Pseudomonas aeruginosa CAUTI

CAUTI Technology Workshop
NIDDK

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CAUTI is caused by specific pathogens associated with the microbiome.

Table 4. Distribution and Rank Order of Selected Pathogens Associated With Cases of Healthcare-Associated Infection (HAI) Reported to the National Healthcare Safety Network, January 2006–October 2007, by Type of HAI

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Overall</th>
<th>CLABSI</th>
<th>CAUTI</th>
<th>VAP</th>
<th>SSI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%) of pathogenic isolates</td>
<td>Rank</td>
<td>No. (%) of pathogenic isolates</td>
<td>Rank</td>
<td>No. (%) of pathogenic isolates</td>
</tr>
<tr>
<td>CoNS</td>
<td>5,178 (15.3)</td>
<td>1</td>
<td>3,900 (34.1)</td>
<td>1</td>
<td>234 (2.5)</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>4,913 (14.5)</td>
<td>2</td>
<td>1,127 (9.9)</td>
<td>4</td>
<td>208 (2.2)</td>
</tr>
<tr>
<td>Enterococcus species</td>
<td>3,028 (3.0)</td>
<td>3</td>
<td>265 (2.3)</td>
<td>2</td>
<td>496 (5.3)</td>
</tr>
<tr>
<td>E. faecalis</td>
<td>1,177 (3.5)</td>
<td>4</td>
<td>627 (5.5)</td>
<td>2</td>
<td>335 (3.6)</td>
</tr>
<tr>
<td>E. faecium</td>
<td>1,888 (5.6)</td>
<td>3</td>
<td>942 (8.2)</td>
<td>2</td>
<td>562 (6.0)</td>
</tr>
<tr>
<td>NOS</td>
<td>1,208 (3.0)</td>
<td>3</td>
<td>265 (2.3)</td>
<td>3</td>
<td>496 (5.3)</td>
</tr>
<tr>
<td>Candida species</td>
<td>2,295 (6.8)</td>
<td>4</td>
<td>673 (5.9)</td>
<td>3</td>
<td>1,361 (14.5)</td>
</tr>
<tr>
<td>C. albicans</td>
<td>2,295 (6.8)</td>
<td>4</td>
<td>673 (5.9)</td>
<td>3</td>
<td>1,361 (14.5)</td>
</tr>
<tr>
<td>Other Candida spp. or NOS</td>
<td>3,028 (3.0)</td>
<td>3</td>
<td>265 (2.3)</td>
<td>2</td>
<td>496 (5.3)</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>3,264 (9.6)</td>
<td>5</td>
<td>669 (5.9)</td>
<td>2</td>
<td>613 (6.5)</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>2,664 (7.9)</td>
<td>6</td>
<td>357 (3.1)</td>
<td>7</td>
<td>938 (10.0)</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>1,956 (5.8)</td>
<td>7</td>
<td>563 (4.9)</td>
<td>5</td>
<td>722 (7.7)</td>
</tr>
<tr>
<td>Enterobacter species</td>
<td>1,624 (4.8)</td>
<td>8</td>
<td>443 (3.9)</td>
<td>6</td>
<td>384 (4.1)</td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td>902 (2.7)</td>
<td>9</td>
<td>252 (2.2)</td>
<td>9</td>
<td>109 (1.2)</td>
</tr>
<tr>
<td>Klebsiella oxytoca</td>
<td>359 (1.1)</td>
<td>10</td>
<td>99 (0.9)</td>
<td>10</td>
<td>85 (0.9)</td>
</tr>
<tr>
<td>Other</td>
<td>5,267 (15.6)</td>
<td>1</td>
<td>1,201 (10.5)</td>
<td>11</td>
<td>1,321 (14.1)</td>
</tr>
<tr>
<td>Total</td>
<td>33,848 (100)</td>
<td>1</td>
<td>11,428 (100)</td>
<td>1</td>
<td>9,377 (100)</td>
</tr>
</tbody>
</table>

Note: Of the 28,502 cases of HAI reported, 4,671 (16.4%) were polymicrobial. CAUTI, catheter-associated urinary tract infection; CLABSI, central line-associated bloodstream infection; CoNS, coagulase-negative staphylococci; NOS, not otherwise specified; SSI, surgical site infection; VAP, ventilator-associated pneumonia.

P. aeruginosa is an important CAUTI pathogen that is NOT associated with the microbiome.

Hidron, et al. *Infection Control Hospital Epidemiol.* 2008
*P. aeruginosa* as a model for biofilm formation

Adopted from Valentini Filloux JBC 2016
Key questions

• Does *P. aeruginosa* form a biofilm on the catheter during CAUTI?
• How does *P. aeruginosa* form a biofilm on the catheter? What biofilm factors are used?
• What is the response of *P. aeruginosa* to urine?
• What is role of quorum-sensing for *P. aeruginosa* CAUTI?
Murine model of catheter-associated urinary tract infection (CAUTI)

Mice are CF-1 outbred mouse to better mimic human populations
Infect for 7-14 days (time when P. aeruginosa is cleared in the absence of catheter

*P. aeruginosa* uses exopolysaccharides to form biofilm on catheters *in vitro*

*Angela Records*

*Stephanie Cole*

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**Cole et al, Infection and Immunity 2014**
*P. aeruginosa* forms a biofilm in the catheter during infection

SEM of the catheter and bladder reveals *P. aeruginosa* only in the interior of the catheter

Cole *et al*, Infection and Immunity 2014
**P. aeruginosa** do not use Pel and Psl exopolysaccharides during CAUTI

1. There is a wide distribution of CFU/organ in outbred mice
2. Most mice with pyelonephritis have bacteria in the bladder
3. Most CFU in the bladder are associated with the catheter
4. *P. aeruginosa* forms biofilm independent of known biofilm exopolysaccharides

Similar results were obtained for PAO1

Cole *et al*, Infection and Immunity 2014
What is triggering PA14 ΔpelD to form a PEL and PSL independent biofilm?

Two possibilities (that are not mutually exclusive):

1. The luminal contents of the bladder triggers a novel biofilm pathway
2. The host response triggers a novel biofilm pathway

Cole et al, Infection and Immunity 2014
Urine can induce PA14 ΔpelD to form biofilm

Cole et al, Infection and Immunity 2014
Urea in urine triggers the alternate \textit{P. aeruginosa} biofilm pathway

\textbf{PA14 $\Delta$pelD}

\textbf{PA14}

Cole \textit{et al}, Infection and Immunity 2014
Urea alters *P. aeruginosa* biofilms morphology

Urea triggers a heterogeneous biofilm for both PA14 and the Δ*pelD* mutant

Cole *et al*, Infection and Immunity 2014
Urea induced *P. aeruginosa* biofilms are sensitive to Dnase I

Conclusion: Urea in urine induces *P. aeruginosa* to form a DNA dependent biofilm

Cole *et al*, Infection and Immunity 2014