Ventilator-Associated Pneumonia (VAP): Pathogenesis, Definitions & Outcomes

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VAP–Washington-9-24-10
“Remember how much you don’t know.”

William Osler
Thinking Outside the Box

- Pathogenesis?
- Diagnosis issues
- Microbiology models key
- **Goals:** better data & patient outcomes
VAP & Intensive Care!!

- ET: 6-21 fold > risk
- > 50% MICU antibiotics
- Mortality = 20%-50%
- Morbidity - huge
- Cost = $15,000 - $40,000

I. Pathogenesis:

Colonization vs Infection (VAT/VAP)
Nasopharyngeal Colonization

Bacteria/Secretions
ETT Cuff leaks, Biofilm

Bacterial Pathogens:
Number, Type & Virulence

Lung Defenses:
Cilia, Humoral, Cellular

Tracheobronchial Colonization

VAT

VAP
BACTERIA: One-Way In & Out!

Colonization

VAT

Route

ETT Cuff & Biofilm

VAP

Bacteremia

Translocation
Biofilm formation: (E-tube)

Attachment | Colonization | Growth

Bulk Fluid

Surface

© 1995 CENTER FOR BIOFILM ENGINEERING MSU—BOZEMAN
Ciliated Tracheal Epithelium

Alveoli
Dynamic Bacterial-Host Interactions

The Chase

This video is from a 16mm movie made in the 1950s by the late David Rogers; Vanderbilt University. It was given to me via Dr. Viktor Najjar, Professor Emeritus at Tufts University Medical School and a former colleague of Rogers.

Written by Tom Stossel, MD. 1999.
Digitally converted by Phil Allen, Ph.D. 1999.
VAP/VAT: Bacterial Pathogens

**NOT**

Viruses: FLU, RSV, HSV

Anaerobes, Legionella, Candida or OIs
MVP > 48 hr: VAT & VAP Overlap

Time

VAT
~3-10%

VAP

Colonized
(<10^6 cfu/ml)
>90%

Nseir, Eur Respir J 2002: 20 1483-89
II. Definitions

VAT

VS

VAP
VAP Surveillance & Outcomes

“The road to success is always under construction"
VAT/VAP Diagnosis = 1+2+3

1. Quantitative Microbiology:  
   - BAL $>10^4$ cfu/ml = VAP  
   - SQ-EA “moderate-heavy” = VAT or VAP  
   - Q-EA $>10^6$ cfu/ml = VAT or VAP

2. Signs/Symptoms = VAT or VAP  
   - Temperature: $>38C/100.4F$ or WBC $>12K$ or $<4K$  
   - New purulent sputum or change in FiO$_2$ or PEEP

3. Radiology: CXR: new & persistent infiltrate, consolidation, cavitation = VAP
VAT/VAP: A Numbers Game!

Orogastric tube (to suction)
Endotracheal tube

Nasopharynx
$10^8$-$10^{10}$ orgs/ml

VAT/VAP
SQ-EA ≥ +++
Q-EA ≥ $10^6$/ml

VAP
BAL > $10^4$/ml

Craven, Sem Resp Dis, 1996
SQ-EA
+++/++++
Mod-Heavy

Q-EA
≥10^{5-6}

Rare, Few Colonization

SQ-ETA Diagnostics
## Diagnostic Tests for Pneumonia in Ventilated Patients: Prospective Evaluation of Diagnostic Accuracy Using Histology as a Diagnostic Gold Standard

CHARLES HUGO MARQUETTE, MARIE-CHRISTINE COPIN, FRÉDÉRIC WALLET, RÉMY NEVIERE, FABIENNE SAULNIER, DANIEL MATHIEU, ALAIN DUROCHER, PHILIPPE RAMON, and ANDRÉ BERNARD TONNEL

<table>
<thead>
<tr>
<th>Q-EA ($\geq 10^6$)</th>
<th>BAL ($\geq 10^4$)</th>
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<tbody>
<tr>
<td>Sens</td>
<td>Spec</td>
</tr>
<tr>
<td>55%</td>
<td>85%</td>
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**SENSITIVITY** vs **SPECIFICITY**
Micro Model & UTI Diagnosis

- **Kass's #** (>10⁵ cfu/ml)
- **UTI symptoms**
  - Pyuria, fever, WBC
  - *Culture: >10⁵ cfu/ml*
- **NOT PERFECT!**
VAT or VAP? Treat? Report?

- 75M intubated >48 hr:
  - Temp >100.4 °F
  - *WBC 11 k (75% polys)
  - ?Tan sputum (>25 PMN)
  - P/F ratio – no change
  - *CXR: infiltrate, ? new
  - *CPIS = 6

- SQ-EA
  - GS: polys/few GNR
  - Cultures: 24-48 hr.

- Dx: VAP or VAT?
- Rx: Treat or not?
- Report HAI or not?
VAT or VAP? Treat? Report?

Clinical
- Temp 100.5 °F
- *WBC 12 k (75% polys)
- ?Tan sputum
- P/F ratio – no change
- *CPIS = 6

Radiology: ?RLL infiltrate

Microbiology
- GS: polys/few GNR
- Cultures: 24-48 hr.

Surveillance EA:
- Q-EA: GNR >10^6 cfu/ml
- SQ-EA: ++++ (heavy)

BAL: >10^4 cfu
When is a Chest “Infiltrate” VAP? Hawthorne or Administrator Effect!

Portable CXRs: Quality???
- Sensitivity = Inflammation; ?Delay
- Specificity = Low for Dx & Rx!
- Key for “VAP” Diagnosis

CHF, ARDS r/o Pn

?RLL Pn vs ?LLL Pn atelectasis
VAT/VAP Principles

1. VAP = an infectious disease!
2. Quantitative microbiology KEY Surveillance cultures?
3. Future: earlier, appropriate, “targeted” therapy?
4. Goal: better outcomes
ATS/IDSA Guidelines for VAP Therapy


1. Early, empiric, appropriate & adequate antibiotics based on MDR risk

2. De-escalate 48-72 hr: based on clinical response & culture results

3. Limit duration: 7-8 days
ARE WE WAITING TOO LONG TO INITIATE THERAPY?

Crude Diagnostics, Definitions, 
DELAY = Increased Bacterial Numbers, More Inflammation, Tissue Damage, Complications & Worse Outcomes?
Surveillance VAT/VAP Model

**Surveillance EAs**
Pathogen GS, C&S

**Diagnosis VAT/VAP**
Q-EA = $10^6$ cfu/ml
SQ-EA = Mod-Heavy

**Earlier, “Targeted” Antibiotics/De-escalation**

ATS/IDSA VAP Model

**VAP Suspected “Broad Spectrum” Antibiotics**
Pathogen EA/BAL
Micro: GS, EA/BAL (48-72 hr Delay)

**De-escalation**
MICU/SICU patients

- Incidence: 3%-11%
- Outcomes: increased ICU LOS, MV days, mortality
- Antibiotics: lower MICU mortality (p<.04)

Nseir, Eur Respir J 2002: 20 1483-89
RCT of VAT Therapy & Outcomes

- VAT: Q-EA ≥ 10⁶, CXR normal
- RCT: Antibiotics vs NO/Delayed therapy:
  - Reduced VAP: 14% vs 47% (p=0.01)
  - Reduced ICU mortality (p<0.05)
  - More MV-free days (p<0.001)
- Good outcomes, but limitations (n=50)

Nseir, *Crit Care* 2008:12:R62
VAT Antibiotic Therapy

Early VAP

Possible VAP

VAP Prevention

IMPROVED PATIENT OUTCOMES
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<th>VAP</th>
<th>VS.</th>
<th>VAT</th>
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<tr>
<td>Temperature, WBC, sputum</td>
<td>Δ PaO₂/FiO₂, &gt;PEEP</td>
<td>+ Pathogen (s)</td>
<td>Δ purulent sputum</td>
</tr>
<tr>
<td>CXR “New infiltrate”</td>
<td>+ Pathogen (s)</td>
<td>-</td>
<td>CXR “Normal”, CHF, ARDS</td>
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<tr>
<td>Microbiology $$$</td>
<td>Microbiology $$$</td>
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<tr>
<td>- Q-EA: &gt;10⁶ CFU/mL</td>
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<td>- BAL &gt;10⁴ CFU/mL</td>
<td>- BAL &lt; 10⁴ CFU/mL</td>
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VA-RTI: A Clinical Model

**EA Surveillance Cultures**
(< \(10^6\) cfu/mL - observe)

**VAT/VAP Dx**
(pathogen \(\geq 10^6\))

**Initiate Therapy**
(“targeted”)

**Reduced VAP**

**Better Outcomes**
VAT/VAP (VA-LRI) Model: Advantages

- Standardized EA/BAL microbiologic diagnoses
- SQ-EA used in most hospitals: Q-EA simple
- Surveillance EA cultures may be useful
- Use of “targeted” vs “empiric” antibiotics
- VA-LRI: EA = endpoint for surveillance or QI

Craven, Clin Infect Dis 2010
VAT/VAP: Suggestions

- Consider use of “VA-RTI” : VAT & VAP
- Focus on aerobic bacteria, “quantitative” cultures
- Target: intubated patients (no tracheostomies)
- Standardize Q-EA, SQ-EA, Q-BAL criteria
- Correlate microbiology data with CXR & clinical signs
- Measure impact of prevention & improved outcomes
VA-RTI (VAT/VAP) Model Issues

- Need better data & confirmatory studies
- Q-EA vs SQ-EA standards needed
- Incidence data & impact of VAT & VAP
- “Clinical” & surveillance data correlation
Thinking Out Side of the Box

- VA-LRI: a surveillance endpoint?
- VAT & VAP may overlap
- VAT/VAP models useful in all hospitals
- Goals: VAP prevention & better outcomes
• Man's mind, once stretched
• by a new idea,
• never regains its original dimension.

•-- Oliver Wendell Holmes
Craven Disclosures

- Research: Pfizer, Bard
- Honoraria: Merck, Pfizer, Ortho-McNeil, Covidien, Sanofi Pasteur, Bard