Diagnosing Ventilator Associated Pneumonia (VAP)

TERRENCE SHENFIELD BS, RRT, RPFT, NPS
UNIVERSITY HOSPITAL

Objectives

- Why is understanding what VAP is important?
- Explain how a patient may get VAP
- Explain why clinical data is not enough to make diagnoses
- Explain why microbiology data is not enough to make diagnoses
- Tools used to screen/identifying patients with VAP that therapist should know
- Using cutting edge medical science to identify who has VAP (biomarkers)

Why is Identifying Who Has VAP Important

- 8-20% of ICU patients
- 27% of all mechanical ventilator patients
- Mortality rates 20 to 50% (up to 70% with multi-resistant organisms)
VAP increases:
- Medical costs
- Ventilator days
- ICU and hospital LOS

Estimated direct cost of excess hospital stay due to VAP is $40,000 per patient

Chest (2002)

Definition of VAP

- Pneumonia that develops in someone who has been intubated
- Typically in studies, patients are only included if intubated greater than 48 hours
  - Early onset = less than 4 days
  - Late onset = greater than 4 days
- Endotracheal intubation increases risk of developing pneumonia by 6 to 21 fold
- Accounts for 90% of infections in mechanically ventilated patients

CDC definition of pneumonia

Table 4. Algorithms for clinically defined pneumonia (PAJ)

<table>
<thead>
<tr>
<th>Lab Abnormality</th>
<th>Signs/Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever or hypothermia</td>
<td>↓</td>
</tr>
<tr>
<td>New or persistent cough</td>
<td>↓</td>
</tr>
<tr>
<td>New sputum</td>
<td>↓</td>
</tr>
<tr>
<td>Chest radiograph</td>
<td>↓</td>
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<tr>
<td>Cyanosis</td>
<td>↓</td>
</tr>
<tr>
<td>New respiratory difficulty</td>
<td>↓</td>
</tr>
</tbody>
</table>

Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health-care-associated infection and criteria for specific types of infection in the acute care setting.
Causative Organisms

- Early onset:
  - Hemophilus influenza
  - Streptococcus pneumoniae
  - Staphylococcus aureus (methicillin sensitive)
  - Escherichia coli
  - Klebsiella
- Late onset:
  - Pseudomonas aeruginosa
  - Acinetobacter
  - Staphylococcus aureus (methicillin resistant)
- Most strains responsible for early onset VAP are antibiotic sensitive. Those responsible for late onset VAP are usually multiple antibiotic resistant


How do you get VAP?

- There are only four routes through which bacteria can reach the lower respiratory tract to cause VAP
  - Hematogenous (spread by way of the bloodstream)
  - Inhalation (improper manipulation of the circuits)
  - Aspiration (this is the main route)

Aspiration

- Aspiration of gastric contents
- Most patients are sedated, or even paralyzed, and cannot cough efficiently
- Once aspirated, the secretions pool above the inflated endotracheal tube cuff
- Cuff leak is associated with introduction of organisms into the distal airspaces
How does a clinician become aware that the patient has VAP?

How do you diagnose VAP?
What tools can the clinician use to determine if patient has VAP?

Tools Used in Diagnosing VAP

- CDC definition of pneumonia
- Clinical Features
- CPIS scores
- Tracheal aspirates
- Bronchoscopic-directed protected specimen brush sampling and quantitative culture
- Blind protected bronchoalveolar lavage (BAL)
- Biomarkers

Limitations of Clinical Diagnoses of VAP

- Chest radiology is very sensitive but not specific
  - Atelectasis
  - ARDS
  - Alveolar hemorrhage
  - Infarction
  - All can be mistaken for pneumonia
- Leukocytosis
- Purulent secretions
- Clinical approach leads to more antibiotic therapy which leads to resistant organisms
Clinical pulmonary infection score (CPIS)

- CPIS is an accepted tool for clinical estimation of ventilator-associated pneumonia (VAP), encompassing five components:
  - Temperature
  - Blood leukocytes
  - Tracheal secretions
  - Oxygenation index
  - Chest X-ray

CPIS was originally described by Pugin and colleagues while comparing bronchoscopic and nonbronchoscopic lavage fluid for the diagnosis of VAP. CPIS score greater than six indicates VAP. Validated CPIS scores to postmortem lung cultures. High false-positive and false-negative rates observed. Sensitivity and specificity poor.

**Table 1** Simplified Version of the Clinical Pulmonary Infection Score (CPIS) Used in This Study

<table>
<thead>
<tr>
<th>Value</th>
<th>Points</th>
</tr>
</thead>
</table>
| Temperature
  - 38.5–38.4°C | 0 |
  - 38.5–38.9°C | 1 |
  - >38.9°C or <36.9°C | 2 |
| Blood leukocytes per mm³
  - <4000 or >11,000 | 0 |
  - 4000–11,000 | 1 |
| Tracheal secretions
  - Few | 0 |
  - Moderate | 1 |
  - Large | 2 |
  - Purulent* | 1 |
| Oxygenation PaO₂/FiO₂, mm Hg
  - >240 or presence of ARDS | 0 |
  - >240 and absence of ARDS | 2 |
| Chest radiograph
  - No infiltrate | 0 |
  - Patchy or diffuse infiltrate | 1 |
  - Localized infiltrate | 2 |

*Add one additional point to the tracheal secretions score if the secretions are purulent.
Sensitivity and specificity made simple!

- **Sensitivity** = probability of a positive test among patients with disease
- **Specificity** = probability of a negative test among patients without disease
- **Prevalence** = probability of disease in the entire population at any point in time
- **Incidence** = probability that a patient without disease develops the disease during an interval

\[
\text{Sensitivity} = \frac{a}{a+c} \\
\text{Specificity} = \frac{d}{b+d}
\]

<table>
<thead>
<tr>
<th></th>
<th>Patients with disease</th>
<th>Patients without disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test is positive</td>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td>Test is negative</td>
<td>c</td>
<td>d</td>
</tr>
</tbody>
</table>

Tracheal aspirates

- Performed by Respiratory Therapist or nurse
- Gram stains (differentiates gram positive and gram negative species)
- Culture and sensitivity
- Tracheal aspirate Gram stains may ... provide a reasonable first-line approach for empiric therapy selection pending acquisition of more invasive specimen types
Tracheal aspirates

- GNR (Gram-negative rods) stains from tracheal aspirates specimens were highly predictive of GNR culture results 89%-91%
- GPC (Gram-positive coccus) stains yielded GPC organisms in 33%-35% culture results
- Tracheobronchial aspirates, $\geq 10^5$ CFU/mL

Protected specimen brushing (PSB)

- Protected specimen brushing (PSB) with the aid of bronchoscopy is the diagnostic method of choice
- Procedure is time and labor intensive and expensive
- Only done by physician
- Fiberoptic bronchoscopy and PSB for quantitative diagnosis of pneumonia

Protected specimen brushing (PSB)

- Bronchoscope was inserted through the endotracheal tube and into the main stem bronchus of the lung suspected of pneumonia by chest roentgenogram
- All lobar bronchi were examined
- A specimen was obtained by expressing and retracting the inner catheter and brush in the standard fashion
Protected specimen brushing (PSB)

- The brush tip was then placed in 1 mL of nonbacteriostatic saline
- Processed by our microbiology laboratory for quantitative culture within 2 hours
- Only those cultures with $10^5$ CFUs/mL (colony forming units) were reported as positive
- Bronchoscopic protected-brush specimens, $>10^3$ colony forming units [CFU]/mL

VAP confirmation values

- Bronchoscopic protected-brush specimens, $>10^3$ colony forming units [CFU]/mL
- Blind BAL, $>10^4$ CFU/mL
- Tracheobronchial aspirates, $>10^5$ CFU/mL

BAL Catheter

- Prepackaged, commercially available telescoping catheter
- BAL Cath- Ballard Medical Products
- Curved tip of the catheter that is directed toward the desired lung
- Can be done by trained Respiratory Therapist
**BAL Catheter**

- Until resistance was met
- Wedged position
- Instill sterile saline
- Processed by our microbiology laboratory for quantitative culture within 2 hours
- Blind BAL, $\geq 10^4$ CFU/mL

**DIAGNOSTIC TESTS: ACCURACY**

- Endotracheal aspiration with quantitative cultures ($>10^6$ cfu/mL)
  - Sensitivity: $76\%$ +9% (range, 38-82%)
  - Specificity: $75\%$ +28% (range, 72-85%)
- Blind bronchial suction
  - Sensitivity: Range, 74-97%
  - Specificity: Range, 74-100%
- Blind mini-BAL
  - Sensitivity: Range, 63-100%
  - Specificity: Range, 66-96%

**DIAGNOSTIC TESTS: ACCURACY**

- Blind PSB
  - Sensitivity: Range, 58-86%
  - Specificity: Range, 71-100%
  - Sensitivity: 73 +18% (range, 42-93%)
  - Specificity: 82 +19% (range, 45-100%)
- Protected specimen brush (Marquette CH, et al. ARRD 193:147:211)
  - Sensitivity: 66 +19% (range, 33-100%)
  - Specificity: 90 +15% (range, 50-100%)
VAP

- Ventilator-associated pneumonia (VAP) is a tremendous problem in the trauma population
- Greater effect on ventilator days and hospital stay than any other nosocomial infection
- Increase in health care costs

VAP

- Clinical diagnosis is problematic
- Invasive means of diagnosis are generally required (PSB, Blind BAL, and Tracheal aspirates)
- Inappropriately low diagnostic thresholds will lead to needless exposure of some patients to antibiotics, with the resultant increase in microbial resistance

VAP

- Use of a threshold that is too high may lead to a lack of diagnostic sensitivity and excess mortality from untreated pneumonia
- Trauma service currently uses BAL in the diagnosis of VAP and uses a diagnostic cutoff of $\geq 10^5$ colony-forming units (CFUs)/mL
VAP

- The goal is to examine the utility of $\geq 10^5$ CFUs/mL as compared with lower diagnostic thresholds with respect to VAP diagnosis and unnecessary antibiotic use.

Journal Of Trauma

- "Optimal Threshold for Diagnosis of Ventilator-Associated Pneumonia Using Bronchoalveolar Lavage" in the Journal Of Trauma, Volume 55(2), August 2003, pp 263-268
- Miller, Preston R. MD; Meredith, J. Wayne MD; Chang, Michael C. MD

VAP in trauma

- The impact of VAP on trauma care is significant
- 20% to 40% of ventilated patients being affected
- Prolonged ventilator requirements and hospital stays
- Clinical methods of VAP diagnosis lack specificity and lead to treatment of large numbers of patients needlessly
Journal Of Trauma

- Trauma surgeons rely on more invasive methods of quantitative culture for diagnosis of VAP
- Common method remains the Blind BAL
- Optimal bacterial count for the diagnosis of VAP varies in the literature

Arguments for Higher Cutoffs

- Proponents of higher cutoffs (≥ 10^5 CFUs/mL) feel that lower thresholds are overly sensitive
- Excessive antibiotic use
- Antibiotic resistance

Arguments for Lower Cutoffs

- Lower thresholds
- Commonly ≥ 10^4 CFUs/mL
- Result in large numbers of untreated patients
- Increased mortality
What the data shows

- Threshold of $\geq 10^5$ CFUs/mL has a low false-negative rate
- Thresholds $<10^5$ CFUs/mL for the diagnosis of VAP in trauma patients would lead to large numbers (>80%) of patients receiving unnecessary antibiotics
- Threshold of $\geq 10^5$ CFUs/mL appears to be appropriate for the diagnosis of VAP in the trauma population.

Biomarkers

- Microbial products activate alveolar macrophages
- Release multiple endogenous mediators locally
  - Tumor necrosis factor
  - Interleukin-1beta
  - Other cytokines
- Problem: no cut off values have been set as of today
  - Currently working on cut off values
- Elastin fiber (EF) in tracheal aspirates corresponds with lung destruction for patients with VAP
  - Sensitivity 32% Specificity 72%

Biomarkers

- sTREM-1 (Soluble triggering receptor expressed on myeloid cells)
- Found in BAL fluid used in determining if there is a bacterial or fungal infection in the lung
- sTREM-1 levels greater than 200pg/ml in BAL fluid
  - Sensitivity 75% and Specificity 84%
- Targets infection and not other lung injury
  - ARDS
  - Pneumonitis
  - Atelectasis
  - ETC…
- Very promising
Biomarkers

- Procalcitonin (PCT)
- Level of procalcitonin raises in response to a proinflammatory stimulus (esp. infection)
- It does not raise significantly with viral or non-infectious inflammations
- Procalcitonin levels may be useful to distinguish bacterial infections from nonbacterial infection
- May help guide therapy and reduce antibiotic use
- Sensitivity 100% and Specificity 75% for patients with VAP
- Very promising

Biomarkers

- C-reactive protein (CRP)
- CRP is useful in the diagnosis of sepsis
- Provoa et al. showed that a CRP > 9.6 mg/dl
- Sensitivity 87% and Specificity 88% for VAP identification
- Daily CRP measurements could be used as a marker of VAP resolution

Questions?