GUIDELINE

GUIDELINE ON SAFER CONCEPTION IN FERTILE HIV-INFECTED INDIVIDUALS AND COUPLES

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Ninety years ago the isolation of insulin transformed the lives of people with type 1 diabetes. Now, models based on empirical data estimate that a 25-year-old person with HIV, when appropriately treated with antiretroviral therapy, can expect to enjoy a median survival of 35 years, remarkably similar to that for someone of the same age with type 1 diabetes. It is high time we normalised the lives of people living positively with HIV. This includes the basic human right to conceive and raise children. HIV-positive individuals may be in serodiscordant relationships or in seroconcordant relationships. As health care providers, it is our responsibility to ensure we understand the opportunities and risks of natural conception in these scenarios, so that we can help our patients to make informed decisions about their own lives. Most of all, it is our duty to make family planning in the setting of positive prevention as safe as we can. This includes informed decisions on contraception, adoption, fostering, conception and prevention of mother-to-child transmission.

Some months ago a dedicated group of individuals, invited and sponsored by the Southern African HIV Clinicians Society, came together in Cape Town to devise guidance in this area, recognising that there are ideal strategies that may be outside the realm of the resource constraints of the public sector or health programmes in southern Africa. This guideline therefore attempts to provide a range of strategies for various resource settings. It is up to us, the providers, to familiarise ourselves with the merits/benefits and risks of each, and to then engage patients in meaningful discussions. All the above, however, is based on the premise and prerequisite that the subject of family planning is actively raised and frequently discussed in our patient encounters.

1. INTRODUCTION

Across South and sub-Saharan Africa, the vast majority of HIV-positive individuals are adults of reproductive age. Before universal access to effective antiretroviral therapy (ART), traditional medical wisdom generally discouraged childbearing because of the risk of HIV transmission (both to uninfected partners and from mother to child) and the reduced survival of infected parents and children. In the era of ART, HIV/AIDS has come to be viewed as a manageable chronic illness. In addition to leading to dramatic reductions in morbidity and mortality of HIV-infected parents, use of highly active antiretroviral therapy (HAART) in Europe and North America has driven the virtual elimination of paediatric HIV infection, and in southern Africa PMTCT programmes have greatly reduced paediatric infections.[1]

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Although many patients feel uncomfortable discussing it with their health care providers, many HIV-infected adults are sexually active. In advanced HIV infection fertility is reduced, but the incidence of pregnancy increases with ART initiation,[2] through increased sexual activity and attitudinal changes in hopes and desires for the future. South Africa has an estimated 1 million births annually, and an estimated 29% of these occur in women living with HIV. Other southern African countries have similar antenatal HIV prevalence rates. A substantial proportion of these pregnancies are unplanned, despite effective contraception being a critical component of the prevention of mother-to-child transmission (PMTCT) of HIV/AIDS programme. However, many HIV-infected women and men want to have children, either immediately or at some time in the future. Reproduction is a basic human right,[3] and for many women having a child is part of their life plan. Indeed, in many parts of southern Africa being without a child attracts significant stigma.[4]

In this context, dealing with issues of fertility and childbearing should be seen as part of routine HIV care. Clinicians are responsible for identifying and supporting the fertility desires of their HIV-infected patients – both in the interests of 'normalising' the lives of people living with this chronic infection, and to help ensure that conception, pregnancy and delivery take place with the least possible risk to the mother, her partner, and the resulting child.

This consensus guideline for the Southern African HIV Clinicians Society has been formulated through a process of consultation with the South African health services in mind. It is designed to assist clinicians to identify patients' fertility desires, and to give safe and effective conception guidance to a presumed fertile couple where one or more partners are HIV infected. We have considered 'resource-intensive' clinical settings, such as the private sector, where technologically advanced assisted reproduction technologies may be available, as well as 'resource-limited' settings such as most public sector health facilities across the region. It is understood that these two levels are often not clearly demarcated, and it is recommended that providers should become familiar with which services documented here are available to patients in their setting. While we present the optimal management for safest conception, there is recognition that state-run and resource-limited clinical settings may not yet facilitate or fund these interventions. In these cases we have attempted to quantify the increased risk that not meeting these standards would incur for your patient. While specialist referral is not contraindicated for those couples in whom one or both partners are suspected of having compromised fertility, these advanced fertility interventions will not be covered in these guidelines.

The guideline is divided into three sections. The first section discusses how the clinician can raise the issue of childbearing and help identify the fertility desires of HIV-infected women and men, with a brief discussion on contraceptive strategies for women who do not wish to become pregnant. The second part focuses on the management of individuals and couples who do desire a pregnancy, with emphasis on the management of HIV disease and co-morbidities before attempting conception. This includes specific conception strategies for HIV-seroconcordant positive couples and serodiscordant couples. Finally, several key issues are discussed, and a series of illustrative scenarios have been appended to the guideline to assist with their understanding and implementation.

The guideline has been devised with an eye on international norms but also with a keen view to local resource issues. The change in the natural history of HIV infection and reduction in MTCT as a result of ART has led to a re-evaluation of the ethical and moral arguments previously used to deny assisted reproduction to HIV-infected patients. Increasingly, parenting is regarded as a realistic option for couples where one or both partners are infected, and the demand for reproductive management is rising. It is also imperative to provide some measure of protection to both the uninfected partner and the uninfected fetus. This guideline attempts to provide some pointers to how this can be done more safely in the southern African context.

2. DISCUSSING FERTILITY AND CHILDBEARING WITH HIV-INFECTED WOMEN AND MEN

The first step towards addressing the issues of fertility and childbearing is to regularly and repeatedly raise these with HIV-infected patients, to understand their desires and related health care needs (Fig. 1). Issues about fertility choices should be discussed with both

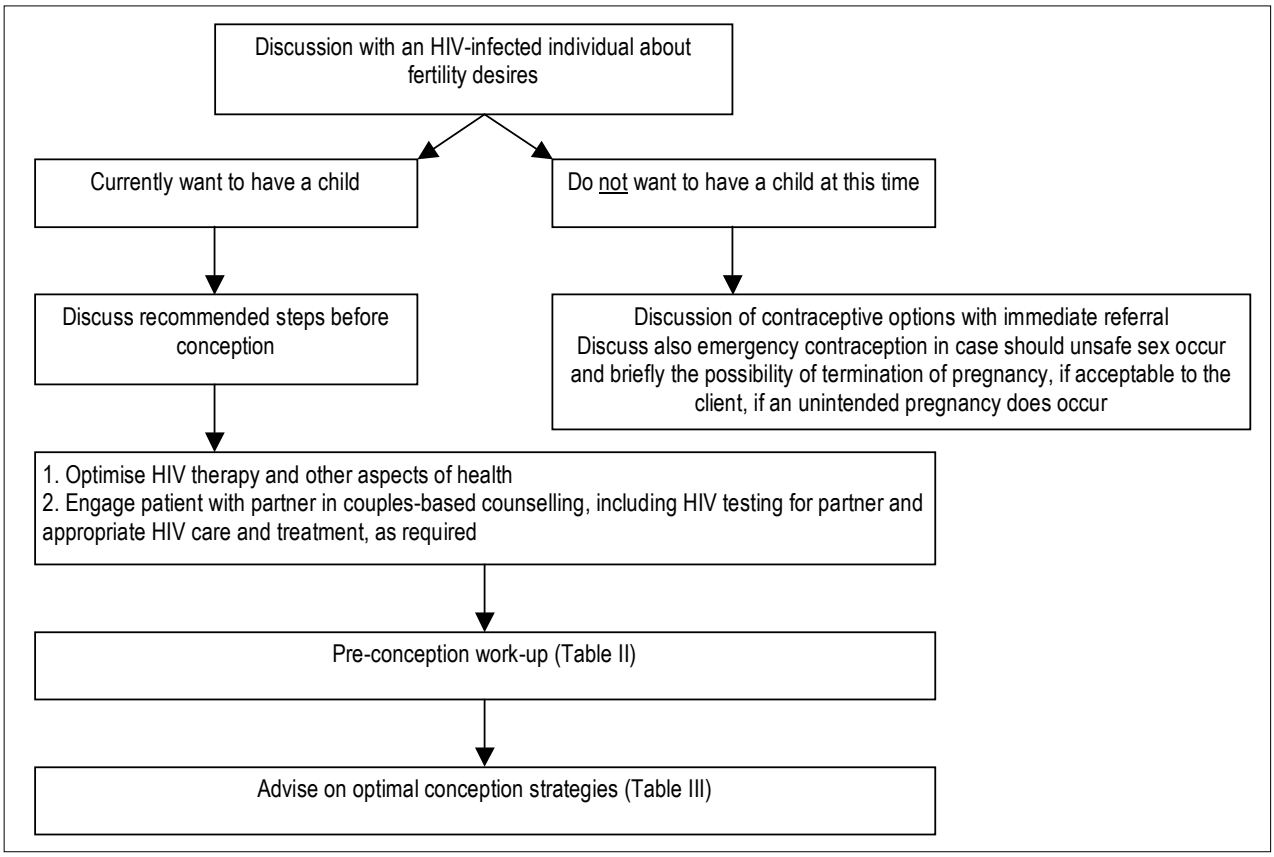


Fig. 1. Flow diagram to approach pregnancy-related issues in HIV-infected women and men.

men and women, and men should be encouraged to bring their partners in for further consultation should this be appropriate. Local research demonstrates that the majority of individuals attending HIV care and treatment services have never had an open discussion about fertility and childbearing with their health care providers.[5] When these discussions do take place, patients report that the tone is strongly judgemental – often discouraging individuals from childbearing regardless of their desires – with an exclusive focus on the need for contraception and condom use.[6]

Ensuring that patients have a basic understanding of HIV transmission and conception is fundamental to safer conception in HIV. Basic information for this can be obtained online in 'Pregnancy in our lives' at http//www.tac.org.za/community/files/file/TreatmentLit/2010/PregnancyInOurLivesEnglish2010.pdf

To introduce this topic, the health care provider may find the following discussion points useful and informative:

- the number of living children, the age of the patient's youngest child, and/or the number of other children the patient may help to care for, and how easy or difficult they find their child care responsibilities
- the health of their existing children, including whether any child is HIV infected
- the partnership status of the patient, the number of children the patient has with their current partner, and perceptions of a partner's desires.

Because of the stigma around sexual activity and pregnancy for HIV-infected individuals, raising issues of fertility and childbearing can be sensitive for many patients. In these discussions, the use of 'normalising' statements – for instance, pointing out that many other patients are grappling with these issues – may help patients to feel comfortable expressing their own thoughts and opinions.

Typically discussions will focus on female patients, but it is critical to note that male partners can have a strong influence on women's fertility-related desires and decisions. These issues are often highly relevant for male patients, and local studies have shown that HIV-infected men are at least as likely as women (often more so) to want another child.[7] Male or female patients may wish to return with their partners to discuss fertility and related issues with the health care provider, and we strongly recommend a couples-based approach to these issues (see below).

Throughout this discussion, the objective of the provider should be to assist patients in arriving at their own informed choice about their fertility desires. Key aspects of information that providers may share which can help the patient arrive at an informed decision include: the patient's current health status and their prognosis; their age; the possibility of HIV transmission if the partner is HIV negative; and the probabilities of having an HIV-negative child given appropriate interventions. Other topics the provider may raise with a patient include: current versus desired family size; partner, family and community influences on fertility desires; whether any existing children are HIV infected; and the current and future resources required in caring for a child. These discussions may include an evaluation of some of the alternatives to childbearing, including adoption (Box 1).

BOX 1. OTHER OPTIONS TO CONSIDER IN MAKING A DECISION AROUND FERTILITY AND CHILDBEARING

In discussing the desire to have a child with HIV-infected women and men, there are several potentially useful options that patients may not be aware of. These include:

- An HIV-infected male partner may consider HIV-negative sperm donations from an HPCSA-accredited facility in South Africa (appropriate accreditation bodies should be sought in other southern African countries), or in low-resource settings from an HIV-negative man.
- Adoption may be possible through an approved facility, or through a social worker. Note that chronic illnesses (including HIV) are not a contraindication, provided the illness is well controlled and the adopting parents are relatively healthy.
- Surrogacy may be an option (i.e. another woman carries the pregnancy for the couple), but this would only be acceptable if the male partner is HIV negative. Surrogacy is not widely practised in South Africa.
- Not to have or formally adopt a child, but to focus on becoming more involved in the care of children in the family or community.

Ultimately these discussions should help to identify the patient's current fertility intentions, which in turn indicate various possible health care interventions. Specifically, providers should encourage patients to decide between:

(a) wanting to become pregnant immediately (i.e. actively trying to conceive), versus
(b) not wanting a child now, but considering a possible pregnancy in the future, versus
(c) the desire to not become pregnant at all.

For patients who remain unsure of their choice, option (b) above (not wanting a child in the present, but reserving the possibility of a child in the future) may be a useful default position, as it holds options open and seeks to emphasise that individuals' fertility intentions may change over time. For example, an HIV-infected woman who does not want a child at present may decide to have a child in the future. Or, a couple who wants a child at present, and has one, may decide afterwards that they do not want more children. As a result, it is important to raise issues of fertility and childbearing at regular intervals during the course of chronic HIV care, even if these are brief discussions to confirm previous decisions. Briefly documenting the discussions between patient and provider can be useful as a reference for future consultations and as a cross-reference in a busy public sector clinic.

3. CONTRACEPTION FOR THE HIV-INFECTED INDIVIDUAL OR COUPLE WHO DOES NOT WANT A CHILD

While this guideline focuses on the needs of individuals and couples who wish to conceive, local research suggests that the majority of HIV-infected individuals are not actively trying to conceive and do not at present want a child.[5,6] HIV care and treatment services are ideally suited to address family planning needs.[8] A range of detailed resources are available on appropriate contraception among HIV-infected women and men (see references). However, a few key points emerge from the literature on this subject.

First, there are a number of effective contraception options that may be used safely by patients living with HIV.[9] Choices may be somewhat restricted in the public sector to barrier methods (such as male and female condoms), injectable progestins and combined oral contraceptive pills. Although availability in the public sector may be limited, intra-uterine contraceptive devices (both copper IUCDs and progesterone IUCDs) are very effective long-acting methods that can be used safely in HIV-infected women, and their use deserves further attention. Male or female sterilisation should be considered for individuals or couples who are certain that they do not wish to become pregnant in the future. In making recommendations about which method to recommend, the efficacy of the different methods should be considered. If a woman is unwell and a pregnancy could impact on her health, a highly effective method should be recommended. If she does not want to use these methods and an unplanned pregnancy would not be a problem, the condom should be considered.

Table I shows the relative effectiveness of the common contraceptive methods, the safety of using each method in HIV-infected women, and whether there is any increased risk of transmission to partners.

HIV-infected women will have the same general contraindications to use as the general population of women.[10]

For women who can negotiate condom use, we strongly recommend that all patients who require effective contraception be advised to practise dual method use – the concurrent use of a highly effective contraceptive method and a male or female condom. Because of the relatively high failure rates of condoms, this approach should be recommended even to women who report consistent condom use. Women who do not currently want a pregnancy but are reluctant to use contraception should be offered contraceptive counselling at every subsequent opportunity.[10,11]

4. THE HIV-INFECTED INDIVIDUAL OR COUPLE WHO WANTS A CHILD

A significant proportion of HIV-infected individuals will desire a child, and may be actively trying to conceive at the time of a clinical consultation. In consulting these individuals, there are several important considerations that the HIV clinician should keep in mind.

Natural conception – unprotected intercourse. The risks of HIV transmission depend on HIV plasma viral load, the presence of sexually transmitted infections, and the length and frequency of exposure.

TABLE I. EFFECTIVENESS OF THE COMMON CONTRACEPTIVE METHODS, AND THEIR SAFETY IN HIV INFECTION

Method	Failure rate/100 woman-years	Impact on disease progression	Increased HIV transmission to partner	Impact on HAART or tuberculosis treatment
Oral combined oral contraceptive	0.2 - 3	No conclusive evidence of harm: can use	No conclusive evidence of harm: can use	Drug interaction with some NNRTIs: do not use Drug interaction with rifampicin and related TB drugs: do not use
DMPA and NET-EN (injectable progestins)	0 - 2	No conclusive evidence of harm: can use	No conclusive evidence of harm: can use	HAART: can use, no need to increase dose or injection frequency TB drugs: can use, no need to increase dose or injection frequency
Male condom	Careful use: 0.4 - 8 Typical use: around 10	None: may prevent re-infection	Barrier method protects partner	N/A
Female condom	Careful use: 5 Typical use: 21	None: may prevent re-infection	Barrier method protects partner	N/A
Copper IUCD	0.1 - 0.3	Evidence on safety reassuring: can use	Limited evidence but reassuring: can use	No interactions
Levonorgestrel IUCD 20	0.1 - 0.3	Limited evidence of safety reassuring: can use	Little evidence but extrapolating from Cu IUCD can use	No interactions
Male and female sterilisation	Female 0 - 0.5 Male 0 - 0.2	No evidence but unlikely: can recommend	No evidence but unlikely: can recommend	N/A

NNRTI = non-nucleoside reverse transcriptase inhibitor.

The impact of HIV viral load. Plasma HIV-1 ribonucleic acid (RNA) levels can be correlated with the sexual transmission of HIV. Viral load is the single greatest risk factor for all transmission modes. ART reduces the plasma and genital HIV viral load in the infected individual to undetectable levels.[12] In a study of 415 HIV serodiscordant couples in Uganda, 21.7% of initially uninfected partners became infected over 30 months of follow-up, translating to a transmission rate of approximately 12 infections per 100 person-years.[13] No transmission events occurred in couples in which the infected partner had a plasma HIV-1 RNA level of less than 1 500 copies/ml, and the transmission risk increased as plasma HIV-1 RNA levels increased. For every 10-fold increase in viral load, there was a >2-fold risk of transmission. Plasma HIV-1 RNA levels generally correlate positively with the concentration of HIV in genital secretions, rectal mucosa and saliva, although inflammation can stimulate local replication.[14] Other studies have shown that transmission events may be observed at a very low plasma HIV-1 RNA level, suggesting that plasma HIV-1 RNA level is not the only determinant of transmission.[15,16] These data suggest that transmission probability drops markedly in people with naturally controlled viral loads or with ART controlled viral loads.[15,16]

Clinical research in discordant couples. Findings from a large multinational clinical study conducted by the HIV Prevention Trials Network (HPTN) recently showed that men and women infected with HIV reduced the risk of transmitting the virus to their sexual partners through initiation of oral ART. The study, known as HPTN 052, was designed to evaluate whether immediate versus delayed use of ART by HIV-infected individuals would reduce transmission of HIV to their HIV-uninfected partners and potentially benefit the HIV-infected individual as well. Findings from the study were reviewed by an independent Data and Safety Monitoring Board (DSMB). The DSMB concluded that initiation of ART by HIV-infected individuals substantially protected their HIV-uninfected sexual partners from acquiring HIV infection, with a 96% reduction in risk of HIV transmission.[17]

So what are the risks for natural conception and unprotected intercourse? One of the difficulties in counselling serodiscordant couples on natural conception methods involving unprotected intercourse is that the risk to the uninfected partner is difficult to quantify, but can certainly not be quoted as zero. Mathematical models cite a risk of 1 in 100 000 per act of intercourse. In practice, viral shedding in semen has been reported to occur even in men fully suppressed on ART.[18]

A recent retrospective study of 551 semen samples analysed in HIV-1-infected men undergoing sperm washing identified 15 cases of detectable HIV-1 in ejaculated semen in men with a long-term undetectable plasma viral load through use of ART, highlighting a need for caution when couples consider a natural conception approach.[19] In the case of serodiscordant couples where the woman is HIV-positive, the evidence is equally concerning: detectable HIV has been identified in follicular fluid and endometrial samples from a series of HIV-positive women undergoing *in vitro* fertilisation (IVF), even when plasma viral load was suppressed fully through the use of ART.[20]

Three studies have analysed infection risk in serodiscordant couples attempting to conceive naturally. The first was a prospective study conducted before the widespread use of ART and examining the risk of unprotected intercourse timed to the fertile window in 96 discordant couples where the male was infected. Four seroconversions were noted in the female partners, 2 during pregnancy and 2 post partum.[21] The seroconversions were identified in couples in whom condom use after conception and outside the fertile window was inconsistent. A more recent, retrospective study attempted to quantify the risks of unprotected intercourse in discordant couples where the man had an undetectable viral load through use of ART for at least 6 months. There were no seroconversions in 62 discordant couples who conceived.[22] Apart from the small sample size, the study is further weakened by the fact that seroconversions were not analysed in couples who failed to conceive, where the risk might be enhanced by repeated exposures. The only study to prospectively assess viral transmission risk in serodiscordant couples attempting to conceive naturally, where the man was fully suppressed on ART and additional pre-exposure prophylaxis (PrEP) was used in the female partner, involved only 22 couples.[23]

4.1 ENGAGING COUPLES

While we typically see patients in individual consultations, ideally HIV care and treatment services should discuss fertility and childbearing jointly with female and male partners. There are several distinct advantages to a couples-based approach. First, because partnerships have an important influence on fertility decisions, consulting with couples can be useful in helping individuals and their partners arrive at appropriate informed decisions about fertility. Second, the health of both partners is important towards safe conception and pregnancy, and delivering care to both partners may therefore be necessary. Third, if a couple is struggling to conceive, there are specific investigations and interventions for both women and men, and investigating and treating one partner only may lead to suboptimal outcomes. However, this entails disclosure of HIV status between partners, which can be a major challenge. At the minimum, the HIV status of both partners must be known and disclosed in order to manage this process safely and effectively

Despite the importance of a couples-based approach, there are circumstances where an individual desires a child but does not know the serostatus of their partner, or desires a child in the absence of a regular partner or a partner who is willing or able to attend the clinic. These situations present particular challenges (see 'Special issues', below).

WHAT SHOULD BE COVERED IN PRECONCEPTION COUNSELLING?

Preconception counselling should ensure an informed choice about reproductive options, including the inherent risks and costs of each treatment and the likely chances of success.

It must include:

- a summary of the available data on safety for each method together with advice on additional methods of reducing risk, such as limiting intercourse to the fertile window, or early initiation of ART
- regular screening for sexually transmitted infections
- the need to identify evidence of reduced fertility or sterility at an early stage in either or both partners
- the possible use of pre-exposure prophylaxis.

The discussion should balance the risk of natural conception with that of more established risk-reduction methods such as sperm washing or risk-free options such as donor insemination. Although timed unprotected intercourse may be the only option for discordant couples in resource-limited settings, this has risk.

Preconceptual counselling should also address:

- The possibility of treatment failure and how the couple would cope if they successfully had a child but the infected parent became more seriously ill or died.
- Those electing to have assisted conception with sperm washing have to understand that this is a risk-reduction method and not a risk-free method.
- When the female partner is HIV-positive they need to understand the risks of MTCT and the methods used.
- They should plan and agree to attend an antenatal clinic once pregnant to ensure that they receive the best possible advice to minimise MTCT risk.

4.2 OPTIMISING HIV THERAPY AND ADDRESSING OTHER HEALTH CONCERNS

As with any chronic condition, optimising the health status of an HIV-infected couple prior to conception is an important step both to facilitate conception and help ensure a safe pregnancy. In the case of HIV, this means:

4.2.1 Documenting the HIV status of both partners. The recommended strategies to conceive vary depending on the serostatus of both partners, with key differences in optimal strategies for HIV-seroconcordant positive couples, and for HIV-serodiscordant partners (where either the male or female partner is HIV infected). HIV counselling and testing is a prerequisite if the HIV status of both partners is not known.

4.2.2 Identifying and managing co-morbidities. This includes HIV-related co-morbidities, most notably opportunistic infections such as tuberculosis (TB), as well as other medical conditions that may influence the pregnancy, such as epilepsy or diabetes. For conditions with short-term management (e.g. TB or acute infections), we recommend delaying attempts at conception until treatment is completed. For chronic conditions that will require treatment throughout pregnancy, it is necessary to avoid potentially teratogenic medications and ensure optimal management before proceeding.

4.2.3 Determination of health status for HIV-infected partners. All HIV-infected patients should undergo thorough clinical assessment and have a CD4 count to determine eligibility for ART before conception. In settings where viral loads are available, these should be included as part of this work-up. However, it should be noted that an undetectable plasma viral load does not necessarily mean that there is an undetectable viral load in the genital tract.

4.2.4 ART initiation as appropriate. Given the benefits of ART in reducing viraemia and reducing the risk of HIV transmission (in addition to its benefits for adult health), ART initiation in eligible individuals and optimisation of appropriate therapy is necessary before proceeding. Ideally, given the data above, any HIV-infected patient wishing to conceive and therefore contemplating unprotected sex should have an undetectable viral load before doing so. This would imply ART for at least 3 - 4 months prior to sexual intercourse. World Health Organization (WHO) guidelines and a number of southern African countries have adopted short-course HAART for PMTCT regardless of CD4, stopping after delivery in women whose baseline count was >350 cells/µl and in whom formula feeding will be implemented, and after cessation of breastfeeding in those women who choose to do so. While current South African national guidelines call for ART initiation in pregnant women with CD4 cell counts <350 cells/µl, clinicians should consider the initiation of ART in a non-pregnant woman with a CD4 count of <350 (ideally this should be <550) cells/µl who is attempting to conceive. It is hoped South African PMTCT guidelines will adopt the strategy of HAART for all pregnant women, continuing HAART for maternal health in women with CD4 <350 cells/µl, and cessation of HAART after pregnancy or breastfeeding in women in whom CD4 counts are >350 cells/µl depending on the infant feeding method of choice. Care is needed in the selection of regimens preconception and in pregnancy, and the risks and advantages of using any antiretroviral with potential teratogenicity (such as efavirenz (EFV)) should be considered in the first trimester. In discordant couples where the man is infected, similar consideration should be given to initiating ART with CD4 counts of >350 (ideally 200 - 550) cells/µl if he and his negative partner are trying to conceive. It is hoped that with the HPTN 052 results[17] (HIV acquisition was reduced by 96% in discordant heterosexual couples where the HIV-infected partner commenced ART at CD4 levels between 350 and 550 cells/µl compared with those in whom it was commenced at 250 cells/µl or with onset of AIDS), the recommendations above can be modified to that described as 'ideal'.

For an ART-eligible HIV-infected woman who conceives while not on ART (and may be diagnosed in pregnancy), therapy should be initiated as soon as possible using pregnancy-friendly regimens (at least by the end of the first trimester), as the duration of ART received during gestation is an important determinant of MTCT risk.[24] For women who are not ART eligible (do not need ART for their own health), PMTCT interventions, focusing on short-course antiretroviral prophylaxis regimens according to national PMTCT guidelines, should be initiated when appropriate (see Box 2). Suggested pregnancy-friendly regimens would include a boosted protease inhibitor (PI) in the first trimester (if the CD4 count is >250 cells/μl) or an EFV-based regimen after the first trimester. A nevirapine-based regimen can be used throughout pregnancy if the starting CD4 count is <250 cells/μl.[25]

BOX 2. PRINCIPLES OF REDUCING MOTHER-TO-CHILD HIV TRANSMISSION

This is not intended to be a comprehensive guide to PMTCT. Please see the reference below for details.

- Ideally all HIV-infected women should already be on ART as part of preconception management; this should be continued throughout pregnancy and breastfeeding.
- If a woman is not on ART, initiate ART as soon as possible irrespective of CD4 cell count, using the appropriate antiretrovirals to avoid teratogenicity, and reduce side-effects and pill burden.
- Women with a baseline CD4 cell count ≤350 cells/μl should continue ART indefinitely for their own health.
- Women with a CD4 cell >350 cells/μl who elect to breastfeed should continue ART until the baby is weaned.
- Women with a baseline CD4 count >350 cells/μl may discontinue ART after delivery.
- In situations where the above cannot be applied, local PMTCT guidelines should be followed.

Additional reading

National Department of Health. The South African Antiretroviral Treatment Guidelines 2010 (2010). http://www.doh.gov.za/aids/index.html

4.2.5. Optimisation of ART. For male or female partners who are either initiating or already established on ART, evidence that therapy is optimised is required before attempting to conceive. This should include evidence of high levels of adherence and immune recovery, and preferably documented virological suppression for at least 4 - 6 months.

4.3 PRECONCEPTION WORK-UP

Table II shows recommended basic investigations that may be undertaken in primary care facilities in the preconception work-up of an HIV-infected couple who desires a child, with adaptations for resource-limited and resource-intensive settings. At a minimum, all women should receive HIV-related investigations as well as syphilis screening, haemoglobin measurement, and physical examination with visual inspection of the cervix for abnormalities and for signs of sexually transmitted infections. Consider a Papanicolau smear (Pap smear) in resource-intensive settings; this may be extended to include a full screen for TORCH infections (congenital infections: toxoplasmosis, rubella, CMV and herpes simplex and other congenital infections) and viral hepatitis, a Pap smear, and a full blood count.

In resource-intensive settings, patients who are struggling to conceive may be referred to specialist fertility services for further work-up, including assessment of luteinising hormone levels in women and sperm assessment in men. Couples found to be non-fertile may be candidates for assisted reproductive technologies.

4.4 SAFER CONCEPTION STRATEGIES

The tools at our disposal to make conception safer in seroconcordant and serodiscordant couples now include (some are proven, some experimental, and they are not listed in any particular order):

- HAART and viral load suppression in the positive partner(s)
- timed, limited, peri-ovulatory, unprotected sex
- intra-uterine insemination
- intravaginal insemination
- male circumcision
- sperm washing

TABLE II. PRECONCEPTION WORK-UP FOR HIV-INFECTED INDIVIDUALS DESIRING A CHILD IN RESOURCE-INTENSIVE AND RESOURCE-LIMITED SETTINGS

	Female partner	Male partner
Resource-intensive strategy	CD4, HIV viral load, hepatitis serology (A); investigations for syphilis, CMV, rubella, HSV, toxoplasmosis; full blood count; Pap smear If on HAART preconception, adaptation of regimen as needed; ensure undetectable HIV Viral load in blood *If difficulty conceiving:* lutenising hormone, referral for fertility assessment	CD4, HIV viral load, syphilis serology; laboratory investigations for other sexually transmitted infections If on HAART preconception, ensure undetectable HIV viral load in blood *If difficulty conceiving:* referral for sperm assessment; fertility assessment
Resource-limited strategy	CD4, syphilis serology, clinical assessment for other sexually transmitted infections; haemoglobin; visual inspection of the cervix ART and undetectable viral load also strongly advised	CD4, syphilis serology; clinical assessment for other sexually transmitted infections ART and undetectable viral load also strongly advised

CMV = cytomegalovirus; HSV = herpes simplex virus.

- surrogate sperm donation
- post-exposure prophylaxis (PEP) in the negative partner
- PrEP in the negative partner.

It is important to note that in deciding which strategies to use for safer conception while in an HIV-positive seroconcordant or discordant relationship, resources, risk and preference may play a role for both the patient and the provider.

Table III shows the recommended conception strategies for serodiscordant and HIV-infected seroconcordant couples, stratified for resource-intensive and resource-limited settings. In all cases where unprotected sex with a positive partner or vaginal insemination with potentially infected semen is considered, both partners should be counselled about the risk of transmission and measures such as ART or prophylaxis, male circumcision, sperm washing and donor insemination. Which of these options are utilised will be determined by available resources

TABLE III. OPTIMAL CONCEPTION SUPPORT STRATEGIES FOR RESOURCE-INTENSIVE AND RESOURCE-LIMITED SETTINGS, ACCORDING TO THE HIV STATUS OF THE COUPLE

	Seroconcordant (male and female HIV infected)	Serodiscordant (male HIV infected)	Serodiscordant (female HIV infected)
Resource-intensive strategy			
Female partner	If on HAART preconception, adaptation of regimen as needed; ensure undetectable HIV viral load in blood; no use of efavirenz in the first trimester among HIV-infected women trying to conceive Conception: consider sperm collection with intra-uterine insemination; self-insemination possible; peri-ovulatory unprotected sexual intercourse only in the face of demonstrated undetectable viral loads If not on HAART preconception, maternal HAART initiation as soon as possible with appropriate regimen	Repeated HIV PCR testing before pregnancy Conception: undectable viral load preferable; sperm washing and intra-uterine insemination Repeated HIV PCR during pregnancy with appropriate management if female partner becomes infected	If on HAART preconception, adaptation of regimen as needed; ensure undetectable HIV viral load in blood Conception: sperm collection with intra-uterine insemination If not on HAART preconception, maternal HAART initiation early in the second trimester
Male partner	Preconception HAART until un-detectable HIV viral load in blood and semen	Preconception HAART until undetectable HIV viral load in blood, semen Conception: sperm assessment; sperm washing with HIV PCR	Ongoing HIV testing; male medical circumcision where appropriate, especially if couple choose peri-ovulatory unprotected sexual intercourse for conception
Resource-limited strategy			
Female partner	If on HAART preconception, adaptation of regimen as needed; ensure high levels of adherence and CD4 monitoring; no use of efavirenz in women trying to conceive Conception: consider sperm collection with self-insemination; peri-ovulatory unprotected sex possible under safe conditions. This would include undetectable viral loads if possible, timed sexual intercourse and limited exposures (see text) If not on HAART prconception, maternal PMTCT initiation asap with appropriate antivirals	Repeated HIV antibody testing before pregnancy Conception: unprotected sex during the fertile period (preferably while on ART with viral load control) Repeated HIV antibody testing during pregnancy with appropriate management if female partner becomes infected Consider use of mono- or dual-therapy PrEP	If on HAART preconception, adaptation of regimen as needed; ensure high levels of adherence and CD4 monitoring; consider ART for conception and pregnancy regardless Conception: sperm collection with self-insemination at the time of ovulation (avoiding spermicide-containing condoms) If not on HAART preconception, maternal PMTCT initiation as soon as possible with appropriate regimen
Male partner	If required, preconception HAART for at least 6 months with intensive adherence support and CD4 monitoring and viral loads monitoring	If required, preconception HAART for at least 6 months with intensive adherence support and CD4 and viral load monitoring	Ongoing HIV testing; male medical circumcision where appropriate, especially if couple choose peri-ovulatory unprotected sexual intercourse for conception

PCR = polymerase chain reaction.

and will determine the level of risk of transmission. Where unprotected exposure is embarked upon this should be in the presence of reasonable expectations for fertility, e.g. no evidence of reduced ovarian reserve or tubal damage, and no more than 6 - 12 cycles of peri-ovulatory sex should be performed unsuccessfully without considering referral for infertility investigation.

4.4.1 Seroconcordant positive couples. In resource-limited settings, sperm conception with self-insemination may be considered. Limited peri-ovulatory unprotected sex is a feasible approach to insemination, although both partners must acknowledge the potential risks associated with superinfection, and have a good understanding of how to time intercourse to the peri-ovulatory window (see Box 3). Superinfection occurs when an already infected individual becomes 're-infected' with another strain of HIV that may or may not be drug sensitive. This is thought to be more common than first thought, although there are few case series. A study in Kenyan sex workers quantified the incidence at 4% per annum.[26] The implications may include increased viral load in someone not on therapy, or infection with a drug-resistant virus in someone who is. Ideally, even in resource-limited settings this risk can be further reduced in seroconcordant couples by ensuring viral load suppression during conception in both partners and self-vaginal inception. In resource-intensive settings, optimal conception may take place under the supervision of a specialist in reproductive medicine. In such contexts, sperm collection and intra-uterine insemination may be optimal. As discussed above, in all settings ART-eligible individuals should be stabilised on optimal therapy prior to conception.

BOX 3. HOW TO DETERMINE A WOMAN'S FERTILE PERIOD

When a couple is living with HIV and attempting conception, determining a woman's fertile period is necessary to time peri-ovulatory intercourse. There are various ways in which a woman's fertile period can be determined. The methods described here presume normal fertility and require minimal resources.

In situations where a woman's fertility may be impaired, more resource-intensive methods (such as day 21 progesterone measurements or serial ultrasound monitoring, with or without ovulation stimulation – clomiphene administration is usually performed in consultation with specialist services) may be used by a reproductive specialist. These more intensive methods may also be used in women living with HIV (who has presumed normal fertility) in order to increase her chance of fertility prediction.

Fertile dates

The average normal duration of a menstrual cycle is 28 days. The first day of a woman's menstrual period is considered to be day 1 of her menstrual cycle. Ovulation is assumed to occur half way through her cycle. Her fertile period would be from 5 days before predicted ovulation up until 1 - 2 days after ovulation. For example, in a woman whose cycle is 28 days long, this would mean that ovulation would be assumed on day 14. The woman's fertile period would therefore occur between days 9 and 16 of her menstrual cycle.

However, menstrual cycle length may differ considerably between women and may even differ from month to month for an individual woman. It is therefore essential that a woman keeps record of her menstrual cycle (typically taking into account the first day of her menstrual period) for at least 4 months in order to determine an average menstrual cycle length. It is important to explain to patients that regular menstrual cycles may not necessarily indicate that ovulation has occurred.

Ovulation prediction kits (for urine and saliva)

A number of over-the-counter products are available that enable ovulation prediction. These methods may utilise sampling and analysis of either urine or saliva, and detect the surge of luteinising hormone that occurs immediately before ovulation.

Basal body temperature (BBT) charting

A woman's body temperature increases by 0.25 - 0.5 ºC during ovulation. Charting a woman's BBT daily will therefore result in a pattern that may assist her in predicting ovulation. For this method of ovulation prediction to be accurate, it is essential that the woman plots her BBT at the same time every day (preferably between 6 and 8 a.m.), before getting out of bed or drinking or eating anything. Attempt conception after the first rise in BBT has been detected. The chances of conceiving after the 3rd day of raised BBT are greatly reduced.

Cervical mucus monitoring

In addition to BBT, a number of other physiological changes occur around the time of ovulation that may be used to help time intercourse. Cervical mucous changes are used most commonly. During non-fertile days, the cervical mucus is thick and acidic. In contrast, during fertile days, the mucus undergoes a change to become thin, profuse, transparent and 'stretchy' (*spinnbarkeit*). A woman's awareness of these changes in her cervical mucus may help her to predict her fertile period.

4.4.2 Serodiscordant couples where the male partner is infected. When the male partner is positive in a serodiscordant relationship he requires optimal medical therapy, including ART when indicated, to minimise the risk of transmission. In resource-limited settings, both partners should be counselled on the risks of transmission, and limited, timed, unprotected intercourse or sperm collection and self-vaginal insemination (Box 4) may be advised. In this scenario, the HIV-negative female partner requires regular HIV antibody testing throughout pregnancy to detect and manage possible seroconversion as soon as possible. In resource-intensive settings, a serodiscordant couple with a positive male partner is an indication for 'sperm washing' and intrauterine insemination, which affords the possibility of conception with minimal risk of male-to-female HIV

BOX 4. LOW-TECHNOLOGY SPERM COLLECTION AND SELF-INSEMINATION TECHNIQUES

Artificial insemination is the process whereby semen is introduced into the female reproductive tract other than by sexual intercourse. It may be intra-uterine or vaginal, the former being a specialist procedure. The latter is a low-risk procedure that can be carried out by a health care provider or by the patient herself.

It is advisable that vaginal insemination be attempted at the most fertile time in the menstrual cycle, which is approximately 2 weeks prior to menses. In a woman with a regular cycle this can be worked out per calendar, but other methodologies include using an ovulation predictor kit, which is commercially available and measures the LH surge. Other indicators include the quality of the cervical mucus and body temperature.

Semen needs to be provided in a clean receptacle, either by male ejaculation into a condom during intercourse or by male ejaculation into a clean specimen jar provided for the purpose. The semen (most men ejaculate 3 - 5 ml) should be inseminated as soon as possible.

Other equipment to carry out the vaginal insemination would include a 'turkey baster' (!), 5 ml plastic syringe or plastic discardable pipette. These items should be supplied to prospective female patients along with the instructions in the appendix.

transmission. PEP/PrEP may also be considered in this setting as protection for the HIV uninfected female partner although this is unproven (see later).

4.4.3 Serodiscordant couples where the female partner is infected. When the female partner is positive in a serodiscordant relationship, there are a wider range of options. It is beneficial for the uninfected male to have been circumcised. If he undergoes a male circumcision procedure, this should be at least 2 months before considering unprotected sex. With the woman's HIV management optimised (viral load undetectable on ART), couples in resource-limited settings may attempt timed peri-ovulatory unprotected sex with appropriate counselling on the risks of transmission. In this case, the male partner may benefit from PrEP or PEP and at the very least will require ongoing HIV testing to identify possible seroconversion. However, it is preferable and feasible to collect the semen of the uninfected male partner and perform vaginal self-insemination around the time of ovulation, thus avoiding the risk of female-to-male transmission. This procedure can easily be taught to the female partner and can be performed with ease in her own home. In addition, if a freshly collected seminal fluid specimen is brought to a clinic, vaginal insemination can easily be performed as a service. In resource-intensive settings, sperm collection and intra-uterine insemination in a female patient with undetectable viral load, would be a preferable option. See Appendix, 'Vaginal artificial self-insemination instructions'.

5. SPECIAL ISSUES

This guideline provides a general approach to safer conception and pregnancy in different situations involving HIV infection. However, there are several potentially common circumstances that are not directly addressed by the strategies described above.

5.1 IS IT EVER APPROPRIATE TO DISCOURAGE PREGNANCY IN AN HIV-INFECTED INDIVIDUAL OR COUPLE?

Ultimately the decision to have a child rests with the patient. However, there are several instances when a clinician may reasonably decide to discourage attempting to have a child. These may include:

- either of the couple has a viral load that cannot be suppressed
- non-disclosure of HIV status to a partner
- documented infertility in either partner
- conditions affecting fertility (although specialist fertility clinics may be able to intervene here)
- medical contraindications, such as active opportunistic/intercurrent infections.

5.2 WHAT IF AN HIV-INFECTED WOMAN DESIRES A CHILD, BUT DOES NOT HAVE A PARTNER?

This raises the question of insemination from alternative sperm sources such as sperm banks, surrogacy and adoption. Should this possibility arise, it is worth knowing what the resources in your area are, what the stipulated eligibilities are and what resources are required for these services. In addition, this situation might be addressed by a sperm donation from a friend, in which case the HIV status of that friend should first be established.

5.3 CAN WE USE PrEP AND/OR PEP TO FACILITATE CONCEPTION WITHOUT HIV TRANSMISSION IN SERODISCORDANT PARTNERS?

PEP for sexual assault survivors has been used for some time, and there is growing interest in PrEP to prevent transmission in serodiscordant partnerships. However, it is important to note that PrEP and/or PEP for discordant couples, initiated before or after sexual intercourse in situations where sperm washing/insemination is not available, have not been validated and could have significant implications for the health of the man, woman or a subsequent child.

While PEP efficacy has not yet been established in a randomised clinical trial, significant data have been collected from cohort studies that suggest that it is an effective intervention. PEP has been recommended for accidental exposure to HIV, either occupational or non-occupational, where the benefits of the medication clearly outweigh the risks. In the case of a serodiscordant couple wanting to conceive, the exposure would be planned. The use of PEP has been reported from a study in men who have sex with men (MSM) in Brazil, who were randomised to take PEP after a risky sexual exposure. The study, conducted by Schecter *et al.*,[27] demonstrated that people have difficulty recognising risk after the fact. This may be due to denial, substance abuse and other factors. Animal models have explored a number of different drug exposures both pre- and/or post-exposure.[28] Current PEP protocols generally state that antiretrovirals have to be given for 28 days after exposure. Some studies have

reported that side-effects related to PEP occur in as many as 77% of users. Currently, then, for every episode of unprotected intercourse, the HIV non-infected partner would take 28 days of antiretrovirals with possible ART-related side-effects.[29]

The evidence for PrEP is also still not well established. The most promising candidate drugs are tenofovir or emtricitabine/tenofovir disoproxil fumarate (FTC/TDF, Truvada). In November 2010, results from a phase III large-scale study, iPrEx, showed that PrEP provided an additional 44% protection from HIV acquisition in men exposed to HIV rectally.[30] The study enrolled 2 499 men and transgender women who have sex with men (who were all at high risk of HIV infection) from Peru, Ecuador, South Africa, Brazil, Thailand and the USA. Half the study subjects were given once-daily oral FTC/TDF and the other half was given a placebo. All subjects received monthly HIV testing and risk-reduction counselling. Among those taking FTC-TDF, 36 became infected with HIV during the trial, compared with 64 in the placebo group.

The FEM-PrEP clinical trial[31] – implemented by FHI in partnership with research centers in Africa – was designed to study whether HIV-negative women who are at higher risk of being exposed to HIV can safely use a daily dose of FTC/TDF to prevent infection. Following a scheduled interim review of the FEM-PrEP study data in March 2011, the Independent Data Monitoring Committee (IDMC) advised that the FEM-PrEP study would be highly unlikely to be able to demonstrate the effectiveness of FTC/TDF in preventing HIV infection in the study population, even if it continued to its originally planned conclusion. The FHI subsequently concurred and has therefore decided to initiate an orderly closure of the study over the next few months. There are a number of possible reasons for the study findings, including low adherence to the study regimen, a true lack of effect of the product among women (v. MSM), or other factors still to be determined.

There is more PrEP research being conducted (Table IV), with the studies on heterosexual transmission being undertaken in Africa in a variety of population groups. There is still much to be learned about effectiveness and real-life implementation, as well as cost-effectiveness.[32]

So what advice can be given to the serodiscordant couple with regard to PrEP? While the results among MSM are promising, and it is likely that PrEP may offer some protection (although whether this will be the case in heterosexual HIV transmission is unknown today), unprotected intercourse with an HIV infected person is never 'no-risk', even if PrEP is partially effective.

6. CASE STUDIES

Case study 1

LM is a 33-year-old woman initiated on EFV, stavudine and lamivudine in May 2005. She responded well to treatment and is currently receiving treatment and care at a down-referral primary health clinic. Her most recent viral load, May 2009, was lower than the detectable limit and her CD4 cell count in January 2010 was 797 cells/µl. She has two children, both over 12 years old, but has no children with her current partner of several years, to whom she has disclosed her status. He is HIV negative.

Initially the patient said that she had no desire to have more children. However, over time she indicated that she and her partner wanted to have a child together. Aside from her ART regimen, she was a good candidate for a safe conception. Upon indicating her intention to conceive, she was referred by study staff for a regimen change. She was told by clinic nurses that a referral was useless as she would need to be up-referred to her initiation site for a regimen change and that up-referrals for regimen changes were not being accepted for planned pregnancies; she should request a regimen change only *after* conceiving. At a subsequent visit on 3 June 2010, the patient had a positive pregnancy test and the same day was up-referred by the primary health centre to her ART initiation site for a regimen change. Upon presenting at the up-referral site with her referral letter, the clinic chose not to accept her back, saying that her current living address was outside their jurisdiction, and referred her elsewhere. The second clinic was willing to receive her, but would not change her regimen or provide an explanation for refusing a regimen change. After 10 weeks of going between clinics the patient was clearly distressed about potential harm that might have been caused to the baby by her current regimen, and after one more failed attempt to receive a regimen change she booked to terminate her planned pregnancy. She had a termination of pregnancy on 25 August, without seeking counselling and discussing her concerns with health care providers or study staff, who might have been able to assuage her fears about the EFV-related risks posed to the baby.

This situation would have been avoided if the patient had: (*i*) received a regimen change when she initially indicated that she was trying to conceive; or (*ii*) failing this, been received by the clinic she was referred to and given an immediate regimen change, as was the expected protocol. Furthermore, had any counselling been provided to her about the actual level of risk associated with EFV-based conceptions, the outcome would probably have been different.[25]

TABLE IV. PrEP RESEARCH IN PROGRESS [32]

Location	Population	Expected completion date
Thailand (CDC)	2 400 injecting drug users	2012
South Africa, Uganda, Zimbabwe (VOICE)	5 000 heterosexual women	2013
Kenya, Uganda (Partners for Prevention)	4 700 serodiscordant heterosexual couples	2013

It is important to note that EFV poses a risk to fetal neural tube development. Neural tube formation occurs at approximately 4 weeks' gestation. The practical point is that unless planned prior to conception, most women on EFV will present after this sensitive time period, making regimen changes both unnecessary and unhelpful. The alternative regimens may be more problematic, e.g. in the case of nevirapine in women with higher CD4 counts (>250 cells/µl), and much more difficult to adhere to in the case of lopinavir/ritonovir (Kaletra). A rule of thumb is not to change unless a pregnant woman on EFV presents at <12 weeks' gestation (first trimester), although one could argue that change is necessary in the case of presentation at >6 weeks.

Case study 2

A nulliparous, 33-year-old HIV-positive woman seeks counselling around safe conception. She had first tested positive for HIV 3 years previously and had been participating in wellness care as her CD4 cell count was still >200 cells/µl. Her partner is HIV positive and on ART. In 2009, the patient's CD4 count was 420 cells/µl. Her most recent CD4 count (June 2010) was 318 cells/µl; a viral load had not been done. The patient desperately wants to conceive, but is worried about MTCT as she is not on ART.

This woman's case is challenging, as she is not indicated to start ART under the national treatment guidelines until her CD4 count drops to 200 cells/µl. However, she is relatively healthy and it may be another year or more before she becomes eligible for ART. The patient understands that as her CD4 count decreases her viral load is rising, and she is worried about a large spike in her viral load around the time of pregnancy if she were to conceive now. On the other hand, if she *were* to conceive, under the new guidelines she would immediately be eligible to start ART as a pregnant woman, since her CD4 count is <350 cells/µl.

What is the best plan of action for this woman if she cannot get started on ART? She can wait for a year or so for her CD4 count to drop and her viral load to spike, start ART and then wait again for another 6 months to achieve virological suppression. At this point she will be 35 and potentially have lowered fertility due to the disease progression and increasing age. Alternatively, she can conceive before ART initiation, with a sub-optimal CD4 cell count and a rising viral load. In this situation she would hope to diagnose the pregnancy as soon as possible, and be initiated onto ART sooner rather than later. The second option allows her to maximise her fertility, particularly now while she is still relatively healthy, but may increase the risk of MTCT and infant mortality, the primary concerns for many HIV-positive women planning to conceive.[14,15] In a resource-intensive setting, the patient would be offered antiretrovirals immediately. There is a potential risk for hypersensitivity and/or hepatotoxicity with nevirapine at a CD4 count of 318 cells/µl. However, EFV is also contraindicated in the first trimester. In South Africa, it would be an option to commence treatment with a boosted PI such as lopinavir or atazanavir. It must be confirmed that both partners are virally suppressed before conception.

WHAT ART IS APPROPRIATE TO USE IN THIS SETTING?

Any woman with reproductive intent who has a CD4 count <250 cells/µl should commence with nevirapine and tenofovir plus lamivudine or FTC. If she is already pregnant and on EFV and presenting in the first trimester, consider changing EFV. If the CD4 count is <250, opt for nevirapine; if >250, opt for a PI, e.g. atazanavir or lopinavir. Note, however, the greater pill burden and possibly greater nausea and vomiting with the latter, especially in the first trimester. If necessary and for simplicity the PI can be changed to EFV in the second or third trimester.

Case study 3

A 24-year-old woman who had been on nevirapine, stavudine and lamivudine since January 2009 indicated that she did not currently want to have any more children. She had a CD4 count of 265 cells/µl and a history of irregular menstrual cycles since HIV diagnosis; she had not menstruated since giving birth 9 months previously. She had a positive pregnancy test during a routine clinic visit in November 2009. She was not prepared for another child and chose to terminate the pregnancy. During her subsequent visit she was encouraged to start family planning, as she indicated that she has difficulty negotiating condom use with her partner. In May 2010, she was diagnosed with a second pregnancy. At this point she went for a second termination of pregnancy in 6 months and was strongly counselled by medical staff to begin using family planning. At her next clinic visit she was still amenorrhoeic. She had a pregnancy test and was given the negative result to present to the clinic nurses in order to initiate an injectable method of family planning. However, she was refused family planning because she was not menstruating. She had a third pregnancy in September 2010.

Amenorrhoea is not uncommon in women, and prolonged amenorrhoea may be more prevalent among HIV-positive women, particularly those with lower CD4 cell counts.[16] Research also suggests that HIV-positive women may be more likely to be ovulating while amenorrhoeic than their HIV-negative counterparts.[17] Policies, whether formally written or just informally followed, to initiate family planning only on the first day of a woman's menstrual cycle are inconvenient for women and result in lower contraceptive uptake and increased rates of unplanned pregnancies. These policies also do not take into consideration HIV-related health concerns, such as an increased risk of amenorrhoea, specific to HIV-positive women. Clear guidelines must be in place to address fertility concerns related to family planning for HIV-positive women.

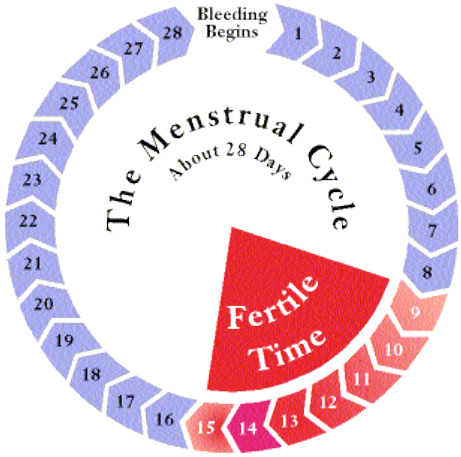
APPENDIX. VAGINAL ARTIFICIAL SELF-INSEMINATION INSTRUCTIONS

Vaginal artificial self-insemination is the process of placing sperm into your vagina without your partner's penis going inside you. This gives you the chance to get pregnant without the risk of passing HIV on to your partner.

Two important things will give you the best opportunity to get pregnant. Firstly, do the artificial insemination at the time of the month when you are the most fertile, and secondly do not wait too long to place his sperm inside you.

How do you know when it is your most fertile time?

The most fertile time in your menstruation cycle is 2 weeks before you get your period, or around day 14 of your cycle.



Other signs to look out for are an increase in your body temperature (if you have a thermometer) or changes in your vaginal discharge. The mucus will become more clear and sticky – you can pull it into strings if you rub it between your fingers.

What you need to do when the time is right.

The first thing to do is to get a sample of sperm from your partner. You can do this in two ways. You can have sex with a condom (don't use one with spermicide) and use the semen that is captured in the end of the condom. The other way is to get your partner to ejaculate into a clean container you can get from the clinic for this purpose. He can do this with your help or on his own.

Once you have the semen sample, don't wait too long. As soon as possible you need to draw the semen into a 5 millilitre (ml) clean plastic syringe without a needle or a bulb pipette (your local clinic can provide you with one). The next thing to do is to get yourself in the right position. Lie on your back with your knees bent. Place a cushion under your hips to get your back flat and your pelvis tipped up.

Make sure you have got all the extra air out of the pipette or syringe and place it into your vagina, a bit like you would a tampon. Don't push it up too far. (This should NOT be painful. If it is, stop what you are doing and report to your clinic.) Then slowly push the semen out of the syringe or pipette backwards into your vagina.

If possible try to stay in this position for an hour. The chance that you will get pregnant might be a bit better if you masturbate and bring yourself to orgasm while you are lying there, although this is not required if you are not used to it.

Lie on back with knees bent | Place a cushion under hips | Slowly push semen from syringe into vagina | Stay on your back for 1 hour

Realistically, the possibility that you will get pregnant is around 5 - 10%. You can try this technique 2 - 4 times during your fertile time. The more often you try, the greater your chance of success.

If you have any questions ask your counsellor or health care provider.

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