INTERPROFESSIONAL PROTOCOL - MUHC

☒ Medication included ☐ No Medication included

THIS IS NOT A MEDICAL ORDER

Title:	**PREVENTION OF MATERNAL TO INFANT HIV INFECTION** Intrapartum, Peripartum, and Postpartum Antiretroviral Therapy/Prophylaxis and Strategies to Prevent Perinatal HIV Transmission
This interprofessional protocol is attached to:	MRC-1378 Pre-printed order for Inpatient Care of Infants born to HIV-Infected Women

1. PURPOSE

To aid in the prevention of perinatal HIV transmission from mother to infant, in the peripartum, intrapartum, and postpartum periods

2. PROFESSIONALS AND PATIENT POPULATION

Professionals:

i) Obstetricians/gynecologists, Maternal Fetal Medicine (MFM) specialists, intensivists, Family Medicine physicians, and nurses who follow HIV-infected pregnant women, who have an understanding of this Interprofessional Protocol.

ii) Pediatricians and nurses who follow infants born to HIV-infected women, who have an understanding of this Interprofessional Protocol.

Patient population:

i) Pregnant women who are infected with HIV.

ii) Infants born to HIV-infected women.

3. ELEMENTS OF CLINICAL ACTIVITY

Professionals are responsible to know the limits and extent of their practice as related to the particular protocol.

PREAMBLE / INTRODUCTION

This protocol is intended to be used as a protocol by physicians/nurses taking care of HIV-infected pregnant women and by physicians/nurses taking care of neonates/infants born to HIV-infected mothers.

Universal screening of all pregnant women, proper identification and treatment as well as follow-up of HIV-infected pregnant women, meticulous intrapartum care, prophylactic antiretroviral (ARV) medications to the infant, and no breastfeeding are all strategies developed to decrease the risk of maternal-infant HIV transmission to nearly negligible levels of less than 2%. This requires close cooperation and communication between the health care teams responsible for these patients from the time of identification of the HIV-infected pregnant woman to the time when her baby is definitely considered not to be infected by HIV.

Close communication is strongly recommended between MUHC services currently based on the following sites:

- the Obstetrical team at the MUHC (Royal Victoria Hospital – RVH),
- the adult HIV care team (Immunodeficiency service at the MUHC (Montreal Chest Institute – MCI)),
- the pediatric Infectious Disease (ID) team, and the pediatric HIV care team (care of the Complex Care Service) at the MUHC (Montreal Children's Hospital – MCH).

1. In the prepartum period, all HIV positive pregnant women should be referred to the MFM clinic of the RVH for transfer of care. These women are at higher risk of antenatal complications including preterm delivery and fetal growth restriction. Prenatal care is provided jointly with the adult HIV team (Immunodeficiency service) at the MCI.
2. The pediatric ID team at the MCH should be contacted by the adult HIV care team (Immunodeficiency service of the MCI) taking care of the HIV-infected pregnant mother in advance of her delivery date in order to familiarize themselves with the mother's health, and any concerns that have arisen during her pregnancy. This will allow the pediatric team to plan ahead for the care of the HIV-exposed newborn.
3. When the HIV-infected pregnant woman is admitted to the case room in labour, the pediatric ID on call team (at the MCH) and the adult HIV care team (Immunodeficiency service at the MCI) should be paged or called by the obstetrics team (RVH) informing them of the imminent delivery and consulted on the care of the newborn HIV-exposed newborn, and the post-partum HIV-infected mother.
4. If a pregnant woman is known to be HIV positive, the latest viral load (VL) and time from admission when VL was measured, should be documented in the Centricity Perinatal information system.
5. In addition to Group B *Streptococcus* status, maternal HIV status, Hepatitis B surface antigen (HBsAg) status, rubella immunity status, and previous genital herpes infection should be documented in the Centricity Perinatal information system upon admission of all pregnant women. If their status is unknown for HIV, HBsAg or rubella immunity, then immediate (STAT) order for testing is mandatory. If there is difficulty in obtaining this information, please contact the Immunodeficiency service at the MCI for the information.
6. In case of preterm premature rupture of membranes, all patients, HIV-positive or not, should follow the same standard practice for obstetrical delivery.

INTRAPARTUM CARE

Intrapartum Antiretroviral Therapy/Prophylaxis

- Intrapartum intravenous zidovudine (ZDV) is recommended for all HIV-infected pregnant women whether on ARV therapy or not and regardless of their antepartum regimen, to reduce perinatal transmission of HIV.
    - According to the most recent version of the US Department of Health and Human Services (DHHS) of the National Institutes of Health (NIH) published July 31, 2012, intrapartum intravenous ZDV is not required for HIV-infected pregnant women who are on Highly Active Antiretroviral Therapy (HAART) and have a RNA viral load (VL) of less than 400 HIV copies/mL near delivery. On the other hand, the UK Guidelines for the management of HIV infection in pregnant women, 2012, do not recommend intrapartum IV ZDV for women on HAART with VL of less than 50 copies/mL at or after 36 weeks of gestation. Some feel that it may be risky to rely on these recommendations as the woman's most recent viral RNA level might not reflect the true VL at delivery. Therefore, for now the MUHC physicians taking care of HIV-infected pregnant women and their newborns recommend intrapartum intravenous ZDV to all HIV-infected pregnant women during labour and delivery regardless of their HIV viral RNA load, and especially if no VL testing was performed at or after 36 weeks of gestation or the report is unavailable at delivery.
- Women who are receiving an antepartum combination ARV treatment regimen should continue this regimen on schedule as much as possible during labour and prior to any scheduled cesarean delivery.

- Women receiving fixed-dose combination regimens that include zidovudine should have zidovudine administered intravenously during labour while other antiretroviral components are continued orally.
- For women who are receiving a stavudine (d4T)-containing antepartum regimen, stavudine should be discontinued during labour while intravenous zidovudine is being administered.

Mode of Delivery

- Elective Caesarean section at 38 weeks of gestation (to help diminish the risk of HIV transmission to the newborn) should be performed in HIV-infected pregnant women in the following circumstances:
    - For women who have a VL of greater than or equal to 1,000 copies/mL, whether or not antepartum ARV drugs have been received,

    and/or:

    - For women with an unknown VL near delivery (e.g. 36 weeks of gestation), whether or not antepartum ARV drugs have been received.
- A planned vaginal delivery is acceptable for women who have a VL of less than 1,000 copies/mL and on HAART during pregnancy.
- It is not clear whether Caesarean delivery after the onset of labour or rupture of membranes provides benefit in preventing perinatal transmission. Management must be individualized based on duration of labour or rupture, VL, and current ARV regimen. Please consult the adult HIV team (Immunodeficiency service at the MCI) for guidance.
- The following obstetrical procedures are not recommended unless they are absolutely warranted for the mother's or the unborn infant's health:
    - Artificial rupture of membranes
    - Use of fetal scalp electrodes for fetal monitoring
    - Delivery with forceps, vacuum extractor, or ventouse
    - Episiotomy
- For infants born to mothers with unknown HIV status, rapid HIV antibody testing of the mother and/or infant is recommended as soon as possible after birth, with initiation of infant antiretroviral prophylaxis immediately if the rapid test is positive.

Table 1. Intrapartum Maternal and Neonatal Zidovudine (ZDV) Dosing for Prevention of Mother-to-Child Transmission of HIV

Maternal Intrapartum Drug	Maternal Dosing	Duration
Zidovudine	2 mg / kg IV over 1 hour, followed by continuous infusion of 1 mg / kg / hour IV	Onset of labour until delivery. Start 3 hours before planned Caesarean delivery and as early as possible before emergency Caesarean delivery

Neonatal Drug	Gestational age	Neonatal Dosing	Duration*
Zidovudine	Greater than or equal to 35 weeks:	**4 mg / kg / dose PO** q 12 hours **OR** **3 mg per kg / dose IV** q 12 hours started as soon as possible and preferably within 6-12 hours of delivery	Birth through 6 weeks
Zidovudine	From 30 to less than 35 weeks	**2 mg / kg / dose PO** q 12 hours **OR** **1.5 mg / kg / dose IV** q 12 hours started as soon as possible and preferably within 6 –12 hours of delivery **THEN** advancing to 3 mg / kg / dose q 12 hours PO **at age 15 days** **OR** 2.3 mg / kg / dose IV q 12 hours **at age 15 days**	Birth through 6 weeks
Zidovudine	Less than 30 weeks	**2 mg / kg / dose PO** q 12 hours **OR**, if unable to tolerate oral agents, **1.5 mg / kg / dose IV** q 12 hours started as soon as possible and preferably within 6 –12 hours of delivery **THEN** advancing to 3 mg / kg / dose q 12 hours PO **at age 4 weeks** **OR** 2.3 mg / kg / dose IV q 12 hours **at age 4 weeks**	Birth through 6 weeks

*A 4-week neonatal chemoprophylaxis regimen is recommended in the United Kingdom and in many other countries. This approach may be considered if there are concerns about adherence or toxicity with the 6-week regimen.

- Decisions regarding the use of other drugs depend on maternal antiretroviral drug exposure, HIV RNA level at or near delivery, resistance testing; and availability of drug formulation and dosing information for newborns.

- Any decision for prophylactic ARV medications in addition to zidovudine should be made in consultation with a pediatric HIV specialist, preferably prior to delivery.

- Most experts feel that the potential benefit of additional antiretroviral drugs may exceed the risk of multiple drug exposure if:

    a) infant born to mother who received antepartum and intrapartum antiretroviral drugs but had suboptimal viral suppression at delivery, particularly if the infant was delivered vaginally
    b) infant born to mother who received only intrapartum antiretroviral drugs
    c) infant born to mother with known ARV drug-resistant virus.

Table 2: Neonatal Dosing for Additional Antiretroviral Drugs to be considered in Selected Circumstances [1]

Neonatal Drug (initiated as soon as possible after delivery)[§]	Neonatal Dosing	Duration
2-drug regimen: Zidovudine and Nevirapine	Zidovudine: For doses see Table 1 above	Zidovudine: Birth through 6 weeks
	Nevirapine: Birth weight 1.5 – 2 kg: 8 mg / dose PO Birth weight greater than 2 kg: 12 mg / dose PO	Nevirapine: 3 doses in 1st week of life - 1st dose less than 48 hours of birth - 2nd dose 48 hours after 1st - 3rd dose 96 hours after 2nd
3-drug regimen: Zidovudine and Lamivudine and Nevirapine	Zidovudine: For doses see Table 1 above	Zidovudine: Birth through 6 weeks
	Lamivudine: 2 mg / kg / dose PO bid	Lamivudine: Birth through 2 weeks
	Nevirapine: Birth weight 1.5 – 2 kg: 8 mg / dose PO Birth weight greater than 2 kg: 12 mg / dose PO	Nevirapine: 3 doses in 1st week of life - 1st dose less than 48 hours of birth - 2nd dose 48 hours after 1st - 3rd dose 96 hours after 2nd

[§] In consultation with a pediatric HIV specialist, preferably prior to delivery.

Infants Born To Mothers with Unknown HIV Infection Status

- For infants born to mothers with unknown HIV status, rapid HIV antibody testing of the mother (or infant if mother not available) is recommended as soon as possible after birth, with initiation of infant ARV prophylaxis immediately if the rapid test is positive.
- If the mother's rapid HIV antibody test is positive, confirmatory antibody testing (e.g., Western blot) should be performed on the mother (or her infant) as soon as possible. If the maternal HIV antibody confirmatory test is positive, a newborn HIV RNA PCR (or HIV DNA PCR if available) should be obtained
- If the confirmatory test is negative, antiretroviral prophylaxis can be discontinued.
- ARV prophylaxis should be initiated as close to the time of birth as possible, preferably within 6 –12 hours of delivery. Infants born to HIV-infected women who have not received antepartum ARV drugs should receive prophylaxis with a combination ARV drug regimen (preferably a 3 drug regimen in consultation with a pediatric HIV/ID specialist), begun as soon after birth as possible.
- Women of unknown HIV status being tested for HIV at or after delivery should be counseled to withhold breast feeding until their HIV status known.

NEONATAL POSTNATAL CARE

Postnatal Management of the HIV-Exposed Neonate

Assessment for Postnatal Care

- Following birth, HIV-exposed infants should have a detailed physical examination.
- A thorough maternal history should be obtained. The HIV-infected mother may be co-infected with other pathogens that can be transmitted from mother to child, such as cytomegalovirus, herpes simplex virus, hepatitis B, hepatitis C, syphilis, toxoplasmosis, or tuberculosis.

Management of Postnatal Care

- Infants born to HIV-infected women who have not received antepartum ARV drugs should receive prophylaxis with a zidovudine and nevirapine and possibly lamivudine regimen, begun as soon after birth as possible. (Consult pediatric ID team)
- The infant should be started on ARV postnatal prophylactic medications ideally as soon as possible after birth or within 6 to 12 hours after delivery. See Tables 1-2 for recommended ARV and doses. Starting prophylaxis after 72 hours of age is unlikely to be beneficial.
- A complete blood count and differential should be performed on the newborn.
- Decisions about the timing of subsequent hematological monitoring will depend on baseline hematologic values, gestational age at birth, clinical condition, receipt of concomitant medications, and maternal antepartum therapy
- Some experts recommend more intensive monitoring of hematologic and serum chemistry and liver function assays during the first few weeks of life for infants exposed to combination antiretroviral therapy in utero or during the neonatal period.
- If hematologic abnormalities are identified while the infant is receiving prophylaxis, decisions on whether to continue infant antiretroviral prophylaxis need to be individualized.
- Routine measurement of serum lactate is not recommended. Measurement of serum lactate may be considered if an infant develops severe clinical symptoms of unknown etiology (particularly neurologic symptoms). Children with in utero/neonatal antiretroviral exposure who develop significant organ system abnormalities of unknown etiology, particularly of the nervous system or heart, should be evaluated for potential mitochondrial dysfunction.
- To prevent *Pneumocystis jiroveci* pneumonia (PCP), all infants born to women with HIV infection should begin PCP prophylaxis at age 4–6 weeks, after completion of the zidovudine prophylaxis regimen; unless there is adequate test information to presumptively exclude HIV infection. The recommended prophylaxis is oral trimethoprim-sulfamethoxazole 5 mg/kg/day (based on the trimethoprim component) divided twice daily for three consecutive days per week.
- HIV-exposed infants should follow the routine primary immunization schedule. Rotavirus vaccine may be given. Other live vaccines should be held until HIV has been presumptively excluded. Infants with known HIV infection may require modifications in the schedule for some live vaccines.

Guidelines for Postnatal Care

- HIV-infected women should NOT breastfeed their infants. HIV-infected mothers who have just given birth should be counseled about this and encouraged to exclusively provide infant formula to their babies.
- Late HIV transmission in infancy has recently been suspected to have occurred as a result of infant consumption of premasticated food given to them from their caregivers. Where appropriate, mothers should be advised of this possibility.
- Follow-up of children with *in utero* or neonatal antiretroviral exposure should continue into adulthood because of the theoretical concerns regarding the potential for carcinogenicity of and mitochondrial dysfunction due to the nucleoside analogue antiretroviral drugs.

Diagnosis of HIV infection in infants less than 18 months of age:

Current recommendations reflect the following:

- HIV infection in infants should be diagnosed using HIV RNA PCR (VL) or DNA PCR virologic tests.
- HIV virologic testing should be performed at **a minimum** at ages **14 - 21 days**, **1 - 2 months**, and **4 - 6 months**.
- Some also perform a virologic test **at birth**, especially if the mother has not been treated with HAART during pregnancy, has not had good virologic control during pregnancy, or if the infant shows signs of *in utero* HIV infection (intrauterine growth retardation, abnormal neurological exam – e.g. hypotonia, or hepatosplenomegaly), or if adequate follow-up of the infant may not be assured.
- If the newborn RNA PCR (VL) or HIV DNA is positive, ARV prophylaxis should be discontinued, a confirmatory test done, and treatment of HIV infection with standard combination antiretroviral therapy started pending the result of the second (confirmatory) test
- A positive HIV virologic test should be confirmed as soon as possible with a second HIV virologic test on a different specimen. Two positive HIV tests constitute a **diagnosis of HIV infection**.
- A positive HIV confirmatory antibody test (Western blot or immunofluorescent antibody (IFA)) at age greater than or equal to 18 months confirms HIV infection with the exception of rare late seroreverters.
- HIV may be **presumptively** excluded in non-breastfed infants with two or more negative virologic tests with one at greater than or equal to 14 days and another at greater than or equal to 1 month of age (or one negative virologic test result obtained at greater than or equal to 2 months of age; or one negative HIV antibody test result obtained at greater than or equal to 6 months of age).
- **Definitive** exclusion of HIV in non-breastfed infants may be based on two negative virologic tests with one obtained at greater than or equal to 1 month and one at greater than or equal to 4 months of age (or two negative HIV antibody tests from separate specimens obtained at greater than or equal to 6 months of age).
- Many experts confirm HIV-negative status with an HIV antibody test at age 12 to 18 months to document seroreversion.
- For both **presumptive** and **definitive** exclusion of HIV infection, the child must have no other laboratory test results (no positive virology or low T lymphocyte CD4 count/percent) or clinical evidence of HIV infection, and not be breastfeeding.
- Definitive exclusion of HIV in a breast fed child is made by lack of HIV antibody at least 6 months after the last exposure to breast milk.

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4. APPROVAL PROCESS

Institutional and professional approval

Committees	Date [yyyy-mm-dd]
☒ Pharmacy and Therapeutics Pediatrics (if applicable)	2013-03-11
☐ Adult Pharmacy and Therapeutics (if applicable)	
☐ MUHC Adult Site Medication Administration Policy (MASMAP) (if applicable)	
☒ MUHC Pediatric Medication Administration Policy (PMAP) (if applicable)	2013-01-16
☒ Clinical Practice Review Committee (if applicable)	2013-01-08
☐ Nursing Executive Committee and Council of Nurses (NEC and CN) (if applicable)	
☐ Multidisciplinary Council (if applicable)	
☐ MUHC Central Executive Committee of Council of Physicians Dentists and Pharmacists Committee (ECPDP) (Obligatory if attached to a collective order) — Final approval Signature of Chairperson: _____	

5. REVIEW DATE

To be updated in maximum of 5 years (2018) or sooner if presence of new evidence or need for practice change.

6. REFERENCES

- Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health *and* Interventions to Reduce Perinatal HIV Transmission in the United States. Available at: http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed November 2, 2012.

  It is emphasized that concepts relevant to HIV management evolve rapidly. The Panel has a mechanism to update recommendations on a regular basis, and the most recent information is available on the AIDS*info* website (http://aidsinfo.nih.gov).

- British HIV Association. Guidelines for the management of HIV infection in pregnant women 2012, VERSION 7. 30 April 2012 *HIV Medicine* (2012), 13 (Suppl. 2), 87–157. Available at http://www.bhiva.org/PregnantWomen2012.aspx. Accessed November 2, 2012.

- Panel on Antiretroviral Therapy and Medical Management of HIV-Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. August 11, 2011; pp 1-268. Available at http://aidsinfo.nih.gov/ContentFiles/lvguidelines/PediatricGuidelines.pdf. Accessed November 2, 2012.