**Ventilator-Associated Pneumonia**

**Definition**

Hospital-Acquired Pneumonia
Occur after receiving Invasive Mechanical Ventilation (IMV)
Some authorities exclude the first 2 days after IMV
Exclude
Home ventilator / Non-invasive ventilator

**Pathogens in VAP**

- Early-onset VAP (< 5 days)
  - *Streptococcus pneumoniae*
  - *Haemophilus influenzae*
  - Enteric GNB
  - MSSA

- Late-onset VAP (> 5 days)
  - *Pseudomonas aeruginosa*
  - *Acinetobacter spp.*
  - MRSA

**Risk Factors for Multidrug-Resistant Pathogens**

- Antimicrobial therapy in preceding 90 d
- Current hospitalization of 5 d or more
- High frequency of antibiotic resistance in the community or in the specific hospital unit
- Presence of risk factors for Health Care-Associated Pneumonia (HCAP):
  - Hospitalization for 2 d or more in the preceding 90 d
  - Residence in a nursing home or extended care facility
  - Home infusion therapy (including antibiotics)
  - Chronic diahysis within 30 d
  - Home wound care
  - Family member with multidrug-resistant pathogens
- Immunosuppressive disease and/or therapy

**Risk of VAP correlates to days of ventilation**

Cumulative hazard of VAP (risk %)

Days of ventilation

- (6.5%)
- (19%)
- (28%)

**Time of onset of pneumonia**

- Risk factor for specific pathogens and outcomes.
- Early-onset HAP and VAP:
  - occurring within the first 4 days of hospitalization
  - carry better prognosis
  - caused by antibiotic sensitive bacteria.
- Late-onset HAP and VAP (5 days or more)
  - caused by multidrug-resistant (MDR) pathogens
  - increased patient mortality and morbidity.
- Patients with early-onset HAP who have received prior antibiotics or who have had prior hospitalization within the past 90 days
  - at greater risk for colonization and infection with MDR pathogens
  - should be treated similar to patients with late-onset HAP or VAP

**Figure for Risk of HAP and VAP**

ATS-IDSA. Am J Respir Crit Care Med Vol 171. pp 388-416, 2005

Kollef, Ewig

**Am J Resp Crit Care Med 1999; 159:138**
Pathogenesis (1)

- Sources of pathogens include healthcare devices, environment (air, water, equipment, and fomites), and commonly the transfer of microorganisms between the patient and staff or other patients.
- A number of host- and treatment-related colonization factors, such as the severity of the patient’s underlying disease, prior surgery, exposure to antibiotics, other medications, and exposure to invasive respiratory devices and equipment, are important in the pathogenesis of VAP.

Pathogenesis (2)

- Aspiration of oropharyngeal pathogens, or leakage of secretions containing bacteria around the endotracheal tube cuff, are the primary routes of bacterial entry into the lower respiratory tract.
- Inhalation or direct inoculation of pathogens into the lower airway, hematogenous spread from infected intravenous catheters, and bacterial translocation from the gastrointestinal tract lumen are uncommon pathogenic mechanisms.

Frequency of ventilator circuit change and the risk of VAP

Randomized, controlled trials

Gastropulmonary hypothesis

- (A) Duodenogastric reflux
- (B) Stomach colonized
- (C) Colonize the esophagus and the hypopharynx
- (D) Contaminated oropharyngeal or gastric secretions pool above ET cuff
- (E) Microaspiration of lower respiratory tract

Secretion pool above ET-tube cuff

Continuous subglottic suction
Pathogenesis (3)

- Infected biofilm in endotracheal tube, with subsequent embolization to distal airways, be important in the pathogenesis of VAP.
- Stomach and sinuses be potential reservoirs of nosocomial pathogens contribute to bacterial colonization of the oropharynx, may vary by the population at risk, and may be decreasing with the changing natural history and management of VAP.

VAP in Maharaj-Chiangmai hospital
March 1999- September 2000

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single pathogen</td>
<td>46%</td>
</tr>
<tr>
<td>Polymicrobial pathogens</td>
<td>51%</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>8.9%</td>
</tr>
<tr>
<td>A. baumanii</td>
<td>8.9%</td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td>7.7%</td>
</tr>
<tr>
<td>S. aureus (MRSA20%)</td>
<td>6.4%</td>
</tr>
<tr>
<td>Others</td>
<td>15%</td>
</tr>
<tr>
<td>Unknown</td>
<td>16%</td>
</tr>
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</table>
**Clinical diagnosis**

- Fever >38.3°C (< 36°C)
- Leukocytosis > 12*10^9 cell/l (leukopenia)
- Pulmonary tracheobronchial secretion
- Abnormal or worsening pulmonary infiltration.

Sensitivity 69-72%  Specificity 42-85%

*Use as initial screening*

**Chest Radiography**

<table>
<thead>
<tr>
<th>Finding</th>
<th>Sens (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air bronchogram</td>
<td>83.3</td>
<td>57.6</td>
<td>51.3</td>
<td>86.0</td>
</tr>
<tr>
<td>Alveolar infiltr.</td>
<td>87.5</td>
<td>25.6</td>
<td>39.5</td>
<td>78.0</td>
</tr>
<tr>
<td>Unilateral</td>
<td>29.5</td>
<td>79.6</td>
<td>35.7</td>
<td>64.0</td>
</tr>
<tr>
<td>Bilateral</td>
<td>66.7</td>
<td>46.5</td>
<td>41.0</td>
<td>86.0</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>29.7</td>
<td>62.8</td>
<td>30.4</td>
<td>61.0</td>
</tr>
<tr>
<td>(lobar or subsegmental)</td>
<td></td>
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</table>

**Limitation of CXR**

1. Portable technique compromises interpretation.
2. Effect of IMV on CXR interpretation.
4. Variable of specific sign on sensitivity and specificity.
5. New or worsening sign on CXR (24hrs), unlikely to be VAP.

**Diagnostic methods for identify pathogens**

- Endotrachial aspiration :EA
- Bronchoscopic sampling :BAL / PSB
- Blood culture
- Pleural fluid culture
- Nonbronchoscopic bronchoalveolar lavage (NB-BAL) collected BAL / protected mini-BAL
- Percutaneous needle aspiration : PLNA
- Lung biopsy

**Endotrachial aspiration , EA**

- For Gram stain and quantitative culture.
- Performs by nonphysician at bedside.
- Sensitivity 47-82%  specificity 75-100%  NPV 73%
- Qualitative culture correlates with invasive methods.
- If culture negative, VAP is unlikely.

**Bronchoalveolar lavage ,BAL**

- Positive when quantitative culture >10^5-10^6 cfu/ml.
- Most studies use 10^4 cfu/ml as cutpoint.
- Present of intracellular organisms increase specificity and PPV.
- Sensitivity (24-100%) specificity(45-100%), varies with : cutpoint, population groups, and prior antibiotic administration.
- Decrease oxygenation for several hours, expense, need for trained bronchoscopist.
Protected specimen brushing (PSB)

- Positive when quantitative culture >10^3 - 10^4 cfu/ml.
- Most studies use 10^3 cfu/ml as cutpoint.
- Sensitivity 39-97% specificity 69-100%.
- More specific than sensitive.
- Limitation as BAL.

Mortality in patients with mechanically ventilated pneumonia

- Overall mortality.
- Pneumonia mortality.
- Pseudomonas or Acinetobacter spp.
- Staphylococcus spp.
- Other organisms.

Impact of BAL data on therapy and outcome of VAP

Diagnosis Conclusions

- Diagnosis of VAP is based on clinical suspicious and patient's stability.
- Basic and noninvasive samplings are effective.
- Invasive methods are expense, may take risk, similar diagnosis efficacy, not reduce mortality, cause delay and change of antibiotics.
- Current antibiotic administration does not modify diagnostic accuracy (culture threshold may be decrease to maintain good accuracy).

When VAP is suspected: 2 options are recommendation

1. Empirical antibiotic therapy:
   - Base on risk factors, local epidemiology data, and preliminary data (nonquantitative testing, qualitative culture)
2. Quantitative procedure: EA, BAL, and PSB
   - Similar sense, specific, PPV, and likelihood ratios.

   - Which choice depends on local expertise, experience, availability, and cost effectiveness.
   - Treatment base on preliminary results.

Prognosis

- Multiple organs dysfunction.
- Bacteremia.
- High virulent organisms.
- Delayed proper treatment.
- Underlying disease.
- Transfer from others ICU.
- Poor clinical parameters: APACHE-III, SAPS-II
- High inflammatory mediators: sICAM, sE-selectin, BPI.
Management of VAP (1)

- Lower respiratory tract culture needs to be collected from all patients before antibiotic therapy, but collection of cultures should not delay the initiation of therapy in critically ill patients.
- Either “semiquantitative” or “quantitative” culture data can be used for the management of patients with HAP.
- Lower respiratory tract cultures can be obtained bronchoscopically or nonbronchoscopically, and can be cultured quantitatively or semiquantitatively.
- Quantitative cultures increase specificity of the diagnosis without deleterious consequences, and the specific quantitative technique should be chosen on the basis of local expertise and experience.
- Negative lower respiratory tract cultures can be used to stop antibiotic therapy in a patient who has had cultures obtained in the absence of an antibiotic change in the past 72 hours.

Management of VAP (2)

- Early, appropriate, broad-spectrum, antibiotic therapy should be prescribed with adequate doses to optimize antimicrobial efficacy.
- An empiric therapy regimen should include agents that are from a different antibiotic class than the patient has recently received.
- Combination therapy for a specific pathogen should be used judiciously in the therapy of HAP, and consideration should be given to short-duration (5 days) aminoglycoside therapy, when used in combination with a β-lactam to treat *P. aeruginosa pneumonia*.
- Linezolid is an alternative to vancomycin, and unconfirmed, preliminary data suggest it may have an advantage for proven VAP due to methicillin-resistant *S. aureus*.

Management of VAP (3)

- Colistin should be considered as therapy for patients with VAP due to a carbapenem-resistant *Acinetobacter species*.
- Aerosolized antibiotics may have value as adjunctive therapy in patients with VAP due to some MDR pathogens.
- De-escalation of antibiotics should be considered once data are available on the results of lower respiratory tract cultures and the patient’s clinical response.
- A shorter duration of antibiotic therapy (7 to 8 days) is recommended for patients with uncomplicated VAP who have received initially appropriate therapy and have had a good clinical response, with no evidence of infection with nonfermenting gram-negative bacilli.

Initial Empirical Antibiotic Therapy for VAP in Patients With Known Risk Factors for Multidrug-Resistant Pathogens, Early Onset, and Any Disease Severity

EMPIRIC THERAPY FOR VAP IN PATIENTS WITH LATE-ONSET DISEASE OR RISK FACTORS FOR MULTIDRUG-RESISTANT PATHOGENS AND ALL DISEASE SEVERITY
VAP Prevention

General prophylaxis

1. Effective infection control measures: staff education, compliance with alcohol-based hand disinfection, and isolation to reduce cross-infection with MDR pathogens should be used routinely.
2. Surveillance of ICU infections, to identify and quantify endemic and new MDR pathogens, and preparation of timely data for infection control and to guide appropriate, antimicrobial therapy in patients with suspected VAP or other nosocomial infections, are recommended.

Intubation and mechanical ventilation

1. Intubation and reintubation should be avoided, as it increases the risk of VAP.
2. Noninvasive ventilation should be used in selected patients with respiratory failure.
3. Orotracheal intubation and orogastric tubes are preferred over nasotracheal intubation and nasogastric tubes to prevent nosocomial sinusitis and to reduce the risk of VAP.
4. Continuous aspiration of subglottic secretions can reduce the risk of early-onset VAP, and should be used.

Noninvasive Mechanical ventilator

5. The endotracheal tube cuff pressure should be maintained at greater than 20 cm H2O to prevent leakage of bacterial pathogens around the cuff into the lower respiratory tract.
6. Contaminated condensate should be carefully emptied from ventilator circuits and condensate should be prevented from entering either the endotracheal tube or inline medication nebulizers.
7. Passive humidifiers or heat-moisture exchangers decrease ventilator circuit colonization, but have not consistently reduced the incidence of VAP, and thus they cannot be regarded as a pneumonia prevention tool.
8. Reduced duration of intubation and mechanical ventilation may prevent VAP and can be achieved by protocols to improve the use of sedation and to accelerate weaning.

9. Maintaining adequate staffing levels in the ICU can reduce length of stay, improve infection control practices, and reduce duration of mechanical ventilation.

**Tracheotomy and VAP**

<table>
<thead>
<tr>
<th></th>
<th>Early tracheotomy</th>
<th>Late tracheotomy</th>
<th>p-value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects</td>
<td>49</td>
<td>13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with HAP</td>
<td>9 (18)</td>
<td>0 (0)</td>
<td>0.001</td>
<td>1.7 (0.3)</td>
</tr>
<tr>
<td>HAP episode 3 days</td>
<td>13</td>
<td>1</td>
<td>0.007</td>
<td></td>
</tr>
<tr>
<td>Duration of MV days</td>
<td>12.9</td>
<td>14.1</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Length of ICU stay</td>
<td>21.1</td>
<td>31.8</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>ICU mortality</td>
<td>7.04</td>
<td>6.67</td>
<td>0.001</td>
<td>0.37 (0.23)</td>
</tr>
</tbody>
</table>

Early tracheotomy: performed <7 days after the initiation of MV
Late tracheotomy: performed >7 days after the initiation of MV.

**Aspiration, body position, and enteral feeding**

1. Patients should be kept in the semirecumbent position (30–45°) rather than supine to prevent aspiration, especially when receiving enteral feeding.

2. Enteral nutrition is preferred over parenteral nutrition to reduce the risk of complications related to central intravenous catheters and to prevent reflux villous atrophy of the intestinal mucosa that may increase the risk of bacterial translocation.

**Modulation of colonization: oral antiseptics and antibiotics**

1. Routine prophylaxis of HAP with oral antibiotics (selective decontamination of the digestive tract or SDD), with or without systemic antibiotics, reduces the incidence of ICU-acquired VAP, has helped contain outbreaks of MDR bacteria but is not recommended for routine use, especially in patients who may be colonized with MDR pathogens.

2. Prior administration of systemic antibiotics has reduced the risk of nosocomial pneumonia in some patient groups, but if a history of prior administration is present at the time of onset of infection, there should be increased suspicion of infection with MDR pathogens.

3. Prophylactic administration of systemic antibiotics for 24 hours at the time of emergent intubation has been demonstrated to prevent ICU-acquired HAP in patients with closed head injury in one study, but its routine use is not recommended until more data become available.

4. Modulation of oropharyngeal colonization by the use of oral chlorhexidine has prevented ICU-acquired HAP in selected patient populations such as those undergoing coronary bypass grafting, but its routine use is not recommended until more data become available.

5. Use daily interruption or lightening of sedation to avoid constant heavy sedation and try to avoid paralytic agents, both of which can depress cough and thereby increase the risk of HAP.
Stress bleeding prophylaxis, transfusion, and hyperglycemia.

1. Comparative data from randomized trials suggest a trend toward reduced VAP with sucralfate, but there is a slightly higher rate of clinically significant gastric bleeding, compared with H2 antagonists. If needed, stress bleeding prophylaxis with either H2 antagonists or sucralfate is acceptable.

2. Transfusion of red blood cell and other allogeneic blood products should follow a restricted transfusion trigger policy; leukocyte-depleted red blood cell transfusions can help to reduce HAP in selected patient populations.

3. Intensive insulin therapy is recommended to maintain serum glucose levels between 80 and 110 mg/dl in ICU patients to reduce nosocomial blood stream infections, duration of mechanical ventilation, ICU stay, morbidity, and mortality.