Review article

# Nosocomial pneumonia

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## Abstract

Nosocomial pneumonia encompasses hospital-acquired pneumonia, healthcare-associated pneumonia and ventilator-associated pneumonia. It is a major infectious problem in the hospitals. Though predominantly caused by endogenous bacteria colonised in the oropharynx and stomach, polymicrobial aetiology is not uncommon. The problem with multidrug resistant strains has been increasing. Hospital environment, equipment and staff are the sources, fomites and carriers of this infection from patient to patient. Diagnosis of nosocomial pneumonia has been simplified by the guidelines. Preventive measures to reduce the incidence of nosocomial pneumonia are simple, effective and economical. They just need to be followed. Empirical antibiotic therapy and de-escalation measures form the back bone of the treatment of nosocomial pneumonia.

**Keywords:** Nosocomial pneumonia, hospital-acquired pneumonia, ventilator-associated pneumonia.

## Definition

Pneumonia contracted by the patient in a hospital is nosocomial pneumonia. It could be a) *Hospital-acquired pneumonia (HAP)*, defined as pneumonia which occurs 48 hours or more after admission to the hospital, which was not incubating at the time of admission b) *Healthcare-associated pneumonia (HCAP)*, defined as pneumonia in a patient who was hospitalised in an acute care hospital for two or more days and within 90 days of the infection; resided in a nursing home or long-term care facility; received recent intravenous antibiotic therapy, chemotherapy, or wound care within the past 30 days of the current infection; or attended a hospital or haemodialysis clinic c) *Ventilator-associated pneumonia (VAP)*, defined as pneumonia that develops after 48 hours of endotracheal intubation and/or mechanical ventilation that was not present before intubation.[1,2]

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Nosocomial pneumonia is the second most common nosocomial infection and is the commonest cause of mortality following a nosocomial infection. The attributable mortality related to nosocomial pneumonia is 33% to 50%.[1] Early-onset HAP and VAP, defined as occurring within the first 4 days of hospitalisation, usually carry a better prognosis, and are more likely to be caused by antibiotic sensitive bacteria (similar to those causing community-acquired pneumonia). Late-onset HAP and VAP (5 days or more) are more likely to be caused by multidrug-resistant (MDR) pathogens, and are associated with increased mortality and morbidity.

## Aetiopathogenesis

The causative organisms for HAP differ significantly from those typically responsible for community-acquired pneumonia. A wide spectrum of bacteria can cause nosocomial pneumonia. It could be polymicrobial as well. Fungal and viral pneumonia are rare and is predominantly seen in immunocompromised patients. Common pathogens include aerobic gram-negative bacilli such as

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*Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae* and *Acinetobacter species*. Infections due to gram-positive cocci, such as *Staphylococcus aureus*, particularly methicillin resistant *Staphylococcus aureus* (MRSA) have been rapidly increasing. Staphylococcal pneumonia is more common in patients with diabetes mellitus, head injury and those hospitalised in intensive care units (ICUs). Early-onset HAP in patients with no prior antibiotic exposure tends to mirror community-acquired pneumonia. The most common pathogens include *Enterobacteraciea*, *Haemophilus influenzae*, *Streptococcus pneumonia*, and methicillin-sensitive *Staphyloccous aureus*. Late-onset HAP with prior antibiotic exposure commonly caused by MDR *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and MRSA presents a greater problem in both the prediction of and empiric treatment.[2,3]

The development of nosocomial pneumonia requires the pathogen to reach the alveoli and host defences to be overwhelmed, either by virulence of the pathogen or by the inoculum size. Aspiration of oropharyngeal pathogens or leakage of bacteria around the endotracheal tube cuff is the primary route of bacterial entry into the trachea. The stomach and sinuses are potential reservoirs for certain bacteria colonising the oropharynx and trachea. Colonisation of the endotracheal tube with bacteria encased in biofilm may result in embolisation into the alveoli during suctioning or bronchoscopy. Haematogenous spread or bacterial translocation from the gastrointestinal tract are rare. Exogenous sources of pathogens include healthcare devices, the environment (air, water, equipment and fomites) and commonly the transfer of microorganisms between the patient and staff or other patients.[1,4]

## Diagnosis of nosocomial pneumonia

Diagnosis encompasses evaluation for presence of nosocomial pneumonia and its causative pathogen. The presence of a new or progressive radiographic infiltrate on chest X-ray plus at least two of the three clinical features (fever greater than 38°C, leukocytosis or leukopaenia and purulent secretions) represents the most accurate combination of criteria to identify nosocomial pneumonia. The next step is to obtain samples of lower respiratory tract secretions for quantitative cultures to find out the causative pathogen. Semi-quantitative cultures cannot be used as reliably as quantitative cultures, to define the presence of pneumonia and the need for antibiotic therapy.[1] Such sample should be obtained before starting/changing the antibiotics. Samples can include an endotracheal aspirate, bronchoalveolar lavage (BAL) sample (bronchoscopy directed or blind) or protected specimen brush (PSB) sample. The diagnostic yield of expectorated sputum in non-intubated patients has not been determined. Tracheal aspirate Gram stain can be used to direct initial empiric antimicrobial therapy. In the absence of any clinical suspicion of HAP, respiratory tract cultures should not be obtained. Clinical pulmonary infection score (CPIS) combines clinical, radiographic, physiological ($PaO_2/FiO_2$) and microbiologic data to provide a single numerical result. When the CPIS exceeded six, good correlation with the presence of pneumonia, as defined by quantitative culture results was found.[5,6] CPIS may be useful for selecting patients for short-course therapy and for monitoring response to treatment.

The diagnostic threshold to discriminate infection from colonisation varies with the technique used and possibly by the clinical probability of infection. Widely accepted diagnostic threshold for diagnosing the infection are $10^6$ colony forming units (cfu)/mL for tracheobronchial aspirate, $10^4$ cfu/mL for BAL sample and $10^3$ cfu/mL for PSB. The choice of method depends on local expertise, experience, availability and cost. Antibiotics can be safely stopped in patients with negative quantitative cultures with no adverse impact on mortality.[1,2,7]

The next step would be to start the treatment with empirical antibiotics. Delay in the initiation of appropriate antibiotic therapy can increase the mortality of VAP and thus therapy should not be postponed for the purpose of performing diagnostic studies in patients who are clinically unstable.[1,7]

## Prevention of nosocomial pneumonia

Several measures in the hospital/ ICU can prevent or reduce the incidence of nosocomial pneumonia.

The respiratory therapist has a major role to play in several of these. Enumerated below are the do's and don'ts to prevent nosocomial pneumonia.[1,2]

## Equipment

1. Avoid intubation and mechanical ventilation when possible. When possible use noninvasive ventilation. Avoid reintubation if possible as it carries a higher chance of VAP.
2. Use oral endotracheal and oral nasogastric tubes rather than nasotracheal and nasogastric tubes to prevent nosocomial sinusitis and VAP.
3. Use endotracheal tubes with provision for continuous subglottic suctioning. This can reduce the risk of early onset VAP by preventing the microaspiration along the tracheal tube cuff.
4. Maintain endotracheal tube cuff pressure at greater than 20 cm $H_2O$ (but < 30 cm $H_2O$ to prevent tracheal mucosal injury) to prevent leakage of bacterial pathogens around the cuff into the lower respiratory tract.
5. Reduce the duration of intubation and mechanical ventilation by protocol driven weaning.
6. There is an absence of evidence about the best sterilisation/disinfection/maintenance procedures for mechanical ventilators. Single-use medical devices should not be reused. Appropriate filters should be used to protect mechanical ventilator circuits from bacterial contamination.
7. Ventilator circuits need not be changed routinely for infection control purposes.[18] New ventilator circuit tubing should be provided for each patient. The maximum duration of time that circuits can be used safely is unknown.
8. Passive humidifiers or heat–moisture exchangers (HME) decrease ventilator circuit colonisation but have not consistently reduced the incidence of VAP. Provided there are no contraindications to their use, HMEs rather than the heated humidifiers may be used. The benefit of use of HMEs *versus* heated humidifiers should be established for each patient and this decision should not be based solely on infection control considerations. Heated humidifiers and HMEs should not be changed routinely and manufacturer's recommendations should be followed.[19]
9. Contaminated condensate should be carefully emptied from ventilator circuits and condensate should be prevented from entering either the endotracheal tube or inline medication nebulisers.
10. Nebulisers should be for single patient use and need to be disinfected and cleaned with sterile water between each use.
11. No recommendation can be made on the use of closed suctioning to reduce the risk of HAP to patients. Closed or open suctioning systems can be used without affecting the risk of VAP. Daily change of suction equipment is not required. Suction equipment may be changed weekly unless it becomes contaminated or damaged.
12. Multiuse self-inflating ventilation bags should be decontaminated according to the manufacturer's guidelines between each patient use.

## General care and procedures in the hospital

1. Enteral route is the preferred route for nutrition. However, enteral feeding can increase the risk of regurgitation and aspiration and hence the incidence of nosocomial pneumonia. Early enteral feeding (from day 1 of intubation) was found to be associated with higher incidence of VAP when compared with late enteral feeding (starting from day five of intubation).[8,9] There is no clear evidence that intermittent feeding (as against continuous feeds), small intestine feeding, the use of metoclopramide or acidification of feeding prevents VAP. Feeds should be delivered with the patient in semirecumbent position (head end elevated by 45°). Enteral feeding should be started at a slow rate and advanced to the target rate over a period of 48 to 72 hours. Volume of residual gastric content and the condition of the patient's abdomen need to be monitored carefully each day. Large-bore nasogastric tubes may increase the risk of aspiration of gastric contents by interfering with normal lower oesophageal sphincter function. There are insufficient data

that support converting a nasogastric tube to a percutaneous endoscopic gastrostomy tube to reduce the risk of aspiration.[10,11]

2. Sedation hold done at least once daily prevents excessive sedation in ventilated patients. This reduces the risk for aspiration. Weaning readiness can be assessed better during periods of sedation hold and helps in faster weaning and extubation. Limiting the use of sedative and paralytic agents is beneficial.
3. Head end elevation or semirecumbent positioning of the patient by 30-45° reduces the likelihood of aspiration and VAP. Patients *should be* kept in a semirecumbent position during enteral feeding. Although this intervention is highly recommended, there is evidence that it is underused in many settings. [10-13]
4. Ulcer prophylaxis to prevent stress ulcers can increase the incidence of nosocomial pneumonia. Both $H_2$ receptor antagonists and antacids are risk factors for HAP in ICU. Sucralfate has a trend toward lower rates of VAP when compared with ranitidine but a higher incidence of gastrointestinal bleeding.[14]
5. Glycaemic control is recommended to reduce nosocomial blood stream infections, duration of mechanical ventilation, ICU stay, morbidity and mortality.
6. Breathing exercises including coughing and early mobilisation during the postoperative recovery period should be encouraged to reduce the risk of pulmonary complications. Incentive spirometry has no role to play in prevention of HAP in the low-risk surgical patient including patients who had no pre-existing pulmonary complications. It should be used in high-risk patients to prevent respiratory complications. No recommendation for use of kinetic therapy (with kinetic bed) to prevent HAP can be made from the evidence available.
7. Oral hygiene of the patients is very important. Poor oral hygiene contributes significantly to the incidence of VAP in intubated patients. Nurses must understand their important role in improving oral hygiene and its effect on rates of pneumonia. Dental plaque may act as a reservoir for pathogenic organisms implicated in pneumonia. Oral care with tooth brushing and use of chlorhexidine mouth rinse reduces the incidence of VAP.
8. Selective Decontamination of Digestive tract (SDD) for routine prophylaxis against HAP using oral antibiotics with or without systemic antibiotics reduces the incidence of VAP but is not recommended for routine use by American Thoracic Society.[1] The British guidelines by BSAC however recommend that where it is anticipated that mechanical ventilation will be required for > 48 h, SDD should be considered for ICU patients in order to prevent the development of VAP. The use of SDD should not be withheld because of concerns about the development of antibiotic resistance.[2]
9. Early tracheostomy (within seven days of mechanical ventilation) has not been shown to favourably impact the incidence of VAP.[15-17]
10. Limited and targeted surveillance of organisms causing nosocomial pneumonia should be carried out. This will help in providing feedback, to assist clinicians in empirical antibiotic selection and on the incidence and susceptibility of organisms causing VAP.

## Personnel

1. Ensure effective infection control measures. Staff hand hygiene should form part of routine care with hands being decontaminated immediately before and after every episode of direct patient contact and after any activity or contact that potentially results in hands becoming contaminated. Hand decontamination after glove removal should be performed.
2. Appropriate personal protective equipment must be used. Use of influenza immunisation in health care workers should be encouraged.
3. Hospital education programmes as part of an overall infection control strategy should form part of the risk reduction measures for nosocomial pneumonia. Adherence to the guidelines is as important as their knowledge. Compliance with the recommendations and guidelines has to be monitored.

## Treatment of nosocomial pneumonia

The most important factor influencing the mortality of nosocomial pneumonia is prompt and adequate empiric treatment. Delays in appropriate antibiotic therapy are associated with increased mortality. Empiric antibiotic therapy should be started based on the general recommendations, knowledge of the predominant pathogens in any specific clinical situation and the local patterns of antibiotic susceptibility. Initial empiric antibiotic therapy for early onset (< five days of admission) HAP or VAP in patients with no known risk factors for MDR pathogens (prolonged duration of hospitalisation *i.e.* five days or more, admission from a healthcare-related facility and recent prolonged antibiotic therapy) is with ceftriaxone or levofloxacin or ampicillin/sulbactam or ertapenem. The causative organisms for such early onset pneumonia closely resemble that of community-acquired pneumonia and include *Streptococcus pneumonia*, *Haemophilus influenza*, *Staphylococcus aureus* (methicillin sensitive) and antibiotic sensitive gram negative bacilli. The initial empiric therapy for nosocomial pneumonia in patients with late-onset disease or risk factors for MDR pathogens (*Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Acinetobacter species*, MRSA) is with antipseudomonal cephalosporin (cefepime, ceftazidime) *or* antipseudomonal carbepenem (reliable choice if *Acinetobacter* or *Klebsiella* is suspected; imipenem or meropenem) *or* beta lactam/ beta lactamase inhibitor (piperacillin–tazobactam) *plus* antipseudomonal fluoroquinolone (ciprofloxacin or levofloxacin) *or* aminoglycoside (amikacin, gentamicin, or tobramycin) *plus* linezolid or vancomycin (preferred if MRSA suspected). Initial therapy should be administered to all patients intravenously, with a switch to oral/enteral therapy in patients with a good clinical response and a functioning intestinal tract. If patients initially receive an appropriate antibiotic regimen, efforts should be made to shorten the duration of therapy from the traditional 14 to 21 days to periods as short as seven days, provided the aetiologic pathogen is not *Pseudomonas aeruginosa*, and that the patient has a good clinical response with resolution of clinical features of infection.[1,2,4,7,20-23]

Monotherapy should be used when possible because combination therapy is often expensive and exposes patients to unnecessary antibiotics, thereby increasing the risk of MDR pathogens and adverse outcomes. Patients who develop nosocomial pneumonia with no risk factors for MDR organisms are likely to respond to monotherapy. Combination therapy should be used if patients are likely to be infected with MDR pathogens. [1,2]

Local instillation or aerosolisation of antibiotics for treatment of nosocomial pneumonia has been tried with aminoglycosides (tobramycin) and polymyxin B. They may be useful to treat microorganisms that are resistant to systemic therapy. Bronchospasm is a common side effect observed with aerosolised antibiotics. Further investigation into the use of aerosolised antibiotics is warranted.

Serial assessment of clinical parameters should be used to assess the response to initial empiric therapy. Chest radiographs are of limited value for defining clinical improvement in severe pneumonia. Radiographic improvement often lags behind clinical parameters. However, the finding of a rapidly deteriorating radiographic pattern, with a follow-up chest radiograph showing progression to multilobar involvement, a greater than 50% increase in the size of the infiltrate within 48 hours, development of cavitary disease or significant pleural effusion should raise concern.[1] Appropriate respiratory tract cultures can be used to define microbiologic resolution. Clinical parameters including white blood cell count and measures of oxygenation and core temperature have been used to assess resolution. Clinical improvement usually takes 48–72 hours and thus therapy should not be changed during this time unless there is rapid clinical deterioration. Nonresponse to therapy is usually evident by third day. The responding patient should have de-escalation of antibiotics, narrowing therapy to the most focused regimen possible on the basis of culture data. De-escalation is an important component of antibiotic therapy which avoids the excessive use of antibiotics and emergence of resistance.[1,2,24] The nonresponding patient should be evaluated for noninfectious mimics of pneumonia,

unsuspected or drug-resistant organisms, other sites of infection, and complications of pneumonia and its therapy. Diagnostic testing should be directed to these likely causes.

Antibiotic cycling or rotation has been advocated as a potential strategy for reducing the emergence of antimicrobial resistance. A class of antibiotics or a specific antibiotic is withdrawn from use for a defined time period and reintroduced at a later point in time in an attempt to limit bacterial resistance to the cycled antimicrobial agents.

## Progress beyond the guidelines

A ventilator bundle was established in 2006 to reduce the incidence of VAP and other adverse events.[25] VAP-bundles are collections of educational materials, guidelines and tools such as checklists that help clinicians deliver best-practice to every patient every time. The role of VAP-prevention bundles is also important to ensure that all patients receive therapy known to be effective. Key components of these bundles include directives for semirecumbent positioning, suction of subglottic secretions, provider hand hygiene and care of ventilator circuits.[26]

When the high volume low pressure (HVLP) cuff of the conventional tracheal tube is inflated in the trachea, excess cuff material folds over itself forming channels. Subglottic secretions collected above the cuff can move along these channels and result in aspiration and VAP. HVLP cuffs of ultrathin polyurethane membrane (thickness of 7 μm, compared with > 50 μm of the conventional polyvinylchloride membrane cuff) have been designed to prevent the formation of folds in the cuff and thus prevent fluid and air leakage. The cuff also has a tapered shape which fits the trachea perfectly. Use of such special endotracheal tube may reduce the incidence of VAP. Another endotracheal tube (Lotrach; Venner Capital, Singapore) with a combination of subglottic secretions drainage, low-volume low-pressure cuff and a device to maintain cuff inflation pressure constant has been proposed for reducing the incidence of VAP. Use of this tube needs further evaluation.[27]

An automatic cuff pressure regulation device which continuously displays the levels of cuff pressure in real time has been described. Cuff pressure less than 20 cm $H_2O$ was less frequently observed when the automatic device was used though the incidence of VAP was similar to the control group.[27]

A device with a balloon (Mucus Shaver; National Institutes of Health, Bethesda, MD) has been designed to remove the biofilm that forms on the inner side of the tracheal tube. The device is introduced through the tube until its tip reaches just beyond the end of the tube. Then the balloon is inflated sufficiently to force the two shaving rings firmly against the wall of the tube. Thereafter, the device is gently retrieved to remove the remaining accumulated mucus from the lumen of the tube. No data regarding VAP prevention with this device are currently available.[27]

## Conclusion

Nosocomial pneumonia is a 'difficult infection'. Consolidated efforts should be made to implement measures to prevent nosocomial pneumonia. Respiratory therapist plays a pivotal role in this. Early diagnosis with a clinical and microbiological strategy and early empirical antibiotic therapy can significantly reduce the morbidity and mortality. De-escalation of the antibiotic therapy should be emphasised to prevent emergence of resistant strains. New research should focus on tackling the problem with MDR organisms.

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