Editorial

Nosocomial Pneumonia: New Concepts on an Old Disease

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Pneumonia is the "captain of the men of death".
William Osler[1]

Despite great strides in medical treatment over the past 20 years, there has been little progress in efforts to prevent or reduce nosocomial pneumonia. Numerous new antibiotics have been developed for treatment, but case fatality rates for patients with bacterial nosocomial pneumonia still exceed 20% and may be as high as 50% in selected populations.[2-4]

Hospital-acquired pneumonia is now the second most common nosocomial infection in the United States[5] and the leading cause of death from nosocomial infection.[6] The lack of success in reducing the incidence of nosocomial pneumonia and its associated fatality can be attributed in part to the fact that hospitalized patients are now older and more likely to have serious underlying disease that may require treatment with immunosuppressive drugs, major surgery, or assisted ventilation. Intubated patients or patients with a tracheostomy and mechanical ventilation have rates of pneumonia that are 4 to 66 times higher than patients who do not require respiratory assistance.[7]

Proper decontamination of respiratory therapy equipment had a major impact on reducing the incidence of necrotizing, gram-negative,bacillary pneumoma in the mechanically ventilated patient.[8,9] but the persistence of high rates of pneumonia in this subset of patients underscores the need for additional research and alternative strategies for intervention[4]

Effective intervention strategies should be based on a complete understanding of pathogenesis of nosocomial pneumonia. Aspiration of bacteria from the nasopharynx is a common event and the major route for bacteria to enter the lung. Why pneumonia occurs in some patients who aspirate and not in others is not well understood, but it is probably related to the amount of material aspirated, the quantity and type of bacteria present in the aspirate, and the ability of the mechanical, cellular, and humoral host defenses to respond effectively.

The importance of pharyngeal colonization in the pathogenesis of pneumonia is well known, but retrograde colonization of the pharynx from the stomach is not widely appreciated in the medical community. During the past decade, several investigators have focused on the role of gastric colonization in the pathogenesis of nosocomial pneumonia in the intubated patient.[10-16] The data of Daschner and co-workers[17] (see pp 59-65) support and extend this concept with data correlating elevated levels of gastric pH to increased rates of nosocomial pneumonia, and further evidence demonstrating retrograde spread of bacteria from the stomach to the nasopharynx.

To what extent and why does bacterial colonization in the stomach occur? Because of the potent bactericidal activity of hydrochloric acid,[18] the stomach is normally sterile at an acid pH of 1. However, if gastric acid is neutralized by the use of antacids, or secretion is blocked by the use of histamine type 2 (H_2 blockers such as cimetidine, ranitidine, or famotidine, gastric colonization with gram-negative bacilli may increase from zero at an acid pH of 1 to more than 100 million/mL at a pH of 6.[11-13,17] Atherton and White initially suggested that the stomach may be a source of bacteria colonizing the respiratory tract of the ventilated patient.[10]) Later work by du Moulin and co-workers" correlated bacterial overgrowth in the stomach with elevated gastric pH in patients receiving antacids and H_2 blockers, and suggested that bacteria in the stomach could cause retrograde colonization of the trachea. These observations have now been confirmed by others.[12,13-17]

The migration of gram-negative bacilli from the stomach to the nasopharynx and ultimately into the lung may occur through a variety of mechanisms. The nasogastric tube, present in nearly all patients receiving mechanical ventilation, probably acts as a conduit for bacteria to ascend into the nasopharynx, as previously demonstrated for bladder catheters by Kass and co-workers.[19] The pres-

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ence of the nasogastric tube also leaves the lower esophageal sphincter incompetent and thereby enhances reflux of bacteria from the stomach to the nasopharynx. Reflux of bacteria into the esophagus may also occur when the patient is supine. If a large inoculum of bacteria is aspirated from the nasopharynx, pulmonary host defenses may be overwhelmed and pneumonia may occur.

How can gastric colonization be reduced in the mechanically ventilated patient? Although previous data suggest that antacids and H_2 blockers were risk factors for nosocomial pneumonia or tracheal colonization in the intensive care unit patient receiving mechanical ventilation [4,10-13] most physicians are reluctant to withhold stress ulcer prophylaxis with antacids or H_2 blockers. The introduction of sucralfate, however, provided an opportunity to examine the importance of the gastric acid barrier in the pathogenesis of nosocomial pneumonia. Sucralfate, compared with antacids and H, blockers, appears to prevent stress bleeding and acts by a "cytoprotective effect" that does not significantly alter gastric pH.[20,21] Two recently published studies suggest that mechanically ventilated intensive care unit patients randomized to sucralfate have lower rates of pneumonia compared with patients given conventional stress ulcer prophylaxis with antacids and/or H, blockers.[15,16] In the study by Driks et al,[15] 7 (12%) of 61 patients in the sucralfate group developed pneumonia compared with 16 (23%) of 69 patients in the antacid and/or H, blocke group. In addition, colonization with gram-negative bacilli was also approximately lO,OOO-fold higher in the stomach, pharynx, and trachea of patients randomized to antacids and/or H, blockers compared with patients treated with sucralfate. In a similar study by Tryba, pneumonia developed in 3 (10%) of 29 patients in the sucralfate group compared with 11 (34%) of the 32 patients in the antacid/H* blocker group.[16]

The lower rates of pneumonia observed in patients treated with sucralfate compared with patients treated with H, blockers and/or antacids have been attributed to alterations in the natural gastric acid barrier, but in vitro data presented by Daschner and co-workers," and similar results by Tryba and Mantey-Stiers** using different methods, suggest that sucralfate may also have an intrinsic antibacterial effect against gram-negative bacilli that is greater than that observed with antacids.

Recently, Pennington[23] stated, ". . . it must be emphasized that nosocomial pneumonia is a discouraging problem. Despite our rather extensive understanding of the pathogenesis of this infectious disease, there is little evidence that significant progress is being made either in preventing or better treating nosocomial pneumonias." Understanding the role of gastric colonization in the pathogenesis of nosocomial pneumonia, coupled with the possibility of now maintaining the natural gastric acid barrier, raises new questions and opens new avenues for investigation and intervention. More information is needed on other effects of gastric colonization, the frequency of reflux, and the risk of the nasogastric tube. Can the observations made on the intubated patient in the intensive care unit be extrapolated to others? How should we manage tube feedings that have been associated with nosocomial pneumonia?[24] Should we consider selective decontamination of the pharynx, stomach, or trachea with different antibiotics as suggested[25,26] or should the use of aerosolized antibiotics be reconsidered?[27] We should be grateful for another small victory over the "captain of the men of death," but the battle lines remain, and the war must continue.

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