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

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We conducted retrospective, comparative analyses of contamination rates for cultures of blood obtained in the emergency rooms of Muhimbili National Hospital (MNH) in Dar es Salaam, Tanzania; Lilongwe Central Hospital (LCH) in central Malawi; and the Duke University Medical Center (DUMC) in the United States. None of the emergency room patients had indwelling intravascular devices at the time that the blood samples for 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. The bloodstream infection rates among the patients at MNH ($n = 513$) and LCH ($n = 486$) were similar (~28%); the contamination rates at the two hospitals were 1.3% (7/513) and 0.8% (4/486), respectively. Of 54 microorganisms isolated from cultures of blood collected in the DUMC emergency room, 26 (48%) were identified as skin contaminants. Cultures of blood collected in the DUMC emergency room were significantly more likely to yield growth of contaminants than the cultures of blood collected in the emergency rooms at MNH and LCH combined (26/332 versus 11/1,003; $P < 0.0001$) or collected in the DUMC inpatient medical service (26/332 versus 7/283; $P < 0.01$). For the 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 when blood samples for culture are obtained in U.S. hospital emergency rooms should help mitigate blood culture contamination rates and the unnecessary microbiology workup of skin contaminants.

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 of as much as 2- to 10-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 type of laboratory investigation is used in excess of need or inappropriately for hospitalized patients (15, 24), blood cultures are considered the "gold standard" for the detection of 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 the provision of 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 bacteremia caused by coagulase-negative staphylococcus (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 the 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, NC. Both African hospitals have >1,000 beds and provide services to patient catchment areas of >2.0 million citizens.

At MNH and LCH, blood samples for culture were obtained from 1995 to 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 patients in Tanzania and Malawi 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 that their blood was drawn.

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 from February through April 1995 (the same period that the Tanzania blood cultures were evaluated). None of the DUMC emergency room patients had in situ intravascular devices at the time that blood was drawn for culture. The second category consisted of blood samples for culture obtained from patients who were already hospitalized in the two DUMC general medicine wards; these patients invariably had in situ

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intravascular devices. At DUMC the cultures of blood collected 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 protocols 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 described previously and included lysis and centrifugation of blood collected in an Isolator tube (Wampole Laboratories, Cranbury, NJ), a Septi-Chek biphasic blood culture bottle (Becton Dickinson Microbiology Systems [BDMS], Cockeysville, MD), and a BACTEC MYCO/F LYTIC blood culture bottle (BDMS) (3, 4). During the same period, DUMC used the BACTEC 9000 (BDMS) blood culture system for the detection of bacteremia and fungemia and the BACTEC 460 (BDMS) system in conjunction with BACTEC 13A bottles (BDMS) for the detection of mycobacteremia.

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

Generally, 70% isopropyl alcohol was used for disinfection of the skin of DUMC emergency room patients; however, we were not able to ascertain how scrupulously the skin was disinfected or the time that was allowed for the 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. For each patient at MNH and LCH, blood was drawn primarily from the antecubital fossa by one of the authors (L.K.A.). It was not possible to ascertain who drew the blood or the site of venipuncture for DUMC patients. For patients admitted via the MNH, LCH, and DUMC emergency rooms, we defined a true-positive blood culture as the 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, on the basis of the findings of seminal studies that have established that these microorganisms are common blood culture contaminants rather than significant causes of community-acquired bacteremia (27, 29, 30, 31). For DUMC inpatients with in situ intravascular devices, the growth of a 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 of blood taken has a 97.1% likelihood of being a contaminant (30). On this basis, we defined the growth of coagulase-negative staphylococcus from a single set of blood samples for culture as contamination.

Data analysis. All data were analyzed by using Epi Info computer software (version 6.04, 2001; Centers for Disease and Prevention, Atlanta, GA). Groups were compared by using the chi-square or Fisher's exact test, where appropriate. Relative risks (RRs) and 95% confidence intervals (CIs) were calculated.

RESULTS

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

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

Organism	No. (%) of isolates[a]
Coagulase-negative *Staphylococcus* spp.[b]	24 (7.2)
Staphylococcus aureus	15 (4.5)
Streptococcus pneumoniae	8 (2.4)
Haemophilus influenzae	2 (0.6)
Group B *Streptococcus* spp.	2 (0.6)
Escherichia coli	1 (0.3)
Propionibacterium spp.[b]	1 (0.3)
Diphtheroids[b]	1 (0.3)

[a] A total of 332 organisms were obtained.
[b] These organisms were deemed contaminants.

United States: DUMC. (i) 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, blood was drawn for culture from 176 (56%) patients while 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 for whom blood for culture was drawn necessarily had fever. Of the 176 patients for whom blood for culture was drawn in the emergency room, 29 (16%) patients had one set of blood cultures, 140 (79.5%) patients had two sets, 5 patients had three sets, and 2 patients had four sets. Thus, there were 332 separate blood draws in the emergency room, all for the 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 cultures of blood 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 two sets of blood cultures.

(ii) 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 for culture from 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 1 set of blood cultures, 52 (45%) had 2 sets, 15 (13%) had 3 sets, 9 (8%) had 4 sets, and 9 (8%) had more than 4 sets (median, 2 sets; range, 1 to 11 sets). The 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

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

Patient no.	No. of blood culture sets[a]	No. of true-positive cultures/total no.	Microorganism
1	3	1/3	*Cryptococcus neoformans*
2	4	2/4	*Escherichia coli*
3	2	2/2	*E. coli*
4	1	1/1	*Staphylococcus aureus*
5	10	2/10	*S. aureus*
6	3	3/3	*S. aureus*
7	1	1/1	*C. neoformans*
8	8	5/8	Polymicrobial growth[b]
9	1	1/1	*S. aureus*

[a] One set is equal to one venipuncture.
[b] The organisms included *Alcaligenes xylosoxidans*, *Enterococcus faecalis*, *Xanthomonas maltophilia*, *Candida albicans*, and *Torulopsis glabrata.*

mycobacterial blood cultures. Of the 24 cultures that were positive for bacterial growth, 7 (29%) yielded bacterial contaminants: *S. epidermidis* (six isolates) and a *Propionibacterium* sp. (one isolate). These seven isolates were deemed probable contaminants because they had each 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 nine inpatients. Thirty-three (12%) of the 283 bacterial cultures were obtained for these nine 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 versus 11/1,003; RR, 7.1; CI, 3.6 to 14.3; $P < 0.0001$) and were significantly more likely to have contaminated blood cultures than DUMC general medicine inpatients (26/332 versus 7/283; RR, 3.2; CI, 1.4 to 7.2; $P < 0.01$). In the two African hospitals, the blood culture contamination rate when povidone-iodine was used for skin cleansing was almost twice the contamination rate when tincture of iodine was used; this difference, however, was not statistically significant (7/517 versus 4/486; RR, 1.7; CI, 0.5 to 5.6; $P = 0.42$).

DISCUSSION

Our analyses compared and contrasted the blood culture contamination rates in large general hospitals in Tanzania and Malawi with the 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 learned 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-positive 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 reflects the use of less scrupulous methods or attention to aseptic technique when blood samples for culture are obtained in the emergency setting or during medical crises.

Our findings that approximately half of the positive cultures of blood collected in the DUMC emergency room and one-third collected in the DUMC inpatient medical service yielded contaminants are consistent with previously published data that suggest that contaminated blood cultures represent about half of all positive blood cultures (7, 16, 28, 29). The underlying reasons for such contamination include limited staff having to cope with a high patient census or multiple emergencies and having to hurry the drawing of blood samples for culture, the use of various techniques to draw blood and inoculate bottles, or unawareness among health care personnel of established guidelines for drawing of blood for culture (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 more than $4,000 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, by 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 the blood culture bottles and the 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 the 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 health care 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 the isolation of *S. epidermidis* 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 cultures of blood 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 compared with the proportion associated with contamination, we classified such positive cultures as contaminants on the basis of 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 for one set of blood cultures performed has a 97.1% probability of being the result of contamination. 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 overestimated. However, this would have rendered the difference between the contamination rates in the DUMC emergency room patients and inpatients even more significant. Second, blood cultures for emergency room patients in Tanzania and Malawi were performed by a single individual in a formal research study setting. In contrast, blood cultures for emergency room patients at DUMC were not obtained as part of a formal study and were carried out by numerous individuals over the study period. Thus, there might have been an inherent bias toward lower contamination rates in the African setting because more care was taken to avoid blood culture contamination in a formal research setting and there was less variability in blood-drawing technique or adherence to basic principles of skin disinfection than there was in the DUMC emergency room. The question naturally arises, then: 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 study at LCH in Malawi, blood cultures continued as part of routine LCH laboratory services were 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 by the use of skin cleansing with locally available isopropyl alcohol and tincture of iodine preparations. Application of these basic principles to the procurement of blood for culture 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 U.S. hospital emergency rooms through the use of better venipuncture and aseptic techniques that were proven effective in settings with substantially fewer resources.

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