Research & Reviews of Pneumonia

Chapter 1

Pathophysiology of Hospital Acquired Pneumonia

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1. Introduction

Pneumonia is an infection of the pulmonary parenchyma resulting from the invasion and overgrowth of microorganisms in the lung parenchyma, break down of host defenses leading to intra-alveolar exudates. Microorganisms gain access to the lower respiratory tract in several ways. The most common being aspiration from the oropharynx [1].

2. Classification and Definition

In the past, pneumonia was typically c1assified as community-acquired (CAP) and hospital-acquired (HAP) or ventilator-associated (VAP) [2]. Since the past few years, however, some patients presenting with onset of pneumonia as outpatients have been found to be infected with the multidrug-resistant (MDR) pathogens previously associated with HAP [3]. Factors responsible for this phenomenon include the widespread use of oral antibiotics, increased use of outpatient IV antibiotic therapy, increased use of day care treatments leading to earlier transfer of patients out of acute-care hospitals to their homes, general aging of the population, and extensive use of immunomodulatory therapies. The potential involvement of these MDR pathogens has led to the designation of a new category of pneumonia-health care-associated pneumonia (HCAP) -that is distinct from CAP. Risk factors associated with HCAP are listed in **Table 1**.

Table 1: Clinical Conditions associated with Healthcare Associated Pneumonia [1]

• Hospitalization for ≥48 h
• Hospitalization for ≥2 days in prior 3 months
• Nursing home or extended care facility residence
• Antibiotic therapy in preceding 3 months
• Chronic dialysis
• Home infusion therapy
• Home wound care
• Family member with MDR infection

3. Definition

3.1. Community acquired Pneumonia: Acute infection of the pulmonary parenchyma that is associated with atleast some symptoms of acute infection, associated with presence of acute infiltrates on chest X-ray or auscultatory findings consistent with pneumonia, in a patient not hospitalized or residing in a long term care facility for ≥14 days before onset of symptoms.

3.2. Hospital acquired Pneumonia: Hospital Acquired Pneumonia (HAP), or Nosocomial Pneumonia (NP) has been defined as pneumonia that develops 48 h or more after admission to a hospital and was not present or incubating at the time of admission.

3.3. Healthcare associated Pneumonia: Infection detected within 48 hours of hospital admission in patients that had previous contact with healthcare service within one year.

4. Defense Mechanisms for Prevention of Respiratory Infection in the Normal Host

Normal healthy individuals harbor variety of mechanisms which prevent the development of pneumonia by the microaspirations which usually occurs during sleep. These defense mechanisms are enumerated in **Table 2**.

Table 2: Normal defense mechanisms

• Anatomy of airway
• Cough reflex
• Mucus
• Mucociliary clearance
• Alveolar macrophages
• Leukocytes
• Immunoglobulins
• Complement
• Lactoferrin
• Basement membrane

5. Pathogenesis of Ventilator associated Pneumonia

Development of pneumonia requires that the pathogens reach the alveoli and that host defenses are overwhelmed by microorganism's virulence or by the inoculum's size. Bacteria can reach the lower respiratory tract either by the blood stream infection or due to colonization

of the mucosa by exogenous or endogenous sources.

6. Endogenous Sources

6.1. Nasal colonization

The upper airway is usually colonized by various micro-organisms. Cross sectional study performed by Piso et al in Swiss refugees [6] showed that 15.7% of the refugees (healthy population) had MRSA colonization.

6.2. Oropharyngeal and gastric colonization

Fibronectin, a component of saliva, inhibits the adhesion of aerobic gram-negative bacilli and promotes the adhesion of normal oral streptococci. In hospitalized patients, the normal oral inhibitory flora gets reduced which promotes colonization of the respiratory pathogens. Thus, the oropharynx of hospitalized patients becomes a reservoir of infected secretions [7].

A gastric pH under 4 prevents bacterial growth in the gastric chamber. In hospitalized patients, treatment with antacid drugs for prevention of stress ulcers leads to an increase the pH of gastric juice. De la Torre et al [8] found that only 10 out of 80 mechanically ventilated patients had no microorganisms on gastric cultures. These 10 patients had a lower mean gastric pH (3.3) than did patients with gastric colonization (mean gastric pH, 4.6). The remaining 70 patients were colonized by either gram positive or gram negative organisms.

The type of microorganism that colonize the stomach is determined by the microorganisms present in the saliva or duodenum. Study conducted by Driks et al [9] showed that non-hospitalized patients treated with H2-blockers had predominant gram-positive bacteria dominating the gastric flora. While hospitalized patients showed colonization predominantly with aerobic gram-negative bacilli.

6.3. Lower airway colonization

The lower airways are found to be colonized in patients with chronic obstructive pulmonary disease and in hospitalized patients. Intubated and mechanically ventilated patients have been shown to have tracheal colonization within the first 24 hours of mechanical ventilation [8]. The pattern of the tracheal colonizing flora changes over time among hospitalized and ventilated patients. Study by Ewig et al [10] showed that theinitial colonization rate of trachea on ICU admission following brain injury was 83%; and *Streptococcus pneumoniae, Haemophilus influenzae,* and *Staphylococcus aureus* were the predominant microorganisms. Similar results were found in the study conducted by Sirvent et al [11]. These microorganisms are responsible for most instances of early-onset pneumonia, suggesting that the aspiration of secretions when the patient becomes unconscious or at the time of intubation does have a role in the develop-

ment of pneumonia.

6.4. Oropharyngeal and gastric aspiration

Normal adults frequently aspirate oropharyngeal secretions during sleep, but host defenses prevent lung infections, and the types of microorganisms aspirated are less virulent. However, the conditions in ill patients especially those in ICU are different. First, as already discussed above, aerobic gram-negative bacilli colonize the dental plaque and oropharynx. Second, the frequent presence of a nasogastric tube gives rise to lower esophageal sphincter incompetence. Third, supine body position of inpatients favors gastric reflux and tracheal aspiration as shown by Torres et al [12]. Torres et al demonstrated that instilling a colloid with technetium via a nasogastric tube and placing patients in a semirecumbent position significantly reduced the radioactivity in tracheal secretions in comparison with patients in a supine position.

7. Exogenous Sources

7.1. Colonization of artificial airways

7.1.1. Ventilator circuits and nebulizer fluids: Condensates of ventilator circuits can be a potential source of microorganisms. The inner parts of the ventilator circuit closest to the patient have the highest rates of contamination and the highest bacterial counts as demonstrated by Craven et al [13]. After 24 hours of use, 80% of the ventilator circuits and the condensates were colonized, predominantly by aerobic gram-negative organisms (76%), gram-positivecocci (21%), and yeast (3%). These microorganisms had frequently been isolated from previous sputum cultures.

7.1.2. Endotracheal tube colonization and Biofilm formation: The endotracheal tube has been described as a reservoir for microorganisms due to the formation of biofilms. The biofilm formed is relatively insensitive to the effects of antibiotics and host defenses, and their fragments can be dislodged by suction catheter or by ventilator gas flow. In 1999, Adair et al [14] performed a study on 20 patients with VAP and 20 controls. They examined endotracheal tubes for the presence of biofilm after extubation, and the relationship with microorganisms that caused VAP. Seventy percent of patients with VAP had identical pathogens isolated from endotracheal biofilm and tracheal secretions (shown by electrophoresis, polymerase chain reaction technique, and susceptibility testing). No pairing of pathogens were observed in controls ($P < .005$).

Thus, the pathogenesis of Ventilator associated Pneumonia can be summarized as shown in **Figure 1**.

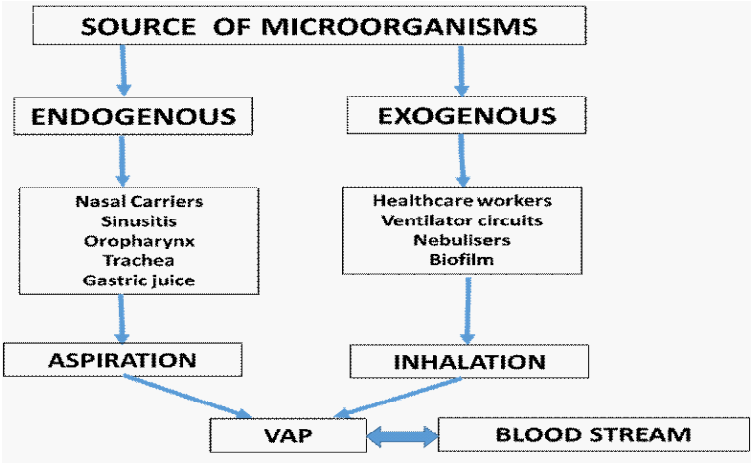

Figure 1: Summary of VAP pathogenesis

8. Histologic characteristics of Ventilator-Associated Pneumonia

In a postmortem study with bilateral multiple biopsy sampling [15], the authors described four evolution stages of pneumonia (**Figure 4**):

An early phase (0–2 days of evolution) shows the presence of capillary congestion with an increased number of polymorphonuclear leukocytes. The alveolar spaces usually show a fibrinous exudate. This is called the stage of edema.

An intermediate phase (3–4 days of evolution) is characterized by the presence of fibrin, a few erythrocytes, and several polymorphonuclear leukocytes within the alveoli. Due to the presence of RBCs, this stage is known as the stage of Red Hepatization.

An advanced phase (5–7 days of evolution) shows polymorphonuclear leukocytes filling up most of the alveoli and macrophages incorporating cellular debris in the cytoplasm. No RBCs are seen extravasating and those already present get lysed. This stage corresponds with successful containment of infection and improvement of gas exchange. This is known as the stage of grey hepatisation.

A resolution phase (> 7 days of evolution) occurs when the inflammatory exudate is eliminated owing to phagocytic activity of mononuclear cells.

As VAP occurs due to microaspiration, a pattern of bronchopneumonia is most common in nosocomial pneumonias, whereas in CAP a lobar pneumonia pattern is seen.

9. Prevention of VAP Based on Pathogenesis

Mechanical ventilation of ICU patients is a common phenomenon in the modern ICUs. Unfortunately, mechanical ventilation is associated with large number of complications including infectious and non-infectious complications. Ventilator associated Pneumonia or Nosocomial Pneumonia is the most common infectious complication.

Understanding the pathogenesis of VAP would help in the development of preventive strategies.

Various strategies can be deviced for the prevention of VAP based on the pathogenesis as given in **Table 3**

Table 3: Measures for prevention of Ventilator Associated Pneumonia based on understanding of VAP pathogenesis [16]

Source of VAP pathogens	Preventive Goal	Specific measures
Aerodigestive colonization	Prevent colonization by exogenous routes	Hand hygiene Adequate PPE
Adequate PPE	Suppress oropharyngeal mucosal colonization	Oral chlorhexidine decontamination Selective digestive tract antimicrobial decontamination Aerosolosed antimicrobials
	Prevent aspiration	Noninvasive ventilation Semirecumbent position ET tube with subglottic suctioning
Contaminated medical therapy equipment	Safe equipment and medical aerosols	Reprocessing of bronchoscopes and respiratory therapy equipment
	Reducing ventilator circuit contamination	Aseptic technique of suctioning Use sterile water
Contaminated water (for *Pseudomonasspp* and *Legionella spp*)	Safe water	Use of sterile water Nosocomial surveillance for respiratory water pathogens Engineering control for contaminated water
Contaminated air (for SARS, *M. tuberculosis* etc)	Safe water	HEPA filteration of air N95 mask Construction policies

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