MANAGEMENT OF HIV-INFECTED WOMEN DURING PREGNANCY AND CHILDBIRTH

BACKGROUND

The probability of mother to child transmission of HIV can be reduced to < 1% with appropriate management. If there is no intervention, the probability of mother to child transmission of HIV in an untreated mother is between 15 and 30%.

Interventions to reduce vertical transmission include:

- Antiretroviral therapy to mother (antepartum +/- intrapartum) and baby (postpartum)
- Elective caesarean section if viral load not fully suppressed
- Caution with invasive obstetric procedures (eg. amniocentesis, fetal scalp monitoring, fetal scalp blood sampling, episiotomy)
- Formula feeding (avoiding breastfeeding) - Some mothers will decide to breastfeed and ideally this decision has been made some time prior to delivery and there has been time for an informed discussion with the woman, the LMC, the neonatologist, the ID HIV CNS and the ID physician.

Pregnant women who are HIV positive must be referred to Christchurch Women's Hospital High Risk Obstetric Team OG3 AND to Infectious Diseases as soon as the pregnancy is confirmed or the HIV positive status identified.

MULTIDISCIPLINARY TEAM

The team is made up of a consistent group of clinicians, and will usually include the following:

TEAM MEMBER	ROLES
Infectious Diseases Specialist	Overall management of HIV related medical care, prescription of antiretrovirals, monitoring of toxicity, treatment of HIV related infections.
Infectious Disease Nurse Specialist	Coordinates HIV outpatient management with the Infectious Diseases (ID) Specialist.
Obstetrician	Supervision of pregnancy care, decisions regarding birth options.
Clinic Midwife / LMC	Assistance with pregnancy care, birth plans, intrapartum care, postnatal care.
Social Worker	Community based support (psychosocial, financial, medications, transport).
Neonatologist	Neonatal medical care, prescription of antiretrovirals, medical follow-up of child.

PRE-PREGNANCY ASSESSMENT AND CARE

All known HIV positive women considering pregnancy should discuss this with their HIV Specialist to allow for appropriate pre-pregnancy assessment and advice. Issues regarding optimisation of HIV treatment, safety of any treatment in pregnancy, mode of birth and breastfeeding should be discussed. All HIV positive women of child bearing age need appropriate contraceptive advice if not considering pregnancy or until medically stable.

Sero-discordant couples should receive preconception advice regarding safe conception. They may also require assisted conception such as sperm washing. They should be referred to fertility service 'Fertility Associates' for this. Recent data confirms that HIV is not transmitted between a couple if the HIV infection partner is on treatment and has a fully suppressed viral load.

Once pregnancy is confirmed a referral should be made directly to the High Risk Obstetric Team OG3 at Christchurch Women's Maternity Services and to Infectious Diseases. Women will be followed up by Infectious Diseases and the High Risk Pregnancy team.

ANTENATAL SCREENING

All pregnant women should be offered antenatal screening for HIV in the first trimester bloods, or when they present/book later in pregnancy. Verbal consent is obtained at the time or the women can opt out of testing. Written consent is not required.

An interpreter should be used for women who do not speak English. It is **NOT** recommended to use a family member or friend as an interpreter.

Patient information leaflets on HIV testing in pregnancy are available through the Ministry of Health (http://www.healthed.govt.nz) in a number of languages.

If an antenatal screening test returns a positive result, a senior person from the laboratory will phone this result through to the health professional who has ordered the test.

The health professional who has ordered the test should contact the on call consultant for Infectious Diseases, Christchurch Hospital for advice and assistance in giving the positive result to the woman and organising urgent follow-up.

A second confirmatory test needs to be performed. This is an HIV EIA and HIV PCR (5 mL serum separator tube and 15 mL EDTA).

PREGNANCY REFERRAL GUIDELINES

All pregnant women who are HIV positive must be referred immediately by telephone to the Infectious Diseases Consultant on call and then a written referral sent to:

Department of Infectious Diseases, Christchurch Hospital
Fax 03 3640 952 Internal Fax 80952

High Risk Obstetric team OG3, at Christchurch Women's Hospital
Fax 03 3644 301 Internal Fax 85301

The High Risk Obstetric team OG3 will then refer to:
Neonatologist responsible for HIV follow-up so arrangements can be made for an antenatal appointment to outline infant care (N. Austin: pager 5001).

PREGNANCY MANAGEMENT

MATERNAL ANTENATAL ANTIRETROVIRAL THERAPY

Combination antiretroviral therapy has been shown to be highly effective in reducing the risk of vertical transmission. These drugs regimens are commonly known as Highly Active Antiretroviral Therapy (HAART).

HIV positive pregnant women should be managed according to the current USA Public Health Service Task Force Recommendations for the Use of Antiretroviral Drugs in Pregnant HIV-infected Women for Maternal Health *and* Interventions to Reduce Perinatal HIV Transmission in the United States. These are available online on the AIDS*Info* website (http://AIDSinfo.nih.gov).

The Infectious Diseases Physician needs to apply for a Subsidy by Special Authority prior to the prescription of HIV medications. The responsibility for selecting, prescribing and monitoring HIV treatment lies with the Infectious Diseases Specialist.

ANTENATAL MONITORING

Drug side effects – women taking antiretrovirals should be closely monitored for both minor and major potential side effects. Some key side effects to be aware of are:

DRUG	SIDE EFFECT
Protease inhibitors *(eg. Kaletra® - (lopinavir+ritonavir), atazanavir, darunavir)*	glucose intolerance and diabetes mellitus, GI intolerance
Truvada® - (tenofovir + emtricitabine)	well tolerated
abacavir in combination with lamivudine as Kivexa®	hypersensitivity reaction (HLA B5701 screening helps predict this)

If an HIV positive woman presents with apparent signs or symptoms of pre-eclampsia, cholestasis or liver dysfunction the differential diagnosis should include a check for potential anti-retroviral toxicity.

It is reasonable to consider the following:

- **At booking**
  - Appropriate referrals as above
  - Booking bloods plus electrolytes, creatinine, liver function, MSU
  - Dating scan if uncertain dates
  - STI infection screen
  - Cervical smear if not done in past year
  - Full medical examination
  - Arrange MSS1 screening (if desired)
  - All women should be offered a Social Worker referral to assess social needs and support services
  - Physiotherapy and dietitian services can be accessed through the High Risk Obstetric Clinic, if appropriate
- **12-16 weeks**
  - MSS1 testing
  - Invasive diagnostic testing (CVS or amniocentesis) is probably safe in women with suppressed viral loads. For women with unsuppressed viral loads, there is likely to be risk of vertical transmission. Decisions need to be made on a case by case basis. NIPT (Non Invasive Prenatal Testing) may be an alternative and should be offered, but this is not publicly funded.
- **18-20 week**:
  - Morphology scan
  - FBC, electrolytes, creatinine, liver function, MSU
  - 75 g/2 hour glucose tolerance test if on protease inhibitors (lopinavir + ritonavir (Kaletra®), atazanavir, danrunavir) or other risk factors
  - Notify the Christchurch Women's Pharmacist of the identity of the HIV positive woman and her expected delivery date so that supplies of intravenous zidovudine for the woman and oral zidovudine for the baby, can be issued to birthing suite well in advance of the EDD [Pharmacist pager 5009].
- **28 weeks**
  - Fetal growth assessment – scan if concerned
  - FBC, electrolytes, creatinine, liver function, MSU
  - HIV viral load and CD4 count
  - 75 g/2 hour glucose tolerance test (if earlier test negative, or not had testing)
  - Anaesthetic review is recommended
- **32 weeks**
  - Fetal growth assessment – scan if concerns
  - Repeat bloods and MSU
  - HIV viral load, if previous detectable viral load or history of pre-term birth
  - Neonatal review and plan completed

- **36 weeks**
  - Fetal growth scan
  - HIV viral load and CD4 count
  - Repeat bloods and MSU

Infections – each woman should be assessed at each visit with regards to the possibility of opportunistic infections.

ANTENATAL COMPLICATIONS

GDM AND PRE-ECLAMPSIA

Glucose impairment and pre-eclampsia have been associated with HAART. Both should be managed in accordance with normal obstetric practice.

PRETERM LABOUR < 34 WEEKS

Preterm birth has been identified as a risk for vertical transmission. An HIV positive woman presenting with threatened preterm labour and intact membranes should have triple swabs taken for microbiology. Betamethasone should be administered in keeping with normal obstetric practice.

There is no evidence for benefit from use of tocolytics in women with HIV infection. Since women with an unsuppressed viral load are at increased risk of sepsis, tocolysis should be avoided. For women with fully suppressed viral load on HAART the decision to treat with tocolytics should be discussed with the consultant on call. It would be reasonable **not** to use tocolysis in this setting.

PRETERM PRELABOUR RUPTURE OF MEMBANES AT 34-37 WEEKS

In the event of preterm pre-labour rupture of membranes after 34 weeks gestation birth should be expedited without delay. Triple swabs should be taken for microbiology and intravenous antibiotics should be prescribed in labour in accordance with the local guidelines on antibiotic prophylaxis in labour. For those women with no other obstetric complication on HAART with a fully suppressed viral load and intending to birth vaginally then induction of labour is the management of choice.

PRETERM PRE-LABOUR RUPTURE OF MEMBRANES < 34 WEEKS

In the event of preterm pre-labour rupture of membranes before 34 weeks gestation the decision to expedite birth will depend on various factors:

- If the mother has an undetectable viral load and is on HAART and if there is no evidence of infection on triple swabs or blood parameters, then the benefits of prolonging gestation probably outweigh any increased risks of vertical transmission. The woman should be managed in the usual way with two doses of betamethasone and ten days of oral erythromycin.
- Birth should be expedited if there is any evidence of infection or at 34 weeks gestation.
- If the woman is not on HAART or has a viral load more than 40 copies per mL, then consideration should be given to earlier birth, which unless there are obvious signs of infection may be delayed

until two doses of betamethasone have been given. The woman's care should be discussed with the Infectious Diseases Consultant on call regarding antiretrovirals during labour and for the infant following birth.

SUSPECTED CHORIOAMNIONITIS

The risks of chorioamnionitis to both mother and baby are increased in the presence of HIV. Therefore there should be a low threshold for administration of broad spectrum intravenous antibiotics where chorioamnionitis is suspected.

MANAGEMENT OF LATE PRESENTING AND UNBOOKED WOMEN

Women presenting late in pregnancy for their first antenatal appointment should be offered HIV testing and if positive appropriate HIV medication needs to be commenced as soon as possible. Any HIV treatment, even started late in pregnancy or intrapartum is associated with a reduction in mother to child transmission.

Unbooked women presenting in labour should be offered an HIV test in labour if there is an opportunity for informed consent. If it is not possible to obtain informed consent prior to birth, an offer should be made for HIV testing shortly after the baby is born. The HIV EIA available through Canterbury Health Laboratories is available 24 hours a day.

If the result is positive:

- Bloods for CD4 count and HIV viral load should be taken.
- The woman's care should be discussed with the Infectious Diseases Consultant on call and started on antiretrovirals as soon as possible. This is likely to include:
  - Intravenous zidovudine infusion
  - HAART
- Dolutegravir plus tenofovir + emtricitabine (Truvada®)
- If possible the woman should undergo LSCS.

Infant antiretroviral therapy should be commenced as soon as possible following birth. Strong consideration should be given to combination anti-retroviral treatment in this situation.

MODE OF BIRTH

A full discussion regarding the mode of birth should take place with each woman. A clear plan must be documented in the notes.

Women whose viral load is less than 40 copies/mL or not detected (fully suppressed) may safely choose a vaginal birth. Caesarean section does not offer additional benefit to reduce vertical transmission of HIV and should be used for usual obstetric indications.

There is no data at present to suggest that spontaneous rupture of membranes in labour increases the risk of vertical transmission for women who have a fully suppressed viral load and are on HAART. Other co-morbidities including chorioamnionitis and preterm labour are associated with an increase in the

risk of vertical transmission and this should be considered when making management decisions (see above for preterm labour and preterm SROM).

Elective Caesarean section is recommended if the viral load is not fully suppressed or if the woman is not on HAART. Elective caesarean section may be indicated for other obstetric reasons and this will be decided in consultation between the woman and her obstetrician.

Delayed Cord Clamping is acceptable practice.

VAGINAL BIRTH

Women should be encouraged to come to hospital at the earliest signs of labour.

The on-call Obstetric Consultant and the anaesthetic team should be notified of the woman's admission.

Confidentiality must be maintained at all times, eg. it is **NOT** necessary to list the diagnosis of HIV on the Flowview board.

Universal infection precautions should be followed by all staff.

A partogram is recommended to record and monitor progress in labour.

There is no indication for artificial rupture of membranes in a spontaneously labouring women making good progress in labour.

Invasive procedures including use of fetal scalp electrodes and fetal pH sampling, episiotomy and assisted vaginal delivery appear safe in women with a completely suppressed viral load. However, the decision to perform them should be made on a case by case basis.

There is no data that suggests an increase in transmission with the use of instrumental delivery.

Caesarean should be performed for the usual obstetric indications.

ELECTIVE CAESAREAN

Anaesthetic review at pre-admission clinic is required.

Whilst the woman is fasting prior to a caesarean section, oral medications should be taken with a sip of water. If food is required for absorption, this should be discussed with the Anaesthetist & Infectious Diseases Consultant.

The woman should be admitted to the birthing suite early on the day of the procedure to allow for intravenous zidovudine infusion to be commenced 3 hours prior to delivery **if required**. (See Appendix B for protocol).

INTRAPARTUM ANTIRETROVIRAL THERAPY

Women who are on antenatal combination antiretroviral treatment should continue this regimen as much as possible during the intrapartum period, to provide maximal virologic effect and to minimize the chance of drug resistance developing.

The woman should bring her own medications with her to ensure access to these. Women who have a fully suppressed viral load do not require additional anti-retroviral treatment intra-partum.

If maternal antiretroviral therapy must be interrupted temporarily (for < 24 hours) all medications (except intravenous zidovudine) should be stopped and reinstituted simultaneously.

INTRAPARTUM INTRAVENOUS ZIDOVUDINE

Intravenous zidovudine during the intrapartum period should be discussed and recommended to all HIV-infected pregnant women with detectable viral loads. For those women with a fully suppressed viral load and are on HAART this may not be necessary, this will be agreed antenatally and documented in the notes and on the plan of care for each individual woman.

If IV zidovudine is required for a woman:

- Check with the birthing suite co-ordinator that supplies of antiretroviral medications are available in the controlled drug cupboard on birthing suite from 24 weeks gestation (if not, contact the Pharmacist).
- The infusion should be commenced when labour is confirmed (see Appendix B for guideline on intravenous zidovudine).

CARE OF THE PLACENTA

It is important that this is discussed with the woman antenatally, as she may not have disclosed her HIV status to family/whānau.

All women should be given the choice of taking their placenta home, as normal. However if an HIV positive woman chooses to keep the placenta, she needs to be aware that the placenta is potentially infectious and any handling should be with gloves and strict hand washing should be adhered to.

POSTPARTUM CARE OF MOTHER AND BABY

A MATERNAL MANAGEMENT

Women with HIV and their babies should be cared for on the maternity ward at Christchurch Women's Hospital. Most women will stay in hospital for 4-5 days.

Confidentiality is paramount. Check the level of disclosure required by the woman. This includes confidentiality of notes and all communication.

Women with HIV may be at higher risk of postnatal infection. Regular observations of pulse, blood pressure and temperature should be performed at least four times a day.

Offer cabergoline (Dostinex® 1 mg for suppression of lactation within first 24 hours unless the woman has decided to breastfeed.

All maternal medications including antiretrovirals should be continued post-partum at the usual dose times. These medications should be brought into hospital by the woman and self-medicated. These must be electronically prescribed in Medchart.

In some women, antiretroviral medication may be stopped postpartum, but would be continued in those women who require antiretrovirals for their own health. In addition a woman who decides to breastfeed should remain on anti-retroviral therapy. This will be decided by the Infectious Diseases Physician. Refer to ID consultant involved and ID nurse specialist, 364 0951 and 027 6777 824 and ensure Neonatologist aware.

Contraceptive advice should be given and a contraceptive plan must be instituted prior to discharge from hospital.

Arrange follow up appointment with Infectious Disease Department prior to discharge.

B INFANT MANAGEMENT

Universal precautions should be adhered to and it is recommended that the baby is handled with gloves until bathed in warm water.

'Skin to skin' procedures

- If the woman has an **undetectable viral load** and on HAART treatment, then 'skin to skin' contact with the mother should be offered as soon as possible after the birth. The baby should then be bathed at a suitable time following this period of skin to skin. It is important for baby to have a bath prior to any intramuscular injections or heel pricks. Following 'skin to skin' time the mother may also need any fluid washed off her skin.
- If the woman has **an unknown or high viral load** then the baby should be bathed immediately after birth prior to skin to skin.

Bathing

It is recommended that the baby is bathed as soon as is practical.

- Bath the baby in warm water to remove any maternal secretions and blood.
- Clean the skin with an aqueous chlorhexidine (alcohol-free) swab before administering any intramuscular injections such as Konakion or breaking the integrity of the skin.

Vitamin K dosing guidelines

Vitamin K (phytomenadione) is recommended to prevent Haemorrhagic disease of the Newborn. Oral Vitamin K 2mg or IM 1mg is appropriate and should be discussed with the woman antenatally.

If the baby requires NICU admission or there is evidence of bleeding or the baby is nil by mouth, vitamin K 1mg should be given intramuscular (after being washed).

Feeding guidelines

National recommendations are that all breastfeeding (including colostrum) should be avoided (MOH: Feeding your baby when you are HIV positive, 2 May 2016). The infant will receive ready-to-feed

formula in hospital. Prior to discharge the family will need to buy formula. The midwife will advise the mother regarding formula feeding.

ID nurse specialist may arrange formula supply if high needs exist.

Some mothers will decide to breastfeed despite advice not to. Ideally this decision has been made some time prior to delivery and there has been time for an informed discussion with the woman, the LMC, the neonatologist, the ID HIV CNS and the ID physician. It is imperative that she remains on effective antiretroviral therapy, that the infant remains on therapy supervised by the neonatologist and that the advice on safest breastfeeding practice is given (e.g. avoid mixed feeding)

Anti-retroviral treatment

Within 6 hours of birth the infant should be administered zidovudine suspension (10 mg/mL) 4 mg/kg every 12 hours for 4 weeks as per Neonatal Drug Profile Guidelines. If possible, doses should be given on an empty stomach and if vomiting occurs within 30 minutes of administering a dose, the dose should be repeated.

If < 35 weeks dose as per NICU drug protocol.

In most cases the 200 mL bottle of zidovudine dispensed for the infant in hospital may be taken home with them and will last for the entire 4 week treatment period. If required an ID specialist can apply for the Special Authority number should there be supply issues, and once issued will allow a subsidised prescription for zidovudine to be dispensed by a community pharmacy. The ward pharmacist and neonatal team can assist with this.

The mother will need education about administration of antiretroviral medication to the baby and should be confident with this before discharge.

Vaccinations

BCG is contra-indicated until the infant is confirmed to be HIV negative**.** Other vaccinations are safe and highly recommended as per the immunisation schedule.

Pneumocystis Prophylaxis

This is no longer routinely used unless there is a risk from the family environment. That is a family member with active PCP.

Monitoring and Follow-up

Day 2

- FBC and HIV proviral DNA to Auckland (2 full EDTA tubes)
- Contact Neonatal Paediatrician responsible for follow-up

Day 14

- FBC and LFT to check for side effects of Zidovudine (anaemia, neutropenia etc.) on Neonatal Unit

6 weeks

- FBC and HIV proviral DNA
- Neonatal outpatient appointment, on the Neonatal Unit

4 months

- FBC and HIV PCR
- Neonatal outpatient appointment, on the Neonatal Unit

APPENDIX A MATERNAL ANTIRETROVIRALS

HIV positive pregnant women should be managed according to the current USA Public Health Service Task Force Recommendations for the Use of Antiretroviral Drugs in Pregnant HIV-infected Women for Maternal Health *and* Interventions to Reduce Perinatal HIV Transmission in the United States. These are available online on the AIDS*Info* website (http://AIDSinfo.nih.gov).

The Infectious Diseases Physician needs to apply for a Subsidy by Special Authority prior to the prescription of HIV medications.

The responsibility for selecting, prescribing and monitoring HIV medication lies with the Infectious Diseases Specialist.

WOMEN ON TREATMENT PRE-PREGNANCY

Women who become pregnant on antiretroviral treatment should usually be continued on this therapy during pregnancy as long as they have an adequate viral response to treatment.

Some medications (especially efavirenz) are contraindicated in pregnancy and this needs to be assessed on a case by case basis.

In those women whose viral load on treatment is not fully suppressed, therapy should ideally be changed before the end of the second trimester. Viral resistance testing should be considered to help guide treatment options.

WOMEN NOT ON TREATMENT PRE-PREGNANCY

Any HIV-infected woman who meets standard criteria for initiation of antiretroviral therapy should receive potent combination antiretroviral therapy, generally consisting of two nucleoside reverse transcriptase inhibitors (NRTIs) plus a reverse transcriptase inhibitor (NNRTI) or protease inhibitor (PI), with continuation of therapy post-partum. This should be started as soon as possible, including in the 1st trimester, as the potential benefits to the mother outweigh the potential fetal risks.

For all women who do not require antiretroviral treatment for their own health, antiretroviral therapy should be discussed and recommended for the prevention of mother to child transmission. This should be commenced after the 1st trimester and by the 26th week of pregnancy, to allow time for antiretroviral effect and allow alteration of medication if side-effects occur.

DRUG REGIMENS

All women should be offered combination antiretroviral treatment to allow for the most efficient reduction in HIV viral load and to prevent HIV resistance to medication developing.

APPENDIX B INTRAVENOUS ZIDOVUDINE ADMINISTRATION

Dosage schedule used in Paediatric AIDS Clinical Trial Group, protocol 076 (JAMA March 16th 1994)

MATERNAL DOSAGE

Day of delivery

Loading dose 2 mg/kg

Maintenance infusion 1 mg/Kg/hour until delivery (or for 12 hours).

Do not mix with any other IV fluid or any other injectable drugs. Therefore administer through a dedicated line.

Preparation

IV zidovudine (Retrovir®) is already in solution

Each vial contains 200 mg/20 mL

It must be diluted before administration, 0.9% sodium chloride or 5% Dextrose can be used as the diluent

Administration of loading dose

2 mg/kg

Example of calculated dose for a woman who weighs 70 Kg:
2 mg x 70 kg = 140 mg of zidovudine required

Add 14 mL (140 mg) of zidovudine solution to 100 mL of 0.9% sodium chloride or 5% Dextrose and infuse via a volumetric pump over one hour.

Administration of maintenance dose

1 mg/kg/hour

Example of calculated dose for a woman who weighs 70 Kg:
1 mg x 70 kg/hour = 70 mg/hour = 840 mg in 12 hours

Add 84 mL (840 mg) of zidovudine solution to 500 mL of 0.9 % sodium chloride or 5% Dextrose and infuse via a volumetric pump as required (up to 12 hours), until baby delivered and cord clamped. Approximately 50 mL/hr.

Stop infusion following birth.

INFANT'S DOSAGE

Oral zidovudine syrup (10 mg/mL) 4 mg/kg twice daily starting within 4-6 hours of birth and continuing for 4 weeks. Check drug sheet if < 35weeks or NBM.

NOTE: even if the woman presents in labour, the loading dose followed by the maintenance regime should always be given.

Routine observations only.