Hospital Acquired Pneumonias
Hospital-acquired pneumonia
Hospital Acquired Pneumonia (HAP)

Hospital acquired pneumonia (HAP) is defined as an infection of the lung parenchyma developing during hospitalization and not present or incubating at the time of admission.

Defined as occurring 48 hrs or more after admission.
HAP in a ventilated patient is referred to as Ventilator associated pneumonias (VAP).

Arising more than 48 – 72 hrs after endotrachael intubation.
Incidence of HAP / VAP

- Second most common nosocomial infection in United States.
- Accounts for almost half of all ICU infections and approx. 60% of all deaths.
- Within the ICU, intubated and mechanically ventilated patients are at substantial risk for VAP.
- Risk of VAP is highest early in the course of hospital stay, being 3% /day during the first 5 days of ventilation, 2% /day during 5-10 days, and 1% /day after this.

Etiological agents

- Gram-negative bacteria (GNB) 55% to 85%
- Gram-positive cocci 20% to 30%
  - Pseudomonas aeruginosa 21%
  - Staphylococcus aureus 20%
  - Enterobacter 9%
Etiologic agents

- Differ according to the population of patients in the ICU, the durations of hospital and ICU stays, and the specific diagnostic methods used.

- Patients with COPD are at increased risk for H. influenzae, Moraxella catarrhalis, or S. pneumoniae infections; cystic fibrosis increases the risk of P. aeruginosa and S. aureas; whereas trauma and neurologic patients are at increased risk of S. aureas infection.
Etiologic agents

Early onset HAP/VAP (occurring within the first 4 days of hospitalization): higher rates of H. Influenzae, S. Pneumoniae, MSSA, or susceptible Enterobacteriaceae.

Late onset HAP/VAP (5 days or more of hospitalization): P. aeruginosa, Acinetobacter spp., MRSA, and multiresistant GNB were more frequent.
Pathogenesis

- **Aspiration of oropharyngeal flora**

- **Inhalation of infected aerosols**

- **Hematogenous spread from remote focus of infection.**

- **Bacterial translocation from gastrointestinal tract.**
Pathogenesis

- Mostly due to microaspiration of oropharyngeal secretions colonized with pathogenic organisms.

- Altered consciousness, abnormal swallowing, depressed gag reflexes, delayed gastric emptying, and decreased gastrointestinal motility: increases the frequency and volume of aspiration in hospitalized patients.

- Colonization by gram-negative bacilli is increased in persons with lower levels of salivary fibronectin, which occurs consequent to alcoholism, diabetes, malnutrition, and other
Other Mechanisms

- Inhalation or direct inoculation of pathogens into the lower airway, hematogenous spread from infected intravenous catheters, and bacterial translocation from gastrointestinal tract lumen are uncommon mechanisms.

- The stomach and sinuses may be potential reservoirs of nosocomial pathogens that contribute to bacterial colonization of the oropharynx.
**Risk factors**

*Host Related*
- Extremes of age
- Severe underlying illness
- Immunosuppression
- Malnutrition
- Alcohol/drug use
- Depressed level of consciousness
- Large volume aspiration
- Comorbid conditions (e.g., diabetes, COPD, etc.)
Risk factors

Device/Treatment Related
- Endotracheal intubation
- Supine position
- Bronchoscopy
- Sedation/paralysis
- Immunosuppressive agents
- Thoracoabdominal surgery and Head/neck surgery
- Mechanical ventilation
- Unplanned extubation/reintubation
- Nasogastric tube placement
- Antibiotic administration
Pathology

Classified as

- Lobar
- Bronchial (most common)
- Interstitial (Pneumocystis)
Clinical features

- Cough with purulent sputum
- Fever
- Pleuritic chest pain
- Dyspnoea
- Haemoptysis
- Altered general well being
Diagnosis

A comprehensive medical history and detailed physical examination should be taken.

Chest radiography: to define the severity of pneumonia and the presence of complications viz effusions or cavitation.

Measure of oxygen saturation.
Diagnosis

- Blood cultures
- Pleural fluid samples
- Expectorated sputum
- Endotracheal aspirates
- FOB with PSB and/or bronchoalveolar lavage (BAL)
Diagnosis

- Hemogram
- Glucose
- Electrolytes
- Liver function tests
- Renal function tests
- ABG
Surveillance

National Nosocomial Infections Surveillance (NNIS) system (initiated in 1970) : Centers for Disease Control and Prevention
NNIS criteria for diagnosis of HAP

A) Rales or dullness to percussion on physical examination of chest AND any of the following:

- New onset of purulent sputum or change in character of sputum
- Organism isolated from blood culture
- Isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy
B) Chest radiographic examination shows new or progressive infiltrate, consolidation, cavitation, or pleural effusion AND any of the following:

- New onset of purulent sputum or change in character of sputum
- Organism isolated from blood culture
- Isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy
- Isolation of virus or detection of viral antigen in respiratory secretions
- Diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for pathogen
Accuracy of criteria

- Post mortem studies have shown that clinical signs of pneumonia are non-specific.
- One study compared autopsy findings with clinical markers of pneumonia (fever, alterations in white blood cell count, purulent sputum with bacterial pathogens, and abnormalities on chest radiographs).
- There is significant overlap in findings in patients with and without pneumonia and these have poor positive predictive value.
- These criterion misdiagnosed the presence or absence of histologically confirmed pneumonia in approximately 1/3 of patients.

Accuracy of criteria

Radiographic findings consistent with pneumonia (alveolar infiltrates, cavities, air bronchograms,) are frequently mimicked by pulmonary hemorrhage.

The clinical criteria also have a poor negative predictive value for VAP.
Other causes of radiographic opacities

- Atelectasis
- Chemical aspiration
- CHF
- Pulmonary hemorrhage
- Pulmonary infarction
- Pulmonary contusion
- Drug reaction
- Bronchogenic carcinoma
Only 42% of mechanically ventilated patients, with fever and new radiographic opacities had VAP.*

Extrapulmonary causes like sinusitis, line infection, UTI etc were common causes of elevated temperature.

*Meduri et al Chest 1994; 106:221-235
Diagnostic strategies for HAP/VAP

Comparing the diagnostic studies is difficult:
- differences in definitions
- patient groups enrolled
- entry criteria
- prior utilization of antibiotics
- the absence of a true “gold standard.”
Diagnostic strategies

Main strategies:
- Blood cultures
- Pleural fluid samples
- Expectorated sputum
- Endotracheal aspirates
- FOB with PSB and/or bronchoalveolar lavage (BAL)
Blood cultures

Very low sensitivity (<20%) in identifying a pathogen in HAP.

The positive predictive value of a positive blood culture for identifying the cause of VAP was 73%.

A positive culture should not be assumed to be originating from lung.
Thoracentesis

Ideally before start of antibiotics or change of therapy.

Chemical and microbiologic evaluation of pleural fluid: detect parapneumonic effusion or empyema.
Expectorated sputum

- Has limited use in diagnosing HAP in nonintubated patients
- Low predictive value
Endotrachael aspirates (EA)

- Least invasive approach in intubated patients.
- Nonquantitative EA has same limitations as expectorated sputum.
- Sensitive but not specific.
- Negative EA, however, is valuable in excluding certain pathogens as causes of HAP.
- Quantitative EA compare reasonably well with more invasive studies for diagnosing HAP with sensitivities ranging from 55-
Endotrachael aspirates

Operating characteristics of EA quantitative cultures, using $10^6$ cfu/ml of respiratory secretions as cutoff point, compared favorably with those of the PSB technique, with higher sensitivity (82 versus 64%) and lower specificity (83 versus 96%).

*Am Rev Respir Dis 1993: 148; 138-144
Endotracheal aspirates

High % of false positive results due to bacterial colonization of the proximal airways observed.

Although quantitative EA cultures can correctly identify patients with pneumonia, microbiologic results cannot be used to infer which microbes present in the trachea are really present in the lungs.
Endotrachael aspirates

Many patients may not be identified by using the cutoff value of $10^6$ cfu/ml.

As soon as a lower threshold is used, specificity declines sharply and over treatment becomes a problem.

Selecting antimicrobial therapy solely on the basis of EA culture results can lead to either unnecessary antibiotic therapy or over treatment with broad spectrum antibiotics.
FOB

Major area of controversy in the diagnosis of HAP is in the utility of bronchoscopy for obtaining samples.

In literature, very broad ranges of sensitivity and specificity for these techniques (i.e., studies have used different criteria with which to compare bronchoscopy).

Provides direct access to the lower airways for sampling bronchial and parenchymal tissues at the site of lung inflammation.
FOB

Specimen types:

- Use of a double lumen catheter with a PSB to collect and calibrate uncontaminated specimens directly from the affected area in the lower respiratory tract.

- BAL for obtaining cells and secretions from a large area of the lung.
False Positive FOB
- Suctioning through the channel
- COPD/Bronchiectasis

False negative FOB
- Poor technique/BAL return
- Antimicrobial therapy (recent changes)
- “Early pneumonia”
Associated occurrence of cardiac arrhythmias, hypoxemia, or bronchospasm is not unusual.*

Transbronchial spread of infection is also remote possibility #.

* Chest 1990: 97; 927–933
# Chest 1992: 102; 557S–564S
Bronchoscopy with PSB

Brush is encased within two catheters

Outer catheter is plugged which prevents contamination of the brush with colonized organisms from the endotracheal tube and airway

After properly positioning, the inner catheter is advanced to dislodge the protective plug

Then, the brush is advanced up to 3 cm distal to the catheter tip

PSB results in sampling of 0.001 to 0.01 ml of secretions
Bronchoscopy with PSB

- Sensitivity and specificity: very wide ranges reported
- At a threshold of $10^3$ cfu/ml, PSB had a sensitivity and specificity of 82% and 89%, respectively.
- Another similar study: PSB had a sensitivity of 36% and specificity of 50%

*Am J Respir Crit Care Med 1995;152:231-240*
Bronchoscopy with PSB

Although in vitro repeatability is excellent and in vivo qualitative recovery is 100%, quantitative results were more variable.

For 14–17% of patients, results of replicate samples fell on both sides of the $10^3 \text{ cfu/ml}$ threshold and cfu counts varied by more than 10–fold for 59 to 67% of samples.*

Reflects irregular distribution of organisms in secretions and the small volume sampled by PSB.
FOB with BAL

- Only 1 ml of actual lung secretions is sampled
- If possible the first 20 ml should be discarded, as it may not represent alveolar material
- A threshold of $10^4$ cfu/ml is utilized in this procedure
Because of the possible risks associated with lung aspiration, it should be reserved for patients who have failed previous empiric treatment, or are immunocompromised and an exact etiology is needed.

A lung aspirate should not be done on patients who are on ventilators, patients with a bleeding diathesis, or in those suspected of infection with *Pneumocystis*.
A study highlighted that patients receiving invasive management had lower mortality rate on day 14 and lower mean sepsis-related organ failure assessment scores on days 3 and 7.*

In addition, the bronchoscopy group had more antibiotic-free days and reduced colonization/infection with *Candida* species.

*Ann Intern Med 2000: 132; 621-630*
Usage of invasive strategies?

In a study in which histological diagnosis of VAP was the “gold-standard” the sensitivity and specificity of quantitative EA, BAL, and PSB were similar.

Threshold values for quantitative EA, BAL, PSB of $10^6$ cfu/ml, $10^4$ cfu/ml, and $10^3$ cfu/ml, respectively, gave sensitivities of 55%, 47%, and 57% and specificities of 85%, 100%, and 88%.
Usage of invasive strategies?

- Invasive diagnostic testing should not be performed early in the course of HAP.

- The false-negative rate for these tests ranges from 30% to 40% and the false-positive rate from 20% to 30%.

Inappropriate initial empiric selection of antibiotics: higher mortality

Wrong initial therapy later corrected by investigations does not improve outcome*

Delays in the administration of appropriate antibiotic treatment was associated with greater mortality.#

*Crit Care Med 2003; 31:2742-2751
#Chest 1997 : 111 ; 676 -685
The initial selection of an antimicrobial agent is almost always made on an empiric basis.

Look into:

a) severity of infection
b) patient-specific risk factors
c) total number of days in hospital before onset.
Empiric treatment

Cover core organisms

- aerobic gram negative bacilli
  - (Enterobacter spp, Escherichia coli, Klebsiella spp, Proteus spp, Serratia marcescens, and Hemophilus influenzae)
- gram-positive organisms such as Streptococcus pneumoniae and Staphyloccoccus aureus.
Mild to moderate HAP – no unusual risk factors

**Core Organisms**

<table>
<thead>
<tr>
<th>Enteric gram-negative bacilli</th>
<th>Cephalosporins (2nd or 3rd generation non-psuedomonal cephalosporin) or Beta-lactam/beta-lactamase inhibitor (ampicillin/sulbactam, ticarcillin/clavulanate, or piperacillin/tazobactam)</th>
</tr>
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<tbody>
<tr>
<td>Streptococcus pneumoniae</td>
<td>Fluoroquinolone/Clind</td>
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Mild to moderate HAP –with risk factors

Core Organisms, plus

Anaerobes (abd surgery, witnessed asp)

Clindamycin (for anerobes) or

Beta-lactam/beta-lactamase inhibitor, (as above)

Staph aureus (coma, head trauma, DM, RF, IV)

+/- Vancomycin (until MRSA ruled out)
Mild to moderate HAP – with risk factors

Core Organisms, plus
Legionella (long term high-dose steroids)

- A macrolide with or without rifampin

- P aeruginosa (prolonged hospital stay, steroids, antibiotics, abnl lungs)

- Treat as severe HAP
Severe HAP (ICU admission, respiratory failure, rapid X-ray changes, severe sepsis, etc.)

- If less than 5 days, attack core group organisms but not monotherapy

- If > 5 days in hospital, cover Psuedomonas and acinetobacter
Severe HAP

**Core Organisms, plus**

- P. aeruginosa
- Acinetobacter sp
- MRSA

**Aminoglycoside*** or Cipro + one of the following:

- antipseudomonal penicillin beta-lac/beta-lac inhibitor
- Ceftaz or cefoperazone
- Imipenem
- Aztreonam
A 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 of HAP 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.

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 that 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 Beta-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*. 
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 HAP, VAP, or HCAP who have received initially appropriate therapy and have had a good clinical response, with no evidence of infection with nonfermenting gram-negative bacilli.
HAP, VAP or HCAP Suspected

Obtain Lower Respiratory Tract (LRT) Sample for Culture (Quantitative or Semi-quantitative) & Microscopy

Unless There Is Both A Low Clinical Suspicion for Pneumonia & Negative Microscopy of LRT Sample, Begin Empiric Antimicrobial Therapy Using Algorithm in Figure 2 & Local Microbiologic Data

Days 2 & 3: Check Cultures & Assess Clinical Response: (Temperature, WBC, Chest X-ray, Oxygenation, Purulent Sputum, Hemodynamic Changes & Organ Function)

Clinical Improvement at 48 - 72 Hours

Cultures -

Search for Other Pathogens, Complications, Other Diagnoses or Other Sites of Infection

Cultures +

Adjust Antibiotic Therapy, Search for Other Pathogens, Complications, Other Diagnoses or Other Sites of Infection

Cultures -

Consider Stopping Antibiotics

Cultures +

De-escalate Antibiotics, if Possible. Treat Selected Patients for 7-8 Days & Reassess
All the best..