VAPs and VACs and IVACs, Oh My!

What’s an Infection Preventionist to do?

Mark L. Metersky, MD, FCCP
Professor, Division of Pulmonary and Critical Care Medicine,
University of Connecticut School of Medicine
Overview

• Review pathophysiology of ventilator-associated pneumonia (VAP)

• Review strategies for preventing VAP
  – Those recommended by IDSA/SHEA
  – Those not routinely recommended by IDSA/SHEA
  – Some not addressed by IDSA/SHEA

• Review the new paradigm of Ventilator Associated Complications
  – Definitions
  – Rationale
  – Usefulness
The Magnitude of the Problem

• Up to 300,000 HAP/VAP per year
• Approximately 10% of ventilated patients affected


• Crude mortality up to 40%
• Attributable mortality controversial, probably around 13%


• No controversy regarding effect upon:
  – Ventilator days 7-12 day excess
  – Hospital LOS 9-13 day increase
  – Cost Excess cost estimated at $40,000


Pathophysiology of VAP

- Essentially all VAP is “aspiration”
- Bacteria get into lungs from:
  - stomach
  - nasopharynx
  - oropharynx
  - ETT/ventilator circuit
  - sub-glottic secretions (above the ETT cuff)
Pathophysiology of VAP

• Prevention of VAP therefore is based on preventing these bacteria from reaching the lung
  – Decrease risk for colonization of upper aerodigestive tract
  – Remove reservoirs of colonized secretions
  – Decrease risk of bacteria which are present from reaching the lungs
You Can’t Get VAP if You Aren’t on a Ventilator

• Appropriate pre-operative evaluation for patients undergoing surgery who may be at risk of respiratory failure

• Use of non-invasive ventilation when feasible, especially:
  – COPD
  – CHF
  – Neuromuscular disease
**Table 2. Serious Complications and Complications Resulting in Death.**

<table>
<thead>
<tr>
<th>VARIABLE*</th>
<th><strong>NONINVASIVE-VENTILATION GROUP (N=32)</strong></th>
<th><strong>CONVENTIONAL-VENTILATION GROUP (N=32)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with complications — no. (%)†</td>
<td>12 (38)</td>
<td>21 (66)</td>
</tr>
<tr>
<td>Patients with complications causing death in ICU — no.</td>
<td>9</td>
<td>15</td>
</tr>
<tr>
<td>No. of complications per patient‡</td>
<td>1.3</td>
<td>1.7</td>
</tr>
<tr>
<td>Death after discharge from ICU — no.</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Complications — total no./no. causing death in ICU (% of group)§</td>
<td>2/2 (6)</td>
<td>4/4 (12)</td>
</tr>
<tr>
<td>Myocardial infarction or cardiogenic shock</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sepsis†</td>
<td>6/5 (19)</td>
<td>11/6 (34)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>3/0 (9)</td>
<td>5/0 (16)</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>1/0 (3)</td>
<td>1/1 (3)</td>
</tr>
<tr>
<td>Polyneuropathy of the critically ill</td>
<td>0/0</td>
<td>1/0 (3)</td>
</tr>
<tr>
<td><strong>Pneumonia‖</strong></td>
<td>1/0 (3)</td>
<td>8/2 (25)§</td>
</tr>
<tr>
<td>Sinusitis‖</td>
<td>0/0</td>
<td>2/0 (6)</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>0/0</td>
<td>1/1 (3)</td>
</tr>
<tr>
<td>Massive blood loss</td>
<td>0/0</td>
<td>1/1 (3)</td>
</tr>
<tr>
<td>Infection at study entry**</td>
<td>2/2 (6)</td>
<td>0/0</td>
</tr>
</tbody>
</table>

An important modifiable risk factor: Length of Mechanical Ventilation

- Each extra day of ventilation is associated with an increase in risk of VAP
- Appropriate use of sedation
  - Minimize sedation
  - Use of short acting sedatives
    - Propofol, dexmedetomidine over benzodiazepines
  - Daily sedation vacations
- Early tracheostomy **not** proven to have benefit
Effect of Daily Interruption of Sedation

Linkage of daily sedation vacations to daily assessment of readiness to wean

• How to get these done reliably?

• Implement respiratory therapist driven protocol

Non-invasive weaning from the ventilator - Ventilator days

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>M (SD)</th>
<th>n</th>
<th>M (SD)</th>
<th>p-value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferrer 2003</td>
<td>21</td>
<td>9.5 (8.3)</td>
<td>22</td>
<td>20.1 (13.1)</td>
<td>19.6%</td>
<td>-10.60 [-17.12, -4.08]</td>
</tr>
<tr>
<td>Girault 1999</td>
<td>17</td>
<td>4.56 (1.85)</td>
<td>16</td>
<td>7.69 (3.79)</td>
<td>38.7%</td>
<td>-3.13 [-5.18, -1.08]</td>
</tr>
<tr>
<td>Hill 2000</td>
<td>12</td>
<td>6.6 (6.93)</td>
<td>9</td>
<td>15.2 (21)</td>
<td>6.4%</td>
<td>-8.60 [-22.87, 5.67]</td>
</tr>
<tr>
<td>Tawfeek 2012</td>
<td>21</td>
<td>12.8 (8.3)</td>
<td>21</td>
<td>22.3 (13.3)</td>
<td>19.0%</td>
<td>-9.50 [-16.21, -2.79]</td>
</tr>
<tr>
<td>Vascchetto 2012</td>
<td>10</td>
<td>7.6 (6)</td>
<td>10</td>
<td>15 (10.8)</td>
<td>16.3%</td>
<td>-7.40 [-15.06, 0.26]</td>
</tr>
</tbody>
</table>

**Subtotal (95% CI)**
81

78

Heterogeneity: $I^2 = 9.14; \chi^2 = 8.07, df = 4 (P = 0.09); I^2 = 50\%$

Test for overall effect: $Z = 3.44 (P = 0.00058)$

Test for subgroup differences: $\chi^2 = 0.06, df = 1 (P = 0.81), I^2 = 0.0\%$
Non-invasive weaning from the ventilator-Pneumonia

<table>
<thead>
<tr>
<th>Study</th>
<th>Noninvasive (N)</th>
<th>Invasive (N)</th>
<th>Risk Difference</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferrer 2003</td>
<td>5/21</td>
<td>13/22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Girault 1999</td>
<td>1/17</td>
<td>1/16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Girault 2011</td>
<td>9/69</td>
<td>10/69</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tawfeek 2012</td>
<td>1/21</td>
<td>8/21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trevisan 2008</td>
<td>1/28</td>
<td>17/37</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Subtotal (95% CI)**: 156/165

**Total events**: 17 (Noninvasive Weaning), 49 (Invasive Weaning)

**Heterogeneity**: $I^2 = 52\%$

**Test for overall effect**: $Z = 2.12 (P = 0.034)$

**Test for subgroup differences**: $I^2 = 1\%$

Early Mobilization

<table>
<thead>
<tr>
<th></th>
<th>Intervention (n=49)</th>
<th>Control (n=55)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Return to independent functional status at hospital discharge</td>
<td>29 (59%)</td>
<td>19 (35%)</td>
<td>0.02</td>
</tr>
<tr>
<td>ICU delirium (days)</td>
<td>2.0 (0.0–6.0)</td>
<td>4.0 (2.0–7.0)</td>
<td>0.03</td>
</tr>
<tr>
<td>Time in ICU with delirium (%)</td>
<td>33% (0.58)</td>
<td>57% (33–69)</td>
<td>0.02</td>
</tr>
<tr>
<td>Hospital delirium (days)</td>
<td>2.0 (0.0–6.0)</td>
<td>4.0 (2.0–8.0)</td>
<td>0.02</td>
</tr>
<tr>
<td>Hospital days with delirium (%)</td>
<td>28% (26)</td>
<td>41% (27)</td>
<td>0.01</td>
</tr>
<tr>
<td>Barthel Index score at hospital discharge</td>
<td>75 (7.5–95)</td>
<td>55 (0–85)</td>
<td>0.05</td>
</tr>
<tr>
<td>ICU-acquired paresis at hospital discharge</td>
<td>15 (31%)</td>
<td>27 (49%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Ventilator-free days*</td>
<td>23.5 (7.4–25.6)</td>
<td>21.1 (0.0–23.8)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

- Duration of mechanical ventilation (days) 3.4 (2.3–7.3) 6.1 (4.0–9.6) 0.02
- Duration of mechanical ventilation, survivors (days) 3.7 (2.3–7.7) 5.6 (3.4–8.4) 0.19
- Duration of mechanical ventilation, non-survivors (days) 2.5 (2.4–5.5) 9.5 (5.9–14.1) 0.04
- Length of stay in ICU (days) 5.9 (4.5–13.2) 7.9 (6.1–12.9) 0.08
- Length of stay in hospital (days) 13.5 (8.0–23.1) 12.9 (8.9–19.8) 0.93
- Hospital mortality 9 (18%) 14 (25%) 0.53

Data are n (%), median (IQR), or mean (SD). ICU=intensive care unit. *Ventilator-free days from study day 1 to day 28. Barthel Index scale 0–100, APACHE II scale 0–71.

Table 3: Main outcomes according to study group

Nasal Colonization and Sinusitis

• Nasogastric tubes and nasotracheal tubes increase the risk for bacterial sinusitis by impairing drainage of secretions from the sinuses


• Randomized trial of oral vs nasal tracheal intubation
  – Decreased incidence of sinusitis, VAP and decreased LOS with orostracheal (all approached but did not reach statistical significance)

The gastro-pulmonary route of pulmonary infection

• The theory that colonization of gastric contents with pathogenic bacteria results in oropharyngeal and then airway colonization

• Leads to VAP when colonized oropharyngeal contents or gastric contents are allowed to reach the lung
The gastro-pulmonary route: Does it exist?

• There is no doubt that increasing stomach pH results in higher bacterial concentration in gastric fluid

• pH can be increased by:
  – Critical illness (inhibits acid secretion)
  – Pharmacologically
    • H2 blockers, PPIs, antacids
  – Enteral feeding
The gastro-pulmonary route: Does it exist?

• How often does gastric colonization precede tracheal colonization?

• Several studies have shown that in ~30% of patients who develop respiratory tract colonization, the same organism was first present in the stomach
  – Dependent upon organism
  – More frequently occurs with E. coli and other enteric Gram negative bacilli
  – Pseudomonas more commonly occurs in trachea/oropharynx first
Small bowel feeding vs gastric feeding

Keeping the stomach contents out of the lungs

- Small bowel feedings compared to gastric feedings
  - Have been associated with lower VAP rates, but no change in mortality
  - Concern with resource use and risks associated with transfer of patient to radiology
Keeping the stomach contents out of the lungs

Avoidance of the supine position

Keeping the stomach contents out of the lungs

• Randomized trial demonstrated decreased VAP rate with use of semi-recumbent position (45°) compared to 0°
  
  – 45° pneumonia in 3/39 (8%)
  – 0° pneumonia in 16/47 (34%)

• Most important during enteral feeding

Failure of semi-recumbent position to prevent VAP

Similar study design, except control group was at 10°, not 0°

<table>
<thead>
<tr>
<th>Variable</th>
<th>Median (Range) or Indicated Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Supine n = 109</td>
</tr>
<tr>
<td>Days in study</td>
<td>5 (0–64)</td>
</tr>
<tr>
<td>Days ventilated</td>
<td>6 (0–64)</td>
</tr>
<tr>
<td>ICU stay, days</td>
<td>10 (0–91)</td>
</tr>
<tr>
<td>Hospital stay, days</td>
<td>24 (0–186)</td>
</tr>
<tr>
<td>Ventilator-associated pneumonia: % of patients (no.)</td>
<td></td>
</tr>
<tr>
<td>Clinically suspected</td>
<td>18.3 (20)</td>
</tr>
<tr>
<td>Microbiologically confirmed</td>
<td>7.3 (8)</td>
</tr>
</tbody>
</table>

Possible explanations for discordant results

• Perhaps 10° is as good as 45°
• van Nieuwenhoven only achieved 22-28°, perhaps 45° is needed
• Draculovic excluded patients with prolonged deviations from appropriate position
• Low overall rate of VAP, limited statistical power to detect a difference
Stress ulcer prophylaxis and VAP

- SHEA/IDSA Guidelines state that stress ulcer prophylaxis should not be used to prevent VAP
  

- True, but this does not address the issue of which agent to use if prophylaxis is going to be used
- Over 20 randomized/controlled trials of sucralfate vs either antacids or H2 blockers (few with PPIs)
- Conflicting results
- At least 7 meta-analyses
  - 4 reported decreased rates of VAP with sucralfate
  - 3 showed non-significant trends toward decreased rates of VAP with sucralfate
Stress ulcer prophylaxis and VAP Cont.

• Effect on VAP is greater in patients receiving enteral nutrition

• Be aware that the usefulness of routine use of stress ulcer prophylaxis is being questioned
Stress ulcer prophylaxis and VAP

Summary of findings

• Sucralfate probably has a small but real effect in diminishing the rate of VAP relative to H2 antagonists

• The mechanism may be due to:
  – Preservation of acidic gastric pH and/or
  – Direct antibacterial effect of sucralfate

• Sucralfate may be associated with a slightly higher risk of upper GI bleeding than H2 blockers

• Recommendation:
  – Consider use of sucralfate instead of H2 blockers or PPIs in ventilated patients except when there are specific risk factors for GI bleeding
Subglottic Secretion Drainage

Incorporated evacuation lumen

Large elliptical dorsal opening

Subglottic area: Volume = 3.6 ± 2 ml
Meta-analysis of Subglottic Secretion Drainage-VAP rates

Subglottic Secretion Drainage

- Seems to be little effect on VAP from Pseudomonas, Gram negative enterics
- Overall, lower ventilator and ICU days associated with subglottic secretion drainage
- Mortality unaffected
- Why not wider uptake?
  - Cost of tube
  - Uncertainty regarding which patients to apply intervention (only useful if prolonged intubation likely)
  - Extubating patients to insert tube not recommended
Subglottic Secretion Drainage Cont.

- SHEA/IDSA recommendation
  - Provide endotracheal tubes with subglottic secretion drainage ports for patients likely to require greater than intubation 48-72 hours of intubation (quality of evidence-Level II)
  - May be cost saving

Interventions that are not recommended for routine use by SHEA/IDSA, but might decrease VAP rates

- Silver impregnated endotracheal tubes
- Chlorhexidine mouth care
- Selective decontamination of the digestive tract
- Small bowel feedings instead of gastric feedings

Silver-impregnated endotracheal tube

- Limitations
  - Not blinded
  - Excess COPD in control group
  - Data not very robust due to small numbers of VAP
  - No decrease in LOS, days of intubation, mortality
  - Antibiotic usage not measured
- Cost
  - Number Needed to Treat to prevent on case of VAP-37
  - Cost ~$90


- SHEA/IDSA- “Generally not recommended”
Silver-impregnated endotracheal tube Cont.
Panchabhai, TS, et al. Oropharyngeal cleansing with 0.2% chlorhexidine for prevention of nosocomial pneumonia in critically ill patients: an open-label randomized trial with 0.01% potassium permanganate as control. Chest. 2009; 135(5):1150-6, 2009
Chlorhexidine Oral Care

- Extensively studied in dental and hand washing literature
- Inexpensive
- No apparent issues of resistance
- Several studies demonstrate lower rate of VAP, nosocomial infections with chlorhexidine mouth care
- Meta-analysis demonstrates clear-cut effect on VAP only in cardiac surgery patients
- Possible effect in non-cardiac surgery patients
Chlorhexidine Oral Care

- Foam swab may be less effective than toothbrush, although there are conflicting results on this issue.
- IDSA/SHEA Guidelines “may lower VAP rates” but insufficient data to determine impact on duration of ventilation, LOS, mortality.
Selective decontamination of the digestive tract (SDD)

- Over 40 published trials, 7 meta-analyses with overwhelming evidence of significant decrease in rate of VAP
- Variable results as to whether benefits as great in medical patients as surgical
- Some meta-analyses show mortality benefit
- Techniques vary
  - Oral vs oral and gastric topical non-absorbable antibiotics
  - Variable use of brief course of systemic antibiotics
    - It is these studies in which a reduction in mortality was noted in the meta-analyses
So why don’t we use SDD?

• Cost
  – Some studies show increased costs, due to the costs of the ABx
• Concern regarding development of resistant organisms, *C. difficile*
• Most trials not done in US
• IDSA/SHEA Guidelines state “insufficient data on possible risks are available”
How do we implement all of the desired interventions?

• Trust the house officers to write it every time?
• Trust the attendings to write it every time?
• Ventilator standing orders/carepath?
  – All relevant orders pre-printed or protocolized
    • Oral hygiene
    • Bed position
    • Daily sedation vacation/weaning assessment
    • Etc.
• Monitor adherence
• Feedback
What is wrong with the old VAP surveillance definition?

- Not reliable
- Not valid
- Subject to bias, elements include:
  - Increased sputum volume
  - Increased purulence
  - Worsened oxygenation
  - Change in lung exam
  - Altered mental status with no other cause
What is wrong with the old VAP definition?

• May lead to:
  – Unconscious bias affecting results
  – Gaming may not be detectable
  – Differences in rates across providers due to different thresholds for defining VAP criteria due to their subjective nature
• Agreement between different adjudicators for diagnosis of VAP is quite low

“We have a lot more tests to go through before we can say for certain we don’t know.”
New Paradigm - Ventilator Associated Conditions (VACs)

- Objective definitions
- Not prone to bias
- Likely reliable
- Level of validity to be determined as use of these definitions increases
Ventilator Associated Complication (VAC)

An increase in daily minimum PEEP > 3 cm H2O or an increase of the daily minimum FiO2 > 0.20 sustained for ≥ 2 calendar days in a patient who had a baseline period of stability or improvement on the ventilator, defined by ≥ 2 calendar days of stable or decreasing daily minimum FiO2 or PEEP
Infection-related Ventilator-associated complication (iVAC)

- An episode of VAC associated with alterations in WBC count (≥12,000 cells/mL or ≤4,000 cells/mL)
- or temperature (>38°C or <36°C) within 2 calendar days of the start of the VAC and ≥4 days of new antibiotics
Possible VAP

• iVAC plus positive culture or other laboratory evidence of infection
• Multiple different ways to meet definition of infection
  – Quantitative culture
  – Positive culture with purulent sputum
  – Non-culture evidence of infection (eg. Urinary antigen, histopathology, DNA amplification)
Rationale

• Many factors can contribute to poor outcomes among patients on ventilators
  – VAP
  – Atelectasis
  – Pulmonary embolism
  – Non-adherence to low tidal volume strategy (protective lung ventilation)
  – Iatrogenic fluid overload
  – Inappropriately prolonged ventilation due to excessive sedation

• Surveillance for only VAP misses other important adverse events *that are often preventable*
Do these events matter?

<table>
<thead>
<tr>
<th>Measure</th>
<th>VAP (n = 148)</th>
<th>Non-VAP (n = 1,172)</th>
<th>P Value</th>
<th>iVAC (n = 65)</th>
<th>Non-iVAC (n = 1,255)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU LOS, median</td>
<td>17.8</td>
<td>9.0</td>
<td>&lt; .0001</td>
<td>22.0</td>
<td>9.3</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>Hospital LOS, median</td>
<td>30.9</td>
<td>22.2</td>
<td>0.01</td>
<td>34.6</td>
<td>22.5</td>
<td>0.03</td>
</tr>
<tr>
<td>Duration of MV, median</td>
<td>13.6</td>
<td>6.2</td>
<td>&lt; .0001</td>
<td>16.9</td>
<td>6.4</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>No. of days on antibiotics</td>
<td>15.5</td>
<td>9.0</td>
<td>&lt; .0001</td>
<td>17.8</td>
<td>9.3</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>Hospital mortality, (%)</td>
<td>32%</td>
<td>34%</td>
<td>0.67</td>
<td>45%</td>
<td>33%</td>
<td>0.07</td>
</tr>
</tbody>
</table>

Can these events be prevented?

- 67 VACs detected prospectively among 1209 patients
- 34 were iVACs
- 18 (53%) deemed potentially preventable
  - Most were probable VAPs, deemed potentially preventable by study definition
  - Causes other than VAP:
    - ARDS
    - Extra-pulmonary infection/inflammation

Summary of Recommended Interventions

- SHEA/IDSA
  - Avoid intubation if possible, through use of non-invasive ventilation
  - Minimize sedation/use daily sedation vacations
  - Daily assessment of readiness to wean
  - Early mobilization
  - Subglottic secretion drainage
  - Elevation of head of bed

Summary of Recommended Interventions Cont.

• Metersky (not directly addressed by SHEA/IDSA)
  – Avoid nasal tubes
  – Consider use of sucralfate instead of H2 blockers or PPI in patients not at high risk for stress gastritis, if stress ulcer prophylaxis is to be used