INCREASING THE SCOPE AND INTENSITY OF INTERVENTIONS TO PREVENT HIV INFECTION IN INFANTS: BEST INTERESTS OF WOMEN AND CHILDREN

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Key messages:

- There is a mismatch between the HIV prevention needs of children and the quality and scope of prevention of mother-to-child transmission (PMTCT) services.
- Although near-elimination of paediatric HIV has taken place in many settings, PMTCT programmes in Africa have little impact so far.
- Given that it is in the child's best interests to detect exposure to HIV shortly after birth and to institute preventive interventions, routine HIV testing may be justified for all infants born to women of unknown HIV status.
- HIV testing for women at child health and immunisation clinics would enable more women to benefit from knowing their status and to receive infant feeding counselling and support.

This year another 460 000 children were infected with HIV in sub-Saharan Africa,[1] signalling an ongoing failure of programmes for PMTCT of HIV and the need to revise existing strategies. Despite initial energetic promotion, in recent years PMTCT has slipped down the policy agenda and coverage of these services remains below 10% in most African countries.[2] Overall impact of current PMTCT programmes on HIV-free survival among infants at a population level is unknown but likely to be low.[3,4] In contrast, in many other settings the risk of transmission is reduced to below 2%, with near-elimination of paediatric HIV.[5-7] In this paper we critique PMTCT strategies used in Africa and argue they require urgent revision. Under-utilised opportunities to prevent HIV infection in infants around childbirth and during breastfeeding are also highlighted. Interventions during chidbirth and postpartum would broaden the present antenatal focus of PMTCT programmes.

BENEFITS OF EARLY KNOWLEDGE OF HIV STATUS

HIV infection will declare itself, commonly with a severe illness that has substantial morbidity and mortality. The earlier in HIV disease that people become aware they are infected, the greater the benefit of care and treatment interventions. Further, to prevent transmission of a communicable disease, infected individuals should be identified as soon as possible after acquisition. Timely diagnosis of HIV confers considerable benefits to the individual and the wider community by facilitating access to care and prevention interventions, and changes in behaviour that accompany knowledge of status.[8,9] Within an enabling policy environment, the role of health workers is to identify early HIV disease and to maximise the benefits of knowing one's status for the infected individual and their susceptible sexual partners and children. Nowhere is this more clearly illustrated than in PMTCT programmes.

Each encounter with a woman in maternal and child health services is an opportunity for the woman to benefit from knowing her HIV status and to prevent further transmission. While the advantages for infants in being HIV-free are implicit, the benefits for women of having an uninfected child need to be highlighted. When giving pre-test information, health care workers should ensure that women are adequately informed of the benefits of PMTCT interventions, and of the emotional and financial consequences of having an HIV-infected child. However, many opportunities to benefit from knowing HIV status are missed with the current emphasis on the individual's right to decline testing and the potential harms associated with testing. The epidemic-long adoption of this approach has, paradoxically, undermined the individual's access to interventions to secure their right to health and that of their sexual partners and children. After decades of over-mystifying HIV testing, the pendulum has slowly swung to principles of public health accompanied by attempts to simplify testing and counselling procedures.[10,11]

Additional efforts to ensure that women directly benefit from PMTCT programmes may increase their acceptability and uptake. Renaming and remarketing of these programmes may be necessary. The name PMTCT ignores men's role in paediatric HIV infection, and fails to acknowledge that women are more than just mothers, and require maximum benefits from an HIV diagnosis, preferably made early in their HIV disease.

DUAL STANDARDS OF CARE: THE OUTCOME GAP

Initiating antiretroviral therapy (ART) for pregnant women helps ensure that benefits of PMTCT programmes accrue to both women and infants. Though given high priority by PMTCT guidelines,[12] ART for pregnant women with indications for treatment has been inadequately operationalised. Guidance is needed on practical aspects of developing well-functioning linkages between antenatal and ART services. For pregnant women, accelerating initiation of ART is often necessary to decrease MTCT risk. Difficulties with timely initiation of ART during pregnancy are compounded by health-seeking patterns, with women often first attending antenatal care late in pregnancy. Measuring CD4 cell counts at the first antenatal visit appears particularly important in reducing delays.[13]

So far, efforts to prevent HIV infection in children have focused on providing short-course ARV regimens for MTCT prophylaxis, most commonly single-dose NVP (sd-NVP). In several African countries, studies have recently investigated the role of triple-ARV regimens used solely for MTCT prophylaxis.[14-17] These regimens are given to women without indications for ART, and are stopped after childbirth (or after weaning). Such interventions bridge the gap in outcomes between infants born to women in Africa (including the South African private sector[18]) and those in the USA, Europe, Brazil and other settings. Long-course triple ARV prophylaxis is the standard of care in high-income countries (since 1998 in the US[19]) as well as in middle-income countries of South America, where more than 90% of HIV-infected women receive triple-ARV prophylaxis.[5,20] Disparities between infant outcomes illustrate stark global inequities: in Africa use of sd-NVP entails a risk of MTCT of about 12%, while elsewhere triple-ARV regimens reduce transmission to below 2%, with little viral resistance. Even in the South African private sector, women receive a standard of care below that provided in the public sector in countries like Brazil.[18]

A recent study in Johannesburg showed that risk for MTCT in women who initiate ART during pregnancy for their own health is lower than in women who do not have indications for ART and receive sd-NVP.[13] This demonstrates the limitations of sd-NVP – infants born to women with high CD4 cell counts had almost a threefold higher risk of HIV infection than infants born to women with advanced HIV disease (at substantially higher baseline risk of MTCT).

Several studies are investigating whether ARV drugs, given either to breastfeeding women or infants, reduce MTCT during breastfeeding.[21] This offers a promising alternative for a problem that causes tremendous difficulties wherever replacement feeding is not feasible. ARV drugs have been shown to reduce MTCT during pregnancy and childbirth in randomised trials, and in observational studies to reduce HIV acquisition after sexual or occupational exposure. Evidence from randomised trials that ARV drugs reduce postpartum transmission is expected in the next years – about 14 years after demonstration that ARV drugs reduce antenatal and intrapartum transmission.

PMTCT ENTRY: THE CHILD'S BEST INTERESTS

In addition to using more effective ARV prophylaxis, to improve impact of PMTCT programmes, several interventions around childbirth and during breastfeeding warrant consideration. These interventions aim to complement and broaden the current antenatal focus of PMTCT programmes. Shortly after childbirth, identifying HIV-exposed infants born to women who have not accessed PMTCT services (either because these services are unavailable or because they declined the offer of HIV testing) would enable HIV-exposed infants to benefit from interventions to reduce their risk of acquiring HIV. Rapid HIV tests, using whole-blood specimens from heel sticks, are especially suited to testing newborns for HIV exposure. Giving ARV post-exposure prophylaxis to infants born to women who did not receive ARV drugs during pregnancy or labour has been shown to reduce MTCT in a randomised trial in Malawi[22] and in South Africa.[23] If ARV prophylaxis is delayed more than 2 days, it is unlikely to have any benefit.[24]

HIV testing is considered part of essential care around childbirth for women of unknown HIV status.[12] In women who decline HIV testing, safeguarding the wellbeing of the child needs to be balanced with protecting the woman's right to privacy. The UN Convention on Rights of the Child (CRC) provides guidance on achieving this balance, stating: 'In all actions concerning children, whether undertaken by public or private social welfare institutions, courts of law administrative authorities or legislative bodies, the best interests of the child shall be a primary consideration.'[25]

South Africa is a signatory of the Convention and in 1995 ratified it, making it legally binding.[26] With evidence that post-exposure prophylaxis for infants is effective, and the high mortality associated with childhood HIV infection, we argue that in the best interests of the child, HIV exposure should be detected, irrespective of the mother's wishes. Using these arguments, consistent with the CRC, the overarching priority is to identify infants exposed to HIV and to deliver interventions to reduce risk of HIV acquisition. With adoption of this policy, all infants born to women of unknown HIV status would be routinely tested for HIV shortly after childbirth.

Disadvantages of routinely testing all newborn infants may include: infringing a woman's right to privacy and deterring women from accessing labour and delivery services. Counselling women in these circumstances would be

challenging, though essential to enable the mother-infant pair to benefit from safer infant feeding. Concerns about deterring attendance at health facilities need to be addressed. So far, inclusion of opt-out HIV testing for adults has not decreased numbers of people attending services and acceptability of such testing has been shown to be high in several reports.[27-31] While these findings are reassuring, they may not reflect outcomes of routine testing of newborns. Routine testing of newborns has occurred in several states in the USA since 1999. With this policy and opt-out testing for pregnant women, HIV testing coverage is near universal.[32] To our knowledge, no reports of decreased attendance at health facilities have been published.[33]

Essentially, a case could be made that the best interests of the infant and the infant's right to preventive health care (article 24 of CRC)[25] supersede the woman's need for autonomy. Further ethical and legal consideration of this scenario is necessary. It is surprising that paediatricians have not been more vociferous advocates for routine testing of newborns, well within the best interests of those they serve. Similarly, children with AIDS could argue that by failing to test them for HIV exposure, the health providers who cared for them around childbirth neglected to protect them from HIV infection and did not act in their best interests, as legally obliged. That would make a fascinating, perhaps winnable, legal test. Schuklenk and Kleinshmidt go further, arguing for mandatory HIV testing for women who decide to carry the fetus to term.[34] They contend that women who choose to carry a fetus to term and choose not to reduce its chances of contracting HIV constitute harm to others. The authors write: 'choosing deliberately not to act to prevent harm when one could have acted without unreasonably high costs to oneself is comparable to similarly deliberate actions that actively produce the same amount of harm'.

POSTPARTUM PMTCT SERVICES

Patient-provider encounters in child health and immunisation clinics could be used to reduce MTCT. For women who have not accessed HIV testing during pregnancy or around childbirth, identifying HIV infection and supporting safer infant feeding could reduce transmission through breastfeeding, which accounts for a third to half of HIV infections in infants. Postpartum testing may be an important measure while coverage of HIV testing in antenatal clinics is being improved. Also, women who previously declined testing may reconsider their decision or form better rapport with the health worker who offers testing. Women are particularly vulnerable to HIV acquisition during pregnancy and postpartum (for reasons of biology and behaviour, such as lower condom use) and retesting of women who tested negative during pregnancy may identify recent infection. During acute HIV infection, risk of transmission to breastfeeding children[35] and sexual partners is high.

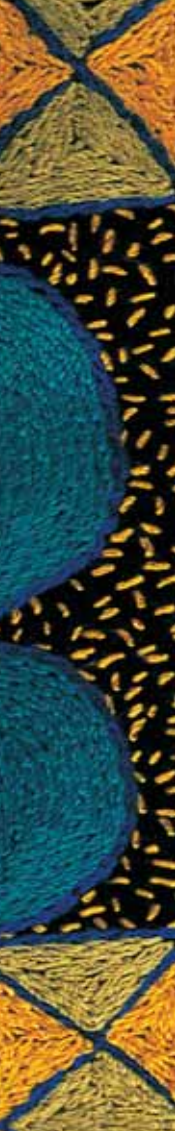
Within child health clinics, postpartum PMTCT services could be built around HIV testing and counselling; infant feeding counselling and support; entry to HIV prevention, care and treatment services; as well as provision of family planning counselling and contraception. Reducing unintended pregnancies among HIV-infected women has been promoted as a key component of PMTCT strategies. Many HIV-infected women have an unmet need for family planning services, especially with shortened lactational amenorrhoea due to replacement feeding or early cessation of breastfeeding. At any time during the breastfeeding period, identifying HIV infection in women or HIV exposure in infants enables them to benefit from infant feeding counselling and support for safer feeding options.

CONCLUSION

In sum, while HIV infection in infants has effectively been eliminated in many settings, in Africa the potential for intervention at each service delivery-point is, so far, underutilised and of low quality. There is an inequitable mismatch between the HIV prevention needs of children and the services provided, necessitating a critical review of prevailing strategies. Despite the level of funding and attention available for HIV interventions, by measures such as coverage, outcomes and equity, PMTCT programmes have performed worse than syphilis control or ART programmes. PMTCT has fallen off the HIV bandwagon and needs to climb back on. For that to occur, stronger bolder national and international leadership is needed, reenergising the current approach with innovative strategies based firmly on public-health principles.

REFERENCES

1. UNAIDS, WHO. *AIDS Epidemic Update: December 2006.* http://www.unaids.org/en/HIV%5Fdata/epi2006/:
2. United Nations General Assembly. Declaration of Commitment on HIV/AIDS: five years later. Follow-up to the outcome of the twenty-sixth special session: implementation of the Declaration of Commitment on HIV/AIDS. Report of the Secretary-General. Sixtieth session, Agenda item 45, 2006.
3. Quaghebeur A, Mutunga L, Mwanyumba F, Mandaliya K, Verhofstede C, Temmerman M. Low efficacy of nevirapine (HIVNET012) in preventing perinatal HIV-1 transmission in a real-life situation. *AIDS* 2004; 18: 1854-1856.
4. Rollins N, Mzolo S, Little K, Horwood C, Newell M-L. HIV prevalence rates amongst 6 week old infants in South Africa: the case for universal screening at immunization clinics. XVI International AIDS Conference, Toronto, Canada, 2006.
5. Mother-to-child transmission of HIV infection in the era of highly active antiretroviral therapy. *Clin Infect Dis* 2005; 40: 458-465.
6. Read J, Cahn P, Losso M, *et al.* A prospective cohort study of HIV-1-infected pregnant women and their infants in Latin America and the Caribbean: the NICHD International Site Development Initiative Perinatal Study. 12th Conference on Retroviruses and Opportunistic Infections, Boston, USA, 22-25 February 2005.
7. United States Public Health Service Task Force. *Public Health Service Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States - October 12, 2006.* http://aidsinfo.nih.gov/ContentFiles/PerinatalGL.pdf:
8. Efficacy of voluntary HIV-1 counselling and testing in individuals and couples in Kenya, Tanzania, and Trinidad: a randomised trial. The Voluntary HIV-1 Counseling and Testing Efficacy Study Group. *Lancet* 2000; 356: 103-112.
9. Marks G, Crepaz N, Senterfitt JW, Janssen RS. Meta-analysis of high-risk sexual behavior in persons aware and unaware they are infected with HIV in the United States: implications for HIV prevention programs. *J Acquir Immune Defic Syndr* 2005; 39: 446-453.
10. World Health Organization, UNAIDS. *Draft WHO/UNAIDS Guidance on Provider-Initiated HIV Testing and Counselling.* 2006. http://www.who.int/hiv/topics/vct/publicreview/en/index.html:
11. Centers for Disease Control and Prevention. *Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings.* 2006. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm:



12. World Health Organization. *Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants in resource-limited settings: towards universal access.* 2006. http://www.who.int/hiv/pub/guidelines/pmtct/en/index.html:
13. Van der Merwe K, Chersich MF, Technau K, Umurungi Y, Conradie F, Coovadia A. Integration of antiretroviral treatment within antenatal care in Gauteng Province, South Africa. *J Acquir Immune Defic Syndr* 2006; 43(5): 577-581.
14. Marazzi M, Germano P, Liotta G, *et al.* Safety of nevirapine-containing antiretroviral triple therapy regimens to prevent vertical transmission in an African cohort of HIV-1-infected pregnant women. *HIV Medicine* 2006; 7: 338–344.
15. Silva A, Serrano D, Leite A, *et al.* Prevention of mother-to-child HIV transmission in Luanda, Angola-Africa. 3rd IAS Conference on HIV Pathogenesis and Treatment, Rio de Janiero, Brazil, 24-27 July 2005.
16. Thomas T, Amornkul P, Mwidau J, *et al.* Preliminary findings: incidence of serious adverse events attributed to nevirapine among women enrolled in an ongoing trial using HAART to prevent mother-to-child HIV transmission. *1*2th Conference on Retroviruses and Opportunistic Infections, Boston, USA, 22-25 February 2005.
17. Tonwe-Gold B, Ekouevi D, Rouet F, *et al.* Highly active antiretroviral therapy for the prevention of perinatal HIV transmission in Africa: mother-to-child HIV transmission plus, Abidjan, Côte d'Ivoire, 2003-2004. 12th Conference on Retroviruses and Opportunistic Infections, Boston, USA, 22-25 February 2005.
18. Hlatshwayo N, Hislop M, Cotton M, Maartens G, Regensberg L. Mother to child HIV transmission prevention (MTCTP) in a managed care setting in South Africa – no role for short-term antiretroviral therapy (ART)? XV International AIDS Conference, 2004.
19. United States Public Health Service Task Force. *Recommendations for use of Antiretroviral Drugs in Pregnant Women Infected with HIV-1 for Maternal Health and for Reducing Perinatal HIV-1 Transmission in the United States.* Rockville, MD: United States Department of Health and Human Services, 1998. http://aidsinfo.nih.gov/ContentFiles/PerinatalGL01301998041.pdf:
20. Shapiro D, Tuolala R, Pollack H, Burchett S. Mother-to-child HIV transmission risk according to antiretroviral therapy, mode of delivery, and viral load in 2895 U.S. women (PACTG 367). 11th Conference on Retroviruses and Opportunistic Infections, San Fransisco, USA, 8-11 February 2004.
21. Gaillard P, Fowler MG, Dabis F, *et al.* Use of antiretroviral drugs to prevent HIV-1 transmission through breast-feeding: from animal studies to randomized clinical trials. *J Acquir Immune Defic Syndr* 2004; 35: 178-187.
22. Taha TE, Kumwenda NI, Hoover DR, *et al.* Nevirapine and zidovudine at birth to reduce perinatal transmission of HIV in an African setting: a randomized controlled trial. *JAMA* 2004, 292: 202-209.
23. Gray GE, Urban M, Chersich MF, *et al.* A randomized trial of two postexposure prophylaxis regimens to reduce mother-to-child HIV-1 transmission in infants of untreated mothers. *AIDS* 2005; 19: 1289-1297.
24. Wade NA, Birkhead GS, Warren BL, *et al.* Abbreviated regimens of zidovudine prophylaxis and perinatal transmission of the human immunodeficiency virus. *N Engl J Med* 1998; 339: 1409-1414.
25. United Nations General Assembly. *Convention on the Rights of the Child.* 1989. http://www.un.org/documents/ga/res/44/a44r025.htm:
26. UNICEF. Convention on the Rights of the Child: signature, ratification and accession. http://www.ohchr.org/english/countries/ratification/11.htm:
27. Greenwald JL, Hall J, Skolnik PR. Approaching the CDC's guidelines on the HIV testing of inpatients: physician-referral versus nonreferral-based testing. *AIDS Patient Care STDs* 2006; 20: 311-317.
28. Jayaraman GC, Preiksaitis JK, Larke B. Mandatory reporting of HIV infection and opt-out prenatal screening for HIV infection: effect on testing rates. *CMAJ* 2003; 168: 679-682.
29. Introduction of routine HIV testing in prenatal care – Botswana, 2004. *MMWR Morb Mortal Wkly Rep* 2004; 53(46): 1083-1086. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5346a2.htm:
30. Perez F, Zvandaziva C, Engelsmann B, Dabis F. Acceptability of routine HIV testing ('opt-out') in antenatal services in two rural districts of Zimbabwe. *J Acquir Immune Defic Syndr* 2006; 41: 514-520.
31. Stanley B, Fraser J, Cox NH. Uptake of HIV screening in genitourinary medicine after change to 'opt-out' consent. *BMJ* 2003, 326: 1174.
32. HIV testing among pregnant women – United States and Canada, 1998-2001. *MMWR Morb Mortal Wkly Rep* 2002; 51(45): 1013-1016.
33. Susman E. Despite the controversy, HIV prenatal testing laws get the job done. *AIDS* 2001;15: N15-16.
34. Schuklenk U, Kleinsmidt A. *Am J Public Health* (in press).
35. Dunn DT, Newell ML, Ades AE, Peckham CS. Risk of human immunodeficiency virus type 1 transmission through breastfeeding. *Lancet* 1992; 340: 585-588.