Oxford Maternal and Perinatal Health Institute

Maternal Health Task Force

The Global Health Network
Enabling research by sharing knowledge

HIV in pregnancy

The Geneva Foundation for Medical Education and Research

On successful completion of this module you should be able to:

- Know the global burden of HIV in pregnancy.
- Describe the screening and diagnostic measures for HIV in general and during and after pregnancy.
- Describe the interventions to prevent HIV transmission in general and in pregnancy (PMTCT).
- Describe the laboratory and clinical monitoring of HIV-positive pregnant women and HIV-exposed newborns.
- Describe the ARV regimens in general and during and after pregnancy.
- Know what complications to expect and how to manage them when a pregnant woman is on ART.
- Know the indications for stopping or substituting ARVs and how to stop or substitute ARVs in a pregnant woman with HIV.
- Identify the common HIV co-infections and measures to reduce morbidity and mortality.

Introduction

The human immunodeficiency virus (HIV) is a ribonucleic acid (RNA) retrovirus that infects the immune cells (especially the CD4 helper T cells) of its human hosts (Chou 2012).

There are two types of HIV: HIV-1 and HIV-2. HIV-1 is responsible for most of HIV infections globally (WHO 2013).

HIV-2 infection is more common in West Africa (Chou 2012).

HIV causes a progressive reduction in the number of immune cells, and leads to Acquired Immunodeficiency Syndrome (AIDS) in most patients if left untreated (Diaz-Rossello 2008).

- AIDS is a life threatening disease characterized by severe dysfunction of the immune system with a CD4 T cell count ≤0.200x 10^9 cells/L (200 cells/mm^3) or one or more AIDS-defining opportunistic infections or neoplastic conditions (Chou 2012).

Chou R, Cantor A, Bougatsos C, Zakher B. Screening for HIV in Pregnant Women: Systematic Review to Update the U.S. Preventive Services Task Force Recommendation. Rockville (MD): Agency for Healthcare Research and Quality (US); 2012.
Diaz-Rossello JL. Perinatal infections transmitted by the mother to her infant: educational material for health personnel. Latin American Center for Perinatology/ Women and Reproductive Health - CLAP/SMR Pan American Health Organization / World Health Organization - PAHO/WHO. 2008.
World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Global burden of HIV in pregnancy

HIV infection is a pandemic disease. Globally, about 35 million individuals were living with HIV in 2013. Of these, 24.7 million were in sub-Saharan Africa and 4.8 million in Asia and the Pacific (UNAIDS 2014).

In 2013, about 16 million individuals living with HIV globally were women aged 15 years and older and 3.2 million were children under 15 years of age (UNAIDS 2014).

More than 90% of HIV-positive pregnant women reside in sub-Saharan Africa (Kendall, 2014).

In 2013, 1.5 million HIV-infected women gave birth globally and there were 240 000 new paediatric infections, amounting to one new infection every two minutes (UNAIDS 2014).

In 2013, 24% of those living with HIV in the United States were women aged 13 years or older and they accounted for 20% of new infections (CDC 2015).

The prevalence of HIV infection amongst women giving birth in the United Kingdom in 2011 was 2.2 per 1000 women giving birth (BHIVA 2014).

HIV is the leading cause of death in women of reproductive age globally; responsible for one quarter of deaths during pregnancy and the six week postpartum period in sub-Saharan Africa (Kendall 2014).

British HIV Association. Management of HIV infection in pregnant women 2012 (2014 interim review). British HIV Association (BHIVA). 2014.
Centers for Disease Control and Prevention. HIV among women: Fact sheet. CDC. 2015.
Kendall T, Danel I. Research and evaluation agenda for HIV and maternal health in sub-Saharan Africa: women and health initiative working paper No. 1. Women and Health Initiative, Harvard School of Public Health: Boston, MA; 2014.
UNAIDS. The gap report. Joint United Nations Programme on HIV/AIDS (UNAIDS). 2014.

Global burden of HIV in pregnancy

Estimated number of pregnant women living with HIV in 2013

Region	Estimate
Asia and the Pacific	74 000
Caribbean	7400
Eastern Europe and central Asia	10 000
Latin America	17 000
Middle East and North Africa	7100
Sub-Saharan Africa	1 300 000
Western and central Europe and North America	12 000
GLOBAL	**1 500 000**

UNAIDS. The gap report. Joint United Nations Programme on HIV/AIDS (UNAIDS). 2014.

Epidemiological definitions

Concentrated HIV epidemic:
Rapid HIV rapid spread in one or more defined subpopulation.
HIV is not well established in the general population.
HIV prevalence is consistently above 5% in at least one defined subpopulation but is below 1% among pregnant women in urban areas.

Generalized HIV epidemic:
HIV is firmly established in the general population.
HIV prevalence consistently exceeds 1% among pregnant women.
Epidemics are mostly mixed and disproportionately affects certain (key) subpopulations.

Mixed epidemics:
HIV acquisition in one or more subpopulations and in the general population.
One or more concentrated epidemics within a generalized epidemic.

Low-level epidemic:
Prevalence of HIV infection has not consistently exceeded 1% in the general population nationally or 5% in any subpopulation.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

HIV testing and counselling

HIV testing and counselling should be voluntary, and observe the five C's of consent, confidentiality, counselling, correct test results and connections to care, treatment and prevention services.

The quality assurance of both testing and counselling is essential. (WHO 2013).

Generalized epidemics

Routine provider-initiated testing and counselling during antenatal, childbirth, postpartum and paediatric care settings.

Test at first antenatal care visit and re-test in the third trimester/ during labour/ shortly after delivery because of high risk of HIV acquisition during pregnancy. (WHO 2013).

Low-level and concentrated epidemics

Provider-initiated testing and counselling during pregnancy. (WHO 2013).

Where feasible, repeat testing in each trimester in women at high and ongoing risk for HIV infection (SOGC 2014).

Society of Obstetricians and Gynaecologists of Canada. Guidelines for the Care of Pregnant Women Living With HIV and Interventions to Reduce Perinatal Transmission. The Society of Obstetricians and Gynaecologists of Canada (SOGC). 2014.
World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Diagnosis and screening for HIV in pregnancy

About half of individuals living with HIV globally do not know their HIV status.

In 2013, 54% of pregnant women in low- and middle-income countries did not get an HIV test done (UNAIDS 2014).

HIV testing and counselling is a gateway to HIV treatment, care and prevention.

Depending on the local context and the epidemic type, strategies for testing and counselling should be mixed, equitable, accessible to all and cost-effective.

Offer pregnant women provider-initiated testing and counselling and linkage to prevention and care for their own health and to prevent new infection in children.

Offer partners voluntary HIV testing and counselling during antenatal care and provide support for mutual disclosure. (WHO 2013).

Tests for HIV diagnosis in pregnant women include:

- Standard tests - the enzyme immunoassay (ELISA) and Western blot protocol is highly (>99%) sensitive and specific.
- Rapid HIV tests- similar accuracy and provide results within hours without requiring a return visit, greater sensitivity with blood-based tests than tests using oral fluids. (AHMAC 2012).

Australian Health Ministers' Advisory Council. National Antenatal Care Guidelines. Australian Government Department of Health. 2012.
UNAIDS. The gap report. Joint United Nations Programme on HIV/AIDS (UNAIDS). 2014.
World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Testing in HIV-exposed infants

Maternal HIV antibody persist in the child up to 15–18 months of age.

Offer early infant diagnosis (EID) using virological tests that detect viral nucleic acid (polymerase chain reaction (PCR) for HIV DNA, RNA or total nucleic acid) or p24 antigen within four to six weeks of birth.

Do HIV serological test at last immunization or 9 months to identify infants who have persisting HIV antibody or have seroreverted.

Do HIV serological test in an infant or child with signs and symptoms suggestive of HIV infection to confirm exposure, then a virological test if child is <18 months of age.

Do a virological testing to diagnose HIV if the infant is seropositive and is >9 months and <18 months old.

Determine the final infant HIV infection status after 18 months and/or six weeks or more after breastfeeding cessation with initial HIV serological testing followed by virological testing for those HIV-positive and <18 months of age.

Recommendations for infant testing vary in resource-rich countries.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Prevention of HIV transmission in pregnancy

Prevention of HIV transmission in pregnancy involves:

1. The prevention of HIV transmission in the general population- to prevent pregnant women from being infected with HIV and reduce the risk of HIV transmission from a pregnant woman to her partner.
2. Prevention of mother-to-child transmission (PMTCT)- to reduce the risk of HIV transmission from a pregnant woman to her baby.

A combination approach is needed for the prevention of HIV transmission in all population. This provides a means for people to access interventions that is appropriate to their specific needs at any point in time and is more impactful than single interventions.

World Health Organization. Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations. WHO. 2014.

1. Prevention of HIV transmission in the general population

Prevention using ARV drugs

Oral pre-exposure prophylaxis of HIV (PrEP)

- The daily use of ARV drugs by HIV-uninfected people to prevent the acquisition of HIV.
- Clinical trials of daily oral PrEP shown to be effective with serodiscordant heterosexual couples.
- Offer daily oral PrEP (TDF or the combination of TDF + FTC) for the uninfected partner in serodiscordant relationship as a possible additional intervention where needed.
- Advise individuals living with HIV in serodiscordant couples starting ART for their own health and to reduce HIV transmission to the uninfected partner.
- Even with a CD4 count ≥350 cells/mm3, offer ART to HIV-positive partners in a serodiscordant couples to reduce HIV transmission to the uninfected partners.

HIV post-exposure prophylaxis

- ART given for a short duration of time to lower the chances of HIV infection acquisition after potential exposure by occupational means or through sexual intercourse.
- Duration of ART is 28 days with the first dose offered as early as possible within 72 hours of exposure.
- The choice of drugs depends on the country's first-line ARV regimen for HIV.
- Offer to sexually assaulted women who present within 72 hours of the assault as appropriate after a joint decision with the woman.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

1. Prevention of HIV transmission in the general population

The following interventions should be used in combination with ARV drugs as appropriate:

- Behavioural interventions.
- Structural and supportive interventions.
- Other biomedical interventions.

Behavioural interventions

Lowers the rate of potential transmission events through targeted information and education using behavioural messages to discourage HIV risk behaviours and encourage protective behaviours like safer drug use, delaying sexual debut, reducing the frequency of unprotected sex with multiple partners, correct and consistent use of male and female condoms and knowledge of own and partner's HIV status.

World Health Organization. Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations. WHO. 2014.

1. Prevention of HIV transmission in the general population

Structural and supportive interventions

Improve the accessibility, uptake and adherence to behavioural and biomedical interventions focusing on providing the social, legal, political and environmental enablers for HIV transmission reduction- legal and policy reform, reducing stigma and discrimination, promoting gender equality and preventing gender-based violence, economic empowerment, access to schooling and supportive interventions to facilitate referrals, adherence, retention and community mobilization.

Other biomedical interventions

Reduce HIV risk practices and/or the probability of HIV transmission per contact event.

Male and female condoms.

Needle and syringe programmes.

Opioid substitution therapy with methadone or buprenorphine- most effective in the treatment for opioid dependence.

Voluntary medical male circumcision- provides up to 66% reduction in the risk of acquisition of HIV for men and offers significant lifetime protection.

World Health Organization. Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations. WHO. 2014.

2. Prevention of mother-to-child transmission (PMTCT)

HIV can be transmitted from mothers to their infants during pregnancy, labour, delivery and breastfeeding.

Without intervention, the risk of transmission is 15−30% in non-breastfeeding populations and 20−45% in breastfeeding mothers (WHO 2010).

In non-breastfeeding settings, up to 50% of HIV transmission from mother to child occurs late in the third trimester (from 36 weeks), during labour, or at delivery if there is no intervention (Diaz-Rossello 2008).

Providing highly effective antiretroviral therapy (ART) and antiretroviral drug (ARV) prophylaxis interventions through prevention of mother-to-child transmission of HIV (PMTCT) programmes can prevent almost all of these infections.

PMTCT can reduce the risk of mother-to-child transmission of HIV (MTCT) to less than 5% in breastfeeding populations and to less than 2% in non-breastfeeding populations (WHO 2010).

PMTCT includes all interventions to prevent transmission of HIV from a mother living with HIV to her infant during pregnancy, labour and delivery or during breastfeeding. It also improves mother's health through early initiation of ART (WHO 2013).

Diaz-Rossello JL. Perinatal infections transmitted by the mother to her infant: educational material for health personnel. Latin American Center for Perinatology/ Women and Reproductive Health - CLAP/SMR Pan American Health Organization / World Health Organization - PAHO/WHO. 2008.
World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

2. Prevention of mother-to-child transmission (PMTCT)

There are four approaches to a comprehensive PMTCT strategy:

1. Primary prevention of HIV infection among women of childbearing age.
2. Prevent unintended pregnancies among women living with HIV.
3. Prevent HIV transmission from women living with HIV to their infants.
4. Provide appropriate treatment, care, and support to mothers living with HIV, their children and families.

Two options are recommended by the World Health Organization (WHO) depending on country programmes:

1. ART to pregnant or breastfeeding women living with HIV for the duration of the risk of mother-to-child transmission (**"Option B"**).
2. Lifelong ART regardless of CD4 cell count based on local circumstances, preferences and values (**"Option B+"**).

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

2. Prevention of mother-to-child transmission (PMTCT)

Provide ART only during the period of risk of mother-to-child transmission ("Option B") with continuing lifelong ART only for those women meeting standard eligibility criteria for the treatment of non-pregnant adults**.**

Relevant in settings with:
- concentrated epidemics,
- lower repeat pregnancy rates and higher family planning coverage,
- high access to CD4 testing,
- high existing coverage of ART for pregnant women who meet the treatment eligibility criteria for non-pregnant individuals, and
- where formula feeding is recommended, available and safe.

Provide Lifelong ART ("Option B+") to all pregnant and breastfeeding women

Particularly relevant in settings with:
- generalized epidemic,
- high repeat pregnancy rates and low family planning coverage (family planning programmes should be instituted),
- low partner testing rates,
- limited access to CD4 testing,
- low existing coverage of ART for pregnant women who meet the treatment eligibility criteria for non-pregnant individuals, and
- long duration of breastfeeding by women living with HIV.

The "Option A" regimen that offers AZT for the mother during pregnancy and single-dose NVP (sd-NVP) plus AZT and 3TC at delivery and for a week postpartum is no longer recommended by WHO.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

2. Prevention of mother-to-child transmission (PMTCT)

Factors associated with the risk of vertical transmission from the mother to her baby include:

- Maternal
  - Advanced maternal HIV disease
  - Maternal antenatal CD4 counts less than 200 cells/mm^3
  - High maternal plasma viral loads
- Obstetric
  - Vaginal delivery
  - Premature rupture of membrane
  - Chorioamnionitis
  - Preterm delivery
- Postnatal
  - Breastfeeding

Diaz-Rossello JL. Perinatal infections transmitted by the mother to her infant: educational material for health personnel. Latin American Center for Perinatology/ Women and Reproductive Health - CLAP/SMR Pan American Health Organization / World Health Organization - PAHO/WHO. 2008.

Laboratory and clinical monitoring- general

Linkage to care and treatment

As with other HIV infected individuals, early enrolment in care will facilitate early assessment of eligibility for ART, timely initiation of ART and access to interventions to prevent further transmission of HIV and other infections and comorbidities, and reduce loss to follow-up.

The following can facilitate linkage to care:

- Linking HIV testing and counselling programmes to prevention, treatment, care and support services.
- Providing on-site or immediate CD4 testing with same-day results.
- Transport assistance to ART site if far from the HIV testing and counselling site.
- Community outreach workers' involvement in the identification of cases lost to follow-up.
- Peers or expert patients support.
- Use of new technologies, like mobile phone text messaging.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Laboratory and clinical monitoring- general

General care for all people infected with HIV, including pregnant women, should be adapted to the type of epidemic and includes:

- Psychosocial counselling and support.
- Disclosure and partner notification.
- Co-trimoxazole preventative therapy (CPT).
- Tuberculosis (TB) counselling, screening and preventive therapy.
- Preventing common fungal infections.
- Preventing sexually transmitted infections and supporting reproductive health needs, including prevention of and screening for cervical cancer.
- Malaria (co-trimoxazole, bed-nets and preventing malaria).
- Selected vaccine-preventable diseases.
- Nutrition.
- Family planning.
- Prevention of mother-to-child transmission (PMTCT).
- Needle and syringe programmes for people who inject drugs.
- Water, sanitation and hygiene.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Laboratory and clinical monitoring- pregnancy

Majority of maternal deaths among women with HIV are from non-obstetric causes, the most risk being in those with advanced disease and least time on antiretroviral therapy (ART). Improved availability of ART and early initiation will reduce maternal morbidity and mortality (Kendall 2014).

- HIV infected pregnant women should receive the minimum package of antenatal visits and pregnancy care recommended for all pregnant women. Clinicians should also:
  - Provide screening for sexually transmitted infections.
  - Provide nutritional counselling and information on infant feeding.
  - Encourage recommended antenatal clinic visits.
  - Manage pregnancy as high-risk in the late third trimester. (WHO 2013).
  - Provide family planning counselling- there are no restrictions to the use of hormonal contraceptives (IATT 2013).

Kendall T, Danel I. Research and evaluation agenda for HIV and maternal health in sub-Saharan Africa: women and health initiative working paper No. 1. Women and Health Initiative, Harvard School of Public Health: Boston, MA; 2014.
IATT, UNICEF, WHO. Toolkit, expanding and simplifying treatment for pregnant women living with HIV. WHO. 2013.
World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Laboratory and clinical monitoring- pregnancy

Recommendations for clinical and laboratory monitoring of HIV-infected pregnant women should be as for non-HIV-infected pregnant women. Other monitoring for her HIV disease are as follows:

At diagnosis

Recommended:

- HIV serology.
- CD4 cell count.
- TB screening.

Desirable:

- Hepatitis B virus (HBV) serology- hepatitis B surface antigen (HBsAg).
- Hepatitis C virus (HCV) serology.
- Cryptococcus antigen if CD4 count ≤100 cells/mm^3 (in settings with a high prevalence of cryptococcal antigenaemia (>3%)).
- Screening for sexually transmitted infections.
- Assessment for major non-communicable chronic diseases and comorbidities. (WHO 2013).

HIV viral load and HIV resistance testing are recommended in resource-rich countries (BHIVA 2014; Palasanthiran 2014; SOGC 2014).

Palasanthiran P, Starr M, Jones C, Giles M. Management of Perinatal Infections. Second edition. Sydney, Australia: Australasian Society for Infectious Diseases; 2014.
British HIV Association. Management of HIV infection in pregnant women 2012 (2014 interim review). British HIV Association (BHIVA). 2014.
Society of Obstetricians and Gynaecologists of Canada. Guidelines for the Care of Pregnant Women Living With HIV and Interventions to Reduce Perinatal Transmission. The Society of Obstetricians and Gynaecologists of Canada (SOGC). 2014.
World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Laboratory and clinical monitoring- labour and delivery

Apart from deaths from non-obstetric causes, women with HIV suffer greater mortality due to puerperal sepsis and obstetric hemorrhage than their HIV-negative counterparts (Kendall 2014).

During labour and delivery:

- Promote facility-based delivery by trained skilled birth attendants.
- Monitor labour using partograph.
- Avoid unnecessary instrumentation.
- Avoid premature rupture of membranes.
- Encourage non-invasive suction of nasogastric secretions in the newborn.
- Wash away blood in the newborn.
- Identify mothers with HIV early and provide ARV drugs to both the mother and the newborn baby. (WHO 2013).

Kendall T, Danel I. Research and evaluation agenda for HIV and maternal health in sub-Saharan Africa: women and health initiative working paper No. 1. Women and Health Initiative, Harvard School of Public Health: Boston, MA; 2014.
World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Laboratory and clinical monitoring- labour and delivery

- Offer rapid HIV testing during labour or immediate postpartum period for all mothers presenting at labour with unknown HIV status.
- Provide ARV treatment to women testing positive and their babies in line with current treatment recommendations.
- Consider extended prophylaxis for infants of mothers who tested positive for HIV.
- Follow universal precautions for all deliveries regardless of the HIV status of the mother.
- Ensure that provision of delivery care is supportive and without stigma.
- In resource-limited settings, indication for caesarean section should be obstetric or medical and not HIV status even though it has been shown to protect against HIV transmission, especially in the absence of ARV drugs or in the case of high viral load. (WHO 2013).
- In resource-rich countries, management of labour and decisions on the mode of delivery vary and are based on whether or not the woman is on ART and her viral load (BHIVA 2014; Palasanthiran 2014; SOGC 2014).

Palasanthiran P, Starr M, Jones C, Giles M. Management of Perinatal Infections. Second edition. Sydney, Australia: Australasian Society for Infectious Diseases; 2014.
British HIV Association. Management of HIV infection in pregnant women 2012 (2014 interim review). British HIV Association (BHIVA). 2014.
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World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Laboratory and clinical monitoring- postnatal care

Encourage all HIV infected women and women of unknown HIV status who deliver outside health facilities to visit a maternal and child health facility as soon as possible after delivery. These women should be medically assessed and HIV interventions initiated or continued as appropriate.

Provide follow-up and linkages to HIV care and treatment and postpartum care for HIV infected women and their infants.

Initial follow up of the HIV-exposed infant should be at the first immunization visit at four to six weeks- emphasize safe feeding practices, review ARV coverage, and offer early infant diagnosis testing.

Schedule the follow-up visit for the HIV infected mother preferably at the same time as the baby- perform a postpartum check, offer family planning counselling, review ARV regimen and provide adherence support. (WHO 2013).

Encourage testing of previous children if their HIV status is unknown (SOGC 2014).

Society of Obstetricians and Gynaecologists of Canada. Guidelines for the Care of Pregnant Women Living With HIV and Interventions to Reduce Perinatal Transmission. The Society of Obstetricians and Gynaecologists of Canada (SOGC). 2014.
World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Laboratory and clinical monitoring- infant feeding

Exclusively breastfeed uninfected infants and infants of unknown HIV status for the first 6 months of live.

Introduce appropriate complementary foods after the first 6 months of exclusive breastfeeding.

Continue breastfeeding for the first 12 months of life and then stop once a nutritionally adequate and safe diet without breast-milk can be provided *(strong recommendation, high-quality evidence for the first 6 months; low-quality evidence for the recommendation of 12 months).*

Aim of WHO recommendations is to improve the HIV-free survival of HIV-exposed infants through ARV drug provision to decrease the risk of HIV transmission and avoidance of malnutrition and higher risk of severe infections in the infants and children from unsafe feeding practices. (WHO, 2013).

Exclusive formula feeding is recommended in resource-rich countries (BHIVA 2014; Palasanthiran 2014; SOGC 2014).

British HIV Association. Management of HIV infection in pregnant women 2012 (2014 interim review). British HIV Association (BHIVA). 2014.
Palasanthiran P, Starr M, Jones C, Giles M. Management of Perinatal Infections. Second edition. Sydney, Australia: Australasian Society for Infectious Diseases; 2014.
Society of Obstetricians and Gynaecologists of Canada. Guidelines for the Care of Pregnant Women Living With HIV and Interventions to Reduce Perinatal Transmission. The Society of Obstetricians and Gynaecologists of Canada (SOGC). 2014.
World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Laboratory monitoring

ART initiation

- CD4 cell count.
- Haemoglobin test for AZT- closely monitor for clinically significant anaemia.
- Blood pressure measurement.
- Urine dipsticks for glycosuria and estimated glomerular filtration rate (eGFR) and serum creatinine for TDF, protein and bilirubin. (WHO 2013)
- Syphilis screening.
- Biochemistry.
- Early infant diagnosis (EID) test. (IATT 2013).
- In defining the clinical stage of a pregnant woman, consider her expected weight gain in relation to the gestational age of the pregnancy and her potential weight loss from HIV (WHO 2010).

IATT, UNICEF, WHO. Toolkit, expanding and simplifying treatment for pregnant women living with HIV. WHO. 2013.
World Health Organization. Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: Recommendations for a public health approach (2010 version). WHO. 2010.
World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Laboratory monitoring

Receiving ART

Recommended:

- CD4 cell count (every 6 months)
- HIV viral load (at 6months after initiating ART and every 12 months thereafter)

Desirable:

- Urine dipstick for glycosuria and serum creatinine for TDF. (WHO 2013).

Additional monitoring of adverse reactions related to antiretroviral drugs will depend on the potential adverse reactions of the antiretroviral agents used (WHO 2010).
High-income countries have different recommendations for laboratory monitoring (BHIVA 2014; Palasanthiran 2014; SOGC 2014).

British HIV Association. Management of HIV infection in pregnant women 2012 (2014 interim review). British HIV Association (BHIVA). 2014.
Palasanthiran P, Starr M, Jones C, Giles M. Management of Perinatal Infections. Second edition. Sydney, Australia: Australasian Society for Infectious Diseases; 2014.
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World Health Organization. Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: Recommendations for a public health approach (2010 version). WHO. 2010.
World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Antiretroviral therapy (ART)

Prior to ART initiation

Discuss with the individuals about their willingness and readiness to initiate ART, the ARV regimen, dosage and scheduling, the likely benefits and possible adverse effects and the required follow-up and monitoring visits.

Do a retesting to confirm HIV diagnosis.

Assess for nutritional status, comorbidities and potentially interacting medications for possible contraindications to HIV medication or dose adjustment.

If the individual declines ART, delay initiation and offer ART at subsequent visits.

In cases of mental health, substance use or other problems that may jeopardise adherence, offer appropriate support, and reassess readiness to for ART initiation at regular intervals.

Provide patient information materials and link to community and peer support, and stress the importance of adherence in the success of treatment.

Request information on any additional medication that are taken, including herbal remedies and nutritional supplements, on a regular basis.

Provide information on condom use, safer sex and avoidance of high risk behaviours to prevent HIV transmission to others (WHO 2013).

HIV-infected women already receiving ART and who become pregnant should also receive appropriate antenatal counselling (WHO 2010).

World Health Organization. Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: Recommendations for a public health approach (2010 version). WHO. 2010.
World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Starting ART in pregnant women living with HIV

WHO recommendations on use of ARVs in pregnant women follows a public health approach (WHO 2013), while in resource rich settings treatment is individualized (SOGC 2014).

Women who are already receiving ART for their own health and have a good immune response should continue. This is to avoid viral rebound, drop in CD4 cell count and subsequent risk of MTCT and HIV disease progression that may result if ART is stopped (WHO 2010).

Initiate triple ARVs (ART) in all HIV infected pregnant and breastfeeding women and maintain for at least the duration of mother-to-child transmission risk. Women meeting treatment eligibility criteria should continue lifelong ART **("Option B"**) (strong recommendation, moderate-quality evidence),

OR

Initiate lifelong ART treatment in all HIV infected pregnant and breastfeeding women-recommended for programmatic and operational reasons, especially in generalized epidemics **("Option B+"**) (conditional recommendation, low-quality evidence).

Stopping ART treatment at the end of the mother-to-child transmission risk period, in women who are not eligible for ART for their own health, may be considered in some countries (conditional recommendation, low-quality evidence). (WHO 2013).

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World Health Organization. Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: Recommendations for a public health approach (2010 version). WHO. 2010.
World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Recommended antiretroviral drugs and adult dosages

Nucleoside reverse-transcriptase inhibitors (NRTIs)

Abacavir (ABC) 300 mg twice daily or 600 mg once daily

Didanosine (ddI) 400 mg once daily (>60 kg) 250 mg once daily (≤60 kg)

Emtricitabine (FTC) 200 mg once daily

Lamivudine (3TC) 150 mg twice daily or 300 mg once daily

Stavudine (d4T) 30 mg twice daily

Zidovudine (AZT) 250−300 mg twice daily

Nucleotide reverse-transcriptase inhibitors (NtRTIs)

Tenofovir (TDF) 300 mg once daily

Non-nucleoside reverse-transcriptase inhibitors (NNRTIs)

Efavirenz (EFV) 600 mg once daily

Etravirine (ETV) 200 mg twice daily

Nevirapine (NVP) 200 mg once daily for 14 days, followed by 200 mg twice daily

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Recommended antiretroviral drugs and adult dosages

Proteases inhibitors (PIs)

Atazanavir (ATV)+ (RTV) ritonavir (ATV/r) 300 mg + 100 mg once daily

Darunavir (DRV)+ ritonavir (DRV/r) 800 mg + 100 mg once daily or 600mg + 100 mg twice daily

Lopinavir (LPV)/ritonavir (LPV/r) 400 mg/100 mg twice daily

On-going tuberculosis (TB) therapy

- In the presence of rifabutin, no dose adjustment required.
- In the presence of rifampicin, adjusted dose of LPV/r (LPV 800 mg + RTV 200 mg twice daily or LPV 400 mg + RTV 400 mg twice daily) or Saquinavir/ ritonavir (SQV/r) (SQV 400 mg + RTV 400 mg twice daily), with close monitoring.

Integrase strand transfer inhibitors (INSTIs)

Raltegravir (RAL) 400 mg twice daily

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

First-line ART for pregnant and breastfeeding women

Two nucleoside reverse-transcriptase inhibitors (NRTIs) and a non-nucleoside reverse-transcriptase inhibitor (NNRTI).

Recommended: TDF + 3TC (or FTC) + EFV as a once-daily fixed-dose combination.

Use in pregnant and breastfeeding women, including pregnant women in the first trimester of pregnancy and women of childbearing age. (*Strong recommendation, but low-quality evidence for pregnant and breastfeeding women*).

Rationale for recommendation

- TDF has limited penetration into breast-milk, which would limit potential toxicity for the breastfeeding infant.
- No increased risk of birth defects with EFV compared with other ARV drugs used during the first trimester of pregnancy.
- Treatment is harmonized across different populations- TB and HIV co-infection and pregnancy.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

First-line ART for pregnant and breastfeeding women

Alternatives first line options:

AZT + 3TC + EFV **OR** AZT + 3TC + NVP **OR** TDF + 3TC (or FTC) + NVP

Do not initiate TDF when the estimated glomerular filtration rate (eGFR) is <50 ml/min, or in long-term-diabetes, uncontrolled hypertension and renal failure.

The evidence that pregnant women with HIV who have high CD4 counts are at increased risk of adverse events from NVP use compared with the general population with HIV is weak but there is need for a lead-in dosing for its initial use and it is not available as a fixed-dose combination with TDF + 3TC (or FTC).

NVP should be used with caution in pregnant women and women who might be pregnant and the risk and benefits and available alternatives considered.

First-line ART regimens may differ in resource rich countries.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Postnatal infant prophylaxis

Start infant prophylaxis as soon as possible after birth or postpartum following a recognized HIV exposure.

Recommended regimen

- Daily NVP for six weeks for infants of mothers who are receiving ART and are breastfeeding.
- Daily NVP (or twice-daily AZT) for four to six weeks for infants receiving replacement feeding.

(Strong recommendation, moderate-quality evidence for breastfeeding infants; strong recommendation, low-quality evidence for infants receiving only replacement feeding).

In special circumstances such as when the mother has had limited ART and is unlikely to be virally suppressed, or where the infant is identified as HIV exposed after birth and is breastfeeding, dosing should be extended beyond 6 weeks of age, with prolonged dosing of up to 12 weeks.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Postnatal infant prophylaxis

Recommended dosing: NVP

Birth to 6 weeks (or 4 weeks if settings with replacement feeding).

Birth-weight- 2000−2499 g- 10 mg once daily.

Birth-weight- ≥2500 g- 15 mg once daily.

Infants weighing <2000 g should receive mg/kg dosing; the suggested starting dose is 2 mg/kg once daily.

6 weeks to 6 months- 20 mg once daily.

>6 months to 9 months - 30 mg once daily.

>9 months until breastfeeding ends - 40 mg once daily.

Recommended dosing: AZT (only recommended in settings with replacement feeding)

Birth to 6 weeks.

Birth-weight- 2000−2499 g- 10 mg twice daily.

Birth-weight- ≥2500 g- 15 mg twice daily.

Infants weighing <2000 g should receive mg/kg dosing; the suggested starting dose is 2 mg/kg twice daily.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

What to expect in the early months of ART

If adherence to ART is good, the following occur in the first six months of treatment:

- Clinical improvement.
- Immunological improvement.
- Virological suppression.
- Complications are also common and the highest death rates occur in the first three months of ART.

Complications of ART:

- Opportunistic infections.
- Immune reconstitution inflammatory syndrome (IRIS).
- Adverse drug reactions like drug hypersensitivity- especially in the first three months of ART.

Risk factors for complications:

- Advanced HIV disease with severe immunodeficiency and existing co-infections and/or comorbidities.
- Severely low haemoglobin.
- Low body mass index.
- Very low CD4 counts.
- Severe malnutrition.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

CD4 recovery

CD4 cell counts generally rises once immune recovery starts following ART initiation.

It increases during the first year of treatment, reaches a plateau, and then further rises during the second year.

It may fail to rise significantly in individuals with persistently severe immunosuppression, especially those with a very low pre-ART CD4 cell count.

Rule out adherence problems or primary non-response to ART where CD4 recovery is poor.

Prophylaxis for opportunistic infections such as co-trimoxazole preventive therapy should continue in individuals with poor CD4 recovery.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Immune reconstitution inflammatory syndrome (IRIS)

A range of clinical signs and symptoms that are possibly associated with immune recovery as a result of ART.

Occurs in 10–30% of individuals initiating ART, commonly within the first 4–8 weeks after ART is initiated.

Presents as:

Paradoxical IRIS

- Opportunistic infection or tumour diagnosed before ART responding initially to treatment but then deteriorating after ART starts.
- Severe and serious and life-threatening forms seen in TB, cryptococcosis, Kaposi's sarcoma and herpes zoster.

Unmasking IRIS

- When initiating ART triggers a disease that was not clinically apparent before ART.

Consider IRIS only when the presentation cannot be explained by a new infection, expected course of a known infection or drug toxicity.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Immune reconstitution inflammatory syndrome (IRIS)

Risk factors:

- ART initiation.
- Disseminated opportunistic infections or tumours.
- A shorter duration of therapy for opportunistic infections before starting ART.

Management:

- Generally self-limiting.
- Interruption of ART is rarely indicated.
- Provide reassurance to prevent discontinuation of or poor adherence to ART.

Reduce occurrence through:

- Earlier HIV diagnosis.
- ART initiation before a decline to below 200 CD4 cells/mm^3 .
- Improved screening for opportunistic infections before ART, especially TB and Cryptococcus.
- Optimal management of opportunistic infections before initiating ART
- Appropriate timing of ART in individuals with opportunistic infections weighing the risk of IRIS after early initiation against high mortality with delayed initiation.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Treatment failure

Treatment failure is defined as a persistently detectable viral load above 1000 copies/ml measured on two consecutive occasions within a three-month interval and with adherence support between measurements, after at least six months of using ARV drugs.

Viral load is a more sensitive and early indicator of treatment failure. Viral load testing is recommended to diagnose and confirm ARV treatment failure (*recommendation- strong, evidence quality level- low*).

If viral load testing is not routinely available, CD4 count and clinical monitoring should be used to diagnose treatment failure, using targeted viral load testing to confirm virological failure where possible (*recommendation- strong, evidence quality level- moderate*).

If available, HBV (HBsAg) serology is also recommended before switching ARV regimen, especially if this testing was not done or if the result was negative at baseline (WHO 2013).

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Clinical failure

Occurrence of new or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4 condition) after 6 months of effective treatment.

Clinical failure should be differentiated from immune reconstitution inflammatory syndrome (IRIS) occurring after initiating ART.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Immunological failure

A fall in CD4 count to the baseline (or below) or persistently low CD4 levels below 100 cells/mm^3 that is not caused by a temporary drop in CD4 cell count due to a current or recent infection (WHO 2013).

Pregnancy related haemodilution causes a drop in the absolute CD4 count in pregnancy. A decrease in the absolute CD4 count from the pre-pregnancy value should thus be interpreted with caution. CD4 cell count may rise by 50-100 cells/mm^3 after delivery (WHO 2010).

According to a systematic review, the sensitivity and positive predictive value for the identification of individuals with virological failure is low using clinical and immunological criteria (WHO 2013).

World Health Organization. Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: Recommendations for a public health approach (2010 version). WHO. 2010.
World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Second-line ART

Aims of World Health Organization recommended second line options are:

- Reduced pill burden
- Usability across populations (adults, adolescents, children, pregnant women and co-infection with TB, HBV and HCV).
- Convenience and efficacy with less toxicity.
- Heat-stable fixed-dose combinations.

Second-line ART should consist of two nucleoside reverse-transcriptase inhibitors (NRTIs) + a ritonavir-boosted protease inhibitor (PI).

That is,

TDF + 3TC (or FTC) + ATV/r or LPV/r (If d4T or AZT was used in the first line regimen).

AZT + 3TC + ATV/r or LPV/r (if TDF was used in first-line ART).

- Heat-stable fixed-dose combinations of ATV/r and LPV/r are the preferred boosted PI options.
- ABC and ddI are alternatives NRTI options but are more complex and costly without clinical advantages.
- DRV/r can be used as an alternative PI and SQV/r in special situations, but may not be available as a heat-stable fixed-dose combination.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Second-line ART

HIV and TB coinfection

- If rifabutin is available use standard PI-containing regimens as recommended for adults and adolescents for second line.
- If rifabutin is not available use same NRTI backbones as recommended for adults and adolescents plus double-dose LPV/r (that is, LPV/r 800 mg/200 mg twice daily) or standard LPV dose with an adjusted dose of RTV (that is, LPV/r 400 mg/400 mg twice daily).

HIV and HBV coinfection

- AZT + TDF + 3TC (or FTC) + (ATV/r or LPV/r)

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Third-line ART

The failure of second-line ART is diagnosed based on the same criteria used for diagnosing the failure of first-line ART.

Evidences guiding third-line strategies are limited and mortality is high among people for whom second-line ART had failed.

Randomized controlled trials conducted in middle- to high-income countries support the efficacy of DRV/r, etravirine (ETV) and raltegravir (RAL), used in combination with optimized background regimen (OBR) chosen by genotyping and phenotyping, in highly ART-experienced patients.

Pharmacokinetic and safety information as well as data on the use of the newer drugs in pregnancy are very limited.

Third-line regimens should include new drugs with minimal risk of cross-resistance to previously used regimens, such as integrase inhibitors and second-generation NNRTIs and Pis.

Patients on a failing second-line regimen with no new ARV options should continue with a tolerated regimen.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Management of ARV toxicities

ABC

Hypersensitivity reaction.

Action:

Substitute with TDF or AZT or d4T if ABC is being used in first-line ART, if it is being used in second-line ART, substitute with TDF.

ATV/r

Electrocardiographic abnormalities (PR interval prolongation) and indirect hyperbilirubinaemia (clinical jaundice).

Action:

Substitute with LPV/r or DRV/r. If boosted PIs are contraindicated and NNRTIs have failed in first-line ART, consider integrase inhibitors.

AZT

Anaemia, neutropaenia, myopathy, lipoatrophy or lipodystrophy and lactic acidosis or severe hepatomegaly with steatosis.

Action:

- If AZT is being used in first-line ART, substitute with TDF or ABC.
- If AZT is being used in second-line ART, substitute with d4T.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Management of ARV toxicities

d4T

Peripheral neuropathy, lipoatrophy or lipodystrophy, lactic acidosis or severe hepatomegaly with steatosis and acute pancreatitis.

Action:

- If d4T is being used in first-line ART, substitute with TDF or AZT or ABC.
- If d4T is being used in second-line ART (after TDF or ABC are used in first-line ART), substitute with AZT.

DRV/r

Hepatotoxicity, severe skin and hypersensitivity reactions.

Action:

- If DRV/r is being used in second-line ART, substituting with ATV/r or LPV/r can be considered.
- When it is used in third-line ART, limited options are available.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Management of ARV toxicities

EFV

Persistent central nervous system toxicity (such as abnormal dreams, depression or mental confusion), hepatotoxicity, convulsions, hypersensitivity reaction, Stevens-Johnson syndrome, potential risk of neural tube birth defects and male gynaecomastia.

Action:

- Switch to NVP. If the person cannot tolerate either NNRTI, use boosted PIs.

The central nervous system side effects usually resolve after a few weeks, but may persist for months or not resolve at all in some cases.

There is no overall increase in the incidence of birth defects for first-trimester EFV exposure compared with other ARV drugs.

ETV

Severe skin and hypersensitivity reactions.

Action: Limited options are available.

LPV/r

Electrocardiographic abnormalities (PR and QT interval prolongation, torsades de pointes), QT interval prolongation, hepatotoxicity, pancreatitis, risk of prematurity, lipoatrophy or metabolic syndrome, dyslipidaemia and severe diarrhoea.

Action:

- ATV/r or DRV/r (if LPV/r is used in second-line ART).
- Consider integrase inhibitors if boosted PIs are contraindicated and treatment with NNRTI in first-line ART has failed.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Management of ARV toxicities

NVP

Hepatotoxicity, severe skin rash and hypersensitivity reaction (Stevens-Johnson syndrome).

Action: Switch to EFV.

If the person cannot tolerate either NNRTI, use boosted PIs

If feasible, monitor hepatic enzymes, especially for women with HIV who have CD4 cell counts >250 cells/mm3 and individuals with HIV who are co-infected with HBV or HCV. The laboratory measurement of liver enzymes has very low predictive value for NVP-containing regimens however.

RAL

Rhabdomyolysis, myopathy and myalgia.

Action: Limited options are available.

TDF

1. Tubular renal dysfunction, Fanconi syndrome, decreases in bone mineral density, lactic acidosis and severe hepatomegaly with steatosis.

Action:

- If TDF is being used in first-line ART, substitute with AZT or d4T or ABC.
- If TDF is being used in second-line ART (after d4T + AZT use in firstline ART), substitute with ABC or ddI.

2. Exacerbation of hepatitis B (hepatic flares) as a result of discontinuation of TDF due to toxicity.

Action: Use alternative drug for hepatitis B treatment (such as entecavir).

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Stopping or substituting ARVs

Do not initiate ART in a pregnant woman who has substantial nausea of pregnancy until the nausea is adequately controlled. Most drugs used to stop nausea in pregnancy can be administered together with ARVs (SOGC 2014).

Discontinue ART in a woman who is already on ARVs and has hyperemesis of pregnancy until this is controlled (SOGC 2014).

Substituting ARVs may become necessary for drug toxicity or to avoid drug interactions (WHO 2013).

Substitute ARVs early in cases of severe adverse drug effects to prevent harm and avoid poor adherence and subsequent drug resistance and treatment failure (WHO 2013).

Resistance may develop if an NNRTI-based regimen is stopped suddenly because of the prolonged half-life of EFV and NVP (WHO 2013).

Society of Obstetricians and Gynaecologists of Canada. Guidelines for the Care of Pregnant Women Living With HIV and Interventions to Reduce Perinatal Transmission. The Society of Obstetricians and Gynaecologists of Canada (SOGC). 2014.
World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Stopping or substituting ARVs

When a NNRTI is to be discontinued, prolong the use of the NRTI backbone for two to three weeks **OR** substitute the NNRTI temporarily with a boosted PI (WHO 2013).

As suggested by pharmacokinetic modelling, if the NRTI backbone included TDF, the tail may not be needed. However, if the NRTI backbone included AZT, the tail should be given (WHO 2013).

If ART is not an NNRTI-based regiment, discontinue all drugs at once and restart all drugs simultaneously to reduce the risk of developing viral resistance during therapy (SOGC 2014).

Resume ART as quickly as possible after discontinuation to reduce the risk of rebound vireamia and the potentially increased risk of vertical transmission (SOGC 2014).

Society of Obstetricians and Gynaecologists of Canada. Guidelines for the Care of Pregnant Women Living With HIV and Interventions to Reduce Perinatal Transmission. The Society of Obstetricians and Gynaecologists of Canada (SOGC). 2014.
World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Co-trimoxazole preventive therapy (CPT)

For prevention of Pneumocystis pneumonia, toxoplasmosis and bacterial infections.

To be implemented as part of the HIV care services.

Start at:

Any WHO stage and CD4 count <350 cells/mm ^{3} (CD4 threshold of <200 cells/mm^3 in some countries) **OR**

WHO 3 or 4 irrespective of CD4 level **OR**

In everyone regardless of CD4 percentage or clinical stage in settings where HIV is highly prevalent or there is high infant mortality due to infectious diseases and limited health infrastructure.

Discontinue therapy:

- In individuals with Stevens-Johnson syndrome, severe liver disease, severe anaemia, severe pancytopaenia.
- Contraindications to co-trimoxazole preventive therapy: severe allergy to sulfa drugs; severe liver disease, severe renal disease and glucose-6-phosphate dehydrogenase (G6PD) deficiency.
- Never or discontinue when CD4 ≥350 cells/mm^3 after 6 months of ART (in settings with high prevalence of bacterial infections or malaria) or CD4 ≥200 cells/mm^3 after 6 months of ART (if initiation is primarily for *Pneumocystis* pneumonia or toxoplasmosis prophylaxis).

Dose of Co-trimoxazole: 960 mg daily.

Monitoring: Clinical at 3-monthly intervals.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Co-infection with Tuberculosis (TB)

The most frequent life-threatening opportunistic infection and a leading cause of death in people living with HIV (WHO 2013).

The risk of active TB is about 10 times higher in HIV-infected pregnant women than in HIV-uninfected women.

Active TB accounts for up to 15% of maternal mortality in some settings.

TB in pregnant women is also associated with prematurity, low birthweight, and perinatal tuberculosis. (WHO 2010).

WHO *Three I's* strategy are:

- intensified TB case-finding
- isoniazid preventive therapy (IPT)
- infection control at all clinical encounters

Screen for TB and offer IPT if none of the symptoms of active TB is reported (current cough, fever, weight loss or night sweats. Other sensitive investigations may be added in settings with high HIV prevalence and a high TB prevalence among people living with HIV (> 10%). (WHO 2013).

For individuals with TB, start antituberculosis treatment first, then initiate ART as soon as clinically possible within the first 8 weeks of treatment.

World Health Organization. Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: Recommendations for a public health approach (2010 version). WHO. 2010.
World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Co-infection with Tuberculosis (TB)

Isoniazid preventive therapy (IPT)

Duration

Minimum of six months of IPT as part of a comprehensive package of HIV.

OR

Minimum of 36 months of IPT.

Contraindications

- Active hepatitis (acute or chronic).
- Regular and heavy alcohol consumption.
- Symptoms of peripheral neuropathy.

Past history of TB is not a contraindication for starting IPT.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Co-infection with Hepatitis B and C

Chronic hepatitis B virus (HBV) infection affects 5–20% of the 33 million people living with HIV worldwide.

Hepatitis C (HCV) affects 5–15% of individuals living with HIV- up to 90% among people who inject drugs.

The burden of co-infection is highest in low- and middle-income countries, particularly in South-East Asia and sub-Saharan Africa for HBV.

There is increasing morbidity and mortality from viral hepatitis among people living with HIV, including those on ART.

A comprehensive approach includes prevention, hepatitis B and HCV screening, HBV vaccination and treatment and care for people with HIV co-infected with HBV and/or HCV (WHO 2013).

Offer routine testing for HBV and HCV infections to all women living with HIV who are recognized to be IDUs.

Counsel all pregnant women with HIV/HBV coinfection about signs and symptoms of liver toxicity. (WHO 2010).

HCV co-infected women without immunity for HBV should be vaccinated against HBV after the first trimester.

ARV against HBV should be continued in a woman who becomes pregnant as there is no evidence of any adverse effect on maternal or neonatal health.

Tenofovir and emtricitabine or lamivudine should form the backbone of ARV regimen in HIV/HBV infection. (BHIVA 2014).

British HIV Association. Management of HIV infection in pregnant women 2012 (2014 interim review). British HIV Association (BHIVA). 2014.
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World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Co-infection with Malaria

Pregnant women with HIV, living in malaria-endemic areas are at increased risk of complications of malaria.

Advise pregnant women living with HIV in areas of stable malaria transmission to routinely use insecticide-treated bed-nets to reduce their exposure to malaria infection.

Offer intermittent preventive treatment during pregnancy in areas of high transmission.

Do malaria parasite testing using either microscopy or a rapid diagnostic test to confirm all suspected malaria cases.

Provide prompt and effective antimalarial treatment regimens treatment using artemisinin-based combination therapies.

Avoid using sulfadoxine-pyrimethamine to treat or prevent malaria among patients with HIV who are receiving co-trimoxazole prophylaxis.

Antimalarial drugs and ARV drugs may share toxicities (particularly sulfa- based drugs) and may have clinically important pharmacokinetic interactions (especially artemesinins, lumefantrine, NNRTIs and PIs).

If possible, avoid amodiaquine-containing artemisinin-based combination regimens in people with HIV receiving AZT, or EFV because of increased risk of neutropaenia in combination with AZT, and hepatotoxicity in combination with EFV.

Monitor people receiving treatment for both HIV and malaria closely for adverse drug reactions.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Co-infection with sexually transmitted infections

Sexually transmitted infections commonly coexist with HIV.

Most are asymptomatic and can cause complications, be transmitted to sexual partners and increase HIV transmission.

HIV infection alters the natural history of sexually transmitted infections.

Provide routine screening, diagnosis and treatment of sexually transmitted infections to identify the infection, provide appropriate treatment and prevent transmission.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Co-infection with cervical cancer

Cervical cancer is preventable and curable if diagnosed and treated early.

Higher risk of pre-cancer and invasive cervical cancer among women living with HIV.

The risk and persistence of human papillomavirus (HPV) infection increases with decreasing CD4 count and increasing HIV viral load.

Invasive cervical cancer is a WHO HIV clinical stage 4 condition.

Follow up women living with HIV closely for evidence of pre-cancerous changes in the cervix, regardless of their ART status or CD4 count and viral load.

Screen all women with HIV for cervical cancer regardless of age.

Provide immediate management for pre-cancerous and cancerous lesions.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

Vaccinations

Assess people living with HIV for eligibility for vaccination at all stages of care.

Offer routine vaccination according to recommended national immunization schedules.

Inactivated vaccines are more effective among people receiving ART and those without immunosuppression. They are safe and can be used with some efficacy in all groups.

Individuals with more severe immunosuppression may be at higher risk of complications from live vaccines.

World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. WHO. 2013.

You have completed the module HIV infection in pregnancy and should now be able to:

- Know the global burden of HIV in pregnancy.
- Describe the screening and diagnostic measures for HIV in general and during and after pregnancy.
- Describe the interventions to prevent HIV transmission in general and in pregnancy (PMTCT).
- Describe the laboratory and clinical monitoring of HIV-positive pregnant women and HIV-exposed newborns.
- Describe the ARV regimens in general and during and after pregnancy.
- Know what complications to expect and how to manage them when a pregnant woman is on ART.
- Know the indications for stopping or substituting ARVs and how to stop or substitute ARVs in a pregnant woman with HIV.
- Identify the common HIV co-infections and measures to reduce morbidity and mortality.

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