Pre-hospital, pre-antibiotic blood cultures for patients with suspected sepsis—a feasibility study

Aileen Harwood, Scott Pearson, Julia Howard, Nicole Jones, Rosie Greenlees, Charlotte Broms, Sharon J Gardiner, Simon C Dalton

Prompt pathogen identification and effective antimicrobial treatment are critical to prevent mortality for patients with sepsis (mate whakatāoke).[1] In Aotearoa New Zealand, Hato Hone St John (HHStJ) play a crucial role in early sepsis management, with Waikato Hospital data revealing that 74% of sepsis cases enter hospital via HHStJ.[2] St John Clinical Procedures and Guidelines[3] state that individuals over 12 years of age with a provisional sepsis diagnosis and at least one of 12 high-risk factors (e.g., systolic blood pressure ≤90mmHg) may be given empiric antibiotics if time to definitive care is over 30 minutes. This accommodates delays due to both distance and emergency department (ED) ramping. The recommended antibiotics are amoxicillin/clavulanic acid with or without gentamicin depending on likely site of infection, or ceftriaxone if meningococcal disease is suspected.[3] The guidelines do not require blood cultures (BCs) to be taken before antibiotic administration, as would be best practice, due to logistical (e.g., short shelf-life of BC bottles),[3] clinical (e.g., contamination) and financial (e.g., cost of BC bottles) concerns. This diminishes pathogen detection in BCs taken subsequently in hospital.[4] Given this, and the substantial pressures across emergency services, there is value in identifying initiatives that could improve sepsis management, including achieving equitable care for those in remote locations.

Here, in a collaboration between HHStJ and Te Whatu Ora – Waitaha Canterbury Emergency Medicine, Microbiology and Infection Management Services at Christchurch Hospital, we conducted a feasibility study to establish a local approach to pre-hospital pre-antibiotic BC collection. We also aimed to assess rates of pathogen and contaminant identification in BCs drawn by HHStJ and ED. This quality improvement initiative was assessed as exempt from Health and Disability Ethics Committee review.

From 21 October 2022 to 21 April 2023, Waitaha Canterbury HHStJ paramedics were asked to draw one set of BCs on insertion of a peripheral intravenous catheter from patients with suspected sepsis before giving intravenous antibiotics as per their guidelines. Paramedics received training on BC collection via resources developed by HHStJ, a microbiology scientist and an emergency medicine specialist. The resources were placed on the HHStJ online learning platform and included a written BC collection protocol, video demonstration and a skill sheet outlining key points for BC collection.

BC collection kits (specimen bag, aerobic and anaerobic culture bottles, vacutainer and request form) were obtained from ED and replaced as used, thus circumventing the logistical and financial barriers mentioned earlier. At handover, paramedics advised ED that BCs had been taken before transferring them with an HHStJ-labelled request form to the laboratory via pneumatic tube. The BCs were registered to ED for follow-up purposes. ED staff were informed of the pilot but were not given explicit advice to draw repeat BCs.

All HHStJ BCs and any subsequent BCs obtained in ED for each patient episode were compiled, reviewed by a clinical microbiologist and analysed descriptively using Microsoft Excel™. A patient episode denotes a separate hospital presentation, rather than a different patient. An isolate was deemed a contaminant following definitions outlined in the recent national BC audit,[5] or as per clinical microbiologist assessment following clinical review.

Table 1 summarises the results of 135 BCs (85 HHStJ, 50 ED) taken from 80 patients across 85 patient episodes. Forty-one patient episodes had repeat BCs in ED, and nine patient episodes had two sets of BCs in ED. Positive results represent both pathogens and probable contaminants.

Of the 85 BCs drawn by HHStJ, 29 were positive and 56 were negative. Of the 29 positive cultures taken by HHStJ, 17 had repeat BCs drawn in ED,

Table 1: Overall summary of blood culture (BC) results.

<table>
<tr><td>Hato Hone St John (HHStJ) (n=85)</td><td></td><td colspan="4">Emergency Department (ED) (n=50)*</td></tr>
<tr><td></td><td></td><td colspan="2">First set (n=41)</td><td colspan="2">Second set (n=9)</td></tr>
<tr><td rowspan="5">Positive</td><td rowspan="5">29</td><td rowspan="2">Positive</td><td rowspan="2">5</td><td>Positive</td><td>1</td></tr>
<tr><td>Negative</td><td>0</td></tr>
<tr><td colspan="4"></td></tr>
<tr><td rowspan="2">Negative</td><td rowspan="2">12</td><td>Positive</td><td>0</td></tr>
<tr><td>Negative</td><td>3</td></tr>
<tr><td colspan="6"></td></tr>
<tr><td rowspan="5">Negative</td><td rowspan="5">56</td><td rowspan="2">Positive</td><td rowspan="2">2</td><td>Positive</td><td>0</td></tr>
<tr><td>Negative</td><td>1</td></tr>
<tr><td colspan="4"></td></tr>
<tr><td rowspan="2">Negative</td><td rowspan="2">22</td><td>Positive</td><td>0</td></tr>
<tr><td>Negative</td><td>4</td></tr>
</table>

Each result represents a single patient episode. Positive BC results include both pathogens and contaminants.
*BCs were repeated in the ED in 41 patient episodes, with nine patient episodes having two sets of repeat BCs.

with 12 of these testing negative. Of the 56 negative cultures by HHStJ, 24 had repeat BCs in ED, with two testing positive.

Table 2 shows the distribution of microorganisms isolated. *Escherichia coli* was the most common pathogen, identified in six HHStJ BCs and three ED BCs. *Staphylococcus aureus* was isolated in four patient episodes. One of these was methicillin (but not gentamicin) resistant (MRSA) and was detected only by HHStJ; this patient received gentamicin and amoxicillin/clavulanic acid pre-hospital. Identification of *Enterococcus faecalis* by HHStJ, but not ED, in another patient episode facilitated diagnosis and treatment of endocarditis. These cases demonstrate the utility of pre-hospital, pre-antibiotic BC collection.

There were 10 probable contaminants isolated from nine BCs drawn from seven patient episodes. In two patient episodes, probable contaminants were isolated by both HHStJ and ED. In one of these, *Proteus mirabilis*, *Staphylococcus capitis* and *Corynebacterium striatum* were isolated from the HHStJ BC, and *C. striatum* was isolated from the ED BC. *P. mirabilis* was assessed as a pathogen and the others were assessed as probable contaminants. In the other, two different contaminants were isolated (mixed coagulase negative staphylococci by HHStJ and *S. capitis* by ED). The remaining five contaminants were isolated by HHStJ.

Post hoc statistical analyses using Chi-squared tests showed the proportion of positive blood cultures was 2.0 (95% CI = 0.96 to 4.17, p=0.024) times higher in samples taken by HHStJ (29/85, 34%; 95% CI = 24.9% to 44.7%) compared with the first set taken in ED (7/41, 17%; 95% CI = 8.2% to 31.6%). The proportion of contaminated samples was 1.7 (95% CI = 0.37 to 7.77, p=0.268) times higher in samples taken by HHStJ (7/85, 8%; 95% CI = 3.8% to 16.3%) compared with the first set taken in ED (2/41, 4.9%; 95% CI = 0.5% to 17.0%).

After excluding contaminants, the HHStJ true pathogen positivity rate (22/85; 26%) exceeded both the ED (6/50; 12%) and the overall Waitaha Canterbury (6.4%)[5] true positive rates, likely reflecting the increased pre-test probability seen in community patients with suspected sepsis and the benefit of pre-antibiotic BCs. The true positivity and contamination rates found in HHStJ BCs align

Table 2: Distribution of bacteria isolated from the blood cultures (BCs).

Species	Hato Hone St John (HHStJ) (n=31*)	Emergency department (ED) (n=8)	Total (n=39*)
Escherichia coli	6	3	9
Coagulase negative staphylococci**	6	1	7
Beta-haemolytic streptococci	5	1	6
Staphylococcus aureus	4	0	4
Proteus mirabilis	2	1	3
*Corynebacterium striatum***	1	1	2
Bacteroides fragilis	1	0	1
Citrobacter species	0	1	1
Enterobacter cloacae	1	0	1
Enterococcus faecalis	1	0	1
Leclercia adecarboxylata	1	0	1
Proteus vulgaris	1	0	1
*Streptococcus parasanguinis***	1	0	1
Streptococcus pneumoniae	1	0	1

*Thirty-nine isolates were detected in 37 sets of BCs. One BC taken by HHStJ grew both the pathogen *Proteus mirabilis* and two contaminants *S. capitis* and *C. striatum*. The repeat BC in the ED grew *C. striatum* only.
**Assessed as contaminants.

with similar studies overseas.[6,7]

Pre-hospital antibiotics were administered by HHStJ in 91% (77/85) of patient episodes—57% as amoxicillin/clavulanic acid with gentamicin (44/77), 34% as amoxicillin/clavulanic acid alone (26/77), and the remaining 9% as gentamicin alone (4/77), ceftriaxone alone (2/77) or ceftriaxone with gentamicin (1/77). Antibiotics were not administered after BCs in five cases due to hospital proximity and in three cases for an undocumented reason.

A limitation of our approach was that only one set of BCs was drawn by HHStJ before antibiotics instead of the two recommended as best practice.[8] Moving forward, two sets of BCs could be obtained by HHStJ before antibiotic administration. Alternatively, repeat BCs could be taken in ED when indicated to address any shortfall, although a lower positivity rate should be anticipated. We propose that ongoing audits of this quality improvement initiative are undertaken, including time from pre-hospital BC collection and antibiotic administration, to time to BC collection in ED. We also recommend review of choice of antibiotics for suspected sepsis by HHStJ—a single dose of ceftriaxone 2g likely strikes a pragmatic balance between expected benefit and harms.

Overall, our results confirmed that pre-hospital, pre-antibiotic BCs had a high rate of pathogen detection without clinically significant contamination or logistical concerns. Pathogen detection is critical to guide antibiotic choice and regimen. Provided that BCs can be expeditiously collected, we advocate that they should be taken before antibiotic administration.

We are pleased to report that, based on this study, HHStJ have formally approved national implementation of pre-hospital, pre-antibiotic BC collection for patients with suspected sepsis

(in an email from N Jones, Hato Hone St John Tāmaki Makaurau Auckland [Nicole.Jones@stjohn.org.nz] in Nov 2023). This is a positive step towards achieving equity in sepsis-related care for those who live remotely. The approach used will be modelled on that described here, including supply of BC kits from receiving hospital EDs and working collaboratively with clinicians at the receiving hospital and associated infection-related services.

COMPETING INTERESTS
Nil.

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