Different interpretations have been provided by Perrella *et al.* [1] to explain the expansion of TCS-δ1+/A13+ cells in the peripheral blood, including selective stimulation of Vδ1 subset by *P. carinii* and/or involvement of this subset in early host defence against the opportunistic infection. The increase of the Vδ2+ cells observed in the lung, i.e., the microenvironment where the immune response against *P. carinii* takes place, strongly suggests the alternative hypothesis that target antigens (including *P. carinii* antigens) and/or environmental stimuli may favour the expansion of the circulating TCR γ/δ cell pool and the later selective migration of Vδ2+/BB3+ cells from the peripheral blood to the lung. In this scenario, the depletion of BB3+ cells in the peripheral blood (and the consequent increase in the relative percentage of A13+/Vδ1+ cells) is likely to represent an epiphenomenon, related to the redistribution of Vδ2+ cells to the sites of PCP-associated inflammation. Further studies are also needed to determine whether HIV infection of pulmonary cells (including alveolar macrophages, pulmonary lymphocytes and fibroblasts) [6] may represent an additional factor accounting for the selective local expansion of Vδ2+ cells.

Acknowledgement

We are grateful to Mr Martin Donach for his help in the preparation of the manuscript.

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Sponsorship: Supported by a grant from Ministero della Sanità, Istituto Superiore di Sanità (MS/ISS), progetto AIDS 1994 and 1995 (Rome, Italy).

Date of receipt: 10 October 1994; accepted 18 October 1994.

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Zidovudine to decrease mother-to-child transmission of HIV-1: is it good for developing countries?

The results of the intermediate analysis of the AIDS Clinical Trials Group (ACTG) 076/Agence Nationale de Recherches sur le SIDA (ANRS) 024 clinical trial conducted in the USA and France have demonstrated the efficacy of zidovudine (ZDV) in reducing the rate of mother-to-child transmission (MTCT) of HIV-1. These findings have already begun to transform clinical practice in industrialized countries, despite the lack of long-term safety data [1]. Africa has the highest incidence of perinatally acquired AIDS [2], but other areas of high incidence/prevalence already exist in developing countries such as Thailand. Decreasing MTCT of HIV-1 must be a public-health priority in this context.

If ZDV can be considered as the gold standard for reducing vertical transmission in the industrialized world, is it time to shift priorities throughout the world? In pursuing such a goal, it is necessary to face not only the critical problem of cost to individuals and health-care systems, but also the uncertainties about the applicability, tolerance, and even the efficacy of prescriptions derived from the ACTG 076 protocol [3].

The efficacy of ZDV has been demonstrated only under specific conditions: 100 mg oral doses five times daily beginning between 14 and 34 weeks of gestation, intravenous infusion during labour and delivery, and administration of ZDV syrup to the neonate four times daily beginning within 24 h of birth for 6 weeks. Leaving aside the cost, this protocol is clearly inapplicable in most developing countries. First, it requires that HIV testing, with pre- and post-test counselling, be performed early in pregnancy. Second, the acceptability of medications to be taken several times daily by mother and neonate may often be poor. Third, intravenous infusions during labour/delivery require admission early in labour and the management of intravenous lines may be ineffective, if not dangerous, in maternities lacking trained personnel and sterile conditions. Finally, whereas the ACTG 076 trial was conducted in a non-breastfeeding population, the relevance of these results may be quite different where infants are breastfed [4].

We therefore suggest that ZDV be introduced in developing countries to decrease MTCT of HIV-1 only if relatively widely applicable protocols are constructed, evaluated and proven to be effective. Among others, the following options may be proposed (Table 1), alone or in combination, considering that late *in utero* and intrapartum HIV transmissions are thought to be predominant in the timing of acquisition of the infection by the future child [5,6]: oral ZDV at the end of pregnancy, with a

simplified daily schedule; an oral loading dose during labour/delivery; syrup to the neonate; oral ZDV to the mother during some or all the breastfeeding period.

Attempts must be made to apply ZDV to reducing postnatal transmission in a context where breastfeeding will not usually be withheld. The proven benefits of breast milk on perinatal morbidity and mortality are widely thought to outweigh the potential risk of HIV transmission in developing countries, leading the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) to recommend breastfeeding regardless of the maternal HIV infection status [7]. If maternal ZDV therapy is to be given throughout the breastfeeding period, it should be prolonged at least 4–6 months, which is the period recommended by UNICEF for exclusive breastfeeding in its recent Baby-Friendly Initiative [8]. On the other hand, there is legitimate concern that postnatal transmission occurring despite maternal ZDV treatment and/or following the end of the therapy may cancel the benefit of decreasing *in utero* and/or intrapartum transmission. The ethical and practical aspects of the controversy over breastfeeding will be correctly addressed only when the actual contribution of breastfeeding to MTCT of HIV-1 is quantified.

Regardless of the protocol chosen, clinical trials must evaluate not only the efficacy but also the tolerance of ZDV in developing countries. Adverse effects may be different and more frequent than in France and the United States; for example, the prevalence of severe anaemia is high in African pregnant women [9]. Well-designed Phase II tolerance studies should therefore be a necessary step in evaluating ZDV in developing countries.

In designing clinical trials of ZDV in developing countries, one must answer several difficult ethical questions. The first is whether the drug can be available afterwards outside of a clinical trial setting [10]. The main obstacle is cost, which calls for effective negotiations between the public-health authorities of the concerned states, bilateral and international agencies such as WHO, and pharmaceutical companies. Another difficult ethical problem is whether to perform a placebo-controlled trial. Panels of experts convened by the ANRS in France and WHO in March and June 1994 stressed that placebo-controlled

Table 1. Comparative advantages and disadvantages of proposed regimens for zidovudine (ZDV) administration to reduce mother-to-child transmission of HIV-1 in developing countries.

	Advantages	Drawbacks
All regimens	Efficacy of ZDV suggested by ACTG 076 data	Long-term effects unknown Adverse effects in women and neonates (e.g., anaemia) unknown No data on women with $<200\times10^6$/l CD4 lymphocytes Effects on postnatal transmission unknown but potentially limited Cost
ACTG 076 protocol	Efficacy in USA–France	Requires trained personnel Compliance difficult Highest cost Requires second trimester HIV testing
Oral ZDV during late third trimester	Most easily acceptable Cost less than ACTG 076 Applicable when testing in third trimester	No impact on early *in utero* transmission Effect on intrapartum transmission unknown No expected effect on postnatal transmission
Intravenous infusion of ZDV in labour	Maximum concentration intrapartum Low cost	Inapplicable in most labour wards where admission occurs in advanced labour Requires sterile material and trained personnel
Oral ZDV booster in labour	Acceptable Low cost	Intrapartum plasma ZDV concentration possibly lower than with intravenous infusion
ZDV syrup to neonate	Possible effect on early postnatal transmission	Efficacy of post-exposure prophylaxis questionable No effect on late postnatal transmission Adverse effects unknown in children Confront with alternatives to breastfeeding
Oral ZDV to mother after delivery	Possible effect on postnatal transmission Adverse effects in neonate lesser than for syrup	Pharmacokinetics of ZDV excretion in colostrum/milk poorly studied Confront with alternatives to breastfeeding

ACTG, AIDS Clinical Trials Group.

trials offer the best option for a rapid and scientifically valid assessment of antiretroviral drug regimens to reduce MTCT of HIV.

ZDV may not be at present the ideal means to decrease MTCT of HIV-1 in developing countries. Non-nucleoside antiretroviral drugs such as nevirapine may also act by reducing the maternal viral load for a short period of time and active/passive immunizations are other potential approaches [11]. Less costly, more accessible alternatives should also be considered. Local disinfection during late pregnancy and labour may be of benefit to decrease HIV transmission by the ascending route and during delivery itself [12]. If such an intervention were to be effective and well tolerated, it could be widely applied even in settings where HIV testing is not available.

The results of the ACTG 076 trial must encourage researchers in developing countries to design and implement trials to determine the tolerance and efficacy of ZDV and other drug strategies that are likely to be widely applicable in the future. Prospects for an effective intervention should also incite public-health authorities to make prenatal HIV testing available. The international health community has a specific responsibility towards reducing the price of antiretrovirals or other interventions and making such measures available in developing countries if they are proven to be effective. Several trials may be necessary in order to evaluate measures that may apply differently in various parts of the world. The development of a common methodological approach is essential in such trials as it has been for observational studies estimating the rate of MTCT of HIV [13,14]. Once evaluated and proven to be efficacious, these measures may ultimately be associated in a comprehensive intervention to tackle the increasing problem of perinatally acquired HIV infection in Africa and other developing countries.

Acknowledgements

This manuscript was prepared in collaboration with the following: C. Badjo, R. Camara, M. Kibora, M. Timite and C. Welffens-Ekra (Abidjan, Côte d'Ivoire); M. Cartoux, F. Fumoux, N. Meda, B. Nacro and T.P. Sanou (Bobo Dioulasso, Burkina Faso); J-B. Hubert and R. Salamon (Bordeaux, France); J. Lange (Geneva, Switzerland); G. Kantarama, J. Ladner, V. Leroy and P. Ntawiniga (Kigali, Rwanda); S. Blanche, F. Brun-Vézinet, E. Chevallier, J-F. Delfraissy, J. Dormont and J-P. Levy (Paris, France).

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Date of receipt: 4 July 1994; revised: 10 October 1994; accepted: 18 October 1994.

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Kaposi's sarcoma involving bone in a patient with AIDS

Kaposi's sarcoma (KS) is the most common AIDS-related neoplasm and a significant cause of morbidity and mortality in patients with AIDS [1]. KS is a multifocal disease, which may involve multiple organs. However, bone involvement is very rare and has been demonstrated in only six cases. We review the cases described in the literature and present a new case of an AIDS patient with cutaneous and pleuropulmonary KS in whom computed tomography (CT) and magnetic resonance imaging (MRI) demonstrated asymptomatic lytic bone lesions in the spine, not evident on bone scan or plain films, and which biopsy showed to be KS.