Analysis of 281,797 Consecutive Blood Cultures Performed over an Eight-Year Period: Trends in Microorganisms Isolated and the Value of Anaerobic Culture of Blood

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The results for 281,797 blood culture sets of specimens collected from adult patients at the Mayo Clinic over an approximately 8-year period (1 November 1984 through 30 November 1992) were analyzed in order to determine whether there were differences in the types of microorganisms isolated over this time and to assess the usefulness of anaerobic culturing of blood. Each blood culture set consisted of two aerobic blood cultures (Septi-Chek [Becton Dickinson, Sparks, MD] and Isolator [Wampole Laboratories, Cranbury, NJ]) and one anaerobic culture (nonvented tryptic or trypticase soy broth [NVTSB; Difco Laboratories, Detroit, or Becton Dickinson]). The relative frequency of isolation of aerobic and facultatively anaerobic gram-positive bacteria and obligately anaerobic bacteria increased over the second half of the 1984–1992 surveillance period. The value of the NVTSB anaerobic blood culture was demonstrated for diagnosing bloodstream infections caused by certain facultatively anaerobic bacteria in addition to obligately anaerobic bacteria and supported the inclusion of the NVTSB anaerobic blood culture as a standard part of the three-component blood culture set used at this institution.

The frequency of aerobic bloodstream infections in hospitals in the United States increased significantly in the 1980s [1]. In contrast, the frequency of anaerobic bloodstream infections decreased [2–8]. As a result, selective rather than routine use of an anaerobic bottle for culturing blood has been proposed. Some studies suggest that this approach is feasible [4, 6, 9–11]; however, other studies do not [12–14].

In an attempt to critically evaluate this issue, we undertook a two-part study to determine (1) the frequency distribution of specific microorganisms causing bloodstream infections in patients at the Mayo Clinic—Rochester Medical Center (Rochester, MN) over an 8-year, 1-month period and (2) the utility of an anaerobic blood culture compared with that of either of two aerobic culture methods for diagnosing these infections.

Materials and Methods

The Mayo Clinic Rochester Microbiology Laboratory services two teaching hospitals (a total of 1,600 beds) and a large multispecialty clinic. Approximately 85% of patients for whom blood cultures are performed are referred to Mayo Clinic Rochester; the remaining patients are residents of Rochester and the surrounding area. Approximately 35,000 blood cultures are performed annually. At Mayo Clinic Rochester, the blood culture set used during the study period consisted of 30 mL of blood distributed equally among the Isolator (I) tube (Wampole Laboratories, Cranbury, NJ); the Septi-Chek (SC) bottle (Becton Dickinson, Sparks, MD), which contains 70 mL of tryptic soy broth and has an attached agar slide; and an anaerobic bottle (a 100-mL, nonvented tryptic soy broth [NVTSB; Difco Laboratories, Detroit] or trypticase soy broth [NVTSB; Becton Dickinson, Sparks, MD] bottle).

When less than 30 mL of blood was obtained, blood culture receptacles were inoculated as follows: the I tube was inoculated first with up to 10 mL if available, followed by the NVTSB bottle with up to 10 mL if available, and then the SC bottle with any remaining blood. All blood culture specimens were drawn by a team of phlebotomists trained and managed by the laboratory. Furthermore, for the first
Table 1. Summary of probable pathogens detected during 1984–1992 by any system.

<table>
<thead>
<tr>
<th>Organism(s)</th>
<th>No. (%) of probable pathogens detected</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All detected</td>
<td>20,456 11,347 9,109</td>
<td></td>
</tr>
<tr>
<td>Aerobic and facultatively anaerobic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>bacteria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staphylococci</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>3,518 (17.2) 1,846 (16.3) 1,672 (18.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><em>Staphylococcus species, coagulase-negative</em></td>
<td>1,831 (9.0) 885 (7.8) 946 (10.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Streptococci</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>658 (3.2) 329 (2.9) 329 (3.6)</td>
<td>.004</td>
</tr>
<tr>
<td><em>Enterococcus faecalis</em></td>
<td>971 (4.8) 478 (4.2) 493 (5.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><em>Enterococcus faecium</em></td>
<td>125 (0.6) 56 (0.5) 60 (0.8)</td>
<td>.016</td>
</tr>
<tr>
<td><em>Streptococcus species, viridans group</em></td>
<td>573 (2.8) 285 (2.5) 288 (3.2)</td>
<td>.005</td>
</tr>
<tr>
<td><em>Streptococcus group B</em></td>
<td>187 (0.9) 74 (0.7) 113 (1.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><em>Streptococcus group A</em></td>
<td>117 (0.6) 72 (0.6) 45 (0.5)</td>
<td>.185</td>
</tr>
<tr>
<td><em>Streptococcus group G</em></td>
<td>82 (0.4) 31 (0.3) 51 (0.6)</td>
<td>.001</td>
</tr>
<tr>
<td>Nutritionally variant streptococci</td>
<td>77 (0.4) 38 (0.3) 39 (0.4)</td>
<td>.279</td>
</tr>
<tr>
<td>Other</td>
<td>146 (0.7) 65 (0.6) 81 (0.9)</td>
<td>.008</td>
</tr>
<tr>
<td>Gram-positive bacilli</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Listeria monocytogenes</em></td>
<td>45 (0.2) 41 (0.4) 4 (0.04)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><em>Corynebacterium jeikeium</em></td>
<td>49 (0.2) 25 (0.2) 24 (0.3)</td>
<td>.530</td>
</tr>
<tr>
<td>Other</td>
<td>472 (2.3) 214 (1.9) 258 (2.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Enterobacteriaceae</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>2,522 (12.3) 1,514 (13.3) 1,008 (11.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>724 (3.5) 370 (3.3) 354 (3.9)</td>
<td>.016</td>
</tr>
<tr>
<td><em>Enterobacter cloacae</em></td>
<td>556 (2.7) 313 (2.8) 243 (2.7)</td>
<td>.692</td>
</tr>
<tr>
<td><em>Serratia marcescens</em></td>
<td>456 (2.2) 370 (3.3) 86 (0.9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><em>Klebsiella oxytoca</em></td>
<td>286 (1.4) 168 (1.5) 118 (1.3)</td>
<td>.262</td>
</tr>
<tr>
<td><em>Enterobacter aerogenes</em></td>
<td>265 (1.3) 169 (1.5) 96 (1.1)</td>
<td>.006</td>
</tr>
<tr>
<td><em>Proteus mirabilis</em></td>
<td>233 (1.3) 147 (1.3) 86 (0.9)</td>
<td>.019</td>
</tr>
<tr>
<td><em>Citrobacter freundii</em></td>
<td>120 (0.6) 64 (0.6) 56 (0.6)</td>
<td>.637</td>
</tr>
<tr>
<td><em>Morganella morganii</em></td>
<td>93 (0.5) 70 (0.6) 23 (0.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><em>Citrobacter diversus</em></td>
<td>44 (0.2) 35 (0.3) 9 (0.1)</td>
<td>.001</td>
</tr>
<tr>
<td>Other</td>
<td>154 (0.8) 90 (0.8) 64 (0.7)</td>
<td>.456</td>
</tr>
<tr>
<td>Other gram-negative bacilli</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>1,204 (5.9) 814 (7.2) 390 (4.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><em>Acinetobacter species</em></td>
<td>198 (1.0) 99 (0.9) 99 (1.1)</td>
<td>.120</td>
</tr>
<tr>
<td><em>Stenotrophomonas maltophilia</em></td>
<td>116 (0.6) 82 (0.7) 34 (0.4)</td>
<td>.001</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>158 (0.8) 106 (0.9) 52 (0.6)</td>
<td>.003</td>
</tr>
<tr>
<td>HACEK group*</td>
<td>55 (0.3) 35 (0.3) 20 (0.2)</td>
<td>.222</td>
</tr>
<tr>
<td>Other</td>
<td>77 (0.4) 41 (0.4) 36 (0.4)</td>
<td>.694</td>
</tr>
<tr>
<td>Obligately anaerobic bacteria</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Bacteroides fragilis</em></td>
<td>920 (4.5) 495 (4.4) 425 (4.7)</td>
<td></td>
</tr>
<tr>
<td><em>Bacteroides fragilis group</em></td>
<td>219 (1.1) 107 (0.9) 112 (1.2)</td>
<td>.048</td>
</tr>
<tr>
<td><em>Bacteroides species, other</em></td>
<td>230 (1.1) 132 (1.2) 98 (1.1)</td>
<td>.556</td>
</tr>
<tr>
<td><em>Bacteroides species, other</em></td>
<td>49 (0.2) 30 (0.3) 19 (0.2)</td>
<td>.417</td>
</tr>
<tr>
<td><em>Prevotella species</em></td>
<td>28 (0.1) 12 (0.1) 16 (0.2)</td>
<td>.179</td>
</tr>
<tr>
<td>* Fusobacterium nucleatum*</td>
<td>36 (0.2) 25 (0.2) 11 (0.1)</td>
<td>.091</td>
</tr>
<tr>
<td><em>Fusobacterium necrophorum</em></td>
<td>16 (0.1) 5 (0.04) 11 (0.1)</td>
<td>.051</td>
</tr>
<tr>
<td><em>Fusobacterium species, other</em></td>
<td>7 (0.03) 6 (0.1) 1 (0.01)</td>
<td>.107</td>
</tr>
<tr>
<td><em>Clostridium perfringens</em></td>
<td>59 (0.3) 31 (0.3) 28 (0.3)</td>
<td>.650</td>
</tr>
<tr>
<td><em>Clostridium septicum</em></td>
<td>34 (0.2) 17 (0.1) 17 (0.2)</td>
<td>.521</td>
</tr>
<tr>
<td><em>Clostridium ramosum</em></td>
<td>29 (0.1) 10 (0.08) 19 (0.2)</td>
<td>.023</td>
</tr>
<tr>
<td><em>Clostridium clostridioforme</em></td>
<td>10 (0.1) 3 (0.03) 7 (0.1)</td>
<td>.105</td>
</tr>
<tr>
<td><em>Clostridium species, other</em></td>
<td>93 (0.5) 63 (0.6) 30 (0.3)</td>
<td>.017</td>
</tr>
<tr>
<td><em>Eubacterium species</em></td>
<td>32 (0.2) 19 (0.2) 13 (0.1)</td>
<td>.656</td>
</tr>
<tr>
<td><em>Actinomyces species</em></td>
<td>9 (0.04) 4 (0.04) 5 (0.1)</td>
<td>.506</td>
</tr>
<tr>
<td><em>Peptostreptococcus species</em></td>
<td>40 (0.2) 24 (0.2) 16 (0.2)</td>
<td>.564</td>
</tr>
<tr>
<td><em>Veillonella species</em></td>
<td>22 (0.1) 7 (0.06) 15 (0.2)</td>
<td>.026</td>
</tr>
<tr>
<td>Other</td>
<td>7 (0.03) 0 (0.0) 7 (0.1)</td>
<td>.003</td>
</tr>
</tbody>
</table>
Table 1. (Continued)

<table>
<thead>
<tr>
<th>Organism(s)</th>
<th>No. (%) of probable pathogens detected</th>
<th>Overall 1984—1988</th>
<th>1989—1992</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yeast and fungi</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Candida albicans</em></td>
<td>1,983 (9.7)</td>
<td>1,182 (10.4)</td>
<td>801 (8.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><em>Candida glabrata</em></td>
<td>376 (1.8)</td>
<td>208 (1.8)</td>
<td>168 (1.8)</td>
<td>.953</td>
</tr>
<tr>
<td><em>Candida parapsilosis</em></td>
<td>359 (1.8)</td>
<td>159 (1.4)</td>
<td>200 (2.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><em>Candida tropicalis</em></td>
<td>254 (1.2)</td>
<td>141 (1.2)</td>
<td>113 (1.2)</td>
<td>.989</td>
</tr>
<tr>
<td><em>Histoplasma capsulatum</em></td>
<td>181 (0.9)</td>
<td>85 (0.7)</td>
<td>96 (1.1)</td>
<td>.021</td>
</tr>
<tr>
<td><em>Cryptococcus neoformans</em></td>
<td>123 (0.6)</td>
<td>91 (0.8)</td>
<td>32 (0.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Other</td>
<td>148 (0.7)</td>
<td>60 (0.5)</td>
<td>88 (1.0)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

NOTE. In the 8-year surveillance period, 7,749 isolates were judged to be probable contaminants: coagulase-negative *Staphylococcus* species (5,261 [67.9%]), *Propionibacterium* species (796 [10.3%]), viridans streptococci (483 [6.2%]), *Bacillus* species (458 [5.9%]), *Corynebacterium* species other than *C. jeikeium* (430 [5.5%]), *Lactobacillus* species (193 [2.5%]), and other species (128 [1.7%]). Aerobic system: Isolator (I; Wampole Laboratories, Cranbury, NJ), Septi-Chek (SC; Becton Dickinson, Sparks, MD). Anaerobic system: Nonvented tryptic soy or trypticase soy broth (NVTSB; Difco Laboratories, Detroit, or Becton Dickinson).

* Haemophilus aphrophilus, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, and Kingella kingae.

Results of 281,797 blood cultures performed during a 24-hour period, two separate venipunctures were routinely performed (two separate sets of blood culture specimens were drawn from separate sites), and if the number of blood cultures ordered over a 24-hour period exceeded four, permission to collect blood for another culture had to be obtained from microbiology personnel. All blood culture specimens were processed in the laboratory within ~4 hours of collection.

The blood culture receptacles (bottles [SC and NVTSB] or tubes [I]) were used as provided by the manufacturer, with no added supplements. Blood culture bottles (SC, NVTSB) were incubated at 35°C in ambient air for a total of 14 days and evaluated at least twice daily in the first 48 hours, once daily for 5 additional days and then once on day 14. For the I tube, the concentrate was inoculated onto the following solid media: sheep blood agar and chocolate blood agar for isolation of bacteria, which were incubated at 35°C in an atmosphere of increased CO₂ for 72 hours; and brain-heart infusion agar, Sabaroud dextrose agar, and inhibitory mold agar for isolation of fungi, incubated at 30°C in ambient air for 21 days. The sheep blood and chocolate blood agar plates were examined twice during the first 24 hours and once daily thereafter. The brain-heart infusion, Sabaroud dextrose, and inhibitory mold agar plates were examined once daily.

The results of 281,797 blood cultures performed during the 8-year, 1-month study period (1 November 1984 through 30 November 1992) were evaluated. For the purposes of the current study, the following microorganisms were categorized as probable contaminants and excluded from further analysis: *Bacillus* species, *Corynebacterium* species (except *Corynebacterium jeikeium*), *Lactobacillus* species, and *Propionibacterium* species. Coagulase-negative *Staphylococcus* species isolates or viridans group *Streptococcus* isolates were considered to be probable pathogens and were included in the data for analysis if they were recovered from ≥2 components (i.e., I, SC, or NVTSB receptacles) in a blood culture set.

The remaining culture results were analyzed. A new episode of bloodstream infection was defined, by means of criteria previously published by Kirkley and colleagues [15], as the initial isolation of a probable pathogen, the subsequent isolation of a different probable pathogen, or the isolation of a previously recovered potential pathogen >5 days after a prior culture was positive for that organism.

For comparing the relative frequencies of isolation of microorganisms for 1984–1988 vs. 1989–1992, P values were calculated on the basis of a two-sided χ² test and/or Fisher's exact test. For each microorganism species, pairwise comparisons of the detection rates between the SC aerobic culture, the I aerobic culture, and the NVTSB anaerobic culture were assessed by means of the sign test. All calculated P values were two-sided, and P-values of <.05 were considered statistically significant.

Results

Of the 281,797 blood cultures performed, 26,001 (9.2%) were positive, and in these positive cultures, 28,205 microorganisms were detected. Seven thousand seven-hundred forty-nine probable contaminants were excluded; thus, 19,068 blood cultures (6.8%) were positive and yielded 20,456 probable pathogens for further evaluation. The frequency distributions
Table 2. Summary of probable pathogens detected by aerobic culture (SC) and/or anaerobic culture (NVTSB) during 1984–1992.

<table>
<thead>
<tr>
<th>Organism(s)</th>
<th>No. of probable pathogens detected</th>
<th>By SC only</th>
<th>By NVTSB only</th>
<th>By both</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All detected</td>
<td>12,126 4,164</td>
<td>1,358 6,604</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aerobic and facultatively anaerobic bacteria</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staphylococci</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>1,870 425</td>
<td>165 1,280</td>
<td></td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td><em>Staphylococcus species</em>, coagulase-negative</td>
<td>1,379 383</td>
<td>91 905</td>
<td></td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Streptococci</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>506 102</td>
<td>48 356</td>
<td></td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td><em>Enterococcus faecalis</em></td>
<td>540 74</td>
<td>96 370</td>
<td></td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><em>Enterococcus faecium</em></td>
<td>74 12</td>
<td>17 45</td>
<td></td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus species</em>, viridans group</td>
<td>484 37</td>
<td>23 424</td>
<td></td>
<td>NS (.093)</td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus group B</em></td>
<td>108 20</td>
<td>19 69</td>
<td></td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus group A</em></td>
<td>78 14</td>
<td>14 50</td>
<td></td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus group G</em></td>
<td>56 9</td>
<td>7 40</td>
<td></td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Nutritionally variant streptococci</td>
<td>59 2</td>
<td>24 33</td>
<td></td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>88 19</td>
<td>16 53</td>
<td></td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Enterobacteriaceae</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>1,704 389</td>
<td>262 1,053</td>
<td></td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>464 93</td>
<td>65 306</td>
<td></td>
<td>.031</td>
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</tr>
<tr>
<td><em>Enterobacter cloacae</em></td>
<td>327 86</td>
<td>40 201</td>
<td></td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td><em>Serratia marcescens</em></td>
<td>261 78</td>
<td>15 168</td>
<td></td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td><em>Klebsiella oxytoca</em></td>
<td>173 36</td>
<td>17 120</td>
<td></td>
<td>.013</td>
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<tr>
<td><em>Enterobacter aerogenes</em></td>
<td>166 40</td>
<td>25 101</td>
<td></td>
<td>NS (.082)</td>
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</tr>
<tr>
<td><em>Proteus mirabilis</em></td>
<td>143 33</td>
<td>19 91</td>
<td></td>
<td>NS (.070)</td>
<td></td>
</tr>
<tr>
<td><em>Citrobacter freundii</em></td>
<td>52 12</td>
<td>6 34</td>
<td></td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><em>Morganella morganii</em></td>
<td>68 17</td>
<td>11 40</td>
<td></td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><em>Citrobacter diversus</em></td>
<td>29 9</td>
<td>8 12</td>
<td></td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>92 27</td>
<td>15 50</td>
<td></td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Other gram-negative bacilli</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>687 502</td>
<td>11 174</td>
<td></td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td><em>Acinetobacter species</em></td>
<td>73 68</td>
<td>1 4</td>
<td></td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td><em>Stenotrophomonas maltophilia</em></td>
<td>48 42</td>
<td>5 5</td>
<td></td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>86 55</td>
<td>3 28</td>
<td></td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>HACEK group*</td>
<td>46 23</td>
<td>3 20</td>
<td></td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>19 19</td>
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<td>Obligately anaerobic bacteria</td>
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<td>59 115</td>
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<td></td>
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<td>96 82</td>
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<td>45 9</td>
<td>18 18</td>
<td></td>
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<td>28 5</td>
<td>10 13</td>
<td></td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><em>Fusobacterium nucleatum</em></td>
<td>28 11</td>
<td>11 6</td>
<td></td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><em>Fusobacterium necrophorum</em></td>
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<td>4 10</td>
<td></td>
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<td></td>
</tr>
<tr>
<td><em>Fusobacterium species</em>, other</td>
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<td>2 4</td>
<td></td>
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<td>11 34</td>
<td></td>
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<td></td>
</tr>
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<td><em>Clostridium septicum</em></td>
<td>22 2</td>
<td>5 15</td>
<td></td>
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<td></td>
</tr>
<tr>
<td><em>Clostridium ramosum</em></td>
<td>24 1</td>
<td>15 8</td>
<td></td>
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</tr>
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<td><em>Clostridium clostridioforme</em></td>
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<td>3 3</td>
<td></td>
<td>.031</td>
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<td><em>Clostridium species</em>, other</td>
<td>83 17</td>
<td>30 36</td>
<td></td>
<td>NS (.079)</td>
<td></td>
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<tr>
<td><em>Eubacterium species</em></td>
<td>29 5</td>
<td>12 12</td>
<td></td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><em>Actinomyces species</em></td>
<td>8 2</td>
<td>4 2</td>
<td></td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><em>Peptostreptococcus species</em></td>
<td>33 8</td>
<td>12 13</td>
<td></td>
<td>NS</td>
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</tr>
</tbody>
</table>

With the exception of Klebsiella pneumoniae, Citrobacter freundii, and Acinetobacter species, all other groups of Enterobacteriaceae and other gram-negative bacilli that were analyzed decreased in relative frequency over the first 4-year time interval (1984–1988) as compared with the second 4-year time interval (1988–1992). Candida albicans and Cryptococcus neoformans also decreased in relative frequency, but other yeasts such as Candida parapsilosis increased in relative frequency, as did the dimorphic fungus Histoplasma capsulatum.

All groups of gram-positive aerobic and facultatively anaerobic cocci and bacilli, with the exception of group A streptococci and Listeria monocytogenes, increased in relative frequency. The relative frequency of isolation for all groups of obligately anaerobic bacteria, when considered together, increased from 4.4% to 4.7%. When individual groups of obligately anaerobic bacteria were studied, members of the Bacteroides fragilis group, Prevotella species, Fusobacterium necrophorum, Clostridium septicum, Clostridium ramosum, Clostridium clostridiiforme, Actinomyces species, and Veillonella species all showed increases in relative frequency.

The overall detection frequencies for probable pathogenic microorganisms for each of the blood culture components for the 8-year, 1-month period (in blood culture sets that contained all three components) were as follows: I aerobic, 78.2%; SC aerobic, 71.7%; and NVTSB anaerobic, 53.1%. For all microorganism groups compared for the SC aerobic and NVTSB anaerobic components (table 2)—with the exception of Enterococcus spp., nutritionally variant streptococci, L. monocytogenes, and obligately anaerobic bacteria—recovery only from the SC aerobic bottle occurred more frequently than did recovery only from the NVTSB anaerobic bottle.

As expected, statistically significantly more obligately anaerobic bacteria were recovered only by the NVTSB anaerobic bottle, including members of the B. fragilis group, C. ramosum, C. clostridiiforme, and Veillonella species. In addition, statistically significantly more nutritionally variant streptococci were recovered only from the NVTSB anaerobic bottle (B. fragilis and members of the B. fragilis group) (table 2). When these comparisons were repeated for bloodstream infections (septic episodes), statistically significant differences that favored the NVTSB component were also observed for B. fragilis and members of the B. fragilis group, C. ramosum, and nutritionally variant streptococci (table 3).

In table 4, the comparisons between the I aerobic and NVTSB anaerobic components are shown. Recovery occurred more frequently in the NVTSB anaerobic culture for Streptococcus pneumoniae, viridans group streptococci, Enterococcus faecium, L. monocytogenes, group A and group G streptococci, nutritionally variant streptococci, Haemophilus influenzae, and every obligately anaerobic group evaluated. These differences were statistically significant for S. pneumoniae, viridans group streptococci, nutritionally variant streptococci, and all groups of obligately anaerobic bacteria except Actinomyces species. When these comparisons were repeated for bloodstream infections (septic episodes), statistically significant differences that favored the NVTSB anaerobic culture were also observed for S. pneumoniae, viridans group streptococci, nutritionally variant streptococci, and all obligately anaerobic bacterial groups except Actinomyces species (table 5).
Table 3. Summary of episodes of bloodstream infections (as defined by the 5-day rule) detected by aerobic culture (SC) and/or anaerobic culture (NVTSB).

<table>
<thead>
<tr>
<th>Organism(s)</th>
<th>No. of detected episodes of bloodstream infections with indicated organism(s)</th>
<th>By SC only</th>
<th>By NVTSB only</th>
<th>By both</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All detected</td>
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<td>1,940</td>
<td>750</td>
<td>3,795</td>
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</tr>
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<td>Aerobic and facultatively anaerobic bacteria</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staphylococci</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
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<td>Staphylococcus aureus</td>
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<td>58</td>
<td>615</td>
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<td>Staphylococcus species, coagulase-negative</td>
<td>868</td>
<td>237</td>
<td>60</td>
<td>571</td>
<td>&lt;.001</td>
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<td>Streptococci</td>
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<td></td>
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<tr>
<td>Streptococcus pneumoniae</td>
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<td>51</td>
<td>27</td>
<td>213</td>
<td>.009</td>
</tr>
<tr>
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<td>43</td>
<td>53</td>
<td>195</td>
<td>NS</td>
</tr>
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<td>35</td>
<td>NS</td>
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<td>14</td>
<td>38</td>
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<td>34</td>
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<td>27</td>
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</tr>
<tr>
<td>Nutritionally variant streptococci</td>
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<td>Other</td>
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<tr>
<td>Other</td>
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<td>3</td>
<td>18</td>
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<tr>
<td>Other</td>
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<td>11</td>
<td>0</td>
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<td>.001</td>
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<td></td>
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<td>69</td>
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<td>55</td>
<td>&lt;.001</td>
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<td>8</td>
<td>14</td>
<td>11</td>
<td>NS</td>
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<td>7</td>
<td>8</td>
<td>NS</td>
</tr>
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<td>8</td>
<td>20</td>
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<td>3</td>
<td>9</td>
<td>NS</td>
</tr>
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<td>7</td>
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<td>NS (.063)</td>
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<td>15</td>
<td>22</td>
<td>21</td>
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<td>8</td>
<td>9</td>
<td>NS</td>
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<td>3</td>
<td>3</td>
<td>NS</td>
</tr>
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<td>Peptostreptococcus species</td>
<td>26</td>
<td>7</td>
<td>9</td>
<td>10</td>
<td>NS</td>
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</table>
Table 3. (Continued)

<table>
<thead>
<tr>
<th>Organism(s)</th>
<th>No. of detected episodes of bloodstream infections with indicated organism(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
</tr>
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<td>Veillonella species</td>
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<td>Other</td>
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<td>Yeast and fungi</td>
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<td>Candida albicans</td>
<td>297</td>
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<td>Candida glabrata</td>
<td>74</td>
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<td>Candida parapsilosis</td>
<td>44</td>
</tr>
<tr>
<td>Candida tropicalis</td>
<td>41</td>
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<tr>
<td>Histoplasma capsulatum</td>
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</tr>
<tr>
<td>Cryptococcus neoformans</td>
<td>19</td>
</tr>
<tr>
<td>Other</td>
<td>18</td>
</tr>
</tbody>
</table>

NOTE. A new episode of bloodstream infection was defined as the initial isolation of a potential pathogen, the subsequent isolation of a different potential pathogen, or the isolation of a previously recovered pathogen >5 days after a prior culture was positive for that organism. This definition was adapted from [15]. The culture systems are defined in the text and in a note to table 1.

1 Haemophilus aphrophilus, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, and Kingella kingae.

Discussion

The results for the first part of our study showed that for our three-component blood culture system, the relative frequency of isolation of aerobic and facultatively anaerobic gram-positive bacteria and obligately anaerobic bacteria increased over the second half of the time period 1984–1992. In contrast, most aerobic and facultatively anaerobic gram-negative bacteria were relatively less frequently isolated from blood cultures over the second half of this period. Although C. albicans and C. neoformans were less frequently isolated, other Candida species and H. capsulatum were more frequently isolated in the second half of the study period.

The increase in the relative frequency of isolation of aerobic and facultatively anaerobic gram-positive bacteria, especially Staphylococcus species, S. pneumoniae, and Enterococcus species, is of particular concern as antimicrobial resistance, including multiple-drug resistance, is becoming more prevalent among these microorganisms. The relative increase in recovery of these microorganisms may be in part related to selective antimicrobial pressures resulting from the use of broad-spectrum antimicrobials such as third-generation cephalosporins, which inhibit many gram-negative bacteria but are less effective or in some cases ineffective against gram-positive bacteria. The relative decrease that we observed in the frequency of C. albicans isolates may relate to the availability of newerazole antifungal drugs and their more frequent use as treatment or prophylaxis for immunoincompetent patients.

The increase in the relative frequency of isolation of obligately anaerobic bacteria, although modest, represented a reversal in the trend we had noted at our institution with this group of organisms in the decade or so preceding the time period evaluated for the current study. We reported a decrease in the relative frequency of obligately anaerobic bacteria isolated from blood cultures at our institution over the period from 1974 to 1988 [2]. Other investigators have reported similar declines in the absolute numbers or frequencies of bacteremias caused by obligately anaerobic bacteria, especially during the late 1970s and throughout the 1980s [3–8], and recently some investigators have reported increases, particularly in the late 1980s and early 1990s [16–18].

Another finding of our study should be stressed. Though the relative frequencies of 4.4% (1984–1988) and 4.7% (1988–1992) for the isolation of obligately anaerobic bac-
Table 4. Summary of probable pathogens detected by aerobic culture (I) and/or anaerobic culture (NVTSB) during 1984–1992.

<table>
<thead>
<tr>
<th>Organism(s)</th>
<th>No. of probable pathogens detected</th>
<th>By NVTSB</th>
<th>By I only</th>
<th>By both</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>16,148</td>
<td>2,205</td>
<td>6,567</td>
<td>7,396</td>
<td>...</td>
</tr>
<tr>
<td>Aerobic and facultatively anaerobic bacteria</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staphylococci</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>2,806</td>
<td>114</td>
<td>1,178</td>
<td>1,514</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><em>Staphylococcus species, coagulase-negative</em></td>
<td>1,818</td>
<td>105</td>
<td>383</td>
<td>1,330</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Streptococci</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>489</td>
<td>112</td>
<td>48</td>
<td>329</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><em>Enterococcus faecalis</em></td>
<td>774</td>
<td>130</td>
<td>161</td>
<td>483</td>
<td>NS (.079)</td>
</tr>
<tr>
<td><em>Enterococcus faecium</em></td>
<td>104</td>
<td>23</td>
<td>21</td>
<td>60</td>
<td>NS</td>
</tr>
<tr>
<td><em>Streptococcus species, viridans group</em></td>
<td>570</td>
<td>59</td>
<td>37</td>
<td>474</td>
<td>.032</td>
</tr>
<tr>
<td><em>Streptococcus group B</em></td>
<td>133</td>
<td>21</td>
<td>39</td>
<td>73</td>
<td>.027</td>
</tr>
<tr>
<td><em>Streptococcus group A</em></td>
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<td>53</td>
<td>NS (.093)</td>
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</tr>
<tr>
<td><em>Streptococcus group G</em></td>
<td>67</td>
<td>21</td>
<td>16</td>
<td>30</td>
<td>NS</td>
</tr>
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<td>Nutritionally variant streptococci</td>
<td>74</td>
<td>43</td>
<td>7</td>
<td>24</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Other</td>
<td>114</td>
<td>27</td>
<td>31</td>
<td>56</td>
<td>NS</td>
</tr>
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<td>Enterobacteriaceae</td>
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</tr>
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<td><em>Escherichia coli</em></td>
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<td>498</td>
<td>1,127</td>
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<td><em>Klebsiella pneumoniae</em></td>
<td>576</td>
<td>83</td>
<td>140</td>
<td>353</td>
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</tr>
<tr>
<td><em>Enterobacter cloacae</em></td>
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<td>67</td>
<td>117</td>
<td>237</td>
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</tr>
<tr>
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<td>122</td>
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</tr>
<tr>
<td><em>Klebsiella oxytoca</em></td>
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<tr>
<td><em>Proteus mirabilis</em></td>
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<td>60</td>
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</tr>
<tr>
<td><em>Citrobacter freundii</em></td>
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<td>29</td>
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<tr>
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</tr>
<tr>
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<td>11</td>
<td>16</td>
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</tr>
<tr>
<td>Other</td>
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<td>18</td>
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<td>52</td>
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<td>Other gram-negative bacilli</td>
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<td></td>
</tr>
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<td><em>Pseudomonas aeruginosa</em></td>
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</tr>
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</tr>
<tr>
<td>Obligately anaerobic bacteria</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td><em>Bacteroides fragilis</em></td>
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<tr>
<td><em>Bacteroides fragilis group</em></td>
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<td>&lt;.001</td>
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<td><em>Bacteroides species, other</em></td>
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<td>&lt;.001</td>
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<td>&lt;.001</td>
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<td>0</td>
<td>&lt;.001</td>
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<td>0</td>
<td>&lt;.001</td>
</tr>
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<td><em>Fusobacterium species, other</em></td>
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</tr>
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<td><em>Clostridium perfringens</em></td>
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<td>2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><em>Clostridium septicum</em></td>
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<td>0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><em>Clostridium ramosum</em></td>
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<td>&lt;.001</td>
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<td><em>Clostridium clostridiosum</em></td>
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<td><em>Clostridium species, other</em></td>
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<td><em>Eubacterium species</em></td>
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<td>1</td>
<td>0</td>
<td>&lt;.001</td>
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<td><em>Actinomyces species</em></td>
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<td>1</td>
<td>2</td>
<td>NS</td>
</tr>
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<td><em>Peptostreptococcus species</em></td>
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Table 4. (Continued).

<table>
<thead>
<tr>
<th>Organism(s)</th>
<th>No. of probable pathogens detected</th>
<th></th>
<th>By NVTSB only</th>
<th>By I only</th>
<th>By both</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Veillonella species</td>
<td>21</td>
<td>21</td>
<td>0</td>
<td>0</td>
<td>&lt;.001</td>
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<td>Other</td>
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<td>6</td>
<td>0</td>
<td>0</td>
<td>.031</td>
<td></td>
</tr>
<tr>
<td>Yeast and fungi</td>
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<td></td>
<td></td>
<td></td>
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<td></td>
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<td>1,229</td>
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<tr>
<td><em>Candida glabrata</em></td>
<td>287</td>
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<td>261</td>
<td>24</td>
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<td></td>
</tr>
<tr>
<td><em>Candida parapsilosis</em></td>
<td>259</td>
<td>0</td>
<td>241</td>
<td>18</td>
<td>&lt;.001</td>
<td></td>
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<tr>
<td><em>Candida tropicalis</em></td>
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<td>158</td>
<td>14</td>
<td>&lt;.001</td>
<td></td>
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<tr>
<td><em>Histoplasma capsulatum</em></td>
<td>159</td>
<td>0</td>
<td>158</td>
<td>1</td>
<td>&lt;.001</td>
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</tr>
<tr>
<td><em>Cryptococcus neoformans</em></td>
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<td>0</td>
<td>99</td>
<td>1</td>
<td>&lt;.001</td>
<td></td>
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<td>112</td>
<td>5</td>
<td>&lt;.001</td>
<td></td>
</tr>
</tbody>
</table>

NOTE. The culture systems are defined in the text and in a note to Table 1. Among the blood culture sets that had both an NVTSB culture and an I culture (with or without an SC culture), 16,148 probable pathogens were isolated by either of these two systems.

The analysis of the two broth bottles in our blood culture system, the aerobic SC and anaerobic NVTSB, showed that the NVTSB anaerobic bottle yielded more isolates and diagnosed more bloodstream infections caused by several facultatively anaerobic bacteria—including *Enterococcus faecalis*, *E. faecium*, and nutritionally variant streptococci—and also recovered as many or more isolates and diagnosed as many or more bloodstream infections caused by all groups of obligately anaerobic bacteria that we analyzed.

The superior recovery of nutritionally variant streptococci by the NVTSB anaerobic bottle may be of particular importance for diagnosing endocarditis caused by this microorganism; however, this condition is rare [20, 21]. Of greater importance may be the ability of the NVTSB anaerobic bottle to yield *Enterococcus* species. These microorganisms have been recently associated with nosocomial outbreaks and are frequently multiple-drug resistant [22–29].

Some clinical laboratories use the lysis centrifugation method for aerobic blood culture (sediment obtained by this method is streaked onto solid media and cultured aerobically) and a nonvented broth bottle for anaerobic culture. Our comparison of the performance of two blood culture systems representative of this approach, the I and NVTSB, showed that the NVTSB anaerobic system not only was a superior system for recovering obligately anaerobic bacteria but also was useful for recovering facultatively anaerobic bacteria.

The NVTSB anaerobic cultures yielded more isolates and diagnosed more bloodstream infections caused by *S. pneumoniae*, *E. faecium*, viridans group streptococci, groups A and G streptococci, nutritionally variant streptococci, and *L. monocytogenes*. The importance of identifying two of these groups of
Table 5. Summary of episodes of bloodstream infections (as defined by the 5-day rule) detected by aerobic culture (I) and/or anaerobic culture (NVTSB).

<table>
<thead>
<tr>
<th>Organism(s)</th>
<th>No. of detected episodes of bloodstream infections with indicated organism(s)</th>
<th>By NVTSB</th>
<th>By I only</th>
<th>By both</th>
<th>P value</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Total</td>
<td>only</td>
<td></td>
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<tr>
<td>All detected</td>
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<td>Aerobic and facultatively anaerobic bacteria</td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Staphylococci</td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<td>386</td>
<td>673</td>
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<td><em>Staphylococcus species, coagulase-negative</em></td>
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<td>228</td>
<td>765</td>
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<td>Streptococci</td>
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<td></td>
<td></td>
<td></td>
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<td><em>Streptococcus pneumoniae</em></td>
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<td>17</td>
<td>196</td>
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<td>24</td>
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<td>4</td>
<td>37</td>
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<td><em>Streptococcus group G</em></td>
<td></td>
<td>42</td>
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<td>10</td>
<td>18</td>
</tr>
<tr>
<td>Nutritionally variant streptococci</td>
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<td>24</td>
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<td>36</td>
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<td>Enterobacteriaceae</td>
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<td></td>
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<td>Other gram-negative bacilli</td>
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<td></td>
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<td><em>Pseudomonas aeruginosa</em></td>
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<td>266</td>
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<td>5</td>
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<td>Other</td>
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<td>42</td>
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<tr>
<td>Obligately anaerobic bacteria</td>
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<td></td>
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<td></td>
</tr>
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<td>2</td>
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</table>
Table 5. (Continued)

<table>
<thead>
<tr>
<th>Organism(s)</th>
<th>Case Total</th>
<th>By NVTSB</th>
<th>By I only</th>
<th>By both</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>By NVTSB</td>
<td>By I only</td>
<td>By both</td>
<td></td>
<td></td>
</tr>
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<td>0</td>
<td>&lt;.001</td>
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<td>Other</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Yeast and fungi</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Candida albicans</td>
<td>364</td>
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<td>274</td>
<td>90</td>
<td>&lt;.001</td>
</tr>
<tr>
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<td>89</td>
<td>11</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Candida parapsilosis</td>
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<td>0</td>
<td>73</td>
<td>9</td>
<td>&lt;.001</td>
</tr>
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<td>1</td>
<td>45</td>
<td>10</td>
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</tr>
<tr>
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<td>&lt;.001</td>
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<td>Other</td>
<td>54</td>
<td>0</td>
<td>51</td>
<td>3</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

NOTE. A new episode of bloodstream infection was defined as the initial isolation of a potential pathogen, the subsequent isolation of a different potential pathogen, or the isolation of a previously recovered pathogen >5 days after a prior culture was positive for that organism. This definition was adapted from [15]. The culture systems are defined in the text and in a note to table 1.

1 Haemophilus aphrophilus, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, and Kingella kingae.

Microorganisms, nutritionally variant streptococci and Enterococcus species, has been stressed previously. S. pneumoniae may be associated with severe life-threatening pneumonia or meningitis, and recently the number of penicillin-resistant strains has increased in the United States [30].

Viridans streptococci are increasingly recognized as the cause of significant infection in immunocompromised hosts and can cause endocarditis, and an increasing number of isolates have been demonstrated to have intermediate or high-level resistance to penicillin [31]. Group A streptococci have recently been shown to cause severe invasive disease, including necrotizing fasciitis and myositis, two conditions frequently associated with bacteremia [32]. Finally, L. monocytogenes may cause significant disease, including meningitis, in immunocompromised patients [33].

Several recent studies have also demonstrated the utility of anaerobic blood culture for recovering facultatively anaerobic bacteria. Martin [12], Murray and colleagues [4], Morris and colleagues [10], and Hellinger and colleagues [34] showed that an anaerobic blood culture was important for recovering not only obligately anaerobic bacteria but also facultatively anaerobic bacteria, including Staphylococcus species, Streptococcus species, Enterococcus species, and members of the family Enterobacteriaceae.

In another study, Mirrett and colleagues [13] demonstrated that for the BacT/Alert automated blood culture system (Organon Teknica, Durham, NC), equal distribution of 10 mL of blood into an anaerobic bottle and an aerobic bottle yielded significantly more microorganisms than if all 10 mL was inoculated into a single aerobic bottle. Again in this study, facultative anaerobic bacteria, including Staphylococcus species and Streptococcus species, were frequently isolated from the anaerobic blood culture bottle.

Some authorities who have advocated the selective use of anaerobic blood culture have targeted patients who have a higher risk for anaerobic bacteremia, including patients who have experienced abdominal or pelvic trauma, have abdominal or pelvic disease (e.g., inflammatory bowel disease or pelvic inflammatory disease), or who have undergone abdominal or pelvic operative procedures [1, 3, 6, 10, 11]. This selective approach assumes that the underlying source of the anaerobic bacteremia will usually always be clinically apparent and that etiologies of anaerobic bacteremia are not changing.

However, Morris and colleagues indicated that the source of the infection was not clinically obvious in 16% of the cases of anaerobic bacteremia that they recently surveyed [10]. Gransden and colleagues observed a statistically significant decline in recent years in the number of cases of anaerobic nosocomial bacteremia arising from what used to be a relatively common source, surgical wounds [8]. One might expect that improved diagnosis, prophylaxis, and treatment of anaerobic infections might effect changes in the sources of bacteremia, especially postsurgically.

As noted previously, enterococcal sepsis is an emerging infectious disease problem in many institutions [22–29] and can occur in clinical settings similar to those associated with anaerobic bacteremia. In addition, Enterococcus species may be associated with urosepsis. One might therefore argue, in view of the results of our comparisons of the aerobic I or aerobic SC
### Table 6. Summary of probable pathogens detected by two aerobic culture methods (SC and/or I).

<table>
<thead>
<tr>
<th>Organism(s)</th>
<th>No. of probable pathogens detected</th>
<th>By SC only</th>
<th>By I only</th>
<th>By both</th>
<th>P value</th>
</tr>
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<td>All detected</td>
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<td>2,430</td>
<td>3,417</td>
<td>8,346</td>
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<td>Aerobic and facultatively anaerobic bacteria</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Staphylococci</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
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<td>Staphylococcus aereus</td>
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<td>1,188</td>
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</tr>
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<td>Clostridium ramosum</td>
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<td>.004</td>
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<td>0</td>
<td>0</td>
<td>NS</td>
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<td>50</td>
<td>2</td>
<td>3</td>
<td>&lt;.001</td>
</tr>
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<td>Eubacterium species</td>
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<td>17</td>
<td>i</td>
<td>0</td>
<td>&lt;.001</td>
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<td>Actinomyces species</td>
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<td>2</td>
<td>1</td>
<td>2</td>
<td>NS</td>
</tr>
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<td>0</td>
<td>0</td>
<td>&lt;.001</td>
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<td>Veillonella species</td>
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<td>0</td>
<td>0</td>
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<td>3</td>
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<td>0</td>
<td>NS</td>
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</table>
Table 6. (Continued)

<table>
<thead>
<tr>
<th>Organism(s)</th>
<th>No. of probable pathogens detected</th>
<th>Total</th>
<th>By SC only</th>
<th>By I only</th>
<th>By both</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yeast and fungi</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Candida albicans</em></td>
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<td>138</td>
<td>336</td>
<td>732</td>
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<tr>
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<td>30</td>
<td>90</td>
<td>173</td>
<td>&lt;.001</td>
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</tr>
<tr>
<td><em>Candida parapsilosis</em></td>
<td>179</td>
<td>22</td>
<td>65</td>
<td>92</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td><em>Candida tropicalis</em></td>
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<td>19</td>
<td>35</td>
<td>91</td>
<td>.040</td>
<td></td>
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<tr>
<td><em>Histoplasma capsulatum</em></td>
<td>160</td>
<td>1</td>
<td>151</td>
<td>8</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td><em>Cryptococcus neoformans</em></td>
<td>5</td>
<td>5</td>
<td>35</td>
<td>45</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>89</td>
<td>9</td>
<td>44</td>
<td>36</td>
<td>&lt;.001</td>
<td></td>
</tr>
</tbody>
</table>

NOTE. The culture systems are defined in the text and in a note to table 1. Among the blood culture sets that had both an SC culture and an I culture (with or without an NVTSB culture), 14,193 probable pathogens were isolated by either of these two systems.

In the current study we did not evaluate the cost-effectiveness of the I system (lysis centrifugation), which requires considerably more preanalytical hands-on time than either the SC or NVTSB broth-based system. To do so would require a formal cost analysis, which is beyond the scope of this article. This analysis should include not only the expenses incurred in the clinical laboratory (processing and reagent costs), but also the savings that might be realized at the bedside if one system more readily detects bloodstream infections than the other.

The diagnosis of endocarditis, especially that caused by fastidious nutritionally variant streptococci, may elude clinicians, and some cases may present as fever of unknown origin. One might also argue, in view of our comparisons of the I or SC cultures with the NVTSB cultures, that when endocarditis or a fever of unknown origin is present, an anaerobic blood culture should be performed. Finally, if a lysis centrifugation system like the I is used as the standard aerobic component of a blood culture system, then one might argue that if bloodstream infections caused by *S. pneumoniae, E. faecium*, viridans streptococci, group A and group G streptococci, or *L. monocytogenes* are possible, the NVTSB anaerobic blood culture should be used.

In summary, the results of the current study demonstrate that the selective targeted use of the NVTSB anaerobic blood culture at our institution would not be feasible.

Although not the focus of the current report, a comparison between the performance of the two aerobic systems, I and SC, was done. These results corroborated the results from a previous study at our institution that also compared these two systems [35]. That study, conducted in 1983, and the current study emphasize the differences in the recovery of microorganisms by these two aerobic blood culturing methods.

The routine use of a high-volume (30 mL) blood culture protocol at our institution is based on previous studies by us and others that showed that the optimal volume of blood for diagnosing bloodstream infection is 20–30 mL per phlebotomy [7, 36]. The importance of blood volume for blood culturing has also been reemphasized recently by Mermel and Maki [37].
Table 7. Summary of episodes of bloodstream infections (as defined by the 5-day rule) detected by two aerobic culture methods (SC and/or I).

<table>
<thead>
<tr>
<th>Organism(s)</th>
<th>No. of detected episodes of bloodstream infections with indicated organism(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
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<tr>
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<tr>
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<tr>
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<tr>
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<td>45</td>
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<tr>
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<td>61</td>
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<tr>
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<td>Proteus mirabilis</td>
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<td>Citrobacter freundii</td>
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### Table 7. (Continued)

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<tr>
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<tr>
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<tr>
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<tr>
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</tr>
<tr>
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<td>48</td>
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</table>

**NOTE.** A new episode of bloodstream infection was defined as the initial isolation of a potential pathogen, the subsequent isolation of a different potential pathogen, or the isolation of a previously recovered pathogen >5 days after a prior culture was positive for that organism. This definition was adapted from [15]. The culture systems are defined in the text and in a note to table 1.

1 Haemophilus arophilus, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, and Kingella kingae.

### References