Effect of Blood Culture Contamination on Antibiotic Use in an Institution With Rapid Laboratory Methods and Phone-Based Clinical Follow-up of Blood Culture Results

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In a multivariate analysis of 30,574 blood culture (BC) results, BC contamination was associated with only a small increase in antibiotic length of therapy compared to no-growth BCs (difference, 0.36 days [95% confidence interval, 0.05–0.67]; P = .02). Stewardship processes at our institution appear to be effective in reducing the impact of BC contamination.

Keywords. antimicrobial stewardship; blood culture; blood culture contamination.

Blood cultures (BCs) are a critical test in the investigation of systemic infection, but up to half of positive blood cultures may be contaminants, usually with skin organisms [1]. BC contamination (BCC) can lead to unnecessary antibiotic prescribing, additional laboratory testing and procedures, prolonged length of stay, and increased costs [1–10]. Many studies on this topic were performed when laboratory methods were slower, only examined inpatient antibiotic use, and did not use a control group against which to compare the effects of BCC [1–6].

In our institution, we have a phone-based program of follow-up for all positive BCs from clinical microbiology (CM). This is combined with rapid laboratory methods, and laboratory comments on reports alerting clinicians to the likelihood of BCC for certain results. The aim of this study was to assess the impact of BCC on overall antibiotic use in an institution with several mitigation processes in place.

METHODS

Setting
Wellington Regional Hospital provides secondary and tertiary services to 500,000 people. It has a full range of medical and surgical services, including hemopoietic stem cell and kidney transplantation. All positive BCs are followed up by CM, with phone-based management advice or direct infectious diseases (ID) referral. Our laboratory uses the BD-BACTEC Plus Aerobic/F and Lytic/10 Anaerobic/F vials. Rapid identification of organisms is performed within 4–8 hours of BC flagging using tube-coagulase for staphylococci and matrix-assisted laser desorption/ionization–time of flight mass spectrometry for all cultures. For suspected BCC, 1 of the following comments is added to the report: “A single isolate of a coagulase-negative Staphylococcus from a blood culture is rarely of clinical significance” or “These organisms usually are contaminants unless repeatedly isolated.”

The above processes were implemented several years before the time period of this study. Each week all positive BCs are classified by the CM registrar and an ID physician according to source and significance using the College of American Pathologists guidelines [11]. Organisms that appear on the Centers for Disease Control and Prevention list of common commensals that are not repeatedly isolated and are not judged to be causing infection are classified as BCC [12]. Blood diversion devices to reduce the risk of BCC are not in use at our institution.

Design
The BC database was matched to inpatient and outpatient electronic dispensing records. BC results were grouped as “pathogen,” “contaminant,” or “no growth” (NG). Data were available for all inpatient dispensing, except the emergency department (ED), for which records were unavailable. ED dispensing was therefore excluded for all patients. Community dispensing records were obtained from the National Pharmaceutical Collection. The national health index number was used to match antibiotic use, laboratory results, demographic and admission/discharge information.

BC results from 1 January 2019 to 31 December 2021 were included, excluding those from the neonatal intensive care unit. Duplicate BCs in the same patient within a 48-hour period were excluded. A hierarchy of BC results was applied so that the overall result for each 48-hour period was ascribed to the highest-priority BC result, with pathogen overriding BCC, and both pathogen and BCC overriding NG. Antibiotic
consumption was calculated for the 14-day period after BC collection, using the length of therapy (LOT) metric, which regards each day where a patient receives ≥1 dose of an antibiotic as 1 LOT, regardless of the number of doses or agents [13]. LOT was also calculated separately for intravenous antibiotics and vancomycin.

**Statistical Analysis**

The χ² test was used to compare categorical variables. Continuous variables were compared using linear regression and the Mann-Whitney test. A multivariate linear regression model was fitted to examine the effect of different patient factors and BCC on LOT. Analysis was performed using Stata version 17 software (StataCorp, College Station, Texas).

**Patient Consent Statement**

Approval was gained from the Capital and Coast District Health Board hospital research and audit committee, and full ethics review was waived as the study formed part of a larger quality improvement exercise for our service. According to local guidelines, individual patient consent was not required.

**RESULTS**

There were 27,292 (89.3%), 997 (3.3%), and 2,285 (7.5%) NG, contaminant, and pathogen BCs, respectively (Table 1). The BCC group had higher inpatient, intravenous, vancomycin, and combined LOT than the NG group. The differences in combined, inpatient, and vancomycin LOT were largest early in the 14-day period, and reduced over time (Figure 1). Conversely, outpatient antibiotic use was higher in the NG group early in the follow-up period. After adjustment for other variables, including early mortality in the BCC group, combined LOT was 0.36 days (95% confidence interval, .05–.67; P = .02) higher in the BCC group compared to NG in the multivariate linear regression model (see full model in the Supplementary Materials).

**DISCUSSION**

The results from this study suggest that in an institution with several relatively simple processes to reduce the postresult impact of BCC, the residual effect on unnecessary antibiotic use is small, particularly when both inpatient and outpatient antibiotic consumption are considered. Combined inpatient/outpatient LOT was only 0.36 days longer (multivariate model) and vancomycin LOT only 0.35 days longer (univariate comparison) in BCC compared to NG BCs. This is in contrast to prior studies on this topic, which have reported larger increases in antibiotic usage [1–3, 7]. For example, Souvenir et al reported an average of 6.5 days of vancomycin therapy for BCC [3], although another more recent analysis reported a smaller difference of 2.5 days for NG compared to 3.5 days in BCC [14].

This analysis shows the value of relatively simple interventions post-BC in reducing unnecessary antimicrobial prescribing. The majority of BCs with coagulase-negative staphylococci (CoNS) are identified within 4 hours of flagging, meaning that vancomycin, in the absence of sepsis, can usually be withheld during this time. The addition of interpretive laboratory comments for BCC reinforces the advice, and we believe has resulted in a good understanding in our institution that most CoNS and other common skin organisms in BCs represent BCC. Phone-based advice is relatively time-efficient, and is integrated as one of the daily tasks performed by CM, which usually takes between 30 and 60 minutes each day (for all BC results, not solely BCC). The trust relationship developed by CM phoning results directly to clinicians improves advice adherence. An added benefit is that some in-person ID consultations are avoided.

This is the largest study on this topic of which we are aware; many of the prior studies had small cohorts often without comparison to NG BCs [1–3, 7]. Almost 80% of patients with NG BCs are given empiric antibiotics at our institution, so to assess antibiotics after BCC without comparison to this group may be misleading. We are also only aware of 1 prior study on BCC that has included outpatient antibiotic consumption, albeit on a small scale [4]. The difference in LOT between BCC and NG groups narrowed with the inclusion of outpatient dispensing, reflecting that the NG group tended to be discharged earlier and receive more antibiotics as outpatients. Finally, many of the prior studies on this topic were performed when laboratory methods were slower [1–4], so overtreatment of BCC while awaiting results may have occurred more frequently.

Strengths of this study include the large sample size and accurate measurement of antibiotic consumption, including outpatient dispensing. We believe the classification of BCs was accurate because it was conducted prospectively shortly after reporting and was based on expert clinical review by the involved clinicians.

This study was performed in a single center and our results may not necessarily apply in other jurisdictions. Phone-based follow-up of all positive BCs may not be feasible in some institutions. We have a low prevalence of methicillin-resistant *Staphylococcus aureus* (5.6% of *S. aureus* in BCs, data not shown), which means that vancomycin can often be avoided. However, many institutions will have similar interventions to ours and New Zealand has similar levels of antibiotic use to many other countries [15–17]. Dispensing data from our ED were unavailable. This will have only affected the LOT analysis if the patient received no antibiotics in any other location on the same day, which would be relatively uncommon. Furthermore, BC results would rarely be available while patients are in ED, so would seldom influence prescribing. Repeat BC results within 48 hours of an index culture were excluded; however, further positives subsequent to this were
included. This means that patients who spend longer in hospital and have more BCs taken may influence the results more than others. However, we feel that this is a better real-world reflection, because each BC in clinical practice has the potential to alter prescribing behavior, and some patients inevitably have a larger impact on overall institutional antibiotic consumption. Outside documentation of clearance of *S. aureus* bacteremia, repeat BCs are predominantly collected at our institution due to a change in patient condition. A change in the patient’s condition will often be accompanied by a change in prescribing behavior, so excluding some BCs over others would mean such changes would not be captured.

In conclusion, we have found that BCC is associated with increases in total antibiotic and vancomycin LOT compared to others having BCs collected; however, these differences are small. This may reflect early stewardship interventions from the clinical laboratory and provides encouragement that relatively simple actions can result in improvements in patient care.

**Table 1. Characteristics and Antibiotic Usage of Different Blood Culture Result Groups**

| Characteristic                                      | No Growth | Contaminant | Pathogen |
|-----------------------------------------------------|-----------|-------------|----------|
| Total BCs                                           | 27,292 (89.3) | 997 (3.3)  | 2,285 (7.5) |
| Individual admissions                               | 21,416 (88.2) | 930 (3.8)  | 1,927 (7.9) |
| Individual patients                                 | 16,240 (86.2) | 907 (4.8)  | 1,700 (9.0) |
| Age, y, median (IQR)                                | 58.6 (34.6–72.9) | 60.2 (37.2–72.9) | 64.8 (50.3–76.0)** |
| Female sex                                          | 12,665 (46.4) | 447 (44.8) | 994 (43.5) |
| Ethnicity                                           |           |             |          |
| NZ Maori                                            | 4,313 (15.8) | 181 (18.2)* | 351 (15.4)** |
| Pacific Islander                                    | 2,878 (10.5) | 98 (9.8)   | 313 (13.7) |
| NZ European/European                                | 16,915 (62.0) | 632 (63.4) | 1,385 (60.6) |
| Asian                                               | 2,509 (9.2)  | 66 (6.6)   | 194 (8.5)  |
| Other/unknown                                       | 677 (2.5)   | 20 (2.0)   | 42 (1.8)   |
| Living in aged residential care                     | 578 (2.1)   | 21 (2.1)   | 81 (3.5)*  |
| Admitting specialty                                 |           |             |          |
| Medical                                             | 9,445 (34.6) | 378 (37.9)** | 965 (42.2)** |
| Surgical                                            | 7,216 (26.4) | 242 (24.3) | 586 (26.9) |
| Hematology/oncology                                 | 4,422 (16.2) | 159 (15.9) | 428 (18.7) |
| ICU                                                 | 817 (3.0)   | 66 (6.6)   | 96 (4.2)   |
| Pediatrics                                          | 2,270 (8.3) | 74 (7.4)   | 61 (2.7)   |
| Obstetrics and gynecology                           | 810 (3.0)   | 15 (1.5)   | 42 (1.8)   |
| Emergency department                                | 1,708 (6.3) | 44 (4.4)   | 88 (3.9)   |
| Unknown                                             | 604 (2.2)   | 19 (1.9)   | 19 (0.8)   |
| BC collected in first 72 h of admission             | 17,797 (65.2) | 608 (61.0)** | 1,525 (66.7)** |
| BC sets per admission, median (IQR)                 | 2 (1–3)     | 2 (1–6)**  | 3 (2–6)**  |
| Length of stay, d, median (IQR)                     |           |             |          |
| Preceding BC collection                             | 1 (0–4)     | 1 (0–6)    | 0 (0–5)**  |
| Following BC collection                             | 4 (2–8)     | 5 (2–11)** | 6 (3–13)** |
| Total                                               | 5 (2–13)    | 7 (3–19)** | 8 (4–18)** |
| Pathogen BC within 14-d window either side         | 17,744 (6.5) | 64 (6.4)  | ...       |
| Death                                               |           |             |          |
| Within 14 d of BC                                   | 1,086 (4.0) | 77 (7.7)** | 214 (9.4)  |
| Within 30 d of BC                                   | 1,714 (6.3) | 92 (9.2)** | 287 (12.6)** |
| Received any antibiotics within 14 d of BC          | 21,812 (79.9) | 866 (86.9)** | 2,285 (96.3)** |
| Antibiotic LOT in the 14 d following BC, d, mean    |           |             |          |
| Inpatient                                           | 4.09       | 4.95**      | 7.08**    |
| Intravenous                                         | 3.25       | 4.13**      | 6.23**    |
| Intravenous vancomycin                              | 0.23       | 0.58**      | 0.88**    |
| Combined inpatient and outpatient                   | 6.61       | 6.99*       | 10.27**   |

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: BC, blood culture; ICU, intensive care unit; IQR, interquartile range; LOT, length of therapy; NZ, New Zealand.

*P < .05 and **P < .01 between groups. For categorical variables with multiple groups, the P-value has been calculated for the group as a whole and is displayed next to the uppermost result. The comparisons displayed in the “Contaminant” column compare the “No growth” group and the “Contaminant” group, and those displayed in the “Pathogen” column compare the “Contaminant” group and the “Pathogen” group.
Supplementary Data

Supplementary materials are available at Open Forum Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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