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 over-diagnosis, 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 test strips. At present, we are performing a validation analysis to compare the test strips. At present, we are performing a validation analysis to compare the test strips. At present, we are performing a validation analysis to compare the test strips. At present, we are performing a validation analysis to compare the test strips. At present, we are performing a validation analysis to compare the test strips. At present, we are performing a validation analysis to compare the test strips. At present, we are performing a validation analysis to compare the test strips. We presume that the HIV antibody–p24 antigen combination ELISA (Axsym; Abbott) was weakly reactive, and an HIV p24 antigen–only ELISA (Nuncisens Easy-Q; bioMérieux), and results of an HIV antibody–p24 antigen combination ELISA (Axsym; Abbott) were negative. However, a fourth-generation HIV antibody–p24 antigen combination ELISA (Axsym; Abbott) was weakly reactive, and an HIV p24 antigen–only ELISA (Elecys; 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 (Amplicor HIV-1; Roche) were positive.

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 roll-out 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.

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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 (Axsym; Abbott) was weakly reactive, and an HIV p24 antigen–only ELISA (Elecys; 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 (Amplicor 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 adult patients is not feasible or warranted, given the rarity of this phenomenon.

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