Correspondence

Seroreversion in Children Infected with HIV Type 1 Who Are Treated in the First Months of Life Is Not a Rare Event

SIR—We read with interest the article by Kassuto et al. [1] regarding the incomplete HIV-1 antibody evolution and seroreversion of 3 of 150 adult patients who initiated HAART early during primary infection. Seroreversion was complete for 1 patient (results of HIV-1/HIV-2 ELISA and HIV-1 Western blot were negative) and partial for 2 other patients (ELISA results for both patients remained positive). Incomplete antibody evolution in 4 patients and partial seroreversion in 1 patient had already been described in 1997 by Lafeuillade et al. [2]; in these patients, the plasma HIV-1 RNA load dropped to <20 copies/mL after early initiation of therapy with zidovudine, didanosine, and lamivudine (treatment began before day 15 of primary HIV-1 infection symptoms), but there was no complete seroreversion. Complete seroreversion in an adult infected with HIV-1 was recently described by Jurriaans et al. [3] in a patient who initiated HAART and immunosuppressive therapy with mycophenolate mofetil during primary HIV-1 infection, but, as is discussed by Kassuto et al. [1] and by Connick [4] in the accompanying editorial commentary, mycophenolate mofetil could have played a role in seroreversion by exerting an inhibitory effect on the humoral immune response. Clearly, incomplete antibody evolution is a rare phenomenon in adults infected with HIV-1 and is linked to very early therapy. Complete seroreversion is even more exceptional.

By contrast, this evolution is more frequent in neonates vertically infected with HIV-1 who are treated in the first months of life. Luzuriaga et al. [5] were the first to describe 2 infants infected with HIV-1 who experienced suppression of viral replication when HAART was initiated before 3 months of age. They had passively acquired maternal HIV-1 antibodies at birth and became seronegative around the age of 12 months. In a later study of 24 infants infected with HIV-1 who initiated therapy at <3 months of age, 15 had suppression of plasma HIV-1 RNA loads to <50 copies/mL, and 14 of 15 became seronegative by 16 months of age [6]. The kinetics of the HIV-1–specific antibody clearance in infants who received early therapy were identical to those observed in uninfected children born to HIV-infected mothers. Some of us and our colleagues [7] have also reported 4 patients who were treated before 2 months of age, among whom 2 experienced a permanent suppression of the viral load and became seronegative. Moreover, analysis of their HIV-1 Western blot pattern suggested transient antibody production, as shown by an increase in the intensity of all the specific protein bands during the first trimester of life, followed by a progressive waning.

Since 1996, there have been 14 infants infected with HIV-1 treated before the age of 2 months in our institution, including the 4 previously reported [7]. After initiation of HAART, plasma HIV-1 RNA loads dropped regularly to <50 copies/mL in 8 of these children during their first months of life. Of these 8 patients, 1 was lost to follow-up before the age of 12 months and 2 had a rapid rebound in viral replication because of a lack of compliance. Of the 5 other patients, 4 had negative results of the HIV-1/HIV-2 ELISA and HIV-1 Western blot before the age of 18 months, and in 1, only low levels of HIV-1 antibodies measured by ELISA persisted. On the basis of the time of the first blood sample in which HIV-1 RNA or DNA was detected, we considered that 2 of these 4 patients acquired the infection intrapartum and that 1 patient acquired the infection in utero. The fourth patient had an undefined time of transmission, because no blood sample was obtained during the first week of life. The patient who acquired the infection in utero remained seronegative until the age of 5.6 years. At that time, the HAART was not administered for 3 weeks. Three months after this transient interruption, the patient's plasma HIV-1 RNA load was again measured at <50 copies/mL, but the results of the HIV-1/HIV-2 ELISA and the HIV-1 Western blot were now positive, which confirmed that the patient was able to mount a humoral response against HIV-1 when the antigenic stimulus was sufficient.

In infants vertically infected with HIV-1 who are treated before the age of 3 months and in whom viral replication is fully and permanently suppressed, clearance of passive, maternally-acquired HIV-1 specific antibodies and absence of active generation of HIV-1 specific antibodies seems to be the rule rather than the exception.

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Invasive Pneumococcal Disease in Children: Changing Serotypes and Clinical Expression of Disease

Sir—In a recent article, Byington et al. [1] provided an interesting analysis of the temporal trends in the incidence of invasive pneumococcal disease (IPD) before and after the introduction of the heptavalent pneumococcal conjugate vaccine (PCV7).

One of the most interesting findings they reported was the significant increase in the incidence of empyema from the prelicensure to the postlicensure period (10.3 vs. 14.3 cases/100,000 children, $P = .013$).

However, the effects of the vaccine do not explain the increased incidence of empyema. Similar increases that clearly preceded the introduction of PCV7 have been reported in the last decade [2, 3]. Furthermore, shifts in the serogroups causing IPD had been observed just before the introduction of PCV7 [4], and the incidence of complicated community-acquired pneumonia has been reported to have decreased since the vaccine was introduced [5].

These changes could be related, at least in part, to the emergence of serogroups that were identified a long time ago as causes of IPD and that reappeared before the introduction of PCV7. Serogroup 1 has been associated with such changes; the percentage of cases of IPD with pleural involvement due to serogroup 1 increased from 24% [6] to 50% [7] between 1993 and 2000 in the United States. It could be that clonal spread of serogroup 1, as has been described in Sweden [8], in conjunction with the phenomenon of antibiotic tolerance [9], explains the reemergence of this serogroup in western societies and, consequently, the increasing number of parapneumonic complications. Also, as reported by Byington et al. [1], the incidence of IPD caused by serogroup 3 has significantly increased between the pre- and postlicensure periods.

We found similar results in a study conducted between 1999 and 2003 in the El Vallés area in the province of Barcelona, Spain. We analyzed the impact of the introduction of PCV7 in 2002. Between 1999 and 2001, the area studied had 19,593 children aged ⩽5 years. From 2002 to 2004, there were 23,382 children aged ⩽5 years in the area. The rate of vaccination was estimated to be ~30%. We did not find a decrease in the global incidence of IPD, but the incidence of empyema increased from 1.7 to 8.5 cases per 100,000 children (OR, 4.5; 95% CI, 0.91–18; $P = .06$) between the 2 periods. Isolates recovered from the pleural fluid were all serotype 1, with the single exception of 1 serotype 4 isolate recovered from a case of empyema in the postlicensure period (authors' unpublished data).

On the basis of all these considerations, we would be very interested in knowing the serotypes that caused empyema in the children described by Byington et al. [1]. This information could indicate whether the increased incidence of empyema reported is an additional effect of PCV7 use. We would also have liked more detailed information about the serotypes that caused IPD in vaccinated children. It is well known that the immunogenicity of PCV7 serotypes is not homogeneous, and vaccine failures have been described previously. Most failures have involved serotypes 19F and 6B [10, 11]. In this context, it could be interesting to know which PCV7 serotypes were identified in the vaccinated children with IPD reported by Byington et al. [1].

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