CORRESPONDENCE

High Incidence of Early Postnatal Transmission of Human Immunodeficiency Virus Type 1 in Bangui, Central African Republic

To the Editor—Postnatal transmission of human immunodeficiency virus type 1 (HIV-1) from infected women to their newborns via breast-feeding occurs commonly in sub-Saharan Africa, in addition to both in utero and peripartum transmission of HIV-1. Indeed, when these children are breast-fed for >6 months, the risk for late postnatal HIV-1 transmission may be as high as 12% [1, 2]. However, the risk of early postnatal HIV-1 transmission (EPT) when a child is breast-fed for <6 months has not been defined by a prospective cohort study.

We evaluated the risk of EPT among the infants of HIV-1-infected women in Bangui, Central African Republic. Forty-three children born to HIV-1-infected women who planned to breast-feed were enrolled at birth. Dried blood samples were collected on filter paper for each child at birth and at 1 and 6 months of age. White blood cells were lysed, DNA was extracted by the phenol-chloroform method, and HIV-1 proviral DNA was detected in parallel by a nested polymerase chain reaction (PCR) on pol and a seminested PCR on tat. The pol primer sets have been optimized to detect HIV-1 variants of diverse geographic origin, including Africa [3]. The tat primer sets (outer primer set: A1 [tat 5563–5590]; 5′-TGAGAGGTCTTCGTGTCTCCGCT-3′ and A2 [tat 5360–5387]; 5′-TGAGGTGTGACATAGCAAGAGGCGT-3′; inner primer set: A2 and A11 [tat 5533–5560]; 5′-TTCCGTGAGGATGAGCTAAGGCTT-3′) were developed in our laboratory (Institut Pasteur) to efficiently detect HIV-1 subtype A originating from Bangui. HIV-1 infection in the children was defined as a positive reaction on both PCRs. Perinatal (in utero or peripartum) HIV infection required positive PCR responses at birth or 1 month; a positive PCR result at 28 days of age has >96% sensitivity for HIV diagnosis in non-breast-fed infants [4]. EPT was defined by a negative PCR result at birth and at 1 month of age, with a positive response at 6 months of age. Fourteen of 43 infants (32%; confidence interval [CI], 19%–49%) were infected perinatally, including 2 neonates with positive PCR results at birth. Eight infants (19%; CI, 8%–33%) were infected in the postnatal period, with the first positive PCR at 6 months of age. Finally, 21 infants (48%; CI, 33%–64%) had persistently negative PCR results at 6 months. The estimated rate of EPT, calculated by dividing the number of children with EPT by the number of children not contaminated in utero or perinatally was 27.6% (8/29).

In the present cohort, almost 20% of children born to women infected with HIV-1 became infected by breast-feeding for <6 months. This high rate of transmission demonstrates that early breast-feeding appears to be an efficient means of transfer of HIV-1 from an infected woman to her child. Moreover, the rate of EPT was almost twice that of late postnatal transmission reported previously [2], suggesting a marked infectivity of early milk. Indeed, large inocula of HIV-1, as evidenced by positivity of HIV-1 p24 antigen and proviral DNA, have been found in colostrum and early breast milk from infected women [5], likely due to the elevated number of mononuclear cells in colostrum. Another possibility may be that strains of HIV-1 from Bangui, consisting mainly of subtypes A and E [6], could have tropism for the mucosae and thus would be readily transmitted via breast-feeding. Half of the infants in this cohort remained uninfected at 6 months of age and were therefore at risk for late postnatal HIV transmission because breast-feeding in Central Africa frequently exceeds 12–18 months.

The strategies for reducing the risk of HIV infection via breast-feeding must take into account the timing of maternal transmission of HIV. One proposal to decrease transmission of HIV has been to limit the duration of breast-feeding to 6 months [2], but this would have no effect on early postnatal HIV-1 infection. Limiting breast-feeding to 3 months, as has also been proposed [7], still does not eliminate the risk of infection from colostrum. The possibility of expressing and discarding colostrum and early milk may help to decrease the rate of early postnatal transmission of HIV. Thus, in sub-Saharan Africa, careful practices may limit the spread of HIV-1 infection to breast-fed infants who cannot be bottle-fed, but advice regarding early breast-feeding must be provided.

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Antiviral CD4 Cell Response in Simian Immunodeficiency Virus–Infected Macaques

To the Editor—In their interesting article, Kent et al. reported on the T cell response of acute human immunodeficiency virus type 1 (HIV-1)–infected macaques [1]. In this model, pig-tailed macaques (Macaca nemestrina) developed virus-specific T helper (Th) cells and cytotoxic T cells (CTLs) after infection with HIV-1. However, unlike most HIV-infected humans, these animals did not develop a virus-induced immunodeficiency.

In rhesus macaques (Macaca mulatta) infected with simian immunodeficiency virus (SIV), the initial virus-specific immune response can be studied in animals subsequently progressing to an AIDS-like disease. Furthermore, the results can be directly compared with findings from animals infected with apathogenic SIV (we used viruses with deletion in regulatory genes). In several experiments, we could show that the pathogenic potential of the inoculated virus influences the resulting immune response in monkeys (reviewed in [2]). Rhesus macaques infected with pathogenic SIV developed virus-specific antibodies and CTLs, but their Th reactivity was strongly reduced [3]. In contrast, rhesus monkeys infected with apathogenic SIV showed a long-lasting, antiviral CTL and Th response [4]. This response was similar to that reported by Kent et al. [1] for HIV-1–infected pig-tail macaques. We have also reported that the virus-specific Th response of animals vaccinated with apathogenic SIV or HIV-2 is critical for protection of the animals against challenge with pathogenic SIV [5, 6]. These data suggest an important role of CD4+ cells in retroviral immunity. This important function might be due not only to immunologic help for other effector cells but possibly to a direct antiviral mechanism of Th cells. An antiviral effect of CD4+ cells has recently been shown in HIV [7] and murine retroviral infections (Friend leukemia virus [8]). In SIV-infected macaques, the virus-specific Th cells developed a rapid dysfunction in the early phase of infection, and the animals subsequently progressed to an AIDS-like disease. The Th dysfunction was associated with impaired cytokine transcription [2], and it has been reported that CD4+ T cells undergo apoptosis to a large extent [9, 10]. Thus, inducing a vigorous and sustained virus-specific Th response seems to be of potential significance for an effective retroviral immunity. This Th reactivity, however, might be hard to achieve against immunodeficiency viruses that have CD4+ T cells as their main target population. In this context, AIDS vaccine research can be conducted only in animal models that closely resemble the pathogenesis of HIV infections in humans.

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Reply

To the Editor—Dittmer and Hunsmann have provided stimulating comments on the role of lentivirus-specific T helper (Th) cell responses in the control of lentivirus infections in macaques and humans [1]. Human immunodeficiency virus type 1 (HIV-1)– and simian immunodeficiency virus (SIV)–specific Th responses are attracting growing interest for their potential effector and helper roles in controlling these infections in vivo. Indeed, Rosenberg et al. [2] have recently shown that HIV-1–specific Th responses inversely correlate with HIV-1 plasma viremia during pathogenic HIV-1 infection of humans [2], and we have recently shown that well-defined human long-term nonprogressors maintain robust HIV-1–specific