Managing Health Care Facility Associated Pneumonias: Diagnosis, Treatment and Prevention

Fredric J. Silverblatt, MD

Pneumonias acquired in a healthcare facility have different epidemiology, risk factors, responsible pathogens, treatments and outcomes than those acquired in the community. Patients with such infections generally have greater mortality and incur greater medical costs. Initially, hospitals were regarded as the major site for this paradigm; more recently, long term care facilities, rehabilitation institutions, dialysis centers and outpatient infusion facilities have also been recognized as posing similar risks. Pneumonias that occur in the ICU carry particularly serious implications. In 2005, a joint committee of the Infectious Diseases Society of America and the American Thoracic Society issued guidelines to help diagnose and manage these infections.[1] Additional research has shown that these infections are not inevitable and that focused, coordinated efforts can reduce their risk and the subsequent serious consequences.

Definitions

The 2005 IDSA/ATS guidelines provided the following definitions:

- A **Hospital-acquired pneumonia (HAP)** is one that presents clinically at 48 or more hours of admission in the absence of evolving, pre-existing infection.
- A **Healthcare-associated pneumonia (HCAP)** is one that occurs in a non-hospitalized patient with one or more of the following risks:
  – Hospitalization in an acute care facility for 2 or more days during the preceding 90 days.
  – Residence in a long term care or rehabilitation facility.
  – Receipt of IV antibiotics, chemotheraphy or wound care within the prior 30 days or attended a hospital or outpatient dialysis center.
- **Ventilator-associated pneumonia (VAP)** refers to a pneumonia that occurs 48-72 h after endotracheal intubation. This is a subset of HAP.

Epidemiology

Pneumonias are the second most common nosocomial infection after urinary tract infections. They carry a high morbidity and mortality rate and account for considerable increase in length of stay and contribute substantially to the rise in hospital expenses.[2] Most cases of HAP occur among patients who are not in the ICU; however, the highest expenses and mortality are found in those admitted to ICUs. This is particularly true for patients who develop VAP. Warren, Shulka et al. compared outcomes and costs of VAP in their ICU. The rate of pneumonia was 127/879 (15.5%) of patients requiring intubation. Infected patients had an increase in length of stay (26 v 4 days), increase in mortality (50 v 34%) and an increase in attributable costs ($118,097).[3] The **Centers for Medicare and Medicaid Services (CMS)** report there were an estimated 30,867 episodes of VAP in American hospitals in 2007 with an average cost of $135,795 per hospital stay.[4] In 2008 the CMS proposed adding VAP to its list of non-reimbursable expenses.

Pathogenesis

For the most part, both nosocomial pneumonias (HAP/VAP and HCAP) and **pneumonias acquired in the community (CAP)**, result from aspiration of oropharyngeal secretions contaminated by potential pathogens. Whereas with CAP those pathogens tend to be *Streptococcus pneumoniae* and other respiratory pathogens with a low rate of antibiotic resistance, in the case of HAP, aspirated material is more likely to be contaminated with organisms resistant to multiple antibiotic. Within a few days of hospitalization, patients undergo replacement of their community flora with "hospital flora" that are more adapted to the hospital environment, i.e., able survive exposure to multiple antibiotics. A similar replacement occurs in non-hospitalized individuals with chronic medical conditions in long term or rehab facilities. Micro aspiration occurs commonly, even among healthy ambulatory individuals, but the virulent hospital organisms are more likely to overwhelm local host in the lower respiratory tract and cause disease. While endotracheal tubes would be expected to protect against aspiration, contaminated secretions can pass into the lower respiratory tract between the outside of the tube and the surface of the trachea.

Other factors that contribute to the risk of HAP are medications and treatments that increase the risk of aspiration or impair the ability of the host to clear aspirated material. Sedatives and many medications for pain blunt the epiglottal reflex. Other medications impair the muco-cilliary elevator mechanism, reducing clearance of aspirated material from the lower respiratory tract. Patients recovering from upper abdominal or thoracic surgery cannot cough without pain and are at greater risk of post-operative pneumonia. Patients on mechanical ventilation are at risk from pooled oral secretions or contaminated solutions from the surfaces of tubing and other components of the ventilator. The normal acidity of gastric fluid inhibits the growth of many potential pathogens and the routine use of H2 blockers and proton pump inhibitors has been linked to the risk of HAP/VAP. The common practice of maintaining intubated patients in a prone position, especially during enteral feeding, facilitates aspiration.[5] Patients can become colonized and then infected from exposure to contaminated environmental surfaces such as the hands and clothing of health care workers, instruments used in patient care and from nearby infected patients.

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Microbiology

Microbial species that are believed to cause nosocomial pneumonias are adapted to the healthcare environment. These include Gram-negative species such as enterobacteraceae (e.g., E. coli, Klebsiella spp, enterobacter spp.), and non-enterobacteraceae Gram negative

species (e.g., *Pseudomonas aeruginosa* and Acinetobacter spp.). Gram-positive organisms include streptococcal spp. and *Staphylococcus aureus* including methicillin-resistant *S. aureus* (MRSA). Many infections are polymicrobial or yield no identifiable pathogen on culture. Anaerobes are often isolated in cases of aspiration pneumonia. Fungi are identified primarily in pneumonias that develop in immunocompromised patients and the recovery of candida or aspergillus species from non- immunocompromised patients is most likely due to colonization of the trachea rather than true infection. Respiratory viruses, e.g. influenza, parainfluenza, adenovirus or respiratory syncitial virus only rarely are the cause pneumonia in hospitalized patients, usually in the setting of an outbreak on the ward or in the community.

Clinical Presentation

HAP should be suspected when patients develop a new infiltrate on chest x-ray plus one or more of these following signs and symptoms -cough, production of purulent sputum, dyspnea, tachypnea, leukocytosis and fever. On physical exam patients may have signs of pulmonary infection such as rales, dullness to percussion and a change from voiced "E" to "A" on auscultation. Hospitalized and/or patients with chronic diseases are often elderly or frail and may present without fever. Because of the greater virulence of nosocomial respiratory pathogens, pulmonary necrosis and extension of the infection to the pleural surface is more common. Involvement of the lower lobes may present with predominantly upper abdominal symptoms. It is nonetheless difficult sometimes to distinguish pneumonia from non-infectious clinical conditions that present in a similar fashion, e.g., pulmonary embolism or adult respiratory distress syndrome.

Diagnostic Studies

Given the high mortality of HAP and the high prevalence of antibiotic-resistant organisms, vigorous efforts should be undertaken to obtain lower respiratory secretions to permit identification of the responsible pathogen(s) and antibiotic sensivities. Positive identification of a pathogen also helps distinguish pneumonia from noninfectious conditions with similar clinical presentation. Optimally, recovery of lower respiratory secretions involves the use of bronchoscopy. The usual technique employs either bronchoalveolar lavage or the use of a protected brush. For intubated patients, a catheter can be inserted into the endotracheal tube and the lower respiratory tree washed with saline. Because small amounts of contaminants usually cannot be avoided with of these techniques, the number of organisms recovered should be quantitated. "Significant" growth is usually defined as 10^4 or greater. Gram stains and, where appropriate, acid-fast and fungal stains should be ordered. Expectorated sputum, or material obtained non-bronchoscopically by deep tracheal suction are much less reliable sources of true, uncontaminated alveolar secretions. In practice, however, bronchoscopy is seldom used for this purpose and the diagnosis of HAP is usually made on clinical and radiological grounds. Blood cultures should be obtained in all cases. While the yield is usually not more than 25%, isolation of a respiratory pathogen from the blood is usually is a reliable indicator of causation.

The increasing use of powerful antibiotics has led to an ever increasing cycle of resistant organisms.

Treatment

Once the decision has been made to use antibiotics, the choice of empiric therapy is based on the presence of risk factors **for multi-drug resistant organisms (MDR);** e.g., a high prevalence of resistant organisms in the clinical setting (consult the institutional "antibiogram"), the use, if any, of prior antibiotic therapy (within 90 days), and the time of onset of disease. Pneumonias that develop early (less than 5 days) are less likely to be caused by MDRs than those which develop later in the admission. and sensitivity data of microbial cultures should be interpreted with the caveats mentioned above. The following recommendations were taken from the IDSA/ATS 2005 guidelines for the management of adults with HAP, VAP and HCAP.

Early onset pneumonias and those who do not have other risk factors for MDS are usually due to antibiotic-sensitive organisms. These include *Streptococcal pneumoniae*, *Haemophilus influenzae*, Methicillin-sensitive *Staphylococcus aureus* and antibiotic-sensitive enteric Gram negative bacilli (E. coli, Klebsiella spp. etc).

- Recommended antibiotic for low risk HAP/VAP/HCAP:
  – Ceftriaxone, 2g, IV q24h Or a respiratory fluoroquinolone (e.g, Levofloxacin 750mg or moxifloxicin 400mg IV/PO q24h

Or

  – Ampicillin/sulbactam (3g IV q 6h)

Or

  – Ertapenem 1g IV q 24h.

For late onset pneumonia or in patients with known risk factors for MDR pathogens the responsible pathogens include, in addition to those listed above for early onset pneumonia, Pseudomonas aeruginosa, Extended beta-lactamase producing strains of E.coli and Klebsiella pneumonia (ESBL) and Acinetobacter spp.

- Recommended initial empiric therapy for MDR pathogens:
  – Antipseudomonal cephalosporin (Cefepime, 1-2g IV q 8-12 h, or Ceftazidime, 2g q 8h)

Or

  – Antipseudomonal carbopenem (imipenem or meropenem, 1 g IV q 8h)

Or

  – Beta-lactam/beta-lactamase inhibitor combination (Piperacillin-tazobactam, 4.5g q6h)

Plus

  – Antipseudomonal fluoroquinolone (ciprofloxacin, 400mg IV q 12h or levofloxacin 750mg IV q 24h)

Or

  – Aminoglycoside (gentamicin or tobramycin, 7mg/kg q24h, or Amikacin 20mg/kg q 24h)

Plus

  – Anti –MRSA therapy (vancomycin 30mg/kg as a single loading dose followed by 15mg/kg q12h, linezolid 600mg q12h)

Doses should be adjusted for abnormal renal function. Trough levels should be obtained for the aminoglycosides and vancomycin. For gentamicin and tobramicin they should be less than 1 microgram, for amikacin they should be less than 4-5 micrograms and for vancomycin they should be between 15-20 micrograms/ml.

Special Pathogens

Empiric treatment should be refined once culture and sensitivity information is returned. Some pathogens that are isolated in patients with HAP or VAP require special consideration because of unusual resistance patterns. *Acinitobacter baumanni* has been implicated in outbreaks of HAP and VAP, particularly in the ICU.[6] Because acinitobacter is found in environmental sites and may be a non-pathogenic colonizer caution must be used in implicating it as a cause of pneumonia unless it is isolated from a normally sterile site or from the blood, or amidst an outbreak. Many strains are highly resistant to antibiotics. The most active agents are imipenem, cefepime, ampicillin/sulbactam, and amikacin. For those strains that are totally resistant to conventional antibiotics, colistin, an antibiotic in use in the '60s but abandoned when less toxic alternatives became available, is recommended in combination with imipemen or ampicillin/sulbactam.

Another organism sometimes recovered from the sputum of hospitalized patients with pneumonia is *Stenotrophomonas maltophilia*. Like acinitobacter, stenotrophomonas is found in the environment and more often colonizes the trachea rather than causes disease; however, it can be a true pathogen particularly in patients with underlying structural lung disease such as cystic fibrosis or in patients on mechanical ventilation.

Stenotrophomonas is best treated with trimethoprin/sulfamethoxazole. **Extended-spectrum beta-lactamase producing strains of enterobacteriaceae (ESBL)** display variable resistance to cephalosporins (e.g. ceftriaxone) and anti-pseudomonal penicillins (e.g. piperacillin/tazobactam). Carbopenems are the most reliable empiric agents against ESBL-producing strains. Ominously, strains of Klebsiella have emerged recently that produce **carbapenemases (KPC)** that bestow the broadest resistance. For such strains, colistin or tigecycline may be the only options.

Prevention

With rates of resistance on the rise and fewer effective antibiotics available, greater efforts need to be made to prevent nosocomial infections including pneumonias. Increasing awareness on the part of healthcare worker of modifiable risk factors has led to reductions of HAP and VAP in those hospitals that have launched such programs . These actions have included increasing compliance with hand-washing protocols using alcohol-based disinfectants, surveillance for introduction of new MDR organisms and isolation of patients so infected. Measures to reduce the risk of VAP include reducing the use of orotracheal intubation by employing non-invasive ventilation techniques whenever possible, careful emptying of contaminated condensates from ventilator circuits, continuous aspiration of subglottic secretions, and keeping patients in the semi recumbent position (30-45 degrees) during enteral feeding. The increasing use of powerful antibiotics, particularly broad-spectrum, highly active agents such as beta-lactam betalactam inhibitor combinations, 3rd and 4th generation cephalosporins, carbopenems (e.g., imipenem-cilastin) and fluoroquinolones has led to an ever increasing cycle of resistant organisms. A program of careful oversight and management of antibiotic use by clinical pharmacists and infectious disease experts (antibiotic stewardship) can minimize the emergence and spread of these problematic pathogens.

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Fredric J. Silverblatt, MD, is Professor of Medicine (Emeritus), The Warren Alpert School of Medicine, Brown University.

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Correspondence

Fredric J. Silverblatt, MD
Roger Williams Medical Center
825 Chalkstone Ave
Providence, RI 02908
e-mail: fsilverblatt@gmail.com