Blood Culture Contamination in Tanzania, Malawi, and the United States: A Microbiological Tale of Three Cities

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ABSTRACT

We conducted retrospective, comparative analyses of contamination rates for blood cultures obtained in the emergency rooms of Muhimbili National Hospital (MNH), Tanzania, Lilongwe Central Hospital (LCH), Malawi, and Duke University Medical Center (DUMC) in the United States. None of these emergency room patients had indwelling intravascular devices at the time the blood cultures were obtained. In addition, we reviewed the contamination rates for a cohort of patients already hospitalized in the DUMC inpatient medical service, most of whom had indwelling intravascular devices. Bloodstream infection rates among MNH (n=513) and LCH (n=486) patients were similar (~28%); contamination rates were 1.3% (7/513) and 0.8% (4/486), respectively. Of 54 microorganisms isolated from DUMC emergency room blood cultures, 26 (48%) were skin contaminants. DUMC emergency room blood cultures were significantly more likely to be contaminated than MNH and LCH emergency room cultures combined (26/332 vs. 11/1003, p <0.0001) or DUMC medical service inpatient cultures (26/332 vs. 7/283, p <0.01).

For MNH and LCH blood cultures, lower contamination rates were observed when skin was disinfected with isopropyl alcohol plus tincture of iodine rather than isopropyl alcohol plus povidone-iodine. In conclusion, blood culture contamination was minimized in sub-Saharan African hospitals with substantially limited resources through scrupulous attention to aseptic skin cleansing and improved venipuncture techniques. Application of these principles to performing blood cultures in United States hospital emergency rooms should help mitigate blood culture contamination rates and unnecessary microbiology work-up of skin contaminants.

Keywords: blood cultures, bloodstream infections, contamination, developing countries, microbiology
BACKGROUND

A study by Washington and the International Collaborative Blood Culture Study Group showed that the number of blood cultures per hospital admission ordered by physicians in the United States exceeds the number ordered by their colleagues abroad by a margin as much as two-fold to ten-fold [26]. In a subsequent editorial [22], Reller posted the question: do physicians in the United States perform too many blood cultures, or do physicians in other countries perform too few? Although published data from hospitals in the United States suggest that this laboratory investigation is used in excess of need or inappropriately in hospitalized patients [15, 24], blood cultures are considered the “gold standard” for detecting bloodstream pathogens and it is therefore more likely that too few blood cultures are performed in less developed settings. In fact, during the past decade, various studies have documented the increasing importance of bloodstream infections in teaching hospitals in sub-Saharan Africa [5, 6, 11, 25]. Although limited financial and human resources often preclude routine blood culture services at many of the large medical facilities in these regions, several reports from sub-Saharan Africa have highlighted the increased occurrence and clinical significance of coagulase-negative staphylococcus bacteremia [1, 2, 8, 13, 14, 17, 18, 19, 21]. This is of concern since blood culture contamination with coagulase-negative staphylococcus remains a perennial problem in developed countries and has enormous implications for less-developed countries, where costs associated with maintaining microbiology laboratories are already prohibitive. With these concerns in mind, we conducted this analytic study to characterize blood culture contamination in two African teaching hospitals and a large tertiary care medical center in the United States.
MATERIALS AND METHODS

Patients and blood culture methods. We conducted retrospective reviews of blood culture data from Muhimbili National Hospital (MNH), a teaching hospital located in Dar es Salaam, Tanzania, Lilongwe Central Hospital (LCH), a large government regional medical center in central Malawi, and Duke University Medical Center (DUMC), a 900-bed tertiary care center in Durham, North Carolina, USA. Both African hospitals have >1000 beds and provide services to patient catchment areas of >2.0 million citizens.

The MNH and LCH blood cultures were obtained during 1995-1998 as part of formal studies of bloodstream infections in febrile adults admitted via the emergency room to the medical inpatient services of both of these institutions (5, 11). All blood specimens obtained from the Tanzania and Malawi patients were drawn through a single venipuncture at the time of initial clinical evaluation in the emergency room; none of these patients had any in situ intravascular devices at the time of blood draw.

The DUMC blood culture data that we reviewed fell into two categories: the first comprised blood cultures performed for patients when they were initially seen in the DUMC emergency room, and who were subsequently admitted to the two general medicine inpatient wards during February through April 1995 (the same period as the Tanzania blood cultures). None of the DUMC emergency room patients had in situ intravascular devices at the time blood was drawn for culture. The second category consisted of blood cultures obtained for patients who were already hospitalized in the two DUMC general medicine wards; these patients invariably had in situ intravascular devices. DUMC blood cultures performed in the emergency room were routine and did not constitute part of any of the formal blood culture studies that were already in progress at DUMC. In contrast, the blood cultures performed in the DUMC general
medicine inpatient wards were obtained according to the working protocol of formal ongoing
evaluation studies of various blood culture systems that were in progress in DUMC at that time.

The blood culture methodology used at MNH and LCH has been previously described, and included lysis and centrifugation of blood collected in an Isolator tube (Wampole Laboratories, Cranbury, NJ), the Septi-Chek™ biphasic blood culture bottle (Becton Dickinson Microbiology Systems [BDMS], Cockeysville, MD), and the BACTEC™ MYCO/F LYTIC blood culture bottle (BDMS) [3, 4]. During the same period, DUMC used the BACTEC 9000 (BDMS) blood culture system for detecting bacteremia and fungemia and the BACTEC 460 (BDMS) system in conjunction with BACTEC 13A bottles (BDMS) for mycobacteremia.

Skin disinfection. For Tanzanian patients, the venipuncture site was disinfected with 70% isopropyl alcohol followed by povidone-iodine; for Malawian patients, skin disinfection was carried out with locally obtained 70% isopropyl alcohol followed by 1-2% tincture of iodine, also locally obtained. For patients in Tanzania and Malawi, the skin disinfectant was allowed to dry for 1-2 minutes before venesection.

Generally, 70% isopropyl alcohol was used for skin disinfection in DUMC emergency room patients; however, we were not able to ascertain how scrupulously the skin was disinfected or the time allowed for skin to dry. Blood cultures for DUMC general medicine inpatients were performed according to the working protocol for the blood culture studies then in progress—i.e., skin disinfection with 70% isopropyl alcohol plus povidone-iodine.

Definitions. One blood culture set consisted of blood from a single venipuncture, regardless of the number of blood culture bottles inoculated. Each MNH and LCH patient had blood drawn
primarily from the antecubital fossa of patients by one of the authors (LKA). It was not possible
to ascertain who drew the blood or the site of venipuncture in DUMC patients. For patients
admitted via the MNH, LCH, and DUMC emergency rooms, we defined a true positive blood
culture as growth of any microorganism (i.e., bacteria, mycobacteria, or fungi) with the
exception of coagulase-negative staphylococcus, *Propionibacterium* spp., *Micrococcus* spp., or
*Corynebacterium* spp., which were classified as contaminants, based on the findings of seminal
studies that have established these microorganisms as common blood culture contaminants rather
than significant causes of community-acquired bacteremia [27, 29, 30, 31]. For DUMC
inpatients with in situ intravascular devices, growth of coagulase-negative staphylococcus in
blood cultures was deemed clinically significant if and only if the organism was isolated from
two or more consecutive sets of blood cultures [27, 29, 30, 31]. In 1997, Weinstein et al.
correlated microbiology data with detailed medical chart and clinical reviews and showed that
one positive culture result for coagulase-negative staphylococcus of only one set taken has a
97.1% likelihood of being a contaminant [30]. On this basis, we defined growth of coagulase-
negative staphylococcus from a single set of blood cultures drawn as contamination.

**Data analysis.** All data were analyzed using Epi Info computer software (Version 6.04, 2001.
Centers for Disease and Prevention, Atlanta, GA). Groups were compared using the Chi square
or Fisher’s exact test, where appropriate. Relative risks (RR) and 95% confidence intervals (CI)
were calculated.
RESULTS

Tanzania and Malawi: MNH and LCH. At MNH, 517 patients had blood cultures performed during the study period. Of these 517 single blood cultures, 145 (28%) grew 155 clinically important organisms (5). For LCH, a total of 486 single blood cultures were obtained; the predominant bloodstream pathogens were similar to Tanzania [3, 4, 6, 11]. The clinical, epidemiologic, and microbiologic significance of the positive blood cultures for patients in both countries have been described previously [5, 6, 11]. Of the 517 MNH blood cultures, 7 (1.3%) yielded organisms that were considered contaminants: three *Staphylococcus epidermidis*, two diphtheroids, one *Micrococcus* sp., and one *Bacillus cereus*. Four (0.8%) of the 486 LCH blood cultures yielded contaminants: two *S. epidermidis*, one *Micrococcus* sp., and one diphtheroid.

United States: DUMC—patients admitted via the emergency room. During the study period, 483 patients were admitted consecutively to the two DUMC general medical wards; 314 (65%) of these patients were admitted from the community via the DUMC emergency room. Of these 314 patients, 176 (56%) had blood drawn for culture whilst they were in the emergency room. Although there were no established or consistently documented criteria for obtaining blood cultures in the DUMC emergency room, microbiology records suggest that some blood cultures were requested because of a patient history of “fever” or a clinical suspicion of deep underlying infection. However, not all DUMC patients who had blood cultures necessarily had fever. Of the 176 patients who had blood drawn for culture in the emergency room, 29 (16%) had one set of blood cultures, 140 (79.5%) patients had two sets, 5 patients had 3 sets, and 2 patients had 4 sets. Thus, there were 332 separate blood draws in the emergency room, all for detection of bacteremia. Of 54 cultures that were positive for bacterial growth, 26 (48%) yielded bacterial
contaminants (Table 1); the overall contamination rate was 7.8% (26/332). The true blood
culture positivity rate was therefore 28/332 (8.4%) and represented blood cultures from 14
patients. Thus, the bloodstream infection rate among those patients for whom blood cultures
were requested, and who were admitted directly to the DUMC general medical wards from the
emergency room was 14/176 (8.0%). All 14 patients had at least 2 sets of blood cultures.

United States: DUMC patients already hospitalized in the general medical wards. During
the study period, another 297 blood cultures were obtained for 115 patients who were already on
the two DUMC general medical wards. The criteria for obtaining blood cultures for most of
these patients remain unknown but included clinical suspicion of sepsis, fever, failed treatment,
or “routine”. These 297 inpatient blood cultures included 283 (95.3%) for bacteria, 8 (2.7%) for
fungi, and 6 (2%) for mycobacteria. Of these 115 patients, 30 (26%) had one set of blood
cultures, 52 (45%) had two sets, 15 (13%) had three sets, 9 (8%) had four sets and 9 (8%) had >4
sets (median: 2 sets; range: 1-11 sets). Positivity rates for the various types of blood cultures
were as follows: 24/283 (8.5%) for bacterial blood cultures; 1/8 (12.5%) for fungal blood
cultures; and 0/6 for mycobacterial blood cultures. Of the 24 cultures that were positive for
bacterial growth, 7 (29%) yielded bacterial contaminants: *S. epidermidis* (six isolates) and
*Propionibacterium* sp. (one isolate). These 7 isolates were deemed probable contaminants
because they each had been isolated from a single set of blood cultures. Hence, the true bacterial
blood culture positivity rate was 17/283 (6.0%) and represented blood cultures for 9 inpatients.
Thirty-three (12%) of the 283 bacterial cultures were obtained for these 9 patients, i.e., 3.7 blood
cultures per patient (Table 2); the remaining 106 patients had 250 cultures, or 2.3 cultures per
patient. The overall bloodstream infection rate for DUMC medical inpatients was 9/115 (7.8%).
Comparison of blood culture contamination. DUMC emergency room patients were significantly more likely to have contaminated blood cultures than MNH Tanzanian and LCH Malawi emergency room patients combined (26/332 vs. 11/1003; RR: 7.1, CI: 3.6-14.3; p <0.0001) or DUMC general medicine inpatients (26/332 vs. 7/283; RR: 3.2, CI: 1.4-7.2; p <0.01). In the two African hospitals, the blood culture contamination rate with povidone-iodine skin cleansing was almost twice the contamination rate when tincture of iodine was used; this difference, however, was not statistically significant (7/517 vs. 4/486, RR: 1.7, CI: 0.5-5.6; p=0.42).


DISCUSSION

Our analyses compare and contrast blood culture contamination rates in large general hospitals in Tanzania and Malawi with rates in a prominent university teaching hospital in the United States. For hospitals both in less-developed countries and in the United States, there are lessons to be learnt from the results of these comparative analyses: (i) coagulase-negative staphylococcus remains an uncommon cause of community-acquired bloodstream infections in adult patients without intravascular devices; and (ii) blood culture contamination rates can be minimized in both these settings through attention to basic aseptic and blood drawing techniques.

For DUMC inpatients, the true positive blood culture and contamination rates were 6.0% and 2.5%, respectively; these findings are consistent with those reported by Weinstein et al. when they studied >10,000 blood cultures and documented true blood culture and contamination rates of 8.1% and 2.3%, respectively [29]. In contrast, the contamination rate of blood cultures performed in the DUMC emergency room was inordinately high (7.8%) and likely reflect less scrupulous methods or attention to aseptic technique when obtaining blood cultures in the emergency setting or during medical crises.

Our finding that approximately half of the positive blood cultures performed in the DUMC emergency room and one-third performed in the DUMC inpatient medical service yielded contaminants are consistent with previously published data that suggest contaminated blood cultures represent about half of all positive blood cultures [7, 16, 28, 29]. Underlying reasons for such contamination include limited staff having to cope with high patient census or multiple emergencies and having to hurry the drawing of blood cultures, varying techniques of drawing blood and inoculating bottles, or unawareness among healthcare personnel of established guidelines for drawing blood cultures [23]. Contamination may be costly to hospitals
in the United States, where incorrect diagnoses based on contaminated blood cultures have been shown to be associated with a per patient median of over $4000 in excess charges, >4 days of excess hospitalization, and substantially increased resource utilization, including laboratory charges [9].

The low blood culture contamination rates in the African hospitals were achieved simply by maintaining meticulous aseptic standards before and during venipuncture, using both alcohol and tincture of iodine (or povidone-iodine) for skin cleansing and allowing the skin to dry properly before venipuncture, and by scrupulously cleaning the rubber diaphragms of blood culture bottles and Isolator tubes with isopropyl alcohol before inoculation with blood or each time that the bottles or Isolator tubes were accessed with a needle. Low blood culture contamination rates were feasible in hospitals with limited resources in less-developed countries and therefore should be achievable, with concerted effort, in tertiary-care hospitals in the United States.

The persisting problem of contamination of blood cultures, reviewed relatively recently by Weinstein [31], has implications for both patient care and laboratory services in developed and less-developed countries. For patients, blood culture contamination results in need for even more cultures, other diagnostic tests, and unnecessary antimicrobial therapy; for the laboratory, comprehensive workup of contaminant isolates adds to the technologist workload and overall healthcare costs [31]. The problem also underscores the difficulty in translating knowledge into practice as has been repeatedly shown by the persisting high blood culture contamination rates and poor hand washing practices in wealthy hospitals in the United States and abroad [10]. With the institution of more critical care facilities in medical centers across Africa, there have been increasing numbers of reports that emphasize the clinical significance of S. epidermidis as a
cause of bacteremia, especially in pediatric populations [2, 12, 18, 20, 21]. Although it is almost
certain that *S. epidermidis* isolated from patients without intravascular devices is likely a result
of blood culture contamination, the significance of this microorganism as a cause of true
bacteremia in patient populations with in situ devices remains uncharacterized in Africa.

Our study had a few limitations: first, *S. epidermidis* was isolated from single sets of
blood cultures drawn from six DUMC inpatients with intravascular devices. Although there
were no chart reviews to determine what proportion of these *S. epidermidis* isolates were
associated with true infections versus contamination, we classified such positive cultures as
contaminants based on work carried out by Weinstein and colleagues in 1997 [30]. In that study,
they showed through detailed reviews of medical charts and microbiology records that one
positive culture result of one set of blood cultures performed has a 97.1% probability of being a
contaminant. If indeed one or more of the six single blood cultures positive for *S. epidermidis*
were truly clinically significant, then the blood culture contamination rate among the DUMC
inpatients might have been over estimated. However, this would have rendered the difference
between the contamination rates in the DUMC emergency room and inpatients even more
significant. Second, blood cultures obtained for emergency room patients in Tanzania and
Malawi were performed by a single individual in a formal research study setting. In contrast,
DUMC emergency room blood cultures were not part of a formal study, and were carried out by
numerous individuals over the study period. Thus, there might have been an inherent bias
towards lower contamination rates in the African setting due to more care being taken to avoid
blood culture contamination in a formal research setting, and less variability in blood drawing
technique or adherence to basic principles of skin disinfection when compared with the DUMC
emergency room. The question naturally arises—is it feasible to achieve low blood culture
contamination rates in the African setting outside the confines of a formal study? Indeed, following the conclusion of the LCH Malawi study, blood cultures continued as part of routine LCH laboratory services, performed by local clinical officers who had been trained in aseptic and blood drawing techniques during the formal studies. Using just tincture of iodine, these clinical officers achieved even lower contamination rates than the 0.8% rate achieved during the formal research period (these data have not been published).

In conclusion, blood cultures enhanced the diagnostic capabilities of medical microbiology laboratories in sentinel hospitals located in two sub-Saharan African countries. In addition, coagulase-negative staphylococcus remains an uncommon cause of community-acquired bacteremia in adult patients from these regions. Blood culture contamination can be minimized through careful drawing of blood under scrupulous aseptic conditions and skin cleaning with locally available isopropyl alcohol and tincture of iodine preparations. Application of these basic principles to blood culture procurement in intensive care units in less-developed countries may help reduce contamination rates and in so doing help characterize the clinical significance of microorganisms like *S. epidermidis* that are increasingly being documented among patients in critical care units. Finally, we have shown that there is scope for reducing blood culture contamination in United States hospital emergency rooms through better venipuncture and aseptic techniques that were proven effective in settings with substantially less resources.
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antibiotics of 115 staphylococcal strains implicated in septicemia in a Tunisian general


TABLE 1. The most frequent organisms isolated from 332 blood cultures obtained for patients admitted to the general medical inpatient service via the emergency room, Duke University Medical Center.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N=332</strong></td>
<td></td>
</tr>
<tr>
<td>Coagulase-negative <em>Staphylococcus</em> sp.⁹</td>
<td>24 (7.2)</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>15 (4.5)</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>8 (2.4)</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>2 (0.6)</td>
</tr>
<tr>
<td>Group B <em>Streptococcus</em> sp.</td>
<td>2 (0.6)</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>1 (0.3)</td>
</tr>
<tr>
<td><em>Propionibacterium</em> sp.⁹</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Diphtheroids⁹</td>
<td>1 (0.3)</td>
</tr>
</tbody>
</table>

⁹ These organisms were deemed contaminants
TABLE 2. Blood culture profiles of the nine culture-positive patients who were already hospitalized in the general medicine inpatient service, Duke University Medical Center.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Number of blood culture sets&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Number of true positive cultures</th>
<th>Microorganism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient #1</td>
<td>3</td>
<td>1/3</td>
<td><em>Cryptococcus neoformans</em></td>
</tr>
<tr>
<td>Patient #2</td>
<td>4</td>
<td>2/4</td>
<td><em>Escherichia coli</em></td>
</tr>
<tr>
<td>Patient #3</td>
<td>2</td>
<td>2/2</td>
<td><em>E. coli</em></td>
</tr>
<tr>
<td>Patient #4</td>
<td>1</td>
<td>1/1</td>
<td><em>Staphylococcus aureus</em></td>
</tr>
<tr>
<td>Patient #5</td>
<td>10</td>
<td>2/10</td>
<td><em>S. aureus</em></td>
</tr>
<tr>
<td>Patient #6</td>
<td>3</td>
<td>3/3</td>
<td><em>S. aureus</em></td>
</tr>
<tr>
<td>Patient #7</td>
<td>1</td>
<td>1/1</td>
<td><em>C. neoformans</em></td>
</tr>
<tr>
<td>Patient #8</td>
<td>8</td>
<td>5/8</td>
<td>Polymicrobial growth&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Patient #9</td>
<td>1</td>
<td>1/1</td>
<td><em>S. aureus</em></td>
</tr>
</tbody>
</table>

<sup>a</sup> One set = one venipuncture

<sup>b</sup> Organisms included *Alcaligenes xylosoxidans, Enterococcus faecalis, Xanthomonas maltophilia, Candida albicans, and Torulopsis glabrata*