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Nosocomial pneumonia: epidemiology and infection control

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Abstract. Elderly, debilitated, or critically ill patients are at high risk for hospital acquired or nosocomial respiratory tract infection. Gram-negative bacilli, *Staphylococcus aureus*, and anaerobes colonizing the oropharynx are the most frequent etiologic agents. Colonization of the oropharynx may be related to the patient's age, underlying disease, nutritional status, prior exposure to antibiotics, supine position, and gastric colonization. Nosocomial pathogens may also be acquired from the hands of hospital personnel, contaminated equipment or fluids. The absence of sensitive and specific methods for accurate diagnosis remain a concern. Despite treatment with appropriate antimicrobial therapy, there is a high mortality and morbidity. Measures for the prevention of nosocomial pneumonia should include compliance with infection control principles, appropriate use of antibiotics, proper patient position, and removal of potential sources of cross colonization.

Key words: Nosocomial pneumonia – Mechanical ventilation – Gastric colonization – Aerobic Gram-negative bacilli – Respiratory therapy equipment

Hospital-acquired pneumonia is presently the second most common cause of nosocomial infection and the leading cause of death from hospital-acquired infection in the United States [1, 2]. Though most cases occur in non-intubated patients, rates of infection are highest in the mechanically ventilated patient [3–5].

Aspiration of bacteria from the oropharynx is an important step in the pathogenesis of pneumonia [6, 7]. Colonization of the patient's oropharynx with nosocomial pathogens appears to be a prerequisite to the development of nosocomial pneumonia [8–10]. Supine position of the patient [11], the presence of a nasogastric tube [3, 12], or reflux of bacteria colonizing the stomach also may increase oropharyngeal colonization and bacterial entry into the lung [13–19].

High mortality rates of nosocomial pneumonia, despite improved treatment with antibiotics [3, 19–23], underscore the need for better preventive efforts. This article will review epidemiology and current strategies for prevention of hospital-acquired pneumonia.

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Epidemiology

Nosocomial pneumonia occurs at a rate of 0.6–1.0 episodes per 100 hospital admissions in the United States [5, 22]. Although most cases occur in non-intubated patients, rates in intubated patients are increased 6–20-fold [3–5].

Nosocomial pneumonia is the leading cause of death from nosocomial infection [2]. Crude fatality rates for patients with nosocomial pneumonia may vary from 20%–50%; rates are generally higher in mechanically ventilated patients in intensive care units [19–24]. Stevens et al. reported fatality rates of 50% for intensive care unit patients with hospital-acquired pneumonia compared to 3.5% for intensive care unit patients without pneumonia [20]. Using a case-control design, Leu and coworkers have suggested that the attributable mortality or mortality due to pneumonia was 33% [21].

In a study of 233 mechanically ventilated patients at Boston City Hospital, the mortality rate for patients with pneumonia was 55% compared to 25% for patients without pneumonia [19]. Although pneumonia was one of 18 variables significantly associated with overall patient mortality, it was not an independent predictor of death. "High-risk" organisms, bilateral infiltrates on chest radiographs and respiratory failure were among the 6 independent risk factors for mortality reported by Celis and co-workers [3]. Nosocomial pneumonia increases a patient's length of stay 7–9 days [21, 25] and the annual cost of diagnosing and treating nosocomial pneumonia may exceed 2 billion dollars per year in the United States [22].

Etiologic agents

Nosocomial pneumonia may be caused by viruses, bacteria or fungi. As shown in Table 1, most of the cases are caused by aerobic Gram-negative bacilli such as *Klebsiella*, *Escherichia coli*, and *Pseudomonas aeruginosa* [26]. Anaerobic bacteria, not collected in the NNIS study summarized in Table 1, have been isolated in approximately 30% of patients, most of whom were not mechanically ventilated [27]. *Legionella pneumophila* may occur in hospitals with a contaminated water supply or cooling tower [28, 29].

Pathogenesis

Aspiration

Aspiration is more frequent in patients with pathologically altered consciousness, abnormal swallowing, depressed gag reflexes, delayed gastric emptying or decreased gastrointestinal motility [6, 7, 30, 31]. Approximately 70% of healthy subjects aspirate during sleep. The number and virulence of bacteria aspirated into the lung are important determinants of the development of pneumonia (Fig. 1). In addition, tracheal intubation may increase colonization of the oropharynx and leakage of bacteria around the cuff increases colonization of the trachea.

Colonization of the oropharynx

Hospitalized patients tend to have high rates of oropharyngeal colonization with aerobic Gram-negative bacilli [8, 9]. Johanson et al. demonstrated Gram-negative bacillary colonization rates of 16% in moderately ill and 57% in critically ill patients [9]; pneumonia occurred in 23% of the colonized patients versus 3.3% of the uncolonized patients [8].

The adherence of Gram-negative bacilli to oropharyngeal epithelial cells is critical for colonization [10, 32]. Host factors and the type of bacteria colonizing the pharynx may affect the adherence. Other risk factors for bacterial colonization and pneumonia are summarized in Table 2.

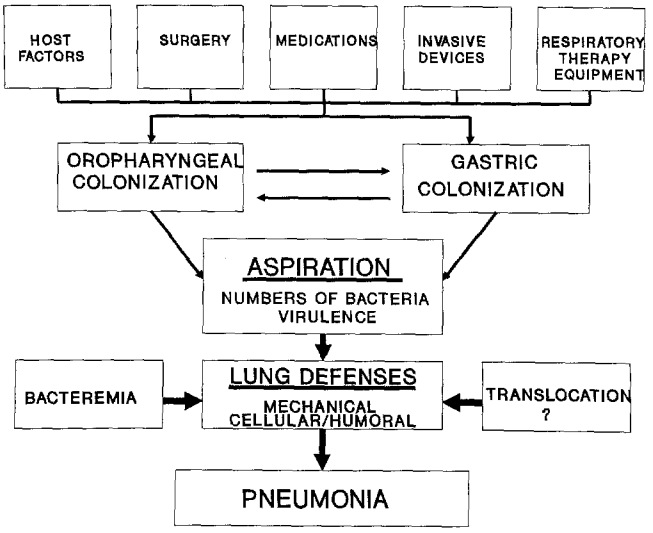

Fig. 1. A summary of mechanisms for colonization of the oropharynx and stomach. Development of pneumonia depends on the virulence and numbers of bacteria aspirated into the lung and the ability of the mechanical, cellular and humoral pulmonary host defenses to protect against infection. Adapted with permission from Craven et al. [74]

Gastric colonization

The stomach is normally sterile at an acid pH, because of the potent bactericidal activity of hydrochloric acid [33]. When gastric acid is absent, the risk of infection and gastric colonization is increased [16, 18, 34–38]. Reduced gastric acid in the intubated patient may result from decreased production, or the use of drugs such as antacids or histamine type-2 (H2) blockers [37]. As shown in Fig. 2, when the gastric pH is ≥ 4, levels of aero-

Table 1. Most frequently reported pathogens associated with nosocomial pneumonia in patients enrolled in the National Nosocomial Infection Study (NNIS) from January 1985 to August 1988 ($n = 15499$ isolates)

Pathogen	Number	%	Rank in 1984
Gram-negative bacilli:	9097	58.7	–
Pseudomonas aeruginosa	2666	17.2	1
Enterobacter spp.	1617	10.4	4
Klebsiella pneumoniae	1140	7.4	3
Escherichia coli	998	6.4	5
Serratia marcescens	695	4.5	6
Proteus mirabilis	527	3.4	7
Acinetobacter spp.	461	3.0	–
Haemophilus influenzae	993	6.4	–
Gram-positive bacilli:	2729	17.6	–
Staphylococcus aureus	2268	14.6	2
Streptococcus pneumoniae	461	3.0	11

Reprinted with permission from Horan et al. [1]

Table 2. Endogenous and exogenous risk factors for oropharyngeal colonization and nosocomial pneumonia

Endogenous factors	Exogenous factors
Host factors	Environmental factors
Genetic (?)	Seasonal trends
Age (extremes)	Cross contamination
Male sex	Air flow/water supply
Chronic disease	Hospitalization
Impaired immunity	Teaching hospital
Malnutrition	Critical care unit
Obesity	Medical/surgical wards
Life style factors	Prolonged length of stay
Smoking	Therapeutic
Alcohol abuse	Sedative/hypnotic drugs
Depressed consciousness	Immunosuppressive therapy
Aspiration	Antacid ± H2 blockers
Prior infection/antibiotics	Invasive devices
Prior surgery	Endotracheal tube
Head and neck	Tracheostomy tube
Thoracic	Nasogastric tube
Abdominal	Intracranial pressure monitor

Adapted with permission from Craven et al. [74]

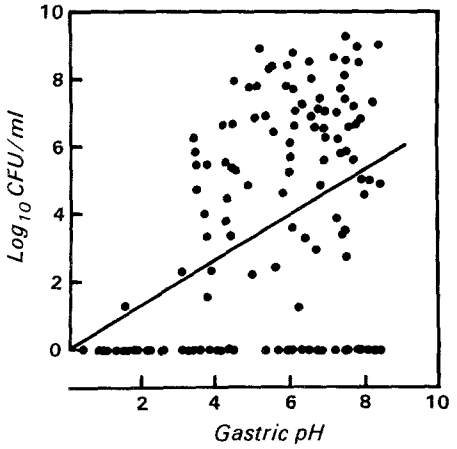

Fig. 2. Correlation between gastric pH and log (10) concentrations of aerobic Gram-negative bacilli/ml of gastric fluid from critical care patients receiving stress ulcer prophylaxis. Linear regression line is calculated by least-squares method. $r = 0.4073$ with 133 degrees of freedom ($p < 0.001$). Reproduced with permission of Du Moulin et al. [16]

bic Gram-negative bacteria may reach 1 – 100 million organisms/ml [14, 16, 35].

Although the frequency of stress bleeding appears to have decreased over the past two decades, most mechanically ventilated, intensive care unit patients continue to receive prophylaxis. Randomized studies of stress bleeding prophylaxis in mechanically ventilated, critical care patients have suggested equal efficacy and decreased rates of pneumonia for patients given sucralfate versus antacids or H2 blockers [15, 18, 38, 39].

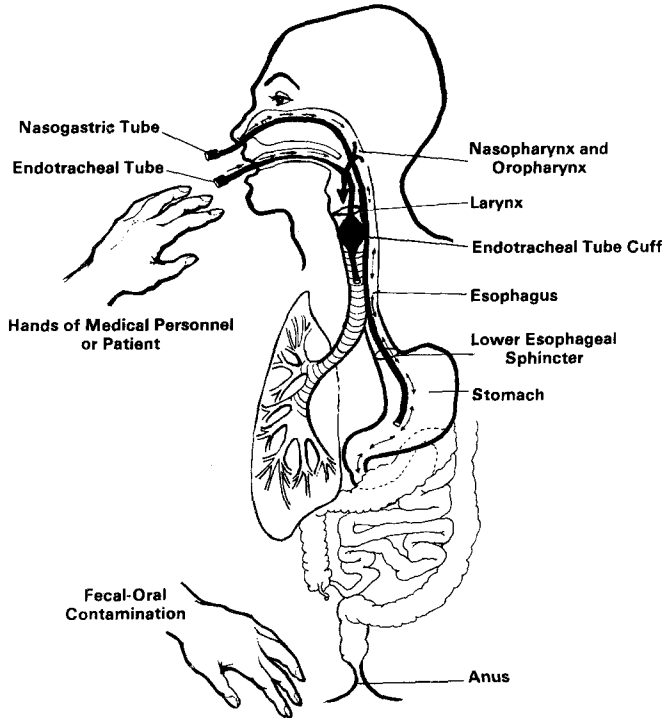

Fig. 3. Schematic diagram depicting routes of oropharyngeal colonization in the intubated patient with a nasogastric tube. In the presence of gastric colonization, the nasogastric tube may increase reflux by making the lower esophageal sphincter incompetent or acting as a conduit for nosocomial pathogens. The *small arrows* represent potential routes of bacterial colonization; the *large arrow* represents the route for aspiration of secretions into the lung. Reprinted with permission from Craven and Driks [75]

Endotracheal and nasogastric tubes

Special efforts should be taken to place the endotracheal tube without trauma to the hypopharynx and to avoid aspiration. The cuff should be maintained at optimal pressure and efforts should be taken to avoid leakage around the cuff when inflated or deflated (Fig. 3). The endotracheal tube may become a nidus for bacteria enmeshed in biofilm or glycocalyx which may dislodge and travel into the tracheobronchial tree [40, 41], increasing the risk of nosocomial pneumonia.

The nasogastric tube may be beneficial for managing gastric secretions, preventing gastric distention, and for administering drugs or feedings, but may increase reflux, oropharyngeal colonization, and subsequent pneumonia [42, 43]. Tube feedings may also increase the volume of gastric contents, intragastric pressure, and the risk of regurgitation [17, 42, 43]. Positioning the patient upright at least 30° appears to reduce the frequency of pulmonary aspiration and gastric reflux that has been reported [11, 44].

Nasotracheal suctioning of the patient

Nasotracheal suctioning is used to obtain sputum specimens or remove secretions from the lower airway. Proper tracheal suctioning of the ventilated patient is needed to prevent the introduction of nosocomial pathogens into the lower respiratory tract. Although more detailed data are needed, a closed tracheal suction system may prevent the drop in arterial oxygen levels, save personnel time and decrease the likelihood of cross contamination from condensate when the circuit is disconnected [45, 46].

Respiratory therapy

The role of respiratory therapy equipment in the pathogenesis and prevention of pneumonia has been reviewed in detail [47, 48]. Important differences in risk are related to the type of respiratory therapy equipment used. In contrast to humidification equipment that warms the air by wicks or bubbles the gas through water, nebulization equipment saturates the inspiratory phase gas with water particles $< 4\mu m$ in diameter [49]. These small, light particles float past host defenses into the patient's terminal bronchioles and alveoli, increasing the risk of pneumonia [49, 50].

Mechanical ventilator circuits

Volume ventilators currently used in most hospitals in the United States have humidifiers to warm and humidify the inspiratory phase gas (Fig. 4). Although the Centers for Disease Control's Guideline for the Prevention of Nosocomial Pneumonia [51] recommends that mechanical ventilator breathing circuits and humidifiers be changed every 24 h, other studies suggest that the interval can be extended to ≥ 48 h [19, 52, 53].

Mechanical ventilators with humidifying cascades often have significant colonization with nosocomial pathogens in the tubing nearest the patient; colonization is low or absent in the distal circuit and humidifier [54, 55]. Of note is that most of the circuit colonization originates from the patient.

Tubing condensate

Tubing condensate may also be contaminated with high numbers of nosocomial pathogens, and therefore simple procedures such as turning the patient or raising the bed rail may cause pneumonia by direct inoculation of bacteria into the patient's tracheobronchial tree [55]. Inappropriate disposal of contaminated condensate may lead to contamination of environmental surfaces and the hands of medical personnel. Heating ventilator tubing will markedly reduce the rate of condensate formation, but heated circuits are expensive. Several devices have been developed to reduce or eliminate tubing condensate. Unfortunately, in-line devices with one-way valves to collect condensate may not fit well into circuits or handle high volumes of condensate. Heat moisture exchangers or artificial noses recycle exhaled heat and moisture, and eliminate the need for a humidifier. Unfortunately, heat moisture exchangers add dead space to the circuit, may increase circuit resistance, and may not provide sufficient humidity for critically ill patients [56, 57].

Medication nebulizers

Medication nebulizers inserted into the inspiratory phase tube of the mechanical ventilator circuit (Fig. 4) may produce bacterial aerosols. In-line medication nebulizers may become contaminated by reflux of tubing condensate or contaminated solutions [58]. If nebulized medications are needed, we recommend the use of in-line nebulizers that can be opened, rinsed with sterile water or saline, and dried between treatments.

Resuscitation bags/spirometers

Resuscitation bags, used for urgent ventilation, are a potential source of nosocomial pathogens [59, 60]. Resuscitation bags may become contaminated with patients' secretions and are difficult to effectively decontaminate. Each patient should have a properly disinfected bag that is not used by other patients.

The spirometer is a well known source for cross contamination of nosocomial pathogens in an intensive care unit [61, 62]. Because the mechanical ventilator tubing is frequently colonized with nosocomial pathogens, devices should not be transferred between patients.

Infection control

Infection control is aimed at identifying potential reservoirs of infection, interrupting transmission between patients and personnel, and preventing or reducing colonization in the host [63]. Surveillance is used for tracking of nosocomial pathogens and eliminating reservoirs of nosocomial pathogens (Table 3). Hospitals with effective surveillance and infection control programs have rates of pneumonia 20% lower than hospitals without such programs [5]. Staff education also appears to be a critical factor. Britt el al. reported a reduction in pneumonia rates from 4.0% – 1.6% with an education and awareness program [64].

Hand colonization is a common source of the transfer of nosocomial pathogens between patients [65, 66]. Hand washing before and after patient contact is an effective means of removing transient bacteria, but this practice is often ignored or inadequately performed.

In a more recent study in a pediatric intensive care unit, rates of nosocomial infection were significantly reduced by the routine use of gowns and gloves for patient contact [67]. These data suggest that similar intervention may be effective in adult units where poor staff compliance with handwashing is well documented. Of note is

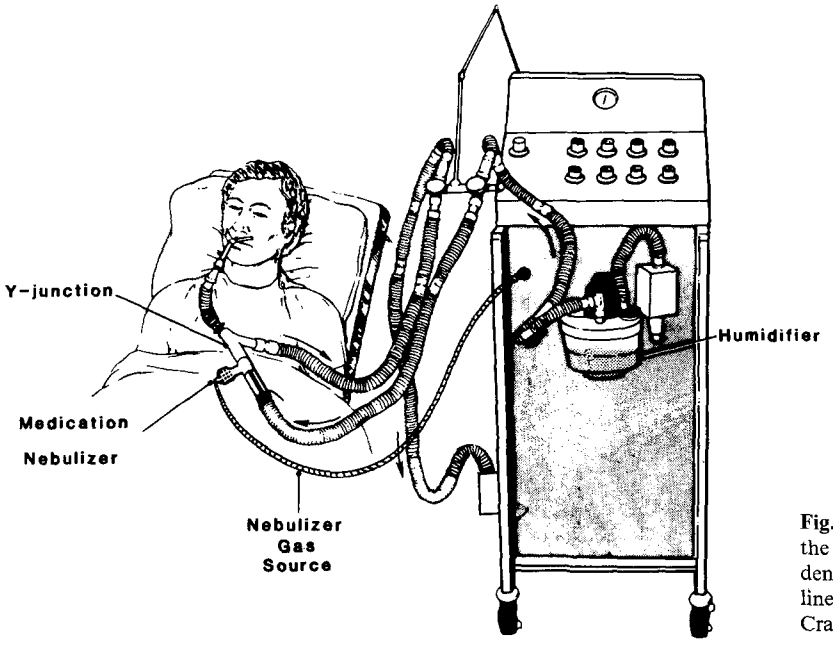

Fig. 4. A mechanically ventilated patient maintained in the upright position. Patient's ventilator circuit has condensate in the dependent portion of the tubing and an in-line medication nebulizer. Reprinted with permission from Craven et al. [52]

Table 3. Summary of methods to reduce the frequency of nosocomial pneumonia in mechanically ventilated patients

General principles
● Treatment of patient's underlying disease
● Keep patient's head elevated at ≥30 degrees
● Review need and drugs used for stress bleeding prophylaxis
● Assess nutritional status and need for tube feeding
● Extubate and remove nasogastric tube as clinically indicated
● Controlled use of antibiotics
Infection control:
● Surveillance in the intensive care unit
● Education and awareness programs
● Handwashing and/or barrier precautions; remove gloves between patients
● Assess technique for suctioning patients
● Consider prophylaxis with systemic and local antibiotics
Respiratory care equipment:
● Discriminate between equipment with nebulizers and humidifiers
● ≥48 h circuit changes (tubing and humidifier) for mechanical ventilators with humidifiers; no changes for circuits with heat moisture exchangers
● Proper removal and attention to tubing condensate
● No transfer of equipment/devices between patients
● Care of in-line medication nebulizers
● Proper disinfection of ventilator tubing, bags and spirometer

Adapted with permission from Craven and Steger [48]

that gloves may become colonized with nosocomial pathogens which can easily be transferred between patients if they are not discarded after patient contact [68, 69].

Selective decontamination of the digestive tract with combinations of antibiotics has been evaluated as a means of reducing nosocomial infection in intensive care unit patients [70–73]. These studies will be discussed in detail in an accompanying article in this issue by Stoutenbeek and others.

Conclusion

Nosocomial pneumonia is the second most common nosocomial infection and the leading cause of death from nosocomial infection in the United States. Mechanically ventilated patients have disproportionately high rates of pneumonia. Due to the high mortality and morbidity of hospital-acquired pneumonia, despite appropriate antibiotic therapy, efforts have been directed at preventive measures. These efforts have included the discrete use of antibiotics, compliance with standard infection control techniques, a knowledge of the risks associated with respiratory therapy equipment, proper patient positioning to reduce the chance of gastric reflux, reduction of gastric overgrowth with bacteria, and the use of selective decontamination of the digestive tract with antibiotics in selected patients.

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