ity of enterovirus infection, it may be best to focus on in-

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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 antiserum, 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 <1:600 was viremic on study
day 0 (day of entry into the study) 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 neutraliz­
ing 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.

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Reference

enterovirus infection: virology, serology, and effects of intravenous im­

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 (EID).” The EID 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 pro­
phylaxis. Although numerous studies have proved that active tu­
berculosis is well controlled in the majority of HIV-infected pa­
tients 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).

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Clinical Infectious Diseases 1996;22:989-9
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1058-4838/96/2202-0052 $02.00
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].

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References