

# **Ventilator-Associated Pneumonia**

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March 17<sup>th</sup>, 2004

# Overview

- How do we define VAP?
- Why do we care?
- Can we prevent it?
- How do we diagnose it?
- How do we treat it?
- Summary

# Definitions

## **Ventilator-Associated Pneumonia (VAP)**

A nosocomial pneumonia (NP) which develops > 48 hours after onset of mechanical ventilation (either by endotracheal intubation or tracheotomy)

# Definitions

- Early Onset
  - Within 3-4 days of MV
  - Less virulent, community acquired organisms (*S.pneumo*, *H.flu*, MSSA)
- Late Onset
  - After 3-4 days of MV
  - More virulent, hospital acquired organisms (*Psuedomonas*, *Acinetobacter*, MRSA)

# A Disclaimer...

## **NO STANDARDIZED DIAGNOSTIC CRITERIA!!**

Difficult to compare and interpret data in

- Epidemiology
- Prevention
- Diagnosis
- Management

# Background

- 2<sup>nd</sup> most common ICU infection
- 80% of all NPs
- Responsible for 1/2 of all ICU antibiotics
- Mortality as high as 80%

# Epidemiology

## Risk of NP in intubated patients

- RR = 10-21 (compared to non-intubated pts)
- Increase with duration of MV
  - Rises 1-3% per day
  - Concentrated over 1<sup>st</sup> 5-10 days of MV

# Incidence

- Incidence ranges from 5-65%
  - Varies with different patient populations
- Kollef et al looked at incidence in different populations
  - CT ICU                    21.6%
  - SICU                        14%
  - MICU                        9.3%
- Trauma, Burns, CNS, Respiratory, Cardiac

# Mortality

- Crude Mortality 24-76%
- Attributable Mortality
  - ❖ 7 matched case control studies
  - ❖ 3 found **NO attributable mortality**
  - ❖ The other four: 15-50%
- Mortality may be secondary to underlying disease

# Groups with increased mortality

- Late onset VAP
- Medical patients (compared to surgical patients)
- Patients with inappropriate initial treatment

# Morbidity

- Heyland, et al
  - Increased ICU stay by 4.3 days
- Rello, et al
  - Large US database; 9,080 ICU patients
  - Patients with VAP had increased LOS
    - Increased Hospital stay (+11.5 days)
    - Increased duration of MV (+9.6 days)
    - Increased ICU stay (+6.1 days)**
  - Cost ~ 40,000\$ per patient

# Pathogenesis

Aspiration

Inhalation

Hematogenous Spread

Bacterial Translocation

# Inhalation

Inhalation of aerosols containing bacteria

- Contaminated RT equipment
- Cross Contamination (Hands)
- Inadequate disinfection/sterilization
- Contaminated solutions/water

# Aspiration

- Depressed level of consciousness - underlying disease, sedation, paralytic agents
- Dysphagia - neuro or esophageal disorders
- Endotracheal tubes (holds vocal cords open)
- Enteral tubes (promotes reflux)
- Maintenance of the supine position

# Bacterial Colonization

- 45% of ICU patients are colonized with GNB within 7 days
- Upper airway
  - Cross contamination, ETT
- GI tract
  - Antacids, H2 blockers, enteral feeds →  
Neutralizes gastric contents
  - Enteral tubes

# Risk Factors

**Table 1. Independent Risk Factors for the development of Ventilator-Associated Pneumonia**

## Host Factors

Serum Albumin < 2.2 g/dl  
Age > 60 years  
ARDS  
COPD, pulmonary disease  
Coma or impaired consciousness  
Burns  
Trauma  
Organ failure  
Severity of illness  
Large volume gastric aspiration  
Gastric colonization and pH  
Upper respiratory tract colonization  
Sinusitis

## Interventional Factors

Re-intubation  
MV > 2 days  
Frequent ventilator circuit changes  
Paralytic agents, sedation  
Nasogastric tube  
Maintenance of supine head position  
H2 blockers, antacids  
Transport out of ICU for tests  
Prior antibiotic use  
Prior use of broad spectrum antibiotics

This table was modified from Chastre et al (8)

# Prevention – Things that Work

Hand washing

Gown/Gloves \*

Non-nasal intubation

Subglottic secretion drainage

Kinetic beds

Semi-recumbent position

Non-invasive positive pressure ventilation

Avoid unnecessary re-intubation

Stress ulcer prophylaxis with sucralfate (instead of H2 blockers or antacids)

# Prevention – Things that do not work

Scheduled changes of ventilator circuits

Closed vs. Open suctioning systems

Motility agents

Chlorhexidate oral rinses

G tubes vs. J tubes

Acidification of tube feeds

Enteral vs. parenteral nutrition

# Prevention – Things that Need More Data

Humidification of the airway

Early tracheostomy

Use of weaning protocols

Immune enhanced enteral feeds

Intratracheal and topical antibiotics

SDD

# Diagnosis

## **NO STANDARDIZED DIAGNOSTIC CRITERIA!!**

Difficult to compare and interpret data in

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# Non-invasive diagnosis

- Clinical Criteria
- Endotracheal aspirate (ETA)
  - Qualitative cultures
  - Quantitative cultures
- Mini – bronchoalveolar lavage (BAL)
- Blind – protected specimen brush (PSB)

# Clinical Criteria

X-ray evidence for new/progressive infiltrate plus 2 or more of the following:

- ❖ Fever
- ❖ Leukocytosis, or
- ❖ Purulent tracheal secretions

- Not reliable
- **Sensitivity 54-72%**
- **Specificity 57-83%**

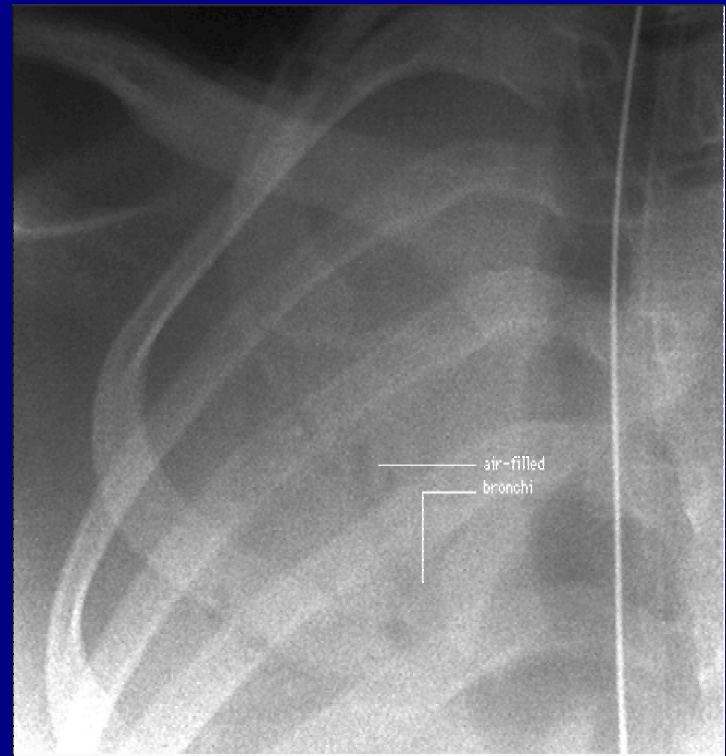
# Torres et al: Compared clinical criteria to autopsy proven VAP

Clinical Criteria	Sensitivity	Specificity
Overall	69%	75%
Fever	55%	58%
Purulent secretions	83%	33%
Infiltrate on x-ray	78%	42%

# Radiographic findings

## Air bronchograms

- Only radiographic sign to correlate with pneumonia
- 64% accuracy



# ETA - Quantity not Quality

- Qualitative cultures
- High sensitivity, 57-88%
- Low specificity, 0-33%
- Not recommended
  - May lead to unnecessary antibiotic use

# Quantity not quality

- **Quantitative cultures**
- Jourdain et al found
  - Cut off of  **$10^6$  CFU/ml** with greatest diagnostic accuracy
  - **Sensitivity 68%**
  - **Specificity 84%**
- **> 10 Epis/LPF = contamination**
  - 85% of ETA should be rejected (Morris)

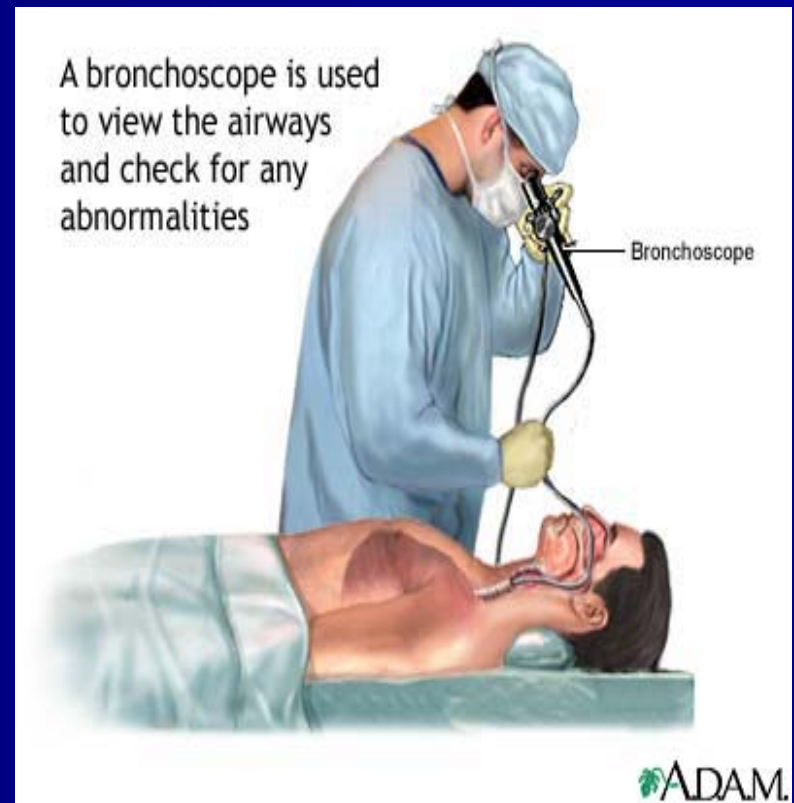
# Mini- BAL, Blind PSB

- Compared to Bronchoscopy
  - ❖ Less invasive
  - ❖ Cheaper
  - ❖ Better tolerated by patient
  - ❖ Easier to use (RTs can do!)
- Mini-BAL → **Sensitivity 78%, Specificity 86%**
- Blind-PSB → **Sensitivity 78%, Specificity 100%**
- Papazian et al: Blind PSB more sensitive than PSB using FOB (82% vs. 42%,  $p = 0.05$ )

# Invasive techniques

## Bronchoscopy

- BAL
- PSB



# Bronchoscopy

## BAL

- Diagnostic threshold  **$10^4$  to  $10^5$  CFU/ml**
- **> 1% Epis/LPF = contamination**
- **Sensitivity 73%, Specificity 83%** (pooled data)

## PSB

- Diagnostic threshold  **$10^3$  CFU/ml**
- **Sensitivity 89%, Specificity 94%** (pooled data)

# Why use Invasive Bronch?

- Does it improve Mortality?
- Decrease Antibiotic usage?
  - Decrease selection pressure, reduce resistance
  - Reduce cost
  - Reduce toxicity
- Rule out VAP, search for other causes of symptoms

# Improved Mortality?

## Sanchez-Nieto

- Prospective randomized trial, N=51
- Invasive vs. Non-invasive diagnosis
- No difference in mortality, duration of MV or length of ICU stay

Other studies with similar findings

# Decrease ABX usage?

A prospective cohort by Heyland et al

- N=141 MV patients with suspected VAP
- Invasive vs. non-invasive diagnosis
- Invasive group
  - Increased confidence in diagnosis ( $p=0.03$ )
  - More comfortable with management plan ( $p=0.02$ )
  - Fewer antibiotics overall ( $p=0.05$ )
  - More likely to have antibiotics discontinued ( $p=0.04$ )

# Treatment

- Initial therapy is empiric
- Start when VAP is suspected, Don't delay
- Individualize to institution
  - Hospital epidemiologic data
- Individualize to patient
  - Surveillance cultures
  - Early onset versus Late onset
  - Prior antibiotic use
  - Use gram stain results if possible

# ATS guidelines

## Mild to Moderate HAP without Risk Factors.

Likely Organisms	Empiric Therapy
Enteric GNB	Second Generation Cephalosporin OR
MSSA*	Beta-lactam/Beta-lactamase PCN** OR
<i>Streptococcus pneumoniae</i>	Floroquinolone

\* MSSA = Methicillin-Sensitive *Staphylococcus Aureus*

\*\* PCN = Penicillin

# ATS guidelines

## Mild to Moderate HAP with Risk Factors.

<b>Risk Factors</b>	<b>Likely Organism</b>	<b>Empiric Therapy</b>
Recent Abdominal Surgery Witnessed Aspiration	Anaerobes	Clindamycin
Coma Head Trauma DM Renal Failure	<i>Staphylococcus Aureus</i>	Vancomycin
Prolonged ICU stay Steroids Prior antibiotics Structural lung disease	<i>Pseudomonas Aeruginosa</i>	Same as Severe HAP

# ATS guidelines

## Severe HAP

### Definition of Severe HAP

- ICU admission
- Need for MV of > 35% oxygen to maintain oxygen saturation > 90%
- Rapid progression of infiltrate on radiograph
- Evidence of sepsis with hypotension or organ dysfunction

### Likely Organisms

*Pseudomonas aeruginosa*

*Acinetobacter baumannii*

Methicillin-Resistant *Staphylococcus aureus*

### Empiric Therapy

Aminoglycoside OR Ciprofloxacin

+

Anti-pseudomonal penicillin OR Imipenim OR Aztreonam

+/-

Vancomycin

# Mono-therapy vs. Combination Therapy

- 45 % of patients with late-onset VAP receive initial inadequate therapy when a single agent is used
- **INADEQUATE INITIAL THERAPY INCREASES MORTALITY!!**

# Mono-therapy vs. Combination Therapy

Is there evidence that 2 are better than 1?

- NO!!
- Cometta et al
  - Imipenem alone vs. Imipenem + Netilmicin
  - Mono therapy as effective as combination
  - No difference in rate of resistance
  - Increased side effects (nephrotoxicity) with Aminoglycoside group

# Scheduled rotation of ABX

- Kollef et al
  - 6 month “before period”: 3<sup>rd</sup> gen ceph
  - 6 month “after period”: fluoroquinolone
  - Decreased incidence of VAP in the after period
    - 6.1 vs. 11.6,  $p = 0.028$
    - Decrease in antibiotic resistant GNB
- What happens after 6 months?

# Length of Treatment

- 7, 14, 21 days? No consensus
- Shorter course may lead to recurrence
- Longer courses may cause toxicity or selection of resistant organisms

# Length of Treatment

Randomized controlled trial by Chastre

Short course: 8 day therapy, n=197

Long course: 15 day therapy, n=204

- Short course -more antibiotic free days
- No difference in mortality, recurrent infection rate, days of MV, length of ICU stay

# Length of Treatment

## Chastre

- In the 8 day group
- Sub-group with VAP caused by non-lactose fermenting GNB
  - increase in recurrence
  - recurrence more likely due to resistant organisms

# UMMS VAP Protocol

**Step 1: Has the patient been on mechanical ventilation through an invasive artificial airway for > 48 hours?**

# UMMS VAP Protocol

**Step 2: In the past 24 hours, did the patient have at least three of the following four criteria present:**

- $T > 101.0^{\circ}\text{F}$  or  $< 97.0^{\circ}\text{F}$ , or  
WBC  $> 12,000$  or  $< 4,000$
- Change in sputum
- Change in chest x-ray c/w infection
- Worsening oxygenation or ventilation

# UMMS VAP Protocol

**Step 3: Is microbiologic confirmation present (both criteria must be present):**

ETA with:

- Moderate to many PMNs and few epithelial cells AND
- Predominant organism that is consistent with GS

And one of the following:

- Blind BAL or PSB with  $> 10^4$  organisms, OR
- Bronchoscopic directed BAL with  $> 10^4$  organisms or PSB with  $> 10^3$  organisms

# UMMS VAP Protocol

Presumptive VAP

No risk factors for resistance

Hospitalization for < 5 days

**Empiric Therapy**

**Ampicillin/Sulbactam**

# UMMS VAP Protocol

Presumptive VAP

No risk factors for resistance

Hospitalization > 5 days

**Empiric Treatment**

**Piperacillin/Tazobactam**

# UMMS VAP Protocol

- Presumptive VAP
- Any risk factor for resistance
- Any duration

**Empiric Therapy**  
**Vancomycin +**  
**Gentamicin +**  
**Piperacillin/Tazobactam**

# UMMS VAP Protocol

## Risk Factors for drug resistance

ABX in last 14 days

Prior culture with MRO

Immunocompromised

Chronic primary lung pathology

Acute or long term care hospitalization  
within 14 days

Tracheostomy for > 5 days

# UMMS VAP Protocol

Recurrent VAP (relapse)

**Empiric Therapy**

**Gentamicin**

**+ Second GNR coverage based on  
prior sensitivities**

**+/- Vancomycin if h/o MRSA**

# Pearls

- No standard for diagnosis
- If VAP is suspected start therapy now
- ↑ mortality with inappropriate therapy
- Guide therapy to individual