The XV International AIDS Conference was held in Bangkok from 11 to 16 July 2004. The theme of the conference was ‘Access for all’. It was an enormous gathering; 10 000 abstracts were accepted for presentation, of which approximately 400 were oral. There were 19 500 attendees from all over the globe with a high representation from Asian countries. South Africa was well represented by a large contingent including politicians, researchers, activists and government officials. The abstracts and presentations which may have an impact on policy and research directions have been reviewed and are summarised.

New World Health Organisation guidelines for the prevention of mother-to-child transmission (PMTCT) of HIV1 were presented at an evening satellite session. The guidelines, available at [http://www.who.int/reproductive-health/rtis/MTCT/](http://www.who.int/reproductive-health/rtis/MTCT/), were compiled by a WHO-convened Technical Consultation on Antiretroviral Drugs and the Prevention of Mother-to-child Transmission of HIV Infection in Resource-limited Settings in Geneva, Switzerland in February 2004. The participants considered the available scientific evidence and the programmatic experience and recommended specific antiretroviral (ARV) regimens according to different clinical situations. The guidelines differ from the recommendations issued by WHO in 2000, which focused mainly on the PMTCT of HIV, by acknowledging the greater access to ARV treatment for women and the desirability of providing ARV treatment for women who need it. They complement other guidelines on treatment issued by the WHO and the 3 by 5 Initiative.

Women may receive ARV drugs during pregnancy as part of combination regimens used to treat their HIV infection or to prevent HIV infection in infants. All efforts should be made to ensure that access to ARV treatment for women is based on their need and eligibility for such treatment. However, ARV regimens for women of childbearing age should be selected considering the possibility of a planned or unintended pregnancy and that ARV drugs may be taken in the first trimester of pregnancy, before a pregnancy is recognised. While triple therapy is widely used in developed countries to prevent HIV transmission in pregnancy, there are concerns about its use for this indication in women where clinical and laboratory monitoring is not readily available.

The key recommendations from the new guidelines are:

1. Women who need ARV treatment for their own health should receive it in accordance with WHO guidelines on ARV treatment. The use of ARV treatment, when indicated, during pregnancy substantially benefits the health of the woman and decreases the risk of HIV transmission to the infant.

2. HIV-infected pregnant women who do not have indications for ARV treatment or do not have access to treatment should be offered ARV prophylaxis to prevent MTCT using one of several ARV regimens known to be safe and effective:

   - Zidovudine (AZT) from 28 weeks of pregnancy plus single-dose nevirapine (NVP) during labour and single-dose NVP and 1-week AZT for the infant. This regimen is highly efficacious, as is initiating AZT later in pregnancy.

   - Alternative regimens based on AZT alone, short-course AZT + lamivudine (3TC) or single-dose NVP (sdNVP) alone are also recommended.
Non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance was a focus of this conference. Specifically the resistance induced by sdNVP to both pregnant mother and the newborn infant attracted much attention. The predominant research method of assessing resistance is to analyse for the presence of viral DNA mutations that are known to confer resistance to specific ARV drugs. The presence of detectable genotypic resistance was reported in three cohorts of women and children. A study of mother-infant pairs recruited from the PMTCT programme in Soweto and Durban who were exposed to single-dose NVP in 2002–2003 was presented. Previous data from this study showed that 40% of women and 45% of children were found to have genotypic resistance to NNRTIs at 7 weeks after delivery. The paper presented at Bangkok reported the fading of genotypic NNRTI resistance to 6 months after the dose of NVP in both mothers and children, and reported the pattern of resistant mutations found. Figs 1 and 2 below show levels of detectable resistance found prior to the NVP dose in pregnant mothers, at 7 weeks after delivery and at 6 months after delivery, respectively. Ninety-eight per cent of the women were infected with clade C HIV.

This study confirmed previous work showing that not only do detectable resistant mutations fade but also the diversity of the mutations diminishes.

A similar study of NVP-induced genotypic resistance in Thailand assessed the pattern of NNRTI-resistant mutations in a population where the predominant HIV subtype is CRF01_AE. Three hundred and ten women with advanced disease who received sdNVP had genotypic resistance assays performed 10 days and 6 weeks after delivery. Overall, the data reported were similar to the work done in South Africa on clade C viruses. NNRTI mutations were found in 38% of the women exposed to sdNVP. Seventy-three per cent of the women with resistance had single-mutation resistance and 27% had at least two mutations. The most common mutation in this study, as in the South African work reported previously, was K103N (65%). However, the second most frequent maternal resistance mutation was G109A (30%), an infrequent mutation in the South African series.

A potential strategy to reduce maternal NNRTI resistance is to not expose the mother to NVP at all. A randomised open label clinical trial was presented that tested two

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**Fig. 1. Graphs of resistance in mothers and infants following single-dose NVP.**

**Resistance among mothers**

- **Baseline (N = 232):** 2.2%
- **7 weeks (N = 458):** 38%
- **6 months (N = 157):** 14%

**Resistance among infants**

- **7 weeks (N = 58):** 42%
- **6 months (N = 21):** 26%

**Fig. 2. Pattern of NNRTI mutations detected in mothers and infants with resistance.**

**Mutations in mothers**

- **K103N**
- **V106A**
- **V106M**
- **Y181C**
- **Y188C**
- **G190A**

**Mutations in infants**

- **K103N**
- **V106A**
- **V106M**
- **Y181C**
- **Y188C**
- **G190A**
interventions to prevent transmission of HIV in infants whose HIV-infected mothers were not able to access antenatal ARVs in PMTCT programmes. This trial, which recruited 1051 infants, was undertaken at the Perinatal HIV Research Unit at Chris Hani Baragwanath Hospital. It compared HIV transmission rates in infants whose mothers did not receive ARVs to prevent MTCT for a variety of reasons. Infants were randomised to receive either:

1. A single dose of NVP (2 mg/kg within 72 hours of delivery) or
2. A 6-week course of twice daily AZT commenced within 24 hours of delivery.

Transmission for the entire group at 12 weeks was 16.3% and transmission in the intention-to-treat analysis is shown in Table I.

Overall, sdNVP was better at reducing transmission than 6 weeks of AZT in this group of infants of mothers who had not accessed an antenatal PMTCT programme. Furthermore, the burden on the health service is markedly reduced by giving a stat post-partum dose compared with ensuring that 6 weeks of AZT are provided and ingested by a newborn. An oral paper reported the genotypic resistance induced by the sdNVP arm in this study. Only 3 of 23 HIV-infected infants whose mothers did not receive NVP and who were randomised to the sdNVP arm were found to have genotypic resistance compared with approximately 45% of infants exposed to maternal NVP in utero and then themselves receiving sdNVP after delivery. The patterns of resistance also differed, with those exposed to only their own sdNVP dose having fewer mutations than those exposed to additional maternal sdNVP as part of HIVNET 012 regimen.

The resistance generated by sdNVP may in part be due to its long half-life. A paper presented by a combined Thai/US group showed NVP plasma levels in 61 women who had recently taken sdNVP to prevent MTCT. Although plasma exposure and $C_{\text{max}}$, were found to be significantly less in pregnant women than in non-pregnant women and men, NVP was detected in women who had delivered up to 21 days post partum, albeit at low concentrations. The median half-life of NVP was 58.3 hours in this study.

The implications of detection of genotypic resistance are uncertain. However, there is recently published evidence that genotypic resistance induced by sdNVP and exposure to sdNVP without the presence of detectable resistance compromises viral response to triple therapy. It is generally agreed that where possible resistance should be minimised. One way of doing this is to avoid NVP altogether. An alternative approach presented at the conference is to provide a short course of Combivir, started simultaneously with maternal sdNVP to cover the ‘tail’ of the prolonged NVP plasma half-life. A study sponsored by Boehringer-Ingelheim, the manufacturers of NVP, and undertaken in South African hospital settings tested the hypothesis that the addition of intrapartum and postpartum Combivir (a fixed dose combination of AZT and 3TC) would reduce maternal NNRTI resistance. Preliminary results of this randomised open-label trial (Table II) providing Combivir post sdNVP to reduce resistance suggest that it is effective in reducing maternal genotypic resistance when compared to sdNVP alone.

**Prevention of Resistance**

**Table I. Transmission Rates by Arm and Timing of Infant HIV PCR Test**

<table>
<thead>
<tr>
<th>Arm</th>
<th>Birth</th>
<th>6 weeks</th>
<th>12 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>sdNVP</td>
<td>7</td>
<td>11.9</td>
<td>14.3</td>
</tr>
<tr>
<td>6 weeks AZT</td>
<td>5.8</td>
<td>13.5</td>
<td>18.1</td>
</tr>
<tr>
<td>p</td>
<td>0.5</td>
<td>0.6</td>
<td>0.4</td>
</tr>
</tbody>
</table>

**Table II. Maternal Resistance by Treatment Arm**

<table>
<thead>
<tr>
<th>Arm</th>
<th>Presence of resistance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2 weeks</td>
</tr>
<tr>
<td>sdNVP</td>
<td>9/18 (50)</td>
</tr>
<tr>
<td>sdNVP, 4 days</td>
<td>120 (5)</td>
</tr>
<tr>
<td>Combivir 4 days</td>
<td>4/43 (10)</td>
</tr>
<tr>
<td>sdNVP, 7 days</td>
<td>3/23 (13)</td>
</tr>
<tr>
<td>Combivir 7 days</td>
<td></td>
</tr>
</tbody>
</table>

Owing to the marked reduction of genotypic resistance in the two Combivir-containing arms, the trial was amended and randomisation to the sdNVP-only arm was stopped. The trial will continue to enrol pregnant women into the two Combivir-containing arms in an attempt to determine the better duration of Combivir cover.

NVP, resistance induced by sdNVP and the ongoing interactions between activists, the South African Medicines Control Council and researchers dominated the news reporting of this conference both in South Africa and internationally. The precipitant for this was a media release emanating from the MCC headlined ‘MCC no longer recommends the use of monotherapy in preventing mother to child transmission’. This was interpreted as a signal of the imminent deregistration of NVP as monotherapy in South Africa for MTCT, and created concern that the PMTCT programme in South Africa was in jeopardy. The Treatment Action Campaign (TAC) then convened a meeting where a
Joint press statement from UNAIDS, UNICEF and the Elizabeth Glazer Paediatric AIDS Foundation was read.12 This meeting was also addressed by representatives of TAC, Médecins Sans Frontières and the UN Secretary General’s special envoy for HIV/AIDS in Africa, Stephen Lewis, who expressed concern that yet another South African NVP spat was diverting attention away from more serious issues of the HIV epidemic. A day later, when the registrar of the MCC clarified the MCC position it became clear that deregistration of NVP was not imminent. Whether this was despite or as a result of the TAC, UN and EGPAF action was unclear.

The impact of maternal AZT on fetal and infant growth in 1,265 infants was assessed in Thailand.13 After adjusting for a variety of potential confounders, the researchers reported that the duration of maternal AZT was statistically significantly associated with increased weight and height at birth. This association persisted for up to 18 months of age, independent of gestational age at birth. Maternal AZT was started at 28 or 35 weeks’ gestation and babies received either 3 days or 6 weeks of AZT after delivery. However, the use of ARVs is not without risk. A single case report14 from the US of an HIV-uninfected baby with extreme hypotonia whose mother was treated with AZT-containing HAART and who was given 6 weeks of AZT after delivery provides isolated evidence of potential toxicity of ARVs. Muscle biopsy showed mitochondrial abnormalities that were attributed to NRTIs.

Rapid testing is gaining acceptability and is of great value in the antenatal clinic where one visit may be the only contact a pregnant woman has with the health service before delivery. A report from Lilongwe15 confirmed the powerful effect of an immediate HIV result on uptake of VCT. This group compared the acceptance of HIV testing and the rate of attendance at post-test counselling in two groups:

1. Pregnant women who were HIV tested using an HIV-ELISA with results obtainable some days later.
2. Women who were able to access a rapid testing algorithm with same-day results.

They used the periods before and after the introduction of rapid testing as comparison periods. The results are summarised in Table III.

In another report from Kigali, Rwanda,16 where rapid tests, infant formula and NVP have been made available in the PMTCT programme, 98% of pregnant women accepted a rapid HIV test of whom 79% attended a post-test counselling session. Of the 21% found to be HIV-infected, 91% took NVP. Notwithstanding the simplicity of the NVP-based PMTCT regimen, an abstract from Malawi17 showed that despite high uptake of VCT less than half the HIV-infected women in their programme were handed a tablet of NVP by 36 weeks of gestation and only 34% of the newborns of HIV-infected mothers received a dose of NVP.

In keeping with the theme of ‘Access for all’, it was gratifying to note the large number of abstracts that summarised the experiences of numerous PMTCT programmes documenting the cascade. Several abstracts from throughout Africa reported on the drop-off in the PMTCT cascade from acceptance of counselling to maternal receipt of NVP. All of them reported rates of maternal HIV-infection of greater than 15%.

Few data were presented on the effectiveness of PMTCT programmes in preventing HIV transmission when implemented on a large scale. A multi-centre collaborative study from Brazil,18 where ARVs are provided free of charge to HIV-infected people, reports data from 63 sites in Brazil for the years 2000 - 2002. The overall MTCT rate of HIV was 6.8%. Ninety-two per cent of the infants received AZT. Higher rates of transmission were reported in women who breast-fed, had a vaginal delivery, and took ARVs incorrectly.

These summarised abstracts represent the papers on MTCT which we believe had the most impact at the conference. Further work on infant feeding and programmatic experiences added to the knowledge base. A searchable archive of all abstracts presented at the Conference (eJIAS abstract finder) is available at [http://www.aids2004.org/](http://www.aids2004.org/).

**REFERENCES**


