HHS Public Access

Author manuscript

Pediatrics. Author manuscript; available in PMC 2019 July 17.

Published in final edited form as:

Pediatrics. 2016 September ; 138(3): . doi:10.1542/peds.2016-1892.

Contraception for HIV-Infected Adolescents

Athena P. Kourtis, MD, PhD, MPH, FAAP, **Ayesha Mirza, MD, FAAP**, and **COMMITTEE ON PEDIATRIC AIDS**

Abstract

Access to high-quality reproductive health care is important for adolescents and young adults with HIV infection to prevent unintended pregnancies, sexually transmitted infections, and secondary transmission of HIV to partners and children. As perinatally HIV-infected children mature into adolescence and adulthood and new HIV infections among adolescentsand young adults continue to occur in the United States, medical providers taking care of such individuals often face issues related to sexual and reproductive health. Challenges including drug interactions between several hormonal methods and antiretroviral agents make decisions regarding contraceptive options more complex for these adolescents. Dual protection, defined as the use of an effective contraceptive along with condoms, should be central to ongoing discussions with HIV-infected young women and couples wishing to avoid pregnancy. Last, reproductive health discussions need to be integrated with discussions on HIV care, because a reduction in plasma HIV viral load below the

---

LEAD AUTHORS
Athena P. Kourtis, MD, PhD, MPH, FAAP
Ayesha Mirza, MD, FAAP
COMMITTEE ON PEDIATRIC AIDS, 2015–2016
Rana Chakraborty, MD, MSc, PhD, FAAP, Chairperson
Ellen Gould Chadwick, MD, FAAP
Elizabeth Montgomery Collins, MD, MPH, FAAP
Echezona Edozie Ezeanolue, MD, MPH, FAAP
Katherine Kai-Chi Hsu, MD, MPH, FAAP
Athena P. Kourtis, MD, PhD, MPH, FAAP
Ayesha Mirza, MD, FAAP
Natella Yurievna Rakhmanina, MD, PhD, FAAP
CONSULTANT
Mobeen Rathore, MD, FAAP
LIAISONS
Kenneth L. Dominguez, MD, MPH – *Centers for Disease Control and Prevention*
George Siberry, MD, MPH, FAAP – *National Institute for Child Health and Human Development*
STAFF
Anjie Emanuel, MPH

FINANCIAL DISCLOSURE: The authors have indicated they do not have a financial relationship relevant to this article to disclose.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

level of detection (an “undetectable viral load”) is essential for the individual’s health as well as for a reduction in HIV transmission to partners and children.

INTRODUCTION

The American Academy of Pediatrics (AAP) recommends that pediatricians develop a working knowledge of existing contraceptive methods for adolescents and has recently published a clinical report to address this issue.[1] Because the evidence base for contraception for HIV-infected adolescents has recently expanded, the goal of this clinical report is to provide a description and rationale for best practices in counseling and administering contraception for adolescents with HIV infection.

HIV type 1–infected adolescents represent an important subgroup within the adolescent population. The availability of combination antiretroviral therapy (cART) in the United States has led to increasing numbers of children who acquired HIV infection through mother-to-child transmission who survive into adolescence and young adulthood. In addition, there is also a growing population of horizontally HIV-infected youth. Reproductive health education for pediatric patients as well as their health care providers represents an important and unmet need in this vulnerable population. Pediatricians providing care for adolescents with HIV infection can help them make informed choices by addressing their contraceptive needs. The AAP recently published a clinical report and accompanying technical report entitled “Contraception for Adolescents.”[1] The American College of Obstetricians and Gynecologists has also issued an opinion statement acknowledging that adolescents who are HIV infected should receive sexual and reproductive health counseling and care.[2] The intent of this clinical report is to address specific considerations and guidance related to contraceptive options available for HIV-infected adolescents.

HIV-INFECTED ADOLESCENTS IN THE UNITED STATES

At the end of 2012, there were an estimated 10 832 people in the United States and 6 dependent areas (American Samoa, Guam, the Northern Mariana Islands, Puerto Rico, the Republic of Palau, and the US Virgin Islands) living with perinatally acquired HIV infection.[3] In 2010, young people aged 13 to 24 years represented 17% of the US population but accounted for an estimated 26% of all new (47 500) HIV infections.[4] This number represented the second largest percentage of new infections in 2010 (the largest group being among those aged 25–34 years [31%]).[5]

Although the majority of new HIV infections among youth occur among gay and bisexual males, female youth in the United States continue to remain vulnerable, with certain ethnic groups at higher risk than others. In 2010, black youth accounted for an estimated 57% of all new HIV infections in youth in the United States, followed by Hispanic/Latino (20%) and white (20%) youth (both male and female).[6] Available data show that a majority of individuals 15 to 24 years of age in the United States do not perceive that they are at risk of acquiring HIV infection and thus are unlikely to take measures to prevent themselves from

contracting HIV. Data also show that more than 60% of HIV-infected youth in the United States do not know that they are infected.[7]

As they age, HIV-infected adolescents are more likely to engage in sexual activity, similar to uninfected youth populations.[8] According to the 2013 Youth Risk Behavior Surveillance conducted by the Centers for Disease Control and Prevention (CDC) among students nationwide in grades 9 through 12, 48.6% of students reported ever having sexual intercourse, with 34% nationwide reporting sexual activity within the 3 months before the survey and 5.6% of students nationwide reporting having had sexual intercourse before the age of 13 years.[9] Among currently sexually active students, 13.7% reported that neither they nor their partner had used any method to prevent pregnancy during the last sexual intercourse.[9] HIV-infected youth can likewise engage in high-risk sexual behaviors, and high rates of unintended pregnancy have been documented in that group.[8, 10, 11] These statistics underscore the importance of reproductive counseling in HIV-infected youth.

Approximately 280 000 HIV-infected women and an estimated 140 000 serodiscordant couples live in the United States, many of whom desire children.[12] Data from a multisite US-based cross-sectional study indicate that there is limited discussion of preconception issues between HIV care providers and their patients.[12, 13] When such discussions do occur, the majority are initiated by patients. Other studies also support this finding.[14, 15] The routine provision of preconception care and counseling for these individuals is a critical need and represents an ongoing challenge. Available data support the fact that unintended pregnancies in this population continue to occur.[11] The estimated number of women with HIV giving birth in the United States increased from 6075 to 6422 births in 2000 to 8650 to 8900 in 2006[16] (a 30% increase). Access to medical care and discussion of fertility intentions may aid in decreasing the risk of an unplanned pregnancy in this population.[12]

REPRODUCTIVE HEALTH ISSUES SPECIFIC TO HIV-INFECTED ADOLESCENTS

Multiple demographic, psychological, sexual, medical, and relationship- based factors play a role in the reproductive decision-making of HIV-infected adolescents and young adults.[12–15] Data suggest that discussions with HIV-infected adolescents about reproductive health led by clinical care providers may not focus as much on family planning but rather on the prevention of sexually transmitted infections (STIs).[17, 18] Discussions about pregnancy prevention may have insufficient content related to pregnancy planning in youth as well as in older women.[19] These findings may reflect general discomfort among pediatric health care providers when addressing issues related to sexuality in adolescent patients and concern for potential drug interactions between certain antiretroviral drugs and hormonal contraception.

The physician-patient relationship also affects reproductive decision-making. Adolescents with chronic medical conditions are faced with many challenges as they transition from pediatric to adult care, including the loss of a long-standing physician-patient relationship.[20, 21] The medical home may represent the only stable environment some of these adolescents have ever known.[22] Once the transition in care from a pediatric to an adult provider occurs, perinatally HIV-infected adolescents, in particular, may have difficulty

expressing their medical needs, particularly those related to sexual and reproductive health. In addition, both perinatally and horizontally HIV-infected youth may experience neurocognitive deficits.[23, 24] This situation can not only make the transition more difficult but also may present ongoing challenges for both retention in care and adherence to life-saving cART. Impairment in cognitive ability and reasoning may also present a major barrier to complicated discussions about reproductive health and contraceptive counseling.

The integration of family planning services within HIV treatment, care, and prevention programs has resulted in an increase in contraceptive use.[25–27] The integration of services is an as-yet underutilized strategy that holds promise, particularly because multiple appointments with different providers pose another barrier to receiving appropriate care. Providers report systemic barriers to providing sexual and reproductive health education, such as overbooked clinics and large patient loads, which limit the length of one-on-one time with patients. In some cases, lack of adequate training on how to effectively provide sexual and reproductive health education and discuss these topics with minors presents an additional barrier.[18] The use of reproductive life planning tools, such as those available on the CDC Web site, may aid providers as they approach these topics with their adolescent patients.[28]

CONFIDENTIALITY AND CONSENT: STATE LAWS

Laws in all 50 states and the District of Columbia allow minors to consent to testing and treatment of STIs. Some states allow, but do not require, a physician to inform a minor's parents that he or she is seeking or receiving STI services when the physician deems it in the minor's best interests. Iowa is the only state that requires that parents be notified if their child tests positive for HIV infection. Laws in 26 states and the District of Columbia explicitly give minors the authority to consent to contraceptive services. Twenty states allow only certain categories of minors to consent to contraceptive services, and 4 states have no relevant policy or case law.[29, 30] Improved access to contraceptive health care with fewer restrictions to family planning reduces unplanned pregnancies and teen births. For example, states with policies that expand access to family planning services for adolescents have been associated with lower teen birth rates, at least for some teenagers.[31]

Familiarity with national and state laws regarding contraceptive treatment of minors is important to provide quality health care to adolescents. Maintaining confidentiality within the limitations permitted by law is paramount to patient trust and the likelihood that an adolescent will return for appropriate guidance and care. Confidentiality is particularly important when sexual behaviors are discussed and may be a major factor in adolescents' decisions to disclose such behaviors to their health care providers and, in turn, use appropriate health services. Because adolescents are often covered by their parents' health insurance, unintended disclosure of health services to parents may further complicate confidentiality. It is important to explain to adolescents when prescribing contraceptive agents that there is a potential for unintended disclosure to parents through health plan communications. The AAP recommends that pediatricians put sexuality education into a lifelong perspective and actively encourage parents to discuss sexuality and contraception

consistent with the family's attitudes, values, beliefs, and circumstances beginning early in the child's life.[32]

Physicians who provide care for adolescent minors have an ethical duty to promote autonomy and advocate for patients to be involved in medical decision-making that affects their care, including reproductive health. However, they also have a responsibility to recognize when the decision-making capacity of the individual minor may compromise such decisions and when decisions are not in the best interest of the patient. Recognizing that situations vary, physicians generally should encourage parental involvement and should try to correct misconceptions that the minor may have about the consequences of parental involvement. The Society for Adolescent Health and Medicine recommends that physicians promote effective communication between adolescents and their parents,[33] a position that is endorsed by the AAP and the American Medical Association.[32, 34]

METHODS OF CONTRACEPTION

Several resources provide indications and specific practice recommendations for the use of particular contraceptive options in HIV-infected females.[1, 2, 35] Detailed guidance about the use of various contraceptive methods in women with medical conditions, including HIV infection, is found in the US Medical Eligibility Criteria for Contraceptive Use.[35] Even though HIV infection alone does not preclude the use of any hormonal contraceptive method,[35] medical conditions and medications used in HIV-infected adolescents may influence contraceptive choices.

This report is based on the AAP technical report on contraception for adolescents[1] but focuses on the appropriateness and considerations of each contraceptive method for HIV-infected adolescents. As in the previous report, contraceptive methods are presented in general order of effectiveness, starting with the most effective reversible methods, the long-acting reversible contraceptive (LARC) methods (contraceptive implants and intrauterine devices [IUDs]). LARC methods usually are ideal contraceptive methods for the adolescent population, because they are user-independent options that eliminate the need for regular adherence for effectiveness. In addition, many HIV-infected adolescents are challenged by daily adherence to cART, so adding an additional medication to which they need to adhere may be undesirable. Hormonal contraceptive methods do not protect against STIs; a barrier method, such as a condom, is recommended for concurrent protection against STIs. Dual method use—the use of a condom in conjunction with a highly effective contraceptive method—should be encouraged for adolescents,[1] because the former can prevent transmission of HIV and other STIs to sexual partners. Recommending dual protection use should be a central component of reproductive health counseling for HIV-infected adolescents.

Progestin Implants

Implants are a highly effective user- and coitus-independent contraceptive method.[1] The progestin implant Nexplanon (Merck, Whitehouse Station, NJ) consists of a single rod containing etonogestrel, the active metabolite of the progestin desogestrel. Implants have a failure rate of less than 1%, a Food and Drug Administration–approved duration of action of

3 years, and very low complication rates.[36] In addition, there is evidence that the effectiveness of the implant is unchanged at 4 years of use.[37] Studies in adolescents have shown that progestin implants are more effective than shorter-acting methods in preventing unintended pregnancy,[38] primarily because they have very low adherence requirements and their typical-use effectiveness approximates perfect-use effectiveness. Changes in menstrual bleeding patterns are the most common side effect and the principal reason for method discontinuation.[39] Data are scant on the effect of progestin implants on bone mineral density.[40, 41]

The efficacy of progestin implants may be impaired by hepatic enzyme–inducing drugs that act on the cytochrome P450 pathway. Implants, in particular, are potentially more vulnerable to the effect of these inducers than other progestin methods, such as injectable contraceptives, because hormonal levels are closer to the lowest therapeutic blood concentration needed for contraceptive efficacy. Emerging evidence indicates reduced levonorgestrel concentrations in women who use levonorgestrel implants and receive efavirenz-containing antiretroviral therapy; contraceptive failures have been described in such women.[42–47] It should be noted that levonorgestrel implants are not available in the United States but are available in several other parts of the world. Several case reports and a pharmacokinetics study also suggest that efavirenz[48] may decrease the efficacy of etonogestrel implants (eg, Nexplanon), although additional data are needed.[47, 49] Failure of the etonogestrel implant was reported in 2 patients receiving efavirenz-based therapy.[50] Prospectively collected data are not yet available to accurately quantify the interaction of efavirenz with progestin implants, to note the time of contraceptive failure, and to comparatively evaluate against other contraceptive options for HIV-infected women. Data on adolescents specifically are not available. Initial concerns about a possible pharmacokinetic interaction of levonorgestrel with nevirapine have not been confirmed by subsequent studies.[45] The National Institutes of Health (NIH) guidance is to use an alternative or additional contraceptive method when efavirenz, nevirapine, or most protease inhibitors (PIs) are administered to HIV-infected individuals.[51, 52] The CDC and the World Health Organization (WHO) state that the benefits of using progestin implants outweigh any risks with concomitant administration of an antiretroviral agent in HIV-infected women.[35, 53]

Intrauterine Devices

IUDs are another type of LARC. Four IUDs currently are approved in the United States: a copper-containing IUD (copper T380-A; ParaGard; Teva North America, North Wales, PA) and 3 levonorgestrel-releasing IUDs (52 mg levonorgestrel; Mirena; Berlax, Montville, NJ; 52 mg levonorgestrel; Liletta; Actavis, San Francisco, CA; and 13.5 mg levonorgestrel; Skyla; Bayer HealthCare Pharmaceuticals, Wayne, NJ). They are appropriate for adolescents and are generally safe and effective methods of contraception with a failure rate of less than 1%.[54, 55] The 13.5-mg

levonorgestrel IUD is approved for 3 years,[56] and the 52-mg levonorgestrel IUD, depending on formulation, is approved for 3 years (Liletta) or 5 years (Mirena), although data for Mirena suggest that it remains effective for up to 7 years.[57] The copper IUD is approved for 10 years, but data support its use for 12 years.[58] Women will continue to have regular

menstrual cycles with the copper IUD; however, these cycles may be heavier with more cramping initially. With the levonorgestrel IUD, menses will become more irregular; however, overall bleeding will be less, with many women experiencing amenorrhea. Individuals with painful menses may have significant improvement of their symptoms with the levonorgestrel IUD.[54]

Despite earlier concerns, IUDs are now considered safe for nulliparous adolescents,[1] because they do not cause tubal infertility in nulliparous women.[35, 59] There is a small risk of pelvic infection after insertion, but this increased risk does not extend beyond the first 21 days after insertion.[60, 61] Although an ongoing active STI or other pelvic infection is a contraindication to IUD placement, an IUD may be inserted in an asymptomatic adolescent at high risk of an STI with screening on the day of insertion. The treatment of any new STI can be subsequently provided without IUD removal.[1, 62] A recent systematic review found an overall low incidence of pelvic inflammatory disease among women with HIV who use IUDs and no differences in infectious complications when comparing IUD complication rates by HIV disease stage; however, the evidence was limited and of fair to poor quality.[63]

HIV infection is not a contraindication to IUD use. The use of an IUD in the context of HIV infection is classified according to CDC US medical eligibility criteria for contraceptive use as category 2, meaning that HIV is a condition for which the advantages of using the IUD generally outweigh theoretical or proven risks.[1, 35] However, the use of an IUD by an individual with advanced HIV disease is classified as category 3, meaning that risks generally outweigh benefits, including the theoretical risk of infection with IUD insertion. Therefore, such women should use an alternative contraceptive method other than an IUD until their immunologic and clinical status improves with cART. For women with an IUD already in place who progress to advanced HIV disease, the IUD can remain in place. However, these women may be at increased risk of pelvic infection.[35, 53]

IUD use did not adversely affect HIV disease progression when compared with hormonal contraceptive use and was not associated with increased risk of HIV transmission to partners.[35] Several small studies have found that levonorgestrel IUDs were not associated with increased genital shedding of HIV.[64, 65] Limited data also suggest that the efficacy of the levonorgestrel IUD is unlikely to be affected by antiretroviral therapy.[64, 66] Furthermore, evidence suggests that there is no higher risk of overall or infectious complications in HIV-infected compared with uninfected women.[65, 67, 68]

Progestin-Only Injectable Contraception

Depot medroxyprogesterone acetate (DMPA), known by the brand name Depo-Provera (Pfizer, New York, NY), is progestin given as a single injection approximately every 13 weeks (up to 15 weeks) with the use of a dose of either 150 mg delivered intramuscularly or 104 mg delivered subcutaneously.[1] This contraceptive method is highly effective at preventing pregnancy, with a 1-year probability of pregnancy of approximately 6% for typical use and 0.2% with perfect use.[1] Similar to the LARC methods, DMPA can be administered to those with contraindications to estrogens and is convenient for many adolescents; however, it requires injections approximately every 13 weeks. Its main side

effects are weight gain, a delayed return to fertility, menstrual bleeding irregularities, and bone mineral loss, which is largely reversible after DMPA discontinuation.[1, 69, 70]

Patients receiving DMPA injections should be counseled about age-appropriate recommendations for supplementation with calcium and vitamin D and regular weight-bearing exercise as well as avoidance of smoking and alcohol to maintain skeletal health.[1] Some providers obtain dual-energy radiograph absorptiometry scans in adolescent patients at baseline when they begin DMPA injections. However, there is no evidence to recommend this practice; moreover, initial bone mineral density losses stabilize by 5 years, with return to pre-use levels on discontinuation of progestin injections.[55] Given the uncertainty surrounding the interaction between progestin-only injectables (particularly DMPA) and the risk of HIV transmission to male partners,[35, 53, 67, 71] as will be discussed later, women with HIV infection need to be informed that progestin-only injectables may or may not increase their risk of HIV transmission to partners. There is insufficient evidence to confirm any risk of disease progression[72]; however, further research is warranted. Women and couples at high risk of HIV who are considering progestin-only injectables should also be informed about and have access to HIV-preventive measures, including male and female condoms.[53] Levels of DMPA do not appear to be reduced by the use of antiretroviral agents (including efavirenz, zidovudine, lamivudine, nevirapine, and nelfinavir)[73–75]; indeed, this agent is largely free of antiretroviral interactions and can be administered with all classes of antiretroviral agents. Although both HIV disease and the antiretroviral agen tenofovir disoproxil fumarate can cause decreases in bone mineral density,[76] the effects of concomitant use of DMPA and tenofovir disoproxil fumarate on adolescent bone health are not known.

Combined Oral Contraceptives

Combined oral contraceptives (COCs) contain an estrogen and a progestin and are available by prescription. They are the most commonly used method of hormonal contraception among adolescents in the United States[1] and are the prototype of other combined methods of birth control, such as the vaginal ring and transdermal patch, which have similar efficacy and clinical profiles. In almost every pill, the estrogen component is ethinyl estradiol in varying amounts, with the “low dose” pill (30–35 μg) being the first line for adolescents.[1] Their typical- use failure rates are 9% in adults and may be higher in adolescents,[1, 77] because they depend on user adherence. Approaches to increase adherence include support from a family member, friend, or partner or cell phone alarms[1] and should include instructions if 1 or more pills are missed. As with all estrogen-containing contraceptive methods, COCs have some contraindications[1, 35]; however, most of these are uncommon in the adolescent. Interactions with several classes of medications, including some antiretroviral agents,[1, 35, 51, 52] are one of the main factors limiting the use of COCs in HIV-infected women. Such interactions lead mainly to a decrease in contraceptive hormonal levels, potentially leading to decreased contraceptive effectiveness, and will be summarized in a later section. A decrease in contraceptive effectiveness of COCs is observed particularly with concurrent administration of a ritonavir-boosted PI; an alternative or additional contraceptive method should be considered when any boosted PI regimen is used. Because nevirapine and efavirenz induce the metabolism of COCs and reduce hormonal levels, an alternative or additional

contraceptive method should also be considered in women who are taking these antiretroviral agents; however, other nonnucleoside reverse transcriptase inhibitors (NNRTIs), such as etravirine and rilpivirine, do not seem to cause the same reduction.[38] COCs do not have any significant interactions with nucleoside reverse transcriptase inhibitors, integrase inhibitors such as raltegravir and dolutegravir, entry inhibitors such as maraviroc, or fusion inhibitors such as enfuvirtide. Preliminary data suggest that elvitegravir/cobicistat may alter hormonal concentrations; the clinical significance of this finding is not fully known, but COCs with greater than 30μg ethinyl estradiol or alternative contraceptives may need to be considered.[51]

Most of the available evidence has found no statistically significant association between the use of COCs and HIV acquisition, HIV transmission to partners, or HIV disease progression; however, the quality of the available evidence is generally considered low.[53, 72, 78, 79]

Contraceptive Vaginal Ring, Transdermal Contraceptive Patch

These methods have efficacy, benefits, side effects, and drug interactions comparable to other combined hormonal methods but represent simpler regimens. Despite the simplified regimen afforded by these methods (weekly for the patch and monthly for the vaginal ring), studies suggest variable rates of acceptability and low long-term continuation rates among adolescents.[78, 80, 81] For HIV-infected adolescents, drug interaction considerations are similar to those of COCs mentioned previously.[35, 52] As with other hormonal methods, a condom should always be used concurrently for STI/HIV protection.

Progestin-Only Pills

Progestin-only pills are not typically recommended as a first-choice method in adolescents, because they require particular timing of pill administration relative to coitus.[1] In addition, they are less effective than other progestin-only methods, including the progestin-containing IUD, implant, and injectables.[1] There is currently no available information regarding the risk of HIV acquisition or transmission to partners with the use of progestin-only pills. On the basis of limited data, progestin levels with progestin-only pills do not appear to be reduced by some PIs,[82] but contraceptive efficacy data are not available. Data on hormonal levels when progestin-only pills are used with other antiretroviral agents, such as efavirenz or nevirapine, are not available.[47] Recommendations for use with antiretroviral drugs are generally the same as those for COCs discussed previously.[35, 51]

Male Condoms

Male condoms are the preferred method of barrier contraception because of their demonstrated ability to decrease the transmission of STIs, including HIV.[1, 79] In addition, they are the most common contraceptive method used by adolescents.[83] They need to be used correctly and consistently with each act of sexual intercourse; therefore, their typical-use failure rate is 18% for all users and can be higher among adolescents, in contrast to a perfect-use failure rate of 2%.[84] Latex condoms should only be used with water-based lubricants[85]; natural membrane condoms do not provide adequate STI protection.[79] The high typical-use failure rate for pregnancy prevention, but added protection from STIs, has led to

the recommendation for dual contraception with a condom plus a highly effective hormonal or other long-acting contraceptive method.[79] More information on condoms can be found in the AAP policy statement on condom use by adolescents.[79] HIV-infected adolescents should always use a condom to prevent HIV transmission to partners.

Emergency Contraception

Several products are available for emergency contraception in the United States, including a progestin-only dedicated emergency contraception product (levonorgestrel-based pill), high-dose combined estrogen-progestin pills, ulipristal acetate (a progesterone receptor modulator), and the copper IUD.[1] All of these methods can prevent pregnancy when initiated up to 5 days after an act of unprotected sexual intercourse but are more effective the earlier they are used. More information on emergency contraception can be found in the AAP policy statement on emergency contraception.[86] Plan B One-Step (levonorgestrel) is approved by the Food and Drug Administration as a nonprescription product for all women of childbearing potential,[87] and generic versions are approved as nonprescription products for adolescent females and women aged ≥17 years, even though proof of age is not required for purchase.[1] Counseling and advance provision of emergency contraception should be a part of anticipatory guidance for adolescents.[1] Recommendations are not different for HIV-infected adolescents; however, drug interactions with antiretroviral agents may need to be considered. Limited evidence suggests that levonorgestrel levels are significantly reduced among women using levonorgestrel emergency contraception who are receiving efavirenz, but no efficacy data are available.[44] Data for interactions of other types of emergency contraception and other antiretroviral agents are not available.[47] However, ulipristal acetate is predominantly metabolized by CYP3A4, so interactions can be expected.[51, 52] The efficacy of the copper IUD is not affected by antiretroviral agents.

Spermicides, Diaphragm, Cervical Cap

HIV infection is a contraindication to the use of spermicides, because there is an increased risk of genital lesions and resulting viral shedding and transmission of HIV associated with nonoxynol-9.[35, 88] Diaphragms and cervical caps are contraindicated in HIV-infected individuals for similar reasons, mainly because of concerns about the spermicide.[89]

Fertility Awareness and Other Periodic Abstinence Methods

Although strict abstinence is obviously an effective means of birth control, it is not a realistic option for adolescents after their sexual debut. Fertility awareness and other periodic abstinence methods are not recommended for adolescents, because they have high failure rates.[1] A condom should always be used by HIV-infected adolescents to prevent the transmission of HIV infection to partners.

Withdrawal

This method has a high contraceptive failure rate,[1] and it provides no STI/HIV protection; therefore, it is not recommended as a contraceptive method.

HORMONAL CONTRACEPTION AND HIV RISK

Concerns have been raised about the effects of hormonal contraception on the risk of HIV acquisition, the risk of HIV transmission from female to male partners, and HIV disease progression. Some observational studies have documented an increased risk of HIV acquisition, transmission, and disease progression associated with changes in the genital tract during contraceptive use.[90–94] Most relevant to this clinical report are the possible associations of hormonal contraception with the risk of HIV transmission to partners and with HIV disease progression. A secondary analysis from 2 longitudinal studies of HIV incidence that followed serodiscordant couples in Africa reported that DMPA use increased the risk of HIV transmission from infected women to their male partners.[95] Among serodiscordant couples in which the HIV-negative partner was male, the rates of HIV transmission were 2.61 per 100 person-years when women used hormonal contraception and 1.51 per 100 person-years when women did not use hormonal contraception ($P = .02$). This study was subject to confounding, because it was not designed to examine HIV risk with hormonal contraception and only a small proportion of women used hormonal contraceptives (11% of total person-years of follow-up).

In addition, these women were not receiving antiretroviral therapy. Indirect evidence on the risk of HIV transmission from female to male partners from 11 studies that assessed genital HIV shedding is mixed.[96] Studies have reported an association between hormonal contraceptive use and increased frequency of shedding of HIV DNA, but not RNA, in the genital tract,[94, 97–99] although this finding has not been consistently documented in all studies.[93, 96] Most studies were cross- sectional, had small sample sizes, and evaluated different markers of transmissibility (HIV DNA versus RNA). Their results are thus difficult to compare or generalize.

Evidence on the effects of hormonal contraception on HIV disease progression was reviewed.[72] Ten cohort studies consistently found no association with hormonal contraceptive use and HIV disease progression compared with nonuse of hormonal contraceptives. One randomized controlled trial found that hormonal contraceptive use was associated with an increased risk of HIV disease progression compared with copper IUD use, but this study had important methodologic shortcomings.[72] Thus, the preponderance of evidence suggests that HIV-infected women can use hormonal contraceptive methods without concerns for HIV disease progression.[72]

A recent WHO[100] consultation concluded that there was, as yet, insufficient evidence to support a change in current guidelines on the use of hormonal contraceptives for women living with HIV or those at high risk of HIV infection.[100] The CDC supports this guidance and has added clarification that strongly encourages condom use and other measures to prevent HIV infection for at-risk women.[35] The WHO encouraged further investigation of the relationship of hormonal contraception and HIV risk. Because most of the available information on HIV risk derives from studies on women who used DMPA or COCs, very limited or no information is currently available on HIV risk related to other hormonal methods, such as progestin implants or progestin-releasing IUDs.

INTERACTIONS OF HORMONAL CONTRACEPTION AND ANTIRETROVIRAL DRUGS

Hormonal contraceptives are primarily metabolized in the liver by the cytochrome P450 system. Antiretroviral agents have varying effects on this metabolic pathway; this is the main biological reason for the interaction between the 2 drug categories, although other metabolic pathways are sometimes involved. Special consideration is necessary for women who use some hormonal methods (ie, combined hormonal contraceptive methods, progestin-only pills, emergency contraceptive pills, or etonogestrel implants) with certain antiretroviral regimens (particularly those containing efavirenz and ritonavir- boosted PIs).[53] In addition, because efavirenz use may be associated with neural tube defects after early fetal exposure, women receiving efavirenz should avoid becoming pregnant, and treatment with efavirenz should be avoided during the first 8 weeks of pregnancy whenever possible.[51]

Data on drug interactions between antiretroviral therapy and hormonal contraceptives come primarily from drug-label pharmacokinetics and limited clinical studies, and the clinical implications of observed alterations in hormonal or antiretroviral levels are not always known. In addition, the magnitude of change in drug levels that may reduce contraceptive efficacy or increase adverse effects is not completely known; therefore, the quality of evidence is deemed low.[35, 100] Up-to-date information regarding drug interactions with antiretroviral agents can be found within the regularly updated CDC, WHO, and NIH guidelines[35, 51–53] Because definitive, high-quality studies on pregnancy rates among women taking hormonal contraceptives and receiving antiretroviral therapy do not exist, dosing recommendations are based on expert opinion.[51] The recommendations referred to in this clinical report are based on the consensus of the NIH expert panel[51] and may be slightly different from those of other sources, including the CDC and the WHO.

A summary of the available evidence on interactions with hormonal contraceptives by antiretroviral class is presented in Table 1. Interactions with hormonal contraceptives may differ among individual antiretroviral agents in each class. In general, nucleoside reverse transcriptase inhibitors and entry inhibitors do not appear to have significant interactions with hormonal contraceptive methods.[51, 53, 101] With regard to NNRTIs, 3 clinical studies, including 1 large study, found that the use of nevirapine-containing cART did not increase ovulation or pregnancy rates in women taking COCs.[102–105] For efavirenz-containing cART, a pharmacokinetic study showed consistently significant decreases in contraceptive hormone levels in women taking COCs, and a small clinical study showed higher ovulation rates in women taking efavirenz-containing cART and COCs.[44, 102, 106] The newer NNRTIs, etravirine and rilpivirine, do not interact with COCs.[101, 107] On the basis of primarily pharmacokinetic data, the efficacy of DMPA is likely not affected by NNRTIs. Efavirenz, but likely not nevirapine, decreases levonorgestrel levels and may decrease contraceptive efficacy in women using levonorgestrel implants[45] or levonorgestrel for emergency contraception[52]; data on interactions of efavirenz with etonogestrel implants are even more scarce.

As mentioned earlier, pharmacokinetic data suggest decreases in COC hormone levels with ritonavir-boosted PIs. For women using ritonavir-boosted PIs who are taking combination

hormonal contraceptives (COC pills, patches, or rings) or progestin-only pills, the use of an alternative or additional method of contraception is recommended.[35, 51, 52] Atazanavir increases ethinyl estradiol concentrations by 50% or more, so with unboosted atazanavir, COCs with concentrations of ethinyl estradiol less than 30μg are needed.[35, 51, 52] On the basis of primarily pharmacokinetic data, the effectiveness of DMPA is likely not affected by PIs.[53] The concomitant use of hormonal contraceptives and preexposure prophylaxis regimens has been evaluated in only a few studies; preexposure prophylaxis was shown to be efficacious in women using DMPA and in their partners.[108] Similarly, concomitant oral tenofovir/emtricitabine use was not associated with changes in plasma levonorgestrel concentrations among women using a levonorgestrel implant in the first year of use.[109]

The efficacy of cART does not appear to be affected by the use of hormonal contraceptive methods on the basis of limited clinical data.[66, 110–114] Very few data are available on whether hormonal contraceptive methods and cART taken together lead to worsening of side effects of contraceptives or increased antiretroviral toxicity. Pharmacokinetic data suggest that COCs, DMPA, and progestin implants are unlikely to have an effect on cART toxicity.[90] Complete information on all contraceptive methods and possible interactions with antiretroviral agents can be found in the CDC-issued Medical Eligibility Criteria for Contraceptive Use[35] and the regularly updated NIH guidance.[51]

CONCLUSIONS

The use of effective contraception is necessary in sexually active HIV-infected adolescents, because it prevents unintended pregnancy, promotes family planning, and prevents mother-to-child transmission of HIV. The promotion of these methods, in conjunction with education regarding dual protection use, is important. However, several of the antiretroviral drugs used in currently recommended regimens for adults and adolescents in the United States[52] have interactions with some hormonal contraceptives, which may limit their efficacy. The evidence on pharmacologic interactions and their clinical significance is still emerging. Interactions of LARCs with antiretroviral agents are particularly important to determine, because LARCs are the most effective contraceptive methods. The effect of hormonal contraceptives on local cervicovaginal concentrations of antiretroviral drugs administered topically or systemically will also need to be studied.[110] There is a need for the development of long-acting, safe, multipurpose prevention technologies that address multiple sexual and reproductive health needs of adolescents and young adults as well as decreased user adherence requirements.[115] Such proof-of-concept technologies might include genitally applied products that can afford antiviral and contraceptive activity and have longer duration of action.[110]

Comprehensive reproductive health counseling and care is an important aspect of care for HIV-infected adolescent females. This care includes the capacity to provide appropriate contraceptive guidance, delivery, and monitoring. Encouraging abstinence,[116] delay of sexual initiation, correct and consistent condom use, and adherence to the antiretroviral regimen are important strategies to improve adolescents' health, prevent unintended pregnancies, and prevent HIV transmission to partners. Clinics and physician practices providing primary care for HIV-infected female adolescents need to include comprehensive

reproductive health counseling and care and have the capability to provide appropriate contraceptive guidance, delivery, and monitoring. Addressing adolescent reproductive health issues in the medical home and during routine visits, where family planning services are integrated into care, along with antiretroviral therapy adherence and risk-reduction counseling, may be one of the best ways to address the sexual and reproductive health needs of HIV-infected adolescents.

ACKNOWLEDGMENT

We thank Dr Lisa Haddad for her helpful comments on the manuscript.

ABBREVIATIONS

AAP	American Academy of Pediatrics
cART	combination antiretroviral therapy
CDC	Centers for Disease Control and Prevention
COC	combined oral contraceptive
DMPA	depot medroxyprogester-one acetate
IUD	intrauterine device
LARC	long-acting reversible contraceptive
NIH	National Institutes of Health
NNRTI	nonnucleoside reverse transcriptase inhibitor
PI	protease inhibitor
STI	sexually transmitted infection
WHO	World Health Organization

REFERENCES

1. Ott MA, Sucato GS; Committee on Adolescence. Contraception for adolescents. Pediatrics. 2014;134(4). Available at: www.pediatrics.org/cgi/content/full/134/4/he1257
2. American College of Obstetricians and Gynecologists; Women's Health Care Physicians. Committee Opinion No. 572: reproductive health care for adolescents with human immunodeficiency virus. Obstet Gynecol. 2013;122(3):721–726 [PubMed: 23963424]
3. Centers for Disease Control and Prevention. HIV Surveillance Report. 2 2015 Available at: www.cdc.gov/hiv/library/reports/surveillance/ Accessed January 4, 2016
4. Centers for Disease Control and Prevention. Estimated HIV incidence in the United States, 2007–2010. HIV Surveillance Supplemental Report. 2012;17(4). Available at: www.cdc.gov/hiv/pdf/statistics_hssr_vol_17_no_4.pdf. Accessed January 4, 2016
5. Centers for Disease Control and Prevention. New HIV infections in the United States. Available at: www.cdc.gov/nchhstp/newsroom//docs/2012/HIV-Infections-2007-2010.pdf. Accessed January 4, 2016
6. Centers for Disease Control and Prevention. HIV among Youth. Available at: www.cdc.gov/hiv/risk/age/youth/index.html?s_cid= tw_std0141316. Accessed January 4, 2016

7. Centers for Disease Control and Prevention. Vital signs: HIV infection, testing, and risk behaviors among youths—United States. MMWR Morb Mortal Wkly Rep. 2012;61(47):971–976 [PubMed: 23190571]
8. Mellins CA, Tassiopoulos K, Malee K, et al.; Pediatric HIV/AIDS Cohort Study. Behavioral health risks in perinatally HIV-exposed youth: co-occurrence of sexual and drug use behavior, mental health problems, and nonadherence to antiretroviral treatment. AIDS Patient Care STDS. 2011;25(7):413–422 [PubMed: 21992620]
9. Kann L, Kinchen S, Shanklin SL, et al.; Centers for Disease Control and Prevention. Youth risk behavior surveillance—United States, 2013. MMWR Suppl. 2014;63(4):1–168. Available at: www.cdc.gov/mmwr/pdf/ss/ss6304.pdf. Accessed January 4, 2016
10. Elkington KS, Bauermeister JA, Santamaria EK, Dolezal C, Mellins CA. Substance use and the development of sexual risk behaviors in youth perinatally exposed to HIV. J Pediatr Psychol. 2015;40(4):442–454 [PubMed: 25476800]
11. Sutton MY, Patel R, Frazier EL. Unplanned pregnancies among HIV-infected women in care-United States. J Acquir Immune Defic Syndr. 2014;65(3):350–358 [PubMed: 24189153]
12. Rahangdale L, Stewart A, Stewart RD, et al.; HOPES (HIV and OB Pregnancy Education Study). Pregnancy intentions among women living with HIV in the United States. J Acquir Immune Defic Syndr. 2014;65(3):306–311 [PubMed: 24525467]
13. Centers for Disease Control and Prevention. HIV among pregnant women, infants, and children. Available at: www.cdc.gov/hiv/risk/gender/pregnantwomen/facts/index.html. Accessed January 4, 2016
14. Finocchario-Kessler S, Bastos FI, Malta M, et al.; Rio Collaborative Group. Discussing childbearing with HIV-infected women of reproductive age in clinical care: a comparison of Brazil and the US. AIDS Behav. 2012;16(1):99–107 [PubMed: 21359541]
15. Steiner RJ, Finocchario-Kessler S, Dariotis JK. Engaging HIV care providers in conversations with their reproductive-age patients about fertility desires and intentions: a historical review of the HIV epidemic in the United States. Am J Public Health. 2013;103(8):1357–1366 [PubMed: 23763424]
16. Whitmore SK, Zhang X, Taylor AW, Blair JM. Estimated number of infants born to HIV-infected women in the United States and five dependent areas, 2006. J Acquir Immune Defic Syndr. 2011;57(3):218–222 [PubMed: 21372725]
17. Fair C, Wiener L, Zadeh S, et al. Reproductive health decision-making in perinatally HIV-infected adolescents and young adults. Matern Child Health J. 2013;17(5):797–808 [PubMed: 22736033]
18. Albright JN, Fair CD. Providers caring for adolescents with perinatally- acquired HIV: current practices and barriers to communication about sexual and reproductive health. AIDS Patient Care STDS. 2014;28(11):587–593 [PubMed: 25290765]
19. Finocchario-Kessler S, Dariotis JK, Sweat MD, et al. Do HIV-infected women want to discuss reproductive plans with providers, and are those conversations occurring? AIDS Patient Care STDS. 2010;24(5):317–323 [PubMed: 20482467]
20. Committee on Pediatric Aids. Transitioning HIV-infected youth into adult health care. Pediatrics. 2013;132(1):192–197 [PubMed: 23796739]
21. Cooley WC, Sagerman PJ; American Academy of Pediatrics; American Academy of Family Physicians; American College of Physicians; Transitions Clinical Report Authoring Group. Supporting the health care transition from adolescence to adulthood in the medical home. Pediatrics. 2011;128(1):182–200 [PubMed: 21708806]
22. Fair CD, Sullivan K, Dizney R, Stackpole A. “It’s like losing a part of my family”: transition expectations of adolescents living with perinatally acquired HIV and their guardians. AIDS Patient Care STDS. 2012;26(7):423–429 [PubMed: 22686235]
23. Nichols SL, Bethel J, Garvie PA, et al. Neurocognitive functioning in antiretroviral therapy-naïve youth with behaviorally acquired human immunodeficiency virus. J Adolesc Health. 2013;53(6): 763–771 [PubMed: 23972941]
24. Mellins CA, Malee KM. Understanding the mental health of youth living with perinatal HIV infection: lessons learned and current challenges. J Int AIDS Soc. 2013;16:18593 [PubMed: 23782478]

25. Baumgartner JN, Green M, Weaver MA, et al. Integrating family planning services into HIV care and treatment clinics in Tanzania: evaluation of a facilitated referral model. Health Policy Plan. 2014;29(5):570–579 [PubMed: 23894070]
26. Berer M HIV/AIDS, sexual and reproductive health: intersections and implications for national programmes. Health Policy Plan. 2004;19(suppl 1):i62–i70 [PubMed: 15452016]
27. Tao AR, Onono M, Baum S, et al. Providers' perspectives on male involvement in family planning in the context of a cluster-randomized controlled trial evaluating integrating family planning into HIV care in Nyanza Province, Kenya. AIDS Care. 2015;27(1):31–37 [PubMed: 25329436]
28. Centers for Disease Control and Prevention. Preconception health and health care: my reproductive life plan. Available at: www.cdc.gov/preconception/documents/reproductivelifeplan-worksheet.pdf. Accessed January 4, 2016
29. Guttmacher Institute. State policies in brief: an overview of Minors' Consent Law. Available at: www.guttmacher.org/statecenter/spibs/spib_OMCL.pdf. Accessed January 4, 2016
30. Guttmacher Institute. State policies in brief: minors' access to STI services. Available at: www.guttmacher.org/statecenter/spibs/spib_MASS.pdf. Accessed January 4, 2016
31. Beltz MA, Sacks VH, Moore KA, Terzian M. State policy and teen childbearing:a review of research studies. J Adolesc Health. 2015;56(2):130–138 [PubMed: 25620298]
32. Committee on Adolescent Health; Committee on Psychosocial Aspects of Child and Family Health. Sexuality education for children and adolescents. Pediatrics. 2001;108(2):498–502. Reaffirmed October 2004 [PubMed: 11483825]
33. Ford C, English A, Sigman G. Confidential health care for adolescents: position paper for the Society for Adolescent Medicine. J Adolesc Health. 2004;35(2):160–167 [PubMed: 15298005]
34. American Medical Association. The AMA code of medical ethics' opinion on confidential services for children and adolescents. AMA J Ethics. 2012;14:778–779. Available at: http://journalofethics.ama-assn.org/2012/10/coet1-1210.html. Accessed January 4, 2016
35. Centers for Disease Control and Prevention. U S. medical eligibility criteria for contraceptive use, 2010. MMWR Recomm Rep. 2010;59(RR-4):1–86
36. Raymond GE. Contraceptive implants In: Hatcher RA, Trussell J, Nelson AL, Cates W Jr, Kowal D, Policar MS, eds. Contraceptive Technology. 20th revised ed Atlanta, GA: Ardent Media, Inc; 2011:193–203
37. McNicholas C, Maddipati R, Zhao Q, Swor E, Peipert JF. Useof the etonogestrel implant and levonorgestrel intrauterine device beyond the U.S. Food and Drug Administration-approved duration. Obstet Gynecol. 2015;125(3):599–604 [PubMed: 25730221]
38. Lewis LN, Doherty DA, Hickey M, Skinner SR. Implanon as a contraceptive choice for teenage mothers: a comparison of contraceptive choices, acceptability and repeat pregnancy. Contraception. 2010;81(5):421–426 [PubMed: 20399949]
39. Darney P, Patel A, Rosen K, Shapiro LS, Kaunitz AM. Safety and efficacy of a single-rod etonogestrel implant (Implanon): results from 11 international clinical trials. Fertil Steril. 2009;91(5):1646–1653 [PubMed: 18423453]
40. Beerthuizen R, van Beek A, Massai R, Mäkäräinen L, Hout J, Bennink HC. Bone mineral density during long-term use of the progestagen contraceptive implant Implanon compared to a non-hormonal method of contraception. Hum Reprod. 2000;15(1):118–122 [PubMed: 10611199]
41. Pongsatha S, Ekmahachai M, Suntornlimsiri N, Morakote N, Chaovisitsaree S. Bone mineral density in women using the subdermal contraceptive implant Implanon for at least 2 years. Int J Gynaecol Obstet. 2010;109(3):223–225 [PubMed: 20206353]
42. Perry SH, Swamy P, Preidis GA, Mwanyumba A, Motsa N, Sarero HN. Implementing the Jadelle implant for women living with HIV in a resource- limited setting: concerns for drug interactions leading to unintended pregnancies. AIDS. 2014;28(5):791–793 [PubMed: 24401645]
43. Tseng A, Hills-Nieminen C. Drug interactions between antiretrovirals and hormonal contraceptives. Expert Opin Drug Metab Toxicol. 2013;9(5):559–572 [PubMed: 23425052]
44. Carten ML, Kiser JJ, Kwara A, Mawhinney S, Cu-Uvin S.Pharmacokinetic interactions between the hormonal emergency contraception, levonorgestrel (Plan B), and efavirenz. Infect Dis Obstet Gynecol. 2012;2012:137192 [PubMed: 22536010]

45. Scarsi K, Lamorde M, Darin K, et al. Efavirenz- but not nevirapine-based antiretroviral therapy decreases exposure to the levonorgestrel released from a sub-dermal contraceptive implant. J Int AIDS Soc. 2014;17(4 suppl 3):19484 [PubMed: 25393993]
46. Scarsi KNS, Byakika-Kibwika P. Levonorgestrel implant + EFV-based ART: unintended pregnancies and associated PK data. In: A report from the Conference on Retroviruses and Opportunistic Infections; February 23–26, 2015; Seattle, WA Abstract 85LB
47. US Agency for International Development. Drug interactions between hormonal contraceptive methods and anti-retroviral medications used to treat HIV. Technical Issue Brief; 10 2014:1–4. Available at: www.cdc.gov/globalaids/resources/pmtct-care/docs/hc_art-brief_final.pdf. Accessed January 4, 2016 [PubMed: 25115034]
48. Vieira CS, Bahamondes MV, de Souza RM, et al. Effect of antiretroviral therapy including lopinavir/ritonavir or efavirenz on etonogestrel-releasing implant pharmacokinetics in HIV-positive women. J Acquir Immune Defic Syndr. 2014;66(4):378–385 [PubMed: 24798768]
49. Kreitchmann R, Innocente AP, Preussler GM. Safety and efficacy of contraceptive implants for HIV-infected women in Porto Alegre, Brazil. Int J Gynaecol Obstet. 2012;117(1):81–82 [PubMed: 22249127]
50. Leticee N, Viard JP, Yamgnane A, Karmochkine M, Benachi A.Contraceptive failure of etonogestrel implant in patients treated with antiretrovirals including efavirenz. Contraception. 2012;85(4):425–427 [PubMed: 22036046]
51. National Institutes of Health. Recommendations for use of antiretroviral drugs in pregnant HIV- 1-infected women for maternal health and interventions to reduce perinatal HIV transmission in the United States. Available at: https://aidsinfo.nih.gov/guidelines/html/3/perinatalguidelines/0. Accessed January 4, 2016
52. National Institutes of Health. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Available at: https://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf. Accessed January 4, 2016
53. World Health Organization. Medical eligibility criteria for contraceptive use 5th ed Executive summary. Geneva, Switzerland: World Health Organization; 2015 Available at:www.who.int/reproductivehealth/publications/family_planning/Ex-Summ-MEC-5/en/. Accessed January 4, 2016
54. Deans G, Schwarz EB. Intrauterine contraceptives (IUCs) In: Hatcher RA, Trussell J, Nelson AL, Cates W Jr, Kowal D, Policar MS, eds. Contraceptive Technology. 20th revised ed Atlanta, GA: Ardent Media, Inc; 2011:147–182
55. Centers for Disease Control and Prevention. U.S. selected practice recommendations for contraceptive use, 2013: adapted from the World Health Organization selected practice recommendations for contraceptive use, 2nd edition. MMWR Recomm Rep. 2013;62(RR-5):1–46. Available at: www.cdc.gov/mmwr/preview/mmwrhtml/rr6205a1.htm. Accessed January 4, 2016
56. Bayer HealthCare Pharmaceuticals. Skyla [package insert]. 2013 Available at: http://labeling.bayerhealthcare.com/html/products/pi/Skyla_PI.pdf. Accessed January 4, 2016
57. Bayer HaelthCare Pharmaceuticals Inc. Mirena [package insert]. 2014 Available at: http://labeling.bayerhealthcare.com/html/products/pi/Mirena_PI.pdf. Accessed January 4, 2016
58. Teva Women's Health I. ParaGuard T 380A [package insert]. 2013 Available at: www.paragard.com/Pdf/ParaGard-PI.pdf. Accessed January 4, 2016
59. Hubacher D, Lara-Ricalde R, Taylor DJ, Guerra-Infante F, Guzmán-Rodríguez R. Use of copper intrauterine devices and the risk of tubal infertility among nulligravid women. N Engl J Med. 2001;345(8):561–567 [PubMed: 11529209]
60. Mohllajee AP, Curtis KM, Peterson HB. Does insertion and use of an intrauterine device increase the risk of pelvic inflammatory disease among women with sexually transmitted infection? A systematic review. Contraception. 2006;73(2):145–153 [PubMed: 16413845]
61. Farley TM, Rosenberg MJ, Rowe PJ, Chen JH, Meirik O. Intrauterine devices and pelvic inflammatory disease: an international perspective. Lancet. 1992;339(8796):785–788 [PubMed: 1347812]
62. Tepper NK, Marchbanks PA, Curtis KMUS. U.S. selected practice recommendations for contraceptive use, 2013. J Womens Health (Larchmt). 2014;23(2):108–111 [PubMed: 24116965]

63. Tepper NK, Curtis KM, Nanda K, Jamieson DJ. Safety of intrauterine devices among women with HIV:a systematic review [published online ahead of print June 22, 2016]. Contraception.10.1016/j.contraception.2016.06.011
64. Heikinheimo O, Lehtovirta P, Suni J, Paavonen J. The levonorgestrel- releasing intrauterine system (LNG- IUS) in HIV-infected women—effects on bleeding patterns, ovarian function and genital shedding of HIV. Hum Reprod. 2006;21(11):2857–2861 [PubMed: 16880227]
65. Lehtovirta P, Paavonen J, Heikinheimo O. Experience with the levonorgestrel- releasing intrauterine system among HIV-infected women. Contraception. 2007;75(1):37–39 [PubMed: 17161122]
66. Heikinheimo O, Lehtovirta P, Aho I, Ristola M, Paavonen J. The levonorgestrel-releasing intrauterine system in human immunodeficiency virus-infected women: a 5-year follow-up study. Am J Obstet Gynecol. 2011;204(2):126.e1–126.e4 [PubMed: 21035781]
67. Morrison CS, Chen PL, Kwok C, et al. Hormonal contraception and the risk of HIV acquisition: an individual participant data meta-analysis. PLoS Med. 2015;12(1):e1001778 [PubMed: 25612136]
68. Stringer EM, Kaseba C, Levy J,et al. A randomized trial of the intrauterine contraceptive device vs hormonal contraception in women who are infected with the human immunodeficiency virus. Am J Obstet Gynecol. 2007;197(2):144.e1–144.e8 [PubMed: 17689627]
69. Pfizer. Depo-provera CI [package insert]. 2010 Available at: www.accessdata.fda.gov/drugsatfda_docs/label/2010/020246s036lbl.pdf. Accessed January 4, 2016
70. Beksinska ME, Kleinschmidt I, Smit JA, Farley TM, Rees HV. Bone mineral density in young women aged 19–24 after 4–5 years of exclusive and mixed use of hormonal contraception. Contraception. 2009;80(2):128–132 [PubMed: 19631787]
71. Polis CB, Phillips SJ, Curtis KM, et al. Hormonal contraceptive methods and risk of HIV acquisition in women: a systematic review of epidemiological evidence. Contraception. 2014;90(4):360–390 [PubMed: 25183264]
72. Phillips SJ, Curtis KM, Polis CB. Effect of hormonal contraceptive methods on HIV disease progression: a systematic review. AIDS. 2013;27(5):787–794 [PubMed: 23135169]
73. Nanda K, Amaral E, Hays M, Viscola MA, Mehta N, Bahamondes L. Pharmacokinetic interactions between depot medroxyprogesterone acetate and combination antiretroviral therapy. Fertil Steril. 2008;90(4):965–971 [PubMed: 17880953]
74. Cohn SE, Park JG, Watts DH, et al.; ACTG A5093 Protocol Team. Depo- medroxyprogesterone in women on antiretroviral therapy: effective contraception and lack of clinically significant interactions. Clin Pharmacol Ther. 2007;81(2):222–227 [PubMed: 17192768]
75. Watts DH, Park JG, Cohn SE, et al. Safety and tolerability of depot medroxyprogesterone acetate among HIV-infected women on antiretroviral therapy: ACTG A5093. Contraception. 2008;77(2):84–90 [PubMed: 18226670]
76. Puthanakit T, Siberry GK. Bone health in children and adolescents with perinatal HIV infection. J Int AIDS Soc. 2013;16:18575 [PubMed: 23782476]
77. Nelson AL. Combined oral contraceptives In: Hatcher RA, Trussell J, Nelson AL, Cates W Jr, Kowal D, Policar MS, eds. Contraceptive Technology. 20th revised ed Atlanta, GA: Ardent Media, Inc; 2011:249–319
78. Stewart FH, Brown BA, Raine TR, Weitz TA, Harper CC. Adolescent and young women's experience with the vaginal ring and oral contraceptive pills. J Pediatr Adolesc Gynecol. 2007;20(6):345–351 [PubMed: 18082856]
79. Committee on Adolescence. Condom use by adolescents. Pediatrics. 2013;132(5):973–981 [PubMed: 28448257]
80. Gilliam ML, Neustadt A, Kozloski M, Mistretta S, Tilmon S, Godfrey E.Adherence and acceptability of the contraceptive ring compared with the pill among students: a randomized controlled trial. Obstet Gynecol. 2010;115(3):503–510 [PubMed: 20177280]
81. Bakhru A, Stanwood N. Performance of contraceptive patch compared with oral contraceptive pill in a high-risk population. Obstet Gynecol. 2006;108(2):378–386 [PubMed: 16880309]
82. Atrio J, Stanczyk FZ, Neely M, Cherala G, Kovacs A, Mishell DR Jr. Effect of protease inhibitors on steady- state pharmacokinetics of oral norethindrone contraception in HIV- infected women. J Acquir Immune Defic Syndr. 2014;65(1):72–77 [PubMed: 24025339]

83. Martinez G, Copen CE, Abma JC. Teenagers in the United States: sexual activity, contraceptive use, and childbearing, 2006–2010 national survey of family growth. Vital Health Stat 23 2011;(6): 1–35
84. Warner L, Steiner MJ. Male condoms In: Hatcher RA, Trussell J, Nelson AL, Cates W Jr, Kowal D, Policar MS, eds. Contraceptive Technology. 20th revised ed Atlanta, GA: Ardent Media, Inc; 2011:371–382
85. Centers for Disease Control and Prevention. Condom fact sheet in brief. Available at: www.cdc.gov/condomeffectiveness/docs/condomfactsheetinbrief.pdf. Accessed January 4, 20160
86. Committee on Adolescence. Emergency contraception. Pediatrics. 2012;130(6):1174–1182 [PubMed: 23184108]
87. US Food and Drug Administration. FDA approves Plan B One-Step emergency contraceptive for use without a prescription for all women of child- bearing potential [news release]. Silver Spring, MD: US Food andDrug Administration; 6 20, 2013 Available at: www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm358082.htm. Accessed January 4, 2016
88. Wilkinson D, Tholandi M, Ramjee G, Rutherford GW. Nonoxynol-9 spermicide for prevention of vaginally acquired HIV and other sexually transmitted infections: systematic review and meta-analysis of randomised controlled trials including more than 5000 women. Lancet Infect Dis. 2002;2(10):613–617 [PubMed: 12383611]
89. Cates W Jr. Vaginal barriers and spermicides In: Hatcher RA, Trussell J, Nelson AL, Cates W Jr, Kowal D, Policar MS, eds. Contraceptive Technology. 20th revised ed Atlanta, GA: Ardent Media, Inc; 2011:391–405
90. US Agency for International Development. Hormonal Contracception and HIV [technical brief]. Washington, DC: US Agency for International Development; 2013
91. Baeten JM, Lavreys L, Overbaugh J. The influence of hormonal contraceptive use on HIV-1 transmission and disease progression. Clin Infect Dis. 2007;45(3):360–369 [PubMed: 17599316]
92. Blish CA, Baeten JM. Hormonal contraception and HIV-1 transmission. Am J Reprod Immunol. 2011;65(3):302–307 [PubMed: 21087338]
93. Roccio M, Gardella B, Maserati R, Zara F, Iacobone D, Spinillo A. Low- dose combined oral contraceptive and cervicovaginal shedding of human immunodeficiency virus. Contraception. 2011;83(6):564–570 [PubMed: 21570555]
94. Mostad SB, Overbaugh J, DeVange DM, et al. Hormonal contraception, vitamin A deficiency, and other risk factors for shedding of HIV-1 infected cells from the cervix and vagina. Lancet. 1997;350(9082):922–927 [PubMed: 9314871]
95. Heffron R, Donnell D, Rees H, et al.; Partners in Prevention HSV/HIV Transmission Study Team. Use of hormonal contraceptives and risk of HIV-1 transmission: a prospective cohort study. Lancet Infect Dis. 2012;12(1):19–26 [PubMed: 21975269]
96. Polis CB, Phillips SJ, Curtis KM. Hormonal contraceptive use and female-to-male HIV transmission: a systematic review of the epidemiologic evidence. AIDS. 2013;27(4):493–505 [PubMed: 23079808]
97. Clemetson DB, Moss GB, Willerford DM, et al. Detection of HIV DNA in cervical and vaginal secretions: prevalence and correlates among women in Nairobi, Kenya. JAMA. 1993;269(22): 2860–2864 [PubMed: 8497089]
98. Kovacs A, Wasserman SS, Burns D,et al.; DATRI Study Group; WIHS Study Group. Determinants of HIV-1 shedding in the genital tract of women. Lancet. 2001;358(9293):1593–1601 [PubMed: 11716886]
99. Wang CC, McClelland RS, Overbaugh J, et al. The effect of hormonal contraception on genital tract shedding of HIV-1. AIDS. 2004;18(2):205–209 [PubMed: 15075537]
100. World Health Organization. Hormonal contraceptive methods for women at high risk of HIV and living with HIV. 2014 Guidance statement. Geneva, Switzerland: World Health Organization; 2014 Available at: http://apps.who.int/iris/bitstream/10665/128537/1/WHO_RHR_14.24_eng.pdf?ua= 1.Accessed January 4, 2016
101. Crauwels HM, van Heeswijk RP, Buelens A, Stevens M, Hoetelmans RM. Lack of an effect of rilpivirine on the pharmacokinetics of ethinylestradiol and norethindrone in healthy volunteers. Int J Clin Pharmacol Ther. 2014;52(2):118–128 [PubMed: 24161160]

102. Landolt NK, Phanuphak N, Ubolyam S, et al. Efavirenz, in contrast to nevirapine, is associated with unfavorable progesterone and antiretroviral levels when coadministered with combined oral contraceptives. J Acquir Immune Defic Syndr. 2013;62(5):534–539 [PubMed: 23187949]
103. Mildvan D, Yarrish R, Marshak A, et al. Pharmacokinetic interaction between nevirapine and ethinyl estradiol/norethindrone when administered concurrently to HIV-infected women. J Acquir Immune Defic Syndr. 2002;29(5):471–477 [PubMed: 11981363]
104. Nanda K, Delany-Moretlwe S, Dubé K, et al. Nevirapine-based antiretroviral therapy does not reduce oral contraceptive effectiveness. AIDS. 2013;27(suppl 1):S17–S25 [PubMed: 24088680]
105. Stuart GS, Moses A, Corbett A, et al. Combined oral contraceptives and antiretroviral PK/PD in Malawian women: pharmacokinetics and pharmacodynamics of a combined oral contraceptive and a generic combined formulation antiretroviral in Malawi. J Acquir Immune Defic Syndr. 2011;58(2):e40–e43 [PubMed: 21921726]
106. Sevinsky H, Eley T, Persson A,et al. The effect of efavirenz on the pharmacokinetics of an oral contraceptive containing ethinyl estradiol and norgestimate in healthy HIV-negative women. Antivir Ther. 2011;16(2):149–156 [PubMed: 21447863]
107. Schöller-Gyüre M, Kakuda TN, Woodfall B, et al. Effect of steady-state etravirine on the pharmacokinetics and pharmacodynamics of ethinylestradiol and norethindrone. Contraception. 2009;80(1):44–52 [PubMed: 19501215]
108. Heffron R, Mugo N, Were E, et al.; Partners PrEP Study Team. Preexposure prophylaxis is efficacious for HIV-1 prevention among women using depot medroxyprogesterone acetate for contraception. AIDS. 2014;28(18):2771–2776 [PubMed: 25493602]
109. Todd CS, Deese J, Wang M, et al.; FEM-PrEP Study Group. Sino-implant (II)® continuation and effect of concomitant tenofovir disoproxil fumarate-emtricitabine use on plasma levonorgestrel concentrations among women in Bondo, Kenya. Contraception. 2015;91(3):248–252 [PubMed: 25459097]
110. Thurman AR, Anderson S, Doncel GF. Effects of hormonal contraception on antiretroviral drug metabolism, pharmacokinetics and pharmacodynamics. Am J Reprod Immunol. 2014;71(6):523–530 [PubMed: 24521428]
111. Polis CB, Nakigozi G, Ssempijja V, et al. Effect of injectable contraceptive use on response to antiretroviral therapy among women in Rakai, Uganda. Contraception. 2012;86(6):725–730 [PubMed: 22717186]
112. Chu JH, Gange SJ, Anastos K, et al. Hormonal contraceptive use and the effectiveness of highly active antiretroviral therapy. Am J Epidemiol. 2005;161(9):881–890 [PubMed: 15840621]
113. Hubacher D, Liku J, Kiarie J, et al. Effect of concurrent use of anti-retroviral therapy and levonorgestrel sub-dermal implant for contraception on CD4 counts: a prospective cohort study in Kenya. J Int AIDS Soc. 2013;16:18448 [PubMed: 23458102]
114. Johnson D, Kempf MC, Wilson CM, Shrestha S. Hormonal contraceptive use and response to antiretroviral therapy among adolescent females. HIV and AIDS Review. 2011;10(3):65–69
115. Friend DR, Clark JT, Kiser PF, Clark MR. Multipurpose prevention technologies: products in development. Antiviral Res. 2013;100(suppl):S39–S47 [PubMed: 24188708]
116. Underhill K, Montgomery P, Operario D. Abstinence-plus programs for HIV infection prevention in high-income countries. Cochrane Database Syst Rev. 2008;1:CD007006

TABLE 1

Interactions of Hormonal Contraceptives With Antiretroviral Drugs by Drug Class

Antiretroviral Class[a]	Hormonal Contraceptive Type				
	Progestin Implants	Levonorgestrel IUD[b]	Progestin Injectables (DMPA)	Combined Hormonal Methods and Progestin-Only Pills	Emergency Contraception
NRTIs	No known interactions	No known interactions	No known interactions	No known interactions	No known interactions
NNRTIs	Potential interaction with efavirenz may limit its contraceptive efficacy; more data are needed	No known interactions	No known interactions	Interactions with efavirenz may decrease hormonal contraceptive levels and contraceptive efficacy; alternative or additional contraceptive methods are recommended	Interactions of levonorgestrel emergency contraception with efavirenz may limit efficacy; possible interactions of ulipristal with NNRTIs; no clinical data
PIs	Potential interaction, very limited clinical data	No known interactions	No known interactions	Interactions with most ritonavirboosted PIs may decrease hormone contraceptive levels and contraceptive efficacy; alternative or additional contraceptive methods are recommended	Possible interaction of ulipristal with elvitegravir/cobicistat; no clinical data
Integrase inhibitors	No known interactions	No known interactions	No known interactions	Possible interaction with elvitegravir/cobicistat	Possible interaction of ulipristal with elvitegravir/cobicistat
Entry/fusion inhibitors	No known interactions	No known interactions	No known interactions	No known interactions	No known interactions

The concurrent use of male condoms for protection against STIs, for additional protection against unintended pregnancy, and for prevention of transmission of HIV infection to partners is always recommended for HIV-infected women. NRTI, nucleoside reverse transcriptase inhibitor.

[a]NRTIs include abacavir, tenofovir, zidovudine, lamivudine, didanosine, emtricitabine, and stavudine; NNRTIs include efavirenz, etravirine, nevirapine, and rilpivirine; PIs include ritonavir-boosted atazanavir, darunavir, fosamprenavir, lopinavir, saquinavir and tipranavir, unboosted atazanavir, fosamprenavir, indinavir, nelfinavir, and ritonavir; integrase inhibitors include raltegravir, dolutegravir, and elvitegravir/cobicistat; entry/fusion inhibitors include maraviroc, vicriviroc, and enfuvirtide

[b]An alternative contraceptive method is recommended for women with severe/advanced clinical HIV disease, until improvement with antiretroviral therapy. If a woman with an IUD develops severe clinical disease, the IUD does not need to be removed, but careful monitoring for pelvic infection is recommended.