

In July 2006, scientist Pablo Barreiro and colleagues published "Reproduction Options for HIV-Serodiscordant Couples," in which they recommended methods for human immunodeficiency virus, or HIV, serodiscordant couples to procreate. An HIV-serodiscordant couple is one in which one partner is HIV-positive, meaning they carry HIV, and the other is HIV-negative, meaning they do not carry the virus. HIV is a virus that can spread by sexual contact and it attacks the immune system, causing a person with the virus to have weakened responses to illnesses. Because HIV can transfer from a pregnant woman to a fetus, fetuses conceived in an HIV-serodiscordant relationship could also be HIV-positive. The article "Reproduction Options for HIV-Serodiscordant Couples" offers HIV-serodiscordant couples options on how to procreate without passing HIV on to each other or their offspring.

HIV is a retrovirus that attacks specialized white blood cells, called CD4 lymphocytes that normally fight disease. A retrovirus is a type of virus that uses ribonucleic acid, or RNA, genetic material, to replicate itself. HIV can spread when an HIV-positive man or woman shares body fluids with an HIV-negative individual. Those fluids include blood, pre-seminal fluid, vaginal fluid, rectal fluid, and breast milk. If left untreated, HIV can lead to acquired human immunodeficiency syndrome, called AIDS, where an individual's CD4 lymphocyte count is too low to fight any type of infection.

The use of highly active antiretroviral therapy, called HAART, reduces the effects of HIV infection that can lead to immunodeficiency, or AIDS. HAART refers to when three or more antiretroviral therapy drugs used in concert with one another, typically in pill form to treat HIV. Antiretroviral therapy encompasses a group of drugs that target retroviruses, such as HIV, and prevent the virus from replicating. The use of multiple drugs in HAART reduces the chance of a person developing a resistance to a single drug because the virus mutated, or changed, quickly and develop resistance to individual drugs. Antiretroviral therapy and HAART do not cure HIV, but they increase the quality of life of an HIV-positive individual. They can also help prevent an HIV-positive individual from transferring the virus to an HIV-negative individual.

In 2006, a group of researchers published an article in *AIDS Reviews* on the many methods an HIV-positive individual might use to prevent transmission of the virus to their HIV-negative partner or infant. The article by Barreiro, and his colleagues Ann Duerr, Karen Beckerman, and Vincent Soriano was originally a literature review in *AIDS Reviews*, a journal that covers various topics within the scope of HIV and AIDS. Both Barreiro and Soriano were medical doctors and researchers in the Department of Infectious Diseases at the Hospital Carlos III in La Paz, Madrid, Spain. Their research focused on infectious diseases, such as HIV. Duerr was also a medical doctor and researcher for the Department of Epidemiology in the School of Public Health and Community Medicine at the University of Washington in Seattle, Washington. Her research included the spread of HIV in Peru, as well as HIV prevention in Africa, Asia, and South America. Beckerman was an obstetrician-gynecologist at the Service of Obstetrics and Gynecology at Newark Beth Israel Medical Center in Newark, New Jersey. Her research included the study of HIV in pregnant women.

In "Reproductive Options for HIV-Serodiscordant Couples," the authors discuss reproductive options for HIV-serodiscordant couples. The authors state that inquiries of fertility and reproduction from HIV-serodiscordant couples continue to increase. For the purpose of the article, the authors define an HIV-serodiscordant couple as a heterosexual couple consisting of a woman and a man. The article consists of several sections, but there are four major parts, detailing different scenarios when discussing the fertility and reproduction of an HIV-serodiscordant couple. The first part of the article details the topics relating to the history of HIV and fertility, the issues HIV poses to HIV-serodiscordant couples and their fertility options, and what medical professionals should discuss with the couples when discussing the couple's reproductive options. In the second part, the authors discuss how assisted reproductive technologies can help couples conceive, and when couples can conceive naturally. In the third part, the authors explain how HAART affects transmission of HIV between partners and between a pregnant woman and fetus. In the fourth part of the article, the authors discuss other issues facing HIV-serodiscordant couples, such as ethics of the medical treatment.

In the introduction, Barreiro, Duerr, Beckerman, and Soriano give a brief history of how HIV can affect fertility and reproduction and the reproductive options for HIV-serodiscordant couples. The authors give a history of how modern medications changed the lives of people affected by HIV

infection. In the early 1980s, several health organizations, such as the Centers for Disease Control and Prevention, or CDC, considered HIV a fatal disease, and discouraged HIV-positive individuals from procreating due to the risk of viral transmission. They recommended alternatives, such as adoption. The authors note that due to treatments such as HAART, there is an increased positive prognosis for HIV positive men and women and it increased the quality of their lives.

Though not stated in the article, before the marketing of HAART drugs, HIV was a life-threatening illness, but with the medication, the illness changed from being life threatening to chronic. Because HAART lowers the risk of transmitting HIV to a partner or fetus, HAART allows for more reproductive options. Maternal-fetal transmission, or vertical transmission, of HIV occurs when the virus transfers from the pregnant woman to the fetus in utero through the placenta. The placenta is an organ that develops during pregnancy that connects the pregnant woman's uterus and the fetus. As they continue with their introduction, Barreiro, Duerr, Beckerman, and Soriano add that there are options outside of natural reproduction for HIV-serodiscordant couples who want children. Natural reproduction is the act of human intercourse without the use of contraceptives. They suggest the use of assisted reproductive technologies, or ARTs, to reduce the risk of HIV transmission. ARTs are reproductive techniques other than natural conception that use medical science to increase the chance of pregnancy, such as in vitro fertilization, or IVF, and sperm washing.

In the first part of the article, the authors talk about what should be discussed when an HIV-positive person or an HIV-serodiscordant couple wants to start a family. Barreiro, Duerr, Beckerman, and Soriano suggest that medical professionals discuss reproduction with HIV-positive clients. They state that HIV-positive men and women who take antiretroviral drugs increase their chances of achieving pregnancy. The researchers propose that the couple plans their pregnancy based on many factors, including whether the male or female partner is HIV-positive and if there are any issues with their fertility that would increase the difficulty of achieving pregnancy. However, one of the most important factors is the couple's viral load or the amount of the virus in the human body. The higher the viral load, the fewer CD4 cells are in the blood, which means the individual is more susceptible to illness. Because HAART can lower and maintain the viral load of HIV, it lowers the risk of transmitting HIV to a partner or fetus.

The authors detail the considerations needed before considering natural conception. The authors strongly suggest that during natural conception attempts HIV-serodiscordant couples should include treatment of both the HIV infection and any other sexually transmitted illness, or STI, such as herpes that they may have. In the preconception consultation, the authors advise that a medical professional discuss with the couple the possibility of vertical transmission, or transmission of HIV from the pregnant woman to fetus. They assert that even with treatment and high CD4 levels, the fetus is still at risk for contracting HIV.

Barreiro, Duerr, Beckerman, and Soriano add that the transmission of HIV in an HIV-serodiscordant relationship varies depending on the couple. In some couples, after several instances of unprotected intercourse, there is no transmission of HIV, whereas in other couples, even one instance of unprotected intercourse can result in transmission of the virus. In that sense, they state that it is important for medical professionals to disclose that they cannot predict the likelihood of an occurrence of an HIV infection during unprotected sexual contact. The authors conclude that section by stating that the preconception consultation should include all possible alternatives to natural conception, such as ARTs, adoption, or helping the couple with the acceptance of not having children.

The authors suggest that to decrease the risk of HIV transmission with HIV-serodiscordant couples, medical professionals should perform routine fertility testing. Undergoing fertility testing can decrease the likelihood of HIV transmission from the HIV-positive partner, because if the couple knows that they are not fertile, then they do not have to risk having unprotected sexual intercourse to procreate, which would reduce the chance of contracting a HIV infection. By undergoing fertility testing, the couple could find out if they could benefit from using ART or if they could use natural conception. Barreiro, Duerr, Beckerman, and Soriano discuss that evidence shows that a decreased CD4 count in HIV-positive women lower chances of conception through IVF. IVF a type of ART in which the egg removed from the woman and fertilized by the man's sperm outside of the body then implanted back into the woman's uterus. The researchers state that HIV-positive men have a lower quality sperm than HIV-negative men. The authors suggest the male partner undergo an evaluation

of his sperm, whereas the female partner should undergo basic hormonal tests, a pelvic ultrasound, and scans of the structure of their reproductive organs to rule out any abnormalities. If any result suggests preemptive issues with fertility, the authors suggest that the medical professional refer the couple to a fertility specialist. However, if an HIV-serodiscordant couple recently gave birth or if there are no abnormalities with the results, the couple can consider pregnancy.

In the second part of the article, Barreiro, Duerr, Beckerman, and Soriano explain different techniques that can assist with becoming pregnant based on the sex of the HIV-positive partner. The authors suggest that HIV-serodiscordant couples can be good candidates for ART. The use of ART in HIV-serodiscordant relationships has generally increased. The researchers state that there is risk of HIV moving between partners and from woman to fetus, or infant. In that scenario, the authors recommend intrauterine insemination as the main option so that a HIV-negative male partner can avoid HIV transmission. In intrauterine insemination, semen obtained using a syringe and inserting the syringe with sperm into the woman's vagina and releasing the sperm. To make that procedure effective, fertility doctors should let the female partner know her most fertile days, based upon hormonal tests and calendar tracking of her menstrual cycle, so the woman can self-inseminate on a fertile day to increase her chances of becoming pregnant. The concern of a couple where the HIV-positive partner is male is male-to-female HIV transmission. The authors note that there is no risk of the fetus infected with HIV from the male when the pregnant woman is HIV-negative. The researchers then add that the only option for such couples in the early years of HIV and fertility research was using donor sperm, which is sperm from another male. They state that using donor sperm was not popular by HIV-serodiscordant couples who wanted to give birth to their own biological offspring.

However, the authors describe that though semen can carry HIV, the individual sperm cells within the semen cannot they lack CD4, CCR5 or CXCR4 receptors for the HIV virus to attach to the sperm cell. A technique called sperm washing implemented to use an HIV-positive male's sperm to impregnate his female HIV-negative partner. Sperm washing consists of separating the sperm from the HIV-infected semen and collecting the sperm. The semen fractionated by gradient centrifugation and the fraction containing the sperm and non-germinal cells is re-suspended and re-centrifuged. In the second part, they use the second centrifugation pellet suspended in a small volume of buffer for the swim up procedure. In this step, the motile spermatozoa move in to the buffer separating the non-motile cells or non-germ cells. The motile cells collected as the purified sperm cells.

Barreiro, Duerr, Beckerman, and Soriano note three options on how to utilize the sperm to fertilize the egg. The options are intrauterine insemination, in vitro fertilization, and intracytoplasmic sperm injection, or ICSI. ICSI is a procedure, which injects a single sperm into the egg. In more than 4500 inseminations, no cases of horizontal transmission, transmission from HIV positive man to HIV negative woman from washed sperm from HIV-positive male partners after undergoing intrauterine insemination. As of 2006, no seroconversions occurred from HIV-negative to HIV-positive, in women who have undergone IVF or ICSI with washed sperm. The average couple requires three to four sessions of any of the procedures to result in a birth rate of sixty to seventy-five percent. The cost of the procedures is not affordable for a substantial portion of the couples.

The second section ends by suggesting a guideline for when to recommend natural conception. The authors state that because assisted reproductive technologies are unattainable for some couples due to their high cost and low efficacy, many HIV-serodiscordant couples must have natural pregnancies, a pregnancy resulting from natural conception. If the HIV-positive partner has a viral load that is detectable in their blood plasma, the researchers do not recommend natural conception. An undetectable viral load refers to a situation when there are too few copies of the virus per milliliter of blood to quantify. The transmission of the virus is less likely from a person with an undetectable viral load in the blood and if the male partner is HIV-positive, the authors recommend a test to detect the levels of the virus in semen. If the result shows no level of the virus in the semen, then they recommend natural conception and state that it is important for the HIV-positive partner to take HAART drugs before the couple considers natural conception.

The third part of the article details how HIV treatment can affect the likelihood of vertical transmission, or maternal-fetal transmission of HIV. The authors compare rates of vertical transmission HIV-positive women to their fetus. They note that in developed countries, such as the US, vertical

transmission occurs in fifteen to twenty-five percent of pregnancies, whereas in underdeveloped countries, such as some African or Asian countries, it occurs in twenty-five to thirty percent of the cases. That shows that the use of HAART decreases the risk of vertical transmission, as HAART is more common in more developed nations. The researchers then state that the use of AZT, a drug that blocks maternal-fetal vertical HIV transmission during pregnancy, reduces the chance of vertical transmission by at least fifty percent. The authors note that if the viral load of the pregnant woman is lower, the risk of vertical transmission decreases. However, there are cases of HIV-positive pregnant women who have an undetectable viral load still give birth to HIV-positive fetuses.

As the article continues, Barreiro, Duerr, Beckerman, and Soriano list guidelines for when couples trying to get pregnant should have unprotected sexual intercourse without passing HIV to the partner. In that section, the authors focus on intercourse generally and not on specifically obtaining a pregnancy. They note that if the HIV-positive partner in the HIV-serodiscordant couple has an undetectable viral load while using HAART, he or she is at a low risk of transmitting the virus. The authors add that even if the HIV-positive partner has an undetectable viral load, the male partner should continue to use a condom, regardless of their HIV status and unprotected sexual intercourse is strongly discouraged after a partner becomes pregnant.

The final part of the article restates the guidelines and gives advice for HIV-serodiscordant couples attempting natural conception. They should not pursue natural conception for more than six ovulation cycles. The researchers note that if no pregnancy occurs after six cycles, the couple should consult a fertility doctor. The authors then add that the HIV-positive partner should be on HAART for no less than six months and have an undetectable viral load before attempts at natural conception occur. Lastly, they advise HIV-serodiscordant couples to have unprotected sexual intercourse three times around ovulation to better their chances of attaining pregnancy.

The final topic is about the ethics of reproduction with HIV-serodiscordant couple. The authors state that their article may receive scrutiny because others may disagree with the options they listed and that some medical professionals may not be supportive of reproductive options for HIV-positive individuals in general. The researchers note that both vertical and horizontal HIV transmission in HIV-serodiscordant couples will always be possible. The vertical transmission is of the highest concern, with the transmission probability of one percent, meaning that one in every one hundred live births will result in an HIV-positive newborn. They relate that to the ethical dilemma of a person carrying an inheritable deadly illness that could infect the newborn. The authors conclude by discussing the debate between natural conception and ART. They reiterate that natural conception may not be an option for some couples, whereas ART, because of the price and infectivity, may not be an option for other couples. They repeat in their conclusion that doctors must counsel HIV-serodiscordant couples about fertility issues.

"Reproductive Options for HIV-Serodiscordant Couples" provided detailed options for HIV-positive people who wanted to start a family and increased literacy on HIV and fertility. Since the article's publication in 2006, scientists have developed new technologies to help lower the risk of transmitting HIV. In 2012, pre-exposure prophylaxis, called PrEP, entered the Pharmaceutical market. PrEP is a drug, sold as a prescription pill under the brand name Truvada that an HIV-negative person in an HIV-serodiscordant relationship can take to block the transmission of HIV. In preventing the sexual transmission of HIV, PrEP is over ninety percent effective when taken daily. In 2018, the Prevention Access Campaign, a health initiative that works to end the stigma of HIV, released a consensus endorsed by over 600 organizations stating that an individual with an undetectable viral load suppressed by HAART drugs cannot pass HIV to their partner. "Reproductive Options for HIV-Serodiscordant Couples" provided detailed options for HIV-positive people who wanted to start a family and increased literacy on HIV and fertility. Since the article's publication in 2006, scientists have developed new technologies to help lower the risk of transmitting HIV. In 2012, pre-exposure prophylaxis, called PrEP, entered the Pharmaceutical market. PrEP is a drug, sold as a prescription pill under the brand name Truvada that an HIV-negative person in an HIV-serodiscordant relationship can take to block the transmission of HIV. In preventing the sexual transmission of HIV, PrEP is over ninety percent effective when taken daily. In 2018, the Prevention Access Campaign, a health initiative that works to end the stigma of HIV, released a consensus endorsed by over 600 organiza-

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