Love in the era of HAART
Reproductive health for men and women affected by HIV

Introduction

Highly active antiretroviral therapy (HAART) has changed HIV from a life sentence to a chronic manageable disease. The average life expectancy of a person newly diagnosed with HIV is approaching, but still not equal to, that of most people without HIV. Modelling, using data from the United States of America, predicts that a 39-year-old entering HIV care can expect to live until 63 years, still short of a 39-year-old without HIV who can expect to live into his 70s. There is still a gap but this is a long way from the 1993 estimate of 6.4 years for a person living with HIV entering care. Single-tablet, once-daily regimens are set to become therapies of choice for those commencing antiretroviral treatment—bringing the expectation, with good drug adherence, of long-term viral suppression and survival.

In many countries, this third decade of the HIV epidemic is characterized by increasing numbers of new infections in women and a lower average age among those women. An increasing number of these women are benefiting from expanded access to antiretroviral treatment. In sub-Saharan Africa, six out of 10 adults receiving antiretroviral (ARV) treatment are women. A substantial proportion of these women will plan to conceive or will have unintended pregnancies. An estimated 19 million unsafe abortions are performed annually. Access to affordable condoms remains the mainstay in the prevention of unintended pregnancies and of HIV transmission. Likewise, in the Western Pacific Region, the estimated number of adult women living with HIV has increased, nearly doubling in 2007 compared to the 2001 estimate (UNAIDS-WHO global database). Surveys among antenatal women have reported a high prevalence of sexually transmitted infections (STI) e.g. 29% with Chlamydia in Fiji in 2005 and 25.5% with at least one STI in Mongolia in 2007. In the 2007–2008 country reports from Cambodia, China, the Lao People’s Democratic Republic and Papua New Guinea on the Progress in health sector responses towards Universal Access, four to six out of every 10 adults receiving ARV therapy were women.

1. Sexual and reproductive health

1.1 Access to services

The HIV epidemic has played a major role in shaping the current understanding of human sexuality and has increased willingness of health care workers to address sexual health in a frank and direct manner (Figure 1).

Figure 1: Men in Myanmar practise using condoms

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The World Health Organization has called on policy-makers and programme managers to improve linkages between programmes for sexual and reproductive health (SRH) and for HIV by integrating key HIV services (voluntary counselling and testing [VCT], prevention of mother-to-child transmission [PMTCT] and antiretroviral therapy [ART]) with key SRH services (family planning, maternal and child health, and management of sexually transmitted infections). Both types of services directly involve men and women who are sexually active and linking them will improve access. Further, those who are infected with HIV are living longer, healthier lives and need services that meet their sexual and reproductive health needs.

A study presented at the 15th Conference on Retroviruses and Opportunistic Infections in 2008 provides support for the integration of prevention into ART programmes. Researchers examined changes in sexual HIV transmission risk behaviour in a cohort of 900 people taking antiretroviral therapy in rural Uganda over a three-year period. Participants were provided with an integrated ART and HIV prevention intervention. There was a 91% reduction in HIV transmission risk that was sustained over a three-year period, with one transmission reported among 64 HIV-discordant couples. The study also found a significant increase in sexual activity for both men and women but no increase in unprotected sex.

Access to PMTCT programmes remains unacceptably low in most countries in the Region. According to the Towards Universal Access Progress Report, little more than 10% of pregnant women in East Asia and the Pacific receive an HIV test and know the result. For many women, this is because they do not seek medical care during their pregnancy. But, with only 12% of antenatal clinics providing HIV testing and counselling, lack of facility coverage for this essential component of antenatal care remains a significant reason why women, even when in care, do not receive an HIV test (Figure 2).

1.2 Vulnerability of women

Women have a higher prevalence of sexual and reproductive ill-health than men. More than half a million women die annually in pregnancy and childbirth from largely preventable causes, almost all of these deaths occurring in resource-constrained settings. Globally, 13% of all maternal deaths are due to the complications of unsafe abortion. More than 340 million new cases of curable sexually transmitted infections occur annually, and sexually transmitted human papillomavirus (HPV) infection, the cause of cervical cancer, is diagnosed in more than 490 000 women and causes 240 000 deaths every year.

The sexual and reproductive health of all women, particularly those living with HIV, is fundamental to their well-being and that of their partners and children. Improving women’s sexual and reproductive health, treating HIV infections and preventing new ones are also important factors in reducing poverty and promoting the social and economic development of communities and countries.

1.3 Sexually transmitted infections (STI)

In addition to the consequences for physical and mental health, STI can cause serious complications for
the fetus and newborn baby, including stillbirth, preterm labour, low-birth weight, congenital syphilis, blindness and pneumonia. Services for preventing, diagnosing and treating STI offer many opportunities for synergy with HIV prevention, care and treatment efforts.

A woman whose sexual partner has an STI should be offered treatment even if the woman is asymptomatic—at least 70% of women with an STI have no symptoms. A syndrome-based approach enables health care workers to provide immediate, highly effective and cost-effective treatment for people with symptoms of STI. Diagnosing the causes of STI often requires sophisticated laboratory facilities, adds to the cost of treatment, may require people with STI to make extra visits to the health facility and almost always delays treatment. Given these considerations and the lack of trained personnel and diagnostic equipment, in many resource-constrained settings, a syndrome-based approach to managing people with STI has been widely adopted.

1.4 Cervical cancer

Invasive cervical cancer is an AIDS-defining illness. Cervical cancer is an important public health priority because of the burden of disease and the potential for effective prevention via screening. In many countries, it is the most common malignancy among women and the leading cause of cancer deaths among women. Women living with HIV have a higher prevalence of human papillomavirus, the cause of cervical cancer. If available, Papanicolaou (PAP) smears should be conducted at least annually in women with HIV infection. Women with previous HPV infection need more frequent screening. In the Western Pacific Region, there are approximately 66,000 women (not specifically HIV positive) living with cervical cancer and 114,200 new cases each year.

2. HIV and pregnancy

2.1 Parenthood

As people with HIV live longer, healthier lives compared to 10 years ago, sexual and reproductive needs will assume more importance, both to individuals and to societies. Under the study title of Life is still going on, researchers conducted in-depth interviews with HIV-positive women and men in the developing country setting of South Africa. Being HIV-positive modified but did not remove reproductive desires, and reproductive intentions differed. Some HIV-positive individuals wished to avoid pregnancy. Fears of partner and infant infection and having a previously infected baby were important factors deterring some individuals from considering having children. The expectations of childbearing that come from families, husbands and society were important influences on women’s reproductive intentions. The researchers also found evidence that knowledge of PMTCT programmes, and ART programmes for those already infected, altered women and men’s attitudes in favour of childbearing.

Most HIV-positive women had not discussed their reproductive desires and intentions with their health care providers because of anticipated negative reactions. The few who had done so perceived the counselling environment to be mostly unsupportive of open discussion on these issues.

In a developed country setting (France), another study examined the desire for a child in heterosexual

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women and men of reproductive age living with HIV. Among 555 women and 699 men who were self-identified as heterosexual, 33% of the women and 20% of the men stated that they expected to have children in the future.3

2.2 The impact of pregnancy on HIV and of HIV on pregnancy

Pregnancy does not adversely affect HIV progression or survival.17 There is a transient decline in CD4 count as a result of haemodilution.18-20 HIVRNA (viral load) levels do not increase during pregnancy, but some studies have reported an increase in viral load postpartum.18

In contrast, the effect of HIV on pregnancy outcomes is considerable. HIV infection is a major cause of maternal mortality in resource-limited settings. In some sub-Saharan African countries with hyper-epidemics, it is the leading cause of maternal mortality, with mortality rates five times those of uninfected women.21 Adverse pregnancy outcomes include spontaneous abortion, stillbirth, perinatal and infant mortality, intrauterine growth retardation, low birth weight, and chorioamnionitis.18

2.3 Prevention of mother-to-child transmission package of services

In 2007, around 370 000 children became infected with HIV, mainly through mother-to-child transmission, 90% of whom live in Africa. Effective prevention of HIV transmission from mother to child involves a package of services, the keys to which are preventing HIV infection among prospective parents, avoiding unwanted pregnancies among HIV-positive women and the prevention of the transmission from HIV-positive mothers to their infants during pregnancy, labour, delivery and breastfeeding.

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The ultimate goal of PMTCT is to reduce maternal and child mortality by delivering a comprehensive package of services that includes primary prevention of HIV infection among women of reproductive age, prevention of unintended pregnancies among women living with HIV, counseling and support on infant feeding, as well as antiretroviral therapy for mothers, cotrimoxazole prophylaxis for mothers and infants, early infant diagnosis and initiation of antiretroviral treatment (Table 1).22

2.4 Infant feeding choices

Women with HIV are advised not to breastfeed if breast-milk substitutes are acceptable, feasible, affordable, sustainable and safe (Figure 3).

If breast-milk substitutes are not available, exclusive breastfeeding is recommended and should be discontinued once an alternative form of feeding becomes feasible.23 Mixed feeding (breastfeeding mixed with bottle feeding of water or formula, or providing other foods) is not recommended because of the higher risk of transmission compared to exclusive breastfeeding.

Current research into reducing transmission of HIV through breastfeeding is focused on prophylactic antiretroviral treatment given to the mother and/or infant during the time of breastfeeding.

Other studies (SIMBA, SWEN, and PEPI) have also demonstrated that extending combination antiretroviral for mothers and infants, even with ongoing breastfeeding, significantly reduces HIV transmission.26-28

2.5 MTCT-Plus –A family-centered approach

MTCT-Plus aims to move beyond interventions aimed solely at preventing infant HIV infection by supporting the provision of specialized care to HIV-infected women, their partners and their children who are identified in MTCT services. MTCT-Plus promotes the treatment of family units. Women who access PMTCT services are subsequently enrolled along with other children in the family and their consenting partners. All family members receive HIV testing and care appropriate to their situation. This may be antiretroviral therapy or regular clinical and/or CD4 monitoring and initiation of treatment when needed. Counselling focuses on prevention of unwanted pregnancies and nutrition. One of the first such programmes, the MTCT-Plus Initiative was established in 2002, and is coordinated by the Mailman School of Public Health at Columbia University. The MTCT-Plus Initiative provides operational funding, medications, training and technical assistance at 13 sites in sub-Saharan Africa and at one site in

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Table 2: Studies of the reduction of transmission of HIV through breastfeeding

<table>
<thead>
<tr>
<th>Study</th>
<th>Methods</th>
<th>Outcomes</th>
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<tr>
<td>MITRA24</td>
<td>HIV-infected pregnant women received zidovudine and lamivudine from week 36 to one week postpartum. Infants received zidovudine and lamivudine from birth to one week of age and then lamivudine alone during breastfeeding (maximum of six months).</td>
<td>Among 398 infants, the cumulative infection or death rate at six months was 8.5%, a reduction of 50% compared to the breastfeeding population of the Petra study in which no antiretroviral was given.</td>
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<tr>
<td>AMATA25</td>
<td>Studied the effectiveness of triple antiretroviral treatment given to women, who formula fed or breastfed, from late pregnancy until seven months after delivery.</td>
<td>Among 176 infants, only one (0.6%) was infected during breastfeeding, and it is believed the mother of this child may have stopped taking her medicine.</td>
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Since its inception, MTCT-Plus has provided care and treatment to more than 13,000 adults and children.

3. Choices for sero-discordant couples

3.1 Sperm washing

Spermatozoa are not infected by HIV. Sperm washing removes HIV from the seminal fluid so that isolated spermatozoa can be artificially inseminated into a HIV-negative woman. During sperm washing, a sample of semen is centrifuged to separate out live sperm from the surrounding fluid and cells (Figure 4). The washed sperm sample is checked by PCR (viral load measurement) to make sure it is HIV negative before artificial insemination into the uninfected female partner. Since 1987, more than 3,600 published attempts have been reported in which processed spermatozoa from HIV-seropositive men were used to establish pregnancy in HIV-seronegative women. Although the data remain observational, sperm washing techniques appear to be relatively safe and effective, offering HIV-serodiscordant couples seeking safe pregnancy an opportunity to have a child. In one European study of 581 discordant couples, the successful pregnancy rate was 70.3% with all female partners remaining HIV negative. A sperm washing service has been available at the Thai Red Cross Anonymous Clinic in Bangkok since 2006.

Fifty three HIV-positive men have used the service. All washed sperm specimens had HIVRNA <50 copies/ml. Of all the couples, 22.6% became pregnant and all pregnant women were HIV-negative after the first trimester of their pregnancy.

4. The Swiss AIDS Commission Statement

Following a review of the published literature, the Swiss Federal Commission for HIV/AIDS announced the first-ever consensus statement that HIV-positive people on effective antiretroviral therapy, with undetectable viral load and without sexually transmitted infections are sexually non-infectious. The statement is valid as long as the person adheres to antiretroviral therapy, is monitored regularly by the treating physician and has a suppressed viral load (<40 copies/ml) for at least six months.

The statement goes on to explain that there is no “proof” that HIV cannot be transmitted from persons on effective ART, but draws a comparison with the 1986 statement that HIV cannot be transmitted by kissing. While the link between kissing and non-transmission of HIV has never been proven, 20 years of experience suggests that it is highly plausible. The Swiss AIDS Commission statement concludes that, while the risk of transmission cannot be scientifically excluded, it is negligibly small.

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4.1 Reaction to the statement

The potential public health implications of the statement are wide-ranging. Reaction has been mixed, from praise for lifting the fear of being a threat to partners, to dismay that the message in the report has the potential for more harm than good with people believing that it is acceptable not to use condoms. Subsequently, Australian researchers analysed the implications of the statement at a population level. Using a mathematical model to estimate the cumulative risk of HIV transmission from effectively treated HIV-infected partners (plasma viral <10 copies per ml) in a population of 10,000 serodiscordant partnerships over 10 years, the expected median number of transmissions would be 215 for female-to-male transmission, 425 for male-to-female transmission and 3,524 for male-to-male transmission. The latter would correspond to an increase in transmission of four times compared to that with current rates of condom use.30

4.2 What are the data?

In addition to the public health implications, the controversy surrounding the Swiss statement lies in the conflicting data. Highly active antiretroviral therapy has been shown to be highly effective in reducing plasma levels of HIV RNA. Spanish researchers studied 393 heterosexual couples in “steady” relationships, of which one partner had been previously diagnosed with HIV infection (index case) and where the non-index partner reported his or her sexual relationship with the index case as the only risk exposure. Between 1991 and 2003, HIV prevalence among partners of index cases not on antiretroviral therapy was 8.6%, whereas no partner was infected in couples in which the index case had been treated with HAART.31 In a smaller study, also from Spain, of 62 HIV-serodiscordant couples, 76 natural pregnancies were documented. Couples were included in the study if only one partner was HIV positive, plasma viral load was <500 copies/mm³ on HAART at the time of natural conception and <50 copies/mm³ at delivery, and HAART was taken during pregnancy by HIV-infected women. All babies born to HIV-infected mothers received prophylaxis with zidovudine during delivery and after birth. Among 68 children, there were nine fetal deaths and one set of twins. Six couples had two consecutive pregnancies and four couples had three pregnancies. There were no cases of HIV seroconversion in the uninfected partners. One case of HIV transmission from mother to baby occurred.

Conversely, in a recent study from France, 5% of 145 HIV-infected men enrolled in an assisted reproductive programme had detectable HIV RNA in semen, even if they had no other sexually transmitted disease and their serum viral load was undetectable for at least six months on antiretroviral treatment.32 An explanation for the detectable semen viral load despite undetectable plasma viral load is that antiretroviral drugs may not penetrate the genital compartment effectively.33 Australian researchers reported sub-therapeutic ARV drug levels in semen among 81 HIV-positive men with undetectable plasma and semen (<250 copies/mm³) viral load.33

5. Finally, sex work

Given the scale of sex work and estimates that it contributes 2%–14% to South-East Asia’s gross domestic product, there is an urgent need to identify which interventions are effective in reducing HIV in sex workers.34

In the first systematic review of HIV and STI prevention interventions in female sex workers in resource-poor countries, researchers looked at two approaches. The first assumed that HIV was an occupational hazard with prevention focused on harm reduction strategies such as empowering sex workers to use condoms and removing structural barriers to safety, such sex work legislation. The second examined strategies to provide STI treatment for sex workers. The effectiveness of either approach has not been assessed systematically. The authors concluded that none of the clinical trials showed an effect on HIV incidence. However, the observational data suggest some evidence for the effectiveness of combination risk-reduction counselling, condom promotion, and regular access to improved STI management in sex workers. Innovative STI delivery methods, such as vouchers, may improve coverage.
The linked response between HIV/AIDS, STI and reproductive health services in Cambodia

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Issues

Linked response strategies are implemented at the operational district level to increase the coverage of HIV and reproductive health including maternal health and prevention of mother-to-child transmission services by strengthening patients’ referrals and follow-up within and between various facility-based services and community-based organizations. In addition, building up the local health management team is very important to support health system strengthening.

Description

The National Center for HIV/AIDS, Dermatology and STD (NCHADS) of the Ministry of Health, Cambodia, started a linked response demonstration project in Neak Loeung Operational District in April 2008, supported by The Clinton Foundation, and a second demonstration project in Kirivong Operational District in Takeo province in June 2008, supported by WHO, the Joint United Nations Programme on HIV/AIDS, United Nations Children's Fund and United Nations Population Fund. Community-based organizations and health staff from HIV, STI, antenatal clinic, maternity and family planning services had an orientation workshop on their respective responsibilities to ensure adequate linkages for referrals and follow-up. Support was provided to community groups to enable referrals and follow-up, including patients’ transportation.

Coordination was organized through regular meetings of the core linked response team and a monitoring and evaluation system was put in place, including a patient tracking system for follow-up of HIV-infected pregnant women and their babies.

Results

In Kirivong Operational District, the percentage of pregnant women who received an HIV test increased from 9% to 84% after the linked response strategy was introduced. When we compared the period of June to November 2007 (before the linked response) with the first six months of the linked response (June to November 2008), the antenatal care (ANC 1) coverage increased from 72% in 2007 to 78% in 2008 and deliveries at health facility from 54% to 58%. No significant change

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Scaling up HIV testing: Update for the Western Pacific Region

Increasing the number of people who know their HIV status is considered a key priority to expanding access to HIV prevention, treatment and care. To achieve this, it is important to strengthen existing testing and counselling services as well as develop innovative strategies to target testing and counselling towards people most at risk of being infected with HIV.\(^{35, 36}\)

It is now widely recognized that inadequate laboratory systems is restricting the scale-up of HIV testing and counselling services in resource-limited settings. To achieve the provision of accurate, reliable and timely laboratory test results, a laboratory quality system is essential. Therefore, the expansion and further development of quality-assured laboratory services as part of a greater framework of health system strengthening will be critical to achieving expansion of HIV testing and counselling services.\(^{37-39}\)

To address concerns over low coverage of HIV testing and counselling in Asia and the Pacific, a technical consultation on scaling up HIV testing and counselling was convened in Phnom Penh, Cambodia, from 4 to 6 June 2007. An urgent need to scale up access to HIV testing and counselling in countries of the Region was recognized and this will require strengthening existing models and combination with other approaches. As recommended in the Phnom Penh meeting, a technical consultation on HIV testing was organized by HIV/AIDS and STI Unit of the World Health Organization Regional Office for the Western Pacific and hosted by the Ministry of Health in Ha Noi, Viet Nam, from 28 to 30 July 2008. The technical consultation provided a forum to discuss issues with HIV testing in the Region, in particular to review a draft guidance document and to identify steps for implementing the guidelines as part of strengthening HIV prevention, care, treatment and support towards universal access.

The meeting recognized that scaling up HIV/AIDS programmes presents an unprecedented opportunity to address integration of quality laboratory services as a whole into health systems.

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Increasing the use of rapid HIV assays

HIV testing in the Western Pacific Region is often carried out using traditional algorithms that rely on a combination of enzyme immunoassay (EIA) and Western blot (WB) with rapid HIV assays used as an initial screening test in some settings. EIA and WB assays require well-resourced laboratories and highly trained staff. WB assays are also costly and require long lead times before the delivery of confirmed testing results. Reducing turnaround times through making better use of rapid technology will be important in scaling up HIV testing and counselling services throughout the Region.

The introduction of good quality, simple and rapid HIV assays and their use in testing algorithms has allowed a substantial decrease in turnaround times. This is beneficial where loss of clients to follow-up is considered a problem. Therefore, rapid HIV assays are recommended where there are efforts to expand access to HIV testing and counselling services, particularly within community settings or health facilities where laboratory services are weak or absent. However, it is important to note that the use of rapid HIV assays does not negate the need for quality systems and sufficiently trained and monitored technicians.

Two important things must be considered when selecting HIV assays for use in testing algorithms:

(1) Both the selection of and the order in which assays are used are of the utmost importance for the final outcome of the testing strategy. The first assay (assay 1) needs to be highly sensitive (at least 99%), and the second assay (assay 2) should be highly specific (at least 98%), while retaining high sensitivity.

(2) An HIV testing algorithm should be validated before countrywide implementation and its performance regularly reviewed. This will require that all HIV testing sites have adequate quality assurance measures in place.

WHO is currently updating its guidance on HIV testing strategies. For more information see http://www.who.int/hiv/topics/vct/en/index.html.

When determining which testing technology is the most appropriate, a number of factors must be considered:

- performance characteristics of assays including sensitivity and specificity, cost, time to perform, shelf life and ease of performance;
- availability of assays, reagents and equipment including consideration of storage conditions;
- the daily specimen throughput (For example, EIA are considered appropriate for medium-to-high throughput (>40 tests/day) and rapid HIV assays are considered appropriate for low-to-medium throughput (~1-100 tests/day)); and
- resources and infrastructure including existing laboratory expertise and personnel, specimen collection and transport methods, the setting in which testing will take place, how they work together as a system and convenience and ability of individuals to return for results.

Adoption of new assays without adequate evaluation should NOT be considered an option. Doing so will compromise the integrity of the testing facility, personnel, and quality of reported results to the patient and/or client. All decisions should be based on sound principles and be guided by a national group of experts.

In conclusion, while the scale-up of HIV testing and counselling is imperative to increasing access to HIV prevention, care and treatment programmes, it is important that it does not result in a substantial decrease in the provision of accurate, reliable and timely HIV test results. Therefore, scaling up HIV testing and counselling services within the Western Pacific Region will require strengthening of existing programmes, implementing new and innovative strategies, making better use of rapid HIV assays and the consideration of quality management systems.
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