DRAFT

Guideline For Prevention Of Healthcare-Associated Pneumonia, 2002

Centers for Disease Control and Prevention
Healthcare Infection Control Practices Advisory Committee

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Healthcare Infection Control Practices Advisory Committee

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EXECUTIVE SUMMARY

The “Guideline for Prevention of Healthcare-associated Pneumonia, 2003" will update, expand, and replace the previously published Centers for Disease Control and Prevention (CDC) "Guideline for Prevention of Nosocomial Pneumonia, 1994.” (1-4) The new guideline is designed to reduce the incidence of pneumonia and other severe, acute lower respiratory tract infections not only in acute-care hospitals, as was the case with the previous edition of the guideline, but also in other healthcare settings, such as ambulatory and long-term care institutions, and other facilities where healthcare is provided. The document is intended for use by infection-control and other healthcare practitioners who are responsible for surveillance, prevention, and control of infections in the healthcare setting.

Developed by the CDC’s Healthcare Infection Control Practices Advisory Committee (HICPAC), the revised guideline updates recommendations for prevention and control of healthcare-associated bacterial pneumonia, especially ventilator-associated pneumonia (VAP); Legionnaires’ disease; invasive pulmonary aspergillosis; respiratory syncytial virus (RSV) infection; and influenza. Among the changes in the recommendations to prevent bacterial pneumonia, especially VAP, are the preferential use of oro-tracheal rather than naso-tracheal tubes in patients who receive mechanically assisted ventilation; the use of an endotracheal tube with a dorsal lumen that allows continuous suctioning of respiratory secretions in the intubated patient’s supraglottic area; the interchangeable use of sucralfate, a histamine-2 (H-2) receptor antagonist, and/or antacid for stress-bleeding prophylaxis in critically ill patients; the use of a heat-moisture exchanger when not otherwise contraindicated in patients receiving mechanically assisted ventilation; and the recommendation to not routinely change breathing circuits of ventilators with humidifiers according to duration of use by patients, and instead, to change the circuits when they malfunction or are visibly contaminated. For prevention of healthcare-associated Legionnaires’ disease, the changes include the recommendations to maintain potable hot water at temperatures not suitable for amplification of *Legionella* spp.; to perform periodic culturing of water samples from the potable water system of a facility’s organ-transplant unit when it is done as part of the facility’s comprehensive program to prevent and control healthcare-associated Legionnaires’ disease; and to initiate an investigation for the source of *Legionella* spp. when one definite or one possible case of laboratory-confirmed healthcare-associated Legionnaires’ disease is identified in an inpatient hematopoietic stem-cell transplant (HSCT) recipient or in two or more HSCT recipients who had visited an outpatient HSCT unit during all or part of the 2-10 day period before illness onset. In the section on aspergillosis, the revised recommendations include the use of a room with high-efficiency particulate air filters rather than laminar airflow, as the protective environment for allogeneic HSCT recipients; use of high-efficiency masks, e.g., N95 respirators, by immunocompromised patients when they leave their rooms for diagnostic testing or other procedures during periods of construction, demolition, renovation, or other dust-generating activity in the facility; and the use of copper 8 quinolinolate for decontamination of structural materials that are implicated in the transmission of aspergillosis. In the RSV section, the new recommendation is to determine, on a case-by-case basis, whether to administer RSV immunoglobulin or monoclonal antibody to infants born prematurely at $\leq$32 weeks of gestational age and infants <2 years who have bronchopulmonary dysplasia, to prevent severe lower respiratory tract RSV infection in these patients. And, in the section on influenza, the new recommendations include the addition of oseltamivir (to amantadine and rimantadine) as a possible prophylactic antiviral agent to be given to all patients without influenza illness in a unit where an institutional outbreak of influenza is recognized; and the addition of oseltamivir and zanamivir (to amantadine and rimantadine) as antiviral agents that can be administered to patients who are acutely ill with influenza in a unit where an influenza outbreak is recognized.

In addition to the revised recommendations, the guideline contains new sections on pertussis and lower respiratory tract infections due to adenovirus and human parainfluenza viruses. Lower respiratory tract infection due to *Mycobacterium tuberculosis* is not addressed in this document, however; it is covered in a separate publication. (5)

This guideline update is the result of a review by CDC staff members of relevant English-language manuscripts that have been published since January 1995 and identified following reference searches using MEDLINE and CURRENT CONTENTS, or obtained from bibliographies of published articles. A working draft of the document was prepared by CDC staff members; reviewed by experts in infection control, intensive-care medicine, pulmonology, respiratory therapy, anesthesiology, internal medicine, and pediatrics; and approved by HICPAC. All recommendations in the guideline,

however, may not reflect the opinions of all reviewers.

INTRODUCTION

Healthcare-associated pneumonia has a major impact on public health because of its associated substantial morbidity and mortality. Because of this, a number of guidelines for its prevention and control have been published. The first CDC Guideline for Prevention of Nosocomial Pneumonia was published in 1981 and addressed the main infection control problems related to hospital-associated pneumonia at the time: the use of large-volume nebulizers that were attached to mechanical ventilators and improper reprocessing, i.e., cleaning and disinfection or sterilization, of respiratory-care equipment. The document also covered the prevention and control of hospital-acquired influenza and RSV infection.

In 1994, the then Hospital Infection Control Practices Advisory Committee (HICPAC) revised and expanded the CDC Guideline for Prevention of Nosocomial Pneumonia to include Legionnaires' disease and pulmonary aspergillosis. HICPAC was established by the Secretary of Health in 1992 to advise the Secretary and the directors of CDC and the National Center for Infectious Diseases, CDC, regarding the prevention and control of hospital-associated infections. The 1994 guideline addressed timely issues regarding the prevention of ventilator-associated pneumonia, e.g., the role of stress-ulcer prophylaxis in the causation of pneumonia and the contentious roles of selective gastrointestinal decontamination and periodic changes of ventilator tubings in the prevention of the infection. The document also presented major changes in the recommendations to prevent and control hospital-associated pneumonia due to *Legionnella* spp. and aspergilli.

In recent years, there has been an increasing demand for guidance on prevention and control of pneumonia and other lower respiratory tract infections in healthcare settings other than the acute-care hospital, probably resulting in part from the progressive shift in the burden and focus of health care in the USA away from inpatient care in the acute-care hospital and towards outpatient and long-term care in various other healthcare settings. In response to this demand, HICPAC, renamed Healthcare Infection Control Practices Advisory Committee in 1998, has revised the guideline to cover these other settings. One major drawback of this endeavor, however, is that organized and well-analyzed infection control data still pertain mainly to the acute-care hospital setting; in comparison, only limited data are available from long-term care, ambulatory, and psychiatric facilities and other healthcare settings, although such data are increasing.

The revised guideline consists of two parts. Part I provides the background for the recommendations that appear in Part II, and includes a discussion of the epidemiology, diagnosis, pathogenesis, modes of transmission, and prevention and control of the following infections: bacterial pneumonia, Legionnaires' disease, pertussis, invasive pulmonary aspergillosis, lower respiratory tract infections caused by RSV, parainfluenza and adenoviruses, and influenza. Part I can be an important resource for educating healthcare personnel. Because education of healthcare personnel is the cornerstone of an effective infection control program, healthcare agencies should give high priority to continuing infection control educational programs for their staff members.

Part II of each section contains the consensus recommendations of HICPAC and addresses such issues as education of healthcare personnel regarding the prevention and control of healthcare-associated pneumonia and other lower respiratory tract infections, surveillance and/or reporting of diagnosed cases of infections, measures to prevent person-to-person transmission of each disease, and reducing host risk to infection.

In this document, as in previously published HICPAC guidelines, each recommendation is categorized on the basis of existing scientific evidence; theoretical rationale; applicability; and economic impact. In addition, however, a new category was created to accommodate recommendations that are made on the basis, wholly or in part, of existing national, state, or local health regulations. The following categorization scheme is applied in this guideline:

CATEGORY IA
Strongly recommended for implementation and strongly supported by well-designed experimental, clinical, or epidemiologic studies.

CATEGORY IB

Strongly recommended for implementation and supported by some clinical or epidemiologic studies and by strong theoretical rationale.

CATEGORY IC
Required for implementation, as mandated by federal and/or state regulation or standard.

CATEGORY II
Suggested for implementation and supported by suggestive clinical or epidemiologic studies or by strong theoretical rationale.

NO RECOMMENDATION; UNRESOLVED ISSUE
Practices for which insufficient evidence or no consensus regarding efficacy exists.

PART I.
ISSUES ON PREVENTION OF HEALTHCARE-ASSOCIATED PNEUMONIA, 2003

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BACTERIAL PNEUMONIA

I. Epidemiology

The epidemiology of healthcare-associated pneumonia varies considerably according to the type of healthcare setting.

A. Hospital-Associated (Nosocomial) Pneumonia

Pneumonia has accounted for approximately 15% of all hospital-associated infections and 27% and 24% of all infections acquired in the medical intensive-care unit (ICU) and coronary care unit, respectively. (6-8) It has been the second most common hospital-associated infection after that of the urinary tract. (6;9) The primary risk factor for the development of hospital-associated bacterial pneumonia is mechanical ventilation (with its requisite endotracheal intubation). (10) CDC's National Nosocomial Infection Surveillance System (NNIS) reported that in 1986-1990 the median rate of ventilator-associated pneumonia (VAP) per thousand ventilator-days in NNIS hospitals ranged from 4.7 in pediatric ICUs to 34.4 in burn ICUs, whereas the median rate of nonventilator-associated pneumonia per 1000 ICU days ranged from 0 in pediatric and respiratory ICUs to 3.2 in trauma ICUs. (10) In other reports, patients receiving continuous mechanical ventilation had 6-21 times the risk of developing hospital-associated pneumonia compared with patients who were not receiving mechanical ventilation. (11-13) Because of this tremendous risk, in the last two decades, most of the research on hospital-associated pneumonia has been focused on VAP. Other major risk factors for pneumonia have been identified in various studies; most of these conditions usually coexist with mechanical ventilation in the same critically ill patients. These include a primary admitting diagnosis of burns, trauma, or disease of the central nervous system; thoraco-abdominal surgery; depressed level of consciousness; prior episode of a large-volume aspiration; underlying chronic lung disease; >70 years of age; 24-hour ventilator-circuit changes; fall-winter season; stress-bleeding prophylaxis with cimetidine with or without antacid; administration of antimicrobial agents; presence of a nasogastric tube; severe trauma; and recent bronchoscopy. (10;12;14-26)

The fatality rates for hospital-associated pneumonia in general, and VAP in particular, are high. For hospital-associated pneumonia, attributable mortality rates of 20%-33% have been reported; in one study, VAP accounted for 60% of all deaths due to hospital-associated infections. (11;14;24;27-29) In studies in which invasive techniques were used to diagnose VAP, the crude mortality rates ranged from 4% in patients with VAP but without antecedent antimicrobial therapy (30) to 73% in patients with VAP caused by *Pseudomonas* or *Acinetobacter* spp., (31) and attributable mortality rates ranged from 5.8% to 13.5%. (32;33) These wide ranges in crude and attributable mortality rates strongly suggest that a patient's risk of dying from VAP is affected by multiple other factors, such as the patient's underlying disease(s) and organ failure, antecedent receipt of antimicrobial agent(s), and the infecting organism(s). (17;24;30-34)

Analyses of pneumonia-associated morbidity have shown that hospital-associated pneumonia can prolong ICU stay by an average of 4.3 days and hospitalization by 4-9 days. (20;27;29;30;32;35) A conservative estimate of the direct cost of excess hospital stay due to pneumonia in 1993 was $1.2 billion a year for the nation. (36)

B. Nursing Home-Associated Pneumonia

In long-term care facilities such as nursing homes, pneumonia is the third most common infection (after those of the urinary tract and skin) acquired by patients (37) and accounts for 13-48% of all nursing home-associated infections. (38;39) Its seasonal variation mirrors that of influenza, suggesting that influenza plays a major role in the occurrence of pneumonia in the elderly.(40)

II. Diagnosis

Healthcare-associated pneumonia, especially VAP, is difficult to diagnose. Traditional criteria for diagnosis have been fever, cough, and development of purulent sputum, in combination with radiologic evidence of a new or progressive pulmonary infiltrate, leukocytosis, a suggestive Gram's stain, and growth of bacteria in cultures of sputum, tracheal aspirate, pleural fluid, or blood. (41-44) Although clinical criteria together with cultures of sputum or tracheal specimens may be sensitive for bacterial pathogens, they are highly nonspecific, especially in patients with VAP; (43;45-48) conversely, culture of blood has a very low sensitivity. (49)

Because of these problems, in 1992, a group of investigators recommended standardized methods for diagnosing pneumonia in clinical research studies of VAP. (50-52) These methods involved bronchoscopic techniques, e.g., quantitative culture of protected specimen brush (PSB) specimen, (53-62) bronchoalveolar lavage (BAL), (54;63-69) and protected BAL (pBAL). (70;71) The reported sensitivities and specificities of these methods have ranged between 70% to 100% and 60% to 100%, respectively, depending on the tests or diagnostic criteria they were compared with. (54;72;73) Because these techniques are invasive, they can cause complications such as hypoxemia, bleeding, or arrhythmia. (48;55;67;74-76) Nonbronchoscopic (NB) or blinded procedures, e.g., NB-pBAL (58;63;77) and NB-PSB, (62;78-80) which utilize blind catheterization of the distal airways, and quantitative culture of endotracheal aspirate (81;82) were developed later.

One randomized, uncontrolled multicenter study in France has shown that in comparison with non-invasive (qualitative cultures of endotracheal aspirate) tests, invasive bronchoscopic technique (PSB or pBAL) for the microbiologic diagnosis of pneumonia was associated with fewer deaths by the 14th day after pneumonia onset, earlier improvement from organ dysfunction, and less antibiotic use. (47) Earlier studies have shown that the use of invasive diagnostic techniques resulted in improved physicians' confidence in their diagnosis and therapeutic management of VAP; (83) however, others have raised questions about the effectiveness of using invasive diagnostic techniques in improving targeted outcomes, i.e., rates of VAP, length of ICU stay, and attributable mortality, (84) and their applicability in daily clinical practice. (85;86)

In an evidence-based assessment of invasive diagnostic tests for VAP, the Clinical Practice Guideline Panel of the American College of Chest Physicians concluded that 1) there is no definitive scientific evidence or expert consensus that quantitative testing produces better clinical outcomes than does empirical treatment; 2) the performance of invasive tests can help in avoiding the administration of antimicrobial agents for clinically insignificant microorganisms, but that no single test has been shown to be clearly superior to another, and 3) when electing to perform an invasive test, the physician should take into consideration the test's sensitivity and specificity, ability to improve patient outcome, potential adverse effects, test availability, and cost. (87)

III. Etiologic Agents

A. Hospital-Associated Pneumonia

The reported distribution of etiologic agents causing hospital-associated pneumonia varies among institutions and settings primarily because of differences in patient populations, diagnostic methods employed, and definitions used. (30;41;53-56;88-92) In general, however, bacteria have been the most frequently isolated pathogens. In most studies, very few anaerobic bacteria and viruses were reported, partly because anaerobic and viral cultures were not performed routinely in the reporting facilities. Similarly, cultures of bronchoscopic specimens from patients with VAP have rarely yielded anaerobes. (26;53;54;56;57;70;93) The bacterial pathogens that have been most frequently associated with nosocomial pneumonia in reports from tertiary-care university hospitals and/or studies of critically ill and/or mechanically ventilated patients in intensive-care units are gram-negative bacilli

(e.g., *Pseudomonas aeruginosa, Proteus* spp., and *Acinetobacter* spp.) and *Staphylococcus aureus*. (53;92) In contrast, the main bacterial pathogens reported to have caused nosocomial pneumonia in one community teaching hospital were *Streptococcus pneumoniae* and *Haemophilus influenzae*. (90) The variation is probably due to differences in patient populations and their underlying illnesses, and in the resident microbial flora of tertiary-care hospitals and community teaching hospitals.

The causative microbial agents of nosocomial pneumonia, including VAP, also vary depending on the length of time the patient has spent in the ICU and/or received mechanically assisted ventilation. This has allowed the classification of nosocomial pneumonia or VAP into either early-onset pneumonia (EOP), if pneumonia develops within 96 hours of the patient's admission to an ICU or intubation for mechanical ventilation, and late-onset pneumonia (LOP), if pneumonia develops after 96 hours of the patient's admission to an ICU or intubation for mechanical ventilation. This categorization can be helpful to clinicians in initiating empiric antimicrobial therapy for cases of nosocomial pneumonia, when the results of microbiologic diagnostic testing are not yet available. EOP has been associated usually with non-multi-antibiotic-resistant organisms such as *Escherichia coli*, *Klebsiella* spp., *Proteus* spp., *S. pneumoniae*, *H. influenzae*, and oxacillin-sensitive *S. aureus*. (94) On the other hand, LOP has been associated with *P. aeruginosa*, oxacillin-resistant *S. aureus*, and *Acinetobacter* spp.--strains that are usually multi-antibiotic-resistant. (94)

B. Nursing Home-Associated Pneumonia

Like cases of community-acquired pneumonia in the elderly, most (up to 79%) cases of nursing home-acquired pneumonia (NHAP) have undetermined etiologies primarily because definitive etiologic diagnosis usually is not rigorously pursued. (95) However, studies documenting the etiologic agents of endemic NHAP have reported the identification of: *S. pneumoniae* in 20%, *S. aureus in 10%,* and *H. influenzae* in 10% of cases; aerobic Gram-negative bacilli, including *K. pneumoniae* and *P. aeruginosa,* in 30% of cases; and normal oropharyngeal flora in 15% of cases. Other than *Chlamydia pneumoniae*, the atypical organisms such as *Mycoplasma pneumoniae* and *Legionella pneumophila* are not significant pathogens in NHAP. (95-97) Viruses such as influenza and RSV have caused outbreaks in nursing homes and have been linked with the occurrence of pneumonia during these outbreaks. (98)

IV. Pathogenesis

Bacteria may invade the lower respiratory tract by micro- or bolus-aspiration of oropharyngeal organisms, inhalation of aerosols containing bacteria, or, less frequently, by hematogenous spread from a distant body site. Bacterial translocation from the gastrointestinal tract had been hypothesized as a mechanism for infection; however, its occurrence in patients with healthcare-associated pneumonia has not been shown. Of the plausible routes, micro-aspiration is believed to be the most important for both healthcare-associated and community-acquired pneumonia. In studies using radioisotope tracers, 45% of healthy adults were found to aspirate during sleep. (41) Persons with abnormal swallowing, such as those who have depressed consciousness, respiratory tract instrumentation and/or mechanically assisted ventilation, gastrointestinal tract instrumentation or diseases, or who have just undergone surgery, especially thoracic and/or abdominal surgery, are particularly likely to aspirate. (13;14;17;26;99)

The high incidence of gram-negative bacillary pneumonia in hospitalized patients appears to be the result of factors that promote colonization of the pharynx by gram-negative bacilli and the subsequent entry of these organisms into the lower respiratory tract. (44;100-104) Although aerobic gram-negative bacilli are recovered infrequently or are found in small numbers in pharyngeal cultures of healthy persons, (100;105) colonization dramatically increases in patients with acidosis, alcoholism, azotemia, coma, diabetes mellitus, hypotension, leukocytosis, leukopenia, pulmonary disease, or endotracheal or nasogastric tubes in place, and in patients given antimicrobial agents. (44;103;104;106)

Oropharyngeal or tracheobronchial colonization by gram-negative bacilli begins with the adherence of the microorganisms to the host's epithelial cells. (102;107-109) Adherence may be affected by multiple factors related to the bacteria (presence of pili, cilia, or capsule, or production of elastase or mucinase), host cell (surface proteins and polysaccharides), and environment (pH and presence of mucin in respiratory secretions). (101;102;107;110-119) Studies indicate that certain substances,

such as fibronectin, can inhibit the adherence of gram-negative bacilli to host cells. (110;112;120) Conversely, certain conditions, such as malnutrition, severe illness, or post-operative state, can increase adherence of gram-negative bacteria. (101;110;114;119;121)

In addition to the oropharynx, the stomach has been postulated to be an important reservoir of organisms that cause healthcare-associated pneumonia,(17;122-126) although the exact role of the stomach in the causation of healthcare-associated pneumonia, specifically VAP, is being critically investigated and debated. (127-130) It appears, however, that the stomach's role may vary depending on the patient's underlying condition(s) and on the prophylactic or therapeutic interventions that the patient receives. (123;131-135) In healthy persons, few bacteria entering the stomach survive in the presence of hydrochloric acid at pH<2. (136;137) However, when gastric pH increases from the normal levels to $\geq$4, microorganisms are able to multiply to high concentrations in the stomach. (134;136;138-140) This can occur in patients with advanced age, (138) achlorhydria, (136) ileus, or upper gastrointestinal disease, and in patients receiving enteral feeding, antacids, or histamine-2 (H-2) antagonists. (123;134;135;140) The contribution of other factors, such as duodeno-gastric reflux and the presence of bile, to gastric colonization in patients with impaired intestinal motility also has been suggested. (133)

Bacteria can also gain entry into the lower respiratory tract of patients through inhalation of aerosols generated primarily by contaminated nebulization devices. In the past, outbreaks of nosocomial pneumonia were related to the use of contaminated large-volume nebulizers, which were humidification devices that produced large amounts of aerosol droplets <4 μm in size, via ultrasound, spinning disk, or the Venturi mechanism. (141-143) Because endotracheal tubes provide direct access to the lower respiratory tract, contaminated aerosol inhalation is particularly hazardous for intubated patients. In contrast to nebulizers that were used as humidification devices for ventilated patients, bubble-through or wick humidifiers primarily increase the water-vapor (or molecular-water) content of inspired gases during mechanical ventilation. Although heated bubble-through humidifiers generate aerosol droplets, they do so in quantities that may not be clinically important; (144;145) wick humidifiers do not generate aerosols.

Rarely, bacterial pneumonia can result from hematogenous spread of infection to the lung from another infection site, e.g., pneumonia resulting from purulent phlebitis or right-sided endocarditis.

V. Risk Factors and Control Measures

Potential risk factors for healthcare-associated bacterial pneumonia have been examined in several large studies. Although specific risk factors may differ slightly between study populations, they can be grouped into the following general categories:1) factors that enhance colonization of the oropharynx and/or stomach by microorganisms, e.g., administration of antimicrobial agents, admission to the ICU, or presence of underlying chronic lung disease; 2) conditions favoring aspiration or reflux, including initial or repeat endotracheal intubation; insertion of nasogastric tube; supine position; coma; surgical procedures involving the head, neck, thorax, or upper abdomen; and immobilization due to trauma or illness; 3) conditions requiring prolonged use of mechanical ventilatory support with potential exposure to contaminated respiratory devices and/or contact with contaminated or colonized hands, mainly of healthcare personnel; and 4) host factors such as extremes of age, malnutrition, and severe underlying conditions, including immunosuppression. (14;16;19;21;24;26;44;146;147)

A. Oropharyngeal, Tracheal, and Gastric Colonization

The association between a patient's predisposition to gram-negative bacillary pneumonia and bacterial colonization of the patient's oropharynx, (42;100) trachea, (134) or stomach (123;140) prompted attempts by researchers to prevent the infection by various means, mainly by local and/or systemic antimicrobial prophylaxis.

Oropharyngeal and tracheal colonization

- Local bacterial interference and aerosolized antimicrobial agents

Early studies centered on utilization of the phenomenon of local bacterial interference (148;149) or

prophylactic aerosolization of antimicrobial agent(s). (150;151) Bacterial interference (with alpha-hemolytic streptococci) was successfully used by some investigators to prevent oropharyngeal colonization by aerobic gram-negative bacilli. (148) However, the efficacy of this method for general use has not been evaluated. Although the use of aerosolized antimicrobial agents resulted in the eradication of common gram-negative bacillary pathogens from the upper respiratory tract and/or a decrease in the incidence of gram-negative-bacillary pneumonia, (150) it had no effect on patient mortality rate (150) and superinfection occurred in some patients receiving the therapy. (150-153) Later, the use of intranasal colistin was shown to have significantly decreased the incidence of gram-negative bacillary and polymicrobial pneumonia in critically ill patients who were compared to historic controls. (154) There was, however, no effect on mortality, and although no increase was detected in the number of cases infected with colistin-resistant microorganisms, the follow-up period was relatively short.

- Oral chlorhexidine rinse

Recently, the antiseptic chlorhexidine gluconate (0.12%) was used successfully as a peri-operative oral rinse to decrease the overall incidence of nosocomial respiratory tract infections in patients who underwent cardiac surgery. (155) However, its use for preventing healthcare-associated pneumonia in other groups of patients at high risk for this infection has not been evaluated.

Oropharyngeal and Gastric Colonization

- Selective Decontamination of the Digestive Tract (SDD)

SDD is the most studied strategy designed to prevent bacterial colonization and lower respiratory tract infection in critically ill and/or mechanically ventilated patients. (156-186) SDD is aimed at preventing oropharyngeal and gastric colonization with aerobic gram-negative bacilli and *Candida* spp., without altering the anaerobic flora. Various SDD regimens use a combination of locally administered nonabsorbable antimicrobial agents, such as polymyxin or colistin, and an aminoglycoside (tobramycin, gentamicin, or, rarely, neomycin) or a quinolone (norfloxacin or ciprofloxacin), coupled with either amphotericin B or nystatin. The local antimicrobial preparation is applied as a paste to the oropharynx and given orally or via the nasogastric tube four times a day. In addition, in many studies, a systemic (intravenous) antimicrobial agent such as cefotaxime or trimethoprim is administered to the patient.

Although most clinical trials, (156-159;161-168;170;171;176-178;181;183-186) including three meta-analyses, (172;179;182) have demonstrated a decrease in the rates of hospital-associated respiratory infections by using SDD, these trials have been difficult to assess because they differ in study design and population, and many have had short follow-up periods. In addition, except for a few reports, (160;163;174;176-178;180) most of these studies utilized nonbronchoscopic methods for the diagnosis of pneumonia.

SDD has not been shown to decrease significantly the duration of mechanical ventilation or ICU stay; however, a decrease in overall antimicrobial use was shown in a few studies (157;167;173;176;181;183;185;186) and, in two meta-analyses, a decrease in mortality was shown in two groups of patients, i.e., critically ill surgical patients and those who received both systemic and local prophylactic antibiotics. (182;184)

SDD is costly; in order to prevent one case of hospital-associated pneumonia or one death due to hospital-associated pneumonia, it was estimated that 6 (range: 5-9) or 23 (range:13-39) patients, respectively, would have to be given SDD. (179)

SDD will probably be found cost-effective for use on subsets of ICU patients, such as trauma and/or critically ill surgical patients. However, there are concerns about the potential for increased bacterial antimicrobial resistance and superinfection with multi-drug resistant pathogens in patients. (30;157;159;160;162;176;187)

- Sucralfate, H-2 blockers, and stress-bleeding prophylaxis

The administration of antacids and H-2 receptor antagonists for prevention of stress bleeding in critically ill, postoperative, and/or mechanically ventilated patients has been associated with gastric bacterial overgrowth (124;139;140;188) and development of pneumonia. (17;124;135;189;190) Sucralfate, a cytoprotective agent that has little effect on gastric pH and may have bactericidal properties of its own, has been suggested as a substitute for antacids and H-2 receptor antagonists. (191-193) The results of clinical trials comparing the risk of pneumonia in patients receiving sucralfate with that in patients given antacids and/or H-2 receptor antagonists have been variable. (124;135;190;191;194-196) Early studies suggested that the use of sucralfate (compared to antacids with or without H-2 receptor antagonists) decreased the risk of pneumonia in ICU patients receiving mechanically assisted ventilation. (124;135;190;191;194) More recent studies, however, including two double-blind studies, failed to demonstrate the advantage of using sucralfate. (197-199) In addition, another study has suggested that patients with acute respiratory distress syndrome who are given sucralfate may even be at a greater risk of developing VAP compared to those who are not. (200)

- Acidified enteral feeding

Because enteral feeding can increase gastric pH (201) and result in gastric and oropharyngeal colonization, an approach advocated to prevent oropharyngeal colonization in patients receiving enteral nutrition is the acidification of enteral feeding. (202) Although the absence of bacteria from the stomach has been confirmed in patients given acidified enteral feeding, the effect on the incidence of pneumonia has not been evaluated. (202)

- Continuous versus intermittent enteral feeding

Continuous enteral feeding of mechanically ventilated patients, a common practice in ICUs, has been associated with increased gastric pH, (134;203) subsequent gastric colonization with gram-negative bacilli, (22;203;204) and a high incidence of pneumonia; (22) whereas intermittent enteral feeding has been associated with lower gastric pH and lower rates of pneumonia. (204) However, a recent study of intermittent enteral feeding in patients who had just had continuous enteral feeding did not corroborate the lowering effect of intermittent enteral feeding on gastric pH or gastric microbial colonization. (205) More studies are needed to determine the utility of intermittent enteral feeding in lowering the rates of pneumonia.

B. Aspiration of Oropharyngeal and Gastric Flora and Nasal-Sinus Secretions

Clinically important aspiration usually occurs in patients who have one or more of the following conditions: a depressed level of consciousness; dysphagia due to neurologic or esophageal disorders; an endotracheal (naso- or oro-tracheal), tracheostomy, or enteral (naso- or oro-gastric) tube in place; and receipt of enteral feeding. (14;206-211)

Placement of an enteral tube may increase nasopharyngeal colonization, cause reflux of gastric contents, or allow bacterial migration via the tube from the stomach to the upper airway. (209;211-214) Gross contamination of the enteral solution during its preparation (215-217) may lead to gastric colonization with gram-negative bacilli.

Prevention of pneumonia in such patients may be difficult; however, placing the patient in a semi-upright position (by elevating the head of the bed at an angle of 30^{o}-45^{o}) has been beneficial, (218;219) probably by preventing aspiration. (214) Gastric contents that were labeled with radioactive material were aspirated via the gastroesophageal route when patients were treated in the supine position. (213;214;219) In two other studies, the supine position (as opposed to the semi-upright position) was a risk factor for pneumonia in patients receiving mechanically assisted ventilation, i.e., significantly higher percentages (23% and 36%) of patients who were supine developed pneumonia compared with 5% and 11% of those who were semi-upright, respectively, either during the first 24 hours of their receipt of mechanically assisted ventilation (220) or during their receipt of both mechanically assisted ventilation and enteral feeding. (218)

On the other hand, other measures that theoretically might be beneficial have yielded equivocal

results, e.g., the use of flexible, small-bore nasogastric tubes, (221) intermittent rather than continuous administration of the enteral feed, (22;204;222) and placement of the enteral tube below the stomach (e.g., in the jejunum). (223-225).

Direct correlations have been reported between naso-tracheal (compared with oro-tracheal) intubation and the occurrence of nosocomial maxillary sinusitis (226;227) and high incidence of pneumonia. (227) These findings suggest that the entry site for endotracheal intubation may affect the incidence of VAP.

C. Mechanically Assisted Ventilation and Endotracheal Intubation

The increased risk for pneumonia in intubated, mechanically ventilated patients is partly due to the carriage of oropharyngeal microorganisms via passage of the endotracheal tube into the trachea during intubation, as well as to depressed host defenses secondary to the patient's severe underlying illness. (14;17;26;228) In addition, bacteria can aggregate on the surface of the tube over time and form a glycocalyx (biofilm) that protects the bacteria from antimicrobial agents or host defenses. (229) Some investigators believe that these bacterial aggregates may become dislodged by ventilation flow, tube manipulation, or suctioning and subsequently embolize into the lower respiratory tract and cause focal pneumonia. (230;231) Removal of the tracheal secretions has been traditionally done by gentle suctioning with the use of aseptic technique. (232;233)

Aspiration of subglottic secretions

In the intubated patient, leakage around the cuff of the endotracheal tube allows bacteria-laden secretions (which pool below the glottis and above the endotracheal-tube cuff) direct access to the lower respiratory tract. (99;234;235) A study showed that the use of an endotracheal tube that has a separate dorsal lumen (which allows continuous suctioning of the pooled secretions) could delay, but not significantly decrease, the occurrence of pneumonia in cardiac-surgery patients. (235) A later study showed that continuous suctioning of subglottic secretions could decrease the incidence of pneumonia in intubated patients: 20 episodes of VAP (confirmed by PSB, BAL, histology, or good clinical response to antimicrobial agents) per 1000 ventilator days occurred in patients who had continuous aspiration of subglottic secretions compared with 40 episodes per 1000 ventilator days in control patients. (232)

Noninvasive positive-pressure ventilation

The increased risk of pneumonia attributable to endotracheal intubation has prompted pulmonologists and intensivists to seek alternative ways of delivering positive-pressure ventilation, i.e., through a face or nose mask, to patients suffering from acute respiratory failure due to various causes. In a recent efficacy study in adult hypoxemic patients, the incidence of pneumonia diagnosed by BAL was shown to be lower (1 [3%] of 32) in those who received positive pressure ventilation through a face mask than in those (8 [25%] of 32) who received the conventional treatment, i.e., intubation and mechanically assisted ventilation (relative risk [RR]: 1.98, 95% confidence interval [CI]: 1.03-3.82). (236) An efficacy study of the use of nasal masks for pneumonia prevention has not been performed. (237)

D. Cross-Colonization Via Hands of Personnel

Pathogens causing healthcare-related pneumonia, such as gram-negative bacilli and *S. aureus*, are ubiquitous in healthcare settings, especially in intensive or critical care areas. (238;239) Transmission of these microorganisms to patients frequently occurs via healthcare personnel's hands that become contaminated or transiently colonized with the microorganisms. (240-245) Procedures such as tracheal suctioning and manipulation of ventilator circuit or endotracheal tubes increase the opportunity for cross-contamination. (245;246) The risk of cross-contamination can be reduced by using aseptic technique and sterile or disinfected equipment when appropriate and eliminating pathogens from the hands of personnel. (12;245;247-249)

In theory, handwashing is an effective way of removing transient bacteria from the hands; (248;249) however, in general, personnel compliance with handwashing has been poor. (250-254) New guidelines for hand hygiene that promote the use of waterless antiseptic preparations may result in

increased personnel compliance and decreased incidence of hand-transmitted infections. (255)

Gloving also helps prevent cross-contamination. (256) Routine gloving (in addition to gowning) was associated with a decrease in the incidence of healthcare-related (RSV) (257) and other ICU infections. (258) However, healthcare-related pathogens can colonize gloves, (259) and outbreaks have been traced to healthcare personnel who did not change gloves after contact with one patient and before providing care to another. (260;261) In addition, gloved hands may get contaminated via leaks in the gloves. (262) Thus, personnel should use gloves properly and decontaminate their hands after gloves are removed. (255;256)

E. Contamination of Devices Used on the Respiratory Tract

Devices used on the respiratory tract for respiratory therapy (e.g., nebulizer), diagnostic examination (e.g., bronchoscope or spirometer), or administration of anesthesia are potential reservoirs or vehicles for infectious microorganisms. (12;263-265) Routes of transmission may be from device-to-patient, (142;144;264-273) from one patient to another, (274;275) or from one body site to the lower respiratory tract of the same patient via hand or device. (275-278) Contaminated reservoirs of aerosol-producing devices, e.g., nebulizers, can allow the growth of hydrophilic bacteria that may be subsequently aerosolized during device use. (141-143;271) Gram-negative bacilli, such as *Pseudomonas* spp. or *Flavobacterium* spp.; *Legionella* spp.; and nontuberculous mycobacteria can multiply to substantial concentrations in nebulizer fluid (270;279-281) and increase the device user's risk of acquiring pneumonia.(142-144;270;271;282-284)

Proper cleaning and sterilization or disinfection of reusable equipment are important components of a program to reduce infections associated with respiratory therapy and anesthesia equipment.(264;266-269;271;285-288) Many devices or parts of devices used on the respiratory tract have been categorized as semicritical in the Spaulding classification system for appropriate sterilization or disinfection of medical devices because they come into direct or indirect contact with mucous membranes but do not ordinarily penetrate body surfaces (See Appendix A), and the associated infection risk following the use of these devices in patients is less than that associated with devices that penetrate normally sterile tissues. (289) Thus, if it is not possible or cost-effective to sterilize these devices by steam autoclave or ethylene oxide, (290) they can be subjected to high-level disinfection by pasteurization at 75^{o}C for 30 minutes (291-294) or by using liquid chemical disinfectants cleared for use on medical instruments by the Food and Drug Administration. (295-297)

Sterile or pasteurized water is preferred over tap or locally prepared distilled water for rinsing off residual liquid chemical sterilant/disinfectant from a respiratory device that has been chemically disinfected, because tap or distilled water may harbor microorganisms that can cause pneumonia. (279;280;298-301) In some hospitals, a tap-water rinse followed by air-drying with or without an alcohol rinse is used. (302) In theory, if complete drying is achieved following a tap-water rinse, the risk of pneumonia associated with the use of the device is probably low. Drying lowers the level of microbial contamination of gastrointestinal endoscopes and washed hands. (303-305) However, many semicritical items used on the respiratory tract (e.g., corrugated tubing, jet or ultrasonic nebulizers, bronchoscopes) are difficult to dry and the degree of dryness of a device is difficult to assess. (294) Data are lacking regarding the safety of routinely using tap water for rinsing reusable semicritical respiratory devices after their disinfection and before they are dried, or between uses of a device on the same patient. (271;287;302;306)

1. Mechanical Ventilators, Breathing Circuits, Humidifiers, Heat-Moisture Exchangers, and In-Line Nebulizers

- a. Mechanical Ventilators

The internal machinery of mechanical ventilators used for respiratory therapy has not been an important source of bacterial contamination of inhaled gas. (307) Thus, routine sterilization or high-level disinfection of the internal machinery is considered unnecessary. Using high-efficiency bacterial filters at various positions in the ventilator breathing circuit had been advocated previously. (308;309) Filters interposed between the machinery and the main breathing circuit can eliminate contaminants from the driving gas and prevent retrograde contamination of the machine by the patient but may also

alter the functional specifications of the breathing device by impeding high gas flows. (308-310) Placement of a filter or condensate trap at the expiratory-phase tubing of the mechanical-ventilator circuit may help prevent cross-contamination of the ventilated patient's immediate environment, (277;311) but the importance of such filters in preventing healthcare-related pneumonia has not been shown.

- b. Breathing circuits, humidifiers, and heat-moisture exchangers

Most U.S. hospitals use ventilators that provide inspired-gas humidification with either bubble-through or wick humidifiers. Because bubble-through humidifiers produce insignificant amounts of aerosol (312) and wick humidifiers produce no aerosol, (145) they do not pose an important risk for pneumonia in patients. In addition, bubble-through humidifiers are usually heated to temperatures that reduce or eliminate bacterial pathogens. (312;313) In general, however, sterile water is still used to fill these humidifiers (314) because tap or distilled water may harbor microorganisms, such as *Legionella* spp., that are more heat-resistant than other bacteria. (283;287;300)

The potential risk for pneumonia in patients using mechanical ventilators with heated bubble-through humidifiers primarily results from the formation of condensate in the inspiratory-phase tubing of unheated ventilator circuits as a result of the difference in the temperatures of the inspiratory-phase gas and ambient air. The condensate and tubing can rapidly become contaminated, usually with bacteria that originate from the patient's oropharynx. (315) In a study by Craven et al., 33% of inspiratory circuits were colonized with bacteria from patients' oropharynx within 2 hours, and 80% within 24 hours, of use. (315) Spillage of the contaminated condensate into the patient's tracheobronchial tree, as can occur during procedures (e.g., suctioning, adjusting the ventilator setting, or feeding or giving hygienic care to the patient) in which the tubing may be moved, may increase the risk of pneumonia in the patient. (315) Thus, in many healthcare facilities, healthcare personnel are trained to prevent such spillage and to drain and discard the fluid periodically. Microorganisms contaminating ventilator-circuit condensate can be transmitted to other patients via hands of the healthcare personnel handling the fluid, especially if the personnel fails to wash hands after handling the condensate.

The role of ventilator-tubing changes in preventing pneumonia in patients using mechanical ventilators with bubble-through humidifiers has been investigated through the years. Initial studies of in-use contamination of mechanical ventilator circuits with humidifiers have shown that neither the rate of bacterial contamination of inspiratory-phase gas nor the incidence of pneumonia was significantly increased when tubing was changed every 24 hours rather than every 8 or 16 hours. (316) Craven et al. later showed that changing the ventilator circuit every 48 hours rather than 24 hours did not result in an increase in contamination of the inspiratory-phase gas or tubing of the ventilator circuits. (317) In addition, the incidence of healthcare-related pneumonia was not significantly higher when circuits were changed every 48 hours rather than every 24 hours. (317) Later reports suggested that the risk for pneumonia may not increase when the interval for circuit change is prolonged beyond 48 hours. Hess et al. showed no increase in the incidence of VAP and a savings of more than $110,000 per year in materials and personnel salaries when breathing circuits were changed every seven days rather than every 48 hours. (318) Dreyfuss and others reported that when the circuits were never changed for the duration of use by a patient, the risk of pneumonia (8 [29%] of 28) was not significantly higher than when the circuits were changed every 48 hours (11 [31%] of 35). (319) More recently, Kollef et al. showed that patients whose breathing circuits were left unchanged indefinitely (unless observed to be grossly contaminated) for the duration of their receipt of mechanical ventilation did not have a higher risk of acquiring pneumonia compared with those whose breathing circuits were changed routinely every 7 days. (320)

These findings indicate that the previous CDC recommendation to change ventilator circuits routinely on the basis of duration of use should be changed to one that is based on visual and/or known contamination of the circuit. This change in recommendation is expected to result in large savings in device use and personnel time for U.S. healthcare facilities. (314;317;320)

Condensate formation in the inspiratory-phase tubing of a ventilator breathing circuit can be decreased by elevating the temperature of the inspiratory-phase gas with a heated wire in the inspiratory-phase tubing. However, in one report, three cases of endotracheal or tracheostomy tube blockage by dried patient secretions were attributed to the decrease in the relative humidity of

inspired gas that results from the elevation of the gas temperature. (321) Therefore, users of heated ventilator tubing should be aware of the advantages and potential complications of using heated tubing.

Condensate accumulation can also be eliminated by using a heat-moisture exchanger (HME). (322-325) An HME recycles heat and moisture exhaled by the patient and eliminates the need for a humidifier. In the absence of a humidifier, no condensate forms in the inspiratory-phase tubing of the ventilator circuit. Thus, bacterial colonization of the tubing is prevented, and the need to routinely change the tubing periodically is obviated. (246) HMEs, however, increase the dead space and resistance to breathing, (326) may leak around the endotracheal tube, and may result in drying of sputum (327) and blockage of the tracheo-bronchial tree. (328;329)

Cook et al reviewed five randomized, controlled studies comparing HMEs and heated humidifiers; the main outcome variable was pneumonia. (330) A significantly lower incidence of pneumonia in the HME patient group was shown in one study; (966) a “tendency” towards lower incidence of pneumonia in the HME group was seen in three other studies, (327;329;331) and no difference in risk was seen in the only study in which PSB was used as a confirmatory method for diagnosing pneumonia. (332) In a later study, Kollef et al. found no difference in the risk of VAP between a group of patients on whom HMEs were used and a comparable group with heated humidifiers.(333)

- c. Small-Volume ("In-Line") Medication Nebulizers

Small-volume medication nebulizers that are inserted in the inspiratory circuit of mechanical ventilators can produce bacterial aerosols. (271) If they become contaminated by condensate in the inspiratory tubing of the breathing circuit, they can increase the patient's risk of pneumonia because the nebulizer aerosol is directed through the endotracheal tube and bypasses many of the normal host defenses against infection. (315)

2. Hand-Held Small-Volume Medication Nebulizers

Hand-held small-volume medication nebulizers can produce bacterial aerosols. They have been associated with healthcare-associated pneumonia, including Legionnaires' disease, as a result of their contamination with medications from multidose vials (334) or with *Legionella*-contaminated tap water used for rinsing and filling the reservoir. (287)

3. Suction Catheters

Tracheal suction catheters can introduce microorganisms into a patient's lower respiratory tract. Currently, two types of suction-catheter systems are used in U.S. hospitals: the open single-use catheter system and the closed multi-use catheter system. The closed-suction system has the advantages of decreased environmental contamination as well as lower costs, especially after it was shown that, notwithstanding the manufacturer-recommended daily catheter changes, the catheter can remain unchanged for an indefinite period without increasing the patient’s risk of healthcare-associated pneumonia. (335;336) However, studies have yielded varied results: earlier studies suggested that the risk for catheter contamination or pneumonia is not different between patients on whom the single-use suction method is used and those on whom the closed multi-use catheter system is used; (330;335;337) but, in one recent study in France, the VAP incidence rate in patients on whom the closed suction system was used was lower than that in those on whom the open system was used. (338)

4. Resuscitation Bags, Oxygen Analyzers, and Ventilator Spirometers

Reusable resuscitation bags are particularly difficult to clean and dry between uses; microorganisms in secretions or fluid left in the bag may be aerosolized and/or sprayed into the lower respiratory tract of the patient on whom the bag is used; in addition, contaminating microorganisms may be transmitted from one patient to another via hands of staff members. (339-341) Oxygen analyzers and ventilator spirometers have been associated with outbreaks of gram-negative respiratory tract colonization and pneumonia resulting from patient-to-patient transmission of organisms via hands of personnel. (274;276) Devices such as these require sterilization or high-level disinfection between

uses on different patients. Education of physicians, respiratory therapists, and nursing staff regarding the associated risks and appropriate care of these devices is essential.

5. Anesthesia Equipment

The contributory role of anesthesia equipment in outbreaks of healthcare-related pneumonia was reported before hospitals implemented routine after-use cleaning and disinfection/sterilization of reusable anesthesia-equipment components that may become contaminated with pathogens during use. (342;343)

➢ a. Anesthesia machine

The internal components of anesthesia machines, which include the gas sources and outlets, gas valves, pressure regulators, flowmeters, and vaporizers, are not considered an important source of bacterial contamination of inhaled gases. (344) Thus, routine sterilization or high-level disinfection of the internal machinery is considered unnecessary.

➢ b. Breathing system or patient circuit

The breathing system or patient circuit, through which inhaled and/or exhaled gases flow to and from a patient, can become contaminated with microorganisms that may originate from the patient's oropharynx or trachea. The breathing system includes the tracheal tube or face mask, inspiratory and expiratory tubing, y-piece, CO_2 absorber and its chamber, the anesthesia ventilator bellows and tubing, humidifier, adjustable pressure-limiting valve, and other devices and accessories. Recommendations for in-use care, maintenance, and reprocessing (i.e., cleaning and disinfection or sterilization) of the components of the breathing system have been published. (345;346) In general, reusable components of the breathing system that directly touch the patient's mucous membranes (e.g., face mask or tracheal tube) or become readily contaminated with the patient's respiratory secretions (e.g., y-piece, inspiratory and expiratory tubing and attached sensors) are cleaned and subjected to high-level disinfection or sterilization between patients. The other parts of the breathing system (e.g., carbon dioxide absorber and its chamber), for which an appropriate and cost-effective schedule of reprocessing has not been firmly determined, (347) are changed, cleaned, and sterilized or subjected to high-level disinfection periodically, according to published guidelines (345;346) and/or manufacturers' instructions.

Using high-efficiency bacterial filters at various positions in the patient circuit, e.g., at the y-piece or on the inspiratory and expiratory sides of the patient circuit, has been advocated (345;348;349) and shown to decrease contamination of the circuit. (349-351) However, the use of bacterial filters to prevent healthcare-associated pulmonary infections has not been shown effective. (352-354)

6. Pulmonary Function Testing Equipment

➢ a. Pulmonary function testing machine

In general, pulmonary function testing machine has not been considered an important source of bacterial contamination of inhaled gas. (355;356) However, because of concern about possible carry-over of bacterial aerosols from an infectious patient-user of the apparatus to the next patient, (275;357) placement of bacterial filters that remove exhaled bacteria between the patient and the testing equipment has been advocated. (275;358) More studies are needed to evaluate the need for, and efficacy of, these filters in preventing healthcare-associated pneumonia. (359)

➢ b. Tubing, connectors, rebreathing valves, and mouthpieces.

Tubing, connectors, rebreathing valves, and mouthpieces may become contaminated with patient secretions during use of the pulmonary-function testing apparatus. Thus, they should be cleaned and subjected to high-level disinfection or sterilization between uses on different patients.

F. Thoracoabdominal Surgical Procedures

Certain patients are at high risk of developing postoperative pulmonary complications, including pneumonia. These persons include those who are more than 70 years of age, are obese, or have chronic obstructive pulmonary disease (COPD). (360-363) Abnormal results from pulmonary function tests (especially decreased maximum expiration flow rate), a history of smoking, the presence of tracheostomy or prolonged intubation, or protein depletion that can cause respiratory-muscle weakness are also risk factors. (19;364;365) Patients who undergo surgery of the head, neck, thorax, or abdomen may suffer from impairment of the normal swallowing and respiratory clearance mechanisms as a result of instrumentation of the respiratory tract, anesthesia, or increased use of narcotics and sedatives; (361;366;367) patients who undergo upper abdominal surgery usually suffer from diaphragmatic dysfunction that results in decreased functional residual capacity of the lungs, closure of airways, and atelectasis. (368;369) Interventions aimed at reducing the postoperative patient's risk for pneumonia and other pulmonary complications have been developed. (370) These include deep breathing exercises, chest physiotherapy, use of incentive spirometry, intermittent positive-pressure breathing (IPPB) and continuous positive airway pressure by face mask. (370-380) Studies evaluating the relative efficacy of these modalities have shown variable results and have been difficult to compare because of differences in outcome variables assessed, patient populations studied, and study design. (373;379-381) Nevertheless, a recent randomized, controlled study showed that chest physiotherapy may not be helpful in preventing postsurgical, VAP, and instead, may cause arterial desaturation.(382) Other studies have found deep breathing exercises, use of incentive spirometry, and IPPB to be beneficial, especially in patients with preoperative pulmonary dysfunction. (373;374;376;377;379-381;383)

G. Other Prophylactic Measures

1. Immunomodulation

- a. Pneumococcal vaccination

Although pneumococci are not a major cause of healthcare-associated pneumonia, they have been identified as etiologic agents of serious healthcare-associated pulmonary infection and bacteremia. (384-387) The following factors render patients at high risk for complications from pneumococcal infections: ≥65 years of age, chronic cardiovascular or pulmonary disease, diabetes mellitus, alcoholism, cirrhosis, CSF leaks, immunosuppression, functional or anatomic asplenia, or HIV infection.

Strains of drug-resistant *S. pneumoniae* have become increasingly common in the United States and in other parts of the world. (388) Up to 35% of isolates submitted to CDC from some locations have intermediate (MIC=0.1-1.0 ug/ml) or high-level (MIC ≥2 ug/ml) resistance to penicillin. (389) Because many of the penicillin-resistant strains of pneumococci are also resistant to other antimicrobial agents such as erythromycin, trimethoprim-sulfamethoxazole, and extended-spectrum cephalosporins, therapeutic management of invasive penumococcal infections, such as pneumonia, becomes difficult and expensive.

The 23-valent vaccine is cost-effective and protective against invasive pneumococcal disease when administered to immunocompetent persons aged ≥2 years, and, although not as effective for immunocompromised patients as for immunocompetent persons, its potential benefits and safety justify its use on this group of patients. (389;390) ACIP recommends the administration of the vaccine to the following: a) immunocompetent persons ≥65 years of age, persons aged 2-64 years who have chronic cardiovascular disease (e.g., congestive heart failure or cardiomyopathy), chronic pulmonary disease (e.g., COPD or ermphysema, but not asthma), diabetes mellitus, alcoholism, chronic liver disease (cirrhosis), or CSF leaks; persons aged 2-64 years who have functional or anatomic asplenia; and persons aged 2-64 who are living in special environments or social settings; and b) immunocompromised persons aged ≥2 years with HIV infection, leukemia, lymphoma, Hodgkin's disease, multiple myeloma, generalized malignancy, chronic renal failure, nephrotic syndrome, or other conditions associated with immunosuppression, such as solid-organ or human-stem-cell transplantation, and persons receiving immunosuppressive chemotherapy, including long-term systemic corticosteroids. (389)

Because two-thirds or more of patients with serious pneumococcal disease have been hospitalized at least once within 4 years before their pneumococcal illness, offering pneumococcal vaccine in healthcare facilities, e.g., at the time of patient discharge or facility visit, should contribute substantially to preventing the disease. (389;391)

b. Use of immune globulin or granulocyte colony-stimulating factor

Intravenous immune globulin (given at 400 mg/kg body weight, once a week) was shown in one study to be efficacious in reducing the overall incidence of nosocomial infections, including gram-negative bacillary pneumonia, in post-operative patients. (392) However, its cost-effectiveness in the prevention of healthcare-associated pneumonia has not been studied. (392)

The use of hyperimmune globulin (100 mg/kg) against exotoxin A, *Klebsiella* spp., and *Pseudomonas aeruginosa* has not been shown to prevent infections due to these microorganisms. (393)

Granulocyte colony-stimulating factor increases the immune response of granulocytopenic patients to infections. It has been administered to patients with chemotherapy-induced febrile neutropenia to decrease the incidence of healthcare-associated infections in general. (394;395) However, its use specifically for preventing pneumonia has not been shown.

- c. Use of glutamine-enriched enteral feeding

Deficiency of glutamine, which is an essential amino acid that is needed for adequate lymphocyte and enterocyte function, may develop in times of severe illness, and contribute greatly to depression of the immune response and increased gut permeability. The intravenous administration of glutamine has been shown to help maintain integrity of the intestines (396) and glutamine-enriched enteral feeding was associated with lower incidences of VAP and bacteremia in multiple- trauma patients. (397)

2. Administration of Antimicrobial Agents

- a. Prophylactic systemic antimicrobial administration

Systemic antimicrobial administration has been a prevalent practice in the prevention of healthcare-related infections, including pneumonia, (398;399) especially in patients who are weaned off mechanical ventilators, postoperative, and/or critically ill. (400) However, with the exception of its use in febrile neutropenic patients (401) or in patients with structural coma, (399) the efficacy of such practice is questionable and the potential exists for superinfection with antimicrobial-resistant microorganisms, which may result from any antimicrobial therapy. (104;398;400;402-406)

- b. Periodic scheduled change in the class of antimicrobial agents used for empiric therapy

Kollef et al. showed that when a scheduled change was made in the class of antimicrobial agents (from a third-generation cephalosporin to a quinolone) used for empiric therapy of suspected gram-negative bacillary infections in patients undergoing cardiac surgery, the incidence of VAP caused by antibiotic-resistant gram-negative bacilli decreased significantly. (407) The authors attributed this finding to the prevention of the emergence of infections by the quinolone that were not suppressed previously by the cephalosporin. However, they also noted the possibility that the decrease in the rate of VAP may have been due to other factors not measured in the study. The use of this approach for the prevention of healthcare-associated pneumonia needs further evaluation.

3. Use of Kinetic Beds or Continuous Lateral Rotational Therapy (CLRT) for Immobilized Patients

Kinetic bed, or CLRT, is used to prevent pulmonary and other complications from prolonged immobilization or bed rest, such as in patients with acute stroke, critical illness, head injury or traction, blunt chest trauma, and/or mechanically assisted ventilation. (408-414) A CLRT bed turns continuously and slowly (from $\leq 40^\circ$ for CLRT to $\geq 40^\circ$ for kinetic therapy) along its longitudinal axis.

Among the hypothesized benefits are improved drainage of secretions within the lungs and lower airways, increased tidal volume, and reduction of venous thrombosis and its sequela, pulmonary embolization. (415-418) Cook et al. reviewed five randomized controlled studies that evaluated the efficacy of CLRT in preventing pneumonia. (408;410-412;414;419) Although all five studies showed a lower incidence of pneumonia in patients placed on CLRT compared to those on standard beds, only the study by Fink et al. showed a significant difference between the two rates i.e., 7/51 (14%) vs 19/48 (40%), respectively, RR=0.35, 95% CI: 0.16-0.75). (412) In addition, in all the studies, one or more patients in the CLRT group had to discontinue treatment because of discomfort, chest pain, or difficulty maintaining IV access, and in all the studies, the diagnosis of pneumonia was based on clinical criteria, including ETA cultures. Four patients would have to be on CLRT instead of the standard bed in order to prevent one case of healthcare-associated pneumonia. Cost-effective studies using more specific diagnostic testing for pneumonia should be done before CLRT becomes routine/standard therapy.

LEGIONNAIRES' DISEASE

Legionnaires' disease is a multi-system illness, with pneumonia, caused by *Legionella* spp. In contrast, Pontiac fever is a self-limited influenza-like illness, without pneumonia, that is associated with *Legionella* spp. (420)

I. Epidemiology

Numerous outbreaks of healthcare-associated Legionnaires' disease have been reported and have provided the opportunity to study the epidemiology of epidemic legionellosis. In contrast, the epidemiology of sporadic (i.e., non-outbreak-related) healthcare-associated Legionnaires' disease has not been well elucidated. However, data suggest that when one case is recognized, the presence of additional cases should be suspected. Of 196 cases of healthcare-associated Legionnaires' disease reported in England and Wales during 1980-1992, 69% occurred during 22 institutional outbreaks (defined as two or more cases occurring at an institution during a 6-month period). (421) Nine percent of cases occurred >6 months before or after an institutional outbreak. Another 13% were in facilities where other sporadic cases (but no outbreaks) were identified. Only 9% occurred at institutions where no outbreaks or additional sporadic cases were identified.

The overall proportion of healthcare-associated pneumonia due to *Legionella* spp. in North America has not been determined, although individual healthcare institutions have reported ranges of 0%-14%. (422-424) During an outbreak, the proportion of healthcare-associated pneumonia due to Legionnaires' disease may be as high as 50%. Because diagnostic tests for *Legionella* spp. infection are not routinely performed on all patients with healthcare-associated pneumonia in most U.S. healthcare facilities, these ranges probably underestimate the incidence of Legionnaires' disease. (425)

Legionella spp. are commonly found in various natural and man-made aquatic environments (426;427) and may enter hospital water systems in low or undetectable numbers. (428;429) Cooling towers, evaporative condensers, heated potable-water-distribution systems within healthcare facilities, and locally produced distilled water can provide a suitable environment for legionellae to multiply. Factors known to enhance colonization and amplification of legionellae in man-made water environments include temperatures of 25-42^{o}C, (430-434) stagnation, (435) scale and sediment, (431) and the presence of certain free-living aquatic amoebae that are capable of supporting intracellular growth of legionellae. (436;437)

A person's risk for acquiring legionellosis following exposure to contaminated water depends on a number of factors, including the type and intensity of exposure and the exposed person's health status. (438-440) Persons with severe immunosuppression from organ transplantation or chronic underlying illnesses, such as hematologic malignancy or end-stage renal disease, are at markedly increased risk for legionellosis. (438;440-445) Persons with diabetes mellitus, chronic lung disease, or non-hematologic malignancy; those who smoke cigarettes; and the elderly are at moderately increased risk. (420) Healthcare-associated Legionnaires' disease also has been reported in patients infected with the HIV virus (446) as well as among neonates and older patients at children's hospitals; the latter cases account for 24% of reported pediatric cases of Legionnaires' disease. (447-450)

Underlying disease and advanced age are not only risk factors for acquiring Legionnaires' disease but also for dying from the illness. In a multivariate analysis of 3,524 cases reported to CDC from 1980 through 1989, immunosuppression, advanced age, end-stage renal disease, cancer, and healthcare-associated acquisition of disease were each independently associated with a fatal outcome. (440) The mortality rate among 803 persons with healthcare-associated cases was 40% compared with 20% among 2,721 persons with community-acquired cases, (440) probably reflecting increased severity of underlying disease in hospitalized patients.

II. Diagnosis

The clinical spectrum of disease due to *Legionella* spp. is broad and ranges from asymptomatic

infection to rapidly progressive pneumonia. Legionnaires' disease cannot be distinguished clinically or radiographically from pneumonia caused by other agents, (451-453) and evidence of infection with other respiratory pathogens does not rule out the possibility of concomitant *Legionella* spp. infection. (454-456)

The diagnosis of legionellosis may be confirmed by any one of the following: isolation of *Legionella* from culture(s) of respiratory secretions or tissues, microscopic visualization of the bacterium in respiratory secretions or tissue by immunofluorescent microscopy, or, for legionellosis due to *L. pneumophila* serogroup 1, detection of *L. pneumophila* serogroup-1 antigens in urine by radioimmunoassay or ELISA, or observation of a fourfold rise in *L. pneumophila* serogroup-1 antibody titer to $\geq$1:128 in paired acute and convalescent serum specimens by use of an indirect immunofluorescent antibody test (IFA). (457-461) A single elevated antibody titer does not confirm a case of Legionnaires' disease because IFA titers $\geq$1:256 are found in 1%-16% of healthy adults. (462-465)

Because the above tests complement each other, performing each test when Legionnaires' disease is suspected increases the probability of confirming the diagnosis. However, because none of the laboratory tests is 100% sensitive, the diagnosis of legionellosis is not ruled out even if one or more of the tests are negative. (458) Of the available tests, the most specific is culture isolation of *Legionella* spp. from any respiratory tract specimen. (458)

III. Modes of Transmission

Inhalation of aerosols of water contaminated with *Legionella* spp. is believed to be the primary mechanism of entry of these organisms into a patient's respiratory tract. (420) In several hospital outbreaks, patients were considered to have been infected from their exposure to contaminated aerosols generated by cooling towers, showers, faucets, respiratory therapy equipment, and room-air humidifiers. (93;270;287;453;466-472) In other studies, aspiration of contaminated potable water or pharyngeal colonizers has been proposed as the mode of transmission to certain patients. (470;473-476) Person-to-person transmission has not been observed.

IV. Definition of Healthcare-Associated Legionnaires' Disease

The incubation period for Legionnaires' disease is generally 2-10 days; (477) thus, for epidemiologic purposes in this document, laboratory-confirmed legionellosis that occurs in a patient who has spent $\geq$10 days continuously in a healthcare facility prior to onset of illness is considered **definite** healthcare-associated Legionnaires' disease, and laboratory-confirmed infection that occurs in a patient who has spent 2-9 days in a healthcare facility before onset of illness is considered **possible** healthcare-associated infection.

V. Prevention and Control Measures

A. Prevention of Legionnaires' Disease in Healthcare Facilities with No Identified Cases (Primary Prevention)

Prevention strategies in healthcare facilities with no cases of healthcare-associated legionellosis have varied by institution, depending on the immunologic status of the patients, the design and construction of the facility, resources available for implementation of prevention strategies, and state and local regulations.

There are at least two schools of thought regarding the most appropriate and cost-effective approach to prevent healthcare-associated legionellosis, especially in facilities where no cases or only sporadic cases of the illness are detected. However, a study comparing the cost-benefit ratios of these strategies has not been done.

The first approach is based on periodic, routine culturing of water samples from the healthcare facility's potable water system, for *Legionella* spp. (478-480) If any sample is culture positive,

diagnostic testing for Legionnaires' disease is recommended for all patients with healthcare-associated pneumonia and the tests are made available to clinicians, either in-house or through a reference laboratory. In-house testing is recommended in particular for facilities with transplant programs. (479) When ≥30% of the samples obtained are culture positive for *Legionella* spp., the facility's potable water system is decontaminated. (479) This approach is based on the premise that no cases of healthcare-associated legionellosis can occur in the absence of *Legionella* spp. from the potable water system, and, conversely, once *Legionella* spp. are cultured from the water, cases of healthcare-associated legionellosis may occur. (473;481) Proponents of this strategy indicate that when physicians are informed that the potable water system of the facility is culture-positive for *Legionella* spp., they are more inclined to conduct the necessary tests for legionellosis. (482) A potential advantage of this approach is the lower cost of culturing a limited number of water samples, if the testing is done infrequently, compared with the cost of routine laboratory diagnostic testing for legionellosis in all patients with healthcare-associated pneumonia in facilities that have had no cases of healthcare-associated legionellosis.

The main argument against this approach is that in the absence of cases, the relationship between the results of water cultures and the risk of legionellosis remains undefined. The bacterium has been frequently present in hospital water systems, (483) often without being associated with known cases of disease. (300;423;484) In a study of 84 hospitals in Quebec, 68% were found to be colonized with *Legionella* spp., and 26% were colonized at >30% of sites sampled; however, cases of Legionnaires' disease were rarely reported from these hospitals. (300) Interpretation of the results of routine culturing of water may be confounded by variable culture results among sites sampled within a single water system and by fluctuations in the concentration of *Legionella* spp. in the same site. (485;486) In addition, the risk of illness following exposure to a given source may be influenced by a number of factors other than the presence or concentration of organisms; these include the degree to which contaminated water is aerosolized into respirable droplets, the proximity of the infectious aerosol to potential host, the susceptibility of the host, and the virulence properties of the contaminating strain. (487-489) Thus, data are insufficient to assign a level of risk for disease even on the basis of the number of colony-forming units detected in samples from the hospital environment. By routinely culturing water samples, many healthcare facilities will have to be committed to water-decontamination programs to eradicate *Legionella* spp. Because of this problem, routine monitoring of water from the hospital's potable water system and from aerosol-producing devices, although instituted in some healthcare facilities and states, (478;480) has not been recommended universally. (490)

The second approach to prevent and control healthcare-associated legionellosis is by:

a) maintaining a high index of suspicion for legionellosis and appropriately using diagnostic tests for legionellosis in patients with healthcare-associated pneumonia who are at high risk of developing the disease and dying from the infection; (423;491)

b) initiating an investigation for a facility source of *Legionella* spp., which may include culturing of facility water for *Legionella* spp., upon identification of one case of definite or two cases of possible healthcare-associated Legionnaires' disease; and

c) routinely maintaining cooling towers and potable-water systems, and using only sterile water for filling and terminal rinsing of nebulization devices. (490;492)

At present, diagnostic testing for legionellosis is underutilized. In one large study, only 19% of hospitals routinely performed testing for legionellosis among patients at high risk for healthcare-associated Legionnaires' disease. (425;442) The establishment of formal testing protocols in healthcare facilities can improve the recognition of cases of healthcare-associated legionellosis and facilitate focused, cost-effective interventions to reduce transmission.

Culturing of the facility water system for legionellae may be appropriate if performed to evaluate the suspected source of infection as part of an outbreak investigation, to assess the effectiveness of water treatment or decontamination protocols, or to evaluate the potential for transmission in healthcare facilities with patients at exceedingly high risk of developing Legionnaires' disease (e.g., hematopoietic stem-cell transplant [HSCT] recipients). Because HSCT recipients are at much higher risk for disease and death from legionellosis compared to most other patients, (425;441;442;493) periodic routine culturing for legionellae in water samples from the transplant unit's potable-water supply may be prudent (494) if performed as part of a comprehensive strategy to prevent Legionnaires' disease in transplant units. However, the optimal method (frequency, number of sites)

for environmental surveillance cultures in transplant units has not been determined, and the cost-effectiveness of this strategy has not been evaluated. (493) In addition, because of the absence of data regarding a “safe” concentration of legionellae in potable water, the goal of an environmental surveillance for legionellae in transplant units, if undertaken, should be to maintain water systems with no detectable legionellae. More importantly, however, clinicians must 1) maintain a high index of suspicion for legionellosis in HSCT recipients who develop healthcare-associated pneumonia and 2) perform diagnostic testing for legionellosis in all HSCT recipients who develop healthcare-associated pneumonia, even when environmental surveillance cultures do not yield legionellae.

In the recently developed Guidelines for the Prevention of Opportunistic Infections in HSCT Recipients, the CDC, Infectious Diseases Society of America, and the American Society of Blood and Marrow Transplantation recommend decontaminating the potable-water system of the transplant unit when legionellae are detected in its water. In addition, and until legionellae are eradicated from the water supply, they recommend that a) HSCT recipients should be restricted from taking showers using the unit water; b) sponge baths should be given to patients using water that is not contaminated with legionellae; c) faucet water in patient rooms or outpatient clinics should not be used so as not to create infectious aerosols, and d) water that is free of legionellae, e.g., sterile or pasteurized water, should be used by transplant recipients for drinking, tooth brushing, or flushing of nasogastric tubes. (469;474;493;495)

Measures aimed at creating an environment that is not conducive to survival or multiplication of *Legionella* spp. have been used in facilities where cases of healthcare-associated legionellosis have been identified. Advocated for all hospitals, (490;496) these measures include routine maintenance of potable water at $\geq 51^{o}$C (124°F) or $<20^{o}$C (68^{o}F) at the tap or chlorination of heated water to achieve 1-2 mg/L free residual chlorine at the tap, especially in areas where immunosuppressed and other high-risk patients are located. (423;473;485;490;495;497-501) If the temperature setting of 51°C is permitted, scalding becomes a possible hazard; one method of preventing scalding is to install preset thermostatic mixing valves. Where buildings cannot be retrofitted, periodically increasing the temperature to at least 66°C (150°F) at the point of use (i.e., faucets) or chlorination followed by flushing can be used to control the growth of *Legionella* spp. (497;499;500) Systems should be inspected annually to ensure that thermostats are functioning properly. Hot or cold water systems that incorporate an elevated holding tank should be inspected and cleaned annually, and lids should be fit tightly to exclude foreign material. The cost-benefit ratio of such measures in facilities that have no identified cases of healthcare-associated legionellosis, however, needs further study.

B. Prevention of Legionnaires' Disease in Healthcare Facilities with Identified Cases (Secondary Prevention)

The indications for a full-scale environmental investigation to search for and subsequently decontaminate identified environmental sources of *Legionella* spp. in healthcare settings remain to be elucidated and probably vary from one healthcare facility to another. In facilities where as few as 1-3 healthcare-associated cases have been identified over a period of up to several months, intensified surveillance for Legionnaires' disease has frequently detected numerous additional cases. (442;467;470;498;502;503) This suggests the need for a low threshold for initiating an investigation following the identification of healthcare-associated, laboratory-confirmed cases of legionellosis. However, when developing a strategy to respond to such an identification, infection-control personnel should consider the level of risk for acquisition of, and mortality from, *Legionella* spp. infection at their particular facility.

The Guidelines for the Prevention of Opportunistic Infections in HSCT Recipients recommend that in a healthcare facility with an HSCT program, the performance of a thorough investigation to identify the source(s) of *Legionella* (and the subsequent disinfection, decontamination, and/or removal of the identified source(s) of *Legionella* spp.) should be done even when only one definite or one possible case of laboratory-confirmed healthcare-associated Legionnaires’ disease is identified in an inpatient HSCT recipient or in two or more HSCT recipients who had visited an outpatient HSCT unit during all or part of the 2-10 day period before illness onset. (493)

An epidemiologic investigation of the source of *Legionella* spp. involves several important steps, including 1) retrospective review of microbiologic and medical records, 2) active surveillance to

identify all recent or ongoing cases of legionellosis, 3) identification of potential risk factors for infection (including environmental exposures, such as showering or use of respiratory-therapy equipment) by line listing of cases; analysis by time, place, and person; and comparison with appropriate controls, 4) collection of water samples from environmental sources implicated by the epidemiologic investigation and from other potential sources of aerosolized water, and 5) subtype-matching between legionellae isolated from patients and environmental samples. (472;504-506) The latter step can be crucial in supporting epidemiologic evidence of a link between human illness and a specific source. (507-509)

In facilities where the cooling towers are found to be contaminated, measures that have been previously published should be used for decontamination. (490;492;493)

In facilities where the heated-water system has been identified as the source of the organism, the system has been decontaminated by pulse (one-time) thermal disinfection or superheating. (490;500) In thermal decontamination, the hot water temperature is raised to 71°-77°C (160°-170°F) and maintained at that level while each outlet around the system is progressively flushed. A minimum flush time of 5 minutes has been recommended; however, the optimal flush time is not known, and longer flush times may be necessary. The number of outlets that can be flushed simultaneously depends on the capacity of the water heater and the flow capability of the system. Appropriate safety procedures to prevent scalding are essential; thus, when possible, flushing should be performed when the building occupants are fewest or least likely to utilize water (e.g., on nights and weekends). For systems where thermal shock treatment is not possible, shock chlorination may provide an alternative. (490;500;510;511) There is, however, less experience with this method of decontamination, and corrosion of metals in the system may result from exposures to high levels of free chlorine. Chlorine should be added, preferably overnight, to achieve a free chlorine residual of at least 2 mg/L (2 ppm) throughout the system. This may require chlorination of the water heater or tank to levels of 20-50 mg/L (20-50 ppm). The pH of the water should be maintained between 7.0 and 8.0. Once the decontamination is complete, recolonization of the hot water systems is likely to occur unless the proper temperatures are maintained or a procedure such as continuous supplemental chlorination is continued. (490;499)

Following either of these procedures, most healthcare facilities maintain heated water at $\geq 51^{o}C$ or $<20^{o}C$ at the tap or chlorinate heated water to achieve 1-2 mg/L free residual chlorine at the tap. (423;473;485;490;497-500) Additional measures, such as physical cleaning or replacement of hot water storage tanks, water heaters, faucets, and showerheads and removal of dead legs in the water-distribution system, may be required because scale and sediment may accumulate and protect organisms from the biocidal effects of heat and chlorine. (431;500) Alternative methods for controlling and eradicating legionellae in water systems, such as treatment of water with ozone, ultraviolet light, or heavy metal ions (i.e., copper/silver ions), have limited the growth of legionellae under laboratory and/or operating conditions. (501;512-520) However, more data are needed regarding the long-term efficacy of these methods. For instance, a recent study suggested that legionellae develop tolerance to copper/silver ion treatment during extended application ($\geq$ 4 years). (521)

Recent, renewed interest in the use of chloramines has arisen primarily because of concerns about adverse health effects associated with by-products of currently used disinfectants. (522) When monochloramine is used for disinfection, the formation of by-products including trihalomethanes and haloacetic acids is minimized. In addition, however, monochloramine reaches distal points in a water system and penetrates into bacterial biofilms better than does free chlorine. (523) A recent study indicated that 90% of hospital outbreaks of Legionnaires' disease that were associated with potable water system could have been prevented if monochloramine rather than free chlorine had been used for residual disinfection. (524) In another study by the same group, in which they compared retrospectively the incidences of nosocomial Legionnaires' disease among hospitals in central Texas, no cases were noted in facilities located in municipalities with monochloramine-treated water. (525) However, additional data are needed regarding the effectiveness of using monochloramine before its routine use as a disinfectant in water systems can be recommended.

Because of a) the high costs of conducting an environmental investigation and eradicating *Legionella* spp. from sources in healthcare facilities (526;527) and b) host-related differences in patient risk for acquiring and dying from legionellosis, the decision to search for and eradicate *Legionella* spp. from sources in a facility should be based, to a large extent, on the type of patient population the facility

serves.

PERTUSSIS

Pertussis is an acute respiratory tract infection caused by *Bordetella pertussis* and typically characterized by progressive, repetitive, and paroxysmal cough that usually lasts for 6-8 weeks. Whooping cough, post-tussive vomiting, and episodes of cyanosis or apnea also may occur, usually in children. In some cases, a chronic cough may persist for several months.

I. Epidemiology

B. pertussis is most noted for causing serious disease during infancy and early childhood. (528;529) The morbidity (e.g., pneumonia, seizures, encephalopathy, and prolonged hospitalization) and mortality due to pertussis had decreased dramatically after routine childhood immunization against pertussis was implemented. (530) However, the disease has not been eradicated, and in the last two decades, the reported incidence of pertussis, including pertussis in adults (both young and elderly), adolescents and older children, has increased. (531-540) It is estimated that 1-2 in 1,000 adolescents and adults contract pertussis each year. (531) These infected adolescents and adults often serve as reservoirs for pertussis in young infants who are unimmunized or incompletely immunized. (541) Pertussis in adults may result in pneumonia, urinary incontinence, and sinusitis. (542)

Outbreaks of pertussis in healthcare settings may follow the introduction of the infection into the facility by admission of infant(s) with pertussis. This may occur during a community outbreak of pertussis, which is often associated with increased hospitalizations and deaths in young children. Adults with cough, including healthcare workers or patient visitors, can also be a major source of pertussis in the healthcare setting, (531;543-548) especially because they can shed the microorganism for prolonged periods before their infection is detected or diagnosed.

II. Diagnosis

The “classic” clinical characteristics of pertussis in infants, i.e., catarrh and paroxysmal cough followed by prolonged convalescence, are usually distinguishable from those of other respiratory tract infections. However, the clinical presentation of pertussis in the previously immunized person (older child, adolescent, or adult) is often, although not always, atypical. (539) The illness may be mild but protracted. Patients may have a prolonged cough lasting for several weeks, and the classic whooping cough is found only in a few cases. (549;550)

Laboratory diagnosis of pertussis is difficult. (551) Of the different laboratory tests that have been developed, the best method for confirmation of pertussis remains culture isolation of *B. pertussis* from nasopharyngeal secretions. (552) The other laboratory tests, i.e., direct fluorescein-conjugated antibody (DFA) tests, polymerase chain reaction (PCR) assays, and serologic assays, are either unstandardized for general use and lack a clear correlation with pertussis illness (PCR and serologic tests), or have low sensitivity and specificity (DFA tests).

DFA tests have been used widely for screening purposes, but some tests have had low sensitivity (38%) and specificity (up to 85% cross-reactivity with normal nasopharyngeal flora) for diagnosing pertussis (551-554) and require a high level of technical care and experienced personnel for accurate interpretation of results. A newer DFA test that uses mouse monoclonal antibody was shown initially to have 65% sensitivity and 99% specificity when compared to culture; (555) however, its actual-use sensitivity and specificity were lower (i.e., <30% and 20%, respectively) when it was utilized in an outbreak investigation in 1999. (556)

PCR assays have been more sensitive than other tests (e.g., they can remain positive for 1-7 days longer than culture isolation tests) in patients who have received antimicrobial therapy for pertussis. In one study, the number of PCR-positive samples was 2.4-fold higher than the number of culture-positive specimens. (557) The sensitivity of PCR, however, decreases with an increase in patient’s age: in one report, the sensitivities of PCR in patients with <10 days of symptoms were 70%, 50%, and 10% in the age groups <1 year, 1-4 years, and $\geq$5 years, respectively. (558) The main disadvantages of PCR are the lack of a universally accepted technique that has been validated

among laboratories and the absence of an established correlation between PCR-positive assays and clinical disease. Thus, it has been recommended that whenever a PCR assay is used to diagnose a suspected case of pertussis, a culture of the patient's nasopharyngeal secretions should be performed at the same time, for confirmation. (556;559)

Serologic assays for pertussis show potential for being a good diagnostic tool. Even single-sample determination of titers of IgG and IgA to various pertussis antigens can be highly sensitive, (554) mostly during the convalescent stage of the disease. For example, a combination of IgG anti-pertussis toxin and IgA anti-filamentous hemagglutinin enzyme-immunoassay testing (using age-specific reference values) had a sensitivity of 81%-89% in diagnosing pertussis from a single serum sample taken 5-10 weeks after symptoms had started. (560) Serologic tests for pertussis, however, are not available for clinical use in the United States, and only one state health department laboratory has a standardized technique in use at the present time. (556;561)

III. Modes of Transmission

Pertussis is transmitted during close contact with an infected person, probably most commonly by direct deposition of *B. pertussis* on the uninfected person's respiratory mucosa, from large droplets generated by the infected person's cough or sneeze. Autoinoculation may also occur when infectious secretions are picked up on hands (directly from the infected person or indirectly from fomites contaminated with the infected person's bacteria-laden secretions) and deposited onto the respiratory mucosa. (562) Patients can also be infected with *B. pertussis* when their nasal mucosa is touched by contaminated hands of other persons, such as healthcare providers, or by contaminated objects.

Transmission of pertussis by the airborne route, i.e., via droplet nuclei carried by air currents over long distances, has not been shown. In one study, *B. pertussis* DNA was recovered from air samples from filters placed as far as 4 meters from the bedside of a patient with pertussis; (563) however, the significance of this finding needs further elucidation.

IV. Control Measures

Vaccination of infants and children against pertussis (even after the infant or child has had pertussis) has been effective in reducing the impact of pertussis worldwide. In the United Sates, recommendations for childhood vaccination include the use of whole cell diphtheria-tetanus-pertussis (DTP) and diphtheria-tetanus-acellular pertussis (DTaP) vaccines. (564)

In recent years, the impetus for universal or selective vaccination of adults with pertussis antigens has become stronger with the development of a "safer" (i.e., less reactogenic) acellular form of vaccine (565) and the greater realization by the medical community and the public, of the increasing prevalence of cases of pertussis in adults and adolescents and its impact on the transmission of the infection. (539) Outbreaks of pertussis in highly immunized populations of children aged 11-12 years (566) and adults have corroborated the finding that vaccine-induced immunity weakens considerably within 6-10 years after vaccination (567) and strongly suggest that booster immunizations for older children, adolescents and adults are necessary for the control of pertussis. However, the safety and efficacy of booster vaccinations in adults and children older than 7 years are still under study. (556)

In healthcare institutions that have had pertussis outbreaks, combinations of control measures have been utilized. (543;545) Successful programs have had several elements in common: a prevailing high index of suspicion for pertussis infection; performance of diagnostic testing on persons with symptoms suggestive of pertussis; prompt initiation of antimicrobial treatment of proven and suspected cases of infection and prophylaxis of exposed patients and healthcare personnel; granting of leave (from work) status to healthcare personnel with suspected pertussis, until after they complete 5 days of antimicrobial therapy for pertussis; and implementation of droplet precautions in addition to standard precautions. (543;545) Droplet and standard precautions include: a) placing a patient with suspected or proven pertussis in a private room or placing a patient with proven pertussis in a room with other patients with proven pertussis and no other infection; b) wearing a mask when entering the room of a person with suspected or proven pertussis and/or when performing procedures and patient-care activities that are likely to generate sprays of respiratory secretions; c) decontaminating hands with soap and water or with a waterless antiseptic agent after touching respiratory secretions or

secretion-contaminated items, whether or not gloves are worn, immediately after gloves are removed, and between patient contacts; (255) d) using clean, nonsterile gloves when touching respiratory secretions and contaminated items or before touching mucous membranes, and removing gloves promptly after use, before touching contaminated items and environmental surfaces, and before going to another patient; e) wearing a clean, nonsterile gown during procedures or patient-care activities that are likely to soil clothing or skin with respiratory secretions, and removing a soiled gown as promptly as possible; and f) handling used patient-care equipment soiled with respiratory secretions in a manner that prevents skin and mucous membrane exposures, contamination of clothing, and transfer of the microorganism to other patients and environments. (256)

The use of a prophylactic antimicrobial agent, most notably erythromycin estolate, for household contacts of patients with pertussis has been effective in preventing culture-positive pertussis but not clinical pertussis. (568;569) In a prospective randomized trial using erythromycin estolate (40 mg/kg/day in 3 divided doses, with a maximum dose of 1 gram) vs placebo for chemoprophylaxis for prevention of secondary cases of pertussis in household contacts of children with culture-positive pertussis, 4 (6.6%) of 61 households randomized to the erythromycin-treatment group vs. 15 (20.3%) of 74 households randomized to the placebo group had culture-positive secondary cases of pertussis; the estimated efficacy of erythromycin prophylaxis in preventing culture-positive pertussis in household contacts was 67.5% (95% confidence interval: 7.6-88.7). There was, however, no difference in the development of respiratory tract symptoms compatible with the case definition of pertussis between the treatment and placebo groups. In addition, medication-associated adverse events were reported in 35% of the erythromycin-treated group vs. 15% of the placebo group. (568) In an earlier review of 14 studies that evaluated the use of erythromycin in preventing secondary transmission of pertussis to close contacts of primary cases, Dodhia and Miller concluded that the protection afforded by such chemoprophylaxis is, at best, modest and inferior to that from administration of whole-cell vaccine. (570) Adverse events, such as nausea, vomiting, and abdominal pain, were reported in association with erythromycin intake in three of the studies. (570) In addition to these reports, post-exposure prophylaxis with erythromycin in neonates has been associated with the development of infantile hypertrophic pyloric stenosis. (571)

Nevertheless, erythromycin remains the drug of choice for treatment of and chemoprophylaxis for pertussis in healthcare centers. In two outbreaks occurring in the healthcare setting, healthcare personnel with prolonged coughing that was possibly pertussis were treated with erythromycin for 14 days, and those with proven or probable pertussis were given a 5-day sick leave during the first 5 days of therapy. (543;544) In one center, a case of nosocomially transmitted pertussis occurred in one of 61 erythromycin-treated healthcare workers; this necessitated treatment of all (exposed) unit personnel with a second course of another antibiotic for 10 days. (544) In the other center, only one case of nosocomially acquired pertussis was identified, in an infant who was not able to complete the prescribed erythromycin prophylaxis. (543)

Other macrolides have been used successfully for eradication of *B. pertussis*; however, data on their clinical efficacy are sparse. In one report, clarithromycin for 7 days (at 500 mg twice a day for adults or 15 mg/kg/day in divided doses for children) and azithromycin for 5 days resulted in the eradication of the microorganism. (572) In another study, treatment of infants and young children with azithromycin for 3 days (at 10 mg/kg/day) or 5 days (at 10 mg/kg on day 1 followed by four days at 5 mg/kg/day) resulted in eradication of *B. pertussis* from 94% and 100% of nasopharyngeal cultures, on days 7 and 14, respectively, after initiation of treatment. (573)

For persons with hypersensitivity and/or intolerance to erythromycin and the other macrolides, trimethoprim-sulfamethoxazole (TMP-SXT) for 14 days (at one double-strength tablet twice a day for adults and 8 mg/kg/day TMP, 40 mg/kg/day SXT a day in 2 divided doses for children) has been successfully used for therapy. (574) TMP-SXT and oxytetracycline for 14 days (at 500 mg four times a day for adults, and 25 mg/kg/day in divided doses for children $\geq$9 years) have been the second-line drugs for chemoprophylaxis. (545)

During institutional outbreaks of pertussis, additional measures have been used to help control the transmission of *B. pertussis*: a) exclusion of healthcare personnel who have symptoms of upper respiratory tract infection from the care of infants and other high-risk patients, including immunocompromised persons such as bone-marrow transplant recipients; and b) limiting visitors to only those who do not have symptoms of a respiratory tract infection and are more than 14 years of

age. (543) Although the exact role of each of these measures in preventing transmission of pertussis has not been determined, their use for control of outbreaks seems prudent. In one outbreak, the administration of acellular pertussis vaccine to healthcare personnel was used safely as an adjunct to chemoprophylaxis. (575) At present, however, there is no pertussis vaccine licensed for use in adults in the U.S.

ASPERGILLOSIS

I. Epidemiology

Aspergillus spp. are ubiquitous fungi, commonly occurring in soil, water, and decaying vegetation. *Aspergillus* spp. have been cultured from unfiltered air, ventilation systems, contaminated dust dislodged during hospital renovation and construction, horizontal surfaces, food, and ornamental plants. (576)

A. fumigatus and *A. flavus* are the most frequently isolated *Aspergillus* spp. in patients with proven aspergillosis. (577;578) Aspergillosis has been recognized increasingly as a cause of severe illness and mortality in highly immunocompromised patients, e.g., patients undergoing chemotherapy and/or organ transplantation (including receipt of hematopoietic stem-cell transplant [HSCT] or solid-organ transplant) and patients with advanced HIV infection, specifically those with CD4 counts of <50/cu mm. (579-588) In addition, patients with chronic lung disease such as chronic granulomatous disease (589) or who are receiving prolonged high-dose corticosteroid therapy also are susceptible to aspergillosis. (590;591)

The most important healthcare-associated infection caused by *Aspergillus* spp. is invasive pulmonary aspergillosis (IPA). (592;593) Outbreaks of IPA have occurred mainly in neutropenic patients, especially those in HSCT units. (585;592;594-601) Although IPA has been reported in recipients of solid-organ transplants (e.g., heart, lung, kidney, or liver), (578;602-608) its incidence in these patients is lower than in recipients of HSCT, (580) probably because neutropenia is less severe in solid-organ transplant recipients and the use of corticosteroids has decreased with the introduction of cyclosporine. (604;609)

The reported attributable mortality from IPA has varied according to patient risk groups. Mortality rates of 90% in recipients of allogeneic HSCT, 13%-80% in patients with aplastic anemia and leukemia, and 68-100% in solid-organ transplant patients have been reported. (610-612) The lower mortality rates observed in some series are probably due to a less specific case-definition of IPA.

II. Pathogenesis

Pulmonary aspergillosis is acquired primarily by inhalation of the fungal spores. In severely immunocompromised patients, primary *Aspergillus* spp. pneumonia results from local lung tissue invasion. (577;593;613) Subsequently, the fungus may disseminate via the bloodstream to involve multiple other deep organs. (577;593;614) A role for nasopharyngeal colonization with *Aspergillus* spp. as an intermediate step before invasive pulmonary disease has been proposed but remains to be elucidated. (615;616) Likewise, colonization of the lower respiratory tract by *Aspergillus* spp., especially in patients with preexisting lung disease such as chronic obstructive lung disease, cystic fibrosis, or inactive tuberculosis, was reported to predispose patients to invasive pulmonary and/or disseminated infection; (577;593;617) however, more recent data have not shown the correlation. (618)

Host defenses against *Aspergillus* spp. involve the mobilization of both macrophages and granulocytes. (619) Alveolar macrophages, by inhibiting germination of fungal conidia, serve as the first line of defense against airborne pulmonary aspergillus infections. After aspergilli germinate and their hyphae invade pulmonary tissue, neutrophils, by secreting microbicidal oxidative metabolites that can damage the fungal hyphae, become the main effector cells involved. Thus, prolonged, severe neutropenia is a risk factor for IPA. (620) And, because a) corticosteroids suppress monocyte/macrophage function that includes the release of both oxidative and non-oxidative metabolites, and b) cyclosporine and tacrolimus (either of which is used in combination with corticosteroids in organ-transplant recipients) inhibit gamma interferon which activates macrophages, their use in organ-transplant recipients increases the recipients' risk of aspergillosis. Low CD4 lymphocyte count, as occurs in patients with severe and/or end-stage HIV infection, decreases the antifungal activity of granulocytes, and chronic granulomatous inhibits granulocyte respiratory burst oxidase activity, resulting in impaired microbicidal phagocytosis.

III. Diagnosis

Diagnosing pneumonia due to *Aspergillus* spp. is often difficult. (621) Clinical signs and symptoms, such as fever, chest pain, cough, malaise, weight loss, and dyspnea are highly variable and nonspecific, and chest x-ray findings can vary from single or multiple nodules with or without cavitation, to widespread infiltrates. (622) The definitive diagnosis of pulmonary aspergillosis requires both histopathologic demonstration of branching, septate, nonpigmented hyphae in lung tissue and isolation of the microorganism in culture. Histologic identification in the absence of a positive culture gives only a probable diagnosis, because aspergillus hyphae are identical to those of *Fusarium* spp., *Scedosporium* spp., and many other non-pigmented molds. The examination of BAL fluid by smear, culture, and/or antigen detection is sometimes helpful, but positive results are obtained in only 50-60% of patients. (623;624)

By itself, culture isolation of *Aspergillus* spp. from respiratory tract specimens of patients may indicate colonization. (625) However, when *Aspergillus* spp. is grown from the sputum of a febrile, neutropenic patient with a new pulmonary infiltrate, it is highly likely that the patient has pulmonary aspergillosis. (626;627) Routine blood cultures are remarkably insensitive for detecting *Aspergillus* spp. (628)

Abnormalities detected by computerized tomography (CT) scanning often precede those detected by plain chest radiograph. (629) In neutropenic patients, the most distinctive lesions are small nodules surrounded by a zone of low attenuation, termed the "halo sign." (630-633) Over time, the nodules may cavitate, resulting in the "crescent sign," a thin air crescent near the edge of the nodule.

Testing for antibodies against aspergillus has seldom proved helpful in diagnosing invasive aspergillosis in neutropenic patients. However, recent results from lung transplant recipients suggest that this procedure might be a useful adjunct to other methods of diagnosis. (634) Techniques have been developed to detect aspergillus galactomannan antigen in serum or urine of infected patients. (635-637) Recently, a sandwich enzyme immunoassay, available in many European countries, has been reported to have a sensitivity of 67-100% and a specificity of 81-99% for detection of galactomannan in serum; however, it is not clear whether this test will allow earlier diagnosis of disease. (638-641) No antigen tests are approved for diagnostic use in the United States.

IV. Risk Factors

Factors related to the host immune status, as well as various environmental exposures, are associated with increased risk of IPA. Severe (absolute neutrophil count [ANC] <500 per cubic millimeter) and prolonged neutropenia is the most important host risk factor for IPA. (620) In addition, deficits in neutrophil function are also associated with IPA; these occur in patients with chronic granulomatous disease, (589) patients receiving supraphysiologic doses of corticosteroids, (642) or patients who develop graft-versus-host disease (GVHD). (643;644) Because HSCT recipients experience the most severe degree of neutropenia, they constitute the population at highest risk for developing invasive aspergillosis. (645;646) The tendency of HSCT recipients to contract severe neutropenia is associated with the type of graft they receive. While both autologous (647) and allogeneic HSCT transplant recipients are severely neutropenic for up to 4 weeks after transplantation, allogeneic transplant recipients may, in addition, develop acute or chronic GVHD. (648) The latter may occur up to several months after the procedure; and the disease and/or its therapy (often with high doses of corticosteroids and other immunosuppressive agents) may result in severe neutropenia.

Recently, a shift in the onset of IPA occurring post transplantation has been observed: IPA now frequently occurs late (>40 days) after receipt of HSCT, i.e., during the period when acute GVHD occurs rather than during the earlier period of neutropenia. (648-650)

In addition to the host's immune system status, other factors related to the organ transplantation procedure may be associated with an increased risk of IPA. Lung-transplant recipients may be at increased risk of IPA because of post-transplantation impairment of local defenses in the bronchial airways. (651)

Hospital-based outbreaks of IPA often have been associated with activities that result in an increase in the count of airborne spores of *Aspergillus* spp. in the hospital environment, such as occurs during building demolition, (652) construction, and/or renovation. (653-661) Other hospital environmental sources that have been associated with IPA outbreaks include bird droppings in air ducts supplying high-risk patient areas (662) and contaminated fireproofing material or damp wood. (654) Recently, hospital water was suggested as a possible vehicle for transmission of aspergilli. *Aspergillus* spp. were cultured from hospital water and water structures; (663;664) and the *A. fumigatus* isolate from one patient who died of invasive aspergillosis had a random-amplified-polymorphic-DNA profile that was similar to that of isolates obtained from water samples from the patient's hospital room. (664) Larger controlled studies, however, are needed to determine the role of water in the transmission of aspergillosis.

Attempts by researchers to identify the healthcare environmental source(s) of airborne *Aspergillus* spp. by establishing an association between the occurrence of IPA cases and either a) the recovery of *Aspergillus* spp. from the air or b) an increased concentration of *Aspergillus* spores in the air have met with difficulties. (665;666) Often, a correlation between patient and environmental isolates could not be demonstrated, (594) and on the rare occasion that some patient and environmental isolates were identical, not all the case-isolates could be matched with those from the environment. (667) The difficulties are due in part to air-sampling problems, the vast genetic diversity of *Aspergillus* isolates, (668) and the limitations of the various subtyping methods for molds. New molecular typing techniques, i.e., karyotyping (669) and DNA endonuclease profiling (now available for *A. fumigatus*), (670;671) have been developed recently and may aid substantially in identifying outbreak sources.

Our current understanding of the transmission of aspergilli in cases of IPA is based mostly on information gathered from outbreak investigations. However, outbreaks of IPA are rare, and the majority of IPA cases occur sporadically. In addition, since little is known about the incubation period of IPA, it is very possible that infections identified in the healthcare facility are acquired outside the hospital. This may occur prior to admission in the ambulatory-care period when patients are still receiving treatment for the underlying disease (outside the hospital setting), or after discharge, during the periods of acute and chronic GVHD that occur many months after transplantation. (672)

V. Control Measures

A. Prevention of Patient Exposure to *Aspergilllus* spp.

Most prevention studies have focused on prevention of IPA in the hospital setting. However, *Aspergillus* spp. are among the most common molds found in the environment, and the period of high risk for IPA among organ-transplant, especially HSCT, patients extends beyond their hospital stay. Therefore, in developing strategies to prevent IPA in HSCT patients, infection control personnel have to consider not only the patient's exposures to the fungus during the patient's immediate post-transplantation period spent in the hospital, but also other exposures (e.g., in ambulatory-care settings) during a later period when the patient, especially the allogeneic HSCT recipient, may again manifest severe neutropenia. Preventing patient exposures to *Aspergillus* spp. outside the hospital is difficult; however, healthcare providers should focus on decreasing the patient's exposure to dusty environments and reducing or eliminating obvious sources or reservoirs of *Aspergillus* spp., such as by removing plants and flowers from rooms where high-risk patients reside or receive medical treatment. (493;576)

In the hospital setting, the provision of a "protective environment" (PE) to house the severely immunosuppressed patient, especially the allogeneic HSCT recipient, has been the cornerstone of prevention of IPA and other airborne infections. Although the exact configuration and specifications of the PE may vary between hospitals, this patient-care area is built to minimize fungal spore counts in air by maintaining a) central or point-of-use high-efficiency particulate air (HEPA) filtration, b) high rates of room-air changes ($\geq$12 per hour), c) directed airflow, incoming at one side of the room and outgoing on the opposite side of the room, d) positive room-air pressure relative to the corridor, and e) well-sealed rooms. (644;673-681) In the 1970s and 1980s, a PE usually was a room with laminar airflow (LAF) consisting of a bank of filters along an entire wall through which air is pumped by blowers into the room at a uniform velocity (90 $\pm$ 20 feet/minute), forcing the air to move in parallel streams or a laminar pattern. (682) The air usually exits at the opposite end of the room, and ultra-high air-change rates (100-400 per hour) are achieved. (644;683) The net effects are essentially

sterile air in the room, minimal air turbulence, minimal opportunity for microorganism build-up, and a consistently clean environment. (644)

The efficacy of an LAF in decreasing the risk of nosocomial aspergillosis in HSCT recipients was demonstrated in one hospital (592) and during outbreaks of aspergillosis related to hospital construction in others. (653;677) However, a resultant reduction in patient morbidity and/or mortality with such a costly and difficult-to maintain system has not been shown conclusively. (684;685) In addition, the past preference for LAF in PE for allogeneic HSCT recipients with aplastic anemia and HLA-identical sibling donors stemmed from the association of the use of regular rooms with a patient mortality rate that was about four times higher than that in patients treated in rooms with LAF. (686) Since the late 1990s, however, the survival of HSCT recipients with aplastic anemia has far exceeded that reported in the 1980s, and no study has been done to determine whether the use of PE with LAF for these patients would result in further improvement in survival. Furthermore, placement of HSCT recipients in a PE with LAF (or HEPA filters) cannot protect the patients against late-occurring invasive aspergillosis (650) and has not been evaluated in solid-organ transplant recipients. Thus, at present, the cost-benefit ratio of utilizing PE with LAF, even for allogeneic HSCT recipients, may not justify its routine use.

The benefit of routinely placing immunosuppressed patients other than allogeneic HSCT recipients in PE has not been shown either. (681) Less expensive alternative systems with lower rates of air changes per hour (but maintained at $\geq$12 per hour) have been used in some centers. (674;675;687-689)

Preventing exposure to aspergillus spores in the healthcare facility also involves the prevention of exposure to hospital demolition, construction, renovation, and dust-generating cleaning activities. (655;660) Recommended measures have been published. (492;655;660;690) In summary, during construction or renovation, facility planners should a) intensify efforts to seal off the transplant unit and keep potentially spore-bearing air from the construction or renovation site from infiltrating the rooms or areas where severely immunosuppressed patients are housed; (691;692) b) clean newly constructed or renovated areas before allowing immunosuppressed patients to enter them, c) minimize aerosolization of *Aspergillus* spores during unit cleaning by using vacuums with HEPA filters and cloth wipes and mop heads that have been premoistened with an FDA-approved hospital disinfectant; (693) and d) allow HSCT recipients to leave the PE only for essential procedures that cannot be performed in the patient rooms, and when the patients must leave the PE, they should be provided with respiratory protection. The most cost-effective respiratory protection for patients who leave their PE has not been determined. In one recent study, however, the use of high-efficiency masks by neutropenic patients who left their hospital rooms during a period of hospital construction was associated with a lower incidence of IPA compared to that during a historical control period. (1065) Although the independent role of the patients' use of high-efficiency masks in the prevention of IPA was not clearly shown this study, it may be prudent, nevertheless, to make immunocompromised patients use a high-efficiency mask, e.g., an N95 respirator, upon leaving their PEs during times when the levels of fungal spores in the environment are expected to be high, i.e., during times of construction, demolition, renovation, or other dust-generating activity in and around the facility. (5;690) For patients who cannot use or tolerate an N95 respirator, a powered air-purifying respirator may be used as substitute. (5)

The use of copper-8-quinolinolate, a topical fungicide that has been used on environmental surfaces contaminated with *Aspergillus* spp. to control a reported outbreak (694) and incorporated in paint or fireproofing material of newly constructed facilities (653;675) may help decrease the environmental spore burden.

B. Modification of Host Risk for Infection

Due to the difficulty of preventing patient exposures to *Aspergillus* spp. in the environment, prevention efforts may be augmented by using chemoprophylaxis to decrease the patient's risk for IPA. Antifungal drug prophylaxis has been used to prevent invasive aspergillosis, but few large comparative trials have been conducted and its usefulness remains controversial. In one meta-analysis, the authors concluded that routine prophylaxis is unjustified. (695) More recently, the results of a large comparative trial suggested that itraconazole oral suspension offers greater protection against aspergillosis than does fluconazole; (696); another study suggested that

itraconazole solution (2.5 mg/kg of body weight twice a day) is at least as effective as oral amphotericin B (500 mg four times a day) in reducing the incidence of proven systemic fungal infection as well as the number of deaths from invasive aspergillosis. (697) In one trial with historical controls, the use of low-dose amphotericin B (up to 0.25 mg/kg/day) prophylaxis reduced deaths from aspergillosis among BMT recipients. (698) However, numerous anecdotal reports of breakthrough invasive aspergillosis occurring while patients are on low-dose parenteral amphotericin B suggest that this form of prophylaxis may be only partially effective. Lipid-based formulations of amphotericin B are less nephrotoxic but significantly more expensive and have not been shown to provide effective prophylaxis. (699) The efficacy of nebulized amphotericin B administered by inhalation as prophylaxis is also unproven. (700;701)

Relapse of invasive aspergillosis, including IPA, occurred after HSCT receipt in about 33% of patients who had previous aspergillosis. (702) Some centers have used either prophylactic intravenous amphotericin B and surgical removal of potentially infected parts of the lung prior to the transplantation, or intravenous amphotericin or itraconazole until the resolution of neutropenia; however, the effectiveness of these measures needs further evaluation. (643;703-705)

VIRAL PNEUMONIA

Viruses can be an important and often underestimated cause of healthcare-associated pneumonia. (706-709) In one prospective study of endemic healthcare-associated infections, approximately 20% of patients with pneumonia had viral infections. (707) Despite advances in diagnosis and treatment of viral respiratory infections, most cases remain undiagnosed and many patients in healthcare facilities remain at high risk for developing severe and sometimes fatal viral infections. (706;710-719) The potential for prolonged patient hospitalization and its attendant increased healthcare costs, the high risk for serious complications of infection for some patients, and the occurrence of nosocomial outbreaks (720;721) underscore the importance of implementing measures to prevent the transmission of respiratory viruses in healthcare facilities.

Healthcare-associated viral respiratory infections 1) usually follow community outbreaks that occur during particular periods every year, (721-725) 2) affect healthy and ill persons, (712;713;726-729) and 3) are usually introduced into healthcare facilities by patients, personnel, or visitors who have acute infections. (730) A number of viruses, including adenoviruses, influenza virus, measles virus, parainfluenza viruses, respiratory syncytial virus (RSV), rhinoviruses, and varicella-zoster virus, can cause healthcare-associated pneumonia. (713;721;730-739) However, adenoviruses, influenza viruses, parainfluenza viruses, and RSV account for most (70%) cases of healthcare-associated pneumonia due to viruses. (740)

This section focuses on the principles and approaches to control healthcare-associated adenovirus, parainfluenza, and RSV infections. Prevention of healthcare-associated influenza is discussed in another section in this document; infections due to other respiratory viral pathogens are addressed in another publication. (256)

RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION

I. Epidemiology

RSV is most noted for causing serious disease during infancy and early childhood. However, infection with RSV confers only limited protective immunity; thus, persons can be repeatedly infected and develop serious disease throughout life. (741-744) The most common manifestation of infection is a mild to moderately severe upper respiratory tract illness, but serious lower respiratory tract disease, e.g., pneumonia or bronchiolitis, can develop in some persons, especially infants, children, and persons with compromised cardiac, pulmonary, or immune systems. (712;714;729;732;745-747) RSV infection in recipients of HSCT has been associated with mortality rates of >50%. (747)

RSV transmission in healthcare settings usually occurs during yearly community outbreaks of RSV infection between December and March and are associated with marked increases in hospitalizations and deaths from pneumonia and bronchiolitis in young children. (742;748) During community outbreaks of RSV infection, children with symptoms of lower respiratory tract disease who are admitted to healthcare facilities often are infected with RSV and can introduce RSV into the healthcare facility. (720;749) RSV-infected personnel and visitors can also introduce RSV into healthcare facilities.

II. Diagnosis

The clinical characteristics of RSV infection are often indistinguishable from those of other viral respiratory tract infections, although an increase in cases of bronchiolitis in young children is highly suggestive of a community outbreak of RSV infection. (750-752) During laboratory-documented community outbreaks of RSV infection, pneumonia or bronchiolitis in a young child can be assumed to be caused by RSV for infection control purposes. In the neonate, the immunosuppressed patient, and the elderly, however, suspicion of RSV infection can be confounded. The RSV-infected neonate can present not so much with respiratory symptoms as with nonspecific symptoms and signs such as poor feeding, increased irritability and apnea, bradycardia, and difficulty breathing. (732;753) The RSV-infected elderly patient can present with exacerbation of underlying cardiac or pulmonary disease and may not be suspected of having a respiratory infection. (754;755) The immunosuppressed patient can remain infected and shed virus for prolonged periods of time without symptoms. (712;756)

Laboratory methods available to diagnose RSV and other viral respiratory infections include traditional tissue culture, shell-vial tissue culture, antigen detection assays, polymerase chain reaction (PCR) assays, and serologic assays. The optimal method for diagnosing infection varies with the patient's age. (745;757;758) In general, diagnostic assays are effective in detecting acute infection in infants and young children, but are relatively insensitive in older children and adults. For example, in infants <6 months of age, virus detection by tissue-culture isolation, antigen detection, or PCR studies is substantially more sensitive than that by serologic tests (i.e., tests to detect a rise in antibody titer between acute- and convalescent-phase serum specimens). (759;760) In previously infected persons and in older children and adults, virus detection is progressively less sensitive; and in adults, serologic studies are substantially more sensitive than virus detection. (758;761) The PCR assay for viral RNA is generally more sensitive than either tissue culture isolation or antigen detection; (761;762) however, its sensitivity in comparison to serology in older children and adults is still unknown.

When specimens are handled appropriately, tissue culture isolation is highly sensitive and specific for detecting infection in infants and young children. Whereas standard viral-isolation studies take days to weeks to detect RSV, the newer shell-vial isolation system can detect RSV within 24 to 48 hours. (763;764)

The most rapid way to detect RSV infection (i.e., in <24 hours) is by antigen-detection using immunofluorescence, enzyme-linked immunoassay, or radioimmunoassay. The reported sensitivity and specificity of these tests, however, can vary between 80% and 95% and may even be lower in

actual practice. (730;765-769)

III. Modes of Transmission

RSV is transmitted during close contact with infected persons, probably most commonly by autoinoculation of infectious secretions that are picked up on hands (directly from the infected person or indirectly from fomites contaminated with the infected person's virus-laden secretions) and deposited onto the conjunctiva or respiratory mucosa; and possibly, but less likely, by droplet spread, i.e., direct deposition of RSV on a person's conjunctiva or respiratory mucosa, from large droplets generated by an infected person's cough or sneeze. (562;749;770;771) Patients can also be infected with RSV when contaminated objects, or hands of other persons such as healthcare providers, touch their conjunctiva or respiratory mucosa. Although RSV is a relatively labile virus and can be inactivated by soap and water and a wide range of disinfectants, (772) it can remain infectious on environmental surfaces for up to 6 hours, sufficiently long to allow the occurrence of transmission via fomite. (771) In studies of RSV outbreaks in healthcare facilities, it is often possible to identify multiple strains of RSV, indicating that multiple sources introduce the virus into the facility. (726;728;773;774) During community outbreaks, RSV-infected patients, healthcare personnel, and visitors are all potential sources of the virus. (775) Infected infants, however, are probably the most effective sources of RSV because they shed high titers of the virus for prolonged periods, and therefore, present a greater chance of contaminating other persons or their environment with infectious respiratory secretions. (776) Healthcare personnel may become infected after exposure in the community (777) or in the healthcare facility, and in turn, infect patients, other healthcare personnel, or facility visitors. (733;778) Patients with suppressed immune systems can remain infectious for prolonged periods of time and be intermittently positive for RSV.

IV. Control Measures

Various combinations of control measures ranging from the simple to the complex have shown some degree of effectiveness in preventing RSV infection and controlling RSV transmission in healthcare facilities.(257;718;778-786) Successful programs have had two elements in common: implementation of standard and contact precautions, (256) and healthcare personnel compliance with these precautions. These precautions include a) hand decontamination with soap and water or a waterless antiseptic agent after touching respiratory secretions or secretion-contaminated items, whether or not gloves are worn, immediately afer gloves are removed, and between patient contacts; (255) b) gloving (with clean, nonsterile gloves) when touching respiratory secretions and contaminated items or before touching mucous membranes, and removing gloves promptly after use, before touching contaminated items and environmental surfaces, and before going to another patient; c) gowning (with a clean, nonsterile gown) during procedures or patient-care activities that are likely to cause soiling of clothing or skin with respiratory secretions, and removing a soiled gown as promptly as possible; d) masking and wearing an eye protector during procedures and patient-care activities that are likely to generate sprays of respiratory secretions; and e) handling used patient-care equipment soiled with respiratory secretions in a manner that prevents skin and mucous membrane exposures, contamination of clothing, or transfer of the virus to other patients and environments. (256) Other precautions include a) cohorting, i.e., placing the infected patient in a private room or in a room with other patients infected with RSV only; and b) limiting patient movement and transport from the room to essential purposes only.

Additional measures may be indicated to control ongoing transmission of RSV in healthcare settings or to prevent transmission to patients at high risk for serious complications of infections, such as those with compromised immune, cardiac, or pulmonary systems. The following additional control measures have been used in various combinations: a) pre-admission screening of patients for RSV infection by rapid laboratory diagnostic tests; b) cohorting of personnel; c) exclusion of healthcare personnel who have symptoms of respiratory tract infection from the care of patients at high risk of severe or fatal RSV infection, e.g., infants, immunocompromised persons such as hemopoietic stem-cell transplant recipients, persons in advanced stages of HIV infection, or persons on prolonged corticosteroid therapy; d) limiting visitors to only those who do not have symptoms of a respiratory tract infection; and e) postponing elective admission of patients at high risk for complications from RSV infection. (718;730;779;782;784) Although the exact role of each of these measures in preventing RSV transmission has not been determined, their use for control of outbreaks seems

prudent.

Recently, two products, immune globulin intravenous (IGIV) with a high titer of RSV neutralizing antibody, and an intramuscular preparation of a humanized monoclonal antibody that neutralizes RSV, have been licensed by the Food and Drug Administration (FDA) and recommended for the prevention of hospitalizations for RSV lower respiratory tract disease in high-risk premature infants, i.e. those born prematurely (at 32 weeks or less of gestational age), and infants who have chronic lung disease. (787) Because these antibody preparations have been shown to prevent hospitalizations for RSV lower respiratory tract disease but not RSV infection, (788-790) their potential effectiveness in controlling nosocomial outbreaks of RSV infection is questionable. Furthermore, the high cost of these products probably makes their use impractical for control or prevention of healthcare-facility outbreaks. Two published cost-benefit studies of the prophylactic treatment have divergent conclusions: one study suggested that the preparations are cost-beneficial when given as recommended in the infant and young child; the other suggested otherwise. (791;792) In the setting of a healthcare-related RSV outbreak, it would seem prudent for attending clinicians to review the status of each hospitalized child and consider the administration of prophylactic RSV antibody preparation to those for whom such prophylaxis is otherwise recommended. (792)

HUMAN PARAINFLUENZA VIRUS INFECTIONS

I. Epidemiology

All four serotypes of human parainfluenza viruses (HPIV 1-4) are associated with a similar range of respiratory tract illnesses, including upper respiratory tract disease, e.g., a cold and/or sore throat; and serious lower respiratory tract illness such as croup, pneumonia, and bronchiolitis. (793) Taken together, the four serotypes of HPIV account for nearly as many cases of respiratory tract disease in children as does RSV. (793-797) HPIV disease is most common in children, but as with RSV, infection confers only limited protective immunity, and persons can become infected and ill repeatedly throughout life. (798) Although the four serotypes can cause similar types of respiratory illness, they each have a unique frequency distribution of the different illnesses and have different epidemiologic features. (793;794;799;800) HPIV-1 is the leading cause of croup in children; and HPIV-2 is a common cause of croup in children. HPIV-3 is less frequently associated with croup than with bronchiolitis and pneumonia. HPIV-4 is infrequently detected presumably because it rarely causes severe disease. Since the early 1970s, the observed peaks in the number of detected cases of HPIV-1 infections in the United States have occurred in the fall of odd-numbered years; the peaks in HPIV-2 infections have occurred yearly in autumn; and peaks in HPIV-3 infections have occurred in late spring and early summer. (793;798-800) The seasonal pattern for HPIV-4 infections has not been defined because of the infection's infrequent detection and the paucity of groups that study the infection.

II. Diagnosis

The patterns of sensitivity of the various laboratory tests for diagnosing HPIV infections simulate those for RSV infections. The sensitivity of serologic tests is low in infants <6 months of age and high in older children and adults, whereas the sensitivity of virus detection by tissue-culture isolation or antigen-detection assays is high in infants and young children and low in adults. (801-803) PCR assays appear to be the most sensitive test for detection of infection in infants and young children; (762;804) however, it is not known whether PCR assays are as sensitive as serologic tests for detecting infection in adults.

III. Modes of Transmission

The modes of transmission of HPIVs have not been well studied but are likely to be similar to those of RSV, i.e., by direct and indirect contact and by large-droplet transmission. The virus is probably transmitted most often when HPIV-contaminated hands or objects touch a susceptible person's eyes, nose, or possibly mouth. Hands or objects can be contaminated directly from secretions of infected persons or by fomites previously contaminated by secretions from infected persons. Droplet transmission may possibly occur when HPIV-laden secretions generated by cough or sneeze from an infected person are directly deposited onto a susceptible person's conjunctivae or nose (or possibly mouth).

IV. Control Measures

The control measures described in the preceding section, "Prevention and Control of RSV Infection," are also applicable for prevention and control of HPIV infections in healthcare settings.

ADENOVIRUS INFECTION

I. Epidemiology

Adenovirus infections occur predominantly in childhood and cause acute upper respiratory illness. (805) Infections may be asymptomatic (806) and infected individuals may shed the virus for months or even years. (807;808) Respiratory disease caused by adenovirus is most prevalent in late winter, spring, and early summer, (806) but it has been observed year-round. Forty-nine species of adenovirus are known to cause human infection, although not all species cause respiratory illnesses. (808) Adenovirus infection of the respiratory tract can lead to symptoms of pharyngitis, (806;809) bronchitis, (806) croup, (806) or pneumonia. (806;810-813) Adenoviruses may also cause diarrhea (814) or conjunctivitis. (806;809;815-817) More serious complications leading to higher morbidity and mortality rates can occur in immunocompromised patients, (818-823) premature infants,(821) and patients with underlying pulmonary or cardiac disease. (806;824) These patients may shed the virus for extended periods of time during which they are likely to infect other high-risk patients. (821;825;826) Adenovirus can also remain latent within lymphatic tissue and become reactivated later upon immunosuppression of the host. (808)

Nosocomial outbreaks of adenovirus infection leading to pneumonia (812;813;826) have occurred in institutional healthcare settings such as intensive care units, (825;826) pediatric chronic care facilities, (827-829) military hospitals, (830) and other healthcare establishments. (812;813) Infection may be introduced from the community into a hospital setting via staff, patients, or visitors.

II. Diagnosis

Clinical signs and symptoms of adenoviral respiratory infections are usually indistinguishable from those of other viral or bacterial respiratory infections. (831) However, respiratory illness in the presence of conjunctivitis is highly suggestive of adenovirus infection. Adenovirus infection can be confirmed by detecting the virus, its antigens, or its DNA, or by detecting a serologic response to infection. The virus is most often isolated from respiratory tract specimens (e.g. nasal swabs or washings, throat swabs, sputum, or bronchoalveolar lavage specimens), ocular specimens in patients with conjunctivitis, or stool specimens. Successful isolation of adenovirus in tissue culture is most likely during the patient's first week of illness. Adenovirus antigens can also be demonstrated in the above-noted specimens by enzyme immunoassay, radioimmunoassay, or immunofluorescence, and adenovirus DNA, by probe hybridization or PCR assays. (832;833) Antigen or viral DNA detection assays have good sensitivity and can be completed in a timely fashion. Serologically, infection can be demonstrated by detecting a 4-fold rise in complement-fixing, binding (e.g., by immunofluorescence or enzyme immunoassays), neutralizing, or hemagglutination-inhibiting antibodies. (808;834) The complement-fixation and binding assays are not serotype-specific but the neutralization and hemagglutination assays are. Endonuclease restriction, PCR, and sequence studies have been used to define distinct strains within adenovirus serotypes and can be used to help confirm linkages between isolates. (833;835-837)

III. Modes of Transmission

The modes of adenovirus transmission have been studied during outbreaks of adenovirus epidemic keratoconjunctivitis or pharyngoconjunctival fever. In these outbreaks, shedding of adenovirus was demonstrated from 3 days before to 14 days after onset of symptoms; viral transmission to contacts was very efficient. (815;838-841) Transmission appears to occur by autoinoculation onto the mucous membranes of the mouth, with hands that have been contaminated with infectious material, such as secretions from the respiratory tract or eye. The virus can also be transmitted by droplets. (813) Transmission by aerosol, the fecal-oral route, contaminated water, and possibly through sexual contact has been suggested, (813;816;842-847) but the exact roles of these modes of transmission in adenovirus-respiratory tract infections is unknown. Since the virus can remain stable on environmental surfaces for prolonged periods of time, fomites are important in the transmission of adenoviruses. (848-851) For example, adenovirus has been reported to retain viability up to 49 days on nonporous surfaces such as plastic or metal and 8 to 10 days on cloth and paper. (848) Because adenovirus is a non-enveloped virus, it is not inactivated by detergents but can be inactivated by

70%-alcohol or chlorox solutions. (809;838;852;853)

IV. Prevention and Control

Control of healthcare-associated outbreaks of adenovirus infections can be very difficult and requires vigorous infection-control procedures, primarily because of the virus' ability to survive for long periods in the environment. (827;830;838-840;854-856) A number of infection control strategies have been studied; strict contact isolation precautions with careful attention to potential transmission by fomites, combined with droplet precautions, have been the key to successful control of transmission in healthcare settings. These measures include use of single-dose drug vials of medicines, careful review of procedures to decontaminate medical and other devices to ensure inactivation of adenovirus, cohorting of patients, use of separate waiting areas in outpatient clinics for infected patients, and postponement of elective admissions to the unit(s) where infected persons are housed. (857;858)

INFLUENZA

I. Epidemiology

Pneumonia in patients with influenza may be due to the influenza virus itself, a secondary bacterial infection, or a combination of both. (859-861) Influenza-associated pneumonia (as well as other influenza complications) can occur in any person but are more common in the very young or old and in persons in any age group with immunosuppression or certain chronic medical conditions, such as severe underlying heart or lung disease. (743;862-868)

Influenza typically occurs annually in the winter from December through April; peak activity in a community usually lasts from 6 to 8 weeks. (869;870) During influenza epidemics in the community, outbreaks in healthcare institutions can occur and are often characterized by abrupt onset and rapid transmission of the infection. (871-875) Most reported institutional outbreaks of influenza have occurred in nursing homes; (876-883) however, outbreaks also have been reported on pediatric and chronic care wards, HSCT units, and medical and neonatal intensive care units. (721;868;872;884)

Influenza is transmitted from person to person primarily via virus-laden large droplets that are generated when infected persons cough, sneeze, or talk; these large droplets can then be directly deposited onto the mucosal surfaces of the upper respiratory tracts of susceptible persons who are near the droplet source. Transmission also may occur by direct (e.g., person-to-person) or indirect (person-object-person) contact. Influenza virus can survive for 24-48 hours on nonporous surfaces and 8-12 hours on porous surfaces such as paper or cloth and can be transmitted to the hands from these surfaces. (885) Airborne transmission by droplet nuclei has been suggested, albeit inconclusively, in some reports; (886-888) however, this route is probably less important than person-to-person spread by either droplet or contact transmission. (889)

The most important reservoirs of influenza virus are infected persons. Infected persons are most infectious during the first 3 days of illness; however, they can shed the virus beginning the day before, and up to 7 or more days after, onset of symptoms. (731;890;891) Children and severely immunodeficient persons may shed virus for longer periods. (892-895) In addition, asymptomatic persons who are infected with influenza virus can shed the virus and potentially be infectious. (896)

II. Diagnosis

Clinically, influenza may be difficult to distinguish from febrile respiratory illnesses caused by other pathogens. During periods when influenza viruses are circulating in the community, clinical definitions that include fever and respiratory symptoms may have positive predictive values ranging from 30% to 81%. (897;898) In addition, infants can manifest a sepsis-like syndrome and 40% of young children can have vomiting or diarrhea. (899;900) Clinically defined influenza-like illness, however, can be useful for evaluating control measures during hospital or nursing-home outbreaks with laboratory-confirmed cases of influenza illness. (901)

Influenza can be diagnosed by virus isolation from respiratory secretions or by serologic conversion; however, recently developed rapid diagnostic tests can allow faster diagnosis and earlier treatment of influenza illness and facilitate prompt initiation of antiviral prophylaxis as part of outbreak control. (902-905) Because rapid tests are generally less sensitive than viral culture and because only viral culture can provide information on circulating influenza virus subtypes and strains, a subset of patients with suspected influenza illness should be tested by viral culture also. (902-906)

III. Surveillance

An active surveillance program for influenza-like illness can help healthcare facilities identify facility-acquired cases of influenza early in their course and prevent influenza from spreading to other patients and healthcare personnel. (907) Before the influenza season, healthcare personnel should be educated regarding recognition of influenza illness, mechanisms for reporting patients with

suspected influenza to those in charge of infection control, use of diagnostic tests for influenza, and use of droplet precautions (in addition to standard precautions) for patients with confirmed or suspected influenza. In addition, infection control personnel should determine the facility-specific threshold levels of influenza or influenza-like illness at which laboratory diagnostic testing for influenza and outbreak control measures should be initiated. For example, an investigation that includes performance of diagnostic laboratory tests on patients and personnel who have influenza-like illness should be considered upon identification of a single case of facility-acquired laboratory-confirmed influenza or a cluster (e.g., ≥3 cases) of facility-acquired influenza-like illness detected within a short period (e.g., 48-72 hours) on the same floor or unit. Laboratory testing for influenza in personnel or patients with influenza-like illness can allow prompt work exclusion of personnel infected with influenza and early initiation of appropriate patient isolation precautions.

IV. Prevention and Control of Influenza

A. Vaccination of Patients and Healthcare Personnel

Vaccination of persons at high risk for complications of influenza and persons who can transmit influenza to high-risk persons, i.e., healthcare personnel and high-risk patients' household members, is the most effective measure for reducing the impact of influenza and should be done before the influenza season each year. (906;908-911) The currently available influenza vaccine is an inactivated trivalent vaccine that is administered by the intramuscular route; a live attenuated trivalent intranasal vaccine is under development. (906) When high vaccination rates are achieved in closed or semi-closed settings, the risk of outbreaks is reduced because of the induction of herd immunity. (912;913) High-risk groups for whom annual vaccination is recommended include persons ≥65 years of age; residents of nursing homes and other long-term-care facilities; persons aged ≥6 months with chronic pulmonary or cardiovascular diseases, including asthma; persons aged ≥6 months with diabetes mellitus, renal dysfunction, hemoglobinopathies, or immunosuppression (including immunosuppression caused by medications or HIV infection); children 6 months-18 years of age who are receiving long-term aspirin therapy and are at risk for Reye syndrome; and women who will be in the second or third trimester of pregnancy during the influenza season. (906) Vaccination of all persons aged 50-64 years also is recommended because of the high prevalence of chronic medical conditions that increase the risk of severe influenza illness in this age group and because of the benefits that healthy persons 50-64 years old obtain from vaccination, i.e., decrease in the risk of influenza and its potential sequelae such as work absenteesim, medical visits, and antibiotic use. (906;914;915)

Healthcare personnel have been implicated in the transmission of influenza to patients; annual vaccination of healthcare personnel, as well as others in close contact with persons at high risk for influenza complications, is recommended. (871;872;906;907;909;916) Vaccination of healthcare personnel is associated with decreased mortality among nursing home residents (910;911) and reduced healthcare personnel illness and absenteeism. (909;917)

Influenza vaccine, however, has been underutilized in institutional settings, even after it became a covered benefit of Medicare Part B. (918) In order to improve vaccination coverage rates among adults, in March 2000, the ACIP published recommendations for the use of the Standing Orders Program (SOP), under which nurses and pharmacists are authorized to administer vaccinations according to an institution- or physician-approved protocol, without an examination of the patient by a physician. (919) ACIP recommended the use of SOP in long-term-care facilities, inpatient and outpatient facilities, managed-care organizations, assisted living facilities, correctional facilities, pharmacies, adult workplaces, and home health care agencies, (919) after SOP programs were shown to be the most effective method of increasing adult vaccination rates. (920;921)

B. Use of Antiviral Drugs

While vaccination of high-risk patients and healthcare personnel is the primary focus of efforts to prevent and control influenza in healthcare settings, the use of antiviral agents can be an important adjunct. (906) Four licensed agents are available in the United States: amantadine, oseltamivir, rimantadine, and zanamivir. Amantadine and rimantadine are chemically related drugs with activity against influenza type A, but not influenza type B. (922-924) Amantadime was approved for influenza A (H2N2) prophylaxis in 1966 and approved for both treatment and prophylaxis in 1976. Rimantadine

was approved for treatment and prophylaxis of influenza A in 1993. (906) Oseltamivir and zanamivir are neuraminidase inhibitors with activity against both influenza A and B viruses. Both drugs were approved in 1999 for the treatment of uncomplicated influenza infections, and oseltamivir was approved in 2000 for prophylaxis. (906) Zanamivir is administered as an inhaled powder while the other three drugs are ingested. The four antiviral drugs differ in age-group indications, pharmacokinetics, side effects, and cost. (906) Additional information about the drugs is available in their respective package inserts.

When administered for treatment within 2 days of illness onset, amantadine and rimantadine can reduce the duration of uncomplicated influenza A illness, and zanamivir and oseltamivir can reduce the duration of uncomplicated influenza A or B illness, by approximately one day. (906;922;923;925-929) None of the four drugs has been demonstrated to be effective in preventing serious influenza-related complications (e.g., bacterial or viral pneumonia or exacerbations of chronic illness).

When administered for prophylaxis before exposure to influenza virus type A, both amantadine and rimantadine are approximately 70-90% effective in preventing illness. (922;924;930) These drugs have been studied extensively as components of influenza-outbreak control programs in nursing homes. (880;922;931-933)

Studies in community settings suggest that oseltamivir and zanamivir are approximately 82-84% effective in preventing febrile influenza illness, although only oseltamivir is currently approved by the FDA for use as prophylaxis. (934-936) The experience with prophylactic use of these agents in institutional settings or among patients with chronic medical conditions is limited, however. (879;937-939)

Anti-influenza virus agents can be used 1) as short-term prophylaxis for high-risk persons who receive their vaccination late in the season; 2) as prophylaxis for persons for whom vaccination is contraindicated; 3) as prophylaxis for immunocompromised persons who may not produce protective levels of antibody in response to vaccination; 4) as prophylaxis, either for the duration of influenza activity in the community or until immunity develops after vaccination, for unvaccinated healthcare workers who provide care to high-risk patients; and 5) when vaccine strains do not closely match the epidemic virus strain. (906)

The decision about which antiviral agent to use as adjunct to vaccination in the prevention and control of healthcare-related influenza is based in part on virologic and epidemiologic surveillance information from the healthcare setting and the community. An antiviral agent can limit the spread of influenza in the healthcare setting if the drug is administered to all or most patients once influenza illnesses begin in the facility. (880;903;937;940;941) Therefore, if an influenza antiviral agent is to be given as prophylaxis to high-risk persons and treatment for infected persons, it should be administered as early in the outbreak as possible to reduce viral transmission. (880;903;906;940)

Side effects from influenza antiviral agents have been reported. Both amantadine and rimantadine are associated with central nervous system (CNS) side effects such as nervousness, insomnia, impaired concentration, mood changes, and light-headedness; however, amantadine is associated with a higher incidence of adverse CNS reactions (13% of healthy adults taking amantadine 200 mg/day) than is rimantadine (6% of healthy adults taking rimantadine 200 mg/day). (924;942) Gastrointestinal side effects occur in approximately 1-3% of persons taking either drug. (924) Serious side effects (e.g., marked behavioral changes, delirium, hallucinations, agitation, and seizures) have been observed mostly among persons with renal insufficiency, seizure disorders, or certain psychiatric disorders, and/or in association with high plasma concentrations. (932;940) Dose reductions of both amantadine and rimantadine are recommended for certain patient groups, such as children <10 years of age, children weighing <40 kg, persons $\geq$65 years of age, and persons with renal insufficiency.

In clinical trials, oseltamivir use was associated with nausea and vomiting although few persons discontinued its use because of these symptoms. (929;935) A reduction in the dose of oseltamivir is recommended for persons with renal insufficiency. (906)

Zanamivir was not associated with significantly different side effects compared to inhaled lactose placebo in clinical trials. (926;928;934) However, respiratory-function deterioration has been

reported in persons taking zanamivir, some of whom had underlying airway disease, e.g., asthma or chronic obstructive pulmonary disease. Because of this risk and the lack of demonstrable efficacy in persons with underlying lung disease, zanamivir is generally not recommended for persons with underlying lung disease. (943)

C. Antiviral Drug Resistance

Drug-resistant viruses can emerge in up to approximately one third of patients who are given either amantadine or rimantadine for treatment of influenza. (923;944;945) Because of the potential risk of transmission of drug-resistant viruses, infected persons taking either amantadine or rimantadine should avoid contact as much as possible with others during treatment and for 2 days after discontinuing treatment. (924;925;945-948) This is particularly important if the contacts involve uninfected high-risk persons. (947;949)

Development of viral resistance to oseltamivir and zanamivir during their use for patient treatment has been identified but does not appear to be frequent. (950-953) However, the experience with oseltamivir or zanamivir for use in influenza outbreak control and the number of tests conducted for viral resistance to either agent have been considerably less than with amantadine or rimantadine. (906) In studies using oseltamivir, 1.3% of post-treatment viral isolates from patients $\geq$13 years of age and 8.6% from patients 1-12 years old had decreased susceptibility to oseltamivir. (951) In clinical trials of zanamivir use, no isolates with reduced susceptibility have been reported and only one resistant isolate from an immune-compromised child on prolonged therapy has been reported, although only a small number of post-treatment isolates have been tested. (943;953)

D. Isolation Precautions and Other Measures

Measures in addition to vaccination and chemoprophylaxis are recommended for control of influenza outbreaks in healthcare facilities. During the patient's infectious stage, droplet precautions (i.e., placing in private rooms, when possible, or cohorting patients who are potentially infectious with influenza or have influenza-like illness; masking by personnel when performing an activity within 3 feet of a person with suspected or proven influenza; limiting to only essential purposes the movement or transport of a potentially infectious patient from his/her room; and, if movement or transport is necessary, minimizing patient dispersal of droplets by making the patient wear a mask, if possible) are recommended in addition to standard precautions for personnel (i.e., handwashing, gloving when handling the patient's respiratory secretions, and gowning when soiling with the patient's respiratory secretions is likely). (256) The added value of placing patients with influenza in negative-pressure rooms has not been assessed. Other measures, although not well studied, may be considered, particularly during severe outbreaks: 1) curtailment or elimination of elective admissions, both medical and surgical; 2) restriction of cardiovascular and pulmonary surgery; 3) restriction of hospital visitors, especially those with acute respiratory illnesses; and 4) work restriction for healthcare personnel with acute respiratory illness. (875;954)

Updated information regarding prevention and control of influenza, including the use of influenza vaccine and antiviral medications, is published annually by the ACIP in the Morbidity and Mortality Weekly Report. (906)

PART II.
RECOMMENDATIONS FOR PREVENTION OF HEALTHCARE-ASSOCIATED PNEUMONIA

Healthcare-Infection Control Practices Advisory Committee

PREVENTION OF HEALTHCARE-ASSOCIATED BACTERIAL PNEUMONIA

I. Staff Education And Infection

Educate healthcare workers regarding the epidemiology of, and infection control procedures for, preventing healthcare-associated bacterial pneumonia in such manner as to ensure worker competency according to the worker's level of responsibility in the healthcare setting.
CATEGORY IB

II. Surveillance

A. Conduct surveillance, using standardized definitions, for bacterial pneumonia in intensive care unit (ICU) patients who are at high risk for healthcare-related bacterial pneumonia (e.g., patients with mechanically assisted ventilation or selected post-operative patients) to determine trends and help identify outbreaks and other potential problems. (955-957) Include data on the causative microorganisms and their antimicrobial susceptibility patterns. (6) Express data as rates (e.g., number of infected patients or infections per 100 ICU days or per 1,000 ventilator-days) to facilitate intrahospital comparisons and trend determination. (955;958-960) Link monitored rates and prevention efforts and feed data back to appropriate healthcare workers. (956)
CATEGORY IB

B. Do not routinely perform surveillance cultures of patients or of equipment or devices used for respiratory therapy, pulmonary-function testing, or delivery of inhalation anesthesia. (961;962) *CATEGORY II*

III. Interruption of Transmission of Microorganisms

A. Sterilization or Disinfection and Maintenance of Equipment and Devices

1. General measures
   a. Thoroughly clean all equipment and devices to be sterilized or disinfected. (295-297)
      CATEGORY IA
   b. Whenever possible, use steam sterilization (by autoclaving) or high-level disinfection by wet heat pasteurization at 76^{o}C for 30 minutes for reprocessing semicritical equipment or devices (i.e., items that come into direct or indirect contact with mucous membranes of the lower respiratory tract) that are not sensitive to heat and moisture. (See examples, Appendix A). Use low-temperature sterilization methods (as approved by the Office of Device Evaluation, Center for Devices and Radiologic Health, Food and Drug Administration) for equipment or devices that are heat or moisture sensitive. (288;289;291;293;296;297;963) Follow disinfection with appropriate rinsing, drying, and packaging, taking care not to contaminate the items in the process. (297)
      CATEGORY IA
   c. When rinsing is necessary after chemical disinfection of reusable semicritical equipment and devices for use on the respiratory tract, use sterile or pasteurized (not distilled, nonsterile) water. (270;279;280;287;298)
      CATEGORY IB
   d. Comply with provisions in the Food and Drug Administration's enforcement document for single-use devices that are reprocessed by third parties. (297;964)
      CATEGORIES IB and IC
2. **Mechanical Ventilators, Breathing Circuits, Humidifiers, Heat and Moisture Exchangers, and Nebulizers**
   a. **Mechanical ventilators**
      (1) Do not routinely sterilize or disinfect the internal machinery of mechanical ventilators.
      CATEGORY IB
   b. **Ventilator circuits with humidifiers**
      (1) Do not change routinely, on the basis of duration of use, the ventilator circuit

(i.e., ventilator tubing and exhalation valve, and the attached humidifier) that is in use on an individual patient. Rather, change the circuit when it is visibly soiled or mechanically malfunctioning. (319;320;965)
CATEGORY IA

(2) Sterilize reusable breathing circuits and bubbling or wick humidifiers, or subject them to high-level disinfection between their uses on different patients. (See Recommendation II-A-1-b, above.) (288;289;291;293;296;297)
CATEGORY IB

(3) Periodically drain and discard any condensate that collects in the tubing of a mechanical ventilator, taking precautions not to allow condensate to drain toward the patient. (315) Decontaminate hands with soap and water or a waterless antiseptic agent after performing the procedure or handling the fluid. (245;255;311)
CATEGORY IA

(4) *No Recommendation* for placing a filter or trap at the distal end of the expiratory-phase tubing of the breathing circuit to collect condensate. (277;311)
UNRESOLVED ISSUE

(5) Do not place bacterial filters between the humidifier reservoir and the inspiratory-phase tubing of the breathing circuit of a mechanical ventilator. (315)
CATEGORY II

c. **Humidifier fluids**

(1) Use sterile or pasteurized water to fill bubbling humidifiers. (145;270;279;280;315)
CATEGORY IB

(2) *No Recommendation* for preferential use of a closed, continuous-feed humidification system.
UNRESOLVED ISSUE

d. **Ventilator breathing circuits with heat-moisture exchangers**

(1) When cost-effective and unless medically contraindicated, use a heat-moisture exchanger (HME) to prevent pneumonia in a patient receiving mechanically assisted ventilation. (329-332;966-968)
CATEGORY II

(2) Change an HME that is in use on a patient when it malfunctions mechanically or becomes visibly soiled.
CATEGORY IB

(3) Do not change *routinely* more frequently than every 48 hours, an HME that is in use on a patient. (969-971)
CATEGORY IB

(4) Do not change routinely (in the absence of gross contamination or malfunction) the breathing circuit attached to an HME while it is in use on a patient. (968)
CATEGORY II

3. **Wall humidifiers**

a. Follow manufacturers' instructions for use and maintenance of wall oxygen humidifiers unless data show that modifying the instructions poses no threat to the patient and is cost-effective. (972-975)
CATEGORY IB

b. Between patients, change the tubing, including any nasal prongs or mask, used to deliver oxygen from a wall outlet.
CATEGORY IB

4. **Small-volume medication nebulizers**: **"in-line" and hand-held nebulizers**

a. Between treatments on the same patient, disinfect; rinse with sterile or pasteurized water; or air-dry small-volume in-line or hand-held medication nebulizers. (271;287)
CATEGORY IB

b. Use only sterile or pasteurized fluid for nebulization, and dispense the fluid into the nebulizer aseptically. (267;270;279;280;287;298;334)

CATEGORY IA

c. If multidose medication vials are used, handle, dispense, and store them according to manufacturers' instructions. (334;976-978)
CATEGORY IB

5. **Mist tents**
   a. Use only mist-tent nebulizers and reservoirs that have undergone sterilization or high-level disinfection and replace them between patients. (979)
   CATEGORY IB
   b. *No Recommendation* regarding the frequency of routinely changing mist-tent nebulizers and reservoirs while in use on one patient. (979)
   UNRESOLVED ISSUE
6. **Other devices used in association with respiratory therapy**
   a. Between their uses on different patients, sterilize or subject to high-level disinfection portable respirometers, oxygen sensors, and other respiratory devices used on multiple patients. (274;276)
   CATEGORY IB
   b.
      (1) Between their uses on different patients, sterilize or subject to high-level disinfection reusable hand-powered resuscitation bags (e.g., Ambu bags). (339-341;980)
      CATEGORY IB
      (2) *No Recommendation* regarding the frequency of changing hydrophobic filters placed on the connection port of resuscitation bags.
      UNRESOLVED ISSUE
7. **Anesthesia machines and breathing systems or patient circuits**
   a. Do not routinely sterilize or disinfect the internal machinery of anesthesia equipment. (344)
   CATEGORY IB
   b. Between uses on different patients, clean reusable components of the breathing system or patient circuit (e.g., tracheal tube or face mask; inspiratory and expiratory breathing tubing; y-piece; reservoir bag; humidifier; and tubing) and then sterilize or subject them to high-level liquid chemical disinfection or pasteurization, in accordance with the device manufacturers' instructions for their reprocessing. (293;296;345;981)
   CATEGORY IB
   c. *No Recommendation* for the frequency of routinely cleaning and disinfecting unidirectional valves and carbon dioxide absorber chambers. (345-347)
   UNRESOLVED ISSUE
   d. Follow published guidelines and/or manufacturers' instructions regarding in-use maintenance, cleaning, and disinfection or sterilization of other components or attachments of the breathing system or patient circuit of anesthesia equipment. (345;346)
   CATEGORY IB
   e. Periodically drain and discard any condensate that collects in the tubing of a breathing circuit, taking precautions not to allow condensate to drain toward the patient. (315) After performing the procedure or handling the fluid, decontaminate hands with soap and water or with a waterless antiseptic preparation. (255)
   CATEGORY IB
   f. *No Recommendation* for placing a bacterial filter in the breathing system or patient circuit of anesthesia equipment. (5;345;346;349-354;982)
   UNRESOLVED ISSUE
8. **Pulmonary-function testing equipment**
   a. Do not routinely sterilize or disinfect the internal machinery of pulmonary-function testing machines between uses on different patients. (355;356)
   CATEGORY II
   b. Unless there is a filter between the mouthpiece and tubing of pulmonary-function testing equipment, sterilize or subject to high-level liquid-chemical disinfection or pasteurization reusable mouthpieces and tubing or connectors between uses on different patients, following the device manufacturers' instructions for their

reprocessing. (297;355;356)
CATEGORY IB

9. **Room-air "humidifiers" and faucet aerators**
   a. Do not use large-volume room-air humidifiers that create aerosols (e.g., by venturi principle, ultrasound, or spinning disk, and thus actually are nebulizers), unless they can be sterilized or subjected to high-level disinfection at least daily and filled only with sterile water. (266;268-270;283;983;984)
   CATEGORY IB
   b. Faucet aerators
      (1) *No Recommendation* on the removal of faucet aerators from areas for immunocompetent patients. (See also section on Legionnaires' Disease, Part II, Section II-C-1-d).
      UNRESOLVED ISSUE
      (2) Remove, clean, and disinfect faucet aerators (and shower heads) in transplant units monthly by using a chlorine bleach solution (i.e., 1:100 dilution of bleach) when *Legionella* spp. are not detectable in the water in these units. (See also section on Legionnaires' Disease, Part II, Section II-C-1-d).(492)
      CATEGORY II
      (3) If *Legionella* spp. are detected in the water of a transplant unit and until *Legionella* spp. are no longer detected by culture, remove faucet aerators in areas for immmunocompromised patients. (See also section on Legionnaires' Disease, Part II, Section II-C-1-d). (492)
      CATEGORY II

B. Interruption of Person-to-Person Transmission of Bacteria

1. **Standard Precautions**
   a. Hand hygiene
   Decontaminate hands with soap and water or with a waterless antiseptic agent after contact with mucous membranes, respiratory secretions, or objects contaminated with respiratory secretions, whether or not gloves are worn. Decontaminate hands, as above, before and after contact with a patient who has an endotracheal or tracheostomy tube in place, and before and after contact with any respiratory device that is used on the patient, whether or not gloves are worn. (241;243;248;249;255;256;262;985)
   CATEGORY IA
   b. Gloving
      (1) Wear gloves for handling respiratory secretions or objects contaminated with respiratory secretions of any patient. (256)
      CATEGORY IB
      (2) Change gloves and decontaminate hands, as above, between contacts with different patients; after handling respiratory secretions or objects contaminated with secretions from one patient and before contact with another patient, object, or environmental surface; and between contacts with a contaminated body site and the respiratory tract of, or respiratory device on, the same patient. (255-257;259;260)
      CATEGORY IA
   c. When soiling with respiratory secretions from a patient is anticipated, wear a gown and change it after soiling occurs and before providing care to another patient. (256;257)
   CATEGORY IB

2. **Care of patients with tracheostomy**
   a. Perform tracheostomy under sterile conditions.
   CATEGORY IB
   b. When changing a tracheostomy tube, use aseptic technique and replace the tube with one that has undergone sterilization or high-level disinfection.
   CATEGORY IB
   c. *No Recommendation* for the routine daily application of topical antimicrobial agent(s) at the tracheostoma.
   UNRESOLVED ISSUE

3. **Suctioning of respiratory tract secretions**
   (See also Section IV-B-1-d, below.)
   a. *No Recommendation* for preferential use of either the multiuse closed-system suction catheter or the single-use open-system suction catheter. (330;335;337;338)
      UNRESOLVED ISSUE
   b. *No Recommendation* on wearing sterile rather than clean gloves when performing endotracheal or tracheal suctioning.
      UNRESOLVED ISSUE
   c. If the closed-system suction is used, change the in-line suction catheter when it malfunctions or becomes visibly soiled. (336)
      CATEGORY IB
   d. If the open-system suction is employed, use a sterile single-use catheter.
      CATEGORY II
   e. Use only sterile or pasteurized fluid to remove secretions from the suction catheter if the catheter is to be used for re-entry into the patient's lower respiratory tract.
      CATEGORY IB

IV. Modifying Host Risk for Infection

A. Measures for Increasing Host Defense Against Infection

1. **Administration of immune modulators**
   a. **Pneumococcal vaccination**
      Vaccinate patients at high risk for severe pneumococcal infections with the 23-valent pneumococcal polysaccharide vaccine. High-risk patients include persons ≥65 years of age; persons aged 2-64 years who have chronic cardiovascular disease (e.g., congestive heart failure or cardiomyopathy), chronic pulmonary disease (e.g., COPD or ermphysema, but not asthma), diabetes mellitus, alcoholism, chronic liver disease (cirrhosis), or CSF leaks; persons aged 2-64 years who have functional or anatomic asplenia; persons aged 2-64 years who are living in special environments or social settings; immunocompromised persons aged ≥2 years with HIV infection, leukemia, lymphoma, Hodgkin's disease, multiple myeloma, generalized malignancy, chronic renal failure, nephrotic syndrome, or other conditions associated with immunosuppression, such as receipt of HSCT, solid-organ transplant, or immunosuppressive chemotherapy, including long-term systemic corticosteroids; and persons in long-term care facilities. (387;389-391;986)
      CATEGORY IA
   b. *No Recommendation* for the routine administration of preparations of granulocyte-colony forming factor or intravenous gamma globulin for prophylaxis against healthcare-associated pneumonia. (392-395)
      UNRESOLVED ISSUE
   c. *No Recommendation* for the routine administration of glutamine for prevention of healthcare-associated pneumonia. (396;397)
      UNRESOLVED ISSUE

B. Precautions for Prevention of Aspiration

Remove devices such as endotracheal, tracheostomy, and/or enteral (i.e., oro- or nasogastric, or jejunal) tubes from patients and discontinue enteral-tube feeding as soon as the clinical indications for these are resolved. (14;17;99;134;207;209;211;229;987-989)
CATEGORY IB

1. **Prevention of aspiration associated with endotracheal intubation**
   a. As much as possible, and unless there are medical contraindications, use noninvasive positive-pressure ventilation delivered continuously by facial or nasal mask, instead of performing endotracheal intubation, in patients with hypoxemia or acute respiratory failure. (236;237)
      CATEGORY II
   b. As much as possible, avoid subjecting patients who have received mechanically assisted ventilation to repeat endotracheal intubations. (147)
      CATEGORY IB

c. Unless contraindicated by the patient's condition, perform orotracheal rather than nasotracheal intubation on patients. (226;227;330)
CATEGORY IB

d. Use an endotracheal tube with a dorsal lumen above the endotracheal cuff to allow drainage (by continuous suctioning) of tracheal secretions that accumulate in the patient's subglottic area. (232;235;330)
CATEGORY IB

e. Before deflating the cuff of an endotracheal tube in preparation for tube removal, or before moving the tube, ensure that secretions are cleared from above the tube cuff.
CATEGORY IB

2. **Prevention of aspiration associated with enteral feeding**
   a. If there is no medical contraindication, elevate at an angle of 30-45^{o} the head of the bed of a patient at high risk for aspiration pneumonia, e.g., a person receiving mechanically assisted ventilation and/or who has an enteral tube in place. (214;218;219;988)
   CATEGORY IB
   b. Routinely verify appropriate placement of the feeding tube. (990-992)
   CATEGORY IB
   c. Routinely assess the patient's intestinal motility (e.g., by auscultating for bowel sounds and measuring residual gastric volume or abdominal girth) and adjust the rate and volume of enteral feeding to avoid regurgitation. (989)
   CATEGORY IB
   d. *No Recommendation* for the preferential use of small-bore tubes for enteral feeding. (221)
   UNRESOLVED ISSUE
   e. *No Recommendation* for preferentially administering enteral feedings continuously or intermittently. (22;204;222)
   UNRESOLVED ISSUE
   f. *No Recommendation* for preferentially placing the feeding tubes, e.g., jejunal tubes, distal to the pylorus. (223-225)
   UNRESOLVED ISSUE
3. **Prevention of oropharyngeal colonization: chlorhexidine oral rinse**
   a. *No Recommendation* on the routine use of an oral chlorhexidine rinse for the prevention of healthcare-associated pneumonia in all post-operative or critically ill patients and/or other patients at high risk for pneumonia. (155)
   UNRESOLVED ISSUE
   b. Use an oral chlorhexidine gluconate (0.12%) rinse during the perioperative period on patients who undergo cardiac surgery. (392)
   CATEGORY II
4. **Prevention of gastric colonization**
   a. Use sucralfate, H2-blockers, and/or antacids interchangeably for stress-bleeding prophylaxis in a patient receiving mechanically assisted ventilation. (191;197-200;993-995)
   CATEGORY II
   b. *No Recommendation* for the routine selective decontamination of the digestive tract (SDD) of all critically ill, mechanically ventilated, or ICU patients to prevent gram-negative bacillary (or *Candida* spp.) pneumonia. (156-187)
   UNRESOLVED ISSUE
   c. *No Recommendation* for routine acidification of gastric feeding. (202)
   UNRESOLVED ISSUE

C. Prevention of Postoperative Pneumonia

1. Instruct preoperative patients, especially those at high risk of contracting pneumonia, regarding taking deep breaths and ambulating as soon as medically indicated in the postoperative period. (376;377;379) High-risk patients include those who will have an abdominal, thoracic, head, or neck operation or who have substantial pulmonary dysfunction, such as patients with COPD, a musculoskeletal abnormality of the chest, or abnormal pulmonary function tests. (361-363;368;369)
CATEGORY IB
2. Encourage all postoperative patients to take deep breaths, move about the bed, and

ambulate unless it is medically contraindicated. (376;377;379;382)
CATEGORY IB

3. Use incentive spirometry on postoperative patients at high risk of developing pneumonia. (See II-B-1, above). (382)
CATEGORY IB

D. Other Prophylactic Procedures for Pneumonia

1. **Administration of antimicrobial agents other than in SDD**
   a. **Systemic antimicrobial prophylaxis**
   Do not routinely administer systemic antimicrobial agents to critically ill or other patients to prevent healthcare-associated pneumonia. (228;398-405)
   CATEGORY IB
   b. *No Recommendation* for a scheduled change in the class of antibiotic that is used for empiric treatment of suspected infections in a particular group of patients. (407)
   UNRESOLVED ISSUE
2. **Use of rotating "kinetic" beds or continuous lateral rotational therapy**
No Recommendation for the routine use of "kinetic" beds or continuous lateral rotational therapy (i.e., placing patients on beds that turn on their longitudinal axes intermittently or continuously) for prevention of healthcare-associated pneumonia in critically ill and/or immobilized patients. (408;410-412;414;419)
UNRESOLVED ISSUE

PREVENTION AND CONTROL OF HEALTHCARE-ASSOCIATED LEGIONNAIRES' DISEASE

I. **Primary Prevention** (Preventing Healthcare-Associated Legionnaires' Disease When No Cases Have Been Documented)

A. Staff Education

Educate according to their level of responsibility in the healthcare setting:

1. physicians, to heighten their suspicion for cases of healthcare-associated Legionnaires' disease and to use appropriate methods for its diagnosis, and
2. patient-care, infection-control, and engineering personnel about measures to control healthcare-associated legionellosis.
   CATEGORY IB

B. Infection and Environmental Surveillance

1. Maintain a high index of suspicion for the diagnosis of healthcare-associated Legionnaires' disease and perform laboratory diagnostic tests for legionellosis on suspected cases, especially in patients who are at high risk of acquiring the disease (e.g., patients who are immunosuppressed, including HSCT or solid-organ-transplant recipients; patients receiving systemic steroids; patients ≥65 years of age; or patients who have chronic underlying disease such as diabetes mellitus, congestive heart failure, and chronic obstructive lung disease).
   (422;438;440;441;447;456;502;503;996;997)
   CATEGORY IA
2. Frequently review the availability and clinicians' use of laboratory diagnostic tests for Legionnaires' disease in the facility, and if clinicians' utilization of the tests on patients with diagnosed or suspected pneumonia is low, implement measures to enhance clinicians' use of the tests, e.g., by conducting educational programs. (425;442)
   CATEGORY IB
3. **Routine culturing of water systems for *Legionella* spp.**
   a. *No Recommendation* on routine culturing of water systems for *Legionella* spp. in healthcare facilities that do not have patient-care areas (i.e., transplant units) for persons at high risk for *Legionella* infection.
      (300;423;473;478;481;482;484;485;492;510;998)
      UNRESOLVED ISSUE
   b. In facilities with HSCT and/or solid-organ transplant programs, perform periodic culturing for legionellae in water samples from the transplant unit's potable water supply (494;999) **as part of a comprehensive strategy** to prevent Legionnaire's disease in transplant units. (492;493)
      CATEGORY II
   c. If such culturing (as in b, above) is undertaken:
      (1) *No Recommendation* on the optimal methods (i.e., frequency, number of sites) for environmental surveillance cultures in transplant units.
      UNRESOLVED ISSUE
      (2) Perform corrective measures aimed at maintaining undetectable levels of *Legionella* spp. in the unit's water system.
      CATEGORY II
      (3) Maintain a high index of suspicion for legionellosis in transplant patients with healthcare-associated pneumonia even when environmental surveillance cultures do not yield legionellae. (425;441)
      CATEGORY IB

C. Use and Care of Medical Devices, Equipment, and Environment

1. **Nebulizers and other devices**
   a. Use sterile or pasteurized (not distilled, nonsterile) water for rinsing nebulization devices and other semicritical respiratory-care equipment after they have been cleaned and/or disinfected. (287;1000)
      CATEGORY IA
   b. Use only sterile or pasteurized (not distilled, nonsterile) water to fill reservoirs of devices used for nebulization. (270;283;287;300;1000)
      CATEGORY IA

c. Do not use large-volume room-air humidifiers that create aerosols (e.g., by venturi principle, ultrasound, or spinning disk) and thus are really nebulizers, unless they can be sterilized or subjected to high-level disinfection daily and filled only with sterile water. (283;1000)
CATEGORY II

d. Faucet aerators and other aerosol-generating devices
   (1) *No Recommendation* on the removal of faucet aerators from areas for immunocompetent patients. (See also Bacterial Pneumonia, Part II, section III-A-9-b).
   UNRESOLVED ISSUE
   (2) When *Legionella* spp. are not detectable in the water in transplant units, remove, clean, and disinfect tap aerators and shower heads in these units monthly by using a chlorine bleach solution (i.e., 1:100 dilution of bleach). (492)
   CATEGORY II
   (3) If *Legionella* spp. are detected in the water of a transplant unit and until *Legionella* spp. are no longer detected by culture, remove faucet aerators in areas for immmunocompromised patients. (492)
   CATEGORY II

2. **Cooling towers**
   a. When a new building is constructed, place cooling towers in such a way that the tower drift is directed away from the facility's air-intake system and design the cooling towers such that the volume of aerosol drift is minimized. (466;490;1001)
   CATEGORIES IA and IC
   b. For cooling towers, install drift eliminators, regularly use an effective biocide, maintain the tower according to manufacturers' recommendations, and keep adequate maintenance records. (466;490;1002)
   CATEGORIES IB and IC
3. **Water-distribution system**
   a. Where practical and allowable by state law, (511) maintain potable water at the outlet at $\geq 51^{o}C$ ($\geq 124^{o}F$) or $<20^{o}C$ ($<68^{o}F$), especially in facilities housing organ-transplant recipients or other high-risk patients. (423;473;485;490;497;499;500) (If water is maintained at $\geq 51^{o}C$, use thermostatic mixing valves to prevent scalding.) (496)
   CATEGORY II
   b. *No Recommendation* on treatment of water with ozone, ultraviolet light, heavy-metal ions, or monochloramine. (512;514-517;523;524;527;1003-1006)
   UNRESOLVED ISSUE
4. **Healthcare facilities with HSCT and/or solid-organ transplant programs**
   If legionellae are detected in the potable water supply of a transplant unit, and until legionellae are no longer detected by culture:
   a. Decontaminate the water supply as per section II-B-2-b-(3)-(a).
   CATEGORY IB
   b. Restrict severely immunocompromised patients from taking showers. (469)
   CATEGORY IB
   c. Use water that is not contaminated with *Legionella* spp. for HSCT patients' sponge baths.
   CATEGORY IB
   d. Provide HSCT patients with sterile water for tooth brushing, drinking, and for flushing nasogastric tubes. (471;474;690;1007)
   CATEGORY IB
   e. Remove aerators from faucets and avoid the use of water from faucets.
   CATEGORY II

II. **Secondary Prevention** (Response to Identification of Laboratory-Confirmed Healthcare-Associated Legionellosis)

A. In Facilities with HSCT and/or Solid-Organ Transplant Patients:
When one inpatient of an HSCT and/or solid-organ transplant unit develops a case of laboratory-confirmed **definite** (i.e., after $\geq$10 days of continuous inpatient stay) or

possible (i.e., within 2-9 days of inpatient stay) healthcare-associated Legionnaires' disease, or when two or more patients develop laboratory-confirmed Legionnaires' disease within 6 months of each other and after having visited an outpatient transplant unit during part of the 2-10 day period prior to illness onset:

1. Contact the local or state health department or CDC if the disease is reportable in the state or if assistance is needed.
   CATEGORIES II and IC
2. In consultation with the facility's infection control team, conduct a combined epidemiologic and environmental investigation (as outlined from II-B-2-b-(1) through III-B-2-b-(5), below) to determine the source(s) of *Legionella* spp. (493) Include, but not limit the investigation to, such potential sources as showers, water faucets, cooling towers, hot water tanks, and carpet cleaner water tanks. (442;453;503) Upon its identification, decontaminate and/or remove the source of *Legionella* spp.
   CATEGORY II
3. If the healthcare facility's potable water system is found to be the source of *Legionella* spp., observe the measures outlined in Section I-C-4, above, regarding the non-use of the facility's potable water by HSCT and solid-organ transplant recipients and decontaminate the water supply as per Section II-B-2-b-(3)-(a)-*i* to *iv*, below.
   CATEGORY IB
4. Do not conduct an extensive facility investigation when an isolated case of possible healthcare-associated Legionnaires' disease occurs in a patient who has had little contact with the inpatient transplant unit during most of the incubation period of the disease.
   CATEGORY II

B. In Facilities That Do Not House Severely Immunocompromised Patients, such as HSCT or Solid-Organ Transplant Recipients:

When a single case of laboratory-confirmed, **definite** healthcare-associated Legionnaires' disease is identified, OR when two or more cases of laboratory-confirmed, **possible** healthcare-associated Legionnaires' disease occur within 6 months of each other:

1. Contact the local or state health department or CDC if the disease is reportable in the state or if assistance is needed.
   CATEGORIES II and IC
2. Conduct an epidemiologic investigation via a retrospective review of microbiologic, serologic, and postmortem data to identify previous cases and begin an intensive prospective surveillance for additional cases of healthcare-associated Legionnaires' disease.
   CATEGORY IB
   a. **If there is no evidence of continued nosocomial transmission,** continue the intensive prospective surveillance for cases for at least 2 months after surveillance is begun.
      CATEGORY II
   b. **If there is evidence of continued transmission:**
      (1) Conduct an environmental investigation to determine the source(s) of *Legionella* spp. by collecting water samples from potential sources of aerosolized water and saving and subtyping isolates of *Legionella* spp. obtained from patients and the environment. (270;287;466-472;504;506;508;509)
      CATEGORY IB
      (2) If a source is not identified, continue surveillance for new cases for at least 2 months, and, depending on the scope of the outbreak, decide on either deferring decontamination pending identification of the source(s) of *Legionella* spp., or proceeding with decontamination of the hospital's water distribution system, with special attention to the specific hospital areas involved in the outbreak.
      CATEGORY II
      (3) If a source of infection is identified by the epidemiologic and environmental investigations, promptly decontaminate it.
      CATEGORY IB
         (a) **If the heated-water system is implicated:**

i. Decontaminate the heated-water system either by superheating or by hyperchlorination. When superheating, raise the hot water temperature to 71°-77°C (160°-170°F) and maintain at that level while progressively flushing each outlet around the system. (A minimum flush time of 5 minutes has been recommended; the optimal flush time is not known, however, and longer flush times may be required.) Post warning signs at each outlet being flushed to prevent scald injury to patients, staff, or visitors. If possible, perform flushing when the building has the fewest occupants (e.g., nights and weekends). For systems where thermal shock treatment is not possible, use shock chlorination as an alternative. Add chlorine, preferably overnight, to achieve a free chlorine residual of at least 2 mg/L (2 ppm) throughout the system. This may require chlorination of the water heater or tank to levels of 20-50 mg/L (20-50 ppm). Maintain the water pH between 7.0 and 8.0. (490;499;500;504;510;526;1008)
CATEGORY IB

ii. Depending on local and state regulations regarding potable water temperature in public buildings, (511) maintain potable water at the outlet at ≥51°C (≥124°F) or <20°C (<68°F), or chlorinate heated water to achieve 1-2 mg/L free residual chlorine at the tap. (423;473;485;492;497-500)
CATEGORY II

iii. *No Recommendation* for treatment of water with ozone, ultraviolet light, or heavy-metal ions or monochloramine. (512;514-518;521)
UNRESOLVED ISSUE

iv. Clean hot-water storage tanks and water heaters to remove accumulated scale and sediment. (492)
CATEGORY IB

(b) **If cooling towers or evaporative condensers are implicated**, decontaminate the cooling-tower system following procedures detailed in the CDC Guideline for Environmental Control in Healthcare Facilities. (490;492)
CATEGORY IB

(4) Assess the efficacy of implemented measures in reducing or eliminating *Legionella* spp. by collecting specimens for culture at 2-week intervals for 3 months.
CATEGORY II

(a) If *Legionella* spp. are not detected in cultures during 3 months of monitoring at 2-week intervals, collect cultures monthly for another 3 months.
CATEGORY II

(b) If *Legionella* spp. are detected in one or more cultures, reassess the implemented control measures, modify them accordingly, and repeat decontamination procedures. Options for repeat decontamination include the intensive use of the same technique used for initial decontamination, or a combination of superheating and hyperchlorination. (1008)
CATEGORY II

(5) Keep adequate records of all infection control measures, including maintenance procedures, and of environmental test results for cooling towers and potable-water systems.
CATEGORY IB

PREVENTION AND CONTROL OF HEALTHCARE-ASSOCIATED PERTUSSIS

I. Staff Education

Educate appropriate personnel, in accordance with their level of responsibility in the healthcare setting, about the epidemiology, modes of transmission, and means of preventing the spread of pertussis. (543;545)
CATEGORY IB

II. Case-Reporting, Disease Surveillance, and Case-Contact Notification

A. Report to the local and/or state health department all confirmed and suspected cases of pertussis. (543)
CATEGORIES II and IC

B. Conduct active surveillance for cases of pertussis until 42 days after the onset of the last pertussis case. (556)
CATEGORY II

C. Notify persons who have had close contact with a case of pertussis in the healthcare setting so that they can be monitored for symptoms of pertussis and/or given appropriate chemoprophylaxis. (Close contact includes the following: face-to-face contact with a case-patient who is symptomatic, e.g., in the catarrhal or paroxysmal period of illness; sharing a confined space in close proximity for a prolonged period of time, such as $\geq$1 hour, with a symptomatic case-patient; or direct contact with respiratory, oral, or nasal secretions from a symptomatic case-patient (e.g., an explosive cough or sneeze on the face, sharing food, sharing eating utensils during a meal, kissing, mouth-to-mouth resuscitation, or performing a full medical examination of the nose and throat). (556)
CATEGORY II

III. Interruption of Pertussis Transmission

A. Vaccination of Adults (for Primary Prevention)
No Recommendation for routinely vaccinating adults, including healthcare workers, with the acellular pertussis vaccine at regular intervals, e.g., every 10 years. (531;556;1009-1012)
UNRESOLVED ISSUE

B. Vaccination (for Secondary Prevention)

1. *No Recommendation* for vaccinating adults, including healthcare workers, during an institutional outbreak of pertussis. (556;575)
   UNRESOLVED ISSUE
2. During an institutional outbreak of pertussis, accelerate scheduled vaccinations to infants and children <7 years of age who have not completed their primary vaccinations, as follows:
   a. **Infants <2 months of age (on initial vaccination)**
      Administer the first dose of the vaccine as early as 6 weeks of age, and the second and third doses at a minimum of 4-week intervals between doses. Give the fourth dose on or after age 1 year and at least 6 months after the third dose. (556;564;1013)
      CATEGORY II
   b. **Other children <7 years of age**
      Administer a DTP or DTaP vaccine dose to all patients who are <7 years of age and are not up-to-date with their DTP/DTaP vaccinations, as follows: administer a fourth dose of DTaP if the child has had three doses of DTaP or DTP, is $\geq$12 months old, and >6 months have passed since the third dose of DTaP or DTP; administer a fifth dose of DTaP or DTP if the child has had four doses of DTaP or DTP, is 4-6 years old, and received the fourth vaccine dose before the fourth birthday. (545;556)
      CATEGORY IB
3. Vaccination of children with a history of well-documented pertussis disease

No Recommendation for administering additional dose(s) of vaccine against pertussis to children who have a history of well-documented pertussis disease (i.e., pertussis illness with either a *B. pertussis*-positive culture or epidemiologic linkage to a culture-positive case). (556;558;564)
UNRESOLVED ISSUE

C. Patient Placement and Management

1. Patients with confirmed pertussis
   Place a patient with diagnosed pertussis in a private room, OR if known not to have any other respiratory infection, in a room with other patient(s) with pertussis until after the first 5 days of a full course of antimicrobial treatment or 21 days after the onset of cough if unable to take antimicrobial treatment for pertussis. (256;556)
   CATEGORY IB
2. Patients with suspected pertussis
   a. Place a patient with suspected pertussis in a private room. After pertussis and no other infection is confirmed, the patient may be placed in a room with other patient(s) who have pertussis, until after the first 5 days of a full course of antimicrobial treatment or 21 days after the onset of cough if unable to take antimicrobial treatment for pertussis. (256;556)
   CATEGORY IB
   b. Perform appropriate diagnostic laboratory tests (for confirmation or exclusion of pertussis) on patients who are admitted with or who develop symptoms of pertussis, to allow for the earliest possible down-grading of infection control precautions to the minimum required for each patient's specific infection(s). (543;547)
   CATEGORY IB

D. Management of Symptomatic Healthcare Personnel

1. In conjunction with Employee Health personnel, perform diagnostic culture of nasopharyngeal secretions for pertussis in healthcare personnel with illness suggestive of pertussis (i.e., unexplained cough illness of >1week duration, paroxysmal cough). (543;545;547)
   CATEGORY IB
2. In conjunction with Employee Health personnel, treat symptomatic healthcare personnel who are proven to have pertussis or personnel who are highly suspected of having pertussis with the same antimicrobial regimen, as detailed for chemoprophylaxis of case-contacts, in F-1 to F-3, below. (543;544)
   CATEGORY IB
3. Restrict symptomatic pertussis-infected healthcare workers from work during the first 5 days of their receipt of antimicrobial therapy. (544;545;1014;1015)
   CATEGORY IB

E. Masking

In addition to observing standard infection-control precautions, wear a mask when performing procedures or patient-care activities that are likely to generate sprays of respiratory secretions, or upon entering the room of a patient with confirmed or suspected pertussis. (256)
CATEGORY IB

F. Use of a Prophylactic Antibiotic Regimen for Contacts of Persons with Pertussis

1. Administer a macrolide to any person who has had close contact with persons with pertussis and who does not have hypersensitivity or intolerance to macrolides. (545;568)
   CATEGORY IB
   a. Use erythromycin (i.e., erythromycin estolate, 500 mg 4 times daily or erythromycin delayed-release tablets, 333 mg 3 times daily for adults, and 40-50 mg/kg day for children) for 14 days. (545;1016-1018)
   CATEGORY IB
   b. For those who are intolerant to erythromycin, use azithromycin for 5-7 days (at 10-12 mg/kg/day) for infants and young children, or for 5 days (at 10 mg/kg on day1 followed by four days at 5 mg/kg/day); or clarithromycin (at 500 mg twice a day for adults or 15-20 mg/kg/day in two divided doses for children) for 10-14 days, respectively. (545;572;1016;1019)
   CATEGORY II

2. For chemoprophylaxis of persons who have hypersensitivity or intolerance to macrolides, use (except in the case of pregnant woman at term, nursing mother, or infant <2 months) trimethoprim-sulfamethoxazole for 14 days (at one double-strength tablet twice a day for adults and 8 mg/kg/day TMP, 40 mg/kg/day SXT a day in 2 divided doses for children). (574;1016;1017)
   CATEGORY II
3. *No Recommendation* for the use of oxytetracycline for 14 days (at 500 mg four times a day for adults, and 25 mg/kg/day in divided doses for children >9 years), (545) or a quinolone (1020) for prophylaxis. (556)
   UNRESOLVED ISSUE

G. Work Exclusion of Asymptomatic Healthcare Workers Exposed to Pertussis

1. Do not exclude from patient care, personnel who remain asymptomatic and who are receiving chemoprophylaxis after an exposure to a case of pertussis (i.e., by direct contact of one's nasal or buccal mucosa with the respiratory secretions of an untreated person who is in the catarrhal or paroxysmal stage of pertussis). (256)
   CATEGORY II
2. Exclude an exposed, asymptomatic healthcare worker who is unable to receive chemoprophylaxis, from providing care to a child <4 years during the period starting 7 days after the worker's first possible exposure until 14 days after his last possible exposure to a case of pertussis. (545)
   CATEGORY II

H. Other Measures

1. Limiting patient movement or transport
   Limit to essential purposes only the movement or transport from the room of a patient with diagnosed or suspected pertussis. If the patient is transported out of the room, ensure that precautions are maintained to minimize the risk of transmission to other patients and of contamination of environmental surfaces or equipment. (256)
   CATEGORY IB
2. Limiting visitors
   Do not allow persons who have symptoms of respiratory infection to visit pediatric, immunosuppressed, or cardiac patients. (256;543;1021)
   CATEGORY IB

PREVENTION AND CONTROL OF HEALTHCARE-ASSOCIATED PULMONARY ASPERGILLOSIS

I. Staff Education and Infection Surveillance

A. Staff Education

Educate healthcare workers according to their level of responsibility regarding infection control procedures to decrease the occurrence of healthcare-associated pulmonary aspergillosis.
CATEGORY II

B. Surveillance

1. Maintain a high index of suspicion for healthcare-associated pulmonary aspergillosis in high-risk patients, including a) patients with severe, prolonged neutropenia (e.g., absolute neutrophil count <500/mm^3 for 2 weeks or <100/mm^3 for 1 week), most notably hemopoietic stem-cell transplant (HSCT) recipients; (579;1022-1025) b) recipients of lung and heart-lung transplants; (1026) c) patients with hematologic malignancies who are receiving chemotherapy, when they are severely neutropenic as defined above; and d) persons receiving prolonged high-dose steroids. (584;606;1023)
CATEGORY IA
2. Maintain surveillance for cases of healthcare-associated pulmonary aspergillosis by periodically reviewing the hospital's microbiologic, histopathologic, and postmortem data.
CATEGORY IB
3. Surveillance cultures
   a. Do not perform routine, periodic cultures of the nasopharynx of asymptomatic, high-risk patients. (580;1027;1028)
   CATEGORY IB
   b. Do not perform routine, periodic cultures of equipment or devices used for respiratory therapy, pulmonary function testing, or delivery of inhalation anesthesia in the HSCT unit, nor of dust in rooms of HSCT recipients. (1027;1028)
   CATEGORY IB
   c. *No Recommendation* for routine microbiologic air sampling before, during, or after facility construction or renovation, or before or during occupancy of areas housing immunocompromised patients. (492)
   UNRESOLVED ISSUE

II. Interruption of Transmission of *Aspergillus* Spp. Spores

A. Planning New Specialized-Care Units for High-Risk Patients

1. **Protected Environment (PE) for allogeneic HSCT recipients**
   a. When constructing new specialized-care units with PE for HSCT recipients, ensure that patient rooms have adequate capacity to minimize accummulation of fungal spores via a) high-efficiency particulate air (HEPA) filtration of incoming air, b) directed room airflow, c) positive air pressure in patient's room in relation to the corridor, d) well-sealed room, and e) high ($\geq$12) air changes per hour. (See *CDC Guideline for Environmental Control in Healthcare Facilities, 2001* for specifications.) (492;679-681)
   CATEGORY IB
   b. Do not use laminar airflow (LAF) routinely in PE. (492;644;650;653;684;685)
   CATEGORY IB
2. **Units for Autologous HSCT and Solid-Organ Transplant Recipients**
   No Recommendation for constructing PE for autologous HSCT or solid-organ-transplant (e.g., heart, liver, lung, kidney) recipients. (See *CDC Guideline for Environmental Control in Healthcare Facilities, 2001*.) (492;681)
   UNRESOLVED ISSUE

B. In Existing Facilities with HSCT Units and No Cases of Healthcare-Associated Aspergillosis

1. **Placement of Patients in PE**
   a. Place allogeneic HSCT recipients in a PE that meets the conditions outlined in Section II-A-1, above.
      CATEGORY IB
   b. *No Recommendation* for routinely placing recipients of autologous HSCT or solid-organ transplants in PE.
      UNRESOLVED ISSUE
2. Maintain air-handling systems in PE and other high-risk patient-care areas according to recommendations in the *CDC Guideline for Environmental Control in Healthcare Facilities, 2001*. (492;679-681)
   CATEGORY IB
3. Use proper dust-control methods for patient-care areas designated for immunocompromised (e.g., HSCT) patients. (492;679-681;693)
   CATEGORY IB
   a. Wet-dust horizontal surfaces daily using cloths moistened with an EPA-registered hospital disinfectant. (657)
      CATEGORY IB
   b. Avoid dusting methods that disperse dust, e.g., feather dusting. (657)
      CATEGORY IB
   c. Keep vacuums in good repair and equip them with HEPA filters for use in high-risk patient-care areas. (657;693)
      CATEGORY IB
   d. Close the doors of immunocompromised patients' rooms when vacuuming corridor floors to minimize patient exposure to airborne dust. (657;693)
      CATEGORY IB
   e. Avoid the use of carpeting in hallways and rooms occupied by immunocompromised patients. (1029)
      CATEGORY IB
   f. Avoid the use of upholstered furniture or furnishings in rooms occupied by immunocompromised patients. (493)
      CATEGORY II
4. Minimize the length of time that immunocompromised patients in PEs are outside their rooms for diagnostic procedures and other activities.
   CATEGORY IB
   a. During periods when construction, renovation, demolition, and/or other dust-generating activities are ongoing in and around the healthcare facility, make the immunocompromised patient wear a mask with high-efficiency, e.g., an N95 respirator, when he/she leaves the PE. (493, 1065)
      CATEGORY II
   b. *No Recommendation* for the specific type of respiratory-protection device, e.g., surgical mask or N95 respirator, for use by an immunocompromised patient who leaves the PE during periods when there is no construction, renovation or other dust-generating activity in progress in or around the healthcare facility. (492)
      UNRESOLVED ISSUE
5. Systematically review and coordinate infection-control strategies with personnel in charge of the facility's engineering, maintenance, central supply and distribution, and catering services. (492;493;576;1030)
   CATEGORY IB
6. When planning construction and renovation activities in and around the facility, assess whether patients at high-risk for aspergillosis are likely to be exposed to high ambient-air spore counts of *Aspergillus* spp. from construction and renovation sites, and, if so, develop a plan to prevent such exposures. (492;493;576;1030;1031)
   CATEGORY IA
7. During construction or renovation activities, construct impermeable barriers between patient-care and construction areas to prevent dust from entering the patient-care areas. (See *CDC Guideline for Environmental Control in Healthcare Facilities, 2000*). (492;653;661)
   CATEGORY IB
8. Direct pedestrian traffic from construction areas away from patient-care areas to limit opening and closing of doors (or other barriers) that may cause dust dispersion, entry

of contaminated air, or tracking of dust into patient-care areas. (492;493;576;598;1030;1032)
CATEGORY IB

9. Do not allow fresh or dried flowers or potted plants in patient-care areas for immunocompromised patients. (576;1033-1036)
CATEGORY IB

C. When a Case of Aspergillosis Occurs

1. Assess whether the infection is healthcare-related or community-acquired. Obtain and use the following information to help in the investigation: background rate of disease at the facility; presence of concurrent or recent cases, as determined by a review of the facility's microbiologic, histopathologic, and postmortem records; length of patient's stay in the facility prior to the onset of aspergillosis; and patient's stay at, visit of, or transfer from other healthcare facilities or other locations within the facility.
CATEGORY IB
2. If there is no evidence indicative of patient acquisition of aspergillosis in the healthcare facility, continue routine maintenance procedures to prevent healthcare-associated aspergillosis, as in Section II-B-1 through II-B-9, above.
CATEGORY IB
3. If evidence of possible facility-acquired infection with *Aspergillus* spp. exists, conduct an epidemiologic investigation and an environmental assessment as detailed in the *CDC Guideline for Environmental Control in Healthcare Facilities, 2000* to determine and eliminate the source of *Aspergillus* spp. (492) If assistance is needed, contact the local or state health department.
CATEGORY IB
4. Use an anti-fungal biocide (e.g., copper-8-quinolinolate) for decontamination of structural materials that are implicated in the transmission of infection. (492;653;1037-1039)
CATEGORY IB

III. Enhancing Host Resistance to Infection

A. *No Recommendation* for the routine administration of antifungal agents (690;696;1040) such as itraconazole oral solution (5 mg/kg/day), (690;696;697;1040) or capsules (500 mg twice a day), (1041) low-dose parenteral amphotericin B (0.1 mg/kg/day), (698) lipid-based formulations of amphotericin B (1 mg/kg/day), (699) or nebulized amphotericin B administered by inhalation (700;1042;1043) as prophylaxis for pulmonary aspergillosis in high-risk patients.
UNRESOLVED ISSUE

B. *No Recommendation* for any specific strategy (e.g., deferral of hematopoietic stem-cell transplantation for a particular length of time or routine prophylaxis with absorbable or intravenous antifungal medications) to prevent recurrence of pulmonary aspergillosis in patients who are to receive HSCT and have a history of pulmonary aspergillosis. (702-704;1044-1047)
UNRESOLVED ISSUE

PREVENTION AND CONTROL OF RESPIRATORY SYNCYTIAL VIRUS, PARAINFLUENZA VIRUS AND ADENOVIRUS INFECTIONS

I. Staff Education and Monitoring and Infection Surveillance

A. Staff Education and Monitoring

1. Educate personnel, in accordance with their level of responsibility in the healthcare setting, about the epidemiology, modes of transmission, and means of preventing the spread of respiratory syncytial virus (RSV), parainfluenza virus, and adenovirus. (786)
   CATEGORY IB
2. Establish mechanisms by which the infection control staff can monitor personnel compliance with the facility's infection control policies regarding these viruses. (786)
   CATEGORY IB

B. Surveillance

1. Establish mechanisms by which the appropriate healthcare personnel are promptly alerted to any increase in the activity of RSV, parainfluenza virus, adenovirus, or other respiratory viruses in the local community.
   CATEGORY IB
2. During periods of increased prevalence of symptoms of viral respiratory illness(es) in the community or healthcare facility, and/or during the RSV and influenza season (which is usually from December through March in most places in the United States), attempt prompt diagnosis of RSV infection, influenza, parainfluenza, or other viral respiratory infection. Use rapid diagnostic techniques as clinically indicated in patients who are admitted to the healthcare facility with respiratory illness and are at high risk for serious complications from the viral infection, e.g., pediatric patients, especially infants, and those with compromised cardiac, pulmonary, or immune function. (718;730;784;786;862)
   CATEGORY IA
3. *No Recommendation* for **routinely** conducting culture-based surveillance for RSV or other respiratory viruses among patients (including immunocompromised patients, such as recipients of hemopoietic stem-cell transplant). (493)
   UNRESOLVED ISSUE

II. Interruption of Transmission of RSV, Parainfluenza Virus, or Adenovirus

A. Prevention of Person-to-Person Transmission

1. **Standard, contact, and droplet precautions**
   a. Hand hygiene
      Decontaminate hands with either soap and water or a waterless antiseptic agent after contact with a patient, or after touching respiratory secretions or fomites potentially contaminated with respiratory secretions, whether or not gloves are worn. (248;256;262;562;749;770;771;782;786)
      CATEGORY IA
   b. Gloving
      (1) Wear gloves for handling patients or respiratory secretions of patients with proven or suspected viral respiratory infection, or fomites potentially contaminated with patient secretions.
      (256;257;749;770;771;779;784;786;1048)
      CATEGORY IA
      (2) Change gloves between patients, or after handling respiratory secretions or fomites contaminated with secretions from one patient before contact with another patient. (256;257;259;786) Decontanimate hands after removing gloves. (See II-A-1-a, above.)
      CATEGORY IA
      (3) After glove removal, ensure that hands do not touch potentially contaminated environmental surfaces or items in the patient's room. (256;786)
      CATEGORY IB

c. Gowning
Wear a gown when soiling with respiratory secretions from a patient is anticipated, e.g., when handling infants with suspected or proven viral respiratory illness, and change the gown after such contact and before caring for another patient. After gown removal, ensure that clothing does not contact potentially contaminated environmental surfaces. (256;257;778;780;784;786)
CATEGORY IB

d. Masking and wearing eye protection
Wear a mask and eye protection or a face shield when performing procedures or patient-care activities that are likely to generate sprays of respiratory secretions from any patient, whether or not the patient has confirmed or suspected viral respiratory tract infection. (256)
CATEGORY IB

e. Patient placement
(1) Place a patient with suspected or diagnosed RSV, parainfluenza, adenovirus, or other viral respiratory tract infection in a private room when possible, OR in a room with other patients with the same infection but no other infection. (256;718;779;782;784;1048)
CATEGORY IB
(2) Promptly perform rapid diagnostic laboratory tests on patients who are admitted with or who develop symptoms of a viral respiratory tract infection after admission to the healthcare facility, to allow for early downgrading of infection control precautions to the minimum required for each patient's specific viral infection. (786;1048)
CATEGORY IB

f. Limiting patient movement or transport
(1) Limit to essential purposes only the movement or transport of a patient with diagnosed or suspected RSV or parainfluenza virus infection from the room. If the patient is transported out of the room, ensure that precautions are maintained to minimize the risk of viral transmission to other patients and of contamination of environmental surfaces or equipment, e.g., by making sure that the patient does not touch other persons' hands or environmental surfaces with hands that have been contaminated with his/her respiratory secretions. (256)
CATEGORY IB
(2) Limit to essential purposes only the movement or transport of a patient with diagnosed or suspected adenovirus infection, from the room. If transport or movement is necessary, minimize patient dispersal of droplets by having the patient wear a mask. (256)
CATEGORY IB

2. **Other measures**

a. Staffing
(1) Restrict healthcare personnel in the acute stages of an upper respiratory tract infection from taking care of infants and other patients at high risk for complications from viral respiratory tract infections (e.g., children with severe underlying cardio-pulmonary conditions, children receiving chemotherapy for malignancy, premature infants, and patients who are otherwise immunocompromised). (256;493;782;784;786)
CATEGORY IB
(2) Perform rapid diagnostic testing on healthcare personnel with symptoms of respiratory tract infection so that their work status can be determined promptly.
CATEGORY II

b. Limiting visitors
Do not allow persons who have symptoms of respiratory infection to visit pediatric, immunosuppressed, or cardiac patients. (256;493;779;786;1048)
CATEGORY IB

c. Use of RSV immune globulin or monoclonal antibody for prevention of RSV infection
Determine on a case-by-case basis whether to administer RSV immune

globulin or monoclonal antibody to infants born prematurely at ≤32 weeks of gestational age and infants <2 years who have bronchopulmonary dysplasia, to prevent severe lower respiratory tract RSV infection in these patients. (787-790)
CATEGORY IB

3. **Control of outbreaks**
   a. Perform rapid screening diagnostic tests for the particular virus(es) known or suspected to be causing the outbreak on patients who are admitted with symptoms of viral respiratory illness, with the intent of promptly cohorting the patients according to their outbreak-virus-infection status as soon as the results of the screening tests are available. (718;730;779;782;784;786;1048) In the interim, admit patients with symptoms of viral respiratory infections to private rooms.
   CATEGORY IB
   b. Personnel cohorting
      (1) During an outbreak of healthcare-associated RSV infection, cohort personnel as much as practical, i.e., restrict personnel who give care to infected patients from giving care to uninfected patients, and vice-versa. (779;782;784)
      CATEGORY II
      (2) *No Recommendation* for routinely cohorting personnel, i.e., restricting personnel who give care to infected patients from giving care to uninfected patients, and vice-versa, during an outbreak of healthcare-associated adenovirus or parainfluenza infection.
      UNRESOLVED ISSUE
   c. Postponing elective patient admissions
      During outbreaks of nosocomial RSV, parainfluenza, or adenovirus infections, postpone elective admission of uninfected patients at high risk for complications from the respiratory viral infection.
      CATEGORY II
   d. Use of RSV immune globulin or monoclonal antibody
      No Recommendation for the use of RSV immune globulin or monoclonal antibody to control outbreaks of RSV infection in healthcare settings.
      UNRESOLVED ISSUE

PREVENTION AND CONTROL OF HEALTHCARE-ASSOCIATED INFLUENZA

I. Staff Education

Provide healthcare personnel continuing education or access to continuing education about the epidemiology, modes of transmission, diagnosis, and means of preventing the spread of influenza, in accordance with their level of responsibility in preventing healthcare-associated influenza. (986;1049-1051)
CATEGORY IB

II. Surveillance

A. Establish mechanism(s) by which facility personnel are promptly alerted about increased influenza activity in the community.
CATEGORY II

B. Establish protocols for intensifying efforts to promptly diagnose cases of facility-acquired influenza:

1. Determine the threshold incidence or prevalence of influenza or influenza-like illness in the facility at which laboratory testing of patients with influenza-like illness is to be undertaken and outbreak control measures are to be initiated. (907)
   CATEGORY II
2. Arrange for laboratory tests to be available to clinicians for prompt diagnosis of influenza, especially during November-April. (902-905)
   CATEGORY IB

III. Modifying Host Risk for Infection

A. Vaccination

1. In acute-care settings (including acute-care hospitals, emergency rooms, and walk-in clinics) or ongoing-care facilities (including physicians' offices, public health clinics, employee health clinics, hemodialysis centers, hospital specialty-care clinics, outpatient rehabilitation programs, or mobile clinics), offer vaccine to inpatients and outpatients at high risk for complications from influenza, beginning in September and throughout the influenza season. (906;1052-1054) Groups at high risk for influenza-related complications include those ≥65 years of age; persons 6 months to <65 years of age with chronic disorders of the pulmonary or cardiovascular system, diabetes mellitus, renal dysfunction, or hemoglobinopathy, or who are immune-compromised, including those with HIV infection; children 6 months-18 years of age who are receiving long-term aspirin therapy; and women who will be in the second or third trimester of pregnancy during the influenza season. (906;916;1055-1059) In addition, offer annual influenza vaccination to all persons 50-64 years of age and to close contacts of children <24 months of age, and encourage vaccination of healthy children 6 months to 24 months of age. (906)
   CATEGORY IA
2. In nursing homes and other long-term care facilities, establish a Standing Orders Program (SOP) for timely administration of vaccine to high-risk persons (as identified in Section III-A-1, above). (906;919;986)
   CATEGORY IA
   a. Obtain consent (if required by state law) for influenza vaccination from every resident or resident's guardian at the time of admission to the facility or anytime afterwards, before the next influenza season. (906;1059;1060)
      CATEGORY IA
   b. Routinely vaccinate all residents (under an SOP and/or with the concurrence of their attending physicians) at one time, annually, before the influenza season. To residents who are admitted during the winter months after completion of the facility's vaccination program, offer the vaccine at the time of their admission. (906;916;1060;1061)
      CATEGORY IA
   c. In settings not included in sections II-A-1 and -2, above, where healthcare is

given, e.g., in homes visited by personnel from home healthcare agencies, vaccinate patients for whom vaccination is indicated, as listed in section III-A-1, above, and refer patient's household members and care givers for vaccination, before the influenza season. (906)
CATEGORY IA

3. Personnel
   a. Each year, vaccinate healthcare personnel before the influenza season. (909-911;915;917) Throughout the influenza season, continue to make vaccine available to newly hired personnel and to those who initially refuse vaccination. If vaccine supply is limited, give highest priority to staff caring for patients at greatest risk for severe complications from influenza infection, as listed in section II-A-1 above. (906)
   CATEGORY IA
   b. Maintain efforts to remove administrative and financial barriers that prevent healthcare workers from receiving the influenza vaccine. (906;1062)
   CATEGORY IA

B. Use of Antiviral Agents (See Section V-C below, Control of Influenza Outbreaks)

IV. Interruption of Person-to-Person Transmission

A. Observe droplet precautions in the care of a patient with confirmed or suspected influenza:
1. Keep a patient for whom influenza is suspected or diagnosed in a private room or in a room with other patients with confirmed influenza, unless there are medical contraindications to doing so. (256)
   CATEGORY IB
2. Wear a mask when working within 3 feet of the patient. (256)
   CATEGORY II\
3. Limit to essential purposes only movement or transport of patient from the room. If patient movement or transport is necessary, have the patient wear a mask, if possible, to minimize droplet dispersal by the patient. (256)
   CATEGORY II

B. Adhere to standard infection control precautions.
1. Hand decontamination after giving care to a patient or after touching a patient or patient's respiratory secretions, whether or not gloves are worn
   a. If hands are visibly dirty or contaminated with proteinaceous material or are visibly soiled with blood or body fluids, wash them with either a non-antimicrobial soap and water or an antimicrobial soap and water. (255)
   CATEGORY IA
   b. If hands are not visibly soiled, use an alcohol-based handrub for their routine decontamination. (255)
   CATEGORY IA
2. Wear gloves if hand contact with patient's respiratory secretions is expected. (256)
   CATEGORY II
3. Wear a gown if soiling of clothes with patient's respiratory secretions is expected.. (256)
   CATEGORY II

C. *No Recommendation* for maintaining negative air pressure in rooms of patients in whom influenza is suspected or diagnosed, or in placing together persons with influenza-like illness in a hospital area with an independent air-supply and exhaust system. (886-889)
UNRESOLVED ISSUE

D. Evaluate, by utilizing the facility's employee health service or its equivalent, personnel with influenza-like illness for their possible removal from duties that involve direct patient contact. Use more stringent guidelines for staff working in certain patient-care areas with patients who are most susceptible to influenza-related complications, e.g., intensive care units, nurseries, and organ-transplant (especially hemopoietic stem-cell transplant) units. (884;954;1063)
CATEGORY IA

E. When influenza outbreaks, especially those characterized by high attack rates and severe illness, occur in the community and/or facility:

1. Curtail or eliminate elective medical and surgical admissions as necessary. (954)
   CATEGORY II
2. Restrict cardiovascular and pulmonary surgery to only emergency cases. (954)
   CATEGORY II
3. Restrict persons with influenza or influenza-like illness from visiting patients in the healthcare facility. (954)
   CATEGORY II
4. Restrict personnel with influenza or influenza-like illness from patient care. (954)
   CATEGORY IB

V. Control of Influenza Outbreaks

A. Determining the Outbreak Strain

Early in the outbreak, perform rapid influenza virus testing on nasopharyngeal swab or nasal wash specimens from patients with recent onset of symptoms suggestive of influenza. In addition, obtain viral cultures from a subset of patients to determine the infecting virus type and subtype. (902-905)
CATEGORY IB

B. Vaccination of Patients and Personnel

Administer current influenza vaccine to unvaccinated patients and healthcare personnel. (880;906;910;911;916)
CATEGORY IA

C. Antiviral Agent Administration

1. **When a facility outbreak of influenza is suspected or recognized:**
   a. Administer amantadine, rimantadine, or oseltamivir as prophylaxis to all patients without influenza illness in the involved unit for whom the antiviral agent is not contraindicated, for 2 weeks or until approximately one week after the end of the outbreak. Do not delay administration of the antiviral agent(s) for prophylaxis unless the results of diagnostic tests to identify the infecting strain(s) can be obtained within 12 to 24 hours after specimen collection. (896;906;924;1061)
   CATEGORY IA
   b. Administer amantadine, rimantadine, oseltamivir, or zanamivir to patients acutely ill with influenza. Choose the agent(s) appropriate for the type(s) of influenza virus circulating in the community. (896;906;924;1061)
   CATEGORY IA
   c. Administer antiviral agent(s) for prophylaxis to unvaccinated personnel for whom it is not medically contraindicated and who are in the involved unit or taking care of high-risk patients. (906)
   CATEGORY IB
   d. *No Recommendation* on the prophylactic administration of zanamivir to patients or personnel. (879;906;934;935;937;938;946)
   UNRESOLVED ISSUE
2. Discontinue the administration of influenza antiviral agents to patients or personnel if laboratory tests confirm or strongly suggest that influenza is not the cause of the facility outbreak. (922)
   CATEGORY IA
3. If the cause of the outbreak is confirmed or believed to be influenza AND vaccine has been administered only recently to susceptible patients and personnel, continue prophylaxis with an antiviral agent until 2 weeks after the vaccination. (1064)
   CATEGORY IB
4. To reduce the potential for transmission of drug-resistant virus, do not allow contact between persons at high risk for complications from influenza and patients or personnel who are taking an antiviral agent for treatment of confirmed or suspected influenza during and for 2 days after the latter discontinue treatment. (923;944;945;947-949)
   CATEGORY IB

APPENDIX A

EXAMPLES OF SEMICRITICAL ITEMS* USED ON THE RESPIRATORY TRACT

Anesthesia device or equipment including:
- face mask or tracheal tube
- inspiratory and expiratory tubing
- Y-piece
- reservoir bag
- humidifier

Breathing circuits of mechanical ventilators
Bronchoscopes and their accessories, except for biopsy forceps ** and specimen brush **
Endotracheal and endobronchial tubes
Laryngoscope blades
Mouthpieces and tubing of pulmonary-function testing equipment
Nebulizers and their reservoirs
Oral and nasal airways
Probes of CO_2 analyzers, air-pressure monitors
Resuscitation bags
Stylets
Suction catheters
Temperature sensors

* Items that directly or indirectly contact mucous membranes of the respiratory tract. They should be sterilized or subjected to high-level disinfection before reuse.

** Considered critical items; they should be sterilized before reuse.

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