ity of enterovirus infection, it may be best to focus on infants, particularly those who are premature, with disseminated disease.

Dennis L. Murray
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Reply

Sir—I appreciate Dr. Murray’s interest in our paper [1]. Two infants in our study were premature: one (intravenous immune globulin group [IVIG]) was born at 35 weeks’ gestation, and the other (control group) was born at 37 weeks’ gestation. Consistent with the observation that prematurity is associated with severe neonatal enterovirus infection, these infants were two of the three sickest patients in our cohort; each had viremia with an echovirus, and each had hepatitis and coagulopathy. Viral isolates were typed by initial screening with pooled antisera, followed by confirmatory testing with type-specific monovalent antisera. As indicated in figure 1 of our paper, one patient in the group that received IVIG containing a neutralization titer of <1:800 was viremic on study day 0 and again on study day 1. The titer of virus in serum of this infant fell from 1.5 × 10^3 50% tissue culture infective dose per mL (TCID_50/mL) on day 0 to 2 × 10^2 TCID_50/mL on day 1. Another patient in the group receiving IVIG with a neutralization titer of <1:800 was viremic on study day 0 and again on study day 1. Viral titers in urine were <6.8 × 10^1 TCID_50/mL on day 0 and 6.8 × 10^1 TCID_50/mL on study day 1. It is difficult to know whether IVIG treatment had an effect in either circumstance.

I agree with Dr. Murray’s conclusion that the variability in the amounts of neutralizing antibody to different enteroviruses within the same and different IVIG preparations and the variability in the course of neonatal enterovirus infections will make proving the clinical efficacy of IVIG in infected neonates challenging. In future studies, larger or repeated doses of IVIG containing high neutralizing antibody titers should be used, and these studies should focus on babies who are likely to have serious disease, including those whose illnesses occur in the first few days of life, those who are premature, and those who manifest multisystem disease.

Mark J. Abzug
Pediatric Infectious Diseases, Department of Pediatrics, University of Colorado School of Medicine/The Children’s Hospital, Denver, Colorado

Reference

Secondary Prophylaxis for Tuberculosis in Patients Infected with Human Immunodeficiency Virus

Sir—In the recent publication of USPHS/IDSA guidelines for the prevention of opportunistic infections in patients infected with HIV [1], one of the recommendations regarding prophylaxis for tuberculosis raises important concerns.

The guidelines state that “Chronic suppressive therapy for a patient who has successfully completed a recommended regimen of treatment for tuberculosis is not necessary (EII).” The EII rating indicates that chronic suppressive therapy is contraindicated on the basis of substantial clinical data. We are not aware of any trial in which outcomes for HIV-infected tuberculosis patients receiving traditional courses of therapy have been compared with those for patients receiving traditional therapy followed by secondary prophylaxis. Although numerous studies have proved that active tuberculosis is well controlled in the majority of HIV-infected patients who receive traditional courses of chemotherapy, relapse rates have been alarmingly high in several series. Relapse rates of 11.4% [2], 9% (in a group receiving 6 months of therapy) [3], and 22.4% [4] have been reported after HIV-infected patients have completed full courses of chemotherapy. The latter two figures were obtained from studies in which high levels of compliance were reported. In a prospective investigation of recurrence rates among HIV-infected individuals vs. those without HIV infection in Kenya, a rate of 17% was found for the HIV-infected group [5]; this rate was 34 times that for the uninfected cohort (95% CI = 3.1–56.2).

References
In the few cases in which paired isolates were available from initial and recurrent infections, the majority of such pairs had identical DNA patterns. Although one cannot deduce from the literature what percentage of tuberculosis “relapses” are actually reinfections or treatment failures secondary to poor compliance, it seems that true relapse of tuberculosis in this population is not an unusual event. Several recent publications have urged consideration of secondary prophylaxis after completion of antituberculous therapy [2, 6, 7].

In our correctional facility we have adopted the practice of offering lifelong prophylaxis with isoniazid to all HIV-infected patients (except those with isoniazid-resistant isolates) who have completed therapy for tuberculosis. In certain settings, especially those characterized by congregate living arrangements, housing with poor ventilation, and populations with high rates of immunodeficiency, every case of active tuberculosis represents a true public health emergency. The catastrophic consequences of such cases have been adequately documented in published descriptions of outbreaks in an HIV ward in an Italian hospital [8] and in a housing facility for HIV-infected persons in San Francisco [9]. We believe that a true relapse rate which approaches that described in the medical literature is unacceptable when considered in the context of a patient population that spends substantial periods in health care facilities for HIV-infected persons, homeless shelters, crack houses, shooting galleries, and/or correctional facilities. This risk is only compounded by the threat of exogenous reinfection in these environments, in which tuberculosis is both endemic and epidemic. The risk-benefit analysis for patients who are returning to private housing situations with immunocompetent adults may be very different.

In the absence of data from a controlled trial, it seems reasonable in settings such as ours to offer ongoing isoniazid therapy, with the goals of decreasing rates of relapsed tuberculosis and perhaps conferring protection against exogenous reinfection. This is a strategy that has proven successful in preventing reactivation of tuberculosis infection in HIV-infected individuals in other clinical settings [10].

Jonathan Shuter and Eran Bellin
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References

Reply

Sir—Drs. Shuter and Bellin question the basis of the USPHS/IDSA recommendation against the use of chronic suppressive antituberculous therapy for HIV-infected persons who have successfully completed a recommended regimen of treatment for tuberculosis [1]. Since there are no comparative clinical trials that specifically address this issue, we agree that categorizing this recommendation as E (i.e., contraindicated) exaggerates the extent of current knowledge; a rating of D (i.e., generally should not be offered) may have been more appropriate.

Several factors have been shown to influence tuberculosis cure rates and treatment outcomes [2]. For persons with HIV infection, some of these factors include treatment with at least two effective drugs (i.e., drugs with in vitro activity against the infecting strain of Mycobacterium tuberculosis); extended duration of therapy (at least 6 months); adherence to the prescribed therapeutic regimen (most commonly achieved through the use of directly observed therapy); severity of immunosuppression (this factor is associated with relatively high mortality among patients with tuberculosis); and probability of reexposure to persons with active tuberculosis, with subsequent reinfection with M. tuberculosis [2-7]. In addition, rifampin-containing antituberculosis regimens are essential in achieving the sterilizing phase associated with a low relapse rate [2].

Drs. Shuter and Bellin cite several references to “alarmingly high” tuberculosis relapse rates. However, some of these reports do not provide the exact nature and duration of drug regimens or the methods used to assess adherence to the regimen. For instance, the study in Zaire compared the effectiveness of a 6-month vs. 12-month antituberculous regimen that contained rifampin for HIV-infected individuals with pulmonary tuberculosis, but no details were given about adherence to therapy [5]. Although the relapse rate after 6 months of therapy was 9.0% for HIV-infected patients, it was not significantly different from the relapse rate of 5.3% observed for patients not infected with HIV (P > .1). Furthermore, among the HIV-infected patients, the relapse rate after 12 months...