Reply to van Griensven et al.

To the Editor—We thank van Griensven et al. [1] for sharing their experience with the lactate point-of-care device. We are also glad that symptomatic hyperlactatemia and lactic acidosis (SH/LA) are becoming a topic of debate and interest in resource-limited settings where stavudine-containing regimens are prescribed for the majority of the patients.

We agree that clinical judgment is crucial in the diagnosis and management of this syndrome; training of health care workers should not only promote the early recognition of symptoms of SH/LA, but should also promote the exclusion of other causes of elevated lactate levels. Although there could be a possibility of overdiagnosis, our case series [2] revealed that 83% of patients had other symptoms of mitochondrial toxicity, suggesting that switching to other drugs would be beneficial for these patients.

After the publication of our case series, the Infectious Diseases Institute received a donation of a point-of-care device (Accutrend Lactate; Roche) [4] with 2000 test strips. At present, we are performing a validation analysis to compare the point-of-care device measurements with measurements from the Makerere University–Johns Hopkins University Core Laboratory, which follows Good Laboratory Practice guidelines and which is certified by the College of American Pathologists.

In addition, we submitted 2 proposals and plan to start the 2 following studies in October 2007.

1. A cross-sectional study involving measurements of serum lactate levels in a cohort of patients receiving antiretroviral treatment (any regimen), to determine the true prevalence of hyperlactatemia. A limitation of the study that we published [2] was that the information was obtained by a review of the charts. Enrolling patients in this cross-sectional study will allow us to design a structured interview to exclude other causes of hyperlactatemia, such as opportunistic infections and transient elevations of lactate levels resulting from exercise or dehydration.

2. A prospective study. Patients with asymptomatic hyperlactatemia will be followed up, and lactate measurements and a structured interview will be performed every 3 months. This will allow us to verify whether subclinical hyperlactatemia rarely progresses to severe disease, as suggested from experience in western countries [3], and that, therefore, regimen changes are not recommended for this category of patients.

We hope that these studies can answer some of the issues raised by van Griensven et al. [1]. Regarding the cost issue, we believe that, in programs in which thousands of patients are receiving stavudine-containing regimens, with consideration of the high mortality rate for SH/LA, measurements of the lactate level should be made. Three years after starting the rollout of free antiretrovirals in Sub-Saharan Africa, antiretroviral treatment programs have had to take into account toxicity issues and to provide tools to manage drug-related complications.

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

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References


HIV-1 Subtype C Seronegative AIDS

To the Editor—We thank Novitsky and colleagues [1] for their interesting report about a seronegative patient infected with HIV-1 subtype C. We too have recently given a seronegative AIDS diagnosis to a patient, the second adult case we have seen at our institution with presumed HIV-1 subtype C infection. This patient received a diagnosis of disseminated tuberculosis and had a CD4+ T cell count of 20 cells/mm3. Results of HIV antibody tests—including rapid (Determine HIV-1/2, Abbott and Capillus; Trinity Biotech) and third-generation ELISA (Dade Behring)—were negative. However, a fourth-generation HIV antibody–p24 antigen combination ELISA (Axysym; Abbott) was weakly reactive, and an HIV p24 antigen–only ELISA (Elecsys; Roche) was also weakly reactive. Viral RNA was detected in the plasma at 2,500,000 IU/mL (Nuclisens Easy-Q; bioMérieux), and results of an HIV DNA PCR (Ampicor HIV-1; Roche) were positive.

We presume that the HIV antibody–p24 antigen combination ELISA was weakly reactive because of the presence of the p24 antigen in the patient’s sample and not because of HIV antibody. This patient had a total serum IgG level of 31.25 g/L, which excludes a primary immune deficiency as a reason for the absence of HIV-specific...
antibody. Formation of immune complexes could explain the apparent seronegative status, but repeated attempts to dissociate these with heat, chaotropic agents, and acid did not yield detectable HIV antibodies or an increase in HIV-p24 antigen titer.

In addition to seeing this rare phenomenon in adults, we have seen it in infants. The most recent case was a 5-month-old child who was admitted to the hospital with Pneumocystis jiroveci and cytomegalovirus pneumonia. This infant had no HIV antibodies detectable with a third-generation ELISA (AxSYM, Abbott); however, results of HIV-p24 antigen ELISA (Elecsys; Roche) and HIV-1 DNA PCR (Amplicor HIV-1; Roche) were positive. Plasma HIV load was 2,600,000 IU/mL (Nuclisens Easy-Q; bioMérieux). An HIV ELISA was performed on the mother during early pregnancy, which was nonreactive; however, the mother tested HIV-antibody positive at the time the infant was tested. We presume she had a primary HIV-1 infection shortly before delivery. This would explain the absence of maternal HIV antibodies in the infant.

We agree with previous publications as to the etiology of this rare phenomenon, thought to be due to rapid propagation of a typical HIV-1 strain in an uncommonly susceptible host [2]. It is hypothesized that there is overwhelming presentation of viral antigens to CD4+ T cells, with resultant HIV-specific clonal depletion of CD4 cells able to respond to HIV antigens. The absence of T cell help is likely to impair both humoral and cellular HIV-specific immune responses [2]. This would explain the high viral load, rapid disease progression, and absence of detectable HIV antibodies in these patients.

With regard to the laboratory diagnosis, fourth-generation HIV antibody–p24 antigen combination ELISAs would detect these cases because of the presence of the HIV-p24 antigen. Introduction of nucleic acid testing into the algorithm of routine HIV-1 screening of adults, we have seen it in infants. The hospital serves a predominantly black and Hispanic community receiving Medicare or Medicaid. It has medical, surgical, substance abuse, psychiatric, obstetrics, gynecology, and neonatal units. There is an oncology service that accounts for <1% of admissions. We routinely use an aerobic and anaerobic blood culture system (Bactec II).

There was no increase in the incidence of anaerobic bacteremia from 2000 to 2006. The total number of positive blood culture results ranged from 1036 to 1454. Anaerobic organisms accounted for <2% of positive blood culture results (range, 0.7%–1.3%). The number of positive anaerobic culture results per 1000 blood cultures performed was 0.73, which is much lower than the rate of 1.68 positive results per 1000 blood cultures that was reported by Lassmann et al. [1] for the period 1993–1996.

Not surprisingly, Bacteroides fragilis accounted for 33% of anaerobes, followed by Peptostreptococcus species (19%) (table 1). The etiology of infections was unknown in 42% of the cases. Thirty-two percent of cases had an abdominal or pelvic source, and 23.5% of cases involved soft-tissue infection.

The mean age of our patients was 61 years (range, 23–103 years), and 55% were male. The mortality rate for these patients

<table>
<thead>
<tr>
<th>Anaerobic organism</th>
<th>2000</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>Total</th>
</tr>
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<tr>
<td>Bacteroides fragilis group</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>5</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>28</td>
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<tr>
<td>Peptostreptococcus species</td>
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<td>1</td>
<td>3</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>16</td>
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<tr>
<td>Other Bacteroides species</td>
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<td>2</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
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<td>2</td>
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<td>1</td>
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<td>10</td>
</tr>
<tr>
<td>Clostridium species</td>
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<td>2</td>
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<tr>
<td>Prevotella and Porphyromonas species</td>
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<td>2</td>
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<td>1</td>
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<td>Fusobacterium species</td>
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<td>0</td>
<td>0</td>
<td>0</td>
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<td>3</td>
</tr>
</tbody>
</table>

**Total** | 18 | 12 | 12 | 12 | 11 | 7 | 13 | 85

We reviewed our experience with anaerobic bacteremia during 2000–2006 at St. Barnabas Hospital, a 450-bed community hospital in the Bronx, New York. The hospital serves a predominantly black and Hispanic community receiving Medicare or Medicaid. It has medical, surgical, substance abuse, psychiatric, obstetrics, gynecology, and neonatal units. There is an oncology service that accounts for <1% of admissions. We routinely use an aerobic and anaerobic blood culture system (Bactec II).

**To the Editor—**We read with interest the article by Lassmann et al. [1] describing the increase in the incidence of anaerobic infections at the Mayo Clinic (Rochester, MN) that could have been due to the increasing number of patients with complex underlying disease. The article reflects the experience in a tertiary-level referral center and may not be valid in a community-based hospital.

References


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**An Increase in the Incidence of Anaerobic Bacteremia: True for Tertiary Care Referral Centers but Not for Community Hospitals?**

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