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Blood Culture Results Before and After Antimicrobial Administration in Patients With Severe Manifestations of Sepsis

A Diagnostic Study

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Background: Administering antimicrobial agents before obtaining blood cultures could potentially decrease time to treatment and improve outcomes, but it is unclear how this strategy affects diagnostic sensitivity.

Objective: To determine the sensitivity of blood cultures obtained shortly after initiation of antimicrobial therapy in patients with severe manifestations of sepsis.

Design: Patient-level, single-group, diagnostic study. (Clinical Trials.gov: NCT01867905)

Setting: 7 emergency departments in North America.

Participants: Adults with severe manifestations of sepsis, including systolic blood pressure less than 90 mm Hg or a serum lactate level of 4 mmol/L or more.

Intervention: Blood cultures were obtained before and within 120 minutes after initiation of antimicrobial treatment.

Measurements: Sensitivity of blood cultures obtained after initiation of antimicrobial therapy.

Results: Of 3164 participants screened, 325 were included in the study (mean age, 65.6 years; 62.8% men) and had repeated blood cultures drawn after initiation of antimicrobial therapy (median time, 70 minutes [interquartile range, 50 to 110 minutes]). Preantimicrobial blood cultures were positive for 1 or more microbial pathogens in 102 of 325 (31.4%) patients. Postantimicrobial blood cultures were positive for 1 or more microbial pathogens in 63 of 325 (19.4%) patients. The absolute difference in the proportion of positive blood cultures between pre- and postantimicrobial testing was 12.0% (95% CI, 5.4% to 18.6%; $P < 0.001$). Sensitivity of postantimicrobial culture was 52.9% (CI, 42.8% to 62.9%). When the results of other microbiological cultures were included, microbial pathogens were found in 69 of 102 (67.6% [CI, 57.7% to 76.6%]) patients.

Limitation: Only a proportion of screened patients were recruited.

Conclusion: Among patients with severe manifestations of sepsis, initiation of empirical antimicrobial therapy significantly reduces the sensitivity of blood cultures drawn shortly after treatment initiation.

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The global burden of morbidity and mortality from sepsis is significant (1). Despite overall improvements in clinical outcomes, patients with sepsis and septic shock have short-term mortality rates approaching 20% (2). Although initial data for new treatments, such as activated protein C (3, 4), intensive insulin therapy (5), levosimendan (6), and ß-blockers (7), were promising, no novel host-directed therapies have consistently demonstrated a reduction in sepsis-associated mortality. The cornerstone of sepsis management continues to be early antimicrobial administration, source control, and supportive care (8–11).

The Surviving Sepsis Campaign guidelines recommend that blood cultures be drawn before starting antimicrobial therapy, with 45-minute delays considered acceptable to achieve this goal (12). However, prompt initiation of effective antimicrobial therapy is a critical determinant of survival (13). Death has been associated with delayed antimicrobial therapy after the onset of septic shock (14–17). Therefore, it is possible that administering antimicrobial agents before obtaining blood cultures could potentially decrease time to treatment and improve outcomes. Although specific microbiological diagnoses and antimicrobial susceptibility testing are important for determining the type and duration of treatment, the diagnostic sensitivity of blood cultures drawn shortly after antimicrobial administration in this population is not known. The purpose of this study was to determine whether the sensitivity of blood cultures decreased after administration of antimicrobial agents in patients with severe manifestations of sepsis.

See also:

Editorial comment

Web-Only
Supplement

METHODS

Study Design

We conducted the FABLED (eFfect of Antimicrobial administration on BLood culture positivity in patients with severe manifestations of sepsis in the Emergency Department) study, a patient-level, single-group, diagnostic study. The protocol was designed by the study management committee and reflects the standard of care in the participating institutions (**Supplement**, available at Annals.org). Seven urban emergency departments across Canada and the United States participated in the study. The research ethics boards at each recruiting center approved the protocol. The investigators remained unaware of the results throughout the enrollment period. The authors vouch for the data and analysis and for the fidelity of this report to the study protocol.

Participants

We recruited adult patients (aged ≥18 years) who presented to the emergency department with severe manifestations of sepsis, who had 2 sets of blood cultures drawn before starting antibiotic therapy, and who were able to have additional sets drawn within 2 hours of empirical antimicrobial administration. The **Supplement** provides detailed inclusion and exclusion criteria. In brief, evidence of a systemic inflammatory response syndrome (18) as well as a presumed or confirmed source of infection in patients was required. Evidence of severity, including systolic blood pressure less than 90 mm Hg at prehospital assessment or in the emergency department or a serum lactate level of 4 mmol/L or greater (19–21), was also required. These markers of severity were chosen because they are more likely to be present in patients with bloodstream infections and are associated with an increased risk for death independent of organ failure or shock (19, 20, 22–24). Moreover, these variables are associated with a sicker patient population that is more likely to benefit from early empirical antimicrobial therapy. Patients were excluded if they had a clinically significant bleeding disorder, a platelet count less than 20 000 × 10^9 cells/L, or an international normalized ratio greater than 6.0 because of the potential risk for harm from the additional venipuncture.

Diagnostic Procedure

Two sets of blood cultures were obtained from study participants before antimicrobial administration. Each set consisted of 1 aerobic and 1 anaerobic culture vial from a single venipuncture site; each set required a separate venipuncture. At 2 participating hospitals, the second set of blood cultures consisted of a single aerobic vial per institutional policy. After administration of the first antimicrobial agent, additional blood cultures were obtained. At 5 institutions, 2 additional sets of blood cultures were drawn with equal blood volumes before and after treatment initiation. At 2 institutions, 1 additional set of blood cultures was drawn after antimicrobial therapy was started because of institutional review board requirements to obtain the smallest acceptable blood culture volume per guideline recommendations (25) (**Supplement**). After treatment initiation, additional sets of blood cultures could be obtained from the same venipuncture to reduce the risk for harm from additional venipunctures.

The protocol stipulated that repeated blood cultures were to be obtained between 30 and 120 minutes after treatment initiation. However, the protocol was amended to include participants with repeated blood cultures up to 240 minutes after antimicrobial therapy because of the difficulties in obtaining repeated blood cultures within 120 minutes of treatment initiation. Antimicrobial agents were administered as standard infusions per routine practice. Blood cultures were obtained and processed at each study site according to local standard operating procedures. All other aspects of clinical care were at the discretion of the treating emergency physician and were based on local institutional guidelines. There were no changes in sepsis protocols throughout the study period.

Written informed consent was obtained from all patients or their surrogate decision maker before enrollment in the study. Given the low probability of harm to participants and the time-dependent nature of the diagnostic procedure, the institutional review boards for all participating institutions approved delayed consent in cases where patients lacked mental capacity and a surrogate decision maker could not be reached. In such cases, retrospective written consent was obtained from patients once they regained capacity or when a surrogate decision maker could be reached. Baseline demographic and clinical data were recorded for all patients.

Outcomes

The primary outcome was to determine the sensitivity of blood cultures obtained within 120 minutes after antimicrobial therapy was initiated in patients with severe manifestations of sepsis. We defined preantimicrobial blood cultures as the reference standard for bacteremia. A noncontaminant organism (25) growing in any of the preantimicrobial blood cultures, but absent from all postantimicrobial blood cultures, was defined as a discordant result. Postantimicrobial blood cultures that grew the same organisms as those obtained before antimicrobial therapy, regardless of the number of positive blood culture vials per set, was defined as a concordant result. In the setting of a polymicrobial bloodstream infection, all noncontaminant organisms recovered in the preantimicrobial blood cultures must have been present in the postantimicrobial blood cultures to have been considered concordant. Contaminant organisms were defined as low-virulence skin flora recovered from a single set of blood cultures when other sets were negative (25) (**Supplement**). All cases of potential contaminants were reviewed by 2 specialists (M.P.C. and C.P.Y.) in infectious diseases and medical microbiology. Appropriate antimicrobial therapy was defined according to Clinical and Laboratory Standards Institute interpretive criteria as administration of an antimicrobial agent to which the pathogen

was susceptible (26). The main secondary outcome was to evaluate the sensitivity of postantimicrobial blood cultures interpreted in the context of microbiological culture results available from other anatomical sites.

Sample Size

On the basis of previously published data (10, 13) and local sepsis epidemiology, we estimated conservatively that 35% of patients with severe manifestations of sepsis would be bacteremic. On the basis of a matched design, preantimicrobial blood culture positivity proportion of 35%, desired power of 90%, 2-tailed α error rate of 5%, and minimum clinically significant difference of 10% in sensitivity, 328 patients were required based on the repeated-measures design of the study. A 10% difference was chosen as the maximum difference in sensitivity between pre- and postantimicrobial blood cultures that would be deemed clinically acceptable through consultation with the infectious disease, emergency medicine, and critical care medicine specialists involved in development of the study protocol.

Statistical Analysis

Data from all hospital centers were consolidated, and the final data set was inspected for errors, outliers, and missing values. All study participants had complete data for the exposures and outcomes of interest. No patients were omitted because of missing data. The statistical unit of analysis was the blood culture pairing for each patient.

The population for primary analysis was defined as any participant recruited to the study in whom both pre- and postantimicrobial (within 240 minutes after initiation of antimicrobial therapy) blood cultures were obtained. An a priori decision was made to analyze the results in the per protocol (PP) population, consisting of participants who had postantimicrobial blood cultures drawn between 30 and 120 minutes after initiation of antimicrobial treatment.

Baseline patient characteristics are presented as proportions for categorical variables, means and SDs for age, and medians and interquartile ranges for nonnormally distributed data. The sample population was described per preantimicrobial blood culture results. Nonnormally distributed variables were compared using the Wilcoxon or the Wilcoxon signed-rank test for unpaired and paired data, respectively. Binary and categorical data were analyzed using the Fisher exact test or chi-square test when unpaired and using the McNemar test when paired. The number and corresponding percentage of patients in each category are presented with exact binomial 95% CIs, where appropriate.

The McNemar chi-square test for paired data was used to compare blood culture results before and after initiation of antimicrobial therapy. Proportions and absolute differences in sensitivity between pre- and postantimicrobial blood cultures are presented with exact binomial 95% CIs. Secondary outcomes evaluating the sensitivity of the postantimicrobial blood cultures as well as all other microbiological culture results available were similarly analyzed. The continuous variable of time between antibiotic administration and postantibiotic blood culture draw was presented in several categories. To optimize the clinical relevance and interpretability of the data, time was categorized as less than 30 minutes, 30 to 60 minutes, 61 to 120 minutes, and 121 to 240 minutes after antibiotic administration.

Role of the Funding Source

The study was funded by a quality improvement initiative by Vancouver Coastal Health and operational grants by the St. Paul's Hospital Foundation Emergency Department Support Fund, the Fonds de Recherche Santé–Québec, and the Maricopa Medical Foundation. The funding agencies had no role in designing the study, analyzing the data, writing the manuscript, or submitting this report for publication.

RESULTS

Patients

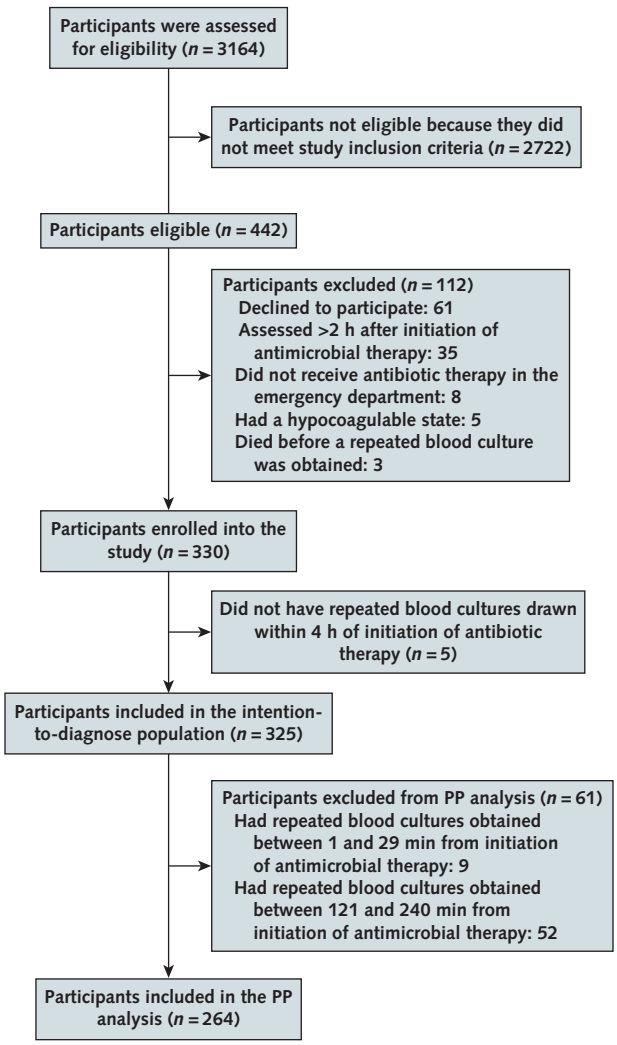
Between November 2013 and September 2018, a total of 330 participants were enrolled in the study (Figure). Five patients did not have postantimicrobial blood cultures drawn per study requirements and were excluded. In total, 325 patients were included in the final analysis. A total of 264 patients had postantimicrobial blood cultures drawn between 30 and 120 minutes after initiation of antimicrobial therapy and were included in the PP analysis.

Patient characteristics are shown in Table 1. The mean age at study enrollment was 65.6 years (SD, 17.7 years), and 204 participants (62.8%) were men. Among all study participants, 141 (43.4%) had a serum lactate level of 4 mmol/L or greater, 123 (37.8%) had systolic blood pressure less than 90 mm Hg, and 61 (18.8%) had both a serum lactate level of 4 mmol/L or greater and systolic blood pressure less than 90 mm Hg. Empirical treatment regimens for most patients included a ß-lactam antibiotic, including piperacillin and tazobactam (n = 197 [60.6%]), a third-generation cephalosporin (n = 76 [23.4%]), or a carbapenem (n = 15 [4.6%]). Baseline characteristics were similar among patients with positive or negative blood cultures before antimicrobial administration; however, patients with positive preantimicrobial blood cultures were more likely to have respiratory failure (19.6% vs. 8.9%).

Microbiology

The median time to repeating blood cultures after initiation of antimicrobial therapy was 70 minutes (interquartile range, 50 to 110 minutes). Blood cultures from 112 patients yielded microbial organisms, including 10 contaminants, before antimicrobial therapy. Postantimicrobial blood cultures from 69 patients yielded microbial organisms, including 6 contaminants. Six pathogens were recovered only from postantimicrobial blood cultures, including 2 from participants who had positive preantimicrobial blood cultures with different pathogens. Three postantimicrobial blood cultures were positive for 1 pathogen, but we did not recover all of the organisms in the preantimicrobial blood culture (Table 2).

Figure. Study flow diagram.



PP = per protocol.

The most commonly isolated pathogens from pre-antimicrobial blood cultures were *Escherichia coli* (*n* = 23 [22.5%]), *Staphylococcus aureus* (*n* = 16 [15.7%]), and *Streptococcus pneumoniae* (*n* = 13 [12.7%]). Twelve participants (3.7%) had polymicrobial blood cultures. A complete list of recovered pathogens is available in the Supplement.

Primary Outcome

Among the entire study population, preantimicrobial blood cultures were positive for 1 or more microbial pathogens in 102 of 325 (31.4%) patients. Postantimicrobial blood cultures were positive for 1 or more microbial pathogens in 63 of 325 (19.4%) patients. The absolute difference in the proportion of positive blood cultures between pre- and postantimicrobial blood cultures was 12.0% (95% CI, 5.4% to 18.6%; $P < 0.001$) (Table 2). Results were similar in an analysis of the PP population (absolute difference, 10.6% [CI, 3.3% to 17.9%]; $P < 0.001$). The sensitivity of postantimicrobial blood cultures was 52.9% (CI, 42.8% to 62.9%) in the entire study population and 56.3% (CI, 44.7% to 67.3%) in the PP population.

Secondary Outcomes

For the entire study population, when the results of cultures from other anatomical sites obtained before or after antimicrobial administration were added to those of postantimicrobial blood cultures, the overall sensitivity increased from 54 of 102 patients to 69 of 102 patients (67.6% [CI, 57.7% to 76.6%]) (Table 3). Results remained consistent in the PP population, with 55 of 80 pathogens recovered in postantimicrobial blood cultures and other cultures (68.8% [CI, 57.4% to 78.7%]). Antimicrobial administration also significantly affected the time required for the blood cultures to become positive for 1 or more microbial pathogens (Supplement).

Adverse Events

No adverse events related to additional venipunctures were reported.

DISCUSSION

Collection of blood cultures before antimicrobial administration in patients with sepsis is a best-practice recommendation (12) and a key component of national quality measures. Although these recommendations may delay initiation of antimicrobial therapy (17), our results suggest that obtaining blood cultures after initiation of empirical treatment reduces sensitivity by approximately 50% when preantimicrobial cultures are positive. Culture sensitivity was reduced at all times after antibiotic administration. This reduction in sensitivity after antimicrobial therapy was not compensated by extending cultures to other anatomical sites and remained meaningful after all microbiological cultures were considered. Microbiological diagnosis is key to optimizing the effectiveness of antimicrobial treatment as well as its safe deescalation. Despite the importance of early antimicrobial administration in this patient population, our results support the Surviving Sepsis Campaign guidelines (12) and suggest that preantimicrobial blood cultures should not be routinely deferred.

Sepsis is a heterogeneous syndrome with evolving clinical criteria (27). Our study was launched before the most recent definitions were published (27). Nonetheless, we enrolled patients with severe manifestations of sepsis, where the sensitivity of postantimicrobial blood cultures has not been previously studied in the setting of a diagnostic study. Previous cohort studies have produced mixed results (28–30). The largest cohort study to date prospectively compared patients sampled before and during antibiotic therapy (29). Although the authors found a statistically significant difference between pre- and postantimicrobial cultures, the fact that postantimicrobial blood cultures were obtained up to 36 hours after treatment initiation limited the clinical implications of their findings.

We performed a diagnostic study using robust methods and compared the results of preantimicrobial blood cultures to postantimicrobial blood cultures

drawn shortly after treatment initiation in the same septic patients. To our knowledge, this is the first report of prospective data quantifying the decrement in blood culture sensitivity from the time of antimicrobial initiation, and our data do not justify administration of antibiotics before blood cultures are obtained. A recent randomized controlled trial in the Netherlands failed to show a benefit from prehospital antibiotic administration (31). We recognize that blood cultures are not 100% sensitive, as some patients may have transient bloodstream infections. Nonetheless, on the basis of our findings, we suggest that patients with severe manifestations of sepsis have blood cultures obtained as soon as possible under aseptic technique, followed immediately by antimicrobial infusion. This would eliminate any delays in treatment while affording maximum microbiological information to guide subsequent therapy.

Our study has several strengths. The repeated measure design of the study and paired statistical analysis allowed us to detect a statistically significant difference of 10% or greater in the proportion of positive blood cultures before and after initiation of antimicrobial therapy. To broaden the clinical applicability of our

Table 1. Patient Characteristics

Variable	Preantimicrobial Blood Culture*		All (*n* = 325)
	Negative (*n* = 223)	Positive (*n* = 102)	
Mean age (SD), *y*	65.4 (17.9)	66.1 (17.2)	65.6 (17.7)
Male, *n (%)*	141 (63.2)	63 (61.8)	204 (62.8)
Comorbidities, *n (%)*			
Hypertension	72 (32.3)	39 (38.2)	111 (34.2)
Diabetes mellitus	57 (25.6)	31 (30.4)	88 (27.1)
Cancer	53 (23.8)	23 (22.5)	76 (23.4)
Chronic obstructive pulmonary disease	28 (12.6)	13 (12.8)	41 (12.6)
Atrial fibrillation	23 (10.3)	14 (13.7)	37 (11.4)
Congestive heart failure	21 (9.4)	16 (15.7)	37 (11.4)
Hepatitis C virus infection	23 (10.3)	9 (8.8)	32 (9.8)
Intravenous drug use	19 (8.5)	8 (7.8)	27 (8.3)
Cerebral vascular disease	20 (9.0)	6 (5.9)	26 (8.0)
Coronary artery disease	14 (6.3)	12 (11.8)	26 (8.0)
Chronic kidney disease	15 (6.7)	10 (9.8)	25 (7.7)
HIV	13 (5.8)	3 (2.9)	16 (4.9)
Median Charlson Comorbidity Index score (IQR)	1 (1–3)	1 (1–3)	1 (1–3)
Initial characteristics in the emergency department, *n (%)*			
Heart rate >90 beats/min	185 (83.0)	82 (80.4)	267 (82.2)
Respiratory rate >20 breaths/min	135 (60.5)	61 (59.8)	196 (60.3)
Temperature >38 °C or <36 °C	106 (47.5)	61 (59.8)	167 (51.4)
Leukocyte count >12 or <4 × 10^9 cells/L	177 (79.4)	78 (76.5)	255 (78.5)
Serum lactate level ≥4.0 mmol/L	137 (61.4)	65 (63.7)	202 (62.2)
Systolic blood pressure <90 mm Hg	127 (57.0)	57 (55.9)	184 (56.6)
Respiratory failure†	20 (8.9)	20 (19.6)	40 (12.3)
Vasopressor requirement	33 (14.8)	18 (17.6)	51 (15.7)
Source of infection, *n (%)*			
Respiratory	85 (38.1)	22 (21.6)	107 (32.9)
Genitourinary	31 (13.9)	27 (26.5)	58 (17.8)
Gastrointestinal	34 (15.2)	21 (20.6)	55 (16.9)
Skin and soft tissue	26 (11.7)	15 (14.7)	41 (12.6)
Other	6 (2.7)	9 (8.8)	15 (4.6)
Unknown	41 (18.4)	8 (7.8)	49 (15.1)
Initial antimicrobial regimen‡, *n (%)*			
Piperacillin–tazobactam	74 (33.2)	36 (35.3)	110 (33.8)
Piperacillin–tazobactam plus vancomycin	27 (12.1)	19 (18.6)	46 (14.2)
Piperacillin–tazobactam plus other antibiotic	29 (13.0)	12 (11.8)	41 (12.6)
Third-generation cephalosporin plus azithromycin	34 (15.2)	5 (4.9)	39 (12.0)
Third-generation cephalosporin	24 (10.8)	13 (12.7)	37 (11.4)
Carbapenem with or without vancomycin	6 (2.7)	9 (8.8)	15 (4.6)
Fluoroquinolone with or without vancomycin	9 (4.0)	3 (2.9)	12 (3.7)
Other	20 (9.0)	5 (4.9)	25 (7.7)

IQR = interquartile range.
* Blood culture obtained before empirical antimicrobial therapy; specimens growing contaminants only were treated as negative.
† Defined as requirement for noninvasive ventilation (bilevel positive airway pressure) or invasive ventilation (endotracheal ventilation).
‡ See the Supplement for a complete list of all antimicrobial regimens used.

Table 2. Proportion of Positive Blood Cultures Before and After Initiation of Antimicrobial Therapy

Time Between Antimicrobial Therapy and Repeated Blood Cultures	Positive Preantimicrobial Blood Culture (*n* = 102), *n*		Negative Preantimicrobial Blood Culture (*n* = 223), *n*		Positive Blood Cultures (95% CI), %		
	Positive Postantimicrobial Blood Culture	Negative Postantimicrobial Blood Culture	Positive Postantimicrobial Blood Culture	Negative Postantimicrobial Blood Culture	Preantimicrobial*	Postantimicrobial	Absolute Difference
<30 min (*n* = 9)	1†	0	0	8	11.1 (0 to 45.7)	11.1 (0 to 45.7)	0.0 (−29.0 to 29.0)
30–60 min (*n* = 124)	29	16	2	77	36.3 (28.4 to 45.1)	25.0 (18.2 to 33.3)	11.3 (−0.1 to 22.7)
61–120 min (*n* = 140)	20‡	15	1	104	25.0 (18.5 to 32.8)	15.0 (10.0 to 21.9)	10.0 (0.7 to 19.3)
121–240 min (*n* = 52)	9	12	1	30	40.4 (28.1 to 54.0)	19.2 (10.6 to 32.1)	21.2 (4.0 to 38.3)
PP population§ (*n* = 264)	49‡	31	3	181	30.3 (25.1 to 36.1)	19.7 (15.3 to 24.9)	10.6 (3.3 to 17.9)
All participants (*n* = 325)	59†‡	43	4	219	31.4 (26.6 to 36.6)	19.4 (15.4 to 24.0)	12.0 (5.4 to 18.6)

PP = per protocol.
* Exact binomial CIs.
† Includes 1 case of polymicrobial bacteremia where the postantimicrobial blood cultures were positive for 1 pathogen but failed to recover all the organisms in the preantimicrobial blood culture.
‡ Includes 2 cases of polymicrobial bacteremia where the postantimicrobial blood cultures were positive for 1 pathogen but failed to recover all the organisms in the preantimicrobial blood culture, as well as 2 postantimicrobial blood cultures that were positive for different organisms than the preantimicrobial blood culture.
§ Defined as patients who had repeated blood cultures between 30 and 120 min from initiation of antimicrobial therapy.

findings, we also considered the results of other microbiological cultures obtained as part of routine care. In both the entire study and PP populations, there would have been a statistically significant decrease in sensitivity if blood cultures had been drawn only after initiation of antimicrobial treatment, with 1 in every 6.7 patients having a false-negative blood culture result. Identifying a microbial pathogen is important for diagnostic certainty, optimizing treatment, and improving clinical outcomes in this patient population (32, 33).

Several aspects of the study results deserve mention. First, there was a proportion of participants who had repeated blood cultures obtained outside the time window specified in the study protocol. Although the results were consistent among both the entire study and PP populations, this variability highlights the real-world challenges of obtaining blood cultures promptly in the emergency department. Second, the proportion of bacteremic patients (31.4%) in this study was slightly lower than expected but similar to a large, randomized controlled trial of a comparable patient population (10). Nonetheless, the primary end point was met in both the entire study and PP populations. Third, the quantity of blood cultured differed among study sites because of local differences in study protocol and laboratory practices. However, total blood volume cultured from a patient at any study site before and after antimicrobial administration was at least 20 mL, which is the minimum suggested by the consensus recommendations of the American Society for Microbiology, and should suffice for pathogen recovery (25). We designed a pragmatic study that reflects the usual care at the participating institutions. Participants were recruited when study investigators were on site to screen and enroll patients into the study. Given that the investigators worked varying hours and days of the week, there is no reason to believe that the study population varied from the general population. Although we recruited only a proportion of participants who were screened, our study population consisted of patients with severe manifestations of sepsis and a conceivably higher microbial burden. As blood cultures drawn after antimicrobial administration still resulted in an important loss of clinical information, our results should therefore be generalizable to other septic patients.

In conclusion, blood culture sensitivity decreased after initiation of empirical antimicrobial therapy. These findings are important in considering the optimal balance between prompt antimicrobial administration and

Table 3. Sensitivity* of Postantimicrobial Blood Cultures Interpreted in the Context of Other Microbiological Culture Results†

Time Between Antimicrobial Therapy and Repeated Blood Cultures	Sensitivity of Postantimicrobial Blood Cultures (95% CI‡), %	Additional Sensitivity From Other Microbiological Cultures (95% CI), %	Overall Sensitivity of Postantimicrobial and Other Microbiological Cultures (95% CI), %
<30 min (*n* = 1)	0 (0.0 to 97.5)	0 (0.0 to 97.5)	0 (0.0 to 97.5)
30–60 min (*n* = 45)	64.4 (48.8 to 78.1)	13.3 (5.1 to 26.8)	77.8 (62.9 to 88.8)
61–120 min (*n* = 35)	45.7 (28.8 to 63.4)	11.4 (3.2 to 26.7)	57.1 (39.4 to 73.7)
121–240 min (*n* = 21)	42.9 (21.8 to 66.0)	23.8 (8.2 to 47.2)	66.7 (43.0 to 85.4)
PP population (*n* = 80)	56.3 (44.7 to 67.3)	12.5 (6.2 to 21.8)	68.8 (57.4 to 78.7)
All participants (*n* = 102)	52.9 (42.8 to 62.9)	14.7 (8.5 to 23.1)	67.7 (57.7 to 76.6)

PP = per protocol.
* We defined preantimicrobial blood cultures as the reference standard for bacteremia. A noncontaminant organism growing in any of the preantimicrobial blood cultures but absent from all postantimicrobial blood cultures was defined as a discordant result. In the setting of a polymicrobial bloodstream infection, all noncontaminant organisms recovered in the preantimicrobial blood cultures must have been present in the postantimicrobial blood cultures to have been considered concordant.
† Other microbiological cultures done as part of routine care and obtained either before or after antimicrobial administration, including urine, sputum, and wound cultures.
‡ Exact binomial CIs.

the need for accurate microbiological data in the care of patients with sepsis.

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Data Sharing Statement: The following data and supporting documents will be made available with publication: deidentified participant data, data dictionary, and statistical/analytic code (contact Matthew P. Cheng; e-mail, mcheng@bwh.harvard.edu). These data will be made available to researchers whose proposed use of the data has been approved, for a specified purpose, with investigator support and with a signed data access agreement (restrictions: none).

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