



衛生防護中心
Centre for Health Protection

Recommended Clinical Guidelines on the Prevention of Perinatal HIV Transmission

Scientific Committee on AIDS and STI (SCAS)

**Centre for Health Protection
Department of Health**



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Scientific Committee on AIDS and STI (SCAS)
has the following terms of reference :

- (a) to advise the Controller of the Centre for Health Protection (CHP) on the scientific basis for the prevention, care and control of HIV/AIDS and STI in Hong Kong;
- (b) to develop recommendations and guidance regarding HIV/AIDS and STI in Hong Kong; and
- (c) to keep under review local and international development of HIV/AIDS and STI.

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Correspondence


Address : 3/F, Wang Tau Hom Jockey Club Clinic
 200 Junction Road East, Kowloon, Hong Kong
Tel : (852) 3143 7281
Fax : (852) 2337 0897
E-mail : aca@dh.gov.hk

Introduction

1. The Universal Antenatal HIV Testing Programme (UATP) was launched in Hong Kong in September 2001. In 2008, rapid HIV testing was introduced in labour wards of all public hospitals to fill up the gap for late-presenting pregnant women without HIV testing during the antenatal period. To assist in the management of HIV positive pregnancy and prevention of perinatal HIV transmission, the Scientific Committee on AIDS and STI (SCAS) published its Recommended Clinical Guidelines on the Prevention of Perinatal HIV Transmission in 2007.¹

2. In the last few years, scientific research and the knowledge base in the area have continued to grow. International recommendations on the use of antiretroviral therapy (ART) in pregnancy and interventions to reduce perinatal HIV transmission have also been updated accordingly.^{2 3} As such, the SCAS embarked on a revision and update of the local clinical guidelines.

3. The Committee finds that the goal and major principles in the 2007 clinical guidelines continue to hold. However, update is needed in the following:

- Use of ART during pregnancy
- Recommended antiretroviral prophylaxis in women who present late and have not received antepartum ART
-  Infant ART prophylaxis



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Goal

4. These clinical guidelines were developed with a view to eradication of mother-to-child-transmission (MTCT) of HIV by the combined approach of early diagnosis and timely evidence-based interventions.

Principles

- I. Universal HIV antibody testing should be performed as part of routine antenatal care for women in Hong Kong, supplemented by rapid testing where necessary.
- II. Clinical management should include that of maternal HIV infection as well as prevention of mother-to-child transmission of HIV.
- III. HIV infected pregnant women who present late would still benefit from use of antiretroviral to reduce mother-to-child transmission.
- IV. The mode of delivery and its management should be considered on the grounds of HIV status as well as obstetric indications.
- V. Paediatric management should be offered to reduce the risk of mother-to-child transmission.
- VI. Multidisciplinary and coordinated efforts should be made to strengthen our knowledge base and practice regarding mother-to-child transmission of HIV in Hong Kong.

Recommendations and rationales

I. Universal HIV antibody testing should be performed as part of routine antenatal care for women in Hong Kong, supplemented by rapid testing where necessary

5. HIV antibody testing for pregnant women should be performed as an integral part of antenatal care. This should not be interpreted as compulsory testing as women are allowed to 'optout'. Since 2001 when universal testing was implemented, there have been high coverage rates consistently exceeding 97%, attesting to wide acceptance of testing. Overall, the prevalence of HIV in antenatal mothers was found to be less than 0.05%.⁴

6. Nevertheless, a decreasing trend of the proportion of deliveries with known maternal HIV status had become obvious by 2006, from 91% in 2003, to 86% in 2004 and 83.4% in 2005 (unpublished data from the Dept of Health). It is likely that this was due to an increasing proportion of women who presented late to obstetric services, e.g. while in labour, thus missing out on antiretroviral prophylaxis and other effective preventive measures offered by an early HIV diagnosis.

7. Conventional HIV antibody testing requires screening with ELISA followed by Western blot for confirmation. Its typical turnaround time is 2 weeks. This is unacceptable when testing is done in late pregnancy, during labour or after delivery, as delay in administration of antiretroviral prophylaxis significantly diminishes its impact. The opportunity of performing an elective caesarean section may also be lost.

8. The new generation of rapid HIV tests is performed at point of care and is highly sensitive and specific. Results are quickly available in terms of minutes. A negative result effectively rules out infection except in those who are in the process of seroconversion. Although confirmation with Western blot is still required, a positive result is highly suggestive and prophylactic interventions should be implemented against MTCT.⁵

9. Provision of rapid test in this situation should not deviate from

the standards of conventional testing. Testing is voluntary and mothers may opt out after explanation is given of testing itself and the effectiveness of available interventions in reducing MTCT.⁶ Overseas studies of rapid test in late presenting women in labour showed that it was feasible and acceptable.⁷ In Hong Kong, rapid testing has been studied in the Voluntary Counselling and Testing service, showing a high degree of client satisfaction.⁸ In a pilot study by a local hospital in 2007, rapid tests were offered to and accepted by all mothers in labour who had not been tested for HIV [unpublished data]. This reinforced the current recommendation that rapid test should be done when necessary to supplement the Universal Antenatal Testing Programme.

II. Clinical management should include that of maternal HIV infection as well as prevention of mother-to-child transmission of HIV

II.A As part of routine medical care, HIV infected women of childbearing potential should receive counselling on contraception to avoid unintended pregnancies. For those who would like to conceive, a careful risk assessment is required.

10. With the availability of combination antiretroviral therapy (cART), HIV disease as we know it today has become a chronic treatable disease with a vastly improved prognosis. Nevertheless, it is still important that HIV infected women of reproductive age receive counselling on effective contraception to avoid unintended pregnancies. Yet, not uncommonly, couples who previously rejected pregnancy are now contemplating children. They should receive information on their risks of MTCT, effectiveness of interventions, and available options of assisted reproduction to assist in their decision. Risk assessment and prevention of horizontal transmission are particularly important for serodiscordant couples.

II.B A woman who is diagnosed HIV positive in the antenatal period shall receive the same standards of care established for HIV-infected nonpregnant patients. cART incorporating ZDV is the recommended regimen to prevent MTCT. To best balance benefits and risks for the mother and her infant, management should involve a physician experienced in HIV medicine.

11. Optimal control of maternal HIV disease is beneficial to reducing MTCT, as both viral load and CD4 cell count are related to transmission. Current major standards of care in HIV disease⁹ are:

- (i) prophylaxis against opportunistic infections based on history and CD4 count; and
- (ii) individualised cART based on viral load, CD4 count and clinical history, the immediate goal of treatment being virological suppression to undetectable levels.

Regular CD4 cell enumeration and viral load testing are indicated and may need to be repeated more frequently to ensure satisfactory control of HIV disease near term. Testing for baseline viral resistance and in the event of suboptimal virologic suppression is recommended to optimize cART regimen.

12. In those with symptomatic disease and low CD4 counts, cART is indicated as soon as possible including in the first trimester. Although ZDV monotherapy is also effective for prevention of MTCT, evidence is now accumulating that cART reduces MTCT to a much greater extent. In PACTG 316, the transmission rate was only 1.5% in a group of women who mostly used combination therapy.¹⁰ In a large European cohort, transmission was only 1.2% in those on cART.¹¹ However, since ZDV has the best evidence, excellent transplacental passage, and a good safety record in this setting, ZDV should be incorporated in the cART regimen. The intrapartum and postpartum components of ZDV continue to be recommended.

13. For those mothers whose HIV disease does not otherwise require treatment, cART as recommended above is still indicated for MTCT prevention after the first trimester.

14. In either case, a physician experienced in HIV Medicine should be involved to assess for the most appropriate antiretroviral regimen based on the clinical stage, pharmacokinetics, toxicity to the mother and foetus, and antiretroviral efficacy, as guided by the CD4 cell count, viral load, viral resistance, and a detailed clinical assessment including that of any known source of infection. The potential adverse effect on disease progression and MTCT of HIV should be made known to the mother to facilitate informed decision.

15. Throughout pregnancy, the HIV physician is responsible for monitoring the response to treatment and applying the usual standards of HIV care, such as various prophylactic treatments. Special considerations, however, should be given to the unique state of pregnancy with its altered pharmacokinetics and propensity to certain adverse effects such as lactic acidosis and hyperglycaemia. The HIV physician should also alert the obstetrician and paediatrician in the event of real or expected anti-retroviral toxicity and unfavourable virological response, as these may impact obstetric and paediatric management. A long term HIV care plan should be put in place which may include a strategy to discontinue therapy postnatally in those mothers who do not otherwise require treatment.

II.C Lamivudine and a protease inhibitor are recommended in addition to zidovudine in the antenatal period, unless otherwise contraindicated.

16. The best regimen for both mother and foetus is one that has the greatest antiretroviral potency, minimal teratogenicity and toxicity, and maximal efficacy in treating HIV disease and decreasing MTCT. A cART regimen typically comprises three drugs: 2 nucleoside reverse transcriptase inhibitors (NRTI) in combination with one protease inhibitor (PI) or one non-nucleoside reverse transcriptase inhibitor (NNRTI). Other than ZDV, lamivudine (3TC) is the other preferred NRTI based on extensive experience of its use in pregnant women. However, for women who are coinfecting with hepatitis B virus (HBV), tenofovir (TDF) plus 3TC or emtricitabine (FTC) is the preferred NRTI backbone. Among the other NRTI, stavudine (d4T) and didanosine (ddI) are not generally recommended because of excessive mitochondrial toxicity and lactic acidosis. Furthermore, d4T and ddI must not be used together in pregnancy.

17. Of the available PIs, Kaletra® (LPV/r) tablet, ritonavir (RTV)-boosted atazanavir (ATV) and ritonavir-boosted saquinavir (SQV) are the preferred options for use in pregnancy. Pharmacokinetic studies suggest that the dose of Kaletra should be increased in the third trimester, to the range of LPV/r 500mg/125mg to 600mg/150mg bid. The use of therapeutic drug monitoring of LPV drug level should be considered.

18. Although nevirapine (NVP) has proven efficacy in preventing MTCT, it should be used with caution, as rash and hepatotoxicity are particularly common in women with a CD4 count above 250/ μ l. The other NNRTI, efavirenz, is teratogenic in monkeys. Neural tube defects have also been reported in humans. In general, this drug is contraindicated in the first trimester. Both NVP and efavirenz have long and often unpredictable half lives. For this reason, development of resistance is a major concern if they are discontinued without cover of other antiretrovirals. If given to the mother, temporary coverage after its discontinuation with 2 NRTIs, e.g. ZDV plus 3TC, of 7 days may be effective. Some experts may add a protease inhibitor and cover for a longer period of time.

19. It cannot be overemphasised that, in order to arrive at an optimal cART regimen, flexibility should be exercised in interpreting these guidelines. Clinical circumstances such as past medical history, anticipated poor adherence, virological failure or potential interactions with other drugs may require deviation from the recommended regimen. Throughout and after pregnancy, close communication among all members of the medical team is required to ensure the best care for the mother and child, and reduce the risk of MTCT to the minimum (Table 1).

II.D For those women who become pregnant while receiving antiretroviral therapy, evaluation should be made of the treatment regarding antiretroviral potency, potential toxicity to the mother and foetus, and prophylactic efficacy against MTCT.

20. For these patients, re-evaluation of the antiretroviral regimen is required with the same considerations applicable to those newly diagnosed in pregnancy. As long as it is potent enough for full viral suppression and well tolerated by the patient, the current cART regimen can be maintained during pregnancy including in the first trimester unless contraindicated. Treatment response has to be reviewed and a viral resistance test is recommended for those with detectable viral loads. Ideally, all pregnancies should be planned so that evaluation could have been made prior to conception regarding the most appropriate regimen.

III. HIV infected pregnant women who present late would still benefit

from use of antiretroviral to reduce mother-to-child transmission

III.A When maternal HIV infection is not diagnosed until labour, or when a known HIV infected woman who has received no prior antiretroviral therapy is in labour, antiretrovirals administered intrapartum and postpartum to the newborn are still indicated to reduce MTCT.

21. In this scenario, the use of rapid HIV test is critical, without which interventions would not even be contemplated. Although the opportunity of a full course of treatment has been lost, commencement of antiretrovirals in labour is still useful to reduce MTCT. The standard 076 regimen of ZDV abbreviated to its intrapartum and postpartum components has been observed to decrease transmission risk, though to a lesser extent.¹² In a recent randomised trial evaluating the safety and efficacy of 3 neonatal antiretroviral regimens for prevention of intrapartum HIV transmission in women who have not received antepartum ART, it was found that combination infant antiretroviral prophylaxis was superior to ZDV alone. Of the two combination regimens, the 2 -drug regimen with ZDV plus NVP is preferable to a 3 -drug regimen with ZDV, nelfinavir (NFV) plus 3TC due to fewer side effects.¹³

22. Therefore, to maximize protection in such a scenario of high MTCT risk, the SCAS recommends the use of ZDV intrapartum to the mother, and a combination of ZDV for 6 weeks plus 3 doses of NVP in the first week postpartum to the newborn (Table 2).

23. It is important that an HIV physician be involved to assist in the management of any complication related to HIV disease and to determine as soon as possible the subsequent treatment plan for the mother.

III.B For infants born to HIV-infected mothers who have not taken antiretroviral therapy during the antenatal and intrapartum periods, the recommended regimen is a total of three doses of nevirapine in combination with 6 weeks of ZDV to be started as soon as possible after birth.

24. Data from a randomised trial showed a lowered HIV

transmission risk with combination infant ART prophylaxis vs ZDV alone in infants born to mothers who had not received antiretroviral therapy during pregnancy.¹³ It is therefore recommended that the infant should receive the same regimen of ZDV plus 3 doses of NVP as soon after birth as possible, as recommended in the above scenario where treatment was begun in labour (Table 3).

25. Combination ART prophylaxis for infant should also be considered (Table 3) in scenarios which are considered to be high risk of MTCT, e.g. mothers who have received antepartum and intrapartum ART but with suboptimal viral suppression at delivery.

26. It is noted that treatment initiated after 48h is likely to be futile and will contribute to viral resistance should infection occur. Thus it should be given only in exceptional cases and after consultation with experts in the field.

IV. The mode of delivery should be considered on the grounds of obstetric indications as well as HIV status

27. For the purpose of MTCT prevention, elective caesarean section confers an independent effect on reducing MTCT in those with a viral load above 1000/ml, and is therefore the preferred mode of delivery in this situation.^{14 15} For those who are able to achieve a lower or undetectable level of viral load before delivery, elective caesarean section *per se* does not offer additional advantage. Furthermore, the operation carries risks of its own which may be further increased in HIV infected women. Important as it should be, the efficacy of elective caesarean section in reducing MTCT is therefore one of many factors, viral and obstetric, in the final decision on the mode of delivery.¹⁶

28. For those mothers who proceed to vaginal delivery, prolonged rupture of membranes (especially if more than 4 hours), invasive foetal monitoring and instrumental delivery should be avoided to reduce MTCT.

V. Paediatric management should be offered to reduce the risk of

mother-to-child transmission

29. A paediatrician experienced in HIV disease and managing babies born to HIV infected mothers should preferably be involved early and before delivery. He would be responsible for completion of the antiretroviral regimen for the neonate and assess for toxicity and congenital defects resulting from maternal use of antiretrovirals. Toxicities that should be ruled out include anaemia secondary to ZDV, lactic acidosis resulting from NRTI, and hyperglycaemia from PI. The infant should also be followed closely for the possibility of HIV infection. Reference should be made to local guidelines in this respect.¹⁷ Of note, BCG vaccination should be withheld until after HIV infection of the infant is ruled out.¹⁸

30. The mother is advised against breast-feeding as it has been estimated that the added risk of transmission by breastfeeding was high at 16.7%.¹⁹ In developing countries, breastfeeding may be justified by its other benefits. In Hong Kong, it is not. Every effort should be made to assist the mother in replacement feeding.

31. At present, the long term effects of antiretrovirals on the future development of the child are not clear. Thus it is important that all such children should be followed by the paediatrician for an extended period of time.

VI. Multidisciplinary and coordinated efforts should be made to strengthen the knowledge base and practice regarding mother-to-child transmission of HIV in Hong Kong

32. Were the goal of eradicating MTCT to be ever possible, it is imperative that all stakeholders, especially obstetricians and paediatricians, be enlisted for their contribution. The fact that optimal prevention of MTCT requires early diagnosis highlights the importance of a strong overall public health programme. Universal antenatal testing supplemented by rapid HIV testing should continue and be closely monitored so that gaps could be filled quickly. Experience of health care providers should also be shared within and across disciplines to identify the model of best practice. It is a most

trying time for the mother who often is also beset with difficult psychosocial circumstances. Overlooking this aspect of care risks non-adherence and failure of otherwise effective interventions. Each and every instance of MTCT is a tragedy and should be reviewed carefully so that improvement can be made.

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Table 1. Recommended antiretroviral prophylaxis against MTCT of HIV

Period and regimen	Dosing	Remarks
Antepartum: cART (ZDV + 3TC + PI or NVP)	<ul style="list-style-type: none"> • ZDV 300 mg po bid • 3TC 150 mg po bid • Kaletra® 2 tablets (LPV 200 mg/RTV 50 mg per tablet) po bid, increased to LPV 500-600 mg/RTV 125-150 mg po bid in 3rd trimester • Saquinavir 1000 mg with RTV 100 mg po bid • Atazanavir 300 mg with RTV 100 mg po qd 	<ul style="list-style-type: none"> • Regimen subject to evaluation by HIV physician • Viral resistance test is recommended • Assess virological response to HAART, esp. near term • Use TDM if necessary • Pre-plan for postnatal treatment • Follow for adverse effects of ARV: <ul style="list-style-type: none"> ♦ Anaemia ♦ Hyperglycaemia ♦ Lactic acidosis • Efavirenz generally contraindicated • Avoid NVP in those with CD4 count >250/μl
Intrapartum: ZDV	<ul style="list-style-type: none"> • Recommended: IV loading dose of 2 mg/kg in 1 h, then 1mg/kg/h till delivery; begin at onset of labour or 3 h before elective caesarean section • Continue antepartum cART regimen 	
Postpartum: cART for mother and ZDV for newborn	<p>Mother:</p> <ul style="list-style-type: none"> • Continue antepartum cART regimen, or • Discontinue under supervision of HIV physician <p>Newborn (to be started as soon after birth as possible and preferably within 6-12 h):</p> <ul style="list-style-type: none"> • ZDV syrup 2 mg/kg po q6h for 6 wk, or • ZDV syrup 4 mg/kg po bid for 6 wk, or • ZDV 1.5 mg/kg IV q6h for 6 wk 	<ul style="list-style-type: none"> • Modify dosage in preterm infants <35 wk gestation: <ul style="list-style-type: none"> ♦ 1.5 mg/kg IV or 2 mg/kg po q12h, then q8h at <ul style="list-style-type: none"> ♦ 2 wk if gestation >30 wk, or ♦ 4 wk if gestation <30 wk • No breastfeeding

cART, combination antiretroviral therapy; ZDV, zidovudine; 3TC, lamivudine; LPV, lopinavir; NVP, nevirapine; RTV, ritonavir; TDM, therapeutic drug monitoring; ARV, antiretroviral.

Table 2. Recommended antiretroviral prophylaxis in women presenting in labour

Period and regimen	Dosing	Remarks
Intrapartum: ZDV	ZDV - <ul style="list-style-type: none"> Recommended: IV bolus of 2 mg/kg over 1 h, then 1mg/kg/h till delivery; begin at onset of labour or 3 h before elective caesarean section 	
Postpartum: ZDV for 6 wk + NVP for 3 doses for newborn	Newborn: ZDV - <ul style="list-style-type: none"> 2 mg/kg po q6h for 6 wk, or 4 mg/kg po bid for 6 wk, or 1.5 mg/kg IV q6h for 6 wk NVP - <ul style="list-style-type: none"> 3 doses in the first week of life (at birth, 48 h after 1st dose, 96 h after 2nd dose) 	<ul style="list-style-type: none"> No breastfeeding Refer to HIV physician for management of maternal HIV disease NVP: 8 mg per dose po if birth weight 1.5-2 kg; 12 mg per dose po if birth weight >2 kg

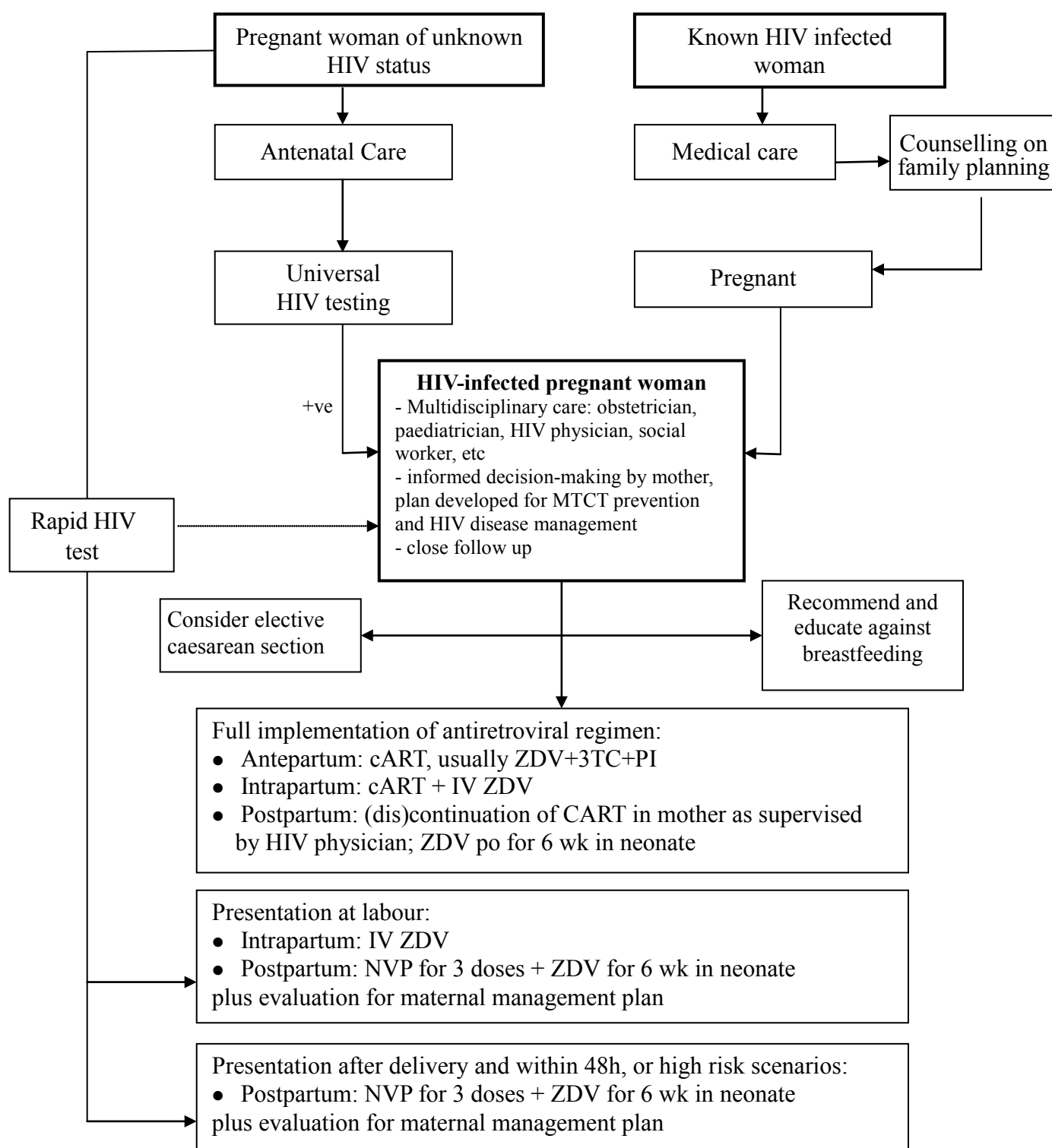
ZDV, zidovudine; 3TC, lamivudine; NVP, nevirapine; ARV, antiretroviral

Table 3. Recommended antiretroviral prophylaxis for infants born to women presenting after delivery or scenarios considered to be high risk of MTCT:

Regimen	Dosing	Remarks
Postpartum: ZDV for 6 wk + NVP for 3 doses for newborn	Immediate use of ZDV: <ul style="list-style-type: none"> 2 mg/kg po q6h for 6 wk, or 4 mg/kg po bid for 6 wk, or 1.5 mg/kg IV q6h for 6 wk NVP: <ul style="list-style-type: none"> 3 doses in the first week of life (at birth, 48 h after 1st dose, 96 h after 2nd dose) 	<ul style="list-style-type: none"> ARV not advised if after 48h of birth No breastfeeding Refer to HIV physician for management of maternal HIV disease No breastfeeding NVP: 8 mg per dose po if birth weight 1.5-2 kg; 12 mg per dose po if birth weight >2 kg

ZDV, zidovudine; 3TC, lamivudine; NVP, nevirapine; ARV, antiretroviral

Algorithm. Overview of management principles in preventing MTCT of HIV



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