Point-of-Care Lactate Testing Predicts Mortality of Severe Sepsis in a Predominantly HIV Type 1–Infected Patient Population in Uganda

Christopher C. Moore, Shevin T. Jacob, Relana Pinkerton, David B. Meya, Harriet Mayanja-Kizza, Steven J. Reynolds, and W. Michael Scheld

1Department of Internal Medicine, Division of Infectious Diseases and International Health, University of Virginia Health System, Charlottesville; 2Division of Intramural Research, National Institutes of Health, Bethesda, and 3Johns Hopkins University School of Medicine, Baltimore, Maryland; and 4Faculty of Medicine, Infectious Diseases Institute, Makerere University, Kampala, Uganda

Background. Prediction of mortality may improve management and outcomes of patients with sepsis in resource-limited settings. Therefore, we evaluated the ability of a hand-held portable whole-blood lactate (PWBL) analyzer to predict mortality of patients who are admitted to the hospital with severe sepsis.

Methods. A prospective observational study enrolled 253 patients at a national referral hospital in Uganda. Inclusion criteria required (1) ≥2 systemic inflammatory response syndrome criteria or thermodyres regulation, (2) hypotension, and (3) suspected infection. A subset of 72 patients had PWBL and standard laboratory serum lactate measured. The primary measured outcome was in-hospital mortality.

Results. Fifty-nine (81.9%) of 72 evaluated patients were infected with human immunodeficiency virus type 1. The in-hospital mortality rate was 25.7% (18 of 70), and the in- and outpatient mortality at 30 days was 41.6% (30 of 72). PWBL was positively associated with in-hospital but not outpatient mortality (P < .001). The receiver operating characteristic area under the curve for PWBL was 0.81 (P < .001). The optimal PWBL concentration for predicting in-hospital mortality (sensitivity, 88.3%; specificity, 71.2%) was ≥4.0 mmol/L. Patients with a PWBL concentration ≥4.0 mmol/L died while in the hospital substantially more often (50.0%) than did those with a PWBL concentration <4.0 mmol/L (7.5%) (odds ratio, 12.3; 95% confidence interval, 3.5–48.9; P < .001). Standard laboratory serum lactate results were inconsistent and less predictive of mortality than were those of PWBL in a multiple logistic regression model.

Conclusion. A PWBL concentration ≥4.0 mmol/L predicts with 81% accuracy a 7-fold higher mortality of patients with sepsis than does a PWBL concentration <4.0 mmol/L. PWBL testing would be useful in places where clinical decisions are limited by lack of laboratory infrastructure and poor reliability.

Received 23 April 2007; accepted 14 September 2007; electronically published 13 December 2007.
Reprints or correspondence: Dr. Christopher C. Moore, Dept. of Internal Medicine, Div. of Infectious Diseases and International Health, University of Virginia Health System, 409 Lane Rd., MR-4 Bldg., Rm. 2111, Charlottesville, VA 22908 (ccm5u@virginia.edu).
Clinical Infectious Diseases 2008;46:215–22
© 2007 by the Infectious Diseases Society of America. All rights reserved. 1058-4838/2008/4602-0010$15.00 DOI: 10.1086/524665

Lactate Predicts Sepsis Mortality in Uganda • CID 2008:46 (15 January) • 215
Table 1. Demographic characteristics and outcomes of the study population.

<table>
<thead>
<tr>
<th>Characteristic or outcome</th>
<th>Value</th>
<th>No. of patients with data available</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean years ± SD</td>
<td>35.7 ± 11.4</td>
<td>72</td>
</tr>
<tr>
<td>Sex, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>38.9</td>
<td>72</td>
</tr>
<tr>
<td>Women</td>
<td>61.1</td>
<td>72</td>
</tr>
<tr>
<td>HIV-1 prevalence, %</td>
<td>81.9</td>
<td>72</td>
</tr>
<tr>
<td>ARVs prescribed, %</td>
<td>13.9</td>
<td>72</td>
</tr>
<tr>
<td>CD4 lymphocyte count, mean lymphocytes/mm³ ± SD</td>
<td>88.6 ± 133.0</td>
<td>59</td>
</tr>
<tr>
<td>SIRS criteria at hospital admission, mean ± SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temperature, °C</td>
<td>37.5 ± 1.5</td>
<td>72</td>
</tr>
<tr>
<td>Heart rate, beats per min</td>
<td>123.1 ± 22.2</td>
<td>72</td>
</tr>
<tr>
<td>Respiratory rate, breaths per min</td>
<td>37.5 ± 13.7</td>
<td>72</td>
</tr>
<tr>
<td>WBC count, cells/mm³</td>
<td>7747.1 ± 7547.9</td>
<td>72</td>
</tr>
<tr>
<td>Blood pressure at hospital admission, mean mm Hg ± SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>79.0 ± 17.5</td>
<td>71</td>
</tr>
<tr>
<td>Diastolic</td>
<td>48.0 ± 20.7</td>
<td>70</td>
</tr>
<tr>
<td>Bicarbonate concentration, mean mmol/L ± SD</td>
<td>21.4 ± 1.6</td>
<td>72</td>
</tr>
<tr>
<td>Received fluid prior to hospital admission, %</td>
<td>6.9</td>
<td>72</td>
</tr>
<tr>
<td>Mortality, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In hospital</td>
<td>25.7</td>
<td>70</td>
</tr>
<tr>
<td>30-Day</td>
<td>27.3</td>
<td>44</td>
</tr>
<tr>
<td>Total</td>
<td>41.6</td>
<td>72</td>
</tr>
<tr>
<td>Days of hospitalization, mean ± SD</td>
<td>6.9 ± 5.42</td>
<td>70</td>
</tr>
</tbody>
</table>

NOTE. ARVs, antiretroviral medicines; SIRS, systemic inflammatory response syndrome.

Lactate concentration—along with mixed venous oxygen saturation, base deficit, and pH—is used to guide early goal-directed therapy of sepsis [13]. Early goal-directed therapy employs fluid resuscitation, vasopressors, and blood transfusion to maximize oxygen delivery to distal tissues. A study of early goal-directed therapy reduced in-hospital mortality of patients admitted with sepsis by 16%, from 46.5% to 30.5%, but this therapeutic strategy relies on expensive laboratory assays [13]. Unfortunately, these technologies are not available in most of sub-Saharan Africa. This resource constraint may lead to increased mortality of patients with sepsis. Therefore, the primary goal of this study was to determine whether a hand-held portable whole-blood lactate (PWBL) analyzer could predict mortality of patients with severe sepsis; the secondary goal was to compare results of PWBL analysis with those of available standard laboratory serum lactate (SLSL) analysis in a resource-limited setting.

METHODS

Patient recruitment. We enrolled 253 patients to study the incidence, management, and outcomes of patients with severe sepsis in a resource-limited setting; within this group, the PWBL concentration was measured consecutively in the first and last 50 patients enrolled. Complete data were available for 72 patients. Consent was obtained from each patient or his or her guardian.

Patients were recruited from the accident and emergency department of Mulago Hospital, a national referral hospital in Kampala, Uganda. Inclusion criteria were age ≥18 years and admission to a medical ward, along with (1) ≥2 systemic inflammatory response syndrome criteria (body temperature >38°C or <36°C; heart rate, >90 beats/min; respiratory rate, >20 breaths/min; or peripheral WBC concentration, >12,000 cells/mm³ or <4000 cells/mm³) or thermodysregulation, (2) systolic blood pressure ≤100 mm Hg, and (3) a suspected infection. Exclusion criteria included acute cerebrovascular events, gastrointestinal hemorrhage, or admission to the surgical or obstetrics and gynecology ward.

Table 2. Prescribed antiretroviral regimens.

<table>
<thead>
<tr>
<th>Antiretroviral regimen</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zidovudine, lamivudine, and efavirenz</td>
<td>3</td>
</tr>
<tr>
<td>Stavudine, lamivudine, and efavirenz</td>
<td>2</td>
</tr>
<tr>
<td>Stavudine, lamivudine, and nevirapine</td>
<td>2</td>
</tr>
<tr>
<td>Zidovudine, stavudine, and nevirapine</td>
<td>1</td>
</tr>
<tr>
<td>Tenofovir, emtricitabine, and efavirenz</td>
<td>1</td>
</tr>
<tr>
<td>Tenofovir, emtricitabine, and lopinavir-ritonavir</td>
<td>1</td>
</tr>
</tbody>
</table>
Figure 1. Histogram of portable whole-blood lactate (PWBL) concentrations of patients who survived in the hospital, compared with PWBL concentrations of patients who died while in the hospital.

Data collection. Background information—including age, sex, HIV-1 serostatus, and prescribed antiretroviral medicines (ARVs)—was recorded. At enrollment, temperature, heart rate, respiratory rate, and blood pressure were measured. The study team observed patients throughout their hospitalizations, but the admitting medical team was responsible for clinical management. To determine outpatient survival, an attempt was made to telephone patients 30 days after their discharge from the hospital.

Laboratory evaluation. A rapid HIV-1 test and malaria smear were performed at Mulago Hospital. A local private clinical laboratory provided results of lactate and bicarbonate analysis. PWBL was obtained by using a lancet to collect a drop of whole blood from the patient’s finger, for analysis by a handheld portable device (Accutrend Portable Lactate Analyzer; Sports Resource Group). This instrument uses enzymatic determination and reflectance photometry of lactate in the plasma portion of whole blood by use of a measurement strip. Results are available within 60 s of blood application. SLSL concentration was obtained by phlebotomy for venous blood samples. Because of hypotension in this study population, a tourniquet was required. Within 2 h of sample collection, the sample was transported in a standard serum tube via a cooler to the clinical laboratory, where blood was centrifuged and serum was removed for use in the lactate assay (Diagnostic Systems International). Because of discrepancies between PWBL and SLSL, clinical laboratory procedures were reviewed. A subset of patients also had a portable serum lactate (PSL) evaluation by an additional hand-held portable lactate analyzer at the time of evaluation of SLSL. At all times, the clinical laboratory personnel were blind to PWBL results. Once values were known, all laboratory results were provided to the patients’ medical team.

Statistical analysis. Data were entered into an EpilInfo database (Centers for Disease Control and Prevention) and were analyzed using SPSS software (SPSS). Descriptive statistics were reported as mean ± SD for all continuous variables, and frequency was reported for all categorical variables. The Student’s paired sample t test and Levine’s test for equality of variance were used to compare mean differences between patient test results. The Wilcoxon signed rank test was applied when distribution assumptions were not met for Student’s paired t test. Statistical significance was defined as P < .05. Results of different lactate tools were compared by plotted mean differences, with limits of agreement (defined as mean difference ± 2 SD) with averaged test score, as recommended by Bland and Altman [14]. Pearson correlations and linear regression were used to describe the strength of the linear relationship between variables. The predictive power of lactate tests for the bivariate mortality outcome variables was assessed using multivariate logistic regression. Covariates were included in the multivariate logistic regression model if they met a P ≤ .20 inclusion criteria.
Figure 2. Bar graph comparing in-hospital mortality (means and SDs) of patients with different portable whole-blood lactate (PWBL) concentrations, with use of Student’s t test.

The receiver operating characteristic (ROC) area under the curve for lactate concentration assessed overall accuracy in mortality prediction. Cutoff lactate concentrations were set and then used to quantitatively calculate sensitivity and specificity in prediction of mortality. The lactate cutoff with the maximum sum of sensitivity and specificity for predicting mortality was reported as the curve inflexion point. ORs were also reported to compare risk of death associated with lactate categories by test type.

Ethical considerations. Approval was obtained from the University of Virginia Institutional Review Board (Charlottesville), Mulago Hospital Office of Director, Makerere University Faculty of Medicine Research Ethics Committee and Infectious Disease Institute Scientific Research Committee (Kampala, Uganda), and Uganda National Council of Science and Technology (Kampala, Uganda).

RESULTS

Patient characteristics and outcomes. The demographic characteristics and outcomes of the study sample are described in table 1. These 72 patients were similar to the larger study population in age (mean age, 35.7 vs. 33.8 years), sex (61.1% vs. 59.1% female), HIV-1 seropositivity (81.9% vs. 86.6%), and ARV status (13.9% vs. 10.6% ARVs prescribed) (table 2). The overall in-hospital mortality rate was 25.7% (18 of 70); 2 patients were lost to follow-up, compared with 24.5% (61 of 249) for the larger group. Follow-up information was available at 30 days for 44 of 52 discharged patients. From this group, 12 (27.3%) of 44 patients died. Complete information was unavailable for 10 enrolled patients, so the total in- and outpatient mortality at 30 days was, at minimum, 41.6% (30 of 72) versus 37.9% for the larger group. None of these differences were statistically significant. Six (8.3%) of 72 patients had malaria parasitemia, of whom none had high-grade 4+ parasitemia.

Lactate concentration and mortality. An independent samples t test comparing PWBL results with in-hospital survival revealed significantly lower PWBL concentrations among survivors (mean ± SD, 3.4 ± 1.5 mmol/L) compared with those who died (mean ± SD, 6.8 ± 4.2 mmol/L; P < .001). Levine’s test for equality of variance showed that PWBL variance was not significantly different between survivors and nonsurvivors. Because of the relatively small sample size, the more-conservative nonparametric Wilcoxon rank sum test was applied and also showed a significant difference in PWBL between survivors and nonsurvivors (P < .001). An ROC value indicated good utility of PWBL for predicting in-hospital mortality (ROC area under the curve, 0.81; 95% CI, 0.71–0.92; P < .001).

Figures 1 and 2 show the frequency and proportion of in-hospital death, as measured by PWBL concentration. A PWBL concentration of 2.6 mmol/L provided very high sensitivity (100%) but low specificity (40.4%) for in-hospital mortality. The ROC curve inflexion point showed that a PWBL concentration of 4.0 mmol/L provides optimal sensitivity (88.3%) and specificity (71.2%) for in-hospital mortality (figure 3). Patients with a PWBL concentration ≥4.0 mmol/L died while hospitalized significantly more often (50.0%) than did those with a PWBL concentration <4.0 mmol/L (7.5%) (OR, 12.3; 95% CI, 3.5–48.9; P < .001).

Figure 3. Receiver operating characteristic curve, with sensitivity on the y-axis and 1–specificity on the x-axis, for prediction of in-hospital mortality on the basis of different portable whole-blood lactate (PWBL) concentrations.
Figure 4. Bland and Altman plots of portable whole blood lactate (PWBL) and standard laboratory serum lactate (SLSL) concentrations (n = 39)

An independent samples t test comparing SLSL results with in-hospital survival revealed significantly lower results for survivors (mean ± SD, 2.1 ± 1.1 mmol/L), compared with non-survivors (mean ± SD, 3.2 ± 2.7 mmol/L; P = .021). The ROC area under the curve for SLSL as a predictor of in-hospital mortality was 0.72 (P = .004). The curve inflexion point showed that a SLSL concentration of 2.0 mmol/L provided optimal sensitivity (77.7%) and specificity (67.3%) for predicting in-hospital mortality. Patients with a SLSL concentration ≥ 2.0 mmol/L died while hospitalized significantly more often (14 [40.0%] of 35 patients) than did those with a SLSL concentration <2.0 mmol/L (4 [11.4%] of 11 patients) (OR, 5.2; 95% CI, 1.5–17.8; P = .004).

To directly compare PWBL and SLSL concentrations in predicting in-hospital mortality, we constructed a 2-step multiple logistic regression model. Mortality prediction power of SLSL was equally poor before and after review of laboratory procedures (Nagelkerke pseudo $R^2 = 0.12$). Step 1 of the model included only SLSL, whereas step 2 included both SLSL and PWBL. In step 1, SLSL concentration was a significant predictor of in-hospital mortality (SLSL ≥ 2.0 mmol/L; OR, 5.2; 95% CI, 1.5–17.9; P = .012). In step 2, entry of PWBL concentration (>4.0 mmol/L; OR, 9.5; 95% CI 2.0–46.7; P < .001) entirely accounted for the predictive utility of SLSL (≥ 2.0 mmol/L, OR, 1.60; 95% CI, 0.34–7.5; P = .65). All predictive value of PWBL for 30-day survival was accounted for by in-hospital mortality. The 12 patients who died after hospital discharge were equally likely to have had a high (≥2.6 mmol/L) or low (<2.6 mmol/L) PWBL concentration at the time of enrollment (30.8% vs. 23.5%; OR, 1.4; P = .74). SLSL concentration was similarly unrelated to 30-day survival.

Lactate concentration, clinical and laboratory evaluation, and mortality. At enrollment, mean systolic blood pressure was 79 mm Hg (range, 40–100 mm Hg), and mean diastolic blood pressure was 48 mm Hg (range, 20–72 mm Hg). Only 5 of 72 patients received intravenous fluids before blood pressure measurement. PWBL results were significantly negatively correlated with patients’ systolic blood pressure ($r = -0.36$; $P = .01$) and diastolic blood pressure ($r = -0.35$; $P = .01$). Mean bicarbonate concentration was 21.4 mmol/L (range, 8–28 mmol/L). There was a small statistically significant negative correlation between bicarbonate and PWBL concentrations ($r = -0.33$; $P = .035$) among all 72 patients. This correlation is higher among patients whose bicarbonate data were collected after the laboratory review ($r = -0.50$; $P < .001$). PWBL was related to neither HIV-1 infection nor ARV status. Patients who received treatment with stavudine-containing regimens had statistically insignificant elevated PWBL concentrations ($n = 5$; 6.4 mmol/L), compared with patients who received non stavudine-containing regimens ($n = 5$; 3.3 mmol/L; $P = .34$). There was no relationship between in-hospital or 30-day survival and patient age, HIV-1 status, ARV status, systolic or diastolic blood pressure, or bicarbonate concentration, with use of a criterion of $P < .20$.

Men were at higher risk of in-hospital death than were women (40.7% vs. 16.3%; OR, 3.5; 95% CI, 1.2–10.8; $P =$...
.024) and had elevated PWBL concentrations, compared with those of women. Sex was included in a multiple logistic regression equation to obtain an adjusted estimate of PWBL concentration as a predictor of in-hospital mortality. The model, including patient sex, showed that patients with PWBL concentrations $\geq 4.0$ mmol/L remained at a substantially increased risk of death (OR, 12.1; 95 CI, 2.9–49.7; $P = .034$). No additional health status indicators were included in the equation, because they were not significantly independently related to mortality.

**Test comparisons.** PWBL and SLSL tests were initially completed for 39 patients. There was a small but significant linear correspondence between test results ($R^2 = 0.23; P = .002$). A Student’s paired-sample $t$ test showed that SLSL concentrations (range, 0.90–3.23 mmol/L) were statistically significantly lower than PWBL concentrations (range, 1.6–17.8 mmol/L) (mean difference, $-2.48$ mmol/L; limits of agreement, 2 SD $\pm$ 5.89 mmol/L; $P < .001$). Figure 4 shows a Bland-Altman analysis of mean difference, with limits of agreement plotted against averaged level (average as measured by both methods). Lactate test differences were highly linearly related ($R^2 = 0.89; P < .001$) to average level of lactate, indicating greater discrepancies at higher lactate concentrations.

Because of these discrepancies, we requested that the laboratory review its procedures and conduct a second set of SLSL tests on 33 more patients. No changes were made in collection or transport of patient blood to the laboratory, and no changes were made in PWBL collection conditions and methods. No specific cause of inaccuracy of SLSL was elucidated. After laboratory review, linear regression of PWBL on SLSL showed closer correspondence of test results ($R^2 = 0.77; P = .007$). The range of test results was similar for SLSL (range, 1.0–13.01) and PWBL (range, 1.6–14.0), but a paired-sample $t$ test revealed that SLSL results remained statistically significantly lower than PWBL results (mean difference, $-1.25$ mmol/L; limits of agreement, 2 SD $\pm$ 2.36 mmol/L; $P < .001$).

A comparison of 33 PSL and PWBL results showed a strong positive linear relationship ($R^2 = 0.80; P < .001$). A paired-sample $t$ test showed that PSL results remained slightly but statistically significantly lower than those of the PWBL (mean difference, $-0.59$ mmol/L; limits of agreement, 2 SD $\pm$ 2.36 mmol/L; $P = .007$). In addition, we compared SLSL with PSL, and we noted a stronger linear relationship ($R^2 = 0.97; P < .001$). A paired-sample $t$ test showed that PSL results were significantly higher than SLSL results (mean difference, 0.66 mmol/L; limits of agreement, 2 SD $\pm$ 1.34 mmol/L; $P < .001$).

**DISCUSSION**

This study of lactate level as a mortality prediction tool for patients with severe sepsis is unique, because we evaluated a predominantly HIV-1–infected patient population in a resource-limited setting. For the first time, we have shown that a hand-held PWBL analyzer is capable of predicting mortality of patients with severe sepsis or septic shock. The instrument can be used quickly and easily by auxiliary medical personnel, who are often at the forefront of care in regions where trained physicians, nurses, and laboratory personnel are scarce [15]. The same instrument has been used in resource-limited settings to evaluate lactic acidosis precipitated by use of ARVs [16].

We found that a PWBL concentration of 2.6 mmol/L was the most sensitive (100%) marker for mortality, because no patient with PWBL $< 2.6$ mmol/L at hospital admission died while in the hospital. However, the low specificity of this value (40.4%) for mortality makes it a poor clinical indicator. Our assessment of the optimal cutoff value for PWBL agrees with those of SLSL studies that 4.0 mmol/L offers the best combined sensitivity (88.3%) and specificity (71.2%) for mortality and should be used in the clinical assessment of septic patients [10, 11, 13]. In our study, the finding of a PWBL concentration $\geq 4.0$ mmol/L meant that the patient had a 7-fold greater chance of dying in the hospital, compared with a value $< 4.0$ mmol/L. Similar to SLSL studies, PWBL outperformed blood pressure assessment and bicarbonate concentration in predicting mortality [13, 17]. We found no significant association between the use of ARVs (including stavudine) and elevated PWBL concentration.

Although PWBL concentration accurately predicted in-hospital mortality, there was no independent association between lactatemia and death at 30 days. This is, perhaps, related to the 82% HIV-1 seropositivity rate of our study population. Not only are HIV-1–infected patients predisposed to bacteremia and, therefore, sepsis, but they are also more likely to contract opportunistic infections and harbor chronic illnesses that cause early mortality. It is also possible that irreparable physiologic harm leads to delayed death, even after recovery from acute sepsis.

Other studies have documented excellent intra-assay precision and strong linear association between PWBL and SLSL [18–20]. One study found that use of PWBL analysis was the cheapest and fastest option, when compared with a bench-top lactate analyzer and SLSL [20]. In our study, PWBL served as a quality assurance tool by identifying SLSL inconsistency. SLSL results improved after a review of laboratory procedures but still remained lower overall than PWBL results. We avoided bias by having laboratory personnel blind to PWBL results. Because association was highest between PSL and SLSL, we suggest that both whole blood and serum can be effectively evaluated by the hand-held lactate analyzer. Although SLSL was somewhat predictive of mortality, PWBL had a better sensitivity (88.3% vs. 77.7%) and specificity (71.2% vs. 67.3%) for mortality and an improved predictive value when compared with...
Lactate Predicts Sepsis Mortality in Uganda • CID 2008;46 (15 January) • 221

SLSL (81% vs. 72%). Although PWBL was a good predictor of in-hospital mortality within this sample, larger studies should be conducted to verify this finding and to examine its use in determining the extent of fluid resuscitation in resource-limited settings.

The lack of reliable laboratory diagnostic testing in resource-limited settings often leads to clinical misdiagnosis [2]. A frequently cited example of this phenomenon is the overdiagnosis of malaria in febrile patients, which often occurs to the exclusion of other diagnoses, notably bacteraemia [21–23]. Six (8.3%) of the patients in our study had malaria parasitemia, of whom none had high-grade 4+ parasitemia, which leads us to believe that patients had sepsis due to infections other than malaria.

The reasons for misdiagnoses are multifactorial but include a lack of both human and material resources. Additionally, as with SLSL in our study, diagnostic inaccuracy can still exist, despite the presence of laboratory equipment [24]. Experts have suggested prioritizing provision of basic accurate laboratory testing in resource-limited settings that should (1) be performed on site in rural primary health care settings, (2) require minimal sample preparation or preservation, (3) be kit based, and (4) be able to be performed with little technical expertise [2]. The use of PWBL concentration in the assessment of septic patients meets this 4-pronged approach to laboratory evaluation.

The World Health Organization promotes clinical treatment algorithms through the Integrated Management of Adult and Adolescent Illness guidelines [25]. PWBL testing can quickly identify patients who require immediate interventions and should be included in evaluation and treatment algorithms for septic patients. PWBL testing could be used in village health posts, for earlier transfer of septic patients to facilities with a higher level of care, and in referral hospitals, for triage of patients to acute care settings where appropriate resuscitation can begin. Therefore, we suggest that PWBL testing be made an important priority for the diagnosis and treatment of severely ill patients in resource-limited settings where the lack of laboratory infrastructure and reliability is a barrier to patient care.

Acknowledgments

We thank the nurses and staff of Mulago Accident and Emergency Department for their assistance in the enrollment of patients for the study and overall dedication to the care of patients at Mulago Hospital. In addition, we are especially grateful to members of the Ugandan sepsis study team—including Dr. Angelo Nganizi, Dr. Kasoji Kimuli, Dr. Cassim Kalisa, and Mr. Samson Omongot—for their dedication and hard work during the study.

Financial support. This study was supported, in part, by the Division of Intramural Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health. C.C.M. and S.T.J. received fellowships from the Pfizer Initiative in International Health at the University of Virginia to support this work. This Initiative was conceived to fund exchange programs of postdoctoral fellows and students between the University of Virginia and several international partners, to conduct research on global health issues. The major purpose of this program is to foster and enhance bidirectional research training. An independent board at the University of Virginia determines which research proposals are funded. Pfizer provided funds to promote the Initiative but has no role in the planning or execution of research protocols, including the study described in our article.

Potential conflicts of interest. W.M.S. serves on the anti-infective advisory board of Pfizer. C.C.M. and S.T.J. received support from fellowships from the Pfizer Initiative in International Health at the University of Virginia. All other authors: no conflicts.

References

9. Rangel-Frausto MS, Pittet D, Costigan M, Hwang T, Davis CS, Wenzel W.M.S. serves on the anti-infective ad-
10. Aduen J, Bernstein WK, Khastgir T, et al. The use and clinical im-