Ventilator-Associated Pneumonia: Diagnosis and Management

Presley Regional Trauma Center
Department of Surgery
University of Tennessee Health Science Center
Memphis, Tennessee
Ventilator Associated Pneumonia

• Acquired infection not present at the initiation of mechanical ventilation
  
  - Pneumonia that occurs > 48 hours after endotracheal intubation
  
  - Caused primarily by micro-aspiration of pooled secretions above ETT cuff
Ventilator Associated Pneumonia

- Prolongs duration of mechanical ventilation by up to 11 days
- Increases LOS by 6–25 days
- Cost ranges from $12 – 40K per episode
- Independently associated with mortality in less severely injured trauma patients (ISS < 25)
Ventilator Associated Pneumonia

- Most common serious infection in surgical ICUs
- Clinical syndrome mimics post-injury and post-surgical systemic inflammation
- Delicate balance between unnecessary and inadequate antimicrobial therapy
- VAP is a surgical disease
VAP Therapy

- VAP represents one of the principal driving forces behind antibiotic usage in the ICU
- Prolonged exposure to unnecessary antibiotics remains a strong predictor for the development of antibiotic resistance
- Determining the optimal duration of definitive antibiotic therapy for VAP remains the key to limiting inappropriate antibiotic exposure
Empiric Antibiotic Therapy

Antibiotic Overuse
- Broad-spectrum regimens
- Unnecessary use
- Prolonged use

Resistance
- Inducible
- Selective

Inadequate Empiric Antibiotic Therapy

Morbidity & Mortality
Ventilator Associated Pneumonia

- issues -

- Prevention
  - Ventilator bundles

- Diagnosis
  - Quantitative cultures to differentiate SIRS
Diagnosis of VAP - challenge -

- Controversial
- Varied Definitions
  - clinical signs and symptoms
  - radiographic evidence
  - laboratory data
  - culture results
- Medical vs surgical patients
Diagnosis of VAP

- evolution -

• Sputum culture
  - simple
  - sensitive, not specific
  - unnecessary antibiotics

• Invasive techniques
  - more labor intensive
  - sensitive & specific
  - more appropriate antibiotics

• Clinical Pulmonary Infection Score
  - simple
  - pulmonary inflammatory response
  - antibiotic duration
CPIS

- Temperature
- Blood leukocytes
- Tracheal secretions
- $\text{PaO}_2 / \text{FiO}_2$
- Chest radiograph

Scores range 0 - 10
CPIS

- Temperature
  - $>36.5 \text{ and } <38.4$ 0 pt
  - $>38.5 \text{ and } <38.9$ 1 pt
  - $>39.0 \text{ and } <36.0$ 2 pt

- Blood leukocytes

- Tracheal secretions

- PaO$_2$ / FiO$_2$

- Chest radiograph
CPIS

- Temperature
- Blood leukocytes
- Tracheal secretions
- PaO\textsubscript{2} / FiO\textsubscript{2}
- Chest radiograph

\[
\begin{align*}
>4,000 \text{ and } & \leq 11,000 \quad 0 \text{ pt} \\
<4,000 \text{ and } & >11,000 \quad 1 \text{ pt}
\end{align*}
\]
CPIS

- Temperature
- Blood leukocytes
- Tracheal secretions
  - few: 0 pt
  - moderate: 1 pt
  - large: 2 pt
  - purulent: +1 pt
- \( \text{PaO}_2 / \text{FiO}_2 \)
- Chest radiograph
CPIS

- Temperature
- Blood leukocytes
- Tracheal secretions
- \( \text{PaO}_2 / \text{FiO}_2 \)
- Chest radiograph

\[
\begin{align*}
>240 \text{ or ARDS} & \quad 0 \text{ pt} \\
\leq 240 \text{ without ARDS} & \quad 1 \text{ pt}
\end{align*}
\]
CPIS

- Temperature
- Blood leukocytes
- Tracheal secretions
- \( \text{PaO}_2 / \text{FiO}_2 \)
- Chest radiograph

- no infiltrate: 0 pt
- patchy / diffuse: 1 pt
- localized: 2 pt
VAP Diagnosis

- Clinical criteria alone – fever, leukocytosis, purulent sputum, CXR infiltrates – are not reliable

- BAL with quantitative cultures
  - Differentiate VAP from SIRS
  - Improve overall survival
Quantitative Cultures
- diagnostic threshold -

Lower Threshold
\(<10^5 \text{CFU/ml}\)
- Prolonged Exposure
- Unnecessary Antibiotics
- Microbial Resistance

Higher Threshold
\(\geq10^5 \text{CFU/ml}\)
- Untreated VAP
- Treatment Delays
- Mortality
Prior Experience
- Memphis & Wake Forest -

- Diagnostic threshold $\geq 10^5$
- FN rates = 11% with $10^4$ organisms
- Mortality rates = 8 to 12% with FN cultures
- Lower threshold $\rightarrow$ unnecessary VAP therapy
- *Diagnostic threshold should be $\geq 10^5$*
$10^4$ BALs

**CS**
- 968 FOB
- 73 False-negatives
- 7.5%

**PS**
- 324 FOB
- 36 False-negatives
- 11%

$p = 0.045$
<table>
<thead>
<tr>
<th></th>
<th>CS</th>
<th>PS</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
<td>39</td>
<td>37</td>
</tr>
<tr>
<td>Injury Severity Score</td>
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<td>35</td>
</tr>
<tr>
<td>GCS Score</td>
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<td>9</td>
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<tr>
<td>24 hr RBC Transfusion</td>
<td>4.5</td>
<td>4.4</td>
</tr>
<tr>
<td>Mortality (%)</td>
<td>5.4</td>
<td>8.3</td>
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<tr>
<td>Antibiotic</td>
<td>n</td>
<td>Charge</td>
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<tr>
<td>-----------------</td>
<td>-----</td>
<td>--------</td>
</tr>
<tr>
<td>Unasyn</td>
<td>311</td>
<td>$280</td>
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<tr>
<td>Vancomycin</td>
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<td>Cefepime</td>
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<td>Primaxin</td>
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<td>$1000</td>
</tr>
<tr>
<td>Bactrim</td>
<td>94</td>
<td>$225</td>
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</tbody>
</table>

Mean charge per VAP episode = $2500
Charge Reduction

968 BALs with $10^4$ CFU/ml

- 313 with VAP from another organism

= 655 episodes unnecessary antibiotics

X $2500$ per $10^4$ unnecessary episode

=
Charge Reduction

968 BALs with $10^4$ CFU/ml
- 313 with VAP from another organism

= 655 episodes unnecessary antibiotics
x $2500$ per $10^4$ unnecessary episode

= $>1.6$ million antibiotic charges
Conclusions

• The results of the current study do not support the purported benefit of a lower diagnostic threshold for VAP

• The diagnostic threshold for VAP in trauma patients should be $\geq 10^5$
Conclusions

• Continued adherence to this diagnostic threshold for quantitative BAL in trauma patients
  - has maintained low false-negative rates
  - reduced patient charges
  - has not increased mortality
Clinical Suspicion of VAP

Bronchoscopy with BAL

≤7 days in ICU
- Ampicillin/sulbactam
  - 3g IV q6h

>7 days in ICU
- Vancomycin 20mg/kg IV q12h +
  - Cefepime 2g IV q8h

Culture Results

<10^5 CFU/ml
- D/C Antibiotics

≥10^5 CFU/ml
- Streamline Antibiotics
Ventilator Associated Pneumonia

- issues -

- Prevention
  - Ventilator bundles

- Diagnosis
  - Quantitative cultures to differentiate SIRS

- Treatment
  - Antibiotic duration
Duration of Therapy

- Resolution of clinical signs may be non-specific in trauma patients with other reasons for systemic inflammation.

- Use of an arbitrary day cutoff or clinical signs may be suboptimal for some resulting in relapse and/or antibiotic resistance due to unnecessary therapy.
Objective Evidence

- Use of a defined bacteriologic strategy overcomes need for arbitrary antibiotic therapy endpoints by objectively identifying patients with MR of VAP

- Optimal duration
  - repeat BAL could be used to guide antimicrobial duration for VAP in trauma patients
    - Mueller et al. 2007
Repeat BAL

- Can safely guide the duration of definitive antibiotic therapy for VAP in critically ill trauma patients
- Resulted in a mean 7-day decrease in the duration of definitive antibiotic therapy for VAP
- Patients with isolated early VAP can be treated for 7 days without repeat BAL
Clinical Signs
- Temperature -

Days of therapy: 0, 4, 7, 10, 14

- 7 Days
- 10 Days
- 14 Days

Temperature range: 35 to 40
Clinical Signs
- White Blood Cell Counts -

Days of therapy
Clinical Signs

- $\text{PaO}_2 / \text{FiO}_2$ -

Days of therapy
Duration of antimicrobial therapy for VAP in trauma patients should be dictated by the causative pathogen:

- 14 days for PA
- 10 or 14 days for MRSA, AB, SM and ENB based on quantitative culture on repeat BAL
Hospital-acquired VAP?

- **PA**
  - Continue Antibiotics for 14 Days

- **MRSA, AB, SM, ENB**
  - Repeat BAL on Day 7 of Appropriate Therapy

VAP pathogens $\leq 10^3$ CFU/ml

- **Yes**
  - Antibiotics 10 Days

- **No**
  - Antibiotics 14 Days
Definitions

- **Appropriate therapy**: at least one antibiotic demonstrates *in vitro* activity against the identified pathogen(s)
- **Microbiological resolution**: $\leq 10^3$ CFU/ml on repeat BAL
- **VAP recurrence**: $>10^5$ CFU/ml on subsequent BAL performed within 2 weeks after cessation of *appropriate* antibiotic therapy
### Antibiotic Days

<table>
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<tr>
<th></th>
<th>MRSA</th>
<th>PA</th>
<th>AB</th>
<th>SM</th>
<th>ENB</th>
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<td><strong>Previous Study</strong></td>
<td>12.5</td>
<td>13.1</td>
<td>10.8</td>
<td>11.1</td>
<td>10.7</td>
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<tr>
<td><strong>Current Study</strong></td>
<td>9.9</td>
<td>14</td>
<td>10</td>
<td>9.7</td>
<td>9.8</td>
</tr>
</tbody>
</table>

Reduction of 4.8 ABx days/VAP episode
Outcome by Pathogen

- Recurrence -

Previous Study | Current Study
---|---
MRSA | 2.0% | 1.5%
p = 0.3
<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Charge/d</th>
<th>Abx d/VAP</th>
<th>VAP/patient</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>
# Antibiotic Charges

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Charge/d</th>
<th>Abx d/VAP</th>
<th>VAP/patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin</td>
<td>$210</td>
<td>-2.6</td>
<td>1.03</td>
</tr>
<tr>
<td>Cefepime</td>
<td>$210</td>
<td>-0.9</td>
<td>1.14</td>
</tr>
<tr>
<td>Cefepime*</td>
<td>$210</td>
<td>0.9</td>
<td>1.01</td>
</tr>
<tr>
<td>Primaxin</td>
<td>$1000</td>
<td>-0.8</td>
<td>1.1</td>
</tr>
<tr>
<td>Bactrim</td>
<td>$225</td>
<td>-1.4</td>
<td>1.1</td>
</tr>
</tbody>
</table>

Mean reduction per patient = $1813.45

* Pseudomonas
Number of bronchoscopies with bronchoalveolar lavage decreased by 30% per patient
30% reduction in #BALs per patient

$1721.64 per patient (BAL + quantitative culture) + 4.8 less antibiotic days per VAP episode

$1813.45 per patient

= $3535.09 per patient
Charge Reduction

30% reduction in #BALs per patient

$1721.64 per patient (BAL + quantitative culture)

+ 4.8 less antibiotic days per VAP episode

$1813.45 per patient

= $3535.09 per patient

$1.35 million over the study period
Conclusions

• Hospital-acquired VAP can be managed effectively by a defined course of therapy dictated solely by the causative pathogen

• Adherence to an established algorithm
  - simplifies the management of VAP
  - reduces antibiotic exposure and adverse effects
  - decreases antibiotic duration and patient charges *without* impacting recurrence
Ventilator Associated Pneumonia - issues -

• Prevention
  ✓ Ventilator bundles

• Diagnosis
  ✓ Quantitative cultures to differentiate SIRS

• Treatment
  ✓ Antibiotic duration
VAP

Diagnostic and management timeline

VAP Suspected

Culture

Empiric Therapy

Final Culture Results

Definitive Therapy

0

< 12h

< 24h

72-96h

10-14d

Temperature

WBC

Sputum

Chest x-ray

Quantitative Invasive

Pathway

Streamline

Duration of therapy
What You Need to Know

Quantitative culture (invasive or non-invasive)
- Accurate identification of pathogen
- Decreases overuse of antibiotics

Diagnostic threshold based on culture
- Differentiate between VAP and VAP-like syndromes
- Overcomes the limitations of clinical diagnosis
What You Need to Know

*Pathway-guided empiric antibiotic therapy*
- Decreases overuse of antibiotics
- Increases frequency of adequate empiric therapy

*Streamlined definitive therapy*
- Decreases overuse of antibiotics
- Decrease antibiotic resistance