Network

Hormonal Contraception and HIV

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Use of hormonal contraceptive methods has greatly improved the well-being of women and their families alike. Two young mothers from KwaZulu Natal, South Africa, walk...
Hormonal contraceptive users need not switch to another contraceptive method.

By Willard Cates, Jr., MD, MPH
President, Research, Family Health International

Charles Morrison, PhD
Senior Epidemiologist, Clinical Research Division, Family Health International

Hormonal contraceptive methods, among the most effective means of preventing pregnancy, have greatly improved the well-being of women and their families alike. However, as the HIV/AIDS pandemic continues unabated, scientists seeking to identify factors that could contribute to the spread of HIV have raised the possibility of an association between hormonal contraceptive use and HIV acquisition.

Research on the topic has been conflicting and inconclusive. However, new data from the largest prospective study ever conducted specifically on this topic help clarify this issue. The FHI-led investigation, conducted among family planning clients in Uganda, Zimbabwe, and Thailand, has found no overall association between the use of combined oral contraceptive (COC) pills or depot-medroxyprogesterone acetate (DMPA) and HIV acquisition. In sum, on the basis of current knowledge about HIV acquisition risks, hormonal contraceptive users who are HIV-negative need not switch to another contraceptive method.

Despite its sophistication and power, this study — funded by the U.S. National Institute of Child Health and Human Development — raised an interesting and unexpected question (see article, page 4): Does the absence of previous genital herpes infection influence the impact, if any, of hormonal contraception on HIV acquisition? Further analyses of the rich data from this study may help provide answers.

Meanwhile, hormonal contraceptive use by HIV-infected women continues to be an important topic for researchers. More women worldwide are learning that they are infected with HIV and many of them do not wish to become pregnant. Uncertainty exists about whether the use of hormonal contraception by HIV-positive women affects their infectivity to male partners or disease progression to AIDS. Research about the infectiousness of HIV-positive hormonal contraceptive users has been limited and inconclusive. As a result, the topic continues to be investigated.

Likewise, some evidence indicates that disease progression may be more rapid if hormonal contraception is used at the time of HIV infection than if it is not used then, but this observation must be confirmed. Further research will also help determine whether hormonal contraceptive use during the later, chronic stage of HIV infection alters the progression to AIDS and the need for antiretroviral (ARV) drug therapy. Finally, clarity about interactions between hormonal contraception and ARV therapy (or other medications used to treat AIDS-related opportunistic infections) is needed. HIV treatment programs are currently scaling up in countries with high HIV prevalence among women, so we need this knowledge as soon as possible.

While hormonal contraception is highly effective against pregnancy, it does not protect against HIV. Thus, HIV-negative hormonal contraceptive users at any risk of infection should, if possible, reduce their number of sex partners and also use condoms consistently and correctly. This long-accepted recommendation remains unchanged regardless of the method of contraception a woman uses. If further research confirms that hormonal contraceptive use at the time of HIV infection speeds disease progression, then women at risk for HIV who continue to use hormonal contraception for protection against pregnancy may have even more incentive to use condoms to protect against infection.

Meanwhile, the possible reproductive health consequences of changing contraceptive methods should be carefully considered. Other than condoms, no contraceptive methods protect against HIV infection. However, some methods provide more protection against pregnancy than others. Women switching to a less effective contraceptive method may be at greater risk for a pregnancy that is both unintended and may have serious health consequences. Pregnancy can result in serious maternal harm or death, especially in some resource-poor settings where childbirth is unsafe or abortion is illegal. In sub-Saharan Africa, for example, as many as one woman in every 16 faces the risk of maternal death in the course of her lifetime. Furthermore, pregnancy itself may increase risk of HIV acquisition.

In the three-country, FHI-led study of hormonal contraceptive use and HIV acquisition, pregnancy did not appear to alter the risk of HIV acquisition. But in a study conducted in Rakai, Uganda, pregnant women were more than twice as likely as non-pregnant, non-lactating women to acquire HIV. Hypothesized reasons for this possibility are that hormonal changes during pregnancy might affect her immune system or vagina.

Again, this finding will need to be confirmed by additional research.

Hormonal contraceptive users who are already HIV-positive and who — in light of limited data about infectivity, disease progression, and drug interactions — wish to continue hormonal contraceptive use can be counseled to do so. Meanwhile, HIV-positive women using hormonal contraception who wish to switch methods should be counseled about other highly effective contraceptive options, such as intrauterine devices and sterilization. Such counseling is especially important because use of contraception by HIV-positive women plays a critical role in preventing mother-to-child transmission of HIV.

References


**Hormonal Contraception and HIV Acquisition**

Study finds no overall association.

**KEY POINTS**

- A recent study has found that hormonal contraceptive use does not increase the risk of HIV acquisition.
- Current knowledge does not indicate a need to change existing recommendations that women at risk of HIV infection may use hormonal contraception with no restrictions.
- Hormonal contraceptive users at any risk of HIV infection should also use condoms consistently and correctly.

Imagine Caroline, a 23-year-old, married woman from Zimbabwe who — like more than a third of women in that country using contraception — takes an oral contraceptive pill each day. By preventing pregnancy at a time in her life when she is not ready to start a family, this highly effective contraceptive provides her with not only peace of mind but also the opportunity to pursue an education and to anticipate the benefits that an education affords. Yet, she worries. Zimbabwe is a place where HIV infection is a clear danger: nearly a quarter of adult Zimbabweans are infected. And Caroline, like so many women in settings where HIV prevalence is high, has heard rumors that use of hormonal contraception may increase her risk of becoming infected with HIV if she is ever exposed to the virus. A thoughtful young woman, she weighs the possible risks and known benefits of continuing to use oral contraception. The idea of acquiring deadly HIV is chilling, and she cannot dismiss it. But she does not want to become pregnant, so she turns to her family planning provider for advice. “What should I do?” she asks.

With some degree of certainty, the provider can now tell her that she does not need to abandon hormonal contraception. This advice is based on new data from the largest prospective study ever conducted on the association between hormonal contraceptive use and HIV acquisition among typical family planning users. The research, funded by the U.S. National Institute of Child Health and Human Development, was conducted by FHI and collaborating institutions* among some 6,100 family planning clients in Uganda, Zimbabwe, and Thailand. The four-year study, published in the January 2, 2007 issue of the journal AIDS, found no overall association between the use of either combined oral contraceptive (COC) pills or depot-medroxyprogesterone acetate (DMPA) and HIV acquisition.¹

This finding — generated by a study with unique methodological strengths when compared with previous studies on the topic (see article, page 5) — is reassuring for women in need of highly effective contraception in settings of high HIV risk. Neither the World Health Organization (WHO) nor the International Planned Parenthood Federation, which have reviewed the study results, plans at this time to change its guidelines for hormonal contraceptive use by such women. In June of 2005, the WHO Family Planning Guideline Steering Group issued a statement that “the study results are reassuring and that the new evidence does not modify the current guidance for contraceptive use,” which states that women at risk of HIV infection or those who are HIV-infected may safely use hormonal contraception.²

The study also examined whether sexually transmitted infections (STIs) modified the relationship between hormonal contraceptive use and HIV acquisition. Among STIs included in the analyses were vaginal infections (trichomoniasis, bacterial vaginosis, and candidiasis), cervical infections (chlamydia and gonorrhea), and infection with herpes simplex virus-2 (HSV-2). The African data showed that only one STI modified the relationship between hormonal contraceptive use and HIV: Among the approximately half of African study participants testing negative for HSV-2 at enrollment, those who used either COCs or DMPA had a statistically significant increased rate of HIV acquisition compared with non-users. This finding was unexpected and has no clear biological mechanism. Thus, as is often the case with unexpected study findings, further research must evaluate this potential association. Of note, the study found that participants who were infected with HSV at the beginning of the study had higher rates of HIV infection than did those women who were HSV-negative at the start. This is consistent with data from many other published studies showing that HSV infection increases the risk of HIV acquisition.

Meanwhile, Dr. Charles Morrison, a senior epidemiologist at FHI and principal investigator for the study, urges a conservative approach. “Our findings should reinforce efforts to counsel all women at risk of HIV infection to use condoms consistently and correctly to prevent HIV acquisition” in addition to their primary contraceptive method, he says. This advice is true for women using any form of contraception, since no contraceptive method besides condoms provides protection against HIV infection.

*Kim Best
Why This Study Is Unique

A possible relationship between hormonal contraceptive use and HIV acquisition has been investigated in approximately 30 studies. However, understanding of this possible relationship has remained poor. Study results have been inconsistent, in part because nearly all these studies have been designed to investigate other research questions and have had important methodological shortcomings. Only 12 prospective studies — the design of which reduces some sources of bias to results — have examined hormonal contraceptive use and HIV infection. Only six of those studies have considered a possible relationship between the use of the injectable hormonal contraceptive depot-medroxyprogesterone acetate (DMPA) and HIV infection.

The present study, funded by the U.S. National Institute of Child Health and Human Development and conducted by FHI researchers and collaborating institutions, is unique and standard-setting in that it is:

- **The only large prospective cohort study designed specifically to evaluate the relationship between the use of low-dose COCs or DMPA and HIV acquisition.** Conducted in Uganda, Zimbabwe, and Thailand, this study involved some 6,100 HIV-negative, 18- to 35-year-old women in three exposure groups of roughly equal size: combined oral contraceptive (COC) users, DMPA users, and women not using hormonal contraception. With this number of study participants, the power of the study to detect a potential association was high. Notably, the study’s prospective cohort design allowed women to continue using their voluntarily chosen contraceptive method.

- **Conducted among family planning clients,** who are considered to be at lower risk of HIV infection than such groups as sex workers or members of HIV-discordant couples. While results of other studies have been conflicting, those that have indicated an increased HIV risk associated with hormonal contraception were generally conducted among very high-risk populations of women, such as sex workers, who have frequent sexual encounters with multiple partners.

- **Methodologically strong in terms of accurate measurement of contraceptive use, identification of the timing of HIV infection relative to hormonal contraceptive use, rigorous and successful follow-up of study participants (who were tested for HIV infection every 12 weeks until they became infected or had been followed for 15 to 24 months, with an overall retention rate of 91 percent), confirmation of the study outcome (HIV incidence) data via stringent algorithms and laboratory audits, and careful measurement of and adjustment for many potential confounding factors.**

For these reasons, this study greatly clarifies what effect hormonal contraceptive use has on HIV acquisition and serves as the strongest study to date exploring this issue. However, unlike a randomized controlled trial, a prospective, observational study cannot provide evidence to establish a direct cause-effect relationship between hormonal contraceptive use and HIV acquisition. While a randomized controlled trial is unlikely to be conducted in the near future, international reproductive health experts will continue to evaluate any additional evidence emerging from other studies.

Kim Best

Reference


References


Questions and Answers

Study of Hormonal Contraceptive Use and HIV Acquisition

How widely is hormonal contraception used?

Worldwide, about 84 million women currently married or in union use combined oral contraceptives (COCs) and about 24 million such women use the injectable depot-medroxyprogesterone acetate (DMPA). Many other women not currently married or in union also use these contraceptive methods.1

What are COCs?

Most oral contraceptives contain both progestin and estrogen and thus are called combined oral contraceptives. The COCs used in this study were low dose (30 micrograms estrogen, 150 micrograms levonorgestrel) monophasic pills.

What is DMPA?

DMPA, known commercially as Depo Provera, is a synthetic form of the natural hormone progesterone. The most widely used injectable contraceptive, it is among the most effective methods of contraception, with typical one-year pregnancy rates of 0.4 percent or lower. DMPA is injected intramuscularly at a dose of 150 milligrams every three months. This decreases the risk of missed doses, such as missing a daily oral contraceptive pill.

Were the pills and injectables used in this study the same as those used in the United States?

The COCs used in this study (Lo-Femenal and Microgynon) are what many women in the United States and other developed countries most commonly use. Similarly, the DMPA used in this study is the same as that used in the United States and in many countries throughout the world.

Are other injectables safe to use?

The World Health Organization’s (WHO’s) Medical Eligibility Criteria for Contraceptive Use currently recommends that women at risk of HIV infection may use all injectables with no restrictions.2

Another progestin-only injectable contraceptive is norethisterone enanthate (NET-EN), known commercially as Noristerat or Noristerat. It differs from DMPA in that it contains a different progestin and is administered every two months at a dose of 200 milligrams. Two combined progestin-estrogen injectable contraceptives, known commercially as Cyclofen and Mesigyna, are administered monthly. Determining whether the differences in dose or types of hormones in these injectables might result in different effects on HIV acquisition would require further research.

(Of note, a recently completed secondary analysis of data collected as part of another study found that use of COCs, NET-EN, or DMPA by South African women from the general population was not associated with increased risk of HIV infection.3)

Could hormonal contraceptives with different dosages of progestins and estrogens than those used by participants in this study pose different risks of HIV acquisition?

Formulations similar to those used in this study are likely to have similar effects. However, more research is needed to investigate this possibility.

Why were Uganda, Zimbabwe, and Thailand selected for this study?

The study was conducted primarily among family planning clients because they are more likely than other women to use hormonal contraception and because it is important to know whether that use increases their risk of HIV acquisition. Also, family planning clients are at relatively low risk of HIV infection. In contrast, many previous analyses of hormonal contraceptive use and HIV acquisition came from studies conducted among women at high risk for HIV infection: commercial sex workers or women seeking medical care for sexually transmitted infections (STIs).

What was done to safeguard the rights of women participating in the study?

The study was designed according to the most rigorous international ethical standards. It was reviewed and approved by the U.S. National Institutes of Health (NIH) and by 12 institutional review and human protection boards in the United States and participating countries.

Why was the study conducted primarily among family planning clients?

The study was conducted primarily among family planning clients because they are more likely than other women to use hormonal contraception and because it is important to know whether that use increases their risk of HIV acquisition. Also, family planning clients are at relatively low risk of HIV infection. In contrast, many previous analyses of hormonal contraceptive use and HIV acquisition came from studies conducted among women at high risk for HIV infection: commercial sex workers or women seeking medical care for sexually transmitted infections (STIs).
All study participants voluntarily agreed to take part in the study, and the study’s prospective cohort design allowed them to continue using their voluntarily chosen contraceptive method. Before the trial began, they were counseled on what the study required of them, as well as the potential risks and benefits of study participation. They were also counseled that they were not obligated to participate and could stop participating at any time.

• Staff emphasized that the effects of hormonal contraceptive use on HIV acquisition — beneficial or harmful — were unknown.

• Everything possible was done to eliminate the possibility that study participants would be exposed to HIV infection. At each regularly scheduled 12-week visit during the study, counselors provided study participants with information on HIV transmission and prevention.

• The use of condoms with all sexual partners was emphasized for protection from HIV. Counseling also included condom negotiation skills, skills-building in partner communication, and demonstration and practice with models of the correct application of condoms. Finally, free condoms were provided.

In addition, highly sensitive tests were used to detect STIs at each study visit. Participants were contacted and treated free of charge for any detected STI, thus reducing the risk of HIV acquisition.

How were the women who became infected with HIV during the study cared for?

All HIV-infected women were encouraged to continue to return for study follow-up visits and were provided their contraceptive methods of choice. Such women were counseled to use condoms consistently, told about the implications of becoming pregnant while HIV-infected, and advised that they should bring their partners for HIV testing and counseling. All participants who became infected with HIV during the study were extensively counseled and given referrals to medical services and to research studies that provided HIV care and treatment. They were also referred to local support groups that offer HIV-related psychological and social services.

In addition, women in Uganda and Zimbabwe (where almost all of the HIV infections occurred) who became HIV-infected during the study were offered the opportunity to enroll in a follow-on study of HIV-infected women. Women in that study received counseling about condom use, reduction in transmission risk, and health maintenance; their choice of contraceptive method and free condoms; diagnosis and treatment for STIs; access to a support group for HIV-infected women and to HIV support counseling; referrals for other HIV support services; referral to an HIV-experienced health care provider (as needed); antiretroviral drug therapy and prophylaxis for pneumonia or tuberculosis, if medically indicated; treatment for malaria and other common infections; Pap smears; daily multivitamins and iron; and referral for treatment to prevent mother-to-child transmission of HIV.

What further analyses can we expect?

Various ancillary studies and secondary analyses will be conducted, ultimately helping international normative bodies set evidence-based standards for the provision of hormonal contraception in countries with high HIV prevalence.

Ancillary studies and secondary analyses will look at whether hormonal contraceptive use is associated with:

1) bacterial vaginosis
2) herpes simplex virus (HSV)
3) chlamydial and gonococcal infection
4) trichomoniasis

They will also evaluate the subsequent impact of these STIs on HIV acquisition. Whether hormonal contraceptive use is associated with human papillomavirus will also be examined.

In addition, ancillary studies among women who become HIV-infected will examine hormonal contraceptive use and its relationship with:

1) genital shedding of HIV (and thus possible HIV transmission to male partners)
2) HIV viral set point (HIV level in the blood after the immune system’s initial response to the virus), progression of HIV infection, and clinical manifestations of HIV/AIDS
3) antiretroviral drug therapy

Finally, the study’s findings related to HIV risk among HSV-negative hormonal contraceptive users will be further analyzed.

Kim Best

References


Research Implications for Users and Providers

Extensive research over decades has shown that combined oral contraceptives (COCs) and the injectable contraceptive depot-medroxyprogesterone acetate (DMPA) are extremely safe and pose few serious side effects.

Recent research suggests that use of COCs and DMPA may increase risk of acquiring chlamydial infection. Otherwise, the body of existing research indicates that hormonal contraceptive use does not appear to increase the overall risk of acquiring other sexually transmitted infections (STIs), including HIV and gonorrhea.

However, hormonal contraceptives do not protect against any STIs, including HIV. This means that family planning providers should counsel users of hormonal contraceptives — as well as other methods — to use condoms consistently and correctly with each sexual act if they are not in a mutually monogamous relationship with an uninfected partner. Providers often assume that men and women in married or steady relationships will not use condoms. But an FHI study conducted among 49 Ugandan women — recruited from the recently published study of hormonal contraceptive use and HIV — and their partners found that stable couples in settings with high fertility and high HIV prevalence may be more likely than commonly thought to use condoms.

Meanwhile, the use of HIV voluntary counseling and testing (VCT) services should be encouraged so more individuals can learn their HIV status. This, in turn, can assist women who do not wish to become pregnant in making contraceptive choices that best meet their needs. For example, some women who learn that they are HIV-positive may strongly wish to prevent pregnancy and thus decide to use a highly effective contraceptive method. VCT programs need to ensure that they provide either contraceptive counseling or referrals for such counseling.

This table suggests actions for hormonal contraceptive users and family planning and VCT providers, based on a couple’s HIV status.

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References


### Actions to Minimize HIV Risks

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<tr>
<th>HIV Status of Couple</th>
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<th>For Family Planning and VCT Providers</th>
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<tr>
<td>Unknown</td>
<td>Seek HIV testing to learn the infection status of both partners. Practice mutual monogamy or, at least, reduce number of sexual partners. Meanwhile, if mutual monogamy cannot be assured, use condoms consistently and correctly to reduce risk of HIV infection in addition to using hormonal contraceptive method to reduce risk of unintended pregnancy. If male condom use not possible, consider option of female condom use.</td>
<td>Encourage both partners to learn their HIV status. Counsel couples on benefits of mutual monogamy. Counsel couples who do not practice mutual monogamy to reduce number of sexual partners and to use a condom at each sexual act. If male condom use not possible, discuss option of female condom use.</td>
</tr>
<tr>
<td>Both HIV-negative, mutually monogamous</td>
<td>Remain monogamous to ensure protection from sexually transmitted HIV infection. Condom use not necessary for prevention of infection. Practice mutual monogamy or, at least, reduce number of sexual partners. Use condoms consistently and correctly with hormonal contraceptive method to reduce risk of HIV infection and other sexually transmitted infections, as well as unintended pregnancy. If male condom use not possible, consider female condom use.</td>
<td>Counsel couples that mutual monogamy will continue to ensure protection from sexually transmitted HIV infection. Condom use not necessary for prevention of infection. Counsel couples on benefits of mutual monogamy. Counsel couples who do not practice mutual monogamy or are not sure that their relationship is mutually monogamous to reduce number of sexual partners and to use a condom at each sexual act. If male condom use not possible, discuss option of female condom use. Note: Even if a couple has tested HIV-negative, one or both individuals could become infected shortly after testing if the relationship is not mutually monogamous.</td>
</tr>
<tr>
<td>Both HIV-negative, not mutually monogamous, or mutual monogamy uncertain</td>
<td>Use condoms consistently and correctly with hormonal contraceptive method to protect uninfected partners from HIV infection (if one partner is HIV-positive) and to protect against both acquisition and transmission of other sexually transmitted infections and new strains of HIV (if both partners are HIV-positive). Consider use of other highly effective, non-hormonal contraceptives (such as the intrauterine device or sterilization), especially if the woman is HIV-infected and concerned about becoming pregnant and transmitting HIV to her child; the possible effect of hormonal contraceptive use on disease progression; or interactions between hormonal contraception and antiretroviral therapy or other drugs used to treat AIDS-related opportunistic infections.</td>
<td>Emphasize consistent and correct condom use with hormonal contraceptive method to protect uninfected partners from HIV infection (if one partner is HIV-positive) and to protect against both acquisition and transmission of other sexually transmitted infections and news strains of HIV (if both partners are HIV-positive). Counsel couples about use of other highly effective, non-hormonal contraceptives (such as the intrauterine device or sterilization), especially if the woman is HIV-infected and concerned about becoming pregnant and transmitting HIV to her child; the possible effect of hormonal contraceptive use on disease progression; or interactions between hormonal contraception and antiretroviral therapy or other drugs used to treat AIDS-related opportunistic infections.*</td>
</tr>
<tr>
<td>One or both partners HIV-positive</td>
<td>Use condoms consistently and correctly with hormonal contraceptive method to protect uninfected partners from HIV infection (if one partner is HIV-positive) and to protect against both acquisition and transmission of other sexually transmitted infections and new strains of HIV (if both partners are HIV-positive). Consider use of other highly effective, non-hormonal contraceptives (such as the intrauterine device or sterilization), especially if the woman is HIV-infected and concerned about becoming pregnant and transmitting HIV to her child; the possible effect of hormonal contraceptive use on disease progression; or interactions between hormonal contraception and antiretroviral therapy or other drugs used to treat AIDS-related opportunistic infections.</td>
<td>Counsel couples about use of other highly effective, non-hormonal contraceptives (such as the intrauterine device or sterilization), especially if the woman is HIV-infected and concerned about becoming pregnant and transmitting HIV to her child; the possible effect of hormonal contraceptive use on disease progression; or interactions between hormonal contraception and antiretroviral therapy or other drugs used to treat AIDS-related opportunistic infections.*</td>
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* Women on antiretroviral therapy generally may use COCs, but medical follow-up may be appropriate due to unanswered questions about the effects of antiretroviral-COC interactions. Non-hormonal methods are recommended for clients taking rifampicin for tuberculosis.
Clients Can Quickly Learn HIV Status

Am I infected with HIV? Is my partner infected with HIV? Most men and women throughout the world do not know the answers to these questions. But, particularly in settings of high HIV prevalence, a sexually active individual who is not in a mutually monogamous relationship with an uninfected partner needs to know. Men and women who learn that they are HIV-infected can seek care and treatment and take steps to avoid infecting their partners. Women who learn they are infected can take steps to avoid infecting any children they might conceive. Even men and women who learn that they are not infected can benefit. If at continuing risk of HIV infection, they can adopt preventive behaviors such as abstaining from sex, being faithful to one sexual partner, and using condoms consistently and correctly.

Testing for HIV infection has been encouraged for many years. Since the mid-1980s, most people seeking testing have had enzyme-linked immunosorbent assay (ELISA) tests. But ELISA tests require a blood sample drawn from a vein, skilled technicians, and a laboratory with reliable water and electricity. Forty to 90 blood specimens must be tested at once for ELISA to be cost-effective. Another disadvantage of ELISA is that the processing of test results takes several days or weeks, requiring clients to return to the testing facility to learn their HIV status. Not surprisingly, up to a third of clients having ELISA tests do not return to receive their results due to disincentives such as travel costs and time.1

Fortunately, some of these obstacles have been reduced with the development and growing availability since 1990 of a variety of new, instrument-free “rapid tests” that allow clients to learn their HIV status immediately and receive counseling about HIV prevention, care, and treatment.

The World Health Organization (WHO), which has called for a major expansion of HIV testing and counseling, has embraced the idea of using rapid HIV tests in many settings.2 The tests can be particularly useful in reaching clients most likely to benefit from knowledge of their HIV status, such as pregnant women and those living in settings of high HIV prevalence.

Advantages of the rapid tests are numerous. Rapid tests use saliva, urine, or finger-prick blood samples to screen for HIV antibodies; sometimes, clients receive results in less than 20 minutes. Like the ELISA tests, rapid tests can screen for HIV-1, HIV-2, and other HIV subtypes. The tests do not require any specialized instruments, and test results can be read visually and interpreted by minimally trained personnel. The rapid tests’ accuracy is comparable to the accuracy of the ELISA tests. (Sensitivity and specificity can be greater than 99 percent.)3 The rapid tests are also comparable in price to the ELISA tests (U.S. $0.40 to U.S. $2 per test through WHO’s bulk procurement scheme). Most rapid test kits have a long shelf life (12 months), can be stored at room temperatures of up to +20°C to +30°C (equivalent to 68°F to 86°F), and do not require water or electricity.

The two most commonly cited disadvantages of the rapid tests are that clients are sometimes reluctant to accept the accuracy of their results and that counselors and clients have less time to prepare for the delivery of results, especially if they are positive.

In general, these tests are well suited for use in HIV voluntary testing and counseling (VCT) centers and resource-constrained facilities, particularly rural areas where the volume of testing is too low to use ELISA tests efficiently. Several programs in Africa, Europe, and the United States are using rapid tests in mobile testing centers to allow people to learn their HIV status quickly and easily.

Like the ELISA tests, the rapid tests provide only initial screening for HIV antibodies and positive results must then be confirmed with another test. WHO has developed testing algorithms of two or three sequential tests (including the initial test) that can reliably confirm HIV test results. HIV rapid tests can take somewhat longer than ELISA tests to detect HIV antibodies (in rare cases, up to three months after infection has occurred). Therefore, persons who have a negative rapid test result but were recently exposed to HIV are counseled to be tested again at least three months after possible infection.

Several dozen brands of rapid test kits are now available on the market worldwide, and many countries are quickly adopting their use. When selecting the kit that best fits their needs, governments and ministries of health are urged to evaluate each kit carefully in terms of cost, availability, and prevalence of particular HIV strains in specific settings.


Chris Parker

References


3. WHO.
Research Implications for Policy-makers

In light of recent research showing no overall association between hormonal contraceptive use and HIV acquisition among women at relatively low risk of HIV infection, no changes should be made in the provision or use of combined oral contraceptives (COCs) or depot-medroxyprogesterone acetate (DMPA). The World Health Organization’s Medical Eligibility Criteria for Contraceptive Use currently states that even women at risk of HIV infection may use hormonal contraception with no restrictions.1

However, no form of contraception other than condoms has been shown to protect women from sexually transmitted infections, including HIV. This means that any sexually active woman not desiring pregnancy and not in a mutually monogamous relationship with an HIV-uninfected partner should consider how best to obtain dual protection against both pregnancy and HIV infection. Dual protection can be achieved by using male latex condoms or female condoms alone or in combination with other contraceptive methods.

Notably, recent research implications for hormonal contraceptive use include the need to carefully balance HIV risks with pregnancy-related risks. These pregnancy-related risks are high in countries where childbirth is unsafe or abortion is illegal, resulting in high maternal and infant mortality and morbidity.

It may be helpful for policy-makers in specific settings to identify the type of HIV epidemic (i.e., low level, concentrated, or generalized) and then determine pregnancy-related risks faced by women of reproductive age. The following table shows the policy implications of balancing relative HIV and pregnancy-related risks.

Balancing Relative HIV and Pregnancy-Related Risks

<table>
<thead>
<tr>
<th>Type of HIV Epidemic*</th>
<th>Risk of pregnancy-related morbidity/mortality</th>
<th>Balanced Relative HIV and Pregnancy-Related Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low risk† (safe childbirth or legal abortion)</td>
<td>High risk† (unsafe childbirth or illegal abortion)</td>
</tr>
<tr>
<td>Low level</td>
<td>Encourage consistent and correct use of client’s preferred contraceptive method.</td>
<td>Encourage use of any contraceptive method that will be highly effective regardless of consistency or correctness of use.‡</td>
</tr>
<tr>
<td>Concentrated</td>
<td>Encourage consistent and correct use of client’s preferred contraceptive method.</td>
<td>Encourage use of any contraceptive method that will be highly effective regardless of consistency or correctness of use.‡</td>
</tr>
<tr>
<td></td>
<td>For women at high risk of HIV, encourage consistent and correct use of condoms (male or female) at each sexual act.</td>
<td>For women at high risk of HIV, encourage consistent and correct use of condoms (male or female) at each sexual act.</td>
</tr>
<tr>
<td>Generalized</td>
<td>Encourage consistent and correct use of condoms (male or female), either alone or in combination with consistent and correct use of client’s preferred contraceptive method, at each sex act.</td>
<td>Encourage consistent and correct use of condoms (male or female) at each sex act and use of any contraceptive method that will be highly effective regardless of consistency or correctness of use.‡</td>
</tr>
</tbody>
</table>

*Low level = HIV prevalence below 5 percent in at-risk subpopulations and below 1 percent among pregnant women; Concentrated = HIV prevalence above 5 percent in at least one at-risk subpopulation but below 1 percent among pregnant women; Generalized = HIV prevalence above 1 percent among pregnant women.

† In general, lifetime risk of maternal death is 1 in 2,800 in developed regions (Europe, Canada, the United States, Japan, Australia, and New Zealand) versus 1 in 61 in developing regions. It is in sub-Saharan Africa, 1 in 16; in South-Central Asia, 1 in 46; in Western Asia, 1 in 120; in South-Eastern Asia, 1 in 140; in Latin America and the Caribbean, 1 in 160; in Northern Africa, 1 in 210; and in Eastern Asia, 1 in 840.


‡ Intrauterine devices, implants, sterilization, and (to a lesser degree) injectables are highly effective methods, providing little or no opportunity for inconsistent or incorrect use.

Reference

Hormonal Contraception and STI Acquisition Explored

By Charles Morrison, PhD
Senior Epidemiologist, Clinical Research Division, Family Health International

Dr. Morrison is an epidemiologist who, for more than a decade, has directed research and published on the relationship between contraception and sexually transmitted infections, including HIV.

Do hormonal contraceptive methods increase women’s risk of acquiring sexually transmitted infections (STIs) other than HIV? This question is of critical concern, given that more than 100 million women worldwide use these methods.\(^1\)

Decreasing STI incidence by identifying and addressing any factors contributing to it is a major public health priority since untreated STIs in women cause important, long-term health consequences. Bacterial STIs — such as chlamydial and gonococcal infection — are associated with pelvic inflammatory disease, chronic pelvic pain, ectopic pregnancy, and infertility. Also, STIs in women may increase the risk of HIV acquisition\(^2\) and transmission to sexual partners.\(^3\)

Existing research on the relationship between hormonal contraceptive use and STIs is limited, and many studies suffer from serious methodological problems.\(^4\) Further high-quality, prospective research is needed to reach informed conclusions about individual contraceptive methods and the risk of acquiring specific STIs. However, based on a review in 2005 of evidence on the topic, the World Health Organization concluded that its existing guidance was appropriate. That guidance places no restrictions on the use of combined oral contraceptives (COCs) or depot-medroxyprogesterone acetate (DMPA) by women at risk of acquiring an STI.\(^5\)

A review of peer-reviewed articles describing research on contraception and STI risk published between January 1966 and December 2004 helps to clarify the matter.\(^6\) The review, conducted by FHI and collaborating institutions,\(^*\) focused largely on prospective studies that assessed contraceptive use prior to infection status. Cross-sectional studies were included but de-emphasized, since such studies cannot determine the sequence of contraceptive exposure and STI outcome, making it impossible to clearly establish the nature of any association. The review found:

- a possible increased risk of acquiring chlamydial infection associated with both the use of COCs\(^7\) and the use of DMPA injections\(^8\)
- no convincing evidence that either COC or DMPA use is associated with the acquisition of gonococcal infection\(^9\)
- insufficient or inconclusive evidence regarding the associations between COC or DMPA use and the risk of acquiring trichomoniasis,\(^10\) human papillomavirus (HPV),\(^11\) herpes simplex virus (HSV),\(^12\) or syphilis\(^13\)

To further clarify the matter, FHI researchers and colleagues are conducting ancillary studies to their recently published prospective study of hormonal contraceptive use and HIV acquisition. These ancillary studies and secondary analyses will investigate whether hormonal contraception affects acquisition of HSV, bacterial vaginosis (BV), chlamydial and gonococcal infection, trichomoniasis, and HPV. They will also assess the role of HSV, BV, and trichomoniasis in HIV acquisition.

No published studies report on STI risk among users of other progestin-only methods including progestin-only pills, the injectable norethisterone enanthate (NET-EN), or the implant Implanon. Likewise, STI risk among users of newer combined hormonal methods such as the patch (Ortho Evra), the ring (NuvaRing), or the combined injectables Cyclofem and Mesigyna has not been evaluated.

**Possible mechanisms of action**

Although further, high-quality research is needed to determine whether hormonal contraceptive use is associated with STI acquisition, such a relationship is plausible for both biological and behavioral reasons. Possible biological mechanisms include:

- increased cervical ectopy (a condition in which the lining usually found inside the cervical canal extends onto the cervix’s outer surface, where exposure to sexually transmitted pathogens is greater) associated with OC use\(^14\)
- changes in the body’s immune system associated with the use of steroids\(^15\)
- direct influence of sex hormones on pathogen virulence, resulting in enhanced susceptibility to infection\(^16\)
- a hypo-estrogenic effect associated with DMPA use, resulting in changes in the vaginal microbial flora or in the vaginal epithelium\(^17\)

\(^*\) FHI and collaborating institutions included the University of California, Los Angeles, the University of Washington, Duke University, the University of California, San Francisco, the University of California, San Diego, the National Institutes of Health, and the International AIDS Vaccine Initiative.
In terms of behavioral factors, women choosing various methods of contraception may differ from one another in the sexual risks they take. Their sexual risk-taking may also change after they begin taking contraceptives.

**Public health, clinical implications**

If a given contraceptive method is shown more conclusively to increase the risk of acquiring certain STIs, counseling strategies should ensure that women understand the association between method use and infection. Until methods that are highly protective against both pregnancy and STIs are available, women at risk of infection should continue to be encouraged to use highly effective contraception to prevent unintended pregnancy together with condoms to help prevent STIs.

However, care should be taken not to cause unwarranted concern about risks associated with contraceptive use. Suggesting an increase in STI risk that has not been shown to exist could result in women stopping a particular contraceptive method without plans to adopt another. This could result in surges in pregnancies that are both unintended and may have serious health consequences. Pregnancy can result in serious maternal harm or death, especially in some resource-poor settings where childbirth is unsafe or women lack access to safe abortions.

The risks and benefits associated with the use of any contraceptive method need to be carefully evaluated by contraceptive providers and users. For many women, increased susceptibility to STIs may be of little concern since their lifestyles, low STI incidence where they live, and other factors may put them at low risk for such infections. Indeed, potential increases in STI risk associated with specific contraceptive methods may not be relevant for large segments of the population in many settings. On the other hand, many women either do not understand that they are at risk of acquiring STIs or do not accurately assess their risks. Thus, for sexually active women not in mutually monogamous relationships with uninfected partners, contraceptive counseling should continue to emphasize the need for condom use and frequent STI screening in addition to highly effective contraception.

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15. Sonnex. *Cue.**
Hormonal Contraceptive Use by HIV-infected Women

Does Hormonal Contraception Increase HIV Infectivity?

Whether hormonal contraceptive use by HIV-infected women increases their risk of infecting sexual partners remains unknown.

Studies addressing this question are limited. Only two such studies have been prospective, and the results of cross-sectional studies of HIV shedding from the genital tract (thought to be a marker of increased infectiousness) are conflicting, perhaps due to relatively small study samples.

How to determine a woman's HIV infectiousness also is unclear. First, the amount of HIV genital shedding necessary to increase infectiousness is unknown. Also, questions remain about the best technique for detecting HIV in genital tract secretions.

Likewise, no consensus exists on what indicators best reflect the risk of HIV infectivity. Various researchers have measured:

- cervical shedding of HIV-1 RNA (a marker of HIV-infected cells)
- cervical shedding of HIV-1 DNA (a measure of cell-free virus and possible viral replication)
- vaginal shedding of HIV
- the presence in cervicovaginal fluid of inflammatory cells, which are thought to be associated with higher HIV loads

But the relative impact of HIV-1 DNA versus HIV-1 RNA shedding on the infectivity of a woman to her partner is uncertain. Also, the significance of vaginal versus cervical HIV shedding is unknown.

Prospective studies

The only prospective study of the direct effect of hormonal contraceptive use on genital tract shedding of HIV, conducted in 2004 among 213 HIV-infected family planning clients in Mombasa, Kenya, detected a significant but modest increase in cervical shedding of HIV-1 DNA after initiation of hormonal contraceptives. However, this increase was noted for hormonal contraceptive use overall; increases were not significant when women were divided into groups based on individual forms of hormonal contraception, including depot-medroxyprogesterone acetate (DMPA), high-dose oral contraceptive pills, low-dose oral contraceptive pills, and progestin-only contraceptive pills. This study also found that the increase in cervical shedding of HIV-1 DNA associated with hormonal contraceptive use overall was not accompanied by an increase in cervical shedding of HIV-1 RNA. Study authors offered the possible explanation that hormonal contraceptive use attracts infected cells to the genital mucosa (evidenced by increased HIV-1 DNA) but does not increase local viral replication in the mucosa (which increased HIV-1 RNA would reflect).

Another prospective study, conducted in 2005 among 967 U.S. women (654 of whom were HIV-infected), found that progestosterone-based contraceptives appeared to raise the number of cervicovaginal inflammatory cells. The presence of these cells is assumed to be associated with increased HIV-1 viral load in genital secretions, but those viral loads were not measured. Another limitation of the study was the small number of participants using progestosterone contraception: 38 HIV-infected women used DMPA and 48 used levonorgestrel implants. As a result, the analysis had little statistical power.

Expected in 2007 are preliminary results from a third prospective study, which is being conducted by FHI researchers and colleagues in Zimbabwe and Uganda. Funded by the U.S. National Institute of Child Health and Human Development, the study is examining the effect of combined oral contraceptive and DMPA use on cervical shedding of HIV-1 RNA among approximately 200 women with early HIV infection. Cervical shedding by these women will be compared with shedding by HIV-infected women not using hormonal contraception.

Another question with few answers at present is whether any association exists between an HIV-infected woman's hormonal contraceptive use and her acquisition of sexually transmitted infections that could enhance HIV shedding. Evidence to date — albeit, mostly from HIV-uninfected women — suggests a possible increased risk of acquiring chlamydial infection associated with both the use of oral contraceptives and DMPA. It is likely that chlamydial infection in women increases genital shedding of HIV.

On the other hand, some evidence suggests that if a woman does not use contraception and experiences an unintended pregnancy, pregnancy itself may promote increased HIV shedding.

Kim Best

References


Analyses consider viral set point, viral diversity

The association between hormonal contraceptive use and clinical progression of HIV has not been studied directly. But the research in Kenya showed associations between hormonal contraceptive use and two strong predictors of HIV disease progression, AIDS, and death: low CD4+ cell counts and high viral set point. CD4+ cells are immune system cells that are destroyed by HIV as the virus replicates. CD4+ count (the number of functioning CD4+ cells per liter of blood) indicates the strength of an infected person’s immune system and whether antiretroviral treatment is needed. Viral set point is the level of HIV in the blood (viral load) after the immune system’s initial response to the virus, generally three or four months after a person is infected.

In the Kenya study, researchers found that median viral set point was significantly higher among women using the injectable contraceptive depot-medroxyprogesterone acetate (DMPA) at the estimated time of HIV infection than it was among women using no hormonal contraception at that time. This difference between the two groups of women persisted during follow-up (median of 34 months). However, continuing use of DMPA did not appear to further increase viral load.

Overall, study participants’ use of oral contraceptive pills was not associated with higher viral set points. But in a subset of 156 HIV-infected sex workers (82 of whom used any hormonal contraception), use of either oral contraceptives or DMPA at the time of HIV infection was associated with acquiring genetically diverse virus populations from one partner. The women who had acquired these genetically diverse virus populations also had significantly higher viral set points and significantly lower CD4+ counts four to 24 months after infection than did those with only one strain of the virus.

The study results suggest that greater viral genetic diversity in early HIV infection could be a mechanism by which hormonal contraception affects viral load and, ultimately, disease progression, says Dr. Ludo Lavreys, former field director of the HIV research site of the University of Washington/University of Nairobi in Mombasa.

Research on the possible relationship between hormonal contraception and HIV disease progression is hampered by the same methodological challenges facing studies of hormonal contraceptive use and the risk of HIV acquisition or transmission (see articles, pages 5 and 14). One strength of the Kenya analyses is that researchers were able to estimate the dates of HIV infection with some precision because data were drawn from a larger prospective study of women who were HIV-negative at enrollment and were subsequently tested each month for HIV.

Does Hormonal Contraception Speed HIV Progression?

Does the use of hormonal contraception during the early stages of HIV infection affect disease progression? Likewise, does its use during the later stages of infection affect disease progression?

These questions cannot be answered yet. The only evidence so far that hormonal contraceptive use might affect HIV disease progression comes from a prospective study conducted among sex workers in Mombasa, Kenya. This evidence suggests that using hormonal contraception at the time of infection — before women know that they are infected — may accelerate HIV-related deterioration of the immune system and thus speed the natural course of the infection.

If other studies confirm this finding, it could provide additional incentive for hormonal contraceptive users who are at high risk of HIV infection to also use condoms consistently for HIV prevention. It could also lead to changes in recommendations for hormonal contraceptive use by women at high risk of HIV infection. To date, however, the evidence of such a risk is considered insufficient to warrant any restrictions on hormonal contraceptive use by women with HIV/AIDS or women at high risk of infection.

But findings from this research among Kenyan sex workers may not apply to other populations, and they have not been confirmed by other studies. For example, data from the large, FHI-led, prospective study of hormonal contraceptive use and HIV acquisition (see article, page 4) and a sub-study of 186 women with primary HIV infection found that hormonal contraceptive use at the time of HIV infection was not significantly associated with a higher HIV viral set point. This data was collected primarily from family planning clients in Uganda and Zimbabwe. Further research among other populations in different geographic areas is needed to clarify the...
Three women from Kampala, Uganda, prepare a meal. A study being conducted in Uganda and Zimbabwe will explore whether hormonal contraception by HIV-infected women affects disease progression.

relationship between hormonal contraceptive use and HIV disease progression.

The limited evidence from Kenya suggests that any impact hormonal contraceptive use may have on HIV disease progression occurs during the early stages of the infection. But as part of their continuing research in Kenya, scientists from the University of Nairobi, Coast Provincial General Hospital in Mombasa, and the University of Washington at Seattle plan to evaluate the relationship between hormonal contraceptive use and HIV disease progression during the later, chronic stage of HIV infection. The study in Uganda and Zimbabwe will also explore whether hormonal contraception affects disease progression over time.

Kathleen Henry Shears

References

Does Pregnancy Speed HIV Progression?

Whether pregnancy affects the course of HIV infection is an important question for HIV-infected women interested in using hormonal contraception. Such women need to weigh the potential — but still unproven — risk of accelerated progression to AIDS among hormonal contraceptive users (see article, page 15) against the risk of an unintended pregnancy resulting from reliance on a less effective contraceptive method.

Because pregnancy itself is thought to suppress immunity, concerns have been raised that pregnancy in HIV-infected women could hasten HIV-related deterioration of the immune system. But the evidence to date suggests that pregnancy does not have such an effect, at least in the short term.

Early reports of pregnancy in HIV-infected women seemed to support the hypothesis that pregnancy accelerates HIV disease progression. However, these studies involved small numbers of women and lacked control groups or the ability to adjust for other factors known to influence disease progression, such as disease stage or time of HIV exposure. A systematic review of studies published from 1983 to 1996 on pregnancy’s effect on HIV progression and survival found a weak association between HIV disease progression and pregnancy in HIV-infected women, but it concluded that the potential for study bias was too great to draw definitive conclusions.

A study published in 2000 was able to control for many potential confounding factors, including time since seroconversion (when virus can be detected in the blood), which occurs about three months after HIV infection. This study, which followed 365 HIV-infected French women — 241 of whom were pregnant — detected no increased risk of HIV progression during pregnancy. Like other prospective studies with similar findings, the French study involved mostly women who had not yet developed symptoms of HIV disease. Therefore, the possibility of increased risk of disease progression among pregnant women with more advanced HIV infection could not be ruled out.

Several studies from developing countries also suggest that pregnancy does not increase the risk of disease progression. In a study among HIV-infected women in Haiti, no statistically significant difference was observed in the rate of progression to AIDS or death between 44 pregnant women and 96 nonpregnant women. And two studies in sub-Saharan Africa — one among 823 pregnant Kenyan women and another that included 229 pregnant women in Malawi — detected no statistically significant differences in immune status between HIV-positive and HIV-negative women during pregnancy.

“Of course, more rigorous studies are needed,” says Dr. Marleen Temmerman, principal investigator of the Kenya study and professor of obstetrics and gynecology at the University of Ghent in Belgium. “But most studies in Europe, the United States, and Africa did not show an impact on disease progression, so if there is any impact at all, it will be a very minimal one.”

Kathleen Henry Shears

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Temmerman M, Nagelkerke N, Bwayo J, et al. Contraceptive methods for HIV-infected women can safely use hormonal contraceptives — including combined oral contraceptives (COCs), the injectables depot-medroxyprogesterone acetate (DMPA) and norethisterone enanthate (NET-EN), and implants such as Norplant. Yet, questions remain about the effects of hormonal contraception on a woman’s HIV infectiousness (see article, page 14) and disease progression (see article, page 15) and about the consequences of interactions between these methods and antiretroviral (ARV) drugs (see articles, pages 20 through 22).

Contraceptive Options for HIV-infected Women

Women with HIV have a right to decide whether they want to become pregnant and bear children. But if an HIV-infected woman chooses not to have children, or wants to space her family, she should be able to make informed, voluntary decisions about contraception and then receive her method of choice. Such use of contraception by HIV-infected women is an important way to reduce HIV-positive births.

HIV-infected women can use most contraceptive methods safely. While weighing the advantages and disadvantages of various methods, however, a woman living with HIV must consider the effects of each method on her own health, risk of infecting others with HIV, and response to HIV/AIDS treatment. Thus, counselors should help each HIV-infected woman assess her contraceptive needs, review all the contraceptive options available to her, and determine whether she and her partner will be able to use a particular method or combination of methods safely, correctly, and consistently.1

Hormonal methods

The World Health Organization (WHO) recommends that HIV-infected women can safely use hormonal contraceptives — including combined oral contraceptives (COCs), the injectables depot-medroxyprogesterone acetate (DMPA) and norethisterone enanthate (NET-EN), and implants such as Norplant. Yet, questions remain about the effects of hormonal contraception on a woman’s HIV infectiousness (see article, page 14) and disease progression (see article, page 15) and about the consequences of interactions between these methods and antiretroviral (ARV) drugs (see articles, pages 20 through 22).

Condoms

Male and female condoms are the only contraceptive methods that can prevent the transmission of sexually transmitted infections (STIs), including HIV. Male condoms can be 97 percent effective in preventing pregnancy if used correctly and consistently; as typically used, they are about 86 percent effective.2 Likewise, male condom use reduces HIV incidence by 80 percent to 97 percent, but only if condoms are used correctly during each act of sexual intercourse with an infected partner.3

Female condoms can be 95 percent effective for pregnancy prevention if used correctly and consistently; as typically used, they are about 79 percent effective.4 No clinical trial has assessed whether female condoms protect against HIV. But estimates based on studies of pregnancy prevention and evidence from laboratory and epidemiological studies of the female condom’s ability to protect against STI pathogens suggest that when used correctly and consistently, the device is likely to be about as effective as a male condom in reducing the risk of HIV and other STIs.5 Consistent condom use can protect an already HIV-infected woman against re-infection with another strain of HIV or from acquiring STIs such as gonorrhea and chlamydial infection. It can also reduce the risk of an HIV-infected woman transmitting the virus to an uninfected partner.6 Even when a woman is unlikely to infect others with HIV because her own infection is controlled by ARV therapy, she should be encouraged to use condoms because treatment may not completely eliminate her risk of infecting others.7

Since condoms as they are typically used are not as effective in preventing pregnancy as are many other contraceptive methods,8 HIV-infected women who do not want to become pregnant should consider using a more effective form of contraception while using condoms for STI protection. Some studies suggest that women with HIV who use more effective contraceptives, such as oral contraceptives or an intrauterine device (IUD), are less likely to use condoms consistently or at all, even with an uninfected partner.9 One U.S. study, however, found that condom use remained consistent among women using condoms and another method simultaneously for dual protection against both infection and pregnancy. Consistency of condom use was reduced only among women who alternated the two methods; for example, using a condom as a backup method after a missed pill.10

Another dual protection option — consistent use of condoms alone — is unpopular with providers because they fear its adoption would increase pregnancy rates. One way to address this concern would be to ensure access to emergency contraception as a backup method of contraception.11

IUDs

A highly effective yet reversible non-hormonal contraceptive method became more available to HIV-infected women in 2004, when WHO removed most of its previously recommended restrictions on use of the IUD by women with HIV. Those restrictions, based on theoretical concerns about increased risk of pelvic inflammatory
Sterilization

The stigma associated with HIV and fear of coming in contact with the blood of HIV-infected women have resulted in some surgeons not wanting to perform sterilizations on such women. However, sterilization offers couples a safe, highly effective, permanent method of contraception. It may be a good option for HIV-positive women and their partners who have decided to forgo or end childbearing, and it raises no particular health concerns for HIV-infected women. If a woman has an AIDS-related illness, however, female sterilization should be postponed until her condition improves. HIV-discordant couples in which the man is HIV-negative and the woman is HIV-positive may want to consider male sterilization because it does not depend on the woman’s health. Studies show a reduction in consistent condom use in couples after one partner has undergone sterilization. As with other methods, couples should be counseled about the importance of using condoms if they might be at risk of HIV infection. This advice is particularly important for discordant couples, to prevent the infected partner from transmitting the virus to the uninfected partner.

Other methods

Barrier methods other than condoms offer only modest protection against pregnancy and are generally not recommended for women with HIV. Frequent use of spermicides containing nonoxynol-9 (N-9) may increase the risk of re-infection with other strains of HIV because N-9 can disrupt the lining of the vagina, making it more vulnerable to infection. Studies have also shown that N-9 offers no protection against STIs.

Diaphragms and cervical caps are not recommended for women with HIV or AIDS and women at high risk of HIV infection because they are usually used with spermicides containing N-9. Studies are under way to determine whether diaphragms offer any protection against STIs and HIV. A protective effect is considered possible because these barrier methods may block entry of pathogens to the cervix, which is the site of infection with gonorrhea and chlamydia and may be more susceptible than the vagina is to HIV infection.

Pregnancy rates of 1 percent to 9 percent with perfect use and 25 percent with typical use are seen for fertility awareness-based methods (natural family planning). These methods require abstaining from sex or using barrier methods only during the fertile days of the menstrual cycle in order to prevent pregnancy. But protected sex throughout the menstrual cycle – even during nonfertile periods – is necessary to prevent HIV transmission to a partner. Therefore, sexually active HIV-infected women and their partners should use male or female condoms consistently throughout the woman’s menstrual cycle.

The use of breastfeeding as a temporary method of contraception (the lactational amenorrhea method) is highly effective in preventing pregnancy for up to six months postpartum in nonmenstruating women who are fully or nearly fully breastfeeding. HIV-infected women who are able to use safe breast milk alternatives to avoid transmitting the virus to their children do not benefit from lactational amenorrhea and will resume ovulating sooner than breastfeeding women. Their future contraceptive needs should be discussed during pregnancy or early in the postpartum period.

In summary, HIV-infected women face few restrictions on their use of modern contraceptive methods. Furthermore, use of effective contraception can play a key role in preventing HIV-positive births.

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HIV-infected women face few restrictions on their use of modern contraceptive methods, including oral contraception. Here, a counselor at a family planning clinic in Kathmandu, Nepal, explains oral contraceptive use to an HIV-uninfected client.
HIV Disclosure Key to Effective Contraception

HIV-infected women's fear of disclosing their serostatus to their regular partners is one of the greatest challenges to providing them with effective contraceptive counseling, says Bernard Mpairwe, senior HIV/AIDS counselor with the Uganda-Case Western Reserve University Research Collaboration at Mulago Hospital in Kampala, Uganda.

When counseling HIV-infected women, Mpairwe and other counselors at the hospital emphasize that condoms are the only contraceptive method that protects against possible transmission of HIV to partners, acquisition of new strains of HIV, and acquisition of other sexually transmitted infections (STIs). They show clients how to use condoms and help them practice negotiating condom use.

But few of the clients use condoms for protection against infection or pregnancy, says Mpairwe, who coordinated counseling at Mulago Hospital for a recent study on hormonal contraception and HIV acquisition (see article, page 4) and currently serves as counseling coordinator for a follow-on study of the effects of hormonal contraceptive use on HIV genital shedding, possible transmission of the virus to male partners, and HIV disease progression. Most study participants believe they are in steady relationships, and the few who use condoms usually do so only with partners outside those relationships. “They fear acquiring a different strain of HIV or other STIs from outside partners,” says Mpairwe. “Of course, sex with a regular partner could pose the same risks, but some women may use condoms only with outside partners because they are better able to negotiate condom use in those situations.”

Condoms have long been stigmatized as methods used primarily in commercial sex or extramarital relationships to prevent STIs. An HIV-positive woman who is not ready to disclose that she has contracted the virus may not want to suggest condom use to a partner because doing so would raise suspicions about her own serostatus. “The fear of disclosure is mainly a fear of being abandoned because the women are financially dependent on their partners,” says Mpairwe. “Their fear of losing their only social and financial support system is greater than the fear of infecting their partners, who may already be infected.”

Failure to disclose can be an obstacle to effective contraception. “We have seen that people who have disclosed find it easier to continue using their methods,” Mpairwe says. This is because they find it less difficult to persuade their partners of the need to prevent a pregnancy and to resist family and societal pressures to bear children. Many of the women in the study who have not disclosed their positive serostatus deal with these pressures by using injectable contraceptives without the knowledge of their partners, Mpairwe notes.

Given their fear of blame, abuse, or even abandonment, how can HIV-infected women be encouraged to disclose their serostatus to regular partners? “I usually advise these women to bring in partners as if they are both being tested for the first time,” Mpairwe says. “Then they can receive their results together and be counseled together.”

Kathleen Henry Shears

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6 Holmes; Gates.


15 WHO; FHI.


17 WHO.

18 FHI.


How Does HIV Therapy Affect Hormonal Contraception?

Key Points

- Certain antiretroviral (ARV) drugs reduce contraceptive hormone levels and could theoretically affect contraceptive efficacy.
- However, women on ARV therapy generally may use hormonal contraceptives.
- Drug treatments for some HIV-related opportunistic infections may interact with hormonal contraceptives.

Limited evidence suggests that certain antiretroviral (ARV) drugs can either raise or lower concentrations of contraceptive hormones in the blood of HIV-infected women using combined oral contraceptives (COCs). Theoretically, lower contraceptive hormone levels could reduce contraceptive efficacy and increase pregnancy risk, while higher levels could increase hormone-related side effects.

Unanswered questions about the effects of ARV-COC interactions have led the World Health Organization (WHO) to caution that, although women on ARV therapy generally may use oral contraceptives, medical follow-up may be appropriate.

Questions about interactions between ARV drugs and COCs center on particular ARV drugs that affect liver enzymes, causing them to speed metabolism of hormonal contraceptives and thus reduce their levels in the blood. These enzyme-inducing ARV drugs include non-nucleoside reverse transcriptase inhibitors (NNRTIs) such as nevirapine and protease inhibitors such as ritonavir.

Reductions in blood levels of contraceptive hormones due to interactions with nevirapine or ritonavir can be substantial. One study showed a 29 percent decrease in levels of ethinyl estradiol and an 18 percent decrease in levels of norethindrone in women taking nevirapine while using a COC containing these hormones. Estrogen levels were reduced by 43 percent when ethinyl estradiol was taken with ritonavir.

Whether such reduced hormone levels affect contraceptive effectiveness is unclear because no studies have looked at actual clinical outcomes. But, anticipating that reduced hormone levels might affect contraceptive effectiveness, some providers recommend prescribing COCs containing 50 micrograms of estrogen rather than the usual 30- or 35-microgram dose for women on enzyme-inducing ARV drugs. The disadvantage of such an approach is that higher doses of estrogen have been associated with an increased risk of side effects such as heart attacks, strokes, serious blood clots, or non-cancerous liver tumors. Moreover, given the proven effectiveness of the ultra-low-dose COC containing 20 micrograms of estrogen, COCs containing 30 or 35 micrograms of estrogen may still be effective even when estrogen levels are somewhat reduced. For now, WHO recommends that COC users on ARV therapy consistently use condoms for HIV prevention, noting that using a condom during each act of sexual intercourse may also compensate for any possible reduction in the effectiveness of the hormonal contraceptive.

“Given the possibility of reduced effectiveness, oral contraceptives may not be the best option for women on ARV treatment who have difficulty remembering to take their pills on time,” says Dr. Irina Yacobson, medical advisor to FHI’s field programs and main author of a recently published provider training module on contraception for women and couples with HIV (available at http://www.fhi.org/en/RH/Training/trainmat/ARVmodule.htm).

On the other hand, some ARV drugs — including the protease inhibitors atazanavir and indinavir — may increase contraceptive hormone levels in the blood. And themajor NNRTI alternative to nevirapine — efavirenz — was found to increase levels of ethinyl estradiol in unpublished studies conducted by the drug manufacturer. ARV drugs that do not appear to affect liver enzymes and are therefore not expected to change levels of contraceptive hormones include nucleoside reverse transcriptase inhibitors (NtRTIs), such as zidovudine, stavudine, and lamivudine; nucleotide reverse transcriptase inhibitors (NtRTIs), such as tenofovir; and fusion inhibitors, such as enfuvirtide. One study found no pharmacokinetic interaction between tenofovir and either deacetyl norgestimate or ethinyl estradiol.

Interactions with other hormonals

Concerns about the impact of ARV drug use on the effectiveness of hormonal contraception focus primarily on COCs. This is because they provide lower doses of hormones than do the other methods and their effectiveness depends on women’s ability to take them correctly. No data are available on interactions between ARV drugs and emergency contraception, but ARV drugs are not expected to substantially influence the efficacy of the higher-dose emergency contraceptive regimens.

Likewise, little is known about interactions between ARV drugs and other methods of hormonal contraception. Since nevirapine reduced levels of progestin in the blood by about 18 percent in a study of COC users, it could similarly reduce progestin levels in...
women using implants or injectables. Such a reduction would probably be too small to influence the efficacy of injectable contraceptives such as depot-medroxy-progestosterone acetate (DMPA) because a dose of DMPA is considered high enough to provide a wide margin of effectiveness. One study by the U.S. Adult AIDS Cooperative Trials Group (ACTG) found no significant changes in DMPA levels among 54 women using ARV regimens that included nevirapine, efavirenz, or the protease inhibitor nelfinavir compared with those in women using other ARV regimens or no ARVs. FHI and the Center for the Research and Control of Maternal-Infant Diseases of Campinas (CEMICAMP) in Campinas, Brazil, are evaluating the effects of a common ARV regimen (zidovudine, lamivudine, and efavirenz) on the pharmacokinetics of DMPA, with results expected in 2007.

The ACTG study did not assess the effects of ARV use on contraceptive hormone levels beyond the 12-week DMPA dosing period. The lack of data on DMPA levels among ARV users after 12 weeks underscores the need for women on ARV therapy to receive their DMPA injections on time.

Clinical outcomes still unknown

No studies of ARV-COC interactions have examined clinical outcomes, such as pregnancy rates or effects on ovulation. In the ACTG research, the researchers observed that suppression of ovulation was maintained in all 54 DMPA users receiving the study ARV regimens. The study was too small to detect statistically significant differences in ovulation between the study and comparison groups, but such differences are unlikely in the absence of any effect of ARV use on DMPA levels.

Finally, drug treatments for some HIV-related opportunistic infections may also interact with hormonal contraceptives. Use of oral contraceptives, contraceptive rings or patches, or implants is not recommended for women taking the antituberculosis drug rifampicin because it is likely to reduce contraceptive effectiveness. WHO advises providers to exercise careful clinical judgment, providing COCs to women on rifampicin only when no other options are available.

How Does Hormonal Contraception Affect HIV Therapy?

Unanswered questions about how contraceptive hormones interact with the immune system and with antiretroviral (ARV) drugs have raised concerns about the response to ARV therapy among HIV-infected women using hormonal contraception.

Until recently, no research had addressed these concerns. But one study, conducted among 154 HIV-infected women participating in the largest prospective study of the impact of HIV infection on U.S. women, found that hormonal contraceptive use did not reduce the effectiveness of the combinations of three or more different ARV drugs known as highly active antiretroviral therapy (HAART). Researchers compared the effects of HAART among 77 hormonal contraceptive users and 77 non-users participating in the Women’s Interagency HIV Study (WIHS). Members of the two groups were matched for age, ethnicity, and pretreatment measures of HIV disease progression (the number of CD4+ immune system cells per cubic millimeter of blood and the level of HIV in the blood).

The analysis revealed no statistically significant differences in immunologic or virologic responses to therapy between women who had been using hormonal contraceptives when they began HAART and non-users. Similar percentages of women in both groups experienced increases in CD4+ cell counts and decreases in viral load to undetectable levels. Moreover, the duration of hormonal contraceptive use before HAART initiation did not affect these positive responses to the therapy.

“The relatively low use of hormonal contraception among WIHS participants limited the statistical power of our study, and therefore our ability to detect very small effects on treatment response,” cautions Dr. Stephen Gange, an author of the study, WIHS principal investigator, and associate professor of epidemiology at Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD, USA. “We also need additional data to assess whether long-term exposure to hormonal contraceptives influences the effectiveness of ARV therapy.”

Researchers would like to know more about the impact of hormonal contraceptive use on HIV therapy.

Reference

**COC-ARV Drug Interactions**

<table>
<thead>
<tr>
<th>Non-nucleoside reverse transcriptase inhibitors (NNRTIs)</th>
<th>Effect of ARV Use on COC Blood Levels</th>
<th>Effect of COC Use on ARV Blood Levels</th>
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<tr>
<td>Atazanavir</td>
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<td>Indinavir</td>
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<td>Zidovudine, stavudine, and lamivudine</td>
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<tr>
<td>Enfurvitide</td>
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* Should not be given to women of childbearing potential unless effective contraception can be ensured.

Note: The ARV combinations recommended by the World Health Organization consist of two NsRTIs and either one NNRTI or one protease inhibitor. Each of the pharmacokinetic studies that produced these data assessed interactions between contraceptive hormones and a single ARV drug, rather than the two- or three-drug combinations taken by the vast majority of HIV-infected patients. In most cases, only one study has been conducted for each drug, and most of the studies have not been published in a peer-reviewed journal.


>{| Women on ARV therapy generally may use hormonal contraception, but possible interactions should be considered. Shown are two healthy women from South Africa, a country where ARV therapy is gradually becoming available to the approximately five and a half million HIV-infected people. |}
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16 WHO. Improving Access to Quality Care in Family Planning: Medical Eligibility Criteria for Contraceptive Use.

Dear Network readers:

FHI is proud to have had support from the U.S. Agency for International Development (USAID) for more than 25 years for our award-winning periodical, Network. Our syntheses of the latest biomedical and programmatic information on reproductive health have been used by many thousands of developing country health professionals to design, implement, and improve health training; as a knowledge resource to support research and writing; and to improve service delivery, health counseling, and policies.

We regret that, due to funding limitations, FHI will no longer be publishing Network. However, we greatly value our relationship with our readers and want to keep you in our communications network.

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Module about contraception for women with HIV

Contraception for Women and Couples with HIV, a training module from FHI and EngenderHealth, is designed to inform providers of family planning or of HIV treatment and care services about the reproductive choices and contraceptive options available to their HIV-positive clients. It summarizes the scientific evidence on contraception for clients with HIV, provides an overview of antiretroviral therapy, and discusses counseling approaches to help HIV-positive clients make informed, voluntary decisions about childbearing and contraception. The module includes PowerPoint slides, a narrative, audience handouts, and reprints of key scientific studies and other sources. Developed for use in southern and eastern Africa with funding from the U.S. Agency for International Development’s (USAID’s) Regional Economic Development Services Office for East and Southern Africa, the module is available at: http://www.fhi.org/en/RH/Training/trainmat/ethicscurr/RETCCREn/index.htm.

Training curriculum about research ethics

Research Ethics Training Curriculum for Community Representatives from FHI informs and empowers community representatives to speak or advocate for research participants worldwide. The 97-page curriculum addresses general principles of research ethics (such as informed consent and ethics committees), their importance, and the role and responsibilities of representatives in the research process. The curriculum provides easy-to-use materials, such as slides, case studies, activities, and facilitator notes, and includes an ethics training certificate from FHI’s Office of International Research Ethics. The curriculum was developed and field-tested in multiple countries, and it is available in print, online, and CD-ROM versions in English, Spanish, French, and Portuguese. To order a copy, please contact: Publications Coordinator, Family Health International, P.O. Box 13950, Research Triangle Park, NC 27709, USA. Telephone: (919) 544-7040. Fax: (919) 544-7261. E-mail: publications@fhi.org. The electronic version is available at: http://www.fhi.org/en/RH/Training/trainmat/ethicscurr/RETCCREn/index.htm.

VCT skills training curriculum

The sixth and newest element of FHI’s Voluntary Counseling and Testing ToolKit is a skills training curriculum that outlines key activities and information needed to prepare people to provide HIV voluntary counseling and testing (VCT) services. Its primary intended audience is VCT trainers at the national, district, and facility levels who are starting or expanding VCT services. The curriculum’s 28 sessions are designed to help trainee counselors understand the prevention-to-care continuum and derive maximum benefit from their practical experience. This resource consists of two parts: a Facilitator’s Guide and a separate Participant’s Manual. The guides are available only in electronic format at this time: http://www.fhi.org/en/HIVAIDS/pub/guide/vcttoolkit.htm.

STI/RTI essential practice guide

Sexually Transmitted and Other Reproductive Tract Infections: A Guide to Essential Practice is a World Health Organization publication, recently developed with the Population Council and FHI. It helps health care managers and practitioners in resource-limited settings around the world meet the needs of individuals who may be at risk of sexually transmitted infections (STIs) and other reproductive tract infections (RTIs). Intended for use in family planning, antenatal, and maternal and child health settings, the guide can be used as a reference manual and a resource to educate and to remind health care workers of the need to consider STIs/RTIs when providing other reproductive health services. Program managers can use it to improve policies, programs, and training on the prevention and management of STIs/RTIs. To order a copy, please contact: World Health Organization, Department of Reproductive Health and Research, Documentation Centre, 1211 Geneva 27, Switzerland. Telephone: 0041 22 791 4447/3346. Fax: 0041 22 791 4189. E-mail: reproductivehealth@who.int. An electronic version is available at: http://who.int/reproductive-health/pages_resources/listing_RTIs_STIs.htm.

Manuals for Christian, Muslim audiences

The manuals Teaching Adults to Communicate with Youth from a Christian Perspective and Teaching Adults to Communicate with Youth from a Muslim Perspective contain six workshops and a participant handbook designed for Christian and Muslim audiences, respectively. The manuals encourage open discussion about sexuality, reproductive health, and HIV in the context of faith communities. Those using the participant handbook practice communication skills and learn factual information taking into account religious teachings and appropriate Bible or Qur’an verses. The manuals provide a forum to clarify Christian and Muslim values about sexuality, reproductive health, and HIV, while providing accurate technical information. They are not designed to promote religion. Developed by the FHI/YouthNet program, they are available at: http://www.fhi.org/Youth/YouthNet/Publications/FLE/index.htm.