Contraceptive risk of HIV long suspected

Animal research showed 15 years ago that progesterone contraceptives could increase infections.

Meredith Wadman

The recent finding that women in seven sub-Saharan Africa countries are nearly twice as likely to acquire HIV if they use a popular, long-acting injectable contraceptive, has incensed AIDS researchers. They say that 15 years of literature has pointed to this increased susceptibility, but that the unwelcome news has been ignored.

The results of a study of 3,790 couples also found that uninfected men were nearly twice as likely to acquire HIV from a female partner using the contraceptive, whose active ingredient is progesterone. The injection, whose generic version costs about US$1.08, is given every three months, and used by more than 90 million women worldwide. The study, published on 4 October in *Lancet Infectious Diseases*¹, also showed that oral contraceptive use by women increased the risk of HIV infection for both women and men with infected partners, but the numbers generated did not rise to statistical significance.

The findings are obliging epidemiologists, infectious-disease specialists and public-health experts to reassess the risks and benefits of the contraceptive, whose branded version, Depo-Provera, is made by Pfizer. The World Health Organization (WHO) is convening a technical consultation early next year at which experts will examine the literature. The aim is to decide whether the WHO’s recommendation for the use of injectable contraceptives should be revised for HIV-infected women, and for female partners of HIV-infected men, in light of the new findings.

But AIDS scientists say that the writing has been on the wall since a study in macaques was published in *Nature Medicine* in 1996². "How many years has it been that the non-human primate model, and other researchers, have been warning about this and being ignored? What, 15 years now? Shocking," John Moore, an HIV scientist at Weill Medical College of Cornell University in New York City, wrote in an e-mail to colleagues and journalists on 5 October.

The 1996 study showed that female rhesus macaques with progesterone implants were 7.7 times more likely to be infected with simian immunodeficiency virus than macaques that had a placebo implant.

Preston Marx, a microbiologist at the Tulane National Primate Research Center in Louisiana and the first author on that paper, says: "It’s not like we did our work and it was published in an obscure journal. There’s absolutely no excuse for people doing contraceptive work to not have known this, and not to have taken this forward in the late ’90s. We should have had this answered [in humans] ten years ago.”

Experts have hypothesized that the thinning of the vaginal mucosa by progesterone (pictured)
makes it easier for HIV to penetrate the vaginal wall in an uninfected woman, and, conversely, for an HIV-positive woman to infect her partner. Other mechanisms at play may include changes in the vaginal microbiota induced by progesterone — specifically, a reduction in hydrogen peroxide-producing *Lactobacillus*, which can kill HIV. Another hypothesis is that progesterone boosts the population of Langerhans cells in the vaginal mucosa, thought to be one of the main targets of HIV in the female genital tract.\(^3\)

Marx believes that public-health and contraceptive experts were hostile to his findings because they did not want to have to cope with a threat to a cheap, accessible and popular contraceptive method that is highly important in the developing world. Instead, he says, they shot the messenger. "I was in one meeting accused of massaging the data. It was real heat."

He notes that intervening human studies have pointed to the same conclusion, particularly a ten-year prospective study study of more than 1,500 sex workers in Mombassa, Kenya.\(^4\)

**Balancing act**

Public-health experts and epidemiologists see the issue differently. Mary Lyn Gaffield, the WHO epidemiologist responsible for developing the organization’s guidelines for family planning, notes that human studies performed since the mid-90s have had methodological limitations. For instance, the risk profile of sex workers is different from that of the general population. Potentially confounding factors, she adds, such as condom use, and the inherent unreliability of self-reporting, mean that "the quality of the evidence is very weak in many of the studies", Gaffield says.

In the current study, she says, "they controlled for many confounding factors, but still hormonal contraceptive use was very, very small. So it warrants us giving a very, very careful look at whether the study prompts a need to warn about the safety or not."

Gaffield notes that there is more in the balance than a woman's risk of HIV infection. Unwanted pregnancies, especially in poor countries, can lead to serious and even fatal complications.

Zdenek Hel, an immunologist at the University of Alabama at Birmingham, was first author on a 2010 review that explored the literature on whether hormone-based contraceptives increase a woman's vulnerability to HIV infection. The review noted that the question remains "highly controversial" and "a topic of intense discussion". It concluded that the epidemiological data thus far were "inconclusive" and that "more comprehensive clinical trials are urgently needed".

Now, says Hel, the new study "may reflect a real and important biological phenomenon and should be taken seriously. This may be the conclusive epidemiological study that we called for."

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**References**

There is an overwhelming evidence from macaque studies, studies in mice, and immunological studies in humans supporting the immunosuppressive function of medroxyprogesterone, the active compound of Depo-Provera. However, it is also important to help to prevent any accusations against Pfizer or other drug companies that sell or distribute Depo-Provera or similar contraceptives. News like this are frequently misinterpreted and drug manufacturers and even academic researchers are easily accused of profiting on HIV-1 epidemic. It is important to remember that contraceptives represent an important tool reducing mother and child mortality, especially in areas with limited resources. World Health Organization has identified the availability and use of effective contraception by HIV-1-infected women wishing to avoid pregnancy as one of the primary strategies for preventing mother-to-child transmission of HIV-1. We should look for viable replacements, contraceptives without the undesired effects.

Zdenek Hel, UAB

if these study turned out to be true then that would be a great problem for Pfizer consumers. Consumers who believe in the effectiveness of these contraceptive yet it seems they'll be needing to look for a new type of contraceptive which is also effective but with no or lesser harmful side effects to human bodies.

Anyway since HIV have been mentioned here, you may wanted to check this article too: http://personalmoneynetwork.com/moneyblog/2011/10/06/costs-of-breast-cancer—Dealing with the costs of breast cancer, it's pretty interesting...:)

>>>It is important to remember that contraceptives represent an important tool reducing mother and child mortality, especially in areas with limited resources.<<<

This is incorrect. Child and mother mortality are things of the distant past with modern medicine. Contraceptives especially chemical ones pose far more risks than benefits. And multigravid women are known to be more healthy because of their multiple pregnancies – for example, studies have found that with every pregnancy, the mother's brain adds neurons – also multi-gravid women who have ovulated less, have been found to have healthier repro systems. Not withstanding children are a blessing to a marriage (95% of humans who have been born have made a positive contribution). Birth control pills, even low dose ones have been named as the more prevalent risk of breast cancer (they are both "cancer initiators" and "Cancer activators"). Those who do not believe me, please view the information on risks of birth control pills (also raise the risk of uterine cancer). Compromising the immune system is a listed risk with any birth control pills as well as weight gain.

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