Diagnosis and Management of Central Line-Associated Blood Stream Infection

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Definitions

- **Colonized Catheter** positive cultures from a catheter without clinical symptoms
- **Exit Site Infection** inflammation or pus within 2 cm of the insertion site
- **Pocket Infection** in a totally implanted device, inflammation or necrosis of overlying skin, or pus in the subcutaneous pocket
- **Tunnel Infection** inflammation along the subcutaneous catheter tunnel
- **Catheter Related Blood Stream Infection** (CRBSI) has the same microbe cultured from the catheter and peripheral blood (CLRBSI = central line-related blood stream infection)
The Impact of CLABSI

➢ 90% of all catheter related BSIs are associated with central-line catheters

• 250,000 cases of (CLABSI) annually in the US
• 80,000 cases occur annually in ICU’s
• The attributable mortality of a CLABSI is 12-25%
• The attributable cost up to $20,000-$56,000 per episode

Attributable Mortality of CLABSI

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>CLABSI Events</th>
<th>Total Events</th>
<th>Control Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>M-H, Random, 95% CI</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blott 2005</td>
<td>49</td>
<td>176</td>
<td>82</td>
<td>315</td>
<td>8.1%</td>
<td>1.10 [0.72, 1.66]</td>
<td></td>
</tr>
<tr>
<td>Cheewinmethasiri 2014</td>
<td>9</td>
<td>44</td>
<td>29</td>
<td>129</td>
<td>6.3%</td>
<td>0.89 [0.38, 2.06]</td>
<td></td>
</tr>
<tr>
<td>Dimick 2001</td>
<td>5</td>
<td>9</td>
<td>53</td>
<td>251</td>
<td>4.3%</td>
<td>4.67 [1.21, 18.00]</td>
<td></td>
</tr>
<tr>
<td>Hajjaj 2014</td>
<td>7</td>
<td>32</td>
<td>10</td>
<td>120</td>
<td>5.4%</td>
<td>3.08 [1.07, 8.88]</td>
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</tr>
<tr>
<td>Higuera 2007</td>
<td>23</td>
<td>55</td>
<td>12</td>
<td>55</td>
<td>6.3%</td>
<td>2.58 [1.12, 5.93]</td>
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<tr>
<td>Hsu 2013</td>
<td>7</td>
<td>16</td>
<td>12</td>
<td>64</td>
<td>4.9%</td>
<td>3.37 [1.05, 10.86]</td>
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<tr>
<td>Kumar 2014</td>
<td>2</td>
<td>28</td>
<td>0</td>
<td>72</td>
<td>1.4%</td>
<td>13.68 [0.64, 294.32]</td>
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<tr>
<td>Leistner 2013</td>
<td>7</td>
<td>40</td>
<td>3</td>
<td>40</td>
<td>4.1%</td>
<td>2.62 [0.63, 10.95]</td>
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<tr>
<td>Olaechea 2013</td>
<td>262</td>
<td>1011</td>
<td>772</td>
<td>4044</td>
<td>8.7%</td>
<td>1.48 [1.26, 1.74]</td>
<td></td>
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<tr>
<td>Pawar 2004</td>
<td>8</td>
<td>35</td>
<td>3</td>
<td>1279</td>
<td>4.2%</td>
<td>126.02 [31.69, 501.22]</td>
<td></td>
</tr>
<tr>
<td>Rello 2000</td>
<td>11</td>
<td>49</td>
<td>17</td>
<td>49</td>
<td>6.1%</td>
<td>0.54 [0.22, 1.33]</td>
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<tr>
<td>Renaud 2001</td>
<td>10</td>
<td>26</td>
<td>7</td>
<td>26</td>
<td>4.9%</td>
<td>1.70 [0.53, 5.48]</td>
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</tr>
<tr>
<td>Rosenthal 2003</td>
<td>77</td>
<td>142</td>
<td>42</td>
<td>142</td>
<td>7.8%</td>
<td>2.82 [1.73, 4.60]</td>
<td></td>
</tr>
<tr>
<td>Smith 2011</td>
<td>4</td>
<td>35</td>
<td>12</td>
<td>1050</td>
<td>4.9%</td>
<td>11.16 [3.41, 36.56]</td>
<td></td>
</tr>
<tr>
<td>Soufir 1999</td>
<td>20</td>
<td>38</td>
<td>20</td>
<td>75</td>
<td>6.4%</td>
<td>3.06 [1.35, 6.92]</td>
<td></td>
</tr>
<tr>
<td>Stevens 2013</td>
<td>56</td>
<td>197</td>
<td>18</td>
<td>201</td>
<td>7.4%</td>
<td>4.04 [2.27, 7.17]</td>
<td></td>
</tr>
<tr>
<td>Warren 2006</td>
<td>21</td>
<td>41</td>
<td>301</td>
<td>1091</td>
<td>7.2%</td>
<td>2.76 [1.47, 5.16]</td>
<td></td>
</tr>
<tr>
<td>Wittekamp 2013</td>
<td>1</td>
<td>2</td>
<td>59</td>
<td>219</td>
<td>1.6%</td>
<td>2.71 [0.17, 44.06]</td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI): 1976 / 9222, 100.0% / 2.75 [1.86, 4.07]

Total events: 579 / 1452

Heterogeneity: Tau² = 0.45; Chi² = 87.14, df = 17 (P < 0.00001); I² = 80%

Test for overall effect: Z = 5.06 (P < 0.00001)
Diagnosis And Management Of Line Sepsis - 1

- Examine patient thoroughly, to identify unrelated sources of infection.

- Carefully examine all catheter insertion sites; gram stain and culture any purulence expressible from insertion site.

- Replace entire delivery system (containers and administration sets). Culture specimen of infusate from each line if:
  - overwhelming septic shock without a source
  - cryptogenic bacteremia/candidemia
 Obtain two 10 to 15-mL blood cultures:
  - If standard (nonquantitative) blood cultures are all that are available, draw 1 from a percutaneous peripheral venipuncture and 1 from the catheter.
  - If quantitative blood culture techniques are available, catheter-drawn cultures can enhance the diagnostic specificity of blood culturing in diagnosis of line sepsis. However, a peripheral percutaneous blood culture must also be drawn concomitantly.
### CRBSI Diagnostic Techniques

<table>
<thead>
<tr>
<th>Techniques without CVC removal</th>
<th>Diagnostic criteria</th>
<th>Accuracy</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simultaneous quantitative blood cultures</td>
<td>Quantitative blood culture drawn through CVC yields CFU count five-fold higher or more than CFU count from simultaneously drawn blood from peripheral vein</td>
<td>93%&lt;sup&gt;22&lt;/sup&gt;</td>
<td>Sensitivity 97–100%&lt;sup&gt;22&lt;/sup&gt;</td>
</tr>
<tr>
<td>Differential time to positivity</td>
<td>Blood culture drawn from CVC becomes positive ≥2 h before simultaneously drawn blood culture from peripheral vein</td>
<td>89–90%&lt;sup&gt;22&lt;/sup&gt;</td>
<td>Specificity 72–87%&lt;sup&gt;22&lt;/sup&gt;</td>
</tr>
<tr>
<td>CVC-drawn quantitative blood culture</td>
<td>Quantitative blood culture from CVC is ≥100 CFU/mL</td>
<td>81–86%&lt;sup&gt;22&lt;/sup&gt;</td>
<td>Specificity 85–96%&lt;sup&gt;22&lt;/sup&gt;</td>
</tr>
<tr>
<td>Acridine orange leucocyte cytopsin</td>
<td>Presence of any bacteria</td>
<td>87%&lt;sup&gt;23&lt;/sup&gt; (96% if followed by Gram stain)&lt;sup&gt;24&lt;/sup&gt;</td>
<td>Specificity 94%&lt;sup&gt;23&lt;/sup&gt; (92% if followed by Gram stain)&lt;sup&gt;24&lt;/sup&gt;</td>
</tr>
<tr>
<td>Endoluminal brush</td>
<td>Quantitative culture with &gt;100 CFU/mL</td>
<td>95%&lt;sup&gt;25&lt;/sup&gt;</td>
<td>Specificity 84%&lt;sup&gt;25&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

| Techniques requiring CVC removal                                  | ≥15 CFU/mL from CVC tip                                                               | 45–84%<sup>26,27</sup>   | Specificity 85%<sup>26,27</sup>                                               | Unable to culture organisms embedded intraluminally                           |
| Quantitative CVC culture: centrifugation, vortexing, sonication   | ≥103 CFU from CVC tip                                                                | 82–83%<sup>22</sup>      | Specificity 89–97%<sup>22</sup>                                               | The cut-off point of ≥103 CFU vs ≥102 CFU is not well defined                 |
| Microscopy of stained CVC: Gram stain and acridine orange staining| Direct visualisation of the microorganisms                                            | 84–100%<sup>28,29</sup> | Specificity 97–100%<sup>28,29</sup>                                          | Labour intensive, impractical                                                   |

CVC=central venous catheter. CFU=colony forming units. CRBSI=catheter-related bloodstream infection.
Suspicion of Line Sepsis: Management of The Device

- Option regarding a peripheral IV or arterial catheter:
  - *Remove and culture catheter*
Suspicion of Line Sepsis: Management of The Device

- Options regarding a short-term CVC:
  - *Purulence* at insertion site
    - or
  - No purulence, but patient *floridly septic without obvious source*:
    - Remove and culture catheter (*and* introducer, if present)
    - Gram stain purulence
    - Re-establish needed access at *new* site
Suspicison of Line Sepsis: Management of The Device

- No purulence, patient not floridly septic:
  - *Leave catheter in place*, pending results of blood cultures
  or
  - *Remove and culture catheter* (and introducer), and re-establish needed access at a *new site*
  or
  - Replace catheter over guidewire
Indications for Culturing an Extracted Intravascular Catheter

- Suspected infection of the catheter
- As part of guidewire catheter exchange
- As part of a clinical study/trial or a QI project

**It must be emphasized that catheters removed in clinical practice should not be routinely cultured and in general it is unacceptable to culture a catheter without accompanying blood cultures.**
Patient with a removable CVC & an acute febrile episode

Mild or moderately ill: (no hypotension or organ failure)
- Blood cultures, 2 sets (1 peripheral)
- If no source of fever identified, remove CVC, culture tip & insert at new site or exchange over a guidewire

Consider antimicrobial therapy

Seriously ill: (hypotension, hypoperfusion, signs & symptoms of organ failure)
- Blood cultures, 2 sets (1 peripheral)
- If no source of fever identified, remove CVC, culture tip & insert at new site, or exchange over a guidewire

Initiate appropriate antimicrobial therapy

Blood cultures (-) & CVC not cultured
- If continued fever & no other source found, remove & culture CVC

Blood cultures (-) & CVC cultures (-)
- Look for another source of infection

Blood cultures (-) & CVC > 15 CFU
- In patients with valvular heart disease or neutropenia, & S. aureus or Candida colonization of CVC, monitor closely for signs of infection & repeat blood cultures accordingly

Blood cultures (+) & CVC > 15 CFU
- See management strategies outlined in Figure 2

Mermel et al, Clin Infect Dis 2001;32:1249-1272
Suggested Guidelines For Changing Catheters Over A Guidewire

1. Indications:
   - Mechanical malfunction or FUO, *without* picture of florid sepsis
   - Patient at very high risk for placement of new catheter due to coagulopathy, morbid obesity, …
   - If patient very septic and could be catheter-related, would *not* place new catheter in old potentially infected site using guidewire. Replace *all* catheters, *new* sites.

2. Same careful *aseptic technique* as for inserting catheter.
   Also replace entire delivery system (tubing and bottle).

3. *Always culture old catheter* unless less than 24 hours old and no signs of systemic infection. If culture subsequently positive, *remove* newly placed catheter

*Routinely* replacing catheters over guidewires as a putative infection control measure is *not* recommended
## Randomized Trial of Scheduled Replacements of Central Venous Catheters in ICU

<table>
<thead>
<tr>
<th>Replacement Protocol</th>
<th>Q3d New Site</th>
<th>Q3d Old Site</th>
<th>As Indicated New Site</th>
<th>As Indicated Old Site</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong># patients</strong></td>
<td>35</td>
<td>40</td>
<td>41</td>
<td>44</td>
</tr>
<tr>
<td><strong># catheters</strong></td>
<td>109</td>
<td>220</td>
<td>94</td>
<td>100</td>
</tr>
<tr>
<td><strong># Bacteremias:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Per 100 catheters</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Per 100 patients</td>
<td>3</td>
<td>10</td>
<td>2</td>
<td>5</td>
</tr>
</tbody>
</table>

Guideline For Replacing A CVC In The Same Site Over A Guidewire-1

- should not be done routinely
- never if purulence at insertion site
- rarely if line sepsis already confirmed microbiologically
  - never, with S. aureus, Bacillus spp, JK diphtheroids, fungi, or mycobacteria
  - never, if evidence of endocarditis, septic thrombosis of great central veins or pulmonary emboli
Guideline For Replacing A CVC In The Same Site Over A Guidewire-2

- Restricted to:
  - very limited sites for new access
  - high risk for access at new site
    eg, severe coagulopathy, morbid obesity...
  - cracked or malfunctioning catheter
  - soft suspicion of line sepsis, not floridly septic
Guideline For Replacing A CVC In The Same Site Over A Guidewire-3

- Protocol:
  - Maximal barrier precautions
  - Two sets of sterile gloves
  - Always culture first catheter, if first catheter infected, remove second(new) catheter ASAP, find new site for central access
Removable central venous catheter (CVC)-related bloodstream infection

Complicated

- Septic thrombosis, endocarditis, osteomyelitis, etc
  - Remove CVC & treat with systemic antibiotic for 4-6 weeks; 6-8 weeks for osteomyelitis

- Coagulase-negative staphylococcus
  - Remove CVC & treat with a systemic antibiotic 5-7 days
    - If catheter is retained, treat with systemic antibiotic +/- antibiotic lock therapy for 10-14 days

Uncomplicated

- S. aureus
  - Remove CVC & treat with a systemic antibiotic for 14 days
    - If TEE (+), extend systemic antibiotic treatment to 4-6 weeks

- Gram-negative bacilli
  - Remove CVC & treat with systemic antibiotic therapy for 10-14 days

- Candida spp.
  - Remove CVC & treat with antifungal therapy for 14 days after last positive blood culture

Line Sepsis: Management of the Longterm Device

- Options regarding surgically-implanted, cuffed Hickman/ Broviac or Hemodialysis catheters or PICCs:
  - Remove at outset if:
    - Tunnel infected
    - Refractory or progressive exit site infection, despite antimicrobial therapy, especially with *Pseudomonas aeruginosa*
    - Evidence of septic thrombosis of cannulated central vein
    - Evidence of endocarditis or septic pulmonary emboli
    - Infecting organism *Bacillus* spp, *Corynebacterium JK*, *Mycobacterium* spp or fungus.

  - Remove later on if:
    - Any of the above absent initially but become manifest later
    - BSI persists ≥3 days despite IV antimicrobial therapy administered through the catheter
Options regarding subcutaneous central ports (e.g. Portacath):

- Cellulitis without BSI: begin antimicrobial therapy - retain port

- Aspirate from port shows organisms on gram-stain or heavy growth in quant culture, or documented port-related bacteremia - remove port
General treatment guidelines

• Remove CVC except in patients with uncomplicated coagulase-negative staphylococci or enterococci bacteremia

• Catheter salvage is an option in patients with uncomplicated CVC infection

• Uncomplicated - defined as:
  ✓ Resolution of bloodstream infection and fever within 72 hours in a patient who:
    ✓ Has no intravascular hardware
    ✓ No endocarditis
    ✓ No supplicative thrombophlebitis

Antibiotic lock therapy

- Indicated in patients when catheter salvage is the goal
- Use in conjunction with systemic antimicrobial therapy
- Dwell times for antibiotic lock solutions should not exceed 48 hours
- Antibiotic concentrations must be increased (100 to 1000 times) to kill bacteria within a biofilm
- *S. aureus* and *Candida* species are less likely to respond to lock therapy

Management Of Line Sepsis-1
Initial Anti-infective Therapy

- Initial empiric regimen must cover MRSA and ESBL+ GNRs:
  - vancomycin (daptomycin or linezolid)
    and
  - ESBL-active broad-spectrum β-lactam
  - Add FQ or AG if septic shock

- Occasionally, guided by Gram stain of insertion site purulence or positive blood cultures
Management Of Line Sepsis-2
Initial Anti-infective Therapy

• Occasionally antifungal therapy begun empirically, before culture results, and should cover fluconazole-resistant, non-albicans strains:
  – Echinocandin

• Modify therapy, when identity and susceptibilities of BSI isolate(s) available, ie for VRE, VMRSA…fungi
Catheter-Associated Septic Shock in the CATSS Database (n=203)

<table>
<thead>
<tr>
<th>Pathogen</th>
<th># patients</th>
<th>% total</th>
<th>% survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>gram negative organisms</td>
<td>70</td>
<td>31.3%</td>
<td>75.7%</td>
</tr>
<tr>
<td>Klebsiella spp</td>
<td>15</td>
<td>7.4%</td>
<td>100%</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>15</td>
<td>7.4%</td>
<td>73.3%</td>
</tr>
<tr>
<td>Enterobacter spp</td>
<td>10</td>
<td>4.9%</td>
<td>70%</td>
</tr>
<tr>
<td>Acinetobacter spp</td>
<td>9</td>
<td>4.4%</td>
<td>77.8%</td>
</tr>
<tr>
<td>E. coli</td>
<td>8</td>
<td>3.9%</td>
<td>12.5%</td>
</tr>
<tr>
<td>Serratia spp</td>
<td>6</td>
<td>3%</td>
<td>100%</td>
</tr>
<tr>
<td>Stenotrophomonas maltophilia</td>
<td>3</td>
<td>1.5%</td>
<td>66.7%</td>
</tr>
<tr>
<td>other gram negative bacilli</td>
<td>4</td>
<td>2.0%</td>
<td>100%</td>
</tr>
<tr>
<td>gram positive organisms</td>
<td>64</td>
<td>31.5%</td>
<td>48.4%</td>
</tr>
<tr>
<td>S. aureus</td>
<td>44</td>
<td>21%</td>
<td>54.5%</td>
</tr>
<tr>
<td>S. faecalis</td>
<td>11</td>
<td>5.4%</td>
<td>45.5%</td>
</tr>
<tr>
<td>S. faecium</td>
<td>7</td>
<td>3.4%</td>
<td>14.3%</td>
</tr>
<tr>
<td>Group A streptococcus spp</td>
<td>2</td>
<td>1%</td>
<td>50%</td>
</tr>
<tr>
<td>yeast/fungi</td>
<td>69</td>
<td>33.99%</td>
<td>24.7%</td>
</tr>
<tr>
<td>C. albicans</td>
<td>40</td>
<td>19.7%</td>
<td>25%</td>
</tr>
<tr>
<td>C. glabrata</td>
<td>19</td>
<td>9.4%</td>
<td>26.3%</td>
</tr>
<tr>
<td>Other yeast</td>
<td>10</td>
<td>5%</td>
<td>10%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>203</strong></td>
<td><strong>100%</strong></td>
<td><strong>51.6%</strong></td>
</tr>
</tbody>
</table>

Central venous catheter related infection accounted for 3.8% of all cases of septic shock.
Mortality as a Function of Adequacy of Empiric Antimicrobial Therapy

### The Benefit of Early vs Late Antibiotics

**Odds Ratio of Survival (95% CI)**

<table>
<thead>
<tr>
<th>Author Yr</th>
<th>No.</th>
<th>Diagnosis</th>
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</thead>
<tbody>
<tr>
<td>Miner 2001</td>
<td>171</td>
<td>meningitis</td>
</tr>
<tr>
<td>Larche 2002</td>
<td>88</td>
<td>Bacteremia/pneumonia*</td>
</tr>
<tr>
<td>Houck 2004</td>
<td>13,771</td>
<td>pneumonia</td>
</tr>
<tr>
<td>Proulx 2005</td>
<td>118</td>
<td>meningitis</td>
</tr>
<tr>
<td>Meehan 1997</td>
<td>14,069</td>
<td>pneumonia</td>
</tr>
<tr>
<td>Gacouin 2002</td>
<td>213</td>
<td>Legionella</td>
</tr>
<tr>
<td>Iregui 2006</td>
<td>107</td>
<td>Vent pneumonia</td>
</tr>
<tr>
<td>Lodise 2003</td>
<td>167</td>
<td>S.aureus</td>
</tr>
<tr>
<td>Kang 2003</td>
<td>123</td>
<td>P. aeruginosa</td>
</tr>
</tbody>
</table>

* Patients with cancer

*Courtesy, C. Natanson, NIH*
Speed of Source Control and Anti-Candida Therapy

Kollef and Kumar, CID 2012
Cumulative Initiation of Effective Antimicrobial Therapy and Survival in Septic Shock

Catheter-Associated Septic Shock

% Survival to Hospital discharge

Time to removal of CVC/initiation of appropriate antibiotics

- 0-3 hours
- 3-6 hours
- 6-12 hours
- 12-24 hours
- >24 hours

Time to antibiotic
Time to CVC removal
Independent risk factors for 30-day all-cause mortality in patients with MDRO CLABSI

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Adjusted HR (95% CI) for 30-day all-cause mortality</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVC not removed</td>
<td>13.5 (6.79–26.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>2.25 (1.35–3.76)</td>
<td>.002</td>
</tr>
<tr>
<td>CHF</td>
<td>1.59 (1.03–2.46)</td>
<td>.035</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>2.28 (1.34–3.87)</td>
<td>.002</td>
</tr>
<tr>
<td>In ICU on date of MDRO CLABSI culture</td>
<td>1.99 (1.33–2.97)</td>
<td>.001</td>
</tr>
</tbody>
</table>
Kaplan–Meier curve for time to death with and without central venous catheter (CVC) removal

Burnham et al. Medicine 2018;97:42
### Results 2X2 table

<table>
<thead>
<tr>
<th>Antibiotic delay</th>
<th>Source control delay</th>
<th>&lt;9 hours</th>
<th>&gt;9 hours</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6 hours</td>
<td>19/20</td>
<td>18/27</td>
<td>37/47</td>
<td>78.7%</td>
</tr>
<tr>
<td></td>
<td>95%</td>
<td>66.7%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;6 hours</td>
<td>23/29</td>
<td>11/50</td>
<td>34/79</td>
<td>43%</td>
</tr>
<tr>
<td></td>
<td>79.3%</td>
<td>22%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>total</td>
<td>42/42</td>
<td>29/77</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>85.7%</td>
<td>37.7%</td>
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</tbody>
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Boxes = n survivors/n (% surv)
Length of treatment

- Length of antimicrobial therapy:
  - ✓ CNS: may retain and treat 10 to 14 days
  - ✓ Enterococcus: may retain and treat 7 to 14 days
  - ✓ S. aureus: remove and treat 4 to 6 weeks
  - ✓ Gram negative bacilli: remove and treat 7 to 14 days; if salvaged, treat 10 to 14 days
  - ✓ Candida species: remove and treated for 14 days; difficult to eradicate without catheter removal

Treatment failure

- No clearance of bacteremia 72 hours after start of antimicrobial therapy or clinical deterioration
- If persistent fever or clinical signs of sepsis, consider work up for:
  - Endocarditis
  - Supprative thrombophlebitis
  - Other metastatic infection
Management Algorithm CLSBSI

Febrile patient with indwelling CVC

Examine local CVC and culture any drainage

- Local signs and symptoms
  - Initiate appropriate therapy
- No local signs and symptoms
  - Check blood culture results

Obtain simultaneous blood cultures via CVC and peripheral vein

- no other source found
  - If possible, exchange and culture CVC
  - Initiate appropriate therapy
- other source found
  - CRBSI management

Check for sources of infection

- Negative blood culture; negative CVC tip
  - Negative peripheral blood culture; positive CVC tip
  - Monitor closely and repeat blood cultures
- Positive blood culture; positive CVC tip
  - CRBSI management

Determine results of DTP or quantitative blood culture*

- Positive CVC blood culture; negative peripheral blood culture
  - Consider antibiotic lock solution
  - CRBSI management
- DTP $\geq 2$ h or quantitative blood culture $\geq 5:1$
- DTP $< 2$ h or quantitative blood culture $< 2:1$
- Positive peripheral blood culture; negative CVC blood culture
  - Look further for other sources of infection
  - Look further for other sources of infection

Raad et al, Lancet Inf Dis 2007;7:645-657
Coagulase-negative Staphylococcus spp

Non-tunnelled CVC
- Remove CVC and treat with ASA for 5-7 days
- May retain CVC and treat with ASA for 7 days and ALT for 10-14 days

Tunneled/implantable CVC
- May retain CVC and treat with ASA for 7 days and ALT for 10-14 days
- If manifestations worsen or persist, remove CVC and treat for 5-7 days

Staphylococcus aureus

Non-tunnelled CVC
- CVC removal is recommended
- ASA for ≥14 days, if transeosophageal echocardiogram is negative

Tunneled/implantable CVC
- If transeosophageal echocardiogram is negative, treat with ASA and ALT for ≥14 days
- Remove CVC if infection is complicated by endocarditis (transeosophageal echocardiogram positive) or septic thrombosis or deep-seated infection and treat with intravenous ASA for 4-6 weeks

Gram-negative bacilli

Non-tunnelled CVC
- CVC removal is recommended
- ASA for 10-14 days

Tunneled/implantable CVC
- CVC removal is recommended
- In absence of other vascular sites, treat with ASA and ALT for 10-14 days and ALT for 14 days
- Remove CVC if there is deterioration or no response, and treat with ASA for 10-14 days

Candida spp

Non-tunnelled or tunnelled CVC
- CVC removal is recommended
- Treat with appropriate antifungal agents for 14 days after last positive blood cultures

If bacteraemia or fungaemia persist, or lack of response after 3 days of CVC removal and initiation of appropriate antibiotics or antifungals

Investigate further the possibility of:
- Septic thrombosis
- Infective endocarditis
- Any other metastatic infection

Kumar, Hemodynamic Monitoring 2013

CVC = central venous catheter
SAT = systemic antimicrobial therapy
ALT = antimicrobial lock therapy
Management Of Life-threatening Infections

**Initial Antibiotic Therapy**

- Based on suspected or identified source
- Don’t forget to consider resistant pathogens
- Start the drugs without delay:

  **ASAP…<1 hour**
If you are not willing to modify the antiinfective regime when culture results become available, why do cultures in the first place?

Always be willing to modify the regimen, based on the culture results and clinical course: simplify, sharpen, delete unnecessary agents.