In order to identify HIV-infected women and offer antiretroviral (ARV) prophylaxis, the South African National Prevention of Mother-To-Child Transmission (PMTCT) of HIV programme recommends 2 HIV tests during pregnancy: at the first antenatal visit and at 32 weeks of gestation. We present two cases that suggest that additional HIV testing strategies are needed to help eliminate the mother-to-child transmission of HIV.

In a longitudinal study on HIV-exposed infants, we recruited infants whose mothers were known to be HIV-infected post partum along with a control group of infants born to HIV-negative women. All women delivering at the Kraaifontein Midwife Obstetric Unit were eligible for enrolment. HIV-exposed infants were matched with HIV-unexposed controls within one month of birth. Mother-infant pairs were recruited within three days of delivery and a CD4 T-cell count was performed on all women regardless of HIV status. In accordance with the study protocol, the infants were reviewed at 2 weeks of age and regularly thereafter. At the 2-week visit, the HIV status of the uninfected mothers was confirmed with an HIV rapid assay using finger-prick blood (Alere Determine HIV 1/2).

Recently, HIV infection was identified on the rapid tests at the 2-week visit in 2 women (Table 1). According to antenatal clinic documentation, both tested negative during pregnancy: at booking (at 21 weeks and 28 weeks of gestation, respectively) and at 32 weeks of gestation, as recommended in the national guideline. Neither infant was born before 38 weeks of gestation. The HIV rapid assay in use in the antenatal clinic at the time was the First Response HIV1-2-0 Card Test (Premier Medical Corporation Ltd, India). According to policy, only a single test is required to screen for HIV. Positive screening tests are confirmed with a second rapid assay (ABON HIV 1/2/0 Tri-Line HIV Rapid Test Device).

Both women elected to breastfeed, although one mother switched to infant formula after one week owing to poor feeding. Her CD4 T-cell count at delivery was 680 x 10^6 cells/l. Her infant was symptomatic at age 2 weeks and was immediately hospitalised, requiring transfer to the intensive care unit. An HIV DNA polymerase chain reaction (PCR) test (AmpliCor HIV-1 DNA prototype assay 1.5) at 2 weeks was positive.

The CD4 count of the second woman was 157 x 10^6 cells/l at delivery. Her baby was well and the HIV DNA PCR at 2 weeks was negative. Daily nevirapine (NVP) for the infant was initiated and the mother was referred for combination antiretroviral therapy (cART) which was commenced within 2 weeks.

Discussion

These two cases raise concerns about antenatal HIV screening and the implications for vertical transmission. As expected, neither woman received any ARV prophylaxis.

A recent Medical Research Council (MRC) report on the effectiveness of the national PMTCT programme in South Africa demonstrated that, among mothers who reported being HIV-negative, 4.1% had infants who were HIV-exposed at 4 - 8 weeks (measured by the presence of HIV antibodies in the infants' blood). A 2007 surveillance study in KwaZulu-Natal (KZN) found that 6.9% of infants whose mothers reported a negative HIV status had similar evidence of exposure (i.e. the
The most likely explanation for our findings is that there is a low incidence of HIV during pregnancy and breastfeeding. Pregnancy poses an increased risk for HIV acquisition by women, even after adjustment for behavioural and other factors; it is also possible that the hormonal and other biological changes associated with pregnancy have a role.\[4,5\] High viral loads during primary HIV infection increase the risk of vertical transmission in utero, peripartum and postpartum,\[6,9\] especially in the absence of ARV prophylaxis. In studies in Botswana and SA, new mothers with negative HIV test results or of unknown HIV status were tested immediately post partum or at infant immunisation visits. The results demonstrated a seroconversion rate of 2.4 - 7.9% during pregnancy and postpartum.\[5,9,12\] These women are at high risk of vertical transmission.\[5,9\] In addition, they are more likely to use mixed feeding practices, placing their infants at greater risk for HIV infection.\[13-15\] In addition, increased incidence of mixed feeding observed in these women is presumably because, having tested HIV-negative, they perceive no risk.

Repeat HIV testing of mothers during late pregnancy, at delivery or at the clinic immunisation visits, would identify women who acquire HIV during pregnancy and in the early post-partum period. The HIV diagnosis of infants whose mothers tested negative during pregnancy is often delayed,\[16,17\] with significant implications for morbidity and mortality.\[18\] Most SA women deliver at a healthcare facility and 99% attend the 6-week vaccination visit.\[19\] Moreover, testing at these time-points shows high uptake,\[18,19,20\] while offering HIV tests to both partners may identify discordant couples and allow counselling on HIV prevention.\[20\] A proviso to this is increasing evidence that, even within discordant partnerships, a significant number of new HIV infections arise from extra-couple transmission.\[20\]

### Conclusion

While the elimination of mother-to-child transmission of HIV is feasible, it will require a modification of current protocols/guidelines to include repeat HIV testing of women at delivery and/or post partum, a quality-control strategy for laboratory testing of a small percentage of negative rapid tests, involvement of male partners in testing and counselling, and an emphasis on exclusive feeding practices, regardless of HIV status.

### Ethics approval

The Mother Infant Health Study (MIHS) is approved by the Ethics Committees of Stellenbosch University and the University of British Columbia.

### Conflict of interest

None.

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### References

5. World Health Organization Department of Essential Health Technologies. HIV Assays: Operational

### Table 1. Patient characteristics

<table>
<thead>
<tr>
<th>Patient</th>
<th>Maternal age (years)</th>
<th>Gestational age, first ANC (weeks)</th>
<th>Gestational age, first HIV test (weeks)</th>
<th>Gestational age, second HIV test (weeks)</th>
<th>Infant date of birth</th>
<th>Maternal CD4+ count at birth (x10^6 cells/l)</th>
<th>Feeding choice</th>
<th>Infant PCR test at 2 weeks</th>
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<td>1</td>
<td>29</td>
<td>21</td>
<td>21</td>
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<tr>
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<td>28</td>
<td>28</td>
<td>32</td>
<td>05/11/2012</td>
<td>157</td>
<td>Breast</td>
<td>Negative</td>
</tr>
</tbody>
</table>

ANC = antenatal clinic visit; PCR = polymerase chain reaction.