Pulmonary: Physiology, VAP, DVT/PE
ACS Surgical Critical Care Update 2013

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Disclosure

Royalties from Wiley-Blackwell
# VAP Diagnostic Strategies

## CLINICAL
- Lung infiltrate that is new or progressing
  +
- > 2 clinical signs of infection
  - Fever/hypothermia
  - Leukocytosis/leukopenia
  - Purulent sputum
  - Decline in oxygenation
- Clinical signs/+culture without an infiltrate:
  - ventilator-associated tracheobronchitis (VAT)

## BACTERIOLOGIC
- Use of quantitative cultures of the lower respiratory tract
  - ESA
  - BAL
  - PSB
- Growth above a set threshold = VAP
Limitations of Both Strategies

- Sensitivity
- Specificity
  - Low specificity (SCX, clinical) leads to over-treatment
- Lack of a “gold standard” for comparison
- “Ventilator-associated” arbitrary
- No consideration of pre-intubation aspiration
Controversies of VAP Diagnosis

- Is the clinical strategy sufficiently accurate?
- Is one diagnostic strategy superior?
- Are outcomes improved with either method?
- Which quantitative threshold should be used?
Radiologic findings nonspecific

Contusions

ARDS

Atelectasis

Cardiogenic Edema
VAP

- No reliable, valid definition of VAP (NHSN)
  - CDC’s healthcare-associated infections (HAIs like CRBSI, CAUTI) surveillance system
    - Standard methodology and definitions to collect data from nearly 5000 healthcare facilities
  - NHSN PNA definitions last updated in 2002
    - Designed for surveillance of all healthcare-associated PNA events and not limited to VAP
    - Need more accurate diagnosis
    - PNA that occurs at the time a ventilator is in place, or within 48 hours after a ventilator has been in place
      - No required duration for the ventilator to qualify as a VAP
  - Surveillance and prevention practices difficult to track
VAP

- **Elements**
  - No required amount of time that ETT must be in place for PNA to count as a VAP
  - CXR – lacks specificity *(not required in new definitions)*
  - Clinical signs/symptoms – lacks sensitivity and specificity; highly subjective
  - Microbiology – lacks sensitivity and specificity; varies among practitioners; what is best practice?
Commentary

Eight initiatives that misleadingly lower ventilator-associated pneumonia rates

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Decline in VAP Rates

- Evidence-based preventive measures
- Ways to lower VAP rates *without improving patient care*
  - Strict interpretation of clinical signs included in surveillance definitions
  - Strict interpretation of CXR findings included in surveillance definitions
  - Requirement for consensus approach to determine if VAP, or physician approval
  - Transferring patients needing prolonged mechanical ventilation
  - Admitting uncomplicated vented postop patients
**CDC**

- VAP Surveillance Definition Working Group
  - Division of Healthcare Quality Promotion
  - CDC Prevention Epicenters
  - Critical Care Societies Collaborative

*No gold standard, valid, reliable definition of VAP*
VAP Definition Modification

- Achieve validity/clinical credibility/reliability
  - Improve accuracy of reporting HAIs
    - Using criteria that are less likely to be influenced by variability in resources, subjectivity, and clinical practices
    - Amenable to electronic data capture
- Comparisons among facilities
- Pay-for-performance

Klompas M. Curr Opin Crit Care 2013 June
http://www.hhs.gov/ash/initiatives/hai/Events/2012-hai-progress-meeting-vae.pdf
Ventilator-Associated Events

- Tiered approach
  - Not intended for use in management of patients
  - Not a clinical definition algorithm

- Tiers 1 and 2
  - Ventilator-associated conditions (VAC)
  - Infection-related complications (IVAC)
  - Potential use for public reporting

- Tier 3
  - Internal use for quality improvement
  - Possible VAP and Probable VAP
Algorithm
(Respiratory Component)

- Patient on mechanical ventilation > 2 days
- Baseline period of stability or improvement, followed by sustained period (> 2 days) of worsening oxygenation
  - Increasing FI02 (>0.20) or PEEP (>3 cmH20)

Ventilator-Associated Condition (VAC)
Algorithm
(Infection/Inflammation Component)

- VAC and
- Evidence of infection/inflammation
  - On or after day 3 of mechanical ventilation
  - Elevated temperature or leukocytosis (SIRS) and
  - New antimicrobial agent continued for ≥ 4 days

Infection-Related Ventilator-Associated Complication (IVAC)
Algorithm
(Additional Evidence)

- VAC and IVAC and
- Positive results of microbiological testing
  - Purulent secretions
    - $\geq 25$ neutrophils and $\leq 10$ squamous cells/LPF
  - Other positive lab evidence
    - Positive SCX, BAL, PSB

*Possible or Probable VAP*
Possible VAP

On or after calendar day 3 of mechanical ventilation and within 2 calendar days before or after the onset of worsening oxygenation, ONE of the following criteria is met:

1) Purulent respiratory secretions (from one or more specimen collections)
   - Defined as secretions from the lungs, bronchi, or trachea that contain ≥25 neutrophils and ≤10 squamous epithelial cells per low power field [lpf, x100].
   - If the laboratory reports semi-quantitative results, those results must be equivalent to the above quantitative thresholds.

2) Positive culture (qualitative, semi-quantitative or quantitative) of sputum*, endotracheal aspirate*, bronchoalveolar lavage*, lung tissue, or protected specimen brushing*

*Excludes the following:
- Normal respiratory/oral flora, mixed respiratory/oral flora or equivalent
- *Candida* species or yeast not otherwise specified
- Coagulase-negative *Staphylococcus* species
- *Enterococcus* species
**Probable VAP**

*(VAC + IVAC)*

On or after calendar day 3 of mechanical ventilation and within 2 calendar days before or after the onset of worsening oxygenation, ONE of the following criteria is met:

1) Purulent respiratory secretions (from one or more specimen collections—and defined as for possible VAP)

AND one of the following (see Table 2):
- Positive culture of endotracheal aspirate*, ≥ 10^5 CFU/ml or equivalent semi-quantitative result
- Positive culture of bronchoalveolar lavage*, ≥ 10^4 CFU/ml or equivalent semi-quantitative result
- Positive culture of lung tissue, ≥ 10^4 CFU/g or equivalent semi-quantitative result
- Positive culture of protected specimen brush*, ≥ 10^3 CFU/ml or equivalent semi-quantitative result

*Same organism exclusions as noted for Possible VAP.*

2) One of the following (without requirement for purulent respiratory secretions):
- Positive pleural fluid culture (where specimen was obtained during thoracentesis or initial placement of chest tube and NOT from an indwelling chest tube)
- Positive lung histopathology
- Positive diagnostic test for *Legionella* spp.
- Positive diagnostic test on respiratory secretions for influenza virus, respiratory syncytial virus, adenovirus, parainfluenza virus, rhinovirus, human metapneumovirus, coronavirus
VAEs

- Identifies a broad range of events in patients on mechanical ventilation, not limited to VAP alone

Requires thinking more broadly about prevention
Which of the following is NOT considered a best practice for the prevention of ventilator-associated pneumonia?

- a. Daily drug sedation holiday
- b. Early tracheostomy
- c. Gastrointestinal and DVT prophylaxis
- d. Elevation of head-of-bed
Which of the following is NOT considered a best practice for the prevention of ventilator-associated pneumonia?

- a. Daily drug sedation holiday
- b. *Early tracheostomy*
- c. Gastrointestinal and DVT prophylaxis
- d. Elevation of head-of-bed
Early (< 7 days) tracheostomy has been shown conclusively to:

- Decrease incidence of VAP
- Decrease mortality
- Decrease hospital and ICU length of stay
- None of the above
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- a. Decrease incidence of VAP
- b. Decrease mortality
- c. Decrease hospital and ICU length of stay
- d. *None of the above*
VAP Bundle

- Reducing complications by improving quality
  - Benchmarking
  - Reducing incidence of VAP

Infectious Diseases Society of America

Centers for Disease Control and Prevention

American Thoracic Society
VAP Bundle

- Daily spontaneous breathing trial
- Daily sedation holiday
- Stress gastritis prophylaxis
- Elevation of head of bed
- DVT prophylaxis
- Daily oral care
  - Chlorhexidine

Craven DE et al. CHEST 2006 July
Am J Respir Crit Care Med 2005 Feb
Not Part of VAP Bundle
(But Is Evidence-Based and Should Be Considered)

- Restrictive blood transfusion policy
- Use of noninvasive positive pressure ventilation
- Continuous aspiration of subglottic secretions
- Strict glycemic control
- **Early tracheostomy**\(^1-5\) in select populations
  - Severe TBI
  - *May* decrease incidence of VAP, mortality, and hospital and ICU length of stay

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3. Rizk EB et al. Neurocrit Care 2011 Dec
4. Young D et al. JAMA 2013 May
5. Gomes SBN et al. Cochrane 2012 Mar

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Which of the following organisms is LEAST likely to require a prolonged course of antibiotics for the treatment of ventilator-associated pneumonia (VAP)?

- a. Acinetobacter
- b. Pseudomonas
- c. Stenotrophomonas
- d. Escherichia
Which of the following organisms is LEAST likely to require a prolonged course of antibiotics for the treatment of ventilator-associated pneumonia (VAP)?

- a. Acinetobacter
- b. Pseudomonas
- c. Stenotrophomonas
- d. *Escherichia*
Length of Treatment

- Chastre J et al.\textsuperscript{1}
  - RCT 401 patients
  - 8 vs. 15 days
  - NFGN rods – similar outcomes; higher recurrence with 8 days of treatment
- Fekih Hassen et al.\textsuperscript{2}
  - RCT 30 patients
  - 7 vs. 10 days
  - Outcomes similar

\textsuperscript{1} JAMA 2003 Nov
\textsuperscript{2} Ann Fr Anesth Rean
Length of Treatment

- **Short course (7-8 days):**
  - Fewer antibiotic days
  - Lower recurrence with MDRO
  - No difference in overall recurrence, mortality, ICU days, ventilator free days

- **Consider longer course (10-14 days)**
  - Acinetobacter, Pseudomonas, Stenotrophomonas, MRSA
  - Higher recurrence of NFGNB with short course
  - Less relapses with long course treatment

Dimopoulos G et al. Chest 2013 June: Short vs. long-duration antibiotic regimens for VAP: a systematic review and meta-analysis
Clinical Suspicion of VAP*

Fiberoptic Bronchoscopy with BAL

Empirc antibiotic therapy based on timing of ICU admission

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

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

Preliminary culture results ≥24 hours

No growth to date
Continue empiric antibiotic therapy

Insignificant
(<100,000 CFU/mL)
Discontinue antibiotic therapy

Significant
(≥100,000 CFU/mL)
Streamline antibiotic therapy

Final culture results

<100,000 cfu/mL
Empiric therapy discontinued

≥100,000 cfu/mL
Definitive antibiotic therapy
Hospital-acquired VAP?

- MRSA, PA: Continue Antibiotics for 14 Days
- AB, SM, ENB: Repeat BAL on Day 7 of Appropriate Therapy

VAP pathogens ≤10³ CFU/ml

- Yes: Antibiotics 10 Days
- No: Antibiotics 14 Days
VTE Epidemiology

- Pulmonary embolism (PE) and deep venous thrombosis (DVT)

- Affects between 600,000 and 2 million patients annually; death in 100,000 to 300,000 per year

- **PE remains the most common preventable cause of in-hospital mortality**

- **Fatal PE is the 3rd most common cause of death in trauma patients who survive the first 24 hours**
# VTE Incidence

<table>
<thead>
<tr>
<th></th>
<th>General Surgery</th>
<th>Trauma</th>
<th>Hip Fx</th>
<th>SCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall DVT</td>
<td>20-30%</td>
<td>58%</td>
<td>50%</td>
<td>70-90%</td>
</tr>
<tr>
<td>Proximal DVT</td>
<td>7%</td>
<td>18%</td>
<td>20%</td>
<td>15%</td>
</tr>
<tr>
<td>PE</td>
<td>0.5%-2%</td>
<td>2-22%</td>
<td>5-25%</td>
<td>5%</td>
</tr>
<tr>
<td>Fatal PE</td>
<td>0.1-0.8%</td>
<td>1%</td>
<td>4-7%</td>
<td>3-5%</td>
</tr>
</tbody>
</table>

*AHRQ - #1 strategy to improve patient safety in hospitals is prevention of VTE*
According to the ACCP, which of the following is not appropriate VTE prophylaxis in the injured patient?

a. LDUH  
b. LMWH  
c. IVCF  
d. Fondaparinux
According to the ACCP, which of the following is not appropriate VTE prophylaxis in the injured patient?

a. LDUH  
b. LMWH  
c. IVCF  
d. Fondaparinux
IVCFs

- Not recommended as prophylaxis (ACCP ‘08 and ‘12)\(^1\)
  - Highest quality is indirect coming from study in patients confirmed with symptomatic, proximal DVT

- 2002 EAST guidelines\(^2\) → level III evidence in favor of
  - Prophylactic placement in very high risk trauma patients who are unable to receive chemoprophylaxis

- More commonly placed for prophylaxis than for treatment

\(^1\)Gould MK et al. CHEST 2012 Feb
\(^2\)Rogers FB et al. J Trauma 2002 July
IVCF

  - *Only RCT of IVCFs in proximal DVT shown to prevent PE*

- 400 patients with proximal DVT, randomized to permanent filter or no filter *AND* to LMWH or LDUH

- Initial non-significant reduction in PE and at 8 years (63% risk reduction), but no difference in mortality

- At 2 years and 8 years → increased DVT, no change in mortality, PTS similar

- *LMWH = LDUH*
**IVCFs**

*Conclusive data lacking that PE and death are reduced when used as prophylaxis, and may increase risk of DVT*

**Retrievable**

- Poor retrieval rates although improved to 60% with a dedicated filter registry in trauma patients
- Most extensively utilized and studied in trauma patients, however there is a lack of high quality literature
  - Decrease in PE and fatal PE
  - Contraindication to chemoprophylaxis

References:

- O’Keeffe T et al. Am Surg 2011 Jan
- Rogers FB et al. J Trauma Acute Care Surg 2012 Feb
Prophylaxis (Chemical)

- **LDUH** (5000 U’s q12 or q8)
  - Major abdominal or thoracic surgery
    - Meta-analyses reduced all DVT (20-40%), proximal DVT, PE and fatal PE

- 2002 EAST guidelines → no support (level II)

- **LDUH 5000 U’s q8 may be as effective as enoxaparin in trauma patients**¹
  - Retrospective, decreased cost, protocol change mid-year

- RCT of LDUH vs. placebo in med-surg ICU patients reduced DVT from 29% to 13%

¹Arnold JD et al.  Am Surg 2010 June
**Prophylaxis (Chemical)**

- **Fondaparinux**
  - Factor Xa inhibitor; blocks thrombin generation by accelerating rate of factor IIa, VIIa, IXa, Xa, Xia, and XIIa inactivation by antithrombin
  - No HIT
  - *No antidote*, long half-life

- Superior (or at least equivalent) to LMWH in *ortho* patients
- Equivalent to dalteparin (LMWH) in *major abdominal surgery* (PEGASUS study)
- Small pilot study in *trauma* patients found 1.2% incidence of DVT with no PE, HIT or major bleeding
Prophylaxis (Chemical)

- **VKA**
- **DTIs**
  - Argatroban
  - Lepirudin
- **Oral agents**
  - **Rivaroxaban** (factor Xa inhibitor)
    - Prophylaxis following TKR/THR
    - No lab monitoring
    - Prothrombin complex concentrate for reversal
  - **Dabigatran** (direct thrombin inhibitor)
    - Prophylaxis following TKR/THR
    - No lab monitoring
    - No antidote; consider HD; no effect with PCC
ASA

- 2012 ACCP¹ guidelines for major general and abdominopelvic surgery in high risk patients (VTE 6%, Caprini ≥ 5, not at risk for bleeding) \textit{AND} contraindication to LMWH or UFH (?HIT)
  - Low dose ASA or fondaparinux or IPC (2C)

- Re-evaluation of a subgroup analysis of the Antiplatelet Trialist Collaborative (1994) in general surgery patients by ACCP found reduced risk of asymptomatic proximal or distal DVT by 48%, symptomatic proximal DVT by 59%, and PE by 57%

- \textit{Low quality evidence:} data with moderate heterogeneity, no blinding in two studies, inconsistent outcomes, imprecision in RR of bleeding, and six studies used fibrinogen scanning for surveillance

¹Gould MK et al. CHEST 2012 Feb
LDUH and Trauma

■ **LDUH** or LMWH or IPC (2012 ACCP - 2C)
  - Low quality evidence in support of asymptomatic proximal DVT which is reduced by 58% with LMWH and by 90% with LDUH plus continuous passive motion (ortho and skeletal trauma patients)

■ Add mechanical prophylaxis in high risk
A 35-year-old woman sustains a 7mm epidural hematoma after being assaulted. According to the Delayed Versus Early Enoxaparin Prophylaxis I (DEEP I) study, enoxaparin may be started safely within ___ hours following injury and a stable head CT?

- a. 24
- b. 48
- c. 72
- d. 96
A 35-year-old woman sustains a 7mm epidural hematoma after being assaulted. According to the Delayed Versus Early Enoxaparin Prophylaxis I (DEEP I) study, enoxaparin may be started safely within ___ hours following injury and a stable head CT?

- a. 24
- b. 48
- c. 72
- d. 96
Incidence of VTE 3-5% when started within 24-48 hours
- Up to 15% when delayed beyond 48 hours

Risk of hemorrhage requiring craniotomy (0.5%) or change in management or outcome (1.1%)

LMWH > LDUH
- Norwood 2008; Dudley 2010; Koehler 2011; Minshall 2011
Traumatic Brain Injury
(Timing of Prophylaxis Highly Controversial)

- Brain Trauma Foundation (*J Neurotrauma* 2007)
  - Level III recommendation for LMWH or LDUH + mechanical
  - Insufficient evidence to support preferred agent, dose, or timing

- Phelan and *The Delayed Versus Early Enoxaparin Prophylaxis I study*¹
  - Low risk TBI patients with progression rates equal to placebo after starting enoxaparin at 24 hours after injury

¹Phelan HA et al. *J Trauma Acute Care Surg* 2012 Dec
**DEEP Study**

- Randomized controlled study of patients with low risk TBI
  - SDH < 8mm
  - EDH < 8mm
  - IPH <2cm
  - Single contusion per lobe
  - SAH with normal angiogram

- Unchanged HCT at 24 hours post-injury
  - Randomized to enoxaparin 30mg SQ BID (n=34) or placebo (n=28)
  - Repeat HCT 48 hours post-injury
  - TBI progression rate of 5.9% with enoxaparin; 3.6% with placebo
    - Rates are similar
    - All were subclinical progression