

Review article

Sexual life and contraception in people living with HIV

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As people living with HIV (PLH) are living longer and healthier lives in the era of highly active antiretroviral therapy, common reproductive health issues are becoming more important. According to WHO, PLH should be offered routine counselling on sexual and reproductive health, so that they can implement informed, healthy, and appropriate decisions. PLH need special attention with regard to the use of contraceptive methods that provide dual protection against HIV/sexually transmitted infection transmission and unintended pregnancies. This article includes literature review on sexual life and contraception in the context of HIV infection including barrier methods, natural methods, sterilization, hormonal contraception, intrauterine device, spermicides/microbicides and emergency contraception. To date, there is no perfect method that provides both protection against HIV transmission and unintended pregnancy. Although male condom remains the principal contraceptive method, its male-controlled usage is its most important obstacle. This article describes the pros and cons of each method for PLH as well as the interaction between hormonal contraceptives and antiretroviral drugs. Many questions remain to be answered. It is therefore important that studies of different methods of contraception in PLH continue.

Keywords: Contraception, family planning, HIV, prevention, sexual life

In the era of highly active antiretroviral therapy (HAART), people living with HIV (PLH) enjoy a significantly improved quality of life. The success achieved in this regard is remarkable. As a result, health professionals are being approached more and more often with issues about common reproductive health [1, 2].

Key elements of reproductive health are sexual life, conception, and contraception, and sexually transmitted diseases (STD), their prevention, diagnosis, and treatment (**Fig. 1**). The interplay between the different elements of reproductive health is complex. The goal of having a healthy sexual life is balanced by the desire for conception or no conception, and for STD avoidance. These relationships are even

more complex when HIV infection comes into play. The objective of this article is to review the literature on sexual life and contraception in the light of HIV infection.

Why is it important to speak about sexual life, contraception and HIV infection?

Sexual life is the basis of reproductive health. PLH have the same sexual needs as the HIV-negative population. HIV-positive men, women, and transgender do practise sex. In 2009, a study from Argentina shows that 84% of people remain sexually active after being diagnosed with HIV infection [3]. Sexual behaviours around the world are extremely diverse. There are many reasons for this - personal preferences, cultural, religious, and other traditions. The management of PLH during their reproductive years is increasingly important. According to the World Health Organization (WHO), PLH should be offered routine counselling on sexual and reproductive health,

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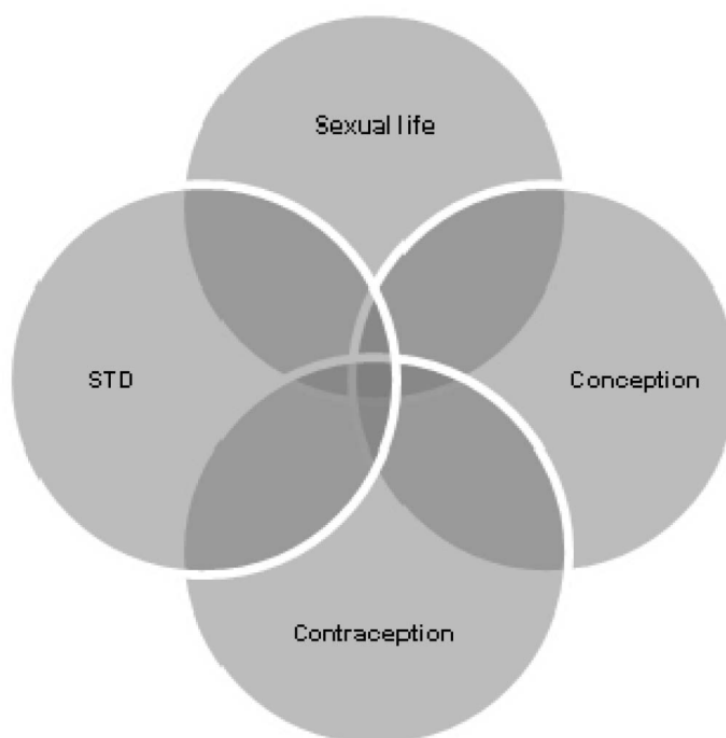


Fig. 1 Elements of reproductive health.

so that they can implement informed, healthy, and appropriate decisions [4].

Millions of new HIV infections occur worldwide each year, predominantly via sexual contacts. In Thailand, where approximately 1% of a population of 62.8 million (2006) is living with HIV, there are close to 14,000 new infections per year. Around 25% of new HIV infections in Thailand are in men who have sex with men (MSM) and there is a 30-40% increase of new infections in married women (12th National Seminar on AIDS, 2009).

As sexual practice is the principal mode of global HIV spread in the 21st century, modern medicine should be able to address the diverse sexual needs of people with and without HIV and give them the possibility to practice sex in a safe way. Appropriate sexual and contraceptive practice would help prevent transmission of HIV and other STDs and prevent unintended pregnancies.

A recent study conducted by the Universities of Cape Town and Columbia, assessed the impact of antiretroviral therapy (ART) on the incidence of pregnancy among over 4,500 HIV-positive women in seven Sub-Saharan African countries [5]. According

to this study the use of ART was associated with an almost 80% increased risk of pregnancy, which may be explained by a series of biological and behavioral factors. The authors do not differentiate between intended and unintended pregnancies, but they conclude that HIV-positive women of childbearing age would benefit from programs that combine starting ART with contraception education and counseling and pregnancy-related care.

Prevention of pregnancy by using contraception is extremely important as it provides the opportunity to plan desired pregnancy in HIV-positive women - or the opposite, to avoid unplanned pregnancy. The latter is particularly relevant when possible harms related to unplanned pregnancy may include teratogenicity from the use of antiretroviral drug such as efavirenz or high-risk of perinatal HIV transmission. In addition, induced abortion - the last resort for ending an unwanted pregnancy - is illegal in many countries including Thailand, for instance [6]. Abortion is not a method of contraception as such and the consequences of illegally induced abortions might be dramatic. Thus, offering a comprehensive choice of contraceptive methods for everyone, including PLH, is crucial.

On the other hand, when an HIV-positive woman wants to become pregnant, providing an effective contraception could be very beneficial to gain time to make the most of HAART before conception. Plasma HIV RNA is an important determinant of the likelihood of spreading HIV to others including the transmission from mother to baby. A sub-study of Staccato performed at one site in Bangkok found that detectable HIV RNA in genital secretions significantly increased in patients with detectable plasma HIV RNA [7]. Therefore, it is important to allow time to optimize HAART before conception in HIV-positive women.

Choosing a highly effective modern method of contraception by PLH does not mean they can stop using condom. The concomitant use of condom remains highly recommended to prevent transmission of STD and HIV to and from others, and super infection of new HIV quasi-species. A statement on behalf of the Swiss Federal Commission for HIV/AIDS in the beginning of 2008 suggests that HIV-infected heterosexual persons on ART with completely suppressed viraemia (“effective ART”) are not sexually infectious, i.e. cannot transmit HIV through sexual contact” when they have been on HAART for at least six months, have undetectable plasma HIV RNA, and have no other STDs [8, 9]. However, this statement is not yet widely adopted and condom use would still prevent STD/HIV transmission in the majority of other PLH who do not meet these particular conditions. Furthermore, the need to prevent unintended pregnancies may still warrant appropriate contraception.

Methods of contraception

A substantial choice of contraceptive methods exists [10, 11]. So far, a perfect method that provides both contraception and prevention of STDs with no side effects, and is completely accepted in all situations, does not exist. The methods of contraception can be divided into two principle groups-barrier and non-barrier methods. The principle advantage of barrier methods, male and female condoms, to the non-barrier methods is that they provide significant protection from STD/HIV in addition to pregnancy prevention. The group of non-barrier methods includes sterilization, hormonal contraception, intrauterine devices, spermicides, and natural methods. Different methods of contraception with their advantages and disadvantages in light of

HIV infection are listed in **Table 1**.

Close to 80% of married Thai women, regardless of their HIV-status, are using some methods of contraception according to the Demographic and Health Surveys Thailand [13]. **Figure 2** shows the percentage of women using certain methods of contraception and how this has changed from 1987 to 2000.

PLH comprise a diverse group with different needs demanding special attention with regard to the use of contraceptive methods. The issues of HIV transmission to the uninfected partner in HIV serodiscordant couples or super-infection in the infected partner in HIV seroconcordant couples are important consideration in counseling PLH on contraceptives. Importantly, systematic contraceptive guidelines for PLH do not exist at present [12, 14, 15].

Barrier methods

Male and female condoms constitute the most popular methods among the barrier group, especially in the prevention of HIV and STDs. These methods, if used properly, give significant protection for both unintended pregnancy and STD/HIV. Unfortunately, male condom cannot answer all the needs, and all too often, it is not used as recommended by health professionals. Male condoms have never been widely accepted in married couples and in particular groups with high sexual risk behavior (MSM, group sex). In addition, as high as 50% of men with HIV infection, especially those who took protease inhibitors (PIs)-based HAART, were reported to have erectile dysfunction, which can make the use of male condom difficult [16, 17].

Female condom is a female controlled contraceptive method, although it is not completely partner independent. Compared to male condom, female condom is more expensive but it can be used in case of erectile dysfunction. Some female condom users complain of difficult insertion and possibility to slip or make a noise when used. Several recent studies assessing the acceptability of female condom among sexual workers [18, 19] demonstrated that the acceptability improved significantly over time (usually several months) with the right education and practice. Nevertheless, female condom so far did not succeed to become very popular among general users.

Table 1. Methods of contraception for people living with HIV.

Methods of contraception	Percentage of pregnancy in the first year of use*	Advantages	Disadvantages
Barrier methods			
Male condom	2%*	<ul style="list-style-type: none"> - reversible method of contraception - good contraceptive effect - significant STD/HIV protection - no additional pill burden - low cost - easy to use - most popular 	<ul style="list-style-type: none"> - effect depends on proper use of the method - partner dependent
Female condom	5%*	<ul style="list-style-type: none"> - reversible method of contraception - independent of erection - less partner dependent when compared to male condom - provides significant STD/HIV protection - no additional pill burden - female controlled method 	<ul style="list-style-type: none"> - effect depends on proper use of the method - difficult to insert, might slip, makes noise - more expensive than male condom
Diaphragm, cervical cap	6%*	<ul style="list-style-type: none"> - reversible method of contraception - no additional pill burden - female controlled method - no STD/HIV protection 	<ul style="list-style-type: none"> - effect depends on proper use of the method - need to be used with nonoxynol-9, thus not appropriate for PLH due to damage of epithelium
Natural methods			
Interrupted intercourse	20 - 30%	<ul style="list-style-type: none"> - no cost - no additional pill burden - partner dependent 	<ul style="list-style-type: none"> - low contraceptive effect - no STD/HIV protection
Abstinence in fertility days of the period			
Sterilization			
Male/female sterilization	0.1-0.5%*	<ul style="list-style-type: none"> - no additional pill burden - partner independent method - no STD/HIV protection 	<ul style="list-style-type: none"> - practically irreversible choice - possible complications during the procedure

Table 1. Methods of contraception for people living with HIV (Continued).

Methods of contraception	Percentage of pregnancy in the first year of use*	Advantages	Disadvantages
Hormonal contraception			
Combined estrogen and progesterone	0.1%*	<ul style="list-style-type: none"> - reversible method of contraception - high contraceptive effect - partner independent method - possible interaction with antiretrovirals and need of higher dosage - no STD/HIV protection 	<ul style="list-style-type: none"> - effect depends on proper use of the method - additional pill burden on daily basis - possible increase in metabolic adverse events
- Combined oral contraceptive pill			
- Combined skin patches			
Progestin only	0.05 – 0.5%*	<ul style="list-style-type: none"> - reversible method of contraception - high contraceptive effect - partner independent method 	<ul style="list-style-type: none"> - effect depends on proper use of the method - need to apply the method on regular basis - possible enhancement of HIV disease progression - possible increase in metabolic adverse events - possible interaction with antiretrovirals and need of higher dosage - no STD/HIV protection
- Pills			
- Injectable			
- Implants			
Intrauterine device			
Copper loaded and releasing	0.6%*	<ul style="list-style-type: none"> - reversible method of contraception 	<ul style="list-style-type: none"> - no STD/HIV protection
Progestrone loaded and releasing	0.1%*	<ul style="list-style-type: none"> - high contraceptive effect - partner independent method - no additional pill burden - user independent method for 5 to 10 years, once inserted 	<ul style="list-style-type: none"> - possible hypermenorrhoea in case of copper IUD
Spermicides, microbicides			
Spermicides, microbicides	15%	<ul style="list-style-type: none"> - partner independent method 	<ul style="list-style-type: none"> - only 1 spermicide (nonoxynol-9, N-9) available on the market, the rest is in development - N-9 not appropriate for PLH, due to damage of vaginal epithelium

* Further information available in 2008 British HIV Association Guidelines for the management of sexual and reproductive health of people living with HIV infection [12].
STD: sexually transmitted disease, N-9: nonoxynol-9, IUD: intrauterine device.

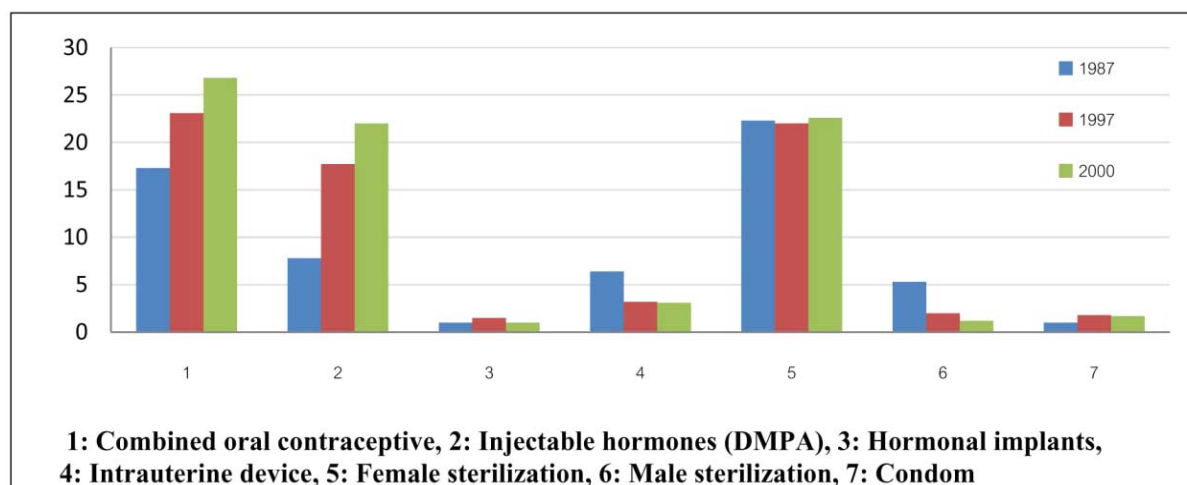


Fig. 2 Reproductive health profile, Thailand 1987-2000. Source: Thailand Demographic and Health Survey, 1987, 1997; Thailand Reproductive Health Profile 2003 [13].

Other examples of the barrier methods of contraception are the diaphragm and the cervical cap. These methods are recommended to be used together with a spermicidal cream, such as nonoxynol-9 (N-9). N-9 on the other hand is not advised to be used in PLH due to its damaging effect on the vaginal epithelium (see spermicides/microbicides below). Therefore, the diaphragm is not recommended to be used in case of HIV infection [12]. The MIRA (Methods for Improving Reproductive Health in Africa) randomized clinical trial in women assessed the effectiveness of the addition of diaphragm with Replen lubricant to routine methods (male condom, counseling) compared to routine methods alone for prevention of HIV infection. It was found that there was no added HIV protective benefit from using the diaphragm and lubricant in addition to male condom. Moreover, it was found that the group randomized to using diaphragm had lower condom use [20]. Therefore, it is currently not recommended that a diaphragm is used or promoted for HIV prevention.

All these advantages and disadvantages of the above barrier methods point to the necessity of studying the rest of the contraceptive methods in PLH, and considering the need of using dual protective methods – one barrier method for STD/HIV prevention and one highly effective contraceptive method for pregnancy prevention [21].

Natural methods

Natural contraception is among the oldest known contraceptive methods in the world. Interrupted sexual

intercourse, the avoidance of sexual intercourse in the fertile days of the month, and infertility during lactation are included in this group. These methods do not require neither any initial preparation apart from basic education nor involve any material cost. However, they are unreliable methods for preventing unintended pregnancies and they do not provide any protection against STD and HIV transmission.

Sterilization

Another method of contraception is sterilization, either male or female, which is widely popular in many countries. In Thailand, female sterilization is much more common than male sterilization and there is insufficient data concerning male sterilization, regardless of HIV status. This method has many advantages as it provides excellent prevention of pregnancy and does not have the side effects of some of the other contraceptive methods. The disadvantage is that sterilization is a virtually irreversible choice and thus might raise serious ethical questions, especially if it is conducted without adequate counseling or if HIV-positive women are forced to undergo the procedure as reported in some African countries [22]. Furthermore, sterilization does not provide any protection from STD and HIV.

Hormonal contraception

Hormonal contraception is a very popular method of contraception around the world. There are two main types of hormonal contraception. The first one is the combined estrogen and progestin type that includes

the combined oral contraceptive pill and the less popular skin patch. The transdermal way of delivering hormones could prove to be of particular interest among HIV-positive women, as it does not have the first-pass metabolism liver effect and thus is expected to interact less with HAART [12]. There have been no detailed studies so far on the use of transdermal hormonal contraception in HIV-positive women. The second one is the progestin-only type that could be delivered as a pill, a depot injection, or an implant. The contraceptive effect achieved with hormonal contraception is among the highest - 0.1 to 0.5 pregnancies per 100 women per year, in case of proper use of the method [12]. Unfortunately, hormonal contraception does not prevent STD and HIV transmission.

There are worries that hormonal contraception might have some serious adverse events on health mainly due to the effect of estrogens [23]. Hormonal contraception is not recommended for obese women, those with high blood pressure, a history of heart disease or blood clots, and some other illnesses, such as breast cancer as it could aggravate these diseases. In general, hormonal contraceptive pill is considered relatively safe for women in good health who do not smoke, regardless of the HIV status of the woman. Hormonal contraception, especially the progestin component, also has some protective effects against cancers of the ovary and of the endometrium.

Data on the effect of hormonal contraception on HIV disease progression is still inconclusive. A study

conducted in Zambia suggested that hormonal contraception might enhance disease progression if administered in HIV-positive women prior to HAART [24]. The researchers randomized 599 HIV-infected women to either a non-hormonal contraceptive method, such as an intrauterine device (IUD), or a hormonal contraception method, such as oral contraceptive pill (OCP) or injectable progestin (depomedroxyprogesteron acetate, DMPA). Disease progression was defined as either death or becoming eligible for ART. They found that OCP or DMPA use was associated with HIV disease progression among women not yet on ART. However, data from a multi-country cohort analysis involving over 4,000 women, published at the end of 2009 by the same group of researchers, provides some reassurance that perhaps hormonal contraception is not associated with HIV disease progression [25].

Another important consideration involving hormonal contraception in HIV positive women is the possible interaction between hormones and antiretroviral drugs, which could require adjusting the dosages of hormones [26-29]. **Table 2** shows the possible interactions between antiretrovirals and ethinyl estradiol and progestin according to the US Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents, December 2009 (30) and the British HIV Association Guidelines, 2008 [12]. More studies are needed in this area, as data on certain ARVs is still limited.

Table 2. Interaction between ethinyl estradiol, progestin and antiretroviral drugs.

Non-nucleoside reverse transcriptase inhibitors	
<i>Nevirapine</i>	↓ EE, ↓ progestin, DMPA no change*
<i>Efavirenz</i>	not fully studied, ↑ EE*
Protease inhibitors	
<i>Saquinavir with Ritonavir</i>	↓ EE*
<i>Lopinavir with Ritonavir</i>	↓ EE, ↓ progestin*
<i>Atazanavir without Ritonavir</i>	↑ EE, ↑ progestin*
<i>Indinavir without Ritonavir</i>	↑ EE, ↑ progestin*
Nucleoside/tide Reverse Transcriptase Inhibitors	no evidence for changes of EE and progestin**
Chemokine Co-Receptor (CCR) 5 antagonist	
<i>Maraviroc</i>	no evidence for changes of EE and progestin*

* Data from US guideline for antiretroviral therapy for adults and adolescents, Dec 2009. **Data from British HIV Association, 2008. EE: ethinyl estradiol, DMPA: depomedroxyprogesterone acetate.

Because of the potential effects of HIV infection, ART, and hormones themselves on body metabolism, we might expect more changes, especially in plasma lipids and glucose tolerance, in HIV-positive women using hormonal contraception. The impact of hormonal contraception on bone density is less studied. Both HIV and hormonal contraception use share a common risk profile for metabolic abnormalities and there is insufficient evidence that hormonal contraception aggravates HIV-associated metabolic dysregulation. A review article from 2008 concludes that denying a woman her choice of contraceptive because of a hypothetical concern is inappropriate as is ignoring the potential for iatrogenic side effects [31]. HIV-positive women who choose to use hormonal contraception may therefore need more careful monitoring and management of potential metabolic abnormalities.

Intrauterine device (IUD)

IUD is the most popular reversible long acting contraceptive method used in the world. It has a very high contraceptive effect (0.6 pregnancies per 100 women per one year, in case of proper use of the method) [12]. At present, there are two main types of IUDs - loaded and releasing either copper or progestin, levonorgestrel, in the uterine cavity. As compared to hormonal contraception, IUD has the advantage of lacking the additional pill burden, the need for regular application, and the adverse events associated with hormonal components in the hormonal contraceptive methods. Progestin releasing IUD has advantage over copper releasing IUD in reducing menstrual bleeding. Hypermenorrhea is one of the possible disadvantages of copper IUDs. An increased incidence of pelvic inflammatory diseases was reported when IUDs were left in the uterine cavity for a period longer than the recommended five years [32]. Several small studies also showed statistically higher incidence of bacterial vaginosis among IUD users as compared to women who did not use any other form of modern contraception [33] or to women using any other method of contraception different from an IUD [34], regardless of their HIV status. Although it is not an absolute contraindication, IUD is not recommended for use in women who have never been pregnant as there is a much higher incidence of adverse effects such as irregular bleeding or hypermenorrhea, dysmenorrhea and expulsion in these women. Similar to sterilization and hormonal

contraception, the IUD has high contraceptive effect but it does not prevent the transmission of STD and HIV, which requires the use of a barrier method in case of an HIV infection or multiple partners (due to higher risk of STD).

A study conducted in Zambia in 2007 reported that IUD is a safe and effective method of contraception in HIV-positive women [35]. The study randomly assigned 303 women to hormonal contraception and 296 women to copper releasing IUD. Women who were assigned to hormonal contraception were more likely to become pregnant than those who were assigned to IUD (4.6 vs. 2.0/100 woman-years). Only one woman who was assigned to the IUD group experienced pelvic inflammatory disease (crude rate, 0.16/100 woman-years), and there was no pelvic inflammatory disease among those women who were assigned to hormonal contraception.

Emergency contraception

Emergency contraception is not a form of contraception to be used on regular basis. As condom is recommended to be used on a regular basis for PLH, emergency contraception should be kept only for emergency situations, such as condom breakage.

Emergency contraception can be achieved either by taking a progestin pill (1.5 mg of levonorgestrel) as soon as possible and not later than 72 hours of unprotected intercourse, or by inserting an IUD up to five days from unprotected sexual intercourse (before the possible implantation of a fertilized egg occurs). According to the 2008 British HIV Association Guidelines for the management of sexual and reproductive health of people living with HIV infection, which quotes a statement of the Faculty of Family Planning and Reproductive Health Care, London [12], the dose of hormonal emergency contraception should be doubled when the woman is taking HAART. There are no studies confirming that the dose increase is required. The Guidelines suggest that perhaps IUD is a more appropriate method for emergency contraception in case the woman is HIV-positive and is on HAART.

Spermicides/microbicides

Last but not least, there is the group of spermicides and microbicides [36, 37]. This is among the oldest groups of contraceptive methods, dating back to ancient Egypt. They are topical agents that can be

applied in the vagina or rectum, either two hours before sexual intercourse or on a daily basis. Spermicides and microbicides are considered one of the female-controlled contraceptive/STD prevention methods which are potentially partner independent.

Nonoxynol-9 (N-9) is the only agent being sold over-the-counter for the prevention of pregnancy and STDs. It kills spermatozooids and different bacterial and viral pathogens, causing STDs. N-9 is quite effective against the HIV in vitro, but it damages the vaginal epithelium and can in fact increase the infectiousness of the surviving HIV in vivo. N-9 is therefore not recommended for use in HIV-positive women and high-risk HIV-negative populations [38].

At present over 50 chemical molecules are being studied, in different stages of clinical development, for the prevention of HIV infection and other STDs, and eventually some of them of pregnancies. In early 2009, there was much excitement in the microbicide research field on the results of the HPTN 035 in 3000 women that showed a 0.5% PRO 2000/5 Gel was 36% protective against HIV compared to no gel [39]. However, in December 2009, the MDP 301 trial in over 9000 women by the UK-based Microbicides Development Program announced their results showing no evidence that PRO 2000 significantly reduced the risk of HIV infection in women [40]. According to the Microbicidal Trial Network [41], this study marks the end of investigations focused on the early generation, novel nonspecific microbicides. The new hope is agents with specific action against HIV, such as antiretroviral drugs. There are already several ongoing trials with Tenofovir gel.

Conclusion

Addressing the sexual needs of PLH is a complex undertaking primarily due to the need to protect against HIV/STD transmission as well as unintended pregnancy. There are over 30 million PLH worldwide, and approximately half of them are women in reproductive age. There are also millions of HIV-positive children in the world who will soon be young adults and start sexual relationships. All of them can benefit from improved reproductive health services.

Health professionals are becoming more aware of the need to provide sexual health advice, contraception and protection against HIV/STD transmission to PLH and their HIV-infected and uninfected partners. Male condom remains the principal barrier method recommended for the majority

of PLH to prevent STD/HIV transmission and unintended pregnancy. One additional highly effective contraceptive method (sterilization, hormonal contraception, or IUD) is recommended for the prevention of unintended pregnancies. Each of these highly effective contraceptive methods has its benefits and risks regardless of HIV infection and there are currently no data to favor one method over another. Use of hormonal contraception, in particular, may cause more concerns in PLH due to potential drug interactions with antiretrovirals and metabolic adverse events. Health professionals should therefore be able to give adequate information to PLH on the pros and cons of each method, so that they can take an informed decision based on their lifestyle, sexual activity, reproductive history, and future fertility plans. Many questions remain to be answered. Therefore, it is important that studies of different methods of contraception in PLH continue.

The authors have no conflict of interest to declare.

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