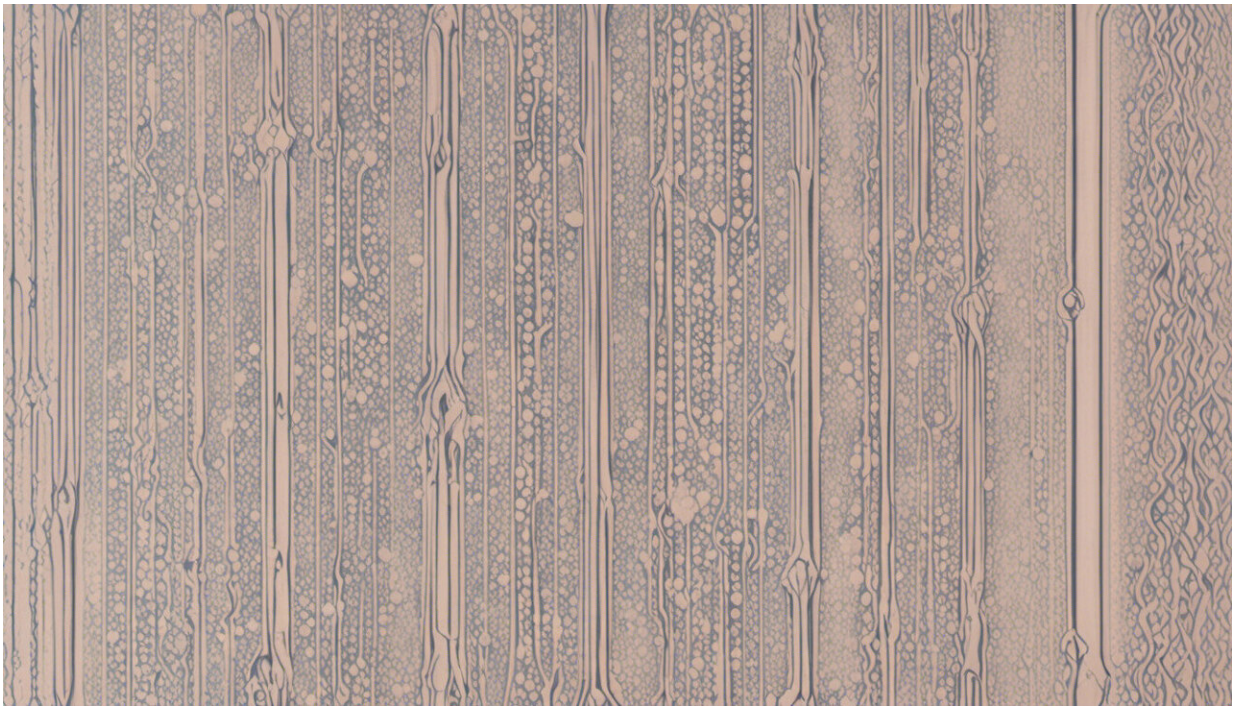
The search for answers to hormonal contraception's role in HIV infection

July 22 2016, by Thomas L. Cherpes



Credit: AI-generated image (disclaimer)

About 75% of HIV-infected people in sub-Saharan African between the ages of 15 and 24 are women. Many factors play a role in this gender imbalance. These include gender-based social disparity and a high prevalence of intergenerational sexual partnerships.

But research suggests certain types of hormonal contraceptives commonly used in this region could also play a role.

Injectable progestin contraceptives, like Depo-Provera, are particularly popular in sub-Saharan Africa. They are effective and convenient. Instead of taking a daily pill, women can receive Depo-Provera injections every three months.

But studies suggest that women using this specific type of contraceptive are more susceptible to HIV. Most recently a large-scale study conducted in Africa found women using injectable progestins were twice as likely to acquire HIV than women using no hormonal contraceptive.

This type of study cannot *prove* a particular type of contraceptive actually makes women more susceptible to infection, as it is just looking for an association between the two.

To really find out if contraceptives make women more susceptible to infection, you need to see how these drugs actually affect the systems that protect the body from infection. Such studies are more difficult to do in humans, so my colleagues and I decided to explore mouse models.

What we learnt from mice

We used mice to learn if Depo-Provera or levonorgestrel (LNG), a progestin used in hormonal intrauterine devices, affect the genital mucosal barrier. This barrier serves as a blockade to prevents virus and bacteria from infecting body tissues. In other words, it is a first line of defense against infection.

Epithelial cells on the surface of genital tract tissues are a vital part of this barrier. They are held tightly together by adhesion molecules that make it difficult for pathogens to penetrate tissue and establish infection.

But we found that mice treated with Depo-Provera or LNG have lower levels of several of these adhesion molecules. This means that genital epithelial cells aren't held together as tightly, tissue becomes more permeable and virus more easily invades.

Our research shows these contraceptives increase mouse susceptibility to infection. But do similar changes in permeability also occur in women?

To find this out, we obtained cervical tissue from US women before and after they started using Depo-Provera. This showed Depo-Provera causes changes to adhesion molecules and tissue permeability similar to those seen in mice.

Where do we go from here?

Sexually transmitted infection and unplanned pregnancy are interconnected public health problems. Countries with a larger burden of infection typically also have higher infant and maternal mortality rates and a great need for effective contraception.

Since Depo-Provera and LNG provide women with effective contraception, we wanted to learn if there are ways to counteract their ability to weaken the mucosal barrier. With this in mind, we also performed studies in which mice were treated with both Depo-Provera and oestrogen.

This combination strengthened the genital mucosal barrier and made mice less susceptible to virus infection. It also suggests a scenario in which women would receive Depo-Provera and a vaginal ring that releases oestrogen and an antiviral microbicide.

Before this can happen, research is needed to determine if Depo-Provera and an oestrogen-releasing vaginal ring protect non-human primates

from viral infection. If positive results are seen, the next logical step would be clinical trials that explore if similar approaches also reduce a woman's risk of acquiring HIV.

This article was originally published on The Conversation. *Read the* original article.

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