ORIGINAL ARTICLE

# Evaluation of White Blood Cell Count, Neutrophil Percentage, and Elevated Temperature as Predictors of Bloodstream Infection in Burn Patients

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**Objective:** To investigate whether specific values of or changes in temperature, white blood cell count, or neutrophil percentage were predictive of bloodstream infection in burn patients.

**Design:** Retrospective review of electronic records.

**Setting:** Intensive care center at the US Army Institute of Surgical Research Burn Center.

**Patients:** Burn patients with blood cultures obtained from 2001 to 2004.

**Main Outcome Measures:** Temperature recorded at the time blood cultures were obtained; highest temperature in each 6-hour interval during the 24 hours prior to this; white blood cell count and neutrophil percentage at the time of obtaining the blood culture and during the 24 hours preceding the blood culture; demographic data; and total body surface area burned.

**Results:** A total of 1063 blood cultures were obtained from 223 patients. Seventy-three people had 140 blood cultures from which microorganisms were recovered. Organisms that were recovered from blood cultures included 80 that were gram negative, 54 that were gram positive, 3 that were mixed gram positive/gram negative, and 3 yeasts. Although white blood cell count and neutrophil percentage at the time of the culture were statistically different between patients with and patients without bloodstream infection, receiver operating characteristic curve analysis revealed these values to be poor discriminators (receiver operating characteristic curve area = 0.624). Temperature or alterations in temperature in the preceding 24-hour period did not predict presence, absence, or type of bloodstream infection.

**Conclusions:** Temperature, white blood cell count, neutrophil percentage, or changes in these values were not clinically reliable in predicting bloodstream infection. Further work is needed to identify alternative clinical parameters, which should prompt blood culture evaluations in this population.

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INFECTION REMAINS THE MAJOR cause of death among patients with burns.[1] Delays in treating infections have been associated with inferior outcomes, necessitating the establishment of parameters that alert physicians to the potential presence of an infection.[2,3] Temperature along with laboratory parameters such as white blood cell (WBC) count and neutrophil percentage or changes in these values are used as markers of probable infection and often trigger further evaluation. White blood cell counts greater than $12 \times 10^3$ cells/mm$^3$ or less than $4 \times 10^3$ cells/mm$^3$ are frequently used as laboratory markers portending possible underlying infectious processes.[4] Temperature elevations of importance are variably defined as 38°C for systemic inflammatory response system, 38.3°C for fever of unknown infection, 38.3°C or 38°C for more than 1 hour for neutropenic fevers, 38°C for hospital- or ventilator-associated pneumonia, and 38.3°C for intensive care unit (ICU) infection.[4-8] In surgical ICUs, 93% of patients meet the definition of systemic inflammatory response system sometime during their admission, which questions the utility of temperature and WBC counts (2 of the criteria for systemic inflammatory response system) as clinical parameters that assess for underlying infection.[9] There is conflicting data as to the utility of these parameters in burn, surgical, and medical patients.[10-13] A recent prospective study revealed that routine postoperative body temperature elevations were not predictive of infection.[14]

Those undergoing therapy for burns often have temperature and WBC count alterations due to infectious and noninfectious etiologies. In our study, we sought to investigate whether temperature, WBC count, and neutrophil percentage at the time cultures were obtained or changes

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**Table 1. Study Population Characteristics**

| Characteristic | Patients With Bacteria-Positive Blood Culture (n = 73) | Patients With Bacteria-Negative Blood Culture (n = 150) |
|---|---|---|
| Mean age, y[a] | 43 | 37 |
| Men, %[b] | 93 | 80 |
| TBSA burned, %[c] | 42.4 | 28.2 |
| No. of deaths (%)[d] | 20 (27) | 12 (8) |

Abbreviation: TBSA, total body surface area.
[a] $P = .03$. Independent samples $t$ test.
[b] $P = .02$. $\chi^2$ Contingency test.
[c] $P < .001$. Mann-Whitney test.
[d] $P < .001$. $\chi^2$ Contingency test.

**Table 2. Most Recovered Bacteria by Blood Culture and Patient**

| Bacteria | No. of Blood Cultures | No. of Patients |
|---|---|---|
| *Pseudomonas aeruginosa* | 48 | 19 |
| Coagulase-negative *Staphylococcus*[a] | 20 | 19 |
| *Klebsiella pneumoniae* | 19 | 14 |
| *Staphylococcus aureus* | 13 | 9 |
| *Acinetobacter baumannii* | 8 | 5 |

[a] No patient had more than 1 coagulase-negative *Staphylococcus*-positive blood culture in a 72-hour period.

in these values in the 24 hours prior could effectively predict positive blood cultures or etiology of bloodstream infections in an ICU burn population.

## METHODS

An electronic medical records review was performed to identify patients with burns admitted from 2001 through 2004 to the US Army Institute of Surgical Research ICU. All patients who underwent blood culture were screened for the presence or absence of growth from the blood culture bottles. Because of access difficulty in most ICU burn patients, usual practice was to obtain blood cultures through central venous catheters, which are changed every 3 days, or arterial catheters, which are changed every 7 days. Indications for cultures typically include elevated temperatures, follow-up blood culture of previously bacteremic patients, and a clinician's impression that the patient had bacteremia manifested by unexplained hypotension or other organ deterioration, for example. Patient data included in this study were age, sex, total body surface area burned, and mortality. For each blood culture obtained, the temperature immediately preceding the collection of blood as well as the highest temperature in each 6-hour interval of the previous 24 hours was recorded. White blood cell count and neutrophil percentage (the differential most reflective of a bacterial or fungal infectious process) at the time nearest the blood culture and 24 hours prior to the culture were included in the evaluation. All blood cultures submitted within 2 hours of each other were grouped and evaluated as a single data point.

Logistic regression analysis was performed to compare the presence or absence of bloodstream infection by WBC count, neutrophil percentage, temperature, and time of collection. The Pearson $\chi^2$ test was used to evaluate categorical values, and the Mann-Whitney test was used to assess noncategorical values. A 1-way nonparametric analysis of variance was used to disclose a difference in total body surface area burned or temperature at the time of blood culture based on the type of bacteria identified (none, gram positive, gram negative [but not mixed], or yeast) because of small numbers. Statistical significance was set at $P < .01$.

## RESULTS

During the study period, 223 patients were admitted to the US Army Institute of Surgical Research ICU, meeting criteria for evaluation, and a total of 1063 blood culture sets were obtained (**Table 1**). Older individuals (47 years old vs 37 years; $P = .03$) with greater total body surface area burned ($P = .001$) had more positive blood cultures, but initial maximum temperatures were not different between those with and those without bloodstream infections. More extensive total body surface area burned was more predictive of gram-negative ($P < .001$) but not gram-positive ($P > .05$) bloodstream infection. Seventy-three patients who had blood cultures obtained (32% of admitted patients) had microorganisms recovered in 140 blood cultures (13% of blood cultures). Gram-negative bacteremia was most commonly detected, with 80 cultures having gram-negative bacteria identified and 54 cultures having gram-positive bacteria identified (**Table 2**). Three cultures were mixed with gram-positive and gram-negative bacteria, and 3 cultures produced yeasts (*Candida albicans* [n = 2] and *Candida tropicalis* [n = 1]). No clinically significant anaerobic bacteria were isolated.

The temperature at the time of obtaining the blood culture along with the preceding highest temperature for each 6-hour interval in the previous 24 hours is shown in **Table 3**. White blood cell count and neutrophil percentage at the time of obtaining the blood culture and the values 24 hours preceding the culture are also presented in Table 3. Temperature and WBC count at the time of obtaining the blood culture were not predictive of bloodstream infection. In addition, temperature at the time of obtaining the blood culture was not predictive of the type of bacteremia, either gram negative or gram positive. Neutrophil percentage at the time of obtaining the blood culture was predictive of bloodstream infection (independent sample $t$ test, $P < .001$); however, the difference in means between the presence or absence of bloodstream infection was only 3.1% (bacteremia [83.2%] vs no bacteremia [80.1%]). By logistic regression, temperature was not predictive of bloodstream infection, but WBC count and neutrophil percentage at the time of obtaining the blood culture were predictive of bloodstream infection. However, receiver operating characteristic curve analysis determined these parameters to be poor discriminators (area under the receiver operating characteristic curve = 0.624; 95% confidence interval, 0.569-0.679; $P < .001$) (**Figure**). Nine blood cultures were associated with temperature recordings at the time of collection of 36.1°C or less, 2 of which revealed the presence of bacteria. Temperature recordings were greater than 40.0°C at the time of collection for 27 blood samples, 4 of which were positive for bacteria.



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**Table 3. Temperature, White Blood Cell Count, and Neutrophil Percentage by Presence or Absence of Bacteria**

| Blood Culture | Mean Highest Temperature | | | | | Mean WBC Count × $10^3$ cells/mm$^3$ (SD) | | Mean Neutrophil Percentage (SD) | |
|---|---|---|---|---|---|---|---|---|---|
| | Time of Culture | Previous 0-6 h | Previous 6-12 h | Previous 12-18 h | Previous 18-24 h | Time of Culture | Previous 24 h | Time of Culture | Previous 24 h |
| Bacteria-positive blood culture | 38.6°C | 38.8°C | 38.3°C | 38.2°C | 38.3°C | 14.1 (8.1) | 13.1 (7.0) | 83.2 (9.5) | 82.9 (8.5) |
| Bacteria-negative blood culture | 38.6°C | 38.9°C | 38.4°C | 38.4°C | 38.4°C | 14.1 (7.7) | 13.9 (7.4) | 80.1 (9.5) | 80.4 (8.8) |

Abbreviation: WBC, white blood cell.

## COMMENT

Rapid identification and treatment of an infection is necessary to prevent excess morbidity and mortality.[2,3] In an assessment of 223 patients with 1063 blood cultures, we were unable to establish temperature or change in temperature in the preceding 24 hours as a parameter that would be clinically useful in predicting bloodstream infection in burn patients in the ICU. White blood cell counts and neutrophil percentages at the time of collecting blood cultures were predictive of bloodstream infection statistically, but these parameters do not appear to be clinically significant.

Fever historically has been the primary clinical parameter used to screen patients for an underlying infection. Fever, whose role has not been clearly elucidated, is a complicated physiologic response to various insults, such as infection, cancer, medications, central nervous system lesion, and rheumatologic disorders.[15] Among patients taking medicine, a higher peak temperature was predictive of microbial infections and predictive of positive blood cultures.[16,17] In a prospective study of postoperative patients, abnormal temperatures were not predictive of infection, potentially causing a false sense of security or anxiety, as patients were afebrile despite underlying infection and others were febrile without an underlying infectious process.[14] In some populations, such as patients in the ICU, the utility of temperature as a marker of infection or shock is hampered, because patients are often febrile despite not being infected.[18,19] Burn injury causes systemic inflammatory response. The magnitude of the changes is roughly a function of burn size that is manifested by increased body temperature, increased WBC count, and increased metabolic rate, which makes diagnosis of infection in the burned patient more difficult. Among burned children, continuous 48-hour fevers have been associated with infection, but the fever peak was not predictive of infection.[10] In an evaluation of the utility of blood cultures in a burned adult population, the highest temperature elevation in the 24 hours before the culture was obtained was not predictive of bloodstream infection.[11] We expanded this evaluation by assessing the temperature at the time of culture and the maximal temperature for the 24 hours prior to obtaining the blood culture. Hypothermia has also been reported to be associated with excess mortality at temperatures below 38°C, with even greater impact when temperatures fall below 36°C.[20,21] Although we did not assess for hypothermia in the 24 hours prior to obtaining blood cultures, at the time blood cultures were obtained, we did not have enough patients with hypothermia to make any meaningful conclusions in our patient population.

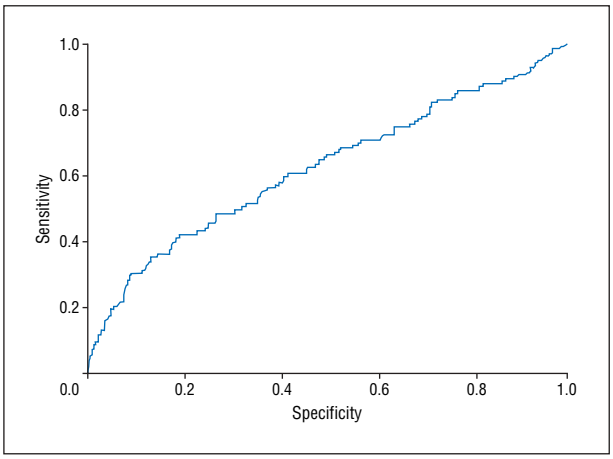


**Figure.** Receiver operating characteristic (ROC) curve analysis for white blood cell count and neutrophil percentage at the time blood cultures were obtained (ROC curve area = 0.624; 95% confidence interval, 0.569-0.679; $P < .001$).

The role of leukocytosis and neutrophilia in predicting bloodstream infection is also of questionable utility, as their etiologies are broad. They include infection, stress, medication, trauma, and abnormal bone marrow production. Among medical patients, WBC counts of $12 \times 10^3/mm^3$ or greater and neutrophilia of 80% or more provided the best discrimination between positive and negative blood cultures.[13] Neutrophils are the part of the differential of WBC counts that are typically the most reflective of bacterial and fungal infections. Among surgical patients, a WBC count of $11 \times 10^3/mm^3$ has been associated with a sensitivity of 0.55 and specificity of 0.38 in the detection of infection.[12] Twenty-two percent of bloodstream infections were not associated with a fever, 32% were not associated with an elevated WBC count, and 6% were not associated with either. Like ours, the study by Crabtree et al[12] was unable to detect an association between fever or WBC count and gram-positive or gram-negative bloodstream infection. In another adult burn population, the mean WBC count 24 hours prior to obtaining blood cultures was also not predictive of



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bloodstream infection.[11] Although WBC count and neutrophil percentage were statistically significant at the time of culture, the ability to discriminate between those with and without bloodstream infection is not possible on clinical grounds, because the values did not reflect clinically significant differences.

Limitations of our study include the retrospective evaluation without controlling for the indications for obtaining blood cultures; however, this did allow us to evaluate the same person across a variety of temperature values. It is also known that blood cultures have an associated contamination rate but also can fail to detect clinically significant bloodstream infection, possibly biasing the results.[21,22] We elected to include all cultures as data points, even coagulase-negative *Staphylococcus*, because of the increased recognition of these organisms as true pathogens. It is also unclear what role asymptomatic bloodstream infection, which potentially occurs in up to 15% of burn patients undergoing wound manipulation, contributes to the findings of this study.[23,24] Finally, we did not control for other infections such as pulmonary, gastrointestinal, and genitourinary infections, as these are nonsterile sites that limit our ability to clearly delineate colonization from infection. Given these limitations, our findings support many of the conclusions drawn from other patient populations (including medical, surgical, and burn patients), regarding parameters that might be clinically useful in predicting bloodstream infection.

Based on the findings of our study, temperature, WBC count, and neutrophil percentage—either at the time of obtaining blood cultures or during the previous 24 hours—are not reflective of bloodstream infection in a burn patient and should not be the sole criteria used to automatically trigger the collection of blood cultures. Further work needs to be performed to determine factors that more reliably predict bloodstream infection.

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## REFERENCES

1. Ekenna O, Sherertz R, Bingham H. Natural history of bloodstream infections in a burn patient population: the importance of candidemia. *Am J Infect Control.* 1993; 21(4):189-195.
2. Ibrahim EH, Sherman G, Ward S, Fraser VJ, Kollef MH. The influence of inadequate antimicrobial treatment of bloodstream infections on patient outcomes in the ICU setting. *Chest.* 2000;118(1):146-155.
3. Kollef MH, Sherman G, Ward S, Fraser VJ. Inadequate antimicrobial treatment of infections: a risk factor for hospital mortality among critically ill patients. *Chest.* 1999;115(2):462-474.
4. Bone RC, Balk RA, Cerra FB, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis: The ACCP/SCCM Consensus Conference Committee, American College of Chest Physicians/Society of Critical Care Medicine. *Chest.* 1992;101(6):1644-1655.
5. Cunha BA. Fever of unknown origin. *Infect Dis Clin North Am.* 1996;10(1):111-127.
6. Hughes WT, Armstrong D, Body GP, et al. 2002 guidelines for the use of antimicrobial agents in neutropenic patients with cancer. *Clin Infect Dis.* 2002; 34(6):730-751.
7. American Thoracic Society and the Infectious Disease Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and health-care associated pneumonia. *Am J Respir Crit Care Med.* 2005;171(4):388-416.
8. O'Grady NP, Barie PS, Bartlett JG, et al. Practice guidelines for evaluating new fever in critically ill adult patients. *Clin Infect Dis.* 1998;26(5):1042-1059.
9. Pittet D, Rangel-Frausto S, Li N, et al. Systemic inflammatory response syndrome, sepsis, severe sepsis and septic shock: incidence, morbidities and outcomes in surgical ICU patients. *Intensive Care Med.* 1995;21(4):302-309.
10. Rodgers GL, Kin J, Long SS. Fever in burned children and its association with infectious complications. *Clin Pediatr (Phila).* 2000;39(9):553-556.
11. Keen A, Knoblock L, Edelman L, Saffle J. Effective limitation of blood culture use in the burn unit. *J Burn Care Rehabil.* 2002;23(3):183-189.
12. Crabtree TD, Pelletier SJ, Antevil JL, Gleason TG, Pruett TL, Sawyer RG. Cohort study of fever and leukocytosis as diagnostic and prognostic indicators in infected surgical patients. *World J Surg.* 2001;25(6):739-744.
13. Walling HW, Manian FA. Predictive value of leukocytosis and neutrophilia for bloodstream infection. *Infect Dis Clin Pract.* 2004;12(1):2-6.
14. Vermeulen H, Storm-Versloot MN, Goossens A, Speelman P, Legenate DA. Diagnostic accuracy of routine postoperative body temperature measurements. *Clin Infect Dis.* 2005;40(10):1404-1410.
15. Hasday JD, Fairchild KD, Shanholts C. The role of fever in the infected host. *Microbes Infect.* 2000;2(15):1891-1904.
16. Bossink AWJ, Groeneveld ABJ, Hack CE, Thijs LG. The clinical host response to microbial infection in medical patients with fever. *Chest.* 1999;116(2):380-390.
17. Groeneveld ABJ, Bossink AWJ, VanMierlo GJ, Hack CE. Circulating inflammatory mediators in patients with fever: predicting bloodstream infection. *Clin Diagn Lab Immunol.* 2001;8(6):1189-1195.
18. Bossink AWJ, Groeneveld ABJ, Koffeman GI, Becker A. Prediction of shock in febrile medical patients with a clinical infection. *Crit Care Med.* 2001;29(1): 25-31.
19. Circiumaru B, Baldock G, Cohen J. A prospective study of fever in the intensive care unit. *Intensive Care Med.* 1999;25(7):668-673.
20. Aube H, Milan C, Blettery B. Risk factors for septic shock in the early management of bacteremia. *Am J Med.* 1992;93(3):283-288.
21. Weinstein MP, Towns ML, Quartey SM, et al. The clinical significance of positive blood cultures in the 1990s: a prospective comprehensive evaluation of the microbiology, epidemiology and outcome of bacteremia and fungemia in adults. *Clin Infect Dis.* 1997;24(4):584-602.
22. Kocoglu ME, Bayram A, Balci I. Evaluation of negative results of BacT/Alert 3D automated blood culture system. *J Microbiol.* 2005;43(3):257-259.
23. Mozingo DW, McMansu AT, Kim SH, Pruitt BA. Incidence of bacteremia after burn wound manipulation in the early post burn period. *J Trauma.* 1997;42 (6):1006-1011.
24. Vindenes H, Bjerknes R. The frequency of bacteremia and fungemia following wound cleaning and excision in patients with large burns. *J Trauma.* 1993; 35(5):742-749.



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