

## **Recommended Clinical Guidelines on the Prevention of Perinatal HIV Transmission (Scientific Committee on AIDS and STI, Centre for Health Protection, November 2018)**

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### **Purpose**

The purpose of this paper is to provide an update on the Recommended Clinical Guidelines on the Prevention of Perinatal HIV Transmission in view of the growing evidences and changing international recommendations in the use of antiretroviral therapy in pregnancy.

### **Introduction**

The Universal Antenatal HIV Testing Programme (UATP) was launched in Hong Kong in September 2001. In 2008, the programme was supplemented with rapid HIV testing in labour wards of public hospitals to fill the gap for late-presenting pregnant women without documented HIV status in the antenatal period. To assist in the management of HIV positive pregnancy and prevention of perinatal HIV transmission, the then Scientific Committee on AIDS published its first Recommended Clinical Guidelines on the Prevention of Perinatal HIV Transmission in 2001, which were subsequently updated in 2007 and 2012 by the Scientific Committee on AIDS and STI (SCAS).<sup>1</sup>

In recent 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.<sup>2,3</sup> In view of such, the SCAS embarked on a revision and update of the local clinical guidelines.

In the course of review, it was noted that the goal and major principles in the 2012 clinical guidelines continued to hold. However, update is needed in the following:

- Consideration of HIV retesting in third trimester in high risk population;
- Use of ART during pregnancy;
- Recommended antiretroviral prophylaxis in women who present late and have not received antepartum ART; and
- Infant ART prophylaxis.

### **Goal**

These clinical guidelines were developed with a view to supporting 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. High risk behaviours should be

avoided during pregnancy and breastfeeding. Repeat testing in the third trimester is recommended where risk exists.

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. High risk behaviors should be avoided during pregnancy and breastfeeding. Repeat testing in the third trimester is recommended where risk exists**

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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 'opt out'. Since 2001 when universal testing was implemented, there have been high coverage rates consistently exceeding 98%, attesting to wide acceptance of testing. In 2016, testing coverage was 100% with an HIV prevalence of 0.02%.<sup>4</sup>

In 2005, it was noticed that the proportion of deliveries with known maternal HIV status had fallen to 83.4% (data from the Dept. of Health), likely due to a rise of women presenting 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.

Conventional HIV antibody testing requires screening with ELISA followed by Western blot for confirmation. Its turnaround time may take up to a week. 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.

The current generation of rapid HIV tests is performed at point of care and is highly sensitive and specific. Results are quickly available in 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 of HIV diagnosis and prophylactic interventions should be implemented against MTCT without delay.<sup>2,5</sup>

Therefore, rapid test should be provided where the mother presents late and without known HIV status. However, testing should not deviate from the standards required 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.<sup>6</sup> Overseas studies of rapid test in late presenting women in labour showed that it was feasible and acceptable.<sup>7</sup> In Hong Kong, rapid testing has been studied in the Voluntary Counselling and Testing service, showing a high degree of client satisfaction.<sup>8</sup> 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 recommendation that rapid test should be done when necessary to supplement the Universal Antenatal Testing Programme.

It cannot be overemphasised that a negative HIV test result does not preclude subsequent acquisition of HIV. As of September 2015, there had been 5 paediatric cases of HIV infection in which a maternal negative result had been obtained in the early antenatal period. These were incidents of MTCT where transmission could have taken place in the late pregnancy period, the intrapartum period or in the postpartum period through breastfeeding. Such occurrence reinforces the need to advise against risk behaviors during pregnancy and breastfeeding.

It is recommended that repeat HIV testing be done in the third trimester between 34 and 36 weeks if there is concern over new HIV acquisition, for example in individuals with the following risk factors: (a) women who inject drugs or whose sex partners do, (b) women who exchange sex for money, (c) women who are sex partners of HIV-infected persons, (d) women who have a new or more than one sex partner during the pregnancy, (e) women who have newly acquired sexually-transmitted infections during pregnancy, and (f) women who originated from areas of unknown or high HIV prevalence, or whose sex partners did<sup>9,10,11</sup>. If there are signs or symptoms compatible with acute HIV infection, HIV testing should also be repeated at any time point during the pregnancy period.

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

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**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.**

With the availability of combination antiretroviral therapy (cART), HIV disease as we know it today has become a chronic treatable condition with 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 child-bearing. They should receive information on their risks of MTCT, effectiveness of interventions, and available options of assisted reproduction to inform 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 shall be initiated or continued for disease treatment and prevention of MTCT. To best balance benefits and risks for the mother and her infant, management should involve a physician experienced in HIV medicine.**

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 disease<sup>12</sup> are:

- (i). prophylaxis against opportunistic infections based on history and CD4 count; and
- (ii). immediate, individualised cART with the goal of virologic 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 delivery. Testing for baseline viral resistance and in the event of suboptimal virologic suppression is recommended to optimise cART regimen.

cART is recommended for all pregnant women diagnosed with HIV regardless of CD4 count and viral load due to the established benefits in their own disease prognosis and in reducing MTCT. In particular, for individuals who are symptomatic, with a low CD4 count of less than 200/uL or a viral load level above 100,000 copies/ml, cART should be initiated as soon as possible including in the first trimester.

For other women, pros and cons of early cART initiation in the first trimester, e.g. early virologic suppression to further reduce the risk of MTCT and potential foetal and neonatal toxicities, should be discussed to arrive at an informed decision. Of note, it has been shown in a large cohort of 12,000 women that those who conceived while on cART attained a 0.19% rate of MTCT against an overall rate of 0.57%.<sup>13</sup> Regardless, all women should preferably have been put on effective cART by 20 weeks of pregnancy, so as to ensure virologic suppression at delivery. Recent studies also confirmed that cART conferred a significantly greater benefit in reducing MTCT.<sup>14</sup> Therefore, ZDV monotherapy can no longer be justified. Similarly, the effectiveness of cART removes the need of routine intrapartum ZDV unless virologic suppression is not achieved at delivery.

A physician experienced in HIV Medicine should be involved to assess for the most appropriate antiretroviral regimen based on the disease 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 effect on disease progression and MTCT of HIV should be made known to the mother to facilitate informed decision.

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 antiretroviral toxicity and unfavourable virologic response, as these may impact obstetric and paediatric management. A long term HIV care plan should be put in place.

### **II.C. cART including 2 nucleoside reverse transcriptase inhibitors as backbone and a third agent is recommended unless otherwise contraindicated.**

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: two nucleoside reverse transcriptase inhibitors (NRTI) in combination with one protease inhibitor (PI), one non-nucleoside reverse transcriptase inhibitor (NNRTI) or one integrase inhibitor (INSTI). ZDV and lamivudine (3TC) have been used extensively in pregnant women. Evidence suggested that tenofovir (TDF)<sup>15-16</sup> and abacavir (ABC)<sup>17</sup> were also safe during pregnancy. Therefore, ABC plus 3TC, TDF plus emtricitabine (FTC), or ZDV plus 3TC, are all acceptable as the backbone NRTI for pregnant women. For women who are coinfecting with hepatitis B virus (HBV), TDF plus 3TC or FTC is preferred. Among the other NRTI, stavudine (d4T) and didanosine (ddI) are not recommended because of excessive mitochondrial

toxicity and lactic acidosis. Furthermore, d4T and ddI must not be used together in pregnancy. Tenofovir alafenamide (TAF) should also be avoided due to limited data in pregnancy.

Of the available PIs, Kaletra® (LPV/r) tablet, ritonavir (RTV)-boosted atazanavir (ATV) and ritonavir-boosted darunavir (DRV) 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 500-600 mg/RTV 125-150 mg bid RTV-boosted DRV should be administered as 600 mg/100 mg twice-daily dosing during pregnancy. If available, therapeutic drug monitoring of PI should be considered. DRV coformulated with cobicistat cannot be recommended in pregnancy because of limited experience.

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/ $\mu$ l. The other NNRTI, efavirenz (EFV), was previously contraindicated in pregnancy due to its association with teratogenicity in monkeys. However, recent studies failed to confirm such findings in humans.<sup>18</sup> Therefore EFV is no longer contraindicated even in the first trimester. Another NNRTI, rilpivriine (RPV), can be considered as an alternative for HIV-infected pregnant women with a pre-treatment viral load less than 100,000 copies/ml.<sup>19</sup> All NNRTI 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.

Raltegravir (RAL), one of the integrase inhibitors, was shown to be safe and well tolerated during pregnancy and was associated with rapid viral decay.<sup>20</sup> This is particularly advantageous for women who present relatively late with a high viral load. It should be given at 400 mg twice daily as there is limited data on once-daily dosing during pregnancy. Dolutegravir (DTG) should be avoided in those women who are pregnant or are trying to conceive. A safety alert has been issued based on an ongoing study in Botswana in which neural tube defects occurred in 4 out of 426 mothers who used DTG while becoming pregnant.<sup>21</sup> Of note, cobicistat-boosted elvitegravir (coformulated either with TDF/FTC or TAF/FTC) and bictegravir, the other INSTIs, cannot be recommended at this time because of limited data on safety.

Clinical circumstances such as past medical history, anticipated poor adherence, virologic failure or potential interactions with other drugs may require deviation from the recommended regimen (Table 1). 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.

#### **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.**

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 generally 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. As a result, treatment may need to be optimised but should not be interrupted. Ideally, all pregnancies should be planned so that evaluation could have been made prior to conception regarding the most appropriate regimen.

**II.E. For women who are on effective cART with a HIV viral load <50 copies/ml close to delivery, intrapartum ZDV is no longer recommended.**

Previous recommendations that intrapartum IV ZDV should be routinely used were based largely on the original 3-part ZDV mono-regimen for MTCT prevention.<sup>22</sup> With the success of cART in fully suppressing HIV in pregnancy, the additional advantage of using IV ZDV was in doubt. A number of recent studies, including a large French cohort,<sup>23</sup> have confirmed that IV ZDV given intrapartum in the presence of viral suppression risks hematologic toxicity without additional benefit in reducing MTCT. Nevertheless, in those situations where viral suppression cannot be confirmed as with late presenting mothers or where adherence is suboptimal, IV ZDV continues to be indicated.

**II.F. In the low risk scenario where the pregnant woman has been on effective cART during pregnancy with virologic suppression, 4 weeks of ZDV monotherapy suffices as infant prophylaxis**

In one study looking into the duration of antiretroviral prophylaxis in infant, investigators found that for low risk cases, four weeks of neonatal prophylaxis had a similar efficacy as a six-week regimen but were associated with fewer hematological side effects.<sup>24</sup> Therefore, if the pregnant woman is on effective cART and has achieved a suppressed viral load with no concerns about adherence, postpartum ZDV as neonatal prophylaxis can be shortened to 4 weeks (Table 1).

**III. HIV infected pregnant women who present late would still benefit from use of antiretroviral to reduce mother-to-child transmission**

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**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 to the mother and postpartum to the neonate are still indicated to reduce MTCT.**

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. As rapid build up of ART levels is important, IV ZDV should be started immediately. Other than ZDV, drugs that cross the placental barrier, such as 3TC and RAL, could also be considered to confer additional pre-exposure prophylaxis for the foetus.

In a randomised trial of neonatal antiretroviral regimens for mothers who have not received antepartum ART, it was also found that combination infant antiretroviral prophylaxis was superior to ZDV alone. Of the two combination regimens that have similar efficacy, the 2-drug regimen (ZDV for 6 wk + 3 doses of NVP in 1 wk) has fewer side effects when compared to a 3-drug regimen (ZDV for 6 wk + nelfinavir (NFV) for 2 wk + 3TC for 2 wk).<sup>25</sup>

Therefore, to maximise protection in such a scenario of high MTCT risk, the SCAS recommends the use of IV 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). It is important that an HIV physician be involved to advise on the management.

**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 combination of**

**ZDV for 6 weeks plus 3 doses of NVP in the first week. Alternatively, a 3-drug regimen consisting of zidovudine, nevirapine and lamivudine can be considered as empiric therapy.**

The SCAS continues to recommend the 2-drug regimen consisting of ZDV for 6 weeks plus 3 doses of NVP in the first week for prophylaxis, started as soon as possible. Alternatively, in these high risk cases where neither antepartum nor intrapartum cART had been given, empiric therapy with a 3-drug regimen of ZDV, treatment dose NVP and 3TC can be considered (Table 3). A Canadian study demonstrated that this 3-drug regimen was well tolerated, albeit associated with such side effects as vomiting, diarrhoea, rash and irritability. Haematological toxicities and lower growth measures were generally reversible after cessation of treatment.<sup>26</sup> As empiric HIV therapy, this regimen could be discontinued and switched to ZDV monotherapy for a total duration of 6 weeks if initial HIV test returned negative. Consultation with experts in the field is advised (Table 3).

It is noted that ART prophylaxis with 2 drugs initiated after 48 hours is likely to be futile and will contribute to viral resistance should infection occur. In this scenario of delayed presentation, consideration may be given to empiric therapy with the three drug regimen if the risk is substantial.

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

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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.<sup>27,28</sup> 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.<sup>29</sup>

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, especially if virologic suppression is not ascertained.

#### **V. Paediatric management should be offered to reduce the risk of mother-to-child transmission**

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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. Of note, BCG vaccination should be withheld until after HIV infection of the infant is ruled out.<sup>30</sup>

Although effective maternal cART coverage during pregnancy and breastfeeding may reduce the post-natal 6-month MTCT rate to the range of 1.1%,<sup>31</sup> this is still unacceptable in settings where alternative to breastfeeding exists and where the goal is the eradication of MTCT. 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.

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**

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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 should be supplemented, if indicated, by rapid HIV testing in the labour ward or repeat testing in third trimester. The programme should 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.



**Table 1. Recommended antiretroviral prophylaxis against MTCT of HIV**

Period and regimen	Dosing	Remarks
Antepartum: cART  NRTI backbone + PI or NNRTI or INSTI  NRTI backbone combination: TDF + FTC (Truvada®) or ABC + 3TC (Kivexa®) or ZDV + 3TC (Combivir®)	<p><u>NRTI</u></p> <ul style="list-style-type: none"> <li>● TDF 300 mg po qd</li> <li>● FTC 200 mg po qd</li> <li>● ABC 300 mg po bid or 600mg po qd</li> <li>● ZDV 300 mg po bid</li> <li>● 3TC 150 mg po bid or 300mg po qd</li> </ul> <p><u>NNRTI</u></p> <ul style="list-style-type: none"> <li>● EFV 600 mg po bedtime</li> <li>● RPV 25 mg qd with food</li> <li>● NVP 200 mg qd for 14 days then 200mg bid</li> </ul> <p><u>PI</u></p> <ul style="list-style-type: none"> <li>● 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 3<sup>rd</sup> trimester</li> <li>● ATV 300 mg with RTV 100 mg po qd</li> <li>● DRV 600 mg with RTV 100mg po bid</li> </ul> <p><u>INSTI</u></p> <ul style="list-style-type: none"> <li>● RAL 400mg po bid</li> </ul>	<ul style="list-style-type: none"> <li>● Regimen subject to evaluation by HIV physician</li> <li>● Viral resistance test is recommended</li> <li>● Assess virologic response to cART, esp. near delivery</li> <li>● Use TDM if necessary</li> <li>● Pre-plan for postnatal treatment</li> <li>● Follow for adverse effects of antiretroviral: <ul style="list-style-type: none"> <li>◆ Anaemia</li> <li>◆ Hyperglycaemia</li> <li>◆ Lactic acidosis</li> </ul> </li> <li>● Avoid starting NVP in those with CD4 count &gt;250/μL; limited PK data of NVP-extended release in pregnancy</li> <li>● Avoid RPV if baseline HIV viral load &gt;100,000 copies</li> <li>● For all ethnicities other than Chinese, limit use of ABC only to those without B*5701</li> <li>● Avoid once-daily dosing for RAL</li> </ul>
Intrapartum: ZDV	<ul style="list-style-type: none"> <li>● ZDV: 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</li> <li>● Continue antepartum cART regimen</li> </ul>	<ul style="list-style-type: none"> <li>● Omit IV ZDV if viral load is suppressed near delivery</li> </ul>
Postpartum: cART for mother and ZDV for newborn	<p>Mother:</p> <ul style="list-style-type: none"> <li>● Continue antepartum cART regimen,</li> </ul> <p>Newborn (to be started as soon after birth as possible and preferably within 6-12 h):</p> <ul style="list-style-type: none"> <li>● ZDV syrup 2 mg/kg po q6h, or 4 mg/kg po bid for 4 wk, or</li> <li>● ZDV 1.5 mg/kg IV q6h for 4 wk</li> </ul>	<ul style="list-style-type: none"> <li>● Modify dosage in preterm infants &lt;35 wk gestation: <ul style="list-style-type: none"> <li>◆ 1.5 mg/kg IV or 2 mg/kg po q12h, then q8h at</li> <li>◆ 2 wk if gestation &gt;30 wk, or</li> <li>◆ 4 wk if gestation &lt;30 wk</li> </ul> </li> <li>● No breastfeeding</li> <li>● Prolong ZDV to 6 weeks with addition of NVP if maternal HIV viral load is not suppressed or doubtful adherence (Table 3).</li> </ul>

cART, combination antiretroviral therapy; TDF, tenofovir; FTC, emtricitabine; ABC, abacavir; ZDV, zidovudine; 3TC, lamivudine; EFV, efavirenz; RPV, rilpivirine; NVP, nevirapine; LPV, lopinavir; RTV, ritonavir; ATV, atazanavir; DRV, darunavir; RAL, raltegravir; TDM, therapeutic drug monitoring; cART, combination antiretroviral therapy.

**Table 2. Recommended antiretroviral prophylaxis in women presenting in labour**

Period and regimen	Dosing	Remarks
Intrapartum: ZDV	ZDV - <ul style="list-style-type: none"> <li>● IV bolus of 2 mg/kg over 1 h, then 1mg/kg/h till delivery</li> <li>● (Then ZDV 300 mg po bid)</li> </ul> (3TC 150 mg po bid) (RAL 400 mg bid)	<ul style="list-style-type: none"> <li>● Consider adding 3TC and RAL to enhance prophylactic effect</li> </ul>
Postpartum: ZDV for 6 wk + NVP for 3 doses for newborn	Newborn: ZDV - <ul style="list-style-type: none"> <li>● 2 mg/kg po q6h for 6 wk, or</li> <li>● 4 mg/kg po bid for 6 wk, or</li> <li>● 1.5 mg/kg IV q6h for 6 wk</li> </ul> NVP - <ul style="list-style-type: none"> <li>● 3 doses in the first week of life (at birth, 48 h after 1<sup>st</sup> dose, 96 h after 2<sup>nd</sup> dose)</li> </ul>	<ul style="list-style-type: none"> <li>◆ No breastfeeding</li> <li>◆ Refer to HIV physician for management of maternal HIV disease</li> <li>◆ NVP: 8 mg per dose po if birth weight 1.5-2 kg; 12 mg per dose po if birth weight &gt;2 kg</li> </ul>

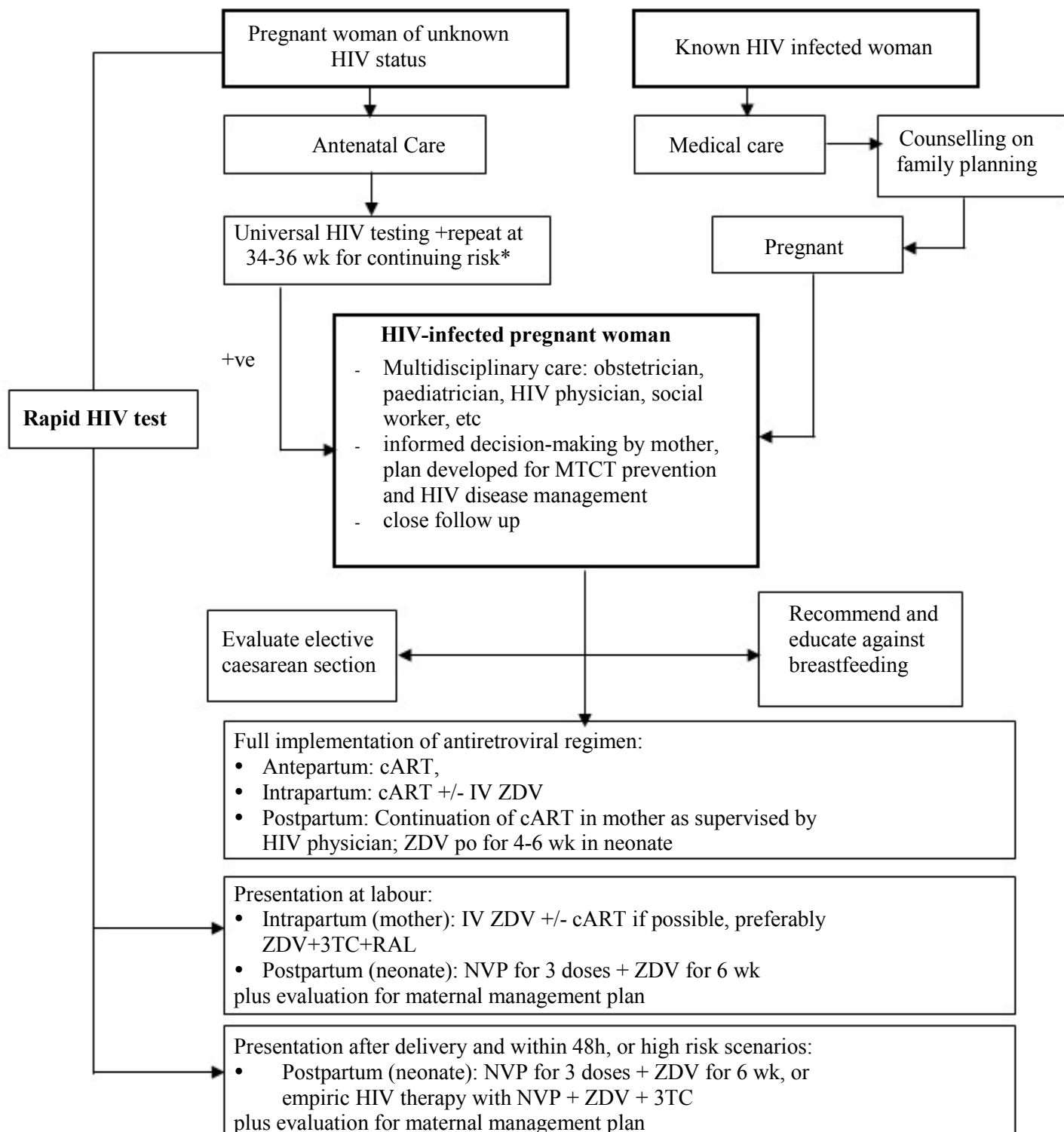
ZDV, zidovudine; 3TC, lamivudine; NVP, nevirapine

**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: 2-drug regimen, or 3-drug regimen as empiric HIV therapy to be started immediately after delivery	<u>2-drug regimen</u> ZDV: <ul style="list-style-type: none"> <li>● 2 mg/kg po q6h for 6 wk, or</li> <li>● 4 mg/kg po bid for 6 wk, or</li> <li>● 1.5 mg/kg IV q6h for 6 wk</li> </ul> NVP: <ul style="list-style-type: none"> <li>● 3 doses in the first week of life (at birth, 48 h after 1<sup>st</sup> dose, 96 h after 2<sup>nd</sup> dose)</li> </ul> <u>3-drug regimen</u> ZDV: <ul style="list-style-type: none"> <li>● 2mg/kg po q6h for 4 wk, or</li> <li>● 4mg/kg po bid for 4 wk</li> </ul> NVP: <ul style="list-style-type: none"> <li>● 2mg/kg po qd for 1 wk then 4mg/kg qd for 1 week then stop</li> <li>● If the mother has received NVP, start with 4mg/kg qd</li> </ul> 3TC: <ul style="list-style-type: none"> <li>● 2mg/kg bd for 2 wk</li> </ul>	<ul style="list-style-type: none"> <li>◆ 2-drug regimen not advised after 48h of birth</li> <li>◆ No breastfeeding</li> <li>◆ Refer to HIV physician for management of maternal HIV disease</li> <li>◆ NVP: 8 mg per dose po if birth weight 1.5-2 kg; 12 mg per dose po if birth weight &gt;2 kg</li> <li>◆ For 3 drug regimen, it is optional to switch to ZDV monotherapy for total of 6 wk if initial neonate HIV PCR test negative</li> <li>◆ Need to monitor for possible side effects, e.g. anemia, rash, GI disturbances</li> </ul>

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

**Algorithm. Overview of management principles in preventing MTCT of HIV**



\*Continuing risk as in women who (i) inject drug or whose partners do, (ii) exchange sex for money, (iii) have HIV infected partners, (iv) have a new or multiple sex partners, (v) have a new STI in pregnancy, (vi) are from areas with unclear or high HIV prevalence, or whose sex partner are

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**Test paper -Recommended Clinical Guidelines on the Prevention of Perinatal HIV Transmission (Scientific Committee on AIDS and STI, Centre for Health Protection, November 2018)**

Expiration Date: 23 December 2019

**CME point # / CNE point: 1 / PEM point: 1 (Midwifery related)**

- Please indicate one answer to each question.
- Answer these on the answer sheet and make submission by fax to Special Preventive Programme, Department of Health.

# Please contact respective authorities directly for CME/CPD accreditation if it is not on listed below.

Accreditors	CME Point
Department of Health <i>(for practising doctors who are not taking CME programme for specialists)</i>	1
Anaesthesiologists	1
Community Medicine	1
Dental Surgeons	1
Emergency Medicine	1
Family Physicians	1
Obstetricians and Gynaecologists	1
Ophthalmologists	0.5
Orthopaedic Surgeons	1
Otorhinolaryngologists	pending
Paediatricians	1
Pathologists	1
Physicians	0
Psychiatrists	1
Radiologists	1
Surgeons	1

1. In its recommendations for prevention of perinatal HIV infection, the Scientific Committee on AIDS and STI abides by the following principles EXCEPT
  - (a) Universal HIV antibody testing should be performed as part of routine antenatal care, supplemented by rapid testing when necessary. Repeat testing in the third trimester is recommended where risk exists.
  - (b) HIV infected pregnant women who present late would still benefit from use of antiretroviral to reduce mother-to-child transmission (MTCT)
  - (c) HIV MTCT considerations override those of obstetric indications in determining the mode of delivery
  - (d) Clinical management should include that of maternal HIV infections as well as prevention of MTCT
  - (e) Paediatric management should be offered to reduce the risk of MTCT
  
2. Which of the following applies to the Universal HIV Antenatal Testing Programme of Hong Kong?
  - (a) Mandatory; women who opt out will be put on empiric antiretroviral therapy
  - (b) One HIV test during the antenatal period suffices
  - (c) Voluntary; women who 'opt in' will sign consent form before testing
  - (d) To guide intervention to prevent MTCT, rapid HIV testing should be done if a pregnant woman without prior antenatal HIV test results presents late in labour
  - (e) If repeat HIV testing is to be done for a pregnant woman with continuing risk of infection, the best time to perform it is at labour



3. Which of the following is NOT a reason to perform a second HIV test in the antenatal period after an initial negative result?
  - (a) The woman habitually injects heroin but she claims to have stopped after becoming pregnant
  - (b) The woman has moved to Hong Kong from a country in Central Asia; you are not familiar with the HIV epidemiology there
  - (c) The woman tells you that her husband is HIV infected
  - (d) The woman tests positive for *Neisseria gonorrhoeae* in her urine
  - (e) All of the above are indications to repeat testing for HIV
  
4. Regarding the initiation of antiretroviral (ARV) for pregnant women known to be HIV infected in the antenatal period,
  - (a) Women with high CD4 count (>200/uL) should defer ARV until after the first trimester
  - (b) Even if a woman has been put on effective ARV while becoming pregnant, this regimen should be reassessed for need of change.
  - (c) HIV physician should not be involved in antenatal care until after delivery to avoid conflict of interest between the best obstetric and HIV outcome.
  - (d) As ARV begun intrapartum has also proved to be effective in preventing MTCT, the newest guideline today allows deferment of ARV until labour
  - (e) All of the above are correct
  
5. Regarding the choice of antiretroviral (ARV) in the antenatal period
  - (a) Doluegravir is one of the recommended options
  - (b) The two-drug combination of Kaletra® and lamivudine is one of the recommended regimens
  - (c) Efavirenz cannot be recommended for use in the first trimester because of the risk of neural tube defect in the newborn
  - (d) Tenofovir cannot be recommended because of its association with unfavourable obstetric outcome
  - (e) Raltegravir is preferred if rapid lowering of viral load is necessary
  
6. For use of protease inhibitor in the antenatal period
  - (a) Dosage of Kaletra® (lopinavir coformulated with ritonavir) should be increased to three tablets BID in the third trimester and reduced back to two tablets BID after delivery
  - (b) Dosage of Prezcoibix® (darunavir coformulated with cobicistat) should be doubled
  - (c) Dosage of atazanavir (boosted by ritonavir) should be doubled
  - (d) TDM (therapeutic drug monitoring) for protease inhibitors cannot be relied upon in pregnancy
  - (e) All of the above are true
  
7. For an HIV infected mother who is delivering vaginally
  - (a) Vacuum extraction, but not forceps, should be used to expedite delivery and reduce the time of contact between the neonate and maternal blood
  - (b) Scalp electrodes should be used in order to detect foetal distress as early as possible
  - (c) Prolonged rupture of membranes should be avoided
  - (d) Vaginal delivery should not happen as all HIV infected mothers should deliver by Cesarean section
  - (e) All of the above are true

8. A 33 year old pregnant lady presents to the hospital in labour. She arrived in Hong Kong two weeks ago. Although she has not undergone antenatal care in Hong Kong, she claims that she has had full workup in her home country, all with normal results. Your preliminary assessment is that the baby is full term; you ask the nurse to prepare a rapid test for HIV and explain to the mother why this is necessary.
- (a) The rapid test result is positive; you explain to the woman that you will need to expedite delivery with forceps or vacuum extraction.
  - (b) The rapid test result is positive; you order an IV bolus of zidovudine stat
  - (c) The rapid test result is positive; you immediately order a conventional serum HIV antibody test and reassure the mother that antiretroviral will be started for her and her baby once the result is confirmed
  - (d) The rapid test result is positive; you proceed to emergency cesarean section because this will reduce the risk of MTCT
  - (e) The woman refuses the rapid test; you ask the nurse to perform the rapid test using blood already drawn for her complete blood picture as it is important to ascertain her HIV status as soon as possible
9. You have been called to see an 18 year old woman who just delivered at her home 24 hours ago. You are unable to retrieve any electronic medical record on her. She admits to having received no antenatal care in Hong Kong and she is not sure about the medical history of the father of her baby. You perform a rapid HIV test for the mother. It is positive.
- (a) You order a two drug regimen for the newborn with oral zidovudine and nevirapine to be started stat
  - (b) You order a three drug regimen for the newborn with oral zidovudine, lamivudine and nevirapine to be started stat
  - (c) You alert the mother to NOT breastfeed even after her own HIV disease is brought under control
  - (d) You explain to the mother she herself will also need to be put on antiretroviral therapy as soon as assessment is done
  - (e) All of the above are appropriate
10. Recent evidence or expert consensus is that
- (a) Extra intrapartum zidovudine is not necessary for an HIV infected mother who achieves undetectable viral load at delivery
  - (b) For an untreated HIV infected mother who presents already in labour, a three-drug daily regimen for empiric therapy (zidovudine, lamivudine, and nevirapine) is now the only option for the neonate
  - (c) To rapidly lower viral load when an HIV infected mother is diagnosed late in the antenatal period, cobicistat-boosted elvitegravir, an integrase inhibitor, may be considered
  - (d) There is no longer justification that neonatal zidovudine should be given for more than 4 weeks
  - (e) All of the above