Ventilator-Associated Pneumonia in the United States

Prof. Lennox Archibald, University of Florida

A Webber Training Teleclass

Ventilator-Associated Pneumonia in the United States: Epidemiology, Diagnosis, and Prevention

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Hosted by Dr. Lynne Sehulster
Centers for Disease Control
Division of Healthcare Quality Promotion

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"For as long as CDC has measured the prevalence of hospital-acquired infections caused by multidrug-resistant organisms, it has been increasing."

Muto CA. Infect Control Hospital Epidemiol 2005; 26:10-12.

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Rates of Resistance Versus Rates of Infection

- Over past decade, CDC has documented downward trend in infection rates in four major anatomic sites:
  - Respiratory tract (VAP)
  - Bloodstream
  - Urinary tract
  - Wounds
- At same time, infection rates due to resistant pathogens are increasing

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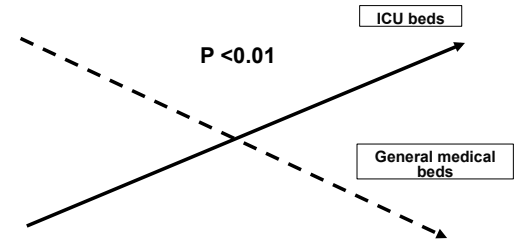
United States Hospitals >500 Beds: 1987-1998 (NNIS Data)



Archibald et al. Clin Infect Dis 1997; 24 :211-5.

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Hospital-Associated Pneumonia

- 31% of all healthcare-associated infections (HAI) in all ICUs
- 27% of all HAI in MICUs
- 28% of all HAI in trauma patients

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Hospital-Associated Pneumonia (NNIS Hospitals)

- Primary risk factor is mechanical ventilation (with its requisite endotracheal intubation)
- 498,998 patients
- 83% of HA pneumonia associated with mechanical ventilation

Richards et al. ICHE 2000; 21:510-15

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Hospital-Associated Pneumonia

- Incidence rates: 4.2-7.7/1000 discharges
- Leading cause of ICU antimicrobial prescribing

Hospital-Associated Pneumonia

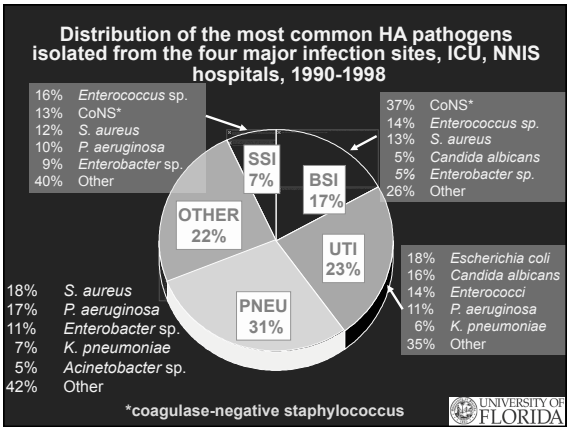
- Morbidity high
- Fatality rates for VAP are high
- Attributable mortality rate: 20%-33%
- VAP account for 60% of all deaths due to hospital-associated infections

Attributable Mortality

- In studies in which invasive techniques were used to diagnose VAP, crude mortality rates had wide range:
  - 4% in patients with VAP but without antecedent antimicrobial therapy
  - 73% in patients with VAP caused by *Pseudomonas spp.* or *Acinetobacter* spp.

Costs

- VAP can prolong ICU stay by an average of 4 - 6 days and hospitalization by 4 - 9 days
- Estimate of the direct cost of excess hospital stay due to VAP is $40,000 per patient



Gram-Negative Pathogens

- 1986 through 2003: 65% of pneumonia episodes
- Proportion of *Acinetobacter* spp. pneumonias has increased:
  4% in 1986 to >7.0% in 2003

Why Are Gram-negative Pneumonias Increasing?

- Adhere to host tissue via microbial adhesions
- Interact with receptors on mucosal surfaces
- Adhesin/receptor interactions define bacterial populations

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Why Are Gram-negative Pneumonias Increasing?

- Changes in adhesins associated with resistant microorganisms or their interactions—trophism
- Hence the underlying role of antimicrobial use!!
- Thus, control of VAP must include control of antimicrobial use in ICUs

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Other Emerging Gram-negative pathogens

- *Stenotrophomonas* spp.
- Extended spectrum beta-lactamase producing pathogens:
  - *Enterobacter cloacae*
  - *Klebsiella pneumoniae*
- Carbapenemase-producing *Klebsiella pneumoniae*

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Where do the bugs come from?

- Patients or other patients or HCW
- Oral cavity
- Stomach
- Intestines
- Air
- Water supply
- Medical equipment
- Work surfaces, white coats, watch straps, stethoscopes, false nails

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Underlying Health Status: Intrinsic Risk Factors

- Age (>70)
- Malnutrition
- Alcohol
- Tobacco
- Severe chronic lung (COPD) and heart disease
- Diabetes
- Connective tissue disorders

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Specific Risk Factors for VAP

- Mechanically assisted ventilation
- Immunosuppression
- Depressed sensorium
- Thoracic-abdominal surgery

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Other Major Risk Factors (I)

- Critically ill—severity of illness
- Primary admitting diagnosis of burns, trauma, or CNS disease
- Thoraco-abdominal surgery (known risk since SENIC in the 1970s)
- Depressed level of consciousness (any cause)
- Prior episode of a large-volume aspiration

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Other Major Risk Factors (II)

- 24-hour ventilator-circuit changes
- Fall-winter season
- Severe trauma
- Recumbent position

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Other Major Risk Factors (III): Invasive Procedures

- Endotracheal or nasal intubation
- Extracorporeal renal support
- Nasogastric tube
- Tracheostomy
- Bronchoscopy

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Risks Related to Therapy

- Recent antimicrobial (anaerobic) therapy
- Immunosuppressive therapy—e.g., steroids; chemotherapy
- Stress-bleeding prophylaxis with cimetidine with or without antacid—results in pH ⇧
- Parenteral nutrition

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Pathogenesis

- Endotracheal intubation
- Mechanical ventilation
- Microaspiration of oropharyngeal secretions
- Upper airway colonization in severely ill patients

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Pathogenesis

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Endotracheal Intubation

- Impairs host-defense mechanisms
- Cough reflex affected
- Mucociliary clearance
- Facilitates VAP, especially when long-term

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Pathogenesis

- Endotracheal intubation
- Mechanical ventilation
- Microaspiration of oropharyngeal secretions
- Upper airway colonization in severely ill patients

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Mechanical Ventilation (I)

- Duration main problem
- Ventilation >24 hrs—key
- Cumulative increased risk of VAP with time
- Decreasing daily risk: 3% per day first week, 2% per day second week, 1% per day third week

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Mechanical Ventilation (II)

- Highest risk during the first 8-10 days of mechanical ventilation
- Lower rates with non-invasive mechanical ventilation (NIV)

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Pathogenesis

- Endotracheal intubation
- Mechanical ventilation
- Microaspiration of oropharyngeal secretions
- Upper airway colonization in severely ill

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Microaspiration of Oropharyngeal Secretions

- Common event
- Upper airway colonization with potentially pathogenic organisms in the severely ill
- Altered mental status—set the stage
- Is it avoidable?

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Microaspiration of Oropharyngeal Secretions

- Raising head of bed at least 10°
- Regular checks of feeding tube position
- Routine assessment of intestinal motility and adjusting feed volumes accordingly
- Small-bore tubes—no consistent evidence

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Pathogenesis

- Endotracheal intubation
- Mechanical ventilation
- Microaspiration of oropharyngeal secretions
- Upper airway colonization in severely ill patients (GNR)

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Gastro-pulmonary route: fact or fiction?

- We are full of bacteria
- What about reports of "no cases of VAP in a year?
  - I have my doubts
- Gut ⟹ stomach ⟹ oropharynx ⟹ trachea ⟹ bronchus ⟹ alveoli

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…we have a basic risk profile—a complex interplay…

- Mechanical ventilation & duration
- Host factors: might be non-modifiable (genetic)
- Ecology of facility: infection control practices and procedures; antimicrobial use
- Contaminated equipment
- Aspiration
  - Oropharynx
  - Gastric
  - Subglottal region
  - Enteral feeding
  - Biofilm

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Oro-pharynx

- Bulk of evidence now that oral cavity is the primary source
- Dental plaque might be playing a role
- Huge confounder: role of Staphylococcus aureus in the oropharynx

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VAP Diagnosis

Clouded by uncertainty, because reference standard has never been established

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What we do know…

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VAP- Diagnosis

- Chest radiology:
  - Very sensitive
  - Typically non-specific
- Wunderink et al. (1992): no radiology signs that correlates well with VAP

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VAP- Diagnosis

- Mistaken for VAP:
  - Lobar or subsegmental atelectasis
  - ARDS
  - Alveolar hemorrhage
  - Infarction
  - Contusion

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So…VAP Diagnosis: Old Paradigm (I)

- Clinical and radiographic signs are non-specific—hence over-diagnosis of VAP
- Signs of upper respiratory colonization equates to infection of lung tissue—this is not true

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VAP Diagnosis: Old Paradigm (II)

- Results in unnecessary prescribing for presumed pneumonia—forceful selective pressure
- One big vicious cycle—back to square 1

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Clinical Diagnosis

- Johanson et al. (1972) criteria
- New or progressive consolidation on chest radiograph AND at least two of the following:
  - Fever (≥38 deg C)
  - Leukocytosis or leukopenia
  - Purulent secretions
- How do these compare with post mortem biopsies?

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… Fàbregas et al. (1999)

- Compared Johanson's criteria with post mortem lung biopsies
- Sensitivity: 69%
- Specificity: not better than 75%
- Despite low accuracy, these criteria were recommended by the American Thoracic Society Consensus Conference on VAP—2005!!!

Other criteria: CDC

- Developed as a tool to describe the epidemiology of hospital-acquired pneumonia—1970
- NNIS hospitals
- Criteria never validated with pathology
- For surveillance purposes
- Aggregated rates of infection for interhospital comparison

Other criteria: Clinical Pulmonary Infection Score (CPIS): Pugin 1991

- Based on 6 variables
  - Fever
  - Leukocytosis
  - Tracheal aspirates
  - Oxygenation
  - Radiographic infiltrates
  - Semi-quantitative cultures of tracheal aspirates with Gram stain
- Total score >6 suggests VAP

Clinical Pulmonary Infection Score

- Compared with pathological diagnoses, sensitivity ~ 75%
- Specificity ~ 42-85%
- Body of literature validating CPIS with BAL for diagnosing VAP

However…

- Limitation: BAL culture is not a true gold standard
- Poor inter-observer agreement in calculating CPIS

VAP- Diagnosis

- Need to differentiate between clinical and surveillance definitions
- Need to consider degree of subjectivity and objectivity in definitions
- They are different: CDC definitions are for surveillance only

What about the utility of BAL?

Meta-Analysis VAP

Alvaro Rea-Neto, Nazah Cherif M Youssef, Fabio Tuche, et al. Critical Care 2008; 12: No 2.

- 572 articles fulfilling the initial search criteria (1966-2007)
- 159 articles were chosen for detailed review
- 64 articles fulfilled the inclusion criteria

Meta-Analysis

- Addition of the results of quantitative bacteriological cultures to clinical criteria (Johanson or CPIS) do not increase the accuracy (sensitivity or specificity) in diagnosing VAP

What about quantitative cultures obtained by different methods?

- BAL
- Protected BAL (pBAL)
- Protected specimen brush (PSB)
- Tracheobronchial aspirate (TBA)

What about quantitative cultures obtained by different methods?

- Quantitative cultures obtained by different methods were equivalent in diagnosing VAP
- Prior antimicrobial use considerably decreased sensitivity of BAL in diagnosing VAP

Meta-Analysis

- Tracheal aspirate has a sensitivity between 44 - 87% and specificity between 31 - 92% (no different than BAL)
- Presence of bacteria on Gram stain (immediate) vs. quantitative culture (two to three days) 79.4 to 86% agreement

Conclusions

- BAL and tracheal aspirate comparable sensitivity and specificity
- Gram stain to assess inflammatory response and quantity of bacteria can serve as an immediate guide
- Quantitative cultures do not add to the clinical criteria
- C-reactive protein, procalcitonin, and soluble triggering receptor expressed on myeloid cells are promising biomarkers in diagnosing VAP

Bronchoalveolar Lavage (BAL) vs. Endotracheal Aspiration (ETA)

- Immunocompetent adults
- Receiving mechanical ventilation
- Suspected VAP after 4 days in ICU
- BAL with quantitative cultures
- ETA with non-quantitative cultures of aspirate
- *Pseudomonas* and MRSA infection or colonization excluded—huge bias in study

NEJM 2006; 355:2619-30
Canadian Critical Care Trials Group

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Bronchoalveolar Lavage (BAL) vs. Endotracheal Aspiration (ETA)

	BAL	ETA	P-value
28-day mortality	18,9%	18.4%	NS
Targeted therapy	74%	75%	NS
Days alive w/o ABx	10.4	10.6	NS
Maximum organ-dysfunction scores (Mean)	8.3	8.6	NS

NEJM 2006; 355:2619-30
Canadian Critical Care Trials Group

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Outcomes

BAL + quantitative cultures of BAL fluid = Endotracheal aspiration + non quantitative culture of aspirate for the following:

- Clinical outcomes
- Antimicrobial use

However, obvious bias despite NEJM publication

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Studies comparing BAL quantitative cultures with pathology

		BAL Sens	BAL Spec
• Balthazar	(2001)	19	94
• Torres	(2000)	83	68
• Fabregas	(1999)	77	58
• Kirtland	(1997)	65	63
• Marquette	(1995)	47	100
• Torres	(1996)	45	55
• Papazian	(1995)	58	95
• Torres	(1994)	50	45
	Mean	55.5 ± 20	72.2 ± 21

Gold standard= Pathology + culture

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Utility of Bronchoscopy in the Diagnosis of VAP

- No evidence that routine bronchoscopy is useful if there is no clinical suspicion of VAP
- Blind BAL has a sensitivity of about 73% with a specificity of 96%

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Bronchoalveolar Lavage (BAL) vs. Endotracheal Aspiration (ETA)

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Non-invasive vs Mechanical Ventilation

Variable	NIV	MVP	P
NI	18%	60%	0.001
NP	8%	22%	0.04
ABX RX	8%	26%	0.01
LOS	9	15	0.02
Vent Days	6	12	0.01
Mortality	4%	26%	0.002

Girou et al. JAMA 2000;284(18):2361-7.

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Bronchoscopy and Mucosal damage

Lundgren R, Hörstedt P, Winblad B. Eur J Respir Dis. 1983 Jan;64(1):24-32

- Respiratory mucosal damage by flexible fiberoptic bronchoscopy in pigs

Lundgren R, Grubbström J, Philipson K, Haglund S, Mossberg B, Camner P. Eur J Respir Dis. 1983 Jan;64 (1):3-8.

- Tracheobronchial clearance after flexible fiberoptic bronchoscopy
- FFB changes mucociliary clearance: practical significance in patients unable to cough

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So, what do we do?

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Lets take a look at the evidence…

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Rule #1

- Do not intubate unless necessary
- Remove ASAP: highest risk during the first 8-10 days of ventilation
- Non-invasive mechanical ventilation (NIV) associated with lower rates—should be encouraged whenever appropriate —multiple studies from France

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What about sedation interruption and weaning protocols?

- Kress et al. NEJM 2000; 342: 1471-7
- Marelich,et al. Chest 2000; 118: 459-67
- No evidence that they reduce VAP
- But probably a “good thing”

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How about modulation of gastric colonization?

- Heyland et al. CCM 1999; 27: 2399
- Acidified parenteral feeds
- Reduced colonization
- Does not translate to reduction in VAP

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Supine body position?

- Drakulovic et al.
- Lancet 1999; 354: 1851-8
- Semirecumbent body position reduces VAP

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Semirecumbent body position: feasibility?

- van Nieuwenhoven CCM 2006; 34:396-402
- 10 degrees: small fluctuations
- 45 degrees: not feasible!
- Standard of care probably 10-30 degrees

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Reducing oropharyngeal aspiration—how effective?

- Subglottal aspiration
- Above cuff & below vocal cords
- At least 5 studies have shown marked reduction in rates

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Topical oral decontamination?

- Koeman et al. Am J Respir Crit Care Med 2006; 173(12): 1297-8 (Marc Bonten's group)
- CHG 2% with and w/o colistin versus a placebo group
- 50-60% reduces incidence of VAP

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Chan et al. BMJ 2007;334:889

- Meta analysis
- 40-50% reduction in VAP incidence with oral antisepsis
- No reduction in mortality
- No reduction in duration of mechanical ventilation or stay in the intensive care

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Selective Digestive Decontamination

- >50 studies
- De Jonge et al. Lancet 2003; 362:1011
- Controlled, randomized, unblinded clinical trial: 934 patients
- Generalizability: single center (low VRE & MRSA)
- Validity: not a cross-over design
- Reduction in mortality & GNR colonization

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Selective Digestive Decontamination

- de Smet et al. NEJM 2009; 360:20-31 January 1, 2009
- In an ICU population in which the mortality rate associated with standard care was 27.5% at day 28, the rate was reduced by an estimated 3.5 percentage points with SDD and by 2.9 percentage points with SOD

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Selective Digestive Decontamination

- Dutch ICUs: No MRSA and no VRE
- The concept works
- SDD=SOD

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How about silver coated ETT?

- Kollef et al. JAMA 2008; 300: 805-13
- 54 centers in North America
- Patients with silver-coated ETT versus those receiving a similar, uncoated tube:
  - Significant reduction in VAP incidence
  - Delayed time to VAP

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However…

- No statistically significant between-group differences observed:
  - Durations of intubation
  - ICU stay
  - Hospital stay
  - Mortality
  - Frequency and severity of adverse events

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Institute for Health Improvement (IHI) Ventilator Bundle

- Elevation of the head of the bed daily:
  - Corresponds to CDC's statement on elevation of head of bed –Category II or aspirations prevention - Category IA
- "Sedation Vacations" and assessment of readiness to extubate
  - Corresponds to CDC's removal of devices - Category IB
- Peptic ulcer disease prophylaxis
  - CDC unresolved issue
- Deep vein thrombosis prophylaxis (?)

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Institute for Health Improvement (IHI) Ventilator Bundle

- No evidence (yet) that VAP bundles reduce the incidence of VAP

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Hospital-Associated Infections Lower Respiratory Infections Modifiable Risk Factors

- **Strong evidence**
  - Semi-recumbent
  - Noninvasive ventilation
  - Continuous lateral rotation
  - Subglottic suctioning
- **Some evidence**
  - Avoid over sedation
  - Avoid paralytics
  - Closed suctioning
  - Oro-tracheal intubation
  - Adequate cuff pressures
  - Avoid H_2 antagonists

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Bottom line in 2011 per evidence-based data

- Non-invasive ventilation if possible
- Oro-tracheal intubation
- Oral versus nasal feeding tubes
- Reduce days of intubation
- Restructure antimicrobial policy
- High level of hygiene
- Semirecumbent: at least 10° if possible
- Chlorhexidine oral care
- Subglottic aspiration

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Sine Qua Non… Surveillance/Education

- Monitor VAP rates; use established benchmarks and definitions of pneumonia (e.g., NHSN definitions/ rates)
- Provide feedback to the staff about the facility's VAP rates
- Reminders about the need for adherence to infection control practices and procedures
- Need to change the culture

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Mechanical Ventilation

- Non-invasive mechanical ventilation (NIV) associated with lower rates—should be encouraged whenever appropriate

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? Stepwise approach

- Canadian Critical Care Society and Canadian Critical Care Trials Group (Dr. Peter Dodek) suggests
- Start with evidence-based basics
- Emphasize good hand hygiene—no randomized trials but still considered effective

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Strategies--summary

1. Semirecumbent positioning—underutilized
2. Continuous subglottic secretion removal (continuous)
3. Oral vs. nasal feeding tubes
4. Targeted oral hygiene (category II); however benign and inexpensive
5. Sedation vacation and weaning assessment—underutilized

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Strategies--summary

6. Stress ulcer prophylaxis
   - Sucralfate shown to reduce gastric bleeding and VAP
   - Studies underpowered
   - CDC category II
   - Role of gastric pH poorly understood
   - Therefore use in high-risk patients
7. Selective digestive tract decontamination
   - Used in Europe
   - Doesn't translate to North America
   - Antimicrobial resistance issues in ICUs

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Strategies--summary

8. Interruption of Person to Person Transmission of Bacteria
   - Standard precautions
   - Care of patients with tracheostomy
   - Suctioning

10. Modifying Host Risks
    - Vaccines -pneumococcal vaccine- Category IA
    - Prevention of aspiration precautions
    - Other prophylactic procedures for pneumonia

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Hospital-Acquired: Diagnosis

- Don't culture intubated patients unless pneumonia suspected; something will grow
- Gram stain with each culture; look for WBCs

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Final Conclusions

- Quantitative BAL cultures:
  - Do not reduce antibiotics use
  - Do not or enhance sensitivity of diagnosis (protected brushing increases the specificity, but markedly reduces sensitivity)
- Bronchoscopy may reduce bacterial clearance (those lacking cough)
- Tracheo-bronchial suction demonstrates similar sensitivity and specificity (less invasive)

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Final Conclusions

- Gram stain in combination with standard tracheo-bronchial culture and clinical criteria should be the standard of care
- Broad spectrum coverage followed by narrowed coverage and short course therapy (7-8 days) promise to reduce the selection of resistant pathogens
- Avoid anti-anaerobic agents if at all possible

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Recent study—2008

- 143 lung tissue specimens examined
- 14 (9.8%) showed histological evidence of an acute pneumonia
- Median age of patients with and without histological evidence of acute pneumonia was 83.6 years and 73.5 years, respectively (P <0.05)
- Most common histological diagnoses were:
  - Acute and chronic heart failure
  - Focal chronic atelectasis
  - Emphysema
  - Pulmonary hypertension
  - Chronic atelectasis.

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Post Mortem Lung Biopsy

- Most common histological diagnoses:
- Acute and chronic passive congestion, consistent with underlying heart failure
- Focal chronic atelectasis
- Emphysema
- Pulmonary hypertension
- Chronic atelectasis.

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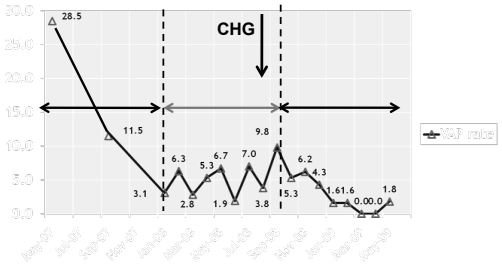
VAP incidence densities
SICU, Shands Hospital



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"Learning is like rowing upstream; not to advance is to fall back" *(Chinese Proverb)*

"Knowing is not enough; we must apply. Willing is not enough; we must do."
—*Johann Wolfgang von Goethe, German poet (1749-1832)*

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Thank you

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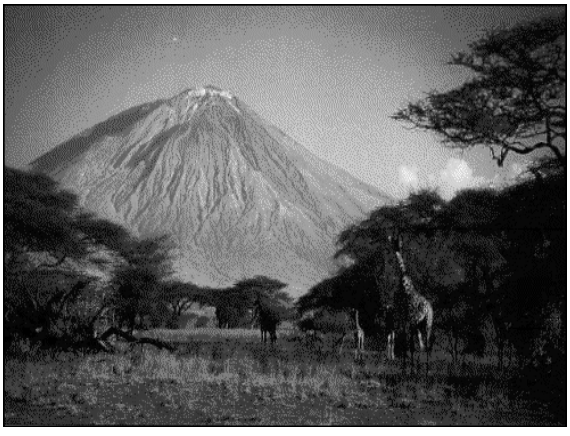

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20 July 11	**(Free WHO Teleclass) Highlights and Results from May 5, 2011 Initiatives Around the World** Speaker: Claire Kilpatrick and Benedetta Allegranzi, WHO Patient Safety Challenge Sponsor: World Health Organization First Global Patient Safety Challenge: Clean Care is Safer Care
11 August 11	**(Free Teleclass) Effects of Narrative as Culture-Centric Health Promotion** Speaker: Dr. Linda Larkey, College of Nursing & Health Innovation, University of Arizona

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