Reply to Filteau

To the Editor—I am in complete agreement with Dr Filteau’s plea that we stop advocating abrupt weaning for human immunodeficiency virus (HIV)-infected women [1]. As correctly stated, early weaning was poorly accepted in our clinical trial population in Zambia and, in intent-to-treat analyses, resulted in no net benefit for HIV-free survival of children born to HIV-infected mothers, and among HIV-infected infants, early weaning resulted in increased mortality [2]. When compliance was taken into account, we observed significant elevations in mortality among uninfected infants and young children whose mothers complied with advice to shorten breast-feeding duration [3]. The increases in uninfected child mortality were so large that they offset the modest number of HIV infections prevented [4]. Thus, there is little to be gained from implementing an intervention (early weaning), albeit with a modest benefit for HIV prevention, which increases mortality among uninfected and HIV-infected children alike.

Our trial was not the only one to report harms of breast-feeding duration. While our research was underway, early weaning started to become the norm in several settings. In some of these sites, distressing increases in morbidity and mortality after weaning were noted relative to historical cohorts with longer breast-feeding durations [5–7]. In part as a response to this accumulating evidence, the World Health Organization revised its recommendations about weaning and now unambiguously discourages abrupt weaning and encourages breast-feeding through 12 months [8].

Demonstration of the effectiveness of antiretroviral drugs when used for longer periods postnatally [9] makes continued breast-feeding an even more attractive option. For women who need therapy for their own health, defined as stage III/IV or CD4 count <350 cells/µL, there is no disagreement that therapy should be initiated promptly and be continued for life [10]. HIV transmission can be brought down to low levels [11,12] and even small increases in uninfected child mortality tip the balance in favor of continued breast-feeding. For women who do not yet need therapy for their own health, either maternal therapy or infant prophylactic regimens work to reduce transmission [13]. Either approach allows breast-feeding to be preserved. Furthermore, our data show that even in the absence of antiretroviral interventions, for women with higher CD4 counts, better outcomes are obtained if women breast-feed [4]. This is because, in this subgroup, postnatal HIV transmission is low enough that the excess mortality caused by shortening breast-feeding overwhelms the small number of HIV infections prevented [4].

However, I strongly disagree with Dr Filteau’s comment that “it is time to stop looking for a mechanism to explain the lower MTCT risk among exclusively breast-fed infants.” Several plausible hypotheses have been tested and found to not be an explanation, but this frustration is not reason to give up. The challenges posed by the HIV epidemic are immense. Central to controlling the epidemic is an effective prophylactic vaccine, and an understanding of at least some of the mechanisms underlying HIV transmission and how these are modulated by natural processes would greatly assist this endeavor. Maintenance of the exclusivity of breast-feeding during the first few months of life is one of the most consistently observed associations in mother-to-child HIV transmission research [14]. When nature gives us clues about how to stop HIV transmission, I am inclined to stop and look. It may turn out that associations between exclusive breast-feeding and HIV transmission are not causal, but our investigation of processes may yield insights into how HIV transmission occurs. It is unfortunate that concepts of exclusive breast-feeding and early, abrupt weaning became intertwined, but it is time to separate these concepts.
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References


Historical Aspects of Leprosy

To the Editor—The picture of the Abbot of Wallingsford with leprosy on the cover of the 15 February 2010 issue of Clinical Infectious Diseases is surprising, because despite the florid skin lesions, the fingers are still intact [1]. The Abbot of Wallingsford sustained some nasal damage and developed a speech impairment that probably indicated laryngeal involvement, which suggests that he had the lepromatous or multibacillary form of the disease. The process of steadily declining health over several years, leading to death, illustrates the course of the untreated disease without the intervention of modern modifying treatment.

Father Damien, who had severe multibacillary leprosy, also had intact fingers with nodules shortly before his death [2], as did the patient with multibacillary leprosy illustrated in Hansen and Loof's book [3]. Hansen described in detail the course of this form of the disease, with increasing bacterial proliferation. Only very rarely was there spontaneous remission with resolution of the skin lesions. In such cases, the patients “become in time anaesthetic, that is, according to our view they recover” [3, p. 80]. In the maculo-anaesthetic form of the disease, discrete lesions appear early, followed by severe sensory loss and disappearance of bacteria. Thus, sensory loss in leprosy is associated with destruction of bacteria and not with their proliferation. The 2 forms are therefore fundamentally different. In untreated multibacillary leprosy, there is continued bacillary proliferation, with death occurring within 8 or 9 years (probably from renal amyloidosis) but without sensory loss or mutilation. In the maculo-anaesthetic form, the bacteria are transient in appearance but are associated with sensory loss and mutilation of digits plus foot ulcers, as well as with a normal life expectancy. There is, therefore, no continuous spectrum of the disease.

This conclusion is, of course, the opposite of the current approach to leprosy, in which “the risk of impaired nerve function is much greater in those with multibacillary disease” [4, p. 194]. Today, leprologists are looking for sensory loss where it only rarely exists [5]. Without the appreciation of the natural history of the disease, there is no chance of understanding the pathogenesis of sensory nerve damage and providing rational therapy.

Patients with paucibacillary leprosy can develop acute sensory loss with simultaneous sensory loss in all 4 limbs [6]. This loss could be attributable to an autoimmune response to an antigen in sensory nerves rather than to a direct invasion of the peripheral nerves by Mycobacterium leprae. Rabbits injected with a homogenate of human peripheral sensory nerve plus adjuvant developed skin lesions similar to those associated with the human form of disease [7]. Electrophysiological studies of the hind limbs showed a specific diminution of the C fiber action potential [8]. Some rabbits developed a state of granulomatous hypersensitivity (ie, skin testing in sensitized animals with a non-myelin) antigen produced an epithelioid cell gran-