HIV-infected individuals, in general they do not provide access to patients with early disease.

In contrast, however, HIV-infected pregnant mothers identified in antenatal clinics and referred to our ART program had a median CD4 cell count (127 cells/\mu L) twice that of patients with TB and exceeding that of the overall treatment cohort (figure 1B). The CD4 cell count distribution also suggests that it is likely that a substantial proportion of antenatal patients also had CD4 cell counts of >200 cells/\mu L. Because the antenatal HIV seroprevalence rate is ∼30% in this community, antenatal clinics represent a key opportunity for identifying many patients with less-advanced immunodeficiency. Treatment of these patients is likely not only to result in better outcomes but also to prevent vertical transmission of HIV. Thus, provision of facilities for HIV testing and CD4 cell count measurement at antenatal clinics warrants prioritization as access to ART is increased in lower-income countries. Furthermore, although costly, provision of CD4 cell count measurements at other voluntary counseling and testing facilities would also help identify other asymptomatic individuals with less-advanced disease who are eligible for ART.

Acknowledgments


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References


Reply to Lawn and Wood

Sir—We agree with Lawn and Wood [1] that patients should be enrolled earlier into antiretroviral treatment (ART) programs. This will benefit HIV-infected individuals and speed up the antiretroviral “rollout” process. Starting ART before patients develop opportunistic infections prevents unnecessary deaths, reduces drug interactions between the antiretrovirals and other drugs, and probably decreases the incidence of immune reactivation inflammatory syndrome. The cost of these complications with their attendant hospitalization is substantial, and these resources are better used for ART.

To start ART earlier, CD4+ lymphocyte counts must be available on a larger, decentralized scale. This will require cheaper and simpler methods for testing CD4+ lymphocyte counts. Ideally, measurement of CD4+ lymphocyte counts should be offered at voluntary counseling and testing sites, antenatal clinics, and tuberculosis (TB) treatment centers. The fact that, in the South African experience, HIV-seropositive patients with TB had a mean CD4+ lymphocyte count of 65 cells/\mu L suggests that these patients were referred for ART when both illnesses were far advanced. Diagnostic and treatment delays for TB must be effectively addressed.

Either the CD4+ lymphocyte count testing should be done at the site where the HIV testing was done or samples should be referred to a reference laboratory with systems that guarantee rapid and reliable return of results. On the basis of CD4+ lymphocyte count results, asymptomatic or paucisymptomatic patients could be referred for early ART. The rollout of CD4+ lymphocyte count testing will not only reduce transportation costs for patients but also enable ART centers to work more efficiently because they will be able to start ART in patients less likely to develop complications and they will not be overwhelmed by patients who do not require treatment.

Earlier initiation of ART in low-income countries must be promoted. This will require additional fiscal and human resources, but, in the long run, the overall cost to society will be substantially less, with reduced health care costs for management of opportunistic infections, including TB, and with more healthy, productive individuals and societies.

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Prevention of Laboratory-Acquired Brucellosis: Significant Side Effects of Prophylaxis

Sir—We describe our experience in responding to a laboratory exposure to *Brucella melitensis*—in particular, the high incidence of adverse events associated with antibiotic prophylaxis. This information may be useful to other laboratories with similar exposures.

A 45-year-old man returned to Australia from Iraq. He presented to the hospital with a cerebrovascular accident and was noted to be febrile and to have a systolic murmur. An echocardiogram demonstrated a vegetation on the aortic valve, and blood cultures grew *B. melitensis* after 2 days. His condition was treated with a combination of rifampicin, doxycycline, and gentamicin, and he had an uneventful recovery.

In the laboratory, the blood cultures were continuously monitored by the BacT/Alert 3D instrument (bioMérieux). When the bottles signaled positive results, they were moved to a class II biological safety cabinet (BSC II), where the bottles were accessed and an aliquot was transferred to a slide and was also placed onto solid agar media. The inoculated media were removed from the cabinet, and plate streaking was performed on an open bench. Initial plate reading and manipulation of the cultures were performed on the open bench, but, within 24 h of the appearance of growth, a presumptive identification of *Brucella* species was made, after which all further manipulation was performed in the BSC II. The organism was confirmed to be *B. melitensis* by a reference laboratory. It was thought that staff may have been exposed to the organism during these procedures.

Staff were interviewed about their exposure and were assigned to high-, medium-, and low-risk groups. Seven staff members were assigned to the high-risk group. These staff manipulated or handled open-plate cultures or potentially inhaled material from the liquid or plate cultures outside the BSC II (i.e., they sniffed the plate, streaked the plate with flamed loops, inspected open-plate cultures, or performed subcultures or biochemical tests). The medium-risk group members were in close proximity while these procedures were being performed (12 staff), and the low-risk group members were working in other areas of the bacteriology laboratory (25 staff). We decided our response would be similar to that reported by Robichaud et al. [1]. After counseling, the high-risk group was offered antimicrobial prophylaxis with rifampicin (450 or 600 mg once daily, depending on body weight) and doxycycline (100 mg twice daily) for 3 weeks. In addition, second-weekly serological testing for brucellosis for 12 weeks was recommended for staff in the high- and medium-risk groups.

All 7 staff members in the high-risk group decided to take prophylaxis. Six started treatment within 1 week after potential exposure, and the seventh started it within 4 weeks after potential exposure, after the exclusion of early pregnancy. Of those 7 staff members, 6 experienced significant side effects associated with the medications. All 6 reported nausea, vomiting, and anorexia. One staff member developed fever and mild hepatitis and required admission to the hospital for monitoring. The symptoms resolved promptly with cessation of the course of antibiotics. One staff member developed minor facial swelling, and another described mild depression and anxiety during antibiotic use. Eight and a half working days were lost because of sick leave among 4 of the staff who received prophylactic antibiotics. Only 4 of the 7 staff completed the treatment course, with 2 staff members missing 2 days of treatment, and 1 missing >5 days. A total of 82% of scheduled serological tests were performed. There were no seroconversions to suggest subclinical infection, and no staff members developed clinical brucellosis during 8 months of follow-up.

No definitive guidelines for the management of potential laboratory exposure to brucellosis are available. Some groups have used postexposure antibiotic prophylaxis, although the effectiveness of this treatment is difficult to measure, and levels of risk are difficult to determine. Robichaud et al. [1] gave prophylaxis with rifampicin and doxycycline to 5 of 6 laboratory technicians, and there were no infections among those 5. The 1 technician who declined prophylaxis developed clinical disease, which suggests that prophylaxis may have been effective. In that study, the regimen was said to be well tolerated, and the adverse effects acceptable. This information was taken into account in our decision to offer prophylaxis to our staff.

We were surprised by the high rate of significant side effects in our treated group and the sick leave that resulted. The lack of infections may indicate that the antibiotic prophylaxis was successful, although it is likely that exposure in our laboratory was limited. The possibility that *Brucella* species were present was quickly recognized, there was minimal manipulation of the culture, and only 1 staff member reported sniffing the plate. Nevertheless, brucellosis is a potentially fatal illness, and any laboratory exposure should be carefully assessed and managed. There may be a role for antibiotic prophylaxis in managing high-risk exposures, but the need for prophylaxis must be balanced against the possibility of significant side effects. Primarily, laboratory protocols should aim to minimize potential laboratory exposures to dangerous pathogens, and laboratory staff should remain vigilant while performing their duties.