Guidelines for the Care of Pregnant Women Living With HIV and Interventions to Reduce Perinatal Transmission: Executive Summary

Abstract

Objective: This guideline reviews the evidence relating to the care of pregnant women living with HIV and the prevention of perinatal HIV transmission. Prenatal care of pregnancies complicated by HIV infection should include monitoring by a multidisciplinary team with experts in this area.

Outcomes: Outcomes evaluated include the impact of HIV on pregnancy outcome and the efficacy and safety of antiretroviral therapy and other measures to decrease the risk of vertical transmission.

Evidence: Published literature was retrieved through searches of PubMed and The Cochrane Library in 2012 and 2013 using appropriate controlled vocabulary (HIV, anti-retroviral agents, pregnancy, delivery) and key words (HIV, pregnancy, antiretroviral agents, vertical transmission, perinatal transmission). Results were restricted to systematic reviews, randomized control trials/controlled clinical trials, and observational studies published in English or French. There were no date restrictions. Searches were updated on a regular basis and incorporated in the guideline to June 2013. Grey (unpublished) literature was identified through searching the websites of health technology assessment and health technology-related agencies, clinical practice guideline collections, clinical trial registries, and national and international medical specialty societies.

Values: The quality of evidence in this document was rated using the criteria described in the Report of the Canadian Task Force on Preventive Health Care (Table 1).

Key Words: HIV, pregnancy, antiretroviral agents, vertical transmission, perinatal transmission

### Table 1. Key to evidence statements and grading of recommendations, using the ranking of the Canadian Task Force on Preventive Health Care

<table>
<thead>
<tr>
<th>Quality of evidence assessment*</th>
<th>Classification of recommendations†</th>
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<tbody>
<tr>
<td>I: Evidence obtained from at least one properly randomized controlled trial</td>
<td>A. There is good evidence to recommend the clinical preventive action</td>
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<tr>
<td>II-1: Evidence from well-designed controlled trials without randomization</td>
<td>B. There is fair evidence to recommend the clinical preventive action</td>
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<tr>
<td>II-2: Evidence from well-designed cohort (prospective or retrospective) or case–control studies, preferably from more than one centre or research group</td>
<td>C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making</td>
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<td>II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category</td>
<td>D. There is fair evidence to recommend against the clinical preventive action</td>
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<tr>
<td>III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees</td>
<td>E. There is good evidence to recommend against the clinical preventive action</td>
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*The quality of evidence reported in these guidelines has been adapted from The Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.69

†Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Preventive Health Care.69

### Recommendations

1. All women living with HIV who are planning a pregnancy or who become pregnant should have their individual situations discussed with experts in the area, with referral to both HIV treatment programs and obstetrical care providers, and an overall plan should be made for their pregnancy care. (II-2A)

2. All pregnant women should be offered HIV testing, with appropriate pre- and post-test counselling, as part of their routine prenatal care in each pregnancy. This testing should be repeated in each trimester in women who are recognized to be at high and ongoing risk for HIV infection. (II-2A)

3. Pregnant women living with HIV should be made aware that with the consistent use of combination antiretroviral therapy and abstinence from breastfeeding, the risk of perinatal transmission is < 1%. (I-A)

4. All pregnant women living with HIV should be treated with combination antiretroviral therapy regardless of baseline CD4 and viral load. (II-2A)

5. Antiretroviral therapy should not be discontinued during the first trimester for obstetrical reasons, but if the woman is not on therapy and there is no urgent medical indication for combination antiretroviral therapy, it can be delayed until after 14 weeks’ gestation. (II-B)

6. All women living with HIV (both those who still have a detectable viral load after exposure to antiretroviral therapy and those who are antiretroviral-naïve) should have their virus genotyped and, if possible, tested for phenotypic resistance to assist in optimizing antiretroviral therapy. It is advisable to discuss the interpretation of the genotype testing and any changes to the antiretroviral therapy with experienced clinicians. Testing for HLA-DRB1*0701, if not done previously, is recommended in case abacavir might be required. (II-2B)

7. A combination antiretroviral therapy regimen including a dual nucleoside reverse transcriptase inhibitor (NRTI) backbone that includes one or more NRTIs and a boosted protease inhibitor should be favoured because there is higher confidence in its safety and efficacy in pregnancy. Whenever possible, antiretrovirals known to cross the placenta to the fetal compartment should be used. (II-2B)

8. Whenever possible drugs with no safety data should be avoided during the period of organogenesis. Efavirenz should not be prescribed in the first trimester of pregnancy because of its possible teratogenicity; however, if exposure has occurred and the neural tube has closed, efavirenz can be continued. Nevirapine should not be started in pregnancy, unless indicated by the woman’s resistance patterns, because it is associated with a high rate of serious adverse outcomes in this situation; however ongoing, pre-pregnancy treatment with nevirapine can be continued through pregnancy if tolerance and efficacy are established. (II-3D)

9. If antiretroviral therapy is discontinued for any reason during pregnancy, all drugs should be discontinued at once (unless the woman is on non-nucleoside reverse transcriptase inhibitors in that case a tail of 2 nucleoside reverse transcriptase inhibitors is recommended for 1 week), and all drugs should be resumed simultaneously to minimize the risk of viral resistance developing during therapy. Antiretroviral therapy should be resumed as quickly as possible after discontinuance to minimize the risk of rebound viremia and the potentially increased risk of vertical transmission. (II-1A)

10. If a pregnant woman has significant nausea of pregnancy, do not begin antiretroviral therapy until her nausea is adequately controlled. Most antiemetics used in pregnancy can be co-administered with antiretrovirals. If the woman is already on antiretrovirals and has hyperemesis of pregnancy, discontinue all antiretrovirals at once, and then reinstate all at once, when nausea and vomiting are controlled (unless the woman is on non-nucleoside reverse transcriptase inhibitors [NNRTIs], in which case a tail of 2 nucleoside reverse transcriptase inhibitors is recommended for 1 week to prevent future NNRTI resistance). (II-2D)

11. Therapy should be individualized to maximize adherence to the prescribed antiretroviral regimen. (III-A)
12. Routine dose adjustment of the combination antiretroviral therapy is not recommended in pregnancy. (III-D)

13. The woman’s clinical, virological, and immunological statuses should be assessed every 4 to 8 weeks during pregnancy, and again 6 weeks postpartum. Routine criteria should be used to assess the woman’s response to, and the possible failure of, antiretroviral therapy. The toxicity of the antiretrovirals should also be monitored at these times. Specific testing should be individualized for the known toxicities of the woman’s antiretroviral therapy regimen. (III-B)

14. As for all pregnant women, all those living with HIV, regardless of age, should be offered, through an informed consent process, dating ultrasound and non-invasive prenatal genetic screening for the most common clinically significant fetal aneuploidies. (III-A)

15. A detailed obstetrical ultrasound at 19 to 20 weeks’ gestation is recommended. Additional ultrasounds, for fetal growth and amniotic fluid volume, are recommended at least each trimester, or as guided by obstetrical indications. (II-3B)

16. As for all pregnant women, those living with HIV should be screened periodically for substance use, and drug addiction should be addressed as needed in conjunction with HIV management. (III-A)

17. Mode of delivery should be discussed in detail with all women:

   a. Women on optimal antiretroviral therapy with acceptable plasma viral load suppression (less than 1000 c/mL) over the last 4 weeks prior to delivery are recommended to have a vaginal delivery in the absence of other obstetrical indications for Caesarean section. If Caesarean section is recommended for obstetrical indications, it can be conducted at 39 weeks, as usual for those indications. (I-A)

   b. Women not on optimal antiretroviral therapy (i.e., no antiretroviral therapy, monotherapy only, or with an incompletely suppressed viral load) should be offered a scheduled pre-labour Caesarian section at approximately 38 weeks’ gestation. (II-2A)

18. Intravenous zidovudine should be initiated as soon as labour onset until delivery, in combination with an oral combination antiretroviral regimen, regardless of mode of delivery, current antiretroviral regimen, or viral load. (III-B)

19. Intrapartum, a single dose of oral nevirapine (200 mg) remains an option in the unusual circumstance of a woman living with HIV who has not received antenatal antiretroviral therapy in pregnancy. (II-2B)

20. Plans for ongoing HIV care should be established prenatally, and unless otherwise indicated, maternal antiretroviral therapy should be continued after delivery and reassessed for ongoing therapy by providers of adult HIV care. (II-1A)

21. HIV-exposed newborns should receive antiretroviral therapy for 6 weeks to prevent vertical transmission of HIV. (I-A)

22. Health care practitioners who care for HIV-exposed newborns should provide timely diagnostic HIV testing: HIV polymerase chain reaction at birth, 1 month, and 3 to 4 months and HIV serology at 18 months (II-A), and they should monitor both short- and long-term outcomes, including screening for adverse effects of antiretroviral therapy and for developmental delay. (III-A).

23. Breast-feeding is not recommended regardless of plasma HIV viral load and use of antiretroviral therapy. (I-E)

24. The pregnancy should be registered with surveillance programs to allow the collection of provincial and national data to guide future pregnancy policies. Women undergoing antiretroviral therapy in pregnancy should also be offered inclusion in appropriate studies. (III-B)

**ABBREVIATIONS**

ALT  alanine aminotransferase
AST  aspartate aminotransferase
cART  combination antiretroviral therapy
EIA  enzyme immunoassay
IV  intravenous
NIH  National Institutes of Health
PCR  polymerase chain reaction
RNA  ribonucleic acid
ZDV  zidovudine