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HIV/AIDS-related Problems in Gynecology

Regine Unkels

INTRODUCTION

In 2009 33.3 million people were living with human immunodeficiency virus (HIV), 2.6 million people were newly infected worldwide and 1.8 million people died in the same year. Young people aged between 15 and 24 years account for 45% of the infections worldwide and approximately 2 million children are living with the virus. Sub-Saharan Africa is most affected with 67% of the people living with HIV/AIDS and 75% of the deaths due to AIDS worldwide; 97% of all new infections in 2009 occurred in middle- or low-income countries[1].

No other disease has had a similar impact on mankind in modern times compared with HIV/AIDS. HIV is a retrovirus which was unknown until the 1980s, when the first cases of a new disease were first identified in the USA. The disease was named acquired immunodeficiency syndrome (AIDS) after its most salient features, death due to infectious diseases through immunodeficiency, and has since then killed more than 25 million people worldwide.

Antiretroviral therapy (ART) was introduced in resource-poor settings reluctantly for the fear of emerging resistance against antiretroviral drugs and lack of sustainability and human resources, but through public pressure and advocacy of international organizations such as Doctors Without Borders (MSF), introduction of adapted ART and care and treatment schemes started to be rolled out with the support of UNAIDS from 2003 onwards. In 2010 approximately 3 million people living with HIV/AIDS had access to ART from the 9 million needing it.

The extent to which the epidemic spread in sub-Saharan Africa and Southeast Asia had significant impact on the economic and social development. The consequences can been seen at all levels of the economy, household and workforce, and at the macroeconomic level. As many societies' economics are based on subsistence farming and agricultural products the impact of HIV/AIDS at the household level is most important. 'HIV/AIDS erodes social capital.'[2] Life expectancy in Southern Africa will decline from 59 years in the late 1980s to 45 years in the years to come, and by now HIV/AIDS is responsible for one in five deaths in this region[2].

Peak age of infection is 20–40 years and peak age of death is 5–10 years later. Without HIV/AIDS these age groups would have the lowest death rate in society. They are also the most important economic actors: parents, teachers, community leaders, nurses and heads of households. Sick people need medical and nursing care. More money foreseen for other things has to be spent on care for a long time. The sick person stops working and carers, mostly women lose time to work, increasing opportunity costs for the family. If the carer is a child, he/she will eventually drop out of school due to lack of time or money. Urban people usually support their rural family. Their sickness or death will have an impact on the rural part of the family as well.

A BRIEF LESSON ON HIV

HIV is a very simple organism, but its potential to survive, reproduce and mutate is enormous. It is transmitted through hetero- and homosexual intercourse, from the pregnant mother to the fetus and during delivery and breastfeeding, through contaminated blood and by sharing contaminated needles or other sharp equipment. Globally, the most important way of transmission however is

heterosexual intercourse. People over 18 months of age can be tested for HIV with rapid field tests taking only a few minutes and more elaborate laboratory tests such as enzyme-linked immunosorbent assay (ELISA) or Western blot immunoassays. Most countries have national standard operational procedures on HIV testing. A test will become positive around 6–12 weeks after infection.

The virus contains two copies of single-stranded ribonucleic acid (RNA) genome and two copies of the enzyme reverse transcriptase (RT) to reproduce in its core, coated with the viral envelope. The virus infects special white blood cells, lymphocytes with a CD4 molecule as the receptor. Within these lymphocytes the two genome copies are turned into double-stranded deoxyribonucleic acid (DNA) genome by the virus' RT, which is integrated in the host's own DNA genome. To create new viruses, more RNA is transcribed to be integrated into new virions, which are released from the host cells which will gradually be destroyed. This will lead in time (10–15 years) to a reduced immunoresponse against diseases which is called acquired immunodeficiency syndrome (AIDS) and eventually the person infected with HIV will die as his or her body will be overwhelmed by infectious diseases and certain forms of cancer where the immune response plays a role. Advanced HIV and AIDS was classified by the World Health Organization (WHO) clinically. This classification is based on prior HIV testing (Table 1).

Today, most healthcare settings at district or regional level can provide HIV counseling and testing. In most district hospitals, CD4 testing and ART are available and all countries have national guidelines on treatment and care for people living with HIV/AIDS. In case you have no such facilities at your health post and you have a patient you suspect of showing HIV-related problems you should start counseling her and refer her for further voluntary counseling and testing (VCT) to the nearest unit providing this service. However, there is still a classification based on clinical symptoms without testing called the Bangui classification: in an adult or adolescent >12 years of age at least two major and at least one minor sign have to be present to diagnose AIDS (Table 2).

This classification can help your decision to refer the patient for VCT and influence your clinical decision on initiation of treatment prior to confirmation of HIV infection but it is always better to convince the patient to go for VCT and if necessary start treatment.

MAGNITUDE OF THE PROBLEM IN GYNECOLOGY

Women living with HIV/AIDS seek care for specific problems in gynecological services all around the world. Recognizing and treating specific gynecological diseases can help to maintain the health of these women for a longer time. Identifying women with HIV/AIDS in your gynecological service will help them to know their sero-status and receive adequate care for HIV/AIDS. This is what this chapter is about.

As seen, both the classifications of HIV disease contain gynecological problems. A total of 15.9 million of the people living with HIV/AIDS (PLWHA) globally are female[1]. Especially in low resource-settings infants depend on their mothers' health and ability to take care of them to survive. Infant mortality and under-5 mortality in HIV-exposed children is two to five times higher than in the non-exposed[3]. These figures show how important women are for the well-being of their families as caregivers and breadwinners.

GYNECOLOGICAL PROBLEMS OF HIV/AIDS

Approximately 89% of female HIV patients experience at least one relevant gynecological problem in 5 years[4]. Gynecological infections are the most common reason to seek care for the first time in HIV-infected women: every time you see a patient is a unique opportunity for HIV counseling and testing. HIV prevalence in gynecological services is often higher than average because women seek help for HIV-related gynecological problems. Frequent problems in HIV-positive women are:

- Sexually transmitted infections (STI)
- Pelvic inflammatory disease (PID)
- Tuberculosis
- Cervical cancer
- Other HIV-related malignancies
- Menstrual disorders
- Miscarriages
- Family planning, infertility.

These topics will be discussed below. Furthermore, procreation in HIV-positive couples is discussed in this chapter.

Table 1 WHO clinical staging of HIV/AIDS for adults and adolescents with confirmed HIV infection

Clinical stage 1
Asymptomatic
Persistent generalized lymphadenopathy
Clinical stage 2
Moderate unexplained weight loss (<10% of presumed or measured body weight)
Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media and pharyngitis)
Herpes zoster
Angular cheilitis
Recurrent oral ulceration
Papular pruritic eruptions
Seborrheic dermatitis
Fungal nail infections
Clinical stage 3
Unexplained severe weight loss (>10% of presumed or measured body weight)
Unexplained chronic diarrhea for longer than 1 month
Unexplained persistent fever (above 37.6°C intermittent or constant, for longer than 1 month)
Persistent oral candidiasis
Oral hairy leukoplakia
Pulmonary tuberculosis (current)
Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis or bacteremia)
Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
Unexplained anemia (<8 g/dl), neutropenia ($<0.5 \times 10^9$ per liter) or chronic thrombocytopenia ($<50 \times 10^9$ per liter)
Clinical stage 4
HIV wasting syndrome
Pneumocystis pneumonia
Recurrent severe bacterial pneumonia
Chronic herpes simplex infection (orolabial, genital or anorectal of more than 1 month's duration or visceral at any site)
Esophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
Extrapulmonary tuberculosis
Kaposi's sarcoma
Cytomegalovirus infection (retinitis or infection of other organs)
Central nervous system toxoplasmosis
HIV encephalopathy
Extrapulmonary cryptococcosis including meningitis
Disseminated non-tuberculous mycobacterial infection
Progressive multifocal leukoencephalopathy
Chronic cryptosporidiosis (with diarrhea)
Chronic isosporiasis
Disseminated mycosis (coccidiomycosis or histoplasmosis)
Recurrent non-typhoidal Salmonella bacteremia
Lymphoma (cerebral or B-cell non-Hodgkin) or other solid HIV-associated tumors
Invasive cervical carcinoma
Atypical disseminated leishmaniasis
Symptomatic HIV-associated nephropathy or symptomatic HIV-associated cardiomyopathy

Table 2 Bangui classification to detect AIDS

Major signs
Weight loss >10% of body weight
Chronic diarrhea for >1 month
Prolonged fever for >1 month
Minor signs
Persistent cough for >1 month
Generalized pruritic dermatitis
History of herpes zoster
Oropharyngeal candidiasis
Chronic progressive or disseminated herpes simplex infection
Generalized lymphadenopathy

Sexually transmitted infections/reproductive tract infections

The most frequent way of transmission of HIV globally is heterosexual intercourse. This way of transmission is shared with other STIs such as chlamydia, trichomonas or syphilis. Those infections can facilitate the transmission of HIV during intercourse and at the same time HIV infection with low immunity can facilitate infection with other STIs. Thus, women with HIV should be routinely screened for other STIs or reproductive tract infections (RTIs) and all out-patient department (OPD) patients who come with symptoms of an STI should be counseled for HIV testing.

Treatment of an STI is the same for HIV-positive and -negative patients but in HIV treatment sometimes needs to be prolonged:

- Vulvovaginal candidiasis was found in 30–70% of HIV-infected women. Depending on CD4 counts episodes can be more frequent, persistent and less susceptible to treatment and often need prolonged treatment (see Chapter 17 on STIs). Severe vulvovaginal candidiasis tends to occur below a CD4 count of 350 cells/mm^3 and is often associated with oral or esophageal thrush which needs general treatment with oral antifungal tablets such as fluconazole.
- Genital herpes simplex may be the first manifestation of AIDS in an HIV-positive patient and is, if persisting for more than a month, an AIDS-defining disease. Here as well episodes tend to be more frequent, more severe and persistent with falling CD4 counts. Presentation of herpetic lesions in HIV may be atypical, e.g. only one ulcer instead of multiple blisters (see Chapter 17 on STIs).
- HIV-positive women have a higher prevalence of syphilis which doesn't respond to a single shot treatment with benzathine penicillin. Primary syphilis should thus be treated like secondary syphilis with benzathine penicillin 2.4 mega units once a week for 3 weeks.

Pelvic inflammatory disease

PID is found more frequently in women living with HIV/AIDS and tends to be more severe with more frequent tubo-ovarian abscesses but often with less pain and lower blood leukocyte counts. Preoperative evaluation of the patient's health is very important since a patient with low CD4 counts tends to have more postoperative complications. A patient with tubo-ovarian abscesses on ultrasound should be thoroughly investigated first, including HIV-antibody testing and, if available, CD4 count to assess eligibility for ART first. If the CD4 count is not available, assess the patient according to the Bangui criteria for HIV/AIDS (Table 2). There are two possibilities for treating such a patient without doing a laparotomy:

1. Medical treatment with ciprofloxacin tablets 250 mg o.d. for 14 days or chloramphenicol tablets 500 mg b.d. for 14 days. Then do another ultrasound to assess response to treatment.
2. If the tubo-ovarian masses on ultrasound are in the pouch of Douglas do a culdotomy under local or general anesthesia. Make sure you explain well what you're about to do to your patient if you use local anesthesia, in order to ensure her cooperation. Put the patient in lithotomy position, disinfect the vagina with iodine or chlorhexidine and do a speculum examination using an Auvard's speculum with an assistant. Put a tenaculum on the posterior lip of the cervix and pull the cervix upwards. Give local anesthesia in the mucosa of the posterior fornix and straight on insert the needle in the abscess as described in Chapter 12 on ectopic pregnancy for culdocentesis. Do not remove the needle and syringe: if pus is coming, make a horizontal incision with a scalpel around the needle in the vaginal wall. Remove the needle and syringe and enlarge the incision with your fingers and try to open up other abscesses nearby in the pouch of Douglas with your finger.

Put a drain or a urinary catheter (30 ml in the balloon) in the incision to keep it open to drain the pus. If necessary you can suture the catheter with absorbable sutures through the cervix. If possible, examine the pus with Gram-stain, Ziehl–Neelsen stain or do a culture. Start antibiotics chloramphenicol or ciprofloxacin for 2 weeks as described above. Remove the drain or catheter if there is only clear fluid coming.

Tuberculosis

Tuberculosis is a big problem for people living with HIV and can easily lead to rapid progression to AIDS and death if untreated. Multiresistant tuberculosis bacilli are emerging more frequently especially in southern Africa and south east Asia. Almost one-third of people living with HIV suffer from tuberculosis and one-third of people suffering from tuberculosis are HIV-positive. Tuberculosis can affect the cervix, uterus, tubes and ovaries as well, causing endomyometritis with menstrual irregularities and amenorrhea, infertility or ectopic pregnancies, and early ovarian failure with early menopause. Peritoneal involvement can mimic ovarian cancer with ascites and miliary implantations leading to unnecessary surgery with serious complications for women living with HIV whose immune system is already low. Alternatively if you cannot differentiate between (extra-ovarial) ovarian cancer and tuberculosis: do a mini-laparotomy and remove some of the affected peritoneum for pathology. You always have to think of tuberculosis in women living with HIV but unfortunately it is very difficult to diagnose, as sputum and Mantoux tests are often negative. If you suspect tuberculosis, a syndromic treatment can be worthwhile initiating for the above-mentioned negative impact of tuberculosis on disease progression. If pathology services are available and you suspect endomyometritis you could perform a manual vacuum aspiration (MVA) (as described in Chapter 10 on postmenopausal bleeding for endometrial sampling) and send the specimen for pathology with the question if tuberculosis is present. Please check with your local tuberculosis coordinator on available guidelines for treatment.

Cervical cancer

This is the second most common cancer in women worldwide. More than 80% of the cases occur in low-resource settings with the highest rate in Asia, especially in India. Most cases of cervical cancer are caused by human papillomavirus (HPV). You will find more information about cervical cancer and HPV in the Chapters 26 and 17 on cervical cancer and STIs. It is best to read these chapters first before going to this section on HIV and cervical cancer as you need to have a basic understanding about the cancer first.

HIV and HPV have common ways of transmission and risk factors. As the immune system has a major role in clearing HPV infections, scientists expected a rise in the rate of cervical cancer with increasing HIV rates, and included cervical cancer in the WHO classification as an AIDS-defining disease, and a decrease with the onset of ART. However, this has not been the case, so the link between HIV and cervical cancer seems to be more complex[5]. Some scientists think that this was due to the fact that before the introduction of ART most HIV-infected women would not live to see their cervical cancer develop; also those who develop it tend to be younger and have a more aggressive form and more rapid progression from cervical intraepithelial neoplasia (CIN) to invasive cancer.

Current evidence shows that women living with HIV have a higher risk for cervical HPV infection and higher rates of viral persistence which increases the risk of CIN, the precursor of cervical cancer. This indeed seems to correlate to CD4 counts as the risk for persistence is twofold in CD4 counts <200 cells/μl[5–7]. The increased prevalence of CIN also seems to be linked to low CD4 counts. The introduction of ART has only shown a moderate or no effect on the prevalence of cervical cancer and CIN in HIV-positive patients although there seems to be a lower incidence of high-grade CIN and a higher rate of regression to low-grade CIN. There is no evidence that ART led to a decrease in cervical cancer among women living with HIV even in the long run. However, as the rate of women with cervical cancer and HIV is high in many resource-poor settings you will find many patients with both diseases and it is worthwhile considering screening for cervical cancer in HIV-positive women and proposing VCT to women with cervical cancer especially when they are young.

Screening tools are the same for HIV-positive and -negative women: in most resource-poor settings direct visual inspection (VIA/VILI) and a see-and-treat approach for abnormal results is the

most feasible approach (see Chapter 26). However, as there is a higher rate for persistence and progression to CIN, women living with HIV need more frequent examinations and should be screened at their initial visit at your clinic once they have tested positive for HIV. If the result is negative, they should come back after 6 months and if this result is negative again, they can come at yearly intervals. The threshold for specialist colposcopic examination in women living with HIV should be low. It is important to look at the perineal and perianal region as well during VIA/VILI as women living with HIV tend to have multifocal disease with higher rates of anal and vulval intraepithelial neoplasia.

HIV-positive women who were treated for CIN have a higher rate of treatment failure and a higher rate of re-occurrence of CIN and need close follow-up especially as they seem to show a more rapid progression from CIN to invasive cancer which normally takes 10–15 years in HIV-negative patients.

Treatment for CIN and cervical cancer is the same in HIV-positive and -negative patients as described in Chapter 26. CIN can be treated using cryotherapy, large loop excision of the transformation zone (LETZ) or electric or knife conization. Invasive cancer should be treated with either surgery (radical hysterectomy) or radio(chemo)therapy which almost always needs referral to specialist care. It is important to know that radiation lowers CD4 counts. Thus you need to assess thoroughly your HIV-positive patient for eligibility for ART and start treatment before referral. Radical hysterectomy is major surgery with increased morbidity and mortality if the patient is in bad health. This needs to be considered as well when choosing the right treatment option for your patient especially as the benefits of chemoradiation will outweigh those of a combination therapy in advanced cases of cancer anyway. There is no scientific evidence available on the influence of ART on chemotherapy but clinical experience with the treatment of lymphoma by chemotherapy shows that this seems to be well tolerated by patients on ART.

Other HIV-related tumors

Experience from industrialized countries shows that people living with HIV/AIDS have an increased risk for developing cancer. Some are very specific for HIV, such as Kaposi sarcoma and are thus classified as AIDS-defining diseases, others only show a higher frequency in people living with HIV/AIDS.

- Non-Hodgkin lymphoma (NHL) and adult Burkitt lymphoma are AIDS-defining diseases and are also associated with immunodepression (CD4 <100 cells/l). Hodgkin lymphoma (HL) shows the same association with immunodepression. Where ART is introduced, the prevalence of NHL, HL and adult Burkitt lymphoma is declining. 'Gynecological' presentations of lymphoma can be abdominal masses with or without acute abdominal pain or kidney problems due to enlarged intra-abdominal lymph nodes. The treatment for lymphoma is chemotherapy and the initiation of ART. NHL can be treated using the COP scheme (cyclophosphamide + vincristine+ prednisolone every 3 weeks for six courses, after this every 3 months).
- Cancers associated with HPV, such as vulval and anal cancer and their precursor lesions, intraepithelial neoplasia, are also associated with HIV/AIDS infection. Their prevalence is linked to immunosuppression as with the other previously described cancers. Gynecological presentations of vulval and anal cancer are commonly chronic ulcers or chronic genital itching and pain with skin changes, such as decoloration, hardening of the skin and easy bleeding. The treatment is the same as for HIV-negative patients but there is a higher rate of treatment failure and recurrence.
- Kaposi sarcoma is associated with herpes simplex virus type 8. It is not surprising thus that Kaposi sarcoma is associated with immunodepression and low CD4 counts. Its frequency is declining with ART. HIV patients with Kaposi sarcoma often have visceral organ involvement and gynecological symptoms can be acute abdominal pain mimicking pelvioperitonitis with ileus. The treatment for Kaposi sarcoma is the initiation of ART and radiotherapy.

Menstrual disorders

Menstrual disorders are a common problem in HIV infection and with women on ART. Especially in advanced stages and progression to AIDS, many women stop having their menstrual period (amenorrhea for more than 6 months). This can be due to wasting with extreme weight loss and stress but also due to underlying chronic diseases such as

tuberculosis either generalized or affecting the female genital organs as described above. With ART or anti-tuberculous treatment the amenorrhea is often reversible leading to ovulation and unplanned pregnancies as fertility and health are restored. If the period doesn't reoccur for more than a year although the patient is treated and puts on weight, she is likely to be post-menopausal. There seems to be an increased rate of early ovarian failure with early menopause in HIV although this is not proven by studies. Chapter 8 describes how you can check for the reasons for amenorrhea. Especially when a woman still wants children and her ovulation induction cannot be achieved either through progesterone or the pill, it is important to counsel her and her partner about the problem of early ovarian failure and the resulting untreatable infertility in order to save her from wasting time and money on useless infertility treatment. Another problem to consider in young women with early ovarian failure is osteoporosis. So it is worthwhile trying everything to restore a menstrual cycle in an amenorrheic woman living with HIV.

Another menstrual problem in HIV is a higher rate of heavy menstrual bleeding (hypermenorrhea) and irregular heavy bleeding (metrorrhagia). The reason for this is not very clear but it is known that people living with HIV/AIDS and those on ART have a higher rate of low platelet counts, which might contribute to the bleeding. Also these patients suffer from anemia more often than patients who are not HIV infected. You should always check full blood count in women living with HIV/AIDS presenting with heavy menstrual periods. Very low platelets (<20,000/μl) could be replaced with whole fresh blood. Stored blood bags do not contain platelets anymore.

Menstrual blood loss can be reduced by using non-steroidal anti-inflammatory drugs (NSAIDs) such as diclofenac tablets 50 mg t.d.s. during the period. If available in your hospital tranexamic acid tablets can be prescribed to reduce blood loss as well, provided the woman doesn't have any thrombosis in her medical history (see also Chapter 9 on treatment of abnormal bleeding).

Heavy bleeding can be avoided by using injectables, implants based on progesterone or levonorgestrel intrauterine devices (IUD)[8]. Many women stop having their periods while using these contraceptive methods. Another way of avoiding menstruation is to continuously use the pill (see Chapter 9). But remember: oral contraceptives decrease the bioavailability of ART in the body.

Miscarriage

Women living with HIV/AIDS have a higher risk of miscarriage due to malfunctioning of the placenta and ascending infections when the mothers immune system is weak. Malaria seems to be more common in HIV-infected pregnant women and can cause miscarriage too. A USAID study found that women living with HIV/AIDS in Africa are 1.47 times more likely to experience miscarriage than non-infected women[9]. Women with recurrent spontaneous abortion should be offered HIV counseling and testing.

Women living with HIV/AIDS have a higher risk of anemia even without being pregnant. When they miscarry they can bleed severely depending on the cause and gestational age. If their CD4 count is very low they can develop severe infection and sepsis. Safe methods to deal with incomplete or missed abortion are shown in Chapter 13 about abortion. All the described methods such as misoprostol or MVA can be used in HIV-infected women. Bleeding after MVA is shorter, so MVA is probably the safer method for severely immunocompromised women, but for all other women living with HIV/AIDS all other methods can also be used safely.

Reproductive health

The majority of women living with HIV is of reproductive age and with the increased availability of ART, healthcare personnel face issues around conception and the desire for children in their HIV-positive patients. A gynecological service is a good place to detect as many HIV infections as possible in order to attach these clients to a care and treatment center (CTC) for HIV as early as possible to receive ART once they become eligible for it. Unfortunately many healthcare workers lack knowledge about issues around procreation in people living with HIV and especially in women with HIV. For a long time women in low-resource settings were, and still are, advised not to become pregnant at all regardless of their age and parity at the time of diagnosis. This advice can lead to harmful consequences as most women feel the need to become pregnant in order to fulfill their role in their society. In some areas with a high prevalence

of HIV, women who do not become pregnant are discriminated against by saying that this is because they have HIV. As a consequence many women with HIV will try to become pregnant regardless of the health providers' advice but will fail to go for antenatal care to the very provider for fear of trouble and discrimination. The prospect of a future planned and well-monitored pregnancy can be a powerful factor for adherence to ART, the advice not to become pregnant could be a cause for depression and ill-adherence. It is more and more recognized that people on ART in resource-poor settings are able to adhere to treatment and can lead a longer and healthier life; why should we deny the prospect of a family to them? The risk of mother-to-child transmission (MTCT) without any preventive measures is 30–40%; using single nevirapine during labor and after delivery has an MTCT rate of 15–20%. The risk of MTCT under ART with high CD4 counts and low viral load, however, can be decreased to <2%. An HIV-positive woman who is well attached to her CTC and feels she can freely speak about her desire for pregnancy to the providers without being harassed has no reason to hide away with this desire and to attempt a pregnancy in secret with all the harmful effects on her family such as partner transmission, new HIV-infection, MTCT, adverse pregnancy outcomes and premature death.

Contraception

Contraception is used as dual protection: against HIV transmission and STI, and unwanted pregnancy. It is important for HIV-positive individuals to protect themselves against an infection with other HIV viruses as this will hamper their immune system and increase the chance of resistance once they take ART. STIs can facilitate new infections through ulcers and local inflammation. The best contraceptive devices to protect against a new HIV infection are condoms which are unfortunately not very reliable in preventing conception unless they are used correctly. Thus it is important to use condoms *and* another method for contraception and HIV prevention (dual protection or contraceptive method mix). You should counsel the clients that it is crucial for them to continue using condoms, even if their partner is HIV positive, in order to avoid new transmission and at the same time to protect themselves and their offspring from the harmful consequences of an unplanned pregnancy. Women with HIV can use the following contraceptives:

- *IUD*: In 2004 WHO changed their guidelines about the use of IUD for women with HIV. There is no increased risk of PID or change in CD4 counts in HIV-positive women or women with AIDS who are well on ART[10]. Levonorgestrel IUD have the advantage that blood loss is absent or slight.
- The method with the lowest failure rate for multiparous women is *tubal ligation* feasible even on district level by mini-lap at any time or post-partum.
- *Contraceptives based on progesterone* such as Norplant® or injectables can be used by women with HIV but the evidence of risk of HIV acquisition is inconclusive at the moment. However, WHO and CDC still recommend progestin-only injectables and implants as contraceptives for women living with HIV[8]. Many women on implants or injectables stop having their period (amenorrhea) which is beneficial to the anemia and thrombocytopenia often associated to HIV and even ART.
- *The contraceptive pill* should be used with caution in women on ART as the use of antiretrovirals lessens contraceptive action as does rifampicin an anti-tuberculous drug. Apart from this it can be used safely and effectively in HIV-positive women. Former concerns that the use of hormonal contraceptives facilitates HIV transmission and progression have been ruled out[10].

Many women with HIV stop having their period while their disease is progressing. When starting ART, ovulation and thus the possibility of becoming pregnant can set in any time. Some HIV-positive women do not want to keep their pregnancy for personal reasons or due to their underlying disease. These women need good counseling on the possibility of pregnancy termination (where legal) (both MVA and misoprostol are safe in HIV-positive women) and should know that if they are on ART the risk of HIV transmission to their child is low.

Planning a pregnancy: pre-conception advise

With the onset of universal ART, life expectancy for people living with HIV/AIDS has started to rise again and couples begin to see a future and start

thinking of a family. Many studies in different settings show that at least one-third of couples living with HIV would like to have children. Studies show that in otherwise healthy women living with HIV pregnancy has no harmful effect on disease progression, but in women with advanced disease, pregnancy can lead to progression to AIDS.

A couple living with HIV who plans to conceive should be well attached to a CTC before attempting to become pregnant. They should be counseled thoroughly about the following in order to make an informed decision[11]:

- The interaction between HIV and pregnancy and possible adverse outcomes for mother and child.
- The risk of HIV transmission to the partners during unprotected intercourse (especially for sero-discordant partners) and to the child before, during and after birth.
- The risk reduction through circumcision of an uninfected male partner.
- The need and options of preventing MTCT (PMTCT) and the need to regularly attend antenatal care and maternal and child health (MCH) services post-partum.
- The necessity to strictly adhere to ART during and after pregnancy and to deliver in a PMTCT facility with a skilled attendant.
- Post-partum contraception.
- Feeding options for the child.

Counseling should not only focus on health issues but also on financial issues such as transport costs and costs of artificial feeding options.

Pregnancy planning in HIV-positive couples must include the following:

- Assessment of eligibility for ART and preconception initiation of ART.
- Subfertility investigations and counseling for *both* partners (the literature shows an increased prevalence of decreased sperm quality and quantity in HIV-infected men!).
- Screening and treatment of STI.

CD4 counts of both partners should be within normal range (around 1000 cells). If your hospital is able to check for viral load, this should be <50 copies. A high CD4 count, however, is a surrogate marker for low viral load and is ok for monitoring if your hospital has no testing facility for viral load.

If the woman is on ART, her regimen should not contain efavirenz as this drug has teratogenic potential. Teratogenicity on spermatozoa has not been documented and clinical practice has not revealed any effect of this kind to date.

To attempt spontaneous conception, the woman should have a regular cycle. If your hospital has an ultrasound machine you can monitor follicle growth as described in Chapter 16 on subfertility. Initially a thorough history as described in Chapter 16 should be taken to identify possible risk factors for subfertility. It is not clear whether there is an increased prevalence of infertility among HIV-positive couples as data are missing.

The couple should have unprotected intercourse on cycle days 11 and 13 only, as described, for 6 months. The rest of the cycle they should use condoms as usual. If after 6 months no pregnancy has occurred, subfertility investigations should start as described in Chapter 16 to minimize the risk of cross-transmission. If they conceive and deliver successfully, their child should be tested for HIV with PCR 6–8 weeks post-partum or with a rapid HIV test after 9 and 18 months.

Sero-discordant couples

This term means that one partner is HIV infected and the other one is not. Data from population-based surveys in five African countries suggest that two-thirds of HIV-positive couples are discordant, so this is an important issue for your clinic. Most studies dealing with the proportion of male or female discordant partners find that the ratio is almost even or a bit higher for men who are HIV positive[12]. The risk of HIV infection for the other partner depends on factors such as co-existing STIs, male circumcision, viral load and disease progression of the infected partner and whether the latter is on ART or not and certainly condom use.

A recent review recommends the following options to reduce transmission:

- Delayed conception after viral suppression through ART
- Intrauterine or intravaginal insemination
- Limited timed unprotected intercourse on fertile days
- Male circumscision in the uninfected male partner
- Pre-exposure prophylaxis with ART for the uninfected partner[13].

Sero-negative partners should be tested for HIV every 3 months while trying to conceive. If

conception and delivery are successful, their children should also be tested as mentioned above.

Female discordance If the woman is HIV positive and the man not, pregnancy should not be attempted naturally where insemination is available and the couple should use condoms during intercourse at all times. The cycle of the woman should be monitored as described in Chapter 16 on subfertility, using a period calendar and assessment of follicle growth by ultrasound. The couple should be taught how to inject sperm into the woman's vagina using a syringe (without needle). During the fertile days of the woman (usually cycle days 11–15) the man should ejaculate in a pot or a condom (without spermicide) and draw the content into the syringe. Either he or the woman should inject the sperm immediately into her vagina. If by this method the woman doesn't conceive after 6 months, further subfertility assessment of both partners should be done as described in Chapter 16.

Male discordance If the man is HIV-infected and his female partner not, the issue is far more complicated. Studies from Uganda and Ghana suggest that transmission rates in sero-discordant couples might be as low as 0.001 per coitus but a recent review found transmission rates as high as 2.0 to 11.8/100 person-years[13–15], but the individual risk is difficult to assess as infection rate depends on so many co-factors and is higher for women than for men due to biological factors such as the surface of vaginal skin, menstrual status and the local presence of lymphocytes. Overall as you can see, the risk of transmission is higher in male discordance and the couple and especially the woman needs good and continuous counseling on her risks. Intrauterine insemination after washing semen has a low risk of transmission, but is not widely available yet. Clearly, the only procedure with no risk of transmission in low-resource settings is adoption or donor sperm. Resorting to a husband's male family members for conception in case the husband is suspected to be infertile is an accepted solution in many cultures and should not be omitted as an option provided the donor is HIV negative and willing to be tested.

The risk of transmission is reduced if the male partner is on ART with low viral load, high CD4 counts and good adherence to therapy and if unprotected intercourse only takes place at a limited period each month during fertile days, e.g. on days 11–15 presuming that the woman has a regular cycle. To reduce unnecessary exposure a complete sterility work-up as described in Chapter 16 on both partners should be done before hand and any necessary treatment should already be accomplished. There is evidence that pre-exposure prophylaxis might decrease the risk for the uninfected female partner and several studies are still ongoing. Results and recommendations from WHO and CDC are expected in 2012[13]. Intrauterine insemination with semen using a 'swim-up' technique as described in Chapter 16 can be considered as the number of lymphocytes in the swim-up will be significantly reduced. If PCR testing for viral parts is done in your facility, you can do this on the washed sperm. If PCR is negative, the risk of HIV transmission is even smaller.

SERVICE INTEGRATION OF HIV/AIDS AND REPRODUCTIVE HEALTH SERVICES

Service integration means that staff, knowledge and capital resources are shared in order to strengthen health services as a whole. HIV/AIDS constitutes a humanitarian crisis with its high burden of disease and its impact on economies and life expectancy in resource-poor settings, disproportionally affecting the poor.

A lot has been done in the fight against HIV/AIDS in the past 5 years and a lot of money has been accorded by international organizations to the regions that are hardest hit by the epidemic. However, HIV/AIDS is only one among other diseases that kill the poor. In 2001 it was responsible for 5.3% deaths globally[16]. As financial resources from governments and donors are limited, funds for the fight against HIV/AIDS are often reallocated from other programs and unfortunately implementation of HIV/AIDS activities has been mostly carried out in a vertical way, meaning that special programs were created with special equipment and special positions which do not take into account that there is already a health system with equipment and staff taking care of routine healthcare such as primary healthcare (PHC) and MCH. Very often staff trained in HIV/AIDS issues don't consider other reproductive health issues in their counseling, such as family planning for women living with HIV/AIDS and the other way round.

Low-resource settings almost all suffer from a human-resource crisis in the health sector. As a

consequence the same staff who was responsible for basic healthcare is now working in HIV/AIDS projects and an already weak PHC system is thus further weakened. Service integration of HIV/AIDS and sexual and reproductive health services is important and obvious:

- 55% of PLWHA are women worldwide.
- Women are more easily infected with HIV/AIDS.
- MTCT occurs in 30–40% of all pregnancies in HIV.
- Every year 80 million women worldwide have unintended pregnancies including HIV-positive women[11].
- >500,000 women die each year from pregnancy-related complications[17].

These services do not only share their clients, they have common objectives as well:

- Safe delivery with knowledgeable, skilled attendants.
- Comprehensive antenatal care services providing focused antenatal care including PMTCT.
- Comprehensive post-partum/post-abortion care with follow-up for women living with HIV/AIDS and their children.
- Skilled family planning services for all women, but especially for women with HIV/AIDS.
- Provision of skilled RTI treatment.
- Empowerment of women.
- Male involvement.

Service integration can also help to solve many problems in vertical HIV/AIDS programs. For example, the weak point of many PMTCT programs is that the focus was put initially on the child, neglecting the mother. As a consequence referral of HIV-positive mothers to a CTC after delivery or during pregnancy for assessment of eligibility for ART often didn't take place and the women were lost to follow-up. Given the fact that, as mentioned above, the mortality of HIV-negative infants is higher when the mother is sick, this will diminish the benefits from PMTCT for the HIV-exposed infant considerably.

In order not to weaken reproductive health services and other PHC services in your health facility you should assess additional activities you are planning on their potential synergistic effect for existing services. For example, if you are planning a home-based care service for people living with HIV/AIDS you should look at who else could profit from community-based (palliative) care, such as people with cancer or paralysis or tuberculosis. Another example is the scaling up of PMTCT activities in an area were most deliveries take place in the community with traditional birth attendants. If you don't tackle the rate of facility-based deliveries or include the traditional birth attendants in your training, your PMTCT program will fail as modified obstetric care methods to avoid HIV transmission during delivery are not applied at community level and many women might miss antiretroviral prophylaxis during delivery. If you integrate PMTCT activities and maternal health activities in this issue you can strengthen both services through one activity.

Here are some more examples of service integration from practical experience that merit a further look:

- Infection prevention and control in the hospital.
- VCT as a routine offer in all hospital services (provider-initiated counseling and testing).
- Condom use and provision.
- Community sensitization on male circumcision (decreases male risk for HIV infection and female risk for cervical cancer) and STI prevention and treatment (decreases risk of HIV transmission and infertility).
- Family planning and pregnancy planning.
- Maternal and infant post-partum care including ART services.
- Universal access to quality antenatal and delivery care, including community-based services.
- Involvement of the public and of patients (traditional healers/birth attendants, religious leaders, male partners).
- Safe blood provision (from opportunistic donations to voluntary donations).
- Cervical cancer screening and treatment.
- Family planning services.

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