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TB and HIV in Healthcare Settings

To the Editor:

Drs. Castro and Dooley (1993;14:65-66) raised some questions about our interpretation of the findings concerning the retrospective comparative evaluation we made of the occupational risk of tuberculosis in healthcare workers (HCWs) assisting HIV-infected and uninfected tuberculosis patients.¹

As stated in the editorial, some of the points already have been clarified,² particularly the most potentially confounding one: that concerning the HIV status of those HCWs who developed tuberculosis. Unlike in the United States, in Italy HIV-infected patients are assisted in the hospitals by regularly employed nurses and HCWs who, in this investigation, have been considered to be HIV-seronegative and had no other immunosuppressive condition.

Drs. Castro and Dooley have calculated the rate of active tuberculosis based on the total number of HCWs. This approach ignores the striking difference in the cumulative number of tuberculosis patients between HIV-infected (85) and uninfected ones (1,079), which represent the source of infection.

In our opinion, this difference must be taken into account when comparing the incidence rates of tuberculosis in the two groups of HCWs. If we consider both the person-years due to HCWs (606 among those caring for HIV-infected patients and 486 among those caring for HIV-uninfected patients) and the cumulative number of tuberculosis patients in calculating the denominator of the two rates, the expected number of HCWs with active tuberculosis is 0.81 among those caring for HIV-infected patients (seven were observed), so that an estimate of the relative risk is $35.4 (7 \times 8.20) \div (2 \times 0.81)$. Using the procedure described by Breslow and Day,³ a 95% confidence interval for the relative risk is 6.8 to 351.5, which is considerably different from that reported by Drs. Castro and Dooley. This result doesn't change if the number of infected patients are given a weight much lower than that given to the number of HCWs; for example, using a square root weight, the 95% confidence interval for the relative risk is 1.9 to 98.7.

Drs. Castro and Dooley also state that there are no reasons to believe that HIV-infected tuberculosis patients may disseminate *Mycobacterium tuberculosis* at a greater extent than expected. They support this notion by quoting only those reports that confirm their view^{4,6} and avoiding any mention of the papers that describe opposing evidence, such as those of Standaert,⁷ Brodt,⁸ and Franchini,⁹ who found a convincing association between cases of HIV-associated tuberculosis and an unexpectedly high spread of tuberculous infection and disease. Along with clinical and epidemiological reports, it could be useful to consider also the "lepromatous-like" pattern shown by HIV-associated tuberculosis in several anatomic areas,^{10,11} including the lungs,^{12,13} where a multibacillary

picture often is seen in a background of aspecific and poorly granulomatous inflammatory reaction, specifically when the most immunosuppressed patients are investigated. In the case of leprosy, another airborne mycobacterial disease, infectiousness is associated rigorously with patients suffering from the lepromatous form of the disease, in whom the specific cellular immune defect makes the affected patient unable to limit bacterial growth.¹⁴ Because severely immunosuppressed patients with HIV infection and tuberculosis display the same histopathological picture seen in cases of lepromatous leprosy, it appears not too hazardous to consider the hypothesis that these (deeply immunosuppressed) patients may disseminate *M. tuberculosis* to a greater extent than immunocompetent tuberculosis patients.

Drs. Castro and Dooley also state that there are reports describing a lower rate of sputum smear positivity for acid-fast bacilli (AFB) in HIV-infected patients compared with seronegative controls. In these reports, however, no information was available on the immune status of those with HIV infection. We believe that, in order to provide the readers with a more comprehensive view of the subject, we also should consider that among HIV-infected patients with tuberculosis, the most immunosuppressed have a higher frequency of positive sputum smears for AFB than those with greater immunity (75% versus 45%), probably reflecting a higher bacillary burden in the setting of greater immunodeficiency.¹⁵ These findings indirectly confirm what we observed in terms of individual immune status of the HIV-infected patients who were identified as the source cases of occupational tuberculosis in our investigation¹; all had signs of

extreme immunosuppression with very low CD+ cell counts.

What we believe, on the basis of these data, is that a possible phenomenon of higher infectiousness of HIV-infected patients with tuberculosis probably is limited to the minority of such patients who develop active disease at an advanced stage of HIV infection, so that on a large scale this should not be considered as a constant feature of tuberculosis/HIV association. In any case, we agree with Drs. Castro and Dooley that those involved in the care of these patients should be aware of such possibility and adequate infection control practices must be ensured in the care centers hosting these patients. Future investigational efforts probably will provide definitive answers to this question.

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The authors reply:

We appreciate the comments of Dr. Di Perri and colleagues, and we would like to respond to some of the points they raise. First, we would like to correct a typographical error that appeared in our editorial.¹ The editorial reads, "When the rate of active tuberculosis is calculated based on the total number of healthcare workers among

those caring for HIV-infected patients (7/135) versus non-HIV infected patients (2/186), the difference is not statistically significant (relative risk, 2.75; 95% confidence interval, 0.58 to 12.96)." This should read "...versus non-HIV infected patients (2/106)..." The relative risk and confidence interval are correct.

Dr. Di Perri raises questions about the appropriate denominator to use in calculating the risk to healthcare workers. In our editorial, we suggested that it would be appropriate to use the number of exposed healthcare workers as the denominator. Dr. Di Perri notes that this approach ignores the difference in the cumulative number of human immunodeficiency virus (HIV)-seropositive and HIV-seronegative tuberculosis patients to which the healthcare workers potentially were exposed. In fact, it would be preferable to use a denominator that takes into account both of these factors. However, in calculating the number of potential source cases to be used in the denominator, it is important to recognize that the infectiousness of patients with tuberculosis is quite variable. It depends on a number of factors, including the site of disease, the presence of cough, the presence of pulmonary cavitation, the presence and the number of acid-fast bacilli on a sputum smear, and the effectiveness and the duration of therapy. Even among patients with similar clinical characteristics, there can be considerable variation in the proportion of contacts who become infected following exposure. This indicates that other factors related to the source patient, the environment, and the person being exposed play an important role in modulating the risk of transmission.

In the nosocomial tuberculosis outbreaks reported during the past two decades, transmission gen-