

GUIDELINES FOR PREVENTING HEALTH-CARE-ASSOCIATED PNEUMONIA, 2003

Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee

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Summary

This report updates, expands, and replaces the previously published CDC "Guideline for Prevention of Nosocomial Pneumonia". The new guidelines are designed to reduce the incidence of health-care-associated pneumonia and other severe, acute lower respiratory tract infections in acute-care hospitals and in other health-care settings (e.g., ambulatory and long-term care institutions) and other facilities where health care is provided.

Among the changes in the recommendations to prevent bacterial pneumonia, especially ventilator-associated pneumonia, are the preferential use of oro-tracheal rather than naso-tracheal tubes in patients who receive mechanically assisted ventilation, the use of noninvasive ventilation to reduce the need for and duration of endotracheal intubation, changing the breathing circuits of ventilators when they malfunction or are visibly contaminated, and (when feasible) the use of an endotracheal tube with a dorsal lumen to allow drainage of respiratory secretions; no recommendations were made about the use of sucralfate, histamine-2 receptor antagonists, or antacids for stress-bleeding prophylaxis. For prevention of health-care-associated Legionnaires disease, the changes include maintaining potable hot water at temperatures not suitable for amplification of Legionella spp., considering routine 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 health-care-associated Legionnaires disease, and initiating an investigation for the source of Legionella spp. when one definite or one possible case of laboratory-confirmed health-care-associated Legionnaires disease is identified in an inpatient hemopoietic 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, and the use of high-efficiency respiratory-protection devices (e.g., N95 respirators) by severely immunocompromised patients when they leave their rooms when dust-generating activities are ongoing in the facility. In the respiratory syncytial virus (RSV) section, the new recommendation is to determine, on a case-by-case basis, whether to administer monoclonal antibody (palivizumab) to certain infants and children aged <24 months who were born prematurely and are at high risk for severe RSV infection. In the section on influenza, the new recommendations include the addition of oseltamivir (to amantadine and rimantadine) for prophylaxis of all patients without influenza illness and oseltamivir and zanamivir (to amantadine and rimantadine) as treatment for 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 caused by adenovirus and human parainfluenza viruses, and refers readers to the source of updated information about prevention and control of severe acute respiratory syndrome.

INTRODUCTION

Because of the high morbidity and mortality associated with health-care-associated pneumonia, several 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-acquired 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 respiratory syncytial virus (RSV) infection.

In 1994, the Healthcare Infection Control Practices Advisory Committee (HICPAC) (then known as the Hospital Infection Control Practices Advisory Committee) revised and expanded the CDC Guideline for Prevention of Nosocomial Pneumonia to include Legionnaires disease and pulmonary aspergillosis (1). HICPAC advises the secretary of Health and the directors of CDC and the National Center for Infectious Diseases about the prevention and control of health-care-associated infections and related adverse events. The 1994 guideline addressed concerns related to preventing ventilator-associated pneumonia (VAP) (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-acquired pneumonia due to *Legionella* spp. and aspergilli.

In recent years, demand has increased for guidance on preventing and controlling pneumonia and other lower respiratory tract infections in health-care 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 United States away from inpatient care in the acute-care hospital and towards outpatient and long-term care in other health-care settings. In response to this demand, HICPAC revised the guideline to cover these other settings. However, infection-control data about the acute-care hospital setting are more abundant and well analyzed compared with those from long-term care, ambulatory, and psychiatric facilities and other health-care settings.

This publication is the complete three-part document, Parts II and III of which have been published recently (2). Part I of the document provides the background for the recommendations and includes a discussion of the epidemiology, diagnosis, pathogenesis, modes of transmission, and prevention and control of the infections. Part I can be an important resource for educating health-care personnel. Because education of health-care personnel is the cornerstone of an effective infection control program, health-care agencies should give high priority to continuing infection-control educational programs for their staff members. Part II contains the consensus HICPAC recommendations for the prevention of the following infections: bacterial pneumonia, Legionnaires disease, pertussis, invasive pulmonary aspergillosis (IPA), lower respiratory tract infections caused by RSV, parainfluenza and adenoviruses, and influenza. Lower respiratory tract infection caused by *Mycobacterium tuberculosis* is not addressed in this document, however; it is covered in a

separate publication (3). HICPAC recommendations address such issues as education of health-care personnel about the prevention and control of health-care-associated pneumonia and other lower respiratory tract infections, surveillance and/or reporting of diagnosed cases of infections, prevention of person-to-person transmission of each disease, and reduction of host risk for infection. Part III provides suggested performance indicators to assist infection-control personnel in monitoring the implementation of the guideline recommendations in their facilities.

The document was prepared by CDC; reviewed by experts in infection control, intensive-care medicine, pulmonology, respiratory therapy, anesthesiology, internal medicine, and pediatrics; and approved by HICPAC. The recommendations are endorsed by the American College of Chest Physicians, American Health Care Association, Association for Professionals of Infection Control and Epidemiology, Infectious Diseases Society of America, Society for Healthcare Epidemiology of America, and Society of Critical Care Medicine.

Key Terms Used In the Guidelines

Protective environment (PE) is a specialized patient-care area, usually in a hospital, with a positive air flow relative to the corridor (i.e., air flows from the room to the outside adjacent space). The combination of high-efficiency particulate air (HEPA) filtration, high numbers (≥ 12) of air changes per hour (ACH), and minimal leakage of air into the room creates an environment that can safely accommodate patients with a severely compromised immune system (e.g., those who have received allogeneic hemopoietic stem-cell transplant [(HSCT)]).

Immunocompromised patients are those patients whose immune mechanisms are deficient because of immunologic disorders (e.g., human immunodeficiency virus [HIV] infection, congenital immune deficiency syndrome, chronic diseases [e.g., diabetes mellitus, cancer, emphysema, or cardiac failure], or immunosuppressive therapy [e.g., radiation, cytotoxic chemotherapy, anti-graft-rejection medication, steroids]). Immunocompromised patients who are identified as high-risk patients have the greatest risk for infection and include persons with severe neutropenia (i.e., an absolute neutrophil count [ANC] of ≤ 500 cells/mL) for prolonged periods of time, recipients of allogeneic HSCT, and those who receive the most intensive chemotherapy (e.g., patients with childhood acute myelogenous leukemia).

Abbreviations Used In the Guidelines

ACIP	Advisory Committee on Immunization Practices
ANC	absolute neutrophil count
BAL	broncho-alveolar lavage
CSF	cerebrospinal fluid
COPD	chronic obstructive pulmonary disease
DFA	direct fluorescein-conjugated antibody
DNA	deoxyribonucleic acid

DTP	diphtheria, tetanus and pertussis
DTaP	diphtheria and tetanus toxoids and acellular pertussis
EOP	early-onset pneumonia
FDA	Food and Drug Administration
GCSF	granulocyte colony-stimulating factor
GVHD	graft-versus-host disease
HEPA	high-efficiency particulate air
HICPAC	Healthcare Infection Control Practices Advisory Committee
HIV	human immunodeficiency virus
HME	heat-moisture exchanger
HPIV	human parainfluenza virus
HSCT	hemopoietic stem-cell transplant
ICU	intensive care unit
IGIV	immune globulin intravenous
IHPS	infantile hypertrophic pyloric stenosis
IPA	invasive pulmonary aspergillosis
LAF	laminar airflow
LAIV	live attenuated influenza vaccine
LOP	late-onset pneumonia
LTCFs	long-term care facilities
NH	nursing home
NHAP	nursing home-associated pneumonia
NIV	noninvasive ventilation
NNIS	National Nosocomial Infection Surveillance
NPPV	noninvasive positive-pressure ventilation
pBAL	protected broncho-alveolar lavage
PE	protective environment
PCR	polymerase chain reaction
PSB	protected-specimen brush
RNA	ribonucleic acid
RSV	respiratory syncytial virus
SARS	severe acute respiratory syndrome
SDD	selective decontamination of the digestive tract
SOP	standing orders program
TMP-SMZ	trimethoprim-sulfamethoxazole
VAP	ventilator-associated pneumonia

PART I. ISSUES ON PREVENTING HEALTH-CARE-ASSOCIATED PNEUMONIA, 2003

HEALTH-CARE-ASSOCIATED BACTERIAL PNEUMONIA

I. EPIDEMIOLOGY

The epidemiology of health-care-associated pneumonia varies considerably according to the type of health-care 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 (4-6). It has been the second most common hospital-associated infection after that of the urinary tract (4;7). The primary risk factor for the development of hospital-associated bacterial pneumonia is mechanical ventilation (with its requisite endotracheal intubation) (8). The CDC's National Nosocomial Infection Surveillance System (NNIS) reported that in 2002, the median rate of VAP per thousand ventilator-days in NNIS hospitals ranged from 2.2 in pediatric ICUs to 14.7 in trauma ICUs (9). 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 (10-12). 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 (8;11;13-25).

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 (10;13;23;26-28). 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 (29) to 73% in patients with VAP caused by *Pseudomonas* or *Acinetobacter* spp. (30), and attributable mortality rates ranged from 5.8% to 13.5% (31;32). 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) (16;23;29-34).

Analyses of pneumonia-associated morbidity have shown that hospital-associated pneumonia can prolong ICU stay by an average of 4.3-6.1 days and hospitalization by 4-9 days (26;28;29;31;33;35;36). An estimate of the direct cost of excess hospital stay due to VAP is

\$40,000 per patient (33).

B. Nursing Home (NH)-Associated Pneumonia (NHAP)

In long-term care facilities (LTCFs) such as NHs, pneumonia is the first or second most common infection (after those of the urinary tract) acquired by patients (37;38), and accounts for 13-48% of all nursing home-associated infections (39;40). Its seasonal variation mirrors that of influenza, suggesting that influenza plays a major role in the occurrence of pneumonia in the elderly (41). NHAP is associated with a high mortality rate. The case-fatality rate of pneumonia in NH residents is reported to be from 6% to 23% (37;38;42;43).

II. DIAGNOSIS

Health-care-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 (44-47). 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 (46;48-51); conversely, culture of blood has a very low sensitivity (52).

In 1992, a group of investigators recommended standardized methods for diagnosing pneumonia in clinical research studies of VAP (53-55). These methods involved bronchoscopic techniques, e.g., quantitative culture of protected specimen brush (PSB) specimen (56-65), bronchoalveolar lavage (BAL) (57;66-72), and protected BAL (pBAL) (73;74). 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 to which they were compared (57;75;76). Because these techniques are invasive, they can cause complications such as hypoxemia, bleeding, or arrhythmia (51;58;70;77-79). Quantitative culture of endotracheal aspirate (80;81) and non-bronchoscopic procedures that utilize blind catheterization of the distal airways, e.g., nonbronchoscopic-pBAL (66;82) and nonbronchoscopic-PSB (65;83;84), were developed later and were shown to approximate the sensitivity and specificity of bronchoscopic techniques (81).

Subsequently, in a randomized, controlled, multicenter study in France, it was 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 (50).

Pneumonia in residents of NHs is also difficult to diagnose because of unavailability of diagnostic tests (especially rapid viral diagnostic tests), the general inability of the patients to provide sputum specimens, and the difficulty of interpreting sputum cultures and chest radiographs (85).

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 (29;44;56-59;86-90). 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 (25;56;57;59;60;73;91). The bacterial pathogens that have been most frequently associated with nosocomial pneumonia in 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* (56;90).

The causative microbial agents of nosocomial pneumonia, including VAP, however, can vary depending on the length of time the patient has spent in the ICU and/or received mechanically assisted ventilation. VAP has been classified 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 pneumonia, when the results of microbiologic diagnostic testing are not yet available. EOP has been associated usually with non-multi-antimicrobial-resistant microorganisms such as *Escherichia coli*, *Klebsiella* spp., *Proteus* spp., *S. pneumoniae*, *H. influenzae*, and oxacillin-sensitive *S. aureus* (92). On the other hand, LOP has been associated with *Pseudomonas aeruginosa*, oxacillin-resistant *S. aureus*, and *Acinetobacter* spp.-- strains that are usually multi-antibiotic-resistant (92).

B. NHAP

Like cases of community-acquired pneumonia in the elderly, most cases (up to 79%) of NHAP have undetermined etiologies primarily because definitive etiologic diagnosis usually is not rigorously pursued (37;85). However, a review of several studies documenting the etiologic agents of endemic NHAP reported the identification of: *S. pneumoniae* in 0-39%, *S. aureus* in 0-33%, *H. influenzae* in 0-19% of cases, and aerobic Gram-negative bacilli in 0-55% of cases (85) (although culture isolation of Gram-negative bacilli from respiratory tract of patients with pneumonia may be confounded by the prevalence of these bacilli as respiratory-tract colonizers of NH residents). Although *Legionella* spp. and *Chlamydia pneumoniae* are not reported very often as etiologic agents (85;93), they have caused outbreaks in LTCFs (94-96). On the other hand, *Mycoplasma pneumoniae* has not been a significant pathogen in NHs (93). Viruses such as influenza and RSV have caused outbreaks in NHs and have been linked with the occurrence of pneumonia during these outbreaks (97).

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 health-care-associated pneumonia has not been shown. Of the plausible routes, micro-aspiration is

believed to be the most important for both health-care-associated and community-acquired pneumonia. In studies using radioisotope tracers, 45% of healthy adults were found to aspirate during sleep (98). 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 (12;13;16;25).

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 microorganisms into the lower respiratory tract (47;99-103). Although aerobic Gram-negative bacilli are recovered infrequently or are found in small numbers in pharyngeal cultures of healthy persons (99;104), 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 (47;102;103;105).

Oropharyngeal or tracheobronchial colonization by Gram-negative bacilli begins with the adherence of the microorganisms to the host's epithelial cells (101;106-108). Adherence may be affected by multiple factors related to the bacteria (e.g., presence of pili, cilia, or capsule, or production of elastase or mucinase), host cell (e.g., surface proteins and polysaccharides), and environment (e.g., pH and presence of mucin in respiratory secretions) (100;101;106;109-118). Studies indicate that certain substances (e.g., fibronectin) can inhibit the adherence of Gram-negative bacilli to host cells (109;111;119). Conversely, certain conditions (e.g., malnutrition, severe illness, or post-operative state) can increase adherence of gram-negative bacteria (100;109;113;118;120).

In addition to the oropharynx, the stomach has been postulated to be an important reservoir of organisms that cause health-care-associated pneumonia (16;121-125), although the exact role of the stomach in the causation of health-care-associated pneumonia, specifically VAP, has been critically investigated and debated (126-129). 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 (122;130-134). In healthy persons, few bacteria entering the stomach survive in the presence of hydrochloric acid at $\text{pH} < 2$ (135). However, when gastric pH increases from the normal levels to ≥ 4 , microorganisms are able to multiply to high concentrations in the stomach (133;135-138). This can occur in patients with advanced age (136), achlorhydria (135), ileus, or upper gastrointestinal disease, and in patients receiving enteral feeding, antacids, or histamine-2 (H-2) antagonists (122;133;134;138). The contribution of other factors (e.g., duodeno-gastric reflux and the presence of bile) to gastric colonization in patients with impaired intestinal motility also has been suggested (132).

The relative importance of oropharyngeal colonization over that of gastric colonization in the development of VAP has been strongly suggested in two studies. In one study, recovery of the etiologic agents of VAP by culture isolation occurred in the following sequence: from the oropharynx initially, then from the tracheo-bronchi and/or stomach (139). In the other study, mechanically ventilated patients who received selective oro-pharyngeal decontamination without concurrent decontamination of the stomach had a 60% lower risk of VAP compared to those who did not have such a treatment (140).

The importance of aspiration of bacteria found in dental plaques in the causation of health-care-associated pneumonia has been invoked by studies in which cultures of dental plaques have yielded pathogenic microorganisms that are prevalent etiologic agents of pneumonia (141;142).

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 respiratory tract infections including pneumonia (143;144) as well as other infections (145) were related to the use of contaminated large-volume nebulizers (i.e., humidification devices that produced large amounts of aerosol droplets <4 µm in size via ultrasound, spinning disk, or Venturi mechanism). Inhalation of contaminated aerosol is particularly hazardous for intubated patients because endotracheal tubes provide direct access to the lower respiratory tract. 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 (146;147); 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 health-care-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 into the respiratory tract or reflux from the gastrointestinal tract (e.g., 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 health-care personnel; and 4) host factors such as extremes of age, malnutrition, and severe underlying conditions, including immunosuppression (13;15;18;20;23;25;47;148-150).

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 (45;99), trachea (133), or stomach (122;138) prompted attempts by researchers to prevent the infection by various means, mainly by local and/or systemic antimicrobial prophylaxis.

Oropharyngeal and/or tracheal colonization

Local bacterial interference and aerosolized antimicrobial agents

Early studies centered on utilization of the phenomenon of local bacterial interference (151;152) or prophylactic aerosolization of antimicrobial agent(s) (153;154). Bacterial interference (with alpha-hemolytic streptococci) was successfully used by some investigators to

prevent oropharyngeal colonization by aerobic Gram-negative bacilli (151). However, the efficacy of this method for general use has not been evaluated. In small studies, aerosolization of antimicrobial agents has been shown to eradicate common Gram-negative bacillary pathogens from the upper respiratory tract and/or decrease the incidence of Gram-negative-bacillary pneumonia (153) or VAP (155); however, no effect on patient mortality rate has been shown (153) and superinfection occurred in some patients receiving the therapy (153;154;156;157). The use of intratracheal colistin was shown to significantly decrease the incidence of gram-negative bacillary and polymicrobial pneumonia in critically ill patients who were compared to historic controls (158). 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.

Selective oropharyngeal decontamination with antimicrobial agents

Recently, a study was conducted to determine the effect of selectively modulating the bacterial colonization of the oropharynx only (without modulating the gastric and intestinal colonization and without the concomitant use of systemic antimicrobial agent[s]) (140). The use of a topical prophylactic preparation containing gentamicin, colistin, and vancomycin resulted in the eradication of oropharyngeal and tracheal colonizers in 75% of the study patients (vs 0 and 9% of 2 groups of controls), prevented acquisition of new oropharyngeal colonizers in 90% of treated patients (vs 41% and 37% of untreated patients), and lowered the incidence of VAP (10%) in study patients (compared to 59% and 63% in two groups of control patients) (140). However, the use of the topical preparation was not associated with shorter duration of ventilation or ICU stay or longer survival in study patients.

Oropharyngeal cleaning and decontamination with an antiseptic agent

Two clinical studies (one in ICU with temporal controls and another in a multi-nursing-home setting using random controls) have shown a decrease in rates of pneumonia, including VAP, upon implementation of a comprehensive oral-hygiene program for patients or residents, respectively (159;160). The oral hygiene programs consisted of frequent toothbrushing and mouth-swabbing with an antiseptic agent; and in the ICU, frequent suctioning of the mouth and subglottic areas of patients receiving mechanically assisted ventilation. More randomized, controlled studies are needed to determine the role of a comprehensive oral-hygiene program in the prevention of VAP or NHAP. However, in the interim, it is prudent for health-care facilities to implement such a program.

Oral chlorhexidine rinse in adult patients undergoing cardiac surgery

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 (161). However, its use for preventing health-care-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 one of the most studied strategies designed to prevent lower respiratory tract infection in critically ill and/or mechanically ventilated patients by preventing bacterial colonization of the digestive tract (162-193). SDD is aimed at preventing oropharyngeal and gastric

colonization with aerobic Gram-negative bacilli and *Candida* spp., without altering the digestive tract's anaerobic flora. Various SDD regimens include 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. Several times a day, the local antimicrobial preparation is applied as a paste to the oropharynx and, except in one study (187), given orally or via the nasogastric tube for gastric decontamination. In addition, however, in many studies, a systemic (i.e., intravenous) antimicrobial agent such as cefotaxime or trimethoprim (TMP) is administered to the patient, thus rendering the regimen nonselective for the oropharynx (187) or oropharynx and stomach.

Although most clinical trials (162-165;167-174;176;177;182-184;187;189-193), including several meta-analyses (178;185;188), have demonstrated a decrease in the rates of hospital-associated respiratory infections with the use of SDD, these studies have been difficult to assess because they differ in study design and population, and many have had short follow-up periods. In addition, except in a few reports (166;169;180;182-184;186), in most of the studies, nonbronchoscopic methods were used to diagnose 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 (163;173;179;182;187;189;191;192), and in two meta-analyses and a primary study, 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 (188;190;193).

The cost of preventing VAP or mortality with the use of SDD has been estimated: in order to prevent one case of hospital-associated pneumonia or one death due to hospital-associated pneumonia, 6 (range: 5-9) or 23 (range:13-39) patients, respectively, would have to be given SDD (185).

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 (29;163;165;166;168;182;194).

Sucralfate, H-2 receptor antagonists, antacids, and stress-bleeding prophylaxis

The administration of antacids and/or H-2 receptor antagonists for prevention of stress bleeding in critically ill, postoperative, or mechanically ventilated patients has been associated with gastric bacterial overgrowth (123;137;138;195) and increased risk for pneumonia (16;123;134;196-198). 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 (199-201). The results of clinical trials comparing the risk of pneumonia in patients receiving sucralfate with that in patients given H-2 receptor antagonists and/or antacids have been variable. Early studies suggested that the use of sucralfate (compared to H-2 receptor antagonists and/or antacids) decreased the risk of pneumonia in ICU patients receiving mechanically assisted ventilation (123;134;198;199;202). More recent studies, however, failed to demonstrate the advantage of using sucralfate (203-205). In addition, another study has suggested that patients with acute respiratory distress syndrome who are administered sucralfate may even be at a greater risk of developing VAP compared to those who are not (206).

Acidified enteral feeding

Because enteral feeding can increase gastric pH (207) and result in gastric colonization, acidification of enteral solutions has been advocated to prevent gastric and tracheal colonization in patients receiving such treatment (208). The absence of “pathogenic” bacteria from the stomachs of patients given acidified enteral feeding has been shown; however, the effect on the incidence of pneumonia has not been evaluated (208;209).

Continuous versus intermittent enteral feeding

Continuous enteral feeding of mechanically ventilated patients, a common practice in ICUs, has been associated with increased gastric pH (133;210), subsequent gastric colonization with Gram-negative bacilli (21;210;211), and a high incidence of pneumonia (21); whereas intermittent enteral feeding has been associated with lower gastric pH and lower rates of pneumonia (211). However, in a cross-over study of intermittent enteral feeding of patients who had just had continuous enteral feeding, intermittent feeding had no lowering effect on gastric pH or gastric microbial colonization (212). In another study that compared intermittent and continuous enteral feeding, intermittent feeding resulted in decreased gastric pH during the “off-feeding” interval; however, the oropharyngeal and tracheal colonization rates and the incidence of VAP were similar in patients who received either treatment (213). More studies are needed to determine the effect of intermittent enteral feeding on the incidence 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 (13;98;214-220).

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 (216;218;221-223). Gross contamination of the enteral solution during its preparation (224-226) 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°-45°) has been beneficial (227), probably by preventing aspiration (223). Gastric contents that were labeled with radioactive material were aspirated via the gastro-esophageal route when patients were treated in the supine position (222;223;228). In two other studies of patients receiving mechanically assisted ventilation, significantly higher percentages (i.e., 23% and 36%) of patients who were supine developed pneumonia compared with 5% and 11% of those who were semi-upright, either during the first 24 hours of receipt of mechanically assisted ventilation (23) or during their receipt of both mechanically assisted ventilation and enteral feeding (227), respectively.

On the other hand, other measures that theoretically might be beneficial have yielded either negative or equivocal results in studies involving small numbers of patients: the use of flexible, small-bore nasogastric tubes did not reduce the incidence of gastroesophageal reflux or microaspiration (229); and placement of the enteral tube below the stomach (e.g., in the jejunum) had variable effects on the rate of aspiration (230-233) and the incidence of pneumonia (234-236).

Direct correlations have been reported between naso-tracheal (rather than oro-tracheal)

intubation and the occurrence of nosocomial maxillary sinusitis (237;238) and high incidence of pneumonia (238). 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 (13;16;25;239). In addition, bacteria can aggregate on the surface of the endotracheal tube over time and form a glycocalyx (i.e., biofilm) that protects the bacteria from antimicrobial agents or host defenses (240). 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 (241;242).

Drainage 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 (243;244). The effect of using an endotracheal tube that has a separate dorsal lumen which allows drainage (i.e., removal by suctioning) of the subglottic secretions has been compared to that of a conventional endotracheal tube (245-248). In the first study in ICU patients, intermittent (i.e., hourly) subglottic secretion drainage was associated with a lower incidence (13% vs 29%) as well as a delayed onset (16.2 ± 11 days vs 8.3 ± 5 days) of VAP (246). Subsequent studies corroborated these findings: lower VAP incidence: 14/76 (18.4%) vs 25/77 (32.5%) (248), and 3/49 (4%) vs 12/56 (16%) (247); and delayed onset of VAP: 12.0 ± 7.1 days vs 5.9 ± 2.1 days (248), and ± 2.3 days vs 2.9 ± 1.2 days (247); albeit the decrease in VAP incidence was not statistically significant: 8/160 (5%) vs 15/183 (8.2%) in one study of patients who had undergone cardiac surgery (245).

Although these randomized, controlled studies showed the beneficial effect of suctioning of subglottic secretions on the incidence of VAP, none showed a corresponding effect on mortality, length of stay in the ICU, or duration of mechanical ventilation. And, although a decision-model cost-effectiveness analysis has shown that as a VAP-prevention strategy, the use of endotracheal tubes that allow aspiration of subglottic secretions may result in savings, the study was hypothetical and based on data extrapolated from several studies instead of one study (249). Larger randomized controlled studies with cost-benefit analysis are needed to determine the exact role of the use these tubes in the overall scheme to prevent VAP and improve secondary outcomes.

Noninvasive ventilation (NIV): Noninvasive positive-pressure ventilation (NPPV):

NIV of patients in acute respiratory failure due to various causes is emerging as a potentially more advantageous method of delivering positive-pressure ventilation than endotracheal tube placement (250-255). NPPV has been shown to reduce the need for, and duration of, intubation, and has resulted in improved survival, particularly in patients with hypercapnic acute respiratory failure due to exacerbation of chronic obstructive pulmonary disease (COPD) (251;252;256;257). In several studies, the use of NPPV resulted in a decreased risk for pneumonia (254;256-260). In one of these studies, the incidence of pneumonia was three times lower (4 [18%] of 50) in those who received NPPV than in those (11 [60%] of 50) who

received the conventional treatment (i.e., intubation and mechanically-assisted ventilation) (258).

Repeat Endotracheal Intubation

Repeat insertion of the endotracheal tube soon after it is removed from a patient who is taken off ventilatory support has been shown to be a risk factor for pneumonia (149). Using NIV instead may help reduce the risk (261).

D. Cross-Colonization Via Hands of Personnel

Pathogens causing health-care-related pneumonia, such as Gram-negative bacilli and *S. aureus*, are ubiquitous in health-care settings, especially in intensive- or critical-care areas (262;263). Transmission of these microorganisms to patients frequently occurs via health-care personnel's hands that become contaminated or transiently colonized with the microorganisms (264-269). Procedures such as tracheal suctioning and manipulation of ventilator circuit or endotracheal tubes increase the opportunity for cross-contamination (269;270). 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 (11;269;271;272).

In theory, handwashing is an effective way of removing transient bacteria from the hands (271;272); however, in general, personnel compliance with handwashing has been poor (273-277). New guidelines for hand hygiene that promote the use of alcohol-based antiseptic preparations may result in increased personnel compliance and decreased incidence of hand-transmitted infections (278).

Gloving also helps prevent cross-contamination (279). Routine gloving (in addition to gowning) was associated with a decrease in the incidence of health-care-related RSV infection (280) and infections occurring in the ICU (281). Gloves, however, can be colonized by pathogens prevalent in the health-care setting (282), and outbreaks have been traced to health-care personnel who did not change gloves after contact with one patient and before providing care to another (283). In addition, gloved hands may get contaminated via leaks in the gloves (284). Thus, personnel should use gloves properly and decontaminate their hands after gloves are removed (278;279).

E. Contamination of Devices Used on the Respiratory Tract

Devices used on the respiratory tract for respiratory therapy (e.g., nebulizers, endotracheal tubes), diagnostic examination (e.g., bronchoscopes or spirometers), or administration of anesthesia are potential reservoirs or vehicles for infectious microorganisms (11;285-287). Routes of transmission may be from device to patient, from one patient to another, or from one body site to the lower respiratory tract of the same patient via hand or device (143;147;286-297). Contaminated reservoirs of aerosol-producing devices, e.g., nebulizers, can allow the growth of hydrophilic bacteria that may be subsequently aerosolized during device use (143;144;292). Gram-negative bacilli (e.g., *Pseudomonas* spp. or *Flavobacterium* spp.; *Legionella* spp.) and nontuberculous mycobacteria can multiply to high concentrations in nebulizer fluid (291;298-300) and increase the device user's risk of acquiring pneumonia (143;144;147;291;292;301-303).

Proper cleaning and sterilization or disinfection of reusable equipment are important components of a program to reduce infections associated with devices used for respiratory

therapy, pulmonary diagnostic tests, or delivery of anesthesia (286;288-290;292;304-308). Most 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), 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 (309). Thus, after they are thoroughly cleaned, they can be subjected to high-level disinfection by either using liquid chemical disinfectants that are cleared by the Food and Drug Administration (FDA) for use on medical instruments (310) or by pasteurization at $\geq 70^{\circ}\text{C}$ for 30 minutes (310-315).

Sterile water is preferred to tap or unsterilized distilled water for rinsing off residual liquid chemical disinfectant from a respiratory device that has been chemically disinfected for reuse, because tap or distilled water may harbor microorganisms that can cause pneumonia (298;299;316-318). However, when rinsing with sterile water is not feasible, rinsing with tap water or filtered water (water passed through 0.2 μ filter), followed by an alcohol rinse and forced-air drying, may be done (310). Forced-air drying has been shown to markedly lower the level of microbial contamination of stored endoscopes, most likely by removing the wet environment favorable for bacterial growth (319;320).

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 reported as an important source of bacterial contamination of inhaled gas. Thus, routine sterilization or high-level disinfection of the internal machinery is considered unnecessary.

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 and wick humidifiers produce no aerosol, they do not pose an important risk for pneumonia in patients (146;321). In addition, bubble-through humidifiers are usually heated to temperatures that reduce or eliminate bacterial pathogens (321;322). In general, however, sterile water is still used to fill these humidifiers (323) because of the potential presence in tap or distilled water, of microorganisms (e.g., *Legionella* spp.) that are more heat-resistant than other bacteria (302;306;317).

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 due to 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 (324). 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 (324). Spillage of the contaminated condensate into the patient's tracheobronchial tree can occur with procedures during which the tubing may be moved (e.g., suctioning, adjusting the ventilator setting, or feeding or giving

hygienic care to the patient) and may increase the patient's risk for pneumonia (324). Thus, in many health-care facilities, personnel are trained to prevent such spillage and drain and discard the fluid periodically. Microorganisms contaminating ventilator-circuit condensate can be transmitted to other patients via hands of the health-care personnel handling the fluid, especially if the personnel fail to decontaminate their 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 for many 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 (325). 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 (326). In addition, ventilatory circuit changes every 24 hours rather than every 48 hours was shown to be a risk factor for VAP in a study of ICU patients who were receiving mechanically assisted ventilatory support (16). Later reports suggested that the risk for pneumonia did not increase when the interval for circuit change was prolonged beyond 48 hours (327;328). 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 (329). Dreyfuss et al. 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 higher than when the circuits were changed every 48 hours (11 [31%] of 35) (330). More recently, Kollef et al. showed that the risk of acquiring pneumonia in patients whose breathing circuits were left unchanged indefinitely for the duration of their receipt of mechanical ventilation (unless the circuit was observed to be grossly contaminated) was not higher than in those whose breathing circuits were changed routinely every 7 days (331). And, Fink et al. found that patients whose circuits were changed every 2 days had >3 times the risk of acquiring VAP compared to those whose circuits were changed every 7 or 30 days (332).

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. health-care facilities (323;326;327;331).

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 (333). 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) (334-337). 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

periodic, routine changing of the tubing is not necessary (270). An HME, however, increases the dead space and resistance to breathing (338), may leak around the endotracheal tube, and may result in drying of sputum (339) and blockage of the tracheo-bronchial tree (340;341). Its effect on the work of breathing (338;342) and the ventilatory drive may cause increased inspiratory neuromuscular activity from the patients, which, if sustained during acute respiratory failure, may lead to inspiratory muscle fatigue (342). Thus, consideration of the economic advantages of the use of an HME should be balanced with its possible negative respiratory effects (342).

In 1998, Cook et al. reviewed five randomized, controlled studies comparing HMEs and heated humidifiers; the main outcome variable was pneumonia (343). A significantly lower incidence of pneumonia in the HME patient group was shown in one study (344), a tendency towards lower incidence of pneumonia in the HME group was seen in three other studies (339;341;345), and no difference in risk was seen in the only study in which PSB was used as a confirmatory method for diagnosing pneumonia (346). 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 (347).

Recently, an HME with an active humidifier (i.e., external heat and moisture added at the patient side of the HME) was designed to offset the device's negative effects (i.e., drying of patient's secretions and increased resistance to airflow) (348;349). However, studies assessing its effects on prevention of pneumonia have not been done.

c. Small-Volume (In-Line) and Hand-held Medication Nebulizers. Small-volume (in-line) medication nebulizers that are inserted in the inspiratory circuit of mechanical ventilators and hand-held liquid-medication nebulizers can produce bacterial aerosols (292). If in-line nebulizers 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 (324). Hand-held small-volume medication nebulizers have been associated with health-care-associated pneumonia, including Legionnaires disease, as a result of their contamination with medications from multidose vials (350-354) or with *Legionella*-contaminated tap water used for rinsing and filling the reservoir (306). Thus, when nebulized liquid medications are used, unit-dose vials are preferable to multi-dose vials. If multidose medication vials are used, the persons who handle, dispense, and store such medications should closely follow the medications' manufacturers' directions to prevent equipment and medication contamination.

2. Suction Catheters

Endotracheal 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 potential advantages of decreased environmental contamination as well as lower costs, especially if it can be corroborated that, notwithstanding the manufacturer-recommended daily catheter changes, the catheter can remain unchanged for an indefinite period without increasing the patient's risk of VAP (355). However, studies that compared the effect of the open single-use catheter system and that of the closed multi-use catheter system on the incidence of VAP have yielded equivocal results. Two studies showed no difference in the incidences of VAP in the two patient groups (356;357) while a third study showed the VAP incidence rate to be

lower (7.32 per 1,000 patient-days) in patients with the closed suction system than (15.89 per 1,000 patient-days) in those who had the open system (358). More studies are needed to determine the effect of the type of suction system on the incidence of VAP.

3. Resuscitation Bags, Ventilator Spirometers and Temperature Probes

Reusable resuscitation bags are particularly difficult to clean and dry between uses; microorganisms in secretions or fluid left in the bag may be aerosolized 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 (359-363). Ventilator spirometers and temperature probes have been associated with outbreaks of Gram-negative bacillary respiratory tract colonization and pneumonia resulting from patient-to-patient transmission of microorganisms (294;295;364;365). Devices such as these require sterilization or high-level disinfection between uses on different patients. Education of physicians, respiratory therapists, and nursing staff about the appropriate care and handling of these devices (in addition to appropriate hand decontamination between patients) is essential.

4. Anesthesia Equipment

The contributory role of anesthesia equipment in outbreaks of health-care-associated pneumonia was reported before hospitals implemented routine after-use cleaning and disinfection/sterilization of reusable components of anesthesia-equipment that may become contaminated with pathogens during use (366;367).

a. Anesthesia machine. The internal components of anesthesia machines (e.g., the gas sources and outlets, gas valves, pressure regulators, flow meters, and vaporizers) are not considered important sources of bacterial contamination of inhaled gases (368). 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, CO₂ 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 (369;370). 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 (371) are changed, cleaned, and sterilized or subjected to high-level disinfection periodically, according to published guidelines (310;369;370) and 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 (369) and shown to decrease contamination of the circuit (372-374). However, the efficacy of bacterial filters in preventing health-care-associated pneumonia has not been shown (375-378).

5. Pulmonary function testing equipment

In general, pulmonary function testing devices (e.g., spirometers, peak flow meters) have not been considered an important source of bacterial contamination of inhaled gas (379;380). However, because of concern about possible carry-over of bacteria from an infectious user of the device to the next patient-user(s) (381), placement of bacterial filters that remove exhaled bacteria between the patient and the testing equipment has been advocated (382). Randomized controlled studies have not been done to evaluate the efficacy of these filters in preventing health-care-associated pneumonia (383).

Whereas high-level disinfection of spirometer tubing and mouthpieces was recommended in the past because these spirometer parts could become contaminated with secretions during patient use (379), recent routine use of filters has obviated the need for such disinfection. Instead, the mouthpiece and the filter are changed between uses by different patients (384).

F. Post-operative State

A preoperative risk index for predicting postoperative pneumonia was recently developed from a study of 160,805 patients who underwent major noncardiac surgery, and validated using another pool of 155,266 surgical patients. The following significant risk factors were identified: type of surgery (abdominal aortic aneurysm repair, thoracic surgery, and emergency surgery); use of general anesthesia; age ≥ 60 years; totally dependent functional status; weight loss greater than 10%; steroid use for chronic conditions; recent history of alcohol use; history of chronic obstructive pulmonary disease; smoking within one year of surgery; impaired sensorium; history of cerebrovascular accident with residual neurologic deficit; low ($<8\text{mg/dL}$) or high ($>22\text{ mg/dL}$) blood urea nitrogen level; and receipt of more than 4 units of blood before surgery (385). These findings echo those from previous studies of risk factors for postoperative pulmonary complications, and underscore the major role of a patient's underlying health status in the occurrence of post-operative pneumonia (18;386).

Interventions aimed at reducing the postoperative patient's risk for pneumonia and other pulmonary complications have been developed; most measures have been geared towards clearing secretions and increasing lung expansion (387-391). These include deep breathing exercises, chest physiotherapy, use of incentive spirometry and continuous positive airway pressure by face mask. The results of studies looking at the effect of each of these maneuvers on the occurrence of postoperative pneumonia, bronchitis, or atelectasis are difficult to compare and interpret because of the relatively small numbers of patients per study; the differences in study design, endpoints, patient populations and surgical procedures; and the potential confounding effects of other forms of treatment (e.g., antibiotic administration, stress-ulcer prophylaxis) received by the study patients (387-397). A common finding among several studies, however, is the association between incentive spirometry and deep breathing exercises on one hand, and a lower incidence of postoperative pulmonary complications (including atelectasis, bronchitis, and clinically diagnosed pneumonia) on the other hand (387-389;391-397).

G. Other Prophylactic Measures

1. Immunomodulation

a. Pneumococcal vaccination. Although pneumococci are not a major cause of health-care-associated pneumonia, they have been identified as etiologic agents of serious health-care-associated pulmonary infection and bacteremia (398-401), and have caused outbreaks in NHs (402). 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, cerebro-spinal fluid (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 (403). In certain areas of the US, approximately 35% of invasive isolates have intermediate (MIC= 0.1-1.0 ug/ml) susceptibility or high-level (MIC ≥ 2 ug/ml) resistance to penicillin (404). Because many of the penicillin-resistant strains of pneumococci are also resistant to other antimicrobial agents (e.g., erythromycin, trimethoprim-sulfamethoxazole [TMP-SMZ], and extended-spectrum cephalosporins), therapeutic management of invasive pneumococcal infections (e.g., pneumonia) becomes difficult and expensive.

The 23-valent vaccine is cost-effective and protective against invasive pneumococcal disease when administered to immunocompetent persons aged ≥ 5 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 (405;406). The Advisory Committee on Immunization Practices (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 emphysema, 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 (405).

Because the 23-valent vaccine does not protect children aged < 2 years, the age group with the highest rate of invasive (e.g., bacteremia, meningitis) and noninvasive pneumococcal disease (i.e., community-acquired pneumonia, acute otitis media, and sinusitis), a 7-valent pneumococcal polysaccharide protein-conjugate vaccine has been recommended for use in all children aged < 2 years and for children aged 24-59 months who are at increased risk for pneumococcal disease (e.g., children with sickle cell disease, HIV infection, and other immunocompromising or chronic medical conditions). ACIP recommends that the vaccine be considered for all children aged 24-59 months, with priority given to children aged 24-35 months, children who are descendants of Alaska natives, American Indians, and African-Americans, and children who attend group day-care centers (407).

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 (408). To further facilitate the implementation of the SOP, in October 2002, the Centers for Medicare and Medicaid Services published an interim final rule that removes the physician-signature requirement from the Conditions of Participation for Medicare and Medicaid in participating hospitals, LTCFs, and home health agencies (where it is allowed under local and state laws) i.e., in these institutions, pneumococcal and

influenza vaccines may be administered to a Medicare or Medicaid patient without a written order from the patient's physician (409).

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 health-care facilities, e.g., at the time of patient discharge or facility visit, should contribute substantially to preventing the disease (405;410).

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 (411). However, its cost-effectiveness in the prevention of health-care-associated pneumonia has not been studied.

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 (412).

Granulocyte colony-stimulating factor (GCSF) increases the immune response of granulocytopenic patients to infections. It has been administered to patients with chemotherapy-induced febrile neutropenia (413-415) and to those with acute traumatic brain injury or cerebral hemorrhage (416) to decrease the incidence of health-care-associated infections in general. However, more studies are needed to determine specifically its efficacy in preventing pneumonia.

c. Use of glutamine-enriched enteral feeding. Deficiency of glutamine, 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 (417) and glutamine-enriched enteral feeding was associated with lower incidences of VAP and bacteremia in multiple-trauma patients (418). However, more studies are needed to define the role, if any, of glutamine administration in the prevention of VAP.

2. Administration of Antimicrobial Agents

a. Prophylactic systemic antimicrobial administration. Studies that evaluated the effect of systemic administration of an antimicrobial agent on the prevention of health-care-associated pneumonia have had conflicting results (419;420). In addition, prophylaxis with systemic antibiotics can potentially cause the emergence of and superinfection with antimicrobial-resistant microorganisms. More studies are needed to resolve this issue.

b. Periodic scheduled change in the class of antimicrobial agents used for empiric therapy of infections. Kollef et al. showed that the incidence of VAP in the ICU caused by antibiotic-resistant Gram-negative bacilli decreased significantly when a scheduled change was made in the class of antimicrobial agents (i.e., from a third-generation cephalosporin to a quinolone) used for empiric therapy of suspected Gram-negative bacillary infections in patients undergoing cardiac surgery (421). The authors attributed this finding to the quinolone's prevention of the emergence of infections 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. In a very similar study, Gruson et al. showed a decrease in the incidence of VAP caused by multi-resistant microorganisms after they instituted a strategy of antibiotic-use control in the medical ICU as follows:

1) restriction of the use of cefetazidime and ciprofloxacin for empiric or definitive therapy; 2) rotation of antimicrobial agents for use in the unit; and 3) supervision and control of antibiotic use by designated personnel (422). The use of this approach specifically to prevent health-care-associated pneumonia needs further evaluation.

3. Turning or Rotational Therapy

Turning or rotational therapy is used to prevent pulmonary and other complications of prolonged immobilization or bed rest as occur in patients with acute stroke, critical illness, head injury or traction, blunt chest trauma, and/or mechanically assisted ventilation (423-429). In the last two decades, automated beds or cushions have been used to provide turning therapy to immobilized patients. These equipment fall into 2 general classes based on the turning angle: the “kinetic” bed (i.e., one that achieves a 62°-angle turn), and the continuous lateral rotational therapy (CLRT) bed (i.e., one that turns $\leq 40^\circ$ along its longitudinal axis). Among the hypothesized benefits of using these beds are improved drainage of secretions within the lungs and lower airways, increased tidal volume, and reduction of venous thrombosis and its sequela, pulmonary embolization (430;431).

Cook et al. reviewed five randomized controlled studies that evaluated the efficacy of CLRT in preventing pneumonia (342;423;425-427;429). 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) (427). 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 and cultures of endotracheal aspirates.

A more recent study also has shown the association of turning therapy and lower incidence of pneumonia (432); however, a decrease in patient mortality was not shown in this or other previous studies (425-427;429;432). One other study reported no beneficial effect on incidence of pneumonia, length of ICU stay, or duration of mechanical ventilation (433).

Turning therapy is expensive; Kirschenbaum et al. estimated CLRT to cost a patient \$100-150/day. In the report by Cook et al., four patients would have to be on CLRT instead of the standard bed in order to prevent one case of health-care-associated pneumonia (342). Cost-effectiveness studies that utilize more specific diagnostic tests for pneumonia should be done before CLRT becomes routine therapy.

HEALTH-CARE-ASSOCIATED 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. (434).

I. EPIDEMIOLOGY

Numerous outbreaks of health-care-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) health-care-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 health-care-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) (435). 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 health-care-associated pneumonia due to *Legionella* spp. in North America has not been determined, although individual health-care institutions have reported ranges of 0%-14% (436-438). During an outbreak, the proportion of health-care-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 health-care-associated pneumonia in most U.S. health-care facilities, these ranges probably underestimate the incidence of Legionnaires disease (439).

Legionella spp. are commonly found in various natural and man-made aquatic environments (440;441) and may enter hospital water systems in low or undetectable numbers (442;443). Cooling towers, evaporative condensers, heated potable-water-distribution systems within health-care facilities, and locally produced distilled water can provide a suitable environment for these microorganisms to multiply. Factors known to enhance colonization and amplification of *Legionella* spp. in man-made water environments include temperatures of 25-42°C (444-448), stagnation (449), scale and sediment (445), and the presence of certain free-living aquatic amoebae that are capable of supporting intracellular growth of *Legionella* spp. (450;451).

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 (452-455). Persons with severe immunosuppression from organ transplantation or chronic underlying illnesses (e.g., hematologic malignancy or end-stage renal disease) are at markedly increased risk for legionellosis (452;454;456-461). Persons with diabetes mellitus, chronic lung disease, or non-hematologic malignancy; those who smoke cigarettes; and the elderly are at moderately increased risk (434). Health-care-associated Legionnaires disease also has been reported in patients infected with the HIV (462;463) 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 (464-467).

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 health-care-associated acquisition of disease were each independently associated with a fatal outcome (454).

The mortality from Legionnaires disease declined markedly between 1980 and 1998: from 34% to 12% for all cases, from 46% to 14% for nosocomial cases, and from 26% to 10% for community-acquired cases (468). It is not clear whether this decline reflects changes in empiric therapy for community- and health-care-associated pneumonia, or detection of milder cases of Legionnaires disease.

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 (469-471), and evidence of infection with other respiratory pathogens does not rule out the possibility of concomitant *Legionella* spp. infection (472;473).

The diagnosis of legionellosis may be confirmed by any one of the following: isolation of *Legionella* sp. 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) (474-477). 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 (478-481).

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 (474). Of the available tests, the most specific is culture isolation of *Legionella* sp. from any respiratory tract specimen (474).

Since the 1990s, the selection of diagnostic tests for Legionnaires disease has changed dramatically (468). The urine antigen has become the most frequent test by which reported cases of Legionnaires disease are detected. Diagnosis by culture and by direct fluorescent antibody and serologic testing decreased significantly. The consequence of this change is that cases of Legionnaires disease caused by species and serogroups other than *L. pneumophila* serogroup 1 have been rarely reported. This may allow undetected transmission of these microorganisms.

Therefore, when the diagnosis of Legionnaires' disease is being considered, patients should be tested with both the urine antigen test and cultures of appropriate respiratory specimens. The use of both tests allows rapid diagnosis of infections due to *L. pneumophila* serogroup 1 and detection and collection of isolates of all *Legionella* species and serogroups (468).

III. MODES OF TRANSMISSION

Inhalation of aerosols of water contaminated with *Legionella* spp. is believed to be the primary mechanism of entry of these microorganisms into a patient's respiratory tract (434). 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 (291;306;471;482-488). In other studies, aspiration of contaminated potable water or pharyngeal colonizers has been proposed as the mode of transmission to certain patients (486;489-492). Person-to-person transmission has not been observed.

IV. DEFINITION OF HEALTH-CARE-ASSOCIATED LEGIONNAIRES DISEASE

The incubation period for Legionnaires disease is generally 2-10 days (493); thus, for epidemiologic purposes in this document, laboratory-confirmed legionellosis that occurs in a patient who has spent ≥ 10 days continuously in a health-care facility prior to onset of illness is considered **definite** health-care-associated Legionnaires disease, and laboratory-confirmed infection that occurs in a patient who has spent 2-9 days in a health-care facility before onset of illness is considered **possible** health-care-associated infection.

V. PREVENTION AND CONTROL MEASURES

A. Prevention of Legionnaires Disease in Health-Care Facilities with No Identified Cases (Primary Prevention)

It is essential that health-care facilities with no cases of health-care-associated legionellosis formulate prevention strategies in accordance with each facility's specific situation. Therefore, these strategies may vary by institution, depending on the immunologic status of the patients, the design and construction of the facility, resources available for implementation of the 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 health-care-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 health-care facility's potable water system, for *Legionella* spp. (494;495). If any sample is culture-positive, diagnostic testing for Legionnaires disease is recommended for all patients with health-care-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 (495). When $\geq 30\%$ of the samples obtained are culture-positive for *Legionella* spp., the facility's potable water system is decontaminated. This approach is based on the premise that no cases of health-care-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 health-care-associated legionellosis may occur (489;496). 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 (497). 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 health-care-associated pneumonia in facilities that have had no cases of health-care-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 (498), often without being associated with known cases of disease (317;437;499). 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 (317). Interpretation of the results of routine culturing of water may be confounded by variable culture results from sites sampled within a single water system and by fluctuations in the concentration of *Legionella* spp. in the same site (500;501). 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 microorganisms; 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 microbial strain (502;503). 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 health-care 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 health-care facilities and in certain locality (494;495), has not been recommended universally (504).

The second approach to prevent and control health-care-associated legionellosis is by

- a) maintaining a high index of suspicion for legionellosis and appropriately using diagnostic tests for legionellosis in patients with health-care-associated pneumonia who are at high risk of developing the disease and dying from the infection (437;505);
- 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 health-care-associated Legionnaires disease;
- c) routinely maintaining cooling towers and potable-water systems, and filling nebulization devices only with sterile fluid (e.g., sterile water or aerosol medication); and
- d) circulating potable water at temperatures not conducive to the amplification of *Legionella* spp. (i.e., storing and distributing cold water below 20°C (68°F) and storing hot water above 60°C (140°F) and circulating it at a minimum return temperature of 51°C [124°F]) (504;506).

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 health-care-associated Legionnaires disease (439;457). The establishment of formal testing protocols in health-care facilities can improve the recognition of cases of health-care-associated legionellosis and facilitate focused, cost-effective interventions to reduce transmission.

Culturing of the facility water system for *Legionella* spp. 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 health-care facilities with patients at exceedingly high risk of developing Legionnaires' disease (e.g., HSCT recipients). Because HSCT recipients are at much higher risk for disease and death from legionellosis compared to most other patients (439;456;457;507), periodic routine culturing for *Legionella* spp. in water samples from the transplant unit's potable-water supply can be done (508) 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 (507). In addition, because of the absence of data regarding a “safe” concentration of *Legionella* spp. in potable water, the goal of an environmental surveillance for *Legionella* spp. in transplant units, if undertaken, should be to maintain water systems with no detectable *Legionella* spp. More importantly, however, clinicians must 1) maintain a high index of suspicion for legionellosis in HSCT recipients who develop health-care-associated pneumonia and 2) perform diagnostic testing (i.e., culture and urine antigen testing) for legionellosis in all HSCT recipients who develop health-care-associated pneumonia, even when environmental surveillance cultures do not yield *Legionella* spp.

In the 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 *Legionella* spp. are detected in its water. In addition, and until *Legionella* spp. 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 *Legionella* spp.; 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 *Legionella* spp., e.g., sterile water, should be used by transplant recipients for drinking, tooth brushing, or flushing of nasogastric tubes (485;490;507;509).

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 health-care-associated legionellosis have been identified. These measures include routine maintenance of potable water at $\geq 51^{\circ}\text{C}$ (124°F) or $< 20^{\circ}\text{C}$ (68°F) at the tap (in localities where it is allowed by state law) 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 (504;510-516). 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. (511;513;514). 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 fit tightly to exclude foreign material.

B. Prevention of Legionnaires Disease in Health-Care 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 health-care settings remain to be elucidated and probably vary from one health-care facility to another. In facilities where as few as 1-3 health-care-associated cases have been identified over a period of up to several months, intensified surveillance for Legionnaires disease has frequently detected numerous additional cases (457;483;486;512;517;518). This suggests the need for a low threshold for initiating an investigation following the identification of health-care-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 health-care facility with an HSCT program, the performance of a thorough investigation to identify the source(s) of *Legionella* spp. (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 health-care-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 (507).

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 *Legionella* spp. isolated from patients and environmental samples (488;519-521). The latter step can be crucial in supporting epidemiologic evidence of a link between human illness and a specific source (522-524).

In facilities where the cooling towers are found to be contaminated, measures that have been previously published should be used for decontamination (504;506).

In facilities where the heated-water system has been identified as the source of the organism, emergency decontamination of the system has been achieved by pulse (one-time) thermal disinfection or superheating (504;513;514;516;525). 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 (526). 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 (457;504;512-514;525;527). 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 (504;513).

Following either of these procedures, most health-care facilities maintain heated water with a minimum return temperature of $\geq 51^{\circ}\text{C}$ (where allowed by state law) or $< 20^{\circ}\text{C}$ at the tap or chlorinate heated water to achieve 1-2 mg/L free residual chlorine at the tap (437;489;500;504;511-514;528).

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 necessary because scale and sediment may accumulate and protect organisms from the biocidal effects of heat and chlorine (445;514). Alternative methods for controlling and eradicating *Legionella* spp. in water systems, such as treatment of water with chlorine dioxide, heavy metal ions (i.e., copper/silver ions), ozone, or ultraviolet light have limited the growth of *Legionella* spp. under laboratory or operating conditions (515;529-542). However, more data are needed regarding the long-term efficacy of these methods (543).

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 (544). 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 (545). 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 (546). In another study that retrospectively compared the incidences of nosocomial Legionnaires disease among hospitals in central Texas, no cases were noted in facilities located in municipalities with monochloramine-treated water (547). And, a survey of 166 US hospitals revealed that in hospitals supplied with municipal water that was disinfected with monochloramine, sporadic cases or outbreaks of facility-acquired Legionnaires disease were less likely to occur (548). However, additional data are needed about the effectiveness of using monochloramine before a recommendation can be made for its routine use as a disinfectant in health-care-facility water systems.

Because of a) the high costs of conducting an environmental investigation and eradicating *Legionella* spp. from sources in health-care facilities (526;549), 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 served by the facility.

HEALTH-CARE-ASSOCIATED PERTUSSIS

Pertussis is a highly infectious 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 (550;551). 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 (552). However, the disease has not been eliminated, 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 (553-561). It is estimated that 1-2 in 1,000 adolescents and adults contract pertussis each year (562). These infected adolescents and adults often serve as reservoirs for pertussis in young infants who are unimmunized or incompletely immunized (563). Pertussis in adults may result in pneumonia, urinary incontinence, or sinusitis (564).

Outbreaks of pertussis in health-care 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 health-care personnel or visitors, can also be a major source of pertussis in the health-care setting (562;565-570), especially because they can shed the microorganism for prolonged periods before the 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 after several weeks of cough. However, the clinical presentation of pertussis in the previously immunized person (older child, adolescent, or adult) is often, although not always, atypical (561). The illness may be mild but protracted. Patients may have a prolonged cough lasting for several weeks, without the classic “whoop” (571;572).

Laboratory diagnosis of pertussis is difficult (573). 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 (574). The other laboratory tests (i.e., direct fluorescein-conjugated antibody [DFA] tests, polymerase chain reaction [PCR] assays, and serologic assays) either have not been standardized or validated for general use (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 (573-576) 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 (577);

however, when it was utilized in an outbreak investigation in 1999, its sensitivity and specificity were only at <30% and 20%, respectively (578).

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 (579;580). In one study, the number of PCR-positive samples was 2.4-fold higher than the number of culture-positive specimens (581). The sensitivity of PCR, however, may decrease 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 ≥ 5 years, respectively (582). The main disadvantages of PCR are the lack of a standardized technique that has been validated among laboratories and the likelihood of false-positive results (583). Thus, it has been suggested that as much as possible, 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 (578;584).

Serologic assays for pertussis show potential to be a good diagnostic tool. Even single-sample determination of titers of IgG and IgA to various pertussis antigens can be highly sensitive mostly during the convalescent stage of the disease (576). For example, a combination of IgG anti-pertussis toxin and IgA anti-filamentous hemagglutinin enzyme-immunoassay testing (using age-specific reference values) had an estimated sensitivity of 81%-89% in diagnosing pertussis from a single serum sample taken 5-10 weeks after symptoms had started (585). Standardized 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 (578;586).

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. Patients can also be infected with *B. pertussis* when their nasal mucosa is touched by contaminated hands of other persons (e.g., health-care personnel), or by contaminated objects.

In one study, *B. pertussis* deoxyribonucleic acid (DNA) was recovered from air samples from filters placed as far as 4 meters from the bedside of a patient with pertussis (587). Transmission of pertussis by the airborne route, however, i.e., via droplet nuclei carried by air currents over long distances, has not been shown.

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 States, current recommendations for childhood vaccination include the use of diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine (588;589).

In recent years, the impetus for universal or selective vaccination of adults with pertussis antigens has become stronger with the development of DTaP (590) and the greater realization by the

medical community and the public, of the high prevalence of cases of pertussis in adults and adolescents and its impact on the transmission of the infection (561). The occurrence of outbreaks of pertussis in highly immunized populations of children aged 11-12 years (591) and adults has corroborated the finding that vaccine-induced immunity weakens considerably within 6-10 years after vaccination (592) and suggests that booster immunizations for older children, adolescents and adults may be necessary for the control of pertussis (593;594). However, the safety and efficacy of booster vaccinations in adults and children older than 7 years are still under study (578).

In health-care institutions that have had pertussis outbreaks, combinations of control measures have been utilized (565;567). 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 health-care personnel; granting of administrative leave (from work) status to health-care 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 (565;567). 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 surgical 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 when hands are visibly soiled, or with an alcohol-based hand rub when hands are not visibly soiled, after touching respiratory secretions or secretion-contaminated items, whether or not gloves are worn (and if gloves are worn, immediately after they are removed) and between patient contacts (278); 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 (279).

The use of a prophylactic antimicrobial agent, most notably erythromycin, for household contacts of patients with pertussis has been effective in preventing culture-positive pertussis (595). Chemoprophylaxis is most effective if administered within 3 weeks of the onset of cough in the index case (578). In an earlier review of 14 studies that evaluated the use of erythromycin for 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 administering whole-cell vaccine; however, some of the contacts in the studies started taking prophylaxis more than 3 weeks after cough onset in the index case (596). Adverse events, such as nausea, vomiting, and abdominal pain, were reported in association with erythromycin intake in three of the studies (596). In addition to these reports, post-exposure prophylaxis with erythromycin in neonates has been associated with the development of infantile hypertrophic pyloric stenosis (IHPS) (597;598). In one study, infants given erythromycin in the first 2 weeks of life had an 8-fold

increased risk for IHPS compared with infants not exposed to erythromycin (598). These findings suggest that erythromycin should be given with caution to very young infants (i.e., those <2 weeks of age). The American Academy of Pediatrics recommends that physicians who prescribe erythromycin to newborn infants should inform parents about the potential risks of IHPS development and signs of IHPS (599).

Nevertheless, erythromycin remains the drug of choice for treatment of and chemoprophylaxis for pertussis in persons who are not hypersensitive to the drug (578;599-601). In two outbreaks occurring in the health-care setting, health-care 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 (565;566). In one center, a case of nosocomial pertussis occurred in one of 61 erythromycin-treated health-care personnel; this necessitated treatment of all (exposed) unit personnel with a second course of another antibiotic for 10 days (566). In the other center, only one case of nosocomial pertussis was identified--in an infant who was not able to complete the prescribed course of prophylaxis with erythromycin (565).

Other macrolides have been found to be active against *B. pertussis* in vitro (602) and have been used successfully for its eradication; 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 (603). 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 5 mg/kg/day on days 2-5) resulted in the eradication of *B. pertussis* from 94% and 100% of nasopharyngeal cultures on days 7 and 14, respectively, after initiation of treatment (604). The incidence of IHPS in infants aged <2 weeks treated with azithromycin or clarithromycin is unknown.

For persons with hypersensitivity and/or intolerance to erythromycin, TMP-SMZ for 14 days (at one double-strength tablet twice a day for adults and 8 mg/kg/day TMP, 40 mg/kg/day sulfamethoxazole (SMZ) in 2 divided doses for children) has been successfully used for therapy (605) and has been the second-line drug for chemoprophylaxis (567;578;599).

During institutional outbreaks of pertussis, additional measures have been used to help control the transmission of *B. pertussis*: a) exclusion of health-care personnel who have symptoms of upper respiratory tract infection from the care of infants and other high-risk patients, including immunocompromised persons such as HSCT recipients; and b) limiting visitors to only those who do not have symptoms of a respiratory tract infection and are aged >14 years (565). Although the exact role of each of these measures in preventing the 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 health-care personnel was used safely as an adjunct to chemoprophylaxis (606). At present, however, there is no pertussis vaccine licensed for use in adults in the U.S.

HEALTH-CARE-ASSOCIATED 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, ornamental plants (607), and recently, water from hospital water system (608).

A. fumigatus and *A. flavus* are the most frequently isolated *Aspergillus* spp. in patients with proven aspergillosis (609-611). Aspergillosis, most notably IPA, has been recognized increasingly as a cause of severe illness and mortality in immunocompromised patients, e.g., patients undergoing chemotherapy and/or organ transplantation (including receipt of HSCT or solid-organ transplant) and patients with advanced HIV infection, specifically those with CD4 counts of <50/cu mm (610-623). In addition, patients with chronic lung disease such as chronic granulomatous disease (624) or who are receiving prolonged high-dose corticosteroid therapy also are susceptible to aspergillosis (625). Outbreaks of IPA have occurred mainly in severely neutropenic patients, especially those in HSCT units (615;621;626-631). Although IPA has been reported in recipients of solid-organ transplants (e.g., heart, kidney, liver, or lung), its incidence in these patients is lower than in recipients of HSCT (610;625;632-637).

The reported attributable mortality from IPA has varied according to patient risk groups. Mortality rates of up to 94% in recipients of allogeneic HSCT, 13%-80% in patients with aplastic anemia and leukemia (including non-allografted, intensely treated neutropenic patients with multiple myeloma), >80% in HIV-infected persons, and 68-100% in solid-organ transplant patients have been reported (610;615;616;621;638-640). 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 (623;641;642). Subsequently, the fungus may disseminate via the bloodstream to involve multiple other deep organs (609;623;643). A role for nasopharyngeal colonization with *Aspergillus* spp. as an intermediate step before invasive pulmonary disease has been proposed but remains to be elucidated (644;645). Likewise, colonization of the lower respiratory tract by *Aspergillus* spp., especially in patients with preexisting lung disease such as COPD, cystic fibrosis, or inactive tuberculosis, was reported to predispose patients to invasive pulmonary or disseminated infection (609;623;646); however, more recent data have not shown the correlation (647).

Host defenses against *Aspergillus* spp. involve the mobilization of both macrophages and granulocytes (648). 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 (649). 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 disease inhibits granulocyte respiratory burst oxidase activity, resulting in impaired microbicidal phagocytosis.

III. DIAGNOSIS

Diagnosing pneumonia due to *Aspergillus* spp. is often difficult (612). 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 (650). 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 (53%-64% sensitivity, 97%-99% specificity, and 75%-84% positive predictive value for IPA), culture (23%-40% sensitivity, 90% specificity, and 24.% positive predictive value for IPA), may be helpful in some cases (651;652).

By itself, culture isolation of *Aspergillus* spp. from respiratory tract specimens of patients may indicate colonization (653). 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 (654;655). Routine blood cultures are remarkably insensitive for detecting *Aspergillus* spp. (656).

Abnormalities detected by computerized tomography (CT) scanning often precede those detected by plain chest radiograph (657). In neutropenic patients, the most distinctive lesions are small nodules surrounded by a zone of low attenuation, termed the "halo sign" (658-661). 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* spp. 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 (662). Techniques have been developed to detect aspergillus galactomannan antigen in serum or urine of infected patients (663-665). 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 (666-669). The variable results obtained by using antibody or antigen assays for confirmation of IPA (670) suggest that more studies are needed to determine the appropriate and cost-effective clinical applications of these tests (671).

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 (>2 weeks) neutropenia is the most important host risk factor for IPA

(615;649). In addition, deficits in neutrophil function are also associated with IPA; these occur in patients with chronic granulomatous disease (624), patients receiving supraphysiologic doses of corticosteroids, or patients who develop graft-versus-host disease (GVHD) (619;629;672). Because HSCT recipients experience the most severe degree of neutropenia, they constitute the population at highest risk for developing invasive aspergillosis (639;673). The tendency of HSCT recipients to contract severe neutropenia is associated with the type of graft they receive. While both autologous (615) 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 (674). 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 (675).

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 (611;629;674-676).

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 (677).

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, construction, and/or renovation (626;678-685). Other hospital environmental sources that have been associated with IPA outbreaks include bird droppings in air ducts supplying high-risk patient areas (686) and contaminated fireproofing material or damp wood (626). Recently, hospital water was suggested as a possible vehicle for transmission of aspergilli. *Aspergillus* spp. were cultured from hospital water and water structures; and *A. fumigatus* isolated 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 (608). Larger, controlled studies, however, are needed to determine the role of water in the transmission of aspergillosis.

Attempts by researchers to identify the health-care 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 (687;688). Often, a correlation between patient and environmental isolates could not be demonstrated (628), 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 (689). The difficulties are due in part to air-sampling problems, the vast genetic diversity of *Aspergillus* isolates (690), and the limitations of the various subtyping methods for molds. Molecular typing techniques, i.e., karyotyping (691) and DNA endonuclease profiling (now available for *A. fumigatus*) (692;693), have been developed 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 health-care facility are acquired outside the hospital. This may occur prior to admission (i.e., during 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 (629;694).

V. CONTROL MEASURES

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

Most prevention studies have focused on IPA acquired in the hospital setting. However, in developing strategies to prevent IPA in HSCT recipients, infection-control personnel have to consider the patient's exposures to the fungus not only during the immediate post-transplantation period in the hospital, but also during a later period when the patient, especially the allogeneic HSCT recipient, may again develop severe neutropenia. Preventing patient exposures to *Aspergillus* spp. outside the hospital is difficult; but health-care providers can focus on decreasing the patient's exposure to dusty environments and reducing or eliminating obvious sources or reservoirs of *Aspergillus* spp., e.g., by removing plants and flowers from rooms where high-risk patients reside or receive medical treatment (e.g., in ambulatory-care settings) (507;695).

In the hospital setting, the provision of a PE to house the severely immunocompromised 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 (≥ 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 or anteroom, and e) well-sealed rooms (619;678;696-705). 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 ± 20 feet/minute), forcing the air to move in parallel streams or a laminar pattern (706). The air usually exits at the opposite end of the room, and ultra-high air-change rates (100-400 per hour) are achieved. The net effects are essentially sterile air in the room, minimal air turbulence, minimal opportunity for microorganism build-up, and a consistently clean environment (619).

The use of rooms with LAF was effective in decreasing the risk of nosocomial aspergillosis during the post-transplantation period in HSCT recipients (619) and in controlling outbreaks of aspergillosis related to hospital construction (678;681). However, a resultant reduction in patient morbidity and/or mortality with such a costly and difficult-to-maintain system has not been shown conclusively (707). 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 (696;708;709). Since the late 1990s, however, the survival of HSCT recipients with aplastic anemia has far exceeded that reported in the 1980s, and no randomized-control 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 (676) 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 immunocompromised patients other than allogeneic HSCT recipients in PE has not been shown either (705). Less expensive alternative systems with lower rates of air changes per hour (but maintained at ≥ 12 per hour) have been used in some centers (699;703;706;710;711).

Preventing exposure to aspergillus spores in the health-care facility also involves prevention of exposure to hospital demolition, construction, renovation, and dust-generating cleaning activities (679;685). Recommended measures have been published (506;507;679;685). In summary, during construction or renovation, facility planners should a) intensify efforts to seal off patient care units that house those at high risk for invasive aspergillosis (i.e., severely immunocompromised patients) and keep potentially spore-bearing air from the construction or renovation site from infiltrating the rooms or areas where severely immunocompromised patients are housed (712;713); b) clean newly constructed or renovated areas before allowing severely immunocompromised 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 pre-moistened with an FDA-approved hospital disinfectant (714), 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 do leave the PE, instruct them to wear high-efficiency masks in areas near building construction or renovation (715). Although the N95 respirator is untested specifically for its efficacy in reducing exposure to *Aspergillus* spp. in hospital construction or renovation areas, it can reduce reliably any aerosol exposure by 90%, with correct fit testing and training of its user (3;716).

A topical fungicide, copper-8-quinolinolate, may be helpful in reducing the environmental fungal spore burden: it was applied on environmental surfaces contaminated with *Aspergillus* spp. to help control a reported outbreak (717) and incorporated in paint or fireproofing material of a newly constructed facility (681).

B. Chemoprophylaxis

Because of the difficulty of preventing patient exposures to *Aspergillus* spp. in the environment, chemoprophylaxis with antifungal agents has been employed in an effort to decrease the patient's risk of IPA (718;719). However, its cost-effectiveness remains controversial.

In trials with historical controls, the use of low-dose amphotericin B (up to 0.25 mg/kg/day) prophylaxis or oral fluconazole was associated with reduced deaths from aspergillosis in HSCT or lung-transplant recipients (720;721). In one study, low-dose amphotericin reduced early systemic fungal infections and improved patient survival (although the latter effect was not directly related to the prevention of fungal infection) (722). 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, although less nephrotoxic than amphotericin B, are significantly more expensive and have not been shown to provide effective prophylaxis against IPA (723). Studies on the efficacy of nebulized amphotericin B administered by inhalation as prophylaxis for IPA have yielded variable results (724-726). Two recent studies suggested that itraconazole oral suspension can offer protection against deep fungal infections (including aspergillosis) that is equal to that from oral

amphotericin B (727) and greater than that from oral fluconazole (728). However, two meta-analyses have found no efficacy with the use of azole antifungal agents (e.g., itraconazole, fluconazole) or low-dose intravenous amphotericin B for chemoprophylaxis against IPA in patients with malignant disease who have severe neutropenia (729;730). In light of these equivocal findings, it has been recommended that when HSCT recipients' respiratory specimens are culture-positive for *Aspergillus* sp., a presumptive diagnosis of acute IPA should be made and preemptive and aggressive treatment (e.g., with intravenous amphotericin) should be started (507).

Relapse of invasive aspergillosis, including IPA, has occurred after HSCT receipt in about 33% of patients who had previous aspergillosis (731). 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 (672;732-736).

HEALTH-CARE-ASSOCIATED VIRAL PNEUMONIA

Viruses can be an important and often underestimated cause of health-care-associated pneumonia (737-740). In one prospective study of endemic health-care-associated infections, approximately 20% of patients with pneumonia had viral infections (738). Despite advances in diagnosis and treatment of viral respiratory infections, most cases remain undiagnosed and many patients in health-care facilities remain at high risk for developing severe and sometimes fatal viral infections (737;741-750). The potential for prolonged patient hospitalization and its attendant increased health-care costs (751-753), the high risk for serious complications of infection for some patients, and the occurrence of nosocomial outbreaks (754;755) underscore the importance of implementing measures to prevent the transmission of respiratory viruses in health-care facilities.

Health-care-associated viral respiratory infections 1) usually follow community outbreaks that occur during particular periods every year (755-759), 2) affect healthy and ill persons (743;744;751;760-763), and 3) are usually introduced into health-care facilities by patients, personnel, or visitors who have acute infections (764). A number of viruses, including adenoviruses, influenza virus, measles virus, parainfluenza viruses, RSV, rhinoviruses, and varicella-zoster virus, can cause health-care-associated pneumonia (744;755;764-772). However, adenoviruses, influenza viruses, parainfluenza viruses, and RSV account for most (70%) cases of health-care-associated pneumonia due to viruses (773).

This section focuses on the principles and approaches to control health-care-associated adenovirus, parainfluenza, and RSV infections. Prevention of health-care-associated influenza is discussed in another section in this document; infections due to other respiratory viral pathogens are addressed in another publication (279).

HEALTH-CARE-ASSOCIATED RSV INFECTION

I. EPIDEMIOLOGY

RSV is most noted for causing serious disease during infancy and early childhood. RSV bronchiolitis has been documented as the leading cause of hospital admissions for infants <1 year of age (774). However, infection with RSV confers only limited protective immunity; thus, persons can be repeatedly infected and develop serious disease throughout life (751;775;776). 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 (743;745;752;763;766;777-779). RSV infection in recipients of HSCT has been associated with mortality rates of >50% (779).

RSV transmission in health-care settings usually occurs during yearly community outbreaks of RSV infection (between December and March in the North American Continent) and are associated with marked increases in hospitalizations and deaths from pneumonia and bronchiolitis in young children (774;780;781). During community outbreaks of RSV infection, children with symptoms of lower respiratory tract disease who are admitted to health-care facilities often are infected with RSV and can introduce RSV into the health-care facility (754;782). RSV-infected personnel and visitors can also introduce RSV into health-care 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 (783;784). 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. However, suspicion of RSV infection in the neonate, the immunosuppressed patient, and the elderly 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 (766;785). 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 (751;786). The immunosuppressed patient can remain infected and shed virus for prolonged periods of time without symptoms (743;787).

Laboratory methods available to diagnose RSV and other viral respiratory infections include traditional tissue culture, shell-vial tissue culture, antigen detection assays, PCR assays, and serologic assays. The optimal method for diagnosing infection varies with the patient's age (777;788;789). 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) (790;791). 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 (789;792). The PCR assay for viral RNA is generally more sensitive than either tissue culture isolation or antigen detection (792-794).

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 (795;796).

The most rapid way to detect RSV infection (i.e., in <24 hours) is by antigen-detection using immunofluorescence, ELISA, 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 (764;797-801).

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 also 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 (782;802-804). Patients can also be infected with RSV when contaminated objects or hands of other persons (e.g., health-care personnel) touch their conjunctiva or respiratory mucosa. RSV can remain viable on environmental surfaces for up to 6 hours, sufficiently long to allow its transmission via fomites (803). In studies of RSV outbreaks in health-care facilities, it is often possible to identify multiple strains of RSV, indicating that multiple sources introduce the virus into the facility (760;762;805;806). During community outbreaks, RSV-infected patients, health-care personnel, and visitors are all potential sources of the virus (807). Infected infants, however, are probably the most effective sources of RSV because they shed high titers of the virus for prolonged periods and require very frequent close contact with their care givers, and therefore, present a greater chance of contaminating other persons or their environment with infectious respiratory secretions (808). Health-care personnel may become infected after exposure in the community or in the health-care facility, and in turn, infect patients, other health-care personnel, or facility visitors (767;809). Patients with suppressed immune systems can remain infectious for prolonged periods of time and be positive for RSV intermittently.

IV. CONTROL MEASURES

Various combinations of control measures ranging from the simple to the complex have been effective in preventing RSV infection and controlling RSV transmission in health-care facilities (280;749;809-817). Successful programs have had two elements in common: implementation of standard and contact precautions (279) and adherence by health-care personnel to these precautions. These precautions include a) hand decontamination with soap and water or an alcohol-based hand rub after touching respiratory secretions or secretion-contaminated items, whether or not gloves are worn, immediately after gloves are removed, and between patient contacts (278); b) gloving (with clean, nonsterile gloves) upon entering an infected patient's room or before handling patients, their respiratory secretions or contaminated items, and removing gloves promptly (and decontaminating

hands) after use, before handling other items or 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 (279). Other precautions include a) placing patients with proven or suspected RSV infection in private rooms or cohorting such patients either by their clinical signs and symptoms or by rapid laboratory testing for RSV (749); and b) limiting patient movement and transport from the room to those for essential purposes only.

Additional measures may be indicated to control ongoing transmission of RSV in health-care settings or prevent transmission to patients at high risk for serious complications of infections (e.g., 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 to facilitate patient placement and prevent exposure of high-risk patients; b) cohorting of personnel; c) exclusion of health-care 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 HSCT 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 (749;764;810;813;815;818;819). Although the exact role of each of these measures in preventing RSV transmission has not been determined, their use for controlling outbreaks and protecting patients who are at the greatest risk for serious disease is prudent.

Recently, two products, immune globulin intravenous (IGIV) with a high titer of RSV neutralizing antibody, and an intramuscular preparation of a humanized mouse monoclonal antibody that neutralizes RSV (palivizumab), have been licensed by the FDA and recommended for the prevention of hospitalizations for RSV lower respiratory tract disease in selected children aged <24 months who were born prematurely at <35 weeks gestational age and infants who have chronic lung disease (820). Palivizumab also is indicated for children with chronic lung disease who have ≥ 2 of the following risk factors: child care attendance, school-aged siblings, exposure to environmental pollutants, congenital abnormality of airways, and severe neuromuscular disease. Palivizumab, which is administered in 5 monthly injections of 15 mg/kg during the RSV season, is the preferred product because of its ease of administration, safety, and effectiveness (820;821).

FDA licensure for the use of palivizumab in other groups of children is under consideration. These children include those who are <24 months of age who have hemodynamically significant cyanotic or acyanotic congenital heart disease, including infants <12 months of age who have congenital heart disease and are most likely to benefit from immunoprophylaxis, i.e., those receiving medication to control congestive heart failure, those with moderate to severe pulmonary artery hypertension, and those with cyanotic heart disease (for which RSV-IGIV is contraindicated) (820).

The role for prophylactic palivizumab administration in other high-risk populations, e.g. those with cystic fibrosis or immune compromise, has not yet been determined. It has been

suggested that RSV-IGIV could be a substitute for standard IGIV in children with severe immunodeficiencies who are receiving monthly infusions of standard IGIV (820).

Paliviumab and RSV-IGIV have been shown to prevent hospitalizations for RSV lower respiratory tract disease (821-825); however, their effectiveness in controlling outbreaks of RSV infection in health-care settings, although suggested in one report (826), needs further study. In addition, the high cost of these products makes their use impractical for control or prevention of health-care-facility outbreaks. Cost-benefit studies of the prophylactic treatment have had varying conclusions: one study suggested that the preparations are cost-beneficial when given as recommended in the infant and young child; the other suggested otherwise (827;828). A third study pointed out that various factors, i.e., changes in the incidence of RSV infection, cost of hospitalization for RSV infection, and cost of palivizumab, may affect the “incremental” cost-effectiveness of palivizumab (829). Thus, in the setting of a health-care-associated RSV outbreak, it is 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.

HEALTH-CARE-ASSOCIATED 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 (e.g., croup, pneumonia, and bronchiolitis) (830). Taken together, the four serotypes of HPIV account for nearly as many cases of respiratory tract disease in children as does RSV (830-834). 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 (835). Although the four serotypes cause similar illnesses, the frequency of occurrence and other epidemiologic features of the illnesses differ from each other (830;831;836;837). 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 (830;835-837). The seasonal pattern for HPIV-4 infections has not been defined because of the infection's infrequent detection and the paucity of studies about 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 (838-840). PCR assays appear to be the most sensitive test for detection of infection in infants and young children (793;841), and was shown recently to be more sensitive than viral culture and antigen detection in adults (842).

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 viruses are 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, nose, or possibly mouth.

IV. CONTROL MEASURES

The control measures described in the preceding section on RSV Infection, also are applicable for prevention and control of HPIV infections in health-care settings.

HEALTH-CARE-ASSOCIATED ADENOVIRUS INFECTION

I. EPIDEMIOLOGY

Adenovirus infections occur predominantly in childhood and cause acute upper respiratory illness (843). Infections may be asymptomatic (844) and infected individuals may shed the virus for months or even years (845;846). Respiratory disease caused by adenovirus is most prevalent in late winter, spring, and early summer (844), but has been observed year-round. Forty-nine species of adenovirus are known to cause human infection, although not all species cause respiratory illnesses (846). Adenovirus infection of the respiratory tract can lead to symptoms of pharyngitis (844;847), bronchitis (844), croup (844), or pneumonia (844;848-851). Adenoviruses may also invade the gastrointestinal tract and cause diarrhea (852), or the conjunctiva and cause conjunctivitis (844;847;853;854). More serious complications leading to higher morbidity and mortality rates can occur in immunocompromised patients (855-858), premature infants (857), and patients with underlying pulmonary or cardiac disease (844;859). These patients may shed the virus for extended periods of time during which they are likely to infect other high-risk patients (857;860;861). Adenovirus can also remain latent within lymphatic tissue and become reactivated later upon immunosuppression of the host (846).

Healthcare-associated outbreaks of adenovirus infection leading to pneumonia (850;851;861) have occurred in hospital ICUs (860;861), pediatric chronic care facilities (862-864), military hospitals (865), and other health-care establishments (850;851). 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 (866). 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 the 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 (867;868). 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 (846;869). 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 (868;870-872).

III. MODES OF TRANSMISSION

The modes of adenovirus transmission have been studied during outbreaks of

keratoconjunctivitis or pharyngoconjunctival fever caused by adenovirus. In these outbreaks, shedding of adenovirus was demonstrated from 3 days before to 14 days after onset of symptoms and viral transmission to contacts was very efficient (873-876). 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 (851). Transmission by aerosol, the fecal-oral route, contaminated water, and possibly through sexual contact, has been suggested (851;853;877-882), 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 (883-886). 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 (883). Because adenovirus is a non-enveloped virus, it is not inactivated by detergents but can be inactivated by 70%-alcohol or chlorox solutions (887;888).

IV. PREVENTION AND CONTROL

Control of health-care-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 (862;865;873-875;889-891). A number of infection control strategies have been studied; adherence to 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 health-care 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 (892;893).

HEALTH-CARE-ASSOCIATED 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 (894-896). Influenza-associated pneumonia (as well as other influenza complications) can occur in any person but are more common in the very young (<24 months of age) or old and in persons in any age group with immunosuppression or certain chronic medical conditions, such as severe underlying heart or lung disease (897-904).

In North America, influenza typically occurs annually in the winter from December through April; peak activity in a community usually lasts from 6 to 8 weeks (905;906). During influenza epidemics in the community, outbreaks in health-care institutions can occur and are often characterized by abrupt onset and rapid spread of the infection (907-911). Most reported institutional outbreaks of influenza have occurred in nursing homes (912-919); however, outbreaks also have been reported on pediatric and chronic care wards, HSCT units, and medical and neonatal ICUs (755;904;908;920).

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-fomite-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 persons' hands from these surfaces (921). Airborne transmission by droplet nuclei has been suggested, albeit inconclusively, in some reports (922-924); however, this route is probably less important than person-to-person spread by either droplet or contact transmission (909).

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 (765;925;926). Children and severely immunodeficient persons may shed virus for longer periods (927-930). In addition, asymptomatic persons who are infected with influenza virus can shed the virus and potentially be infectious (931).

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% (932;933). In addition, infants can manifest a sepsis-like syndrome and 40% of young children can have vomiting or diarrhea (925;934). 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 (935).

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 (936-940). 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

(and allow antiviral-susceptibility testing when needed), a subset of patients with suspected influenza illness should be tested by viral culture also (936-939;941).

III. SURVEILLANCE

An active surveillance program for influenza-like illness can help health-care facilities identify facility-acquired cases of influenza early in their course and prevent influenza from spreading to other patients and health-care personnel (942). Before the influenza season, health-care personnel should be trained to recognize influenza illness and made aware of the available mechanisms for reporting patients with suspected influenza to those in charge of infection control. In addition, they should learn about the use of diagnostic tests for influenza as well as the use of droplet precautions (in addition to standard precautions) for patients with confirmed or suspected influenza. 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. In LTCFs, an active surveillance for influenza as well as for pneumonia can help identify facility-acquired cases of influenza.

IV. PREVENTION AND CONTROL OF INFLUENZA

A. Vaccination of Patients and Health-Care Personnel

Vaccination of persons at high risk for complications of influenza and persons who can transmit influenza to high-risk persons, i.e., health-care 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 (941;943-946). Both an inactivated and a live attenuated influenza vaccine (LAIV) are now available. The inactivated vaccine is administered by the intramuscular route and is approved for use in persons aged 6 months and older; LAIV is administered via a nasal spray and is approved for use only in healthy persons aged 5-49 years (941). There are no data assessing the risk of transmission of virus from LAIV recipients to immunosuppressed contacts. In the absence of such data, use of the inactivated influenza vaccine is preferred for vaccinating household members, health-care personnel, and others who have close contact with immunosuppressed individuals because of the theoretical risk that a live attenuated vaccine virus could be transmitted to, and cause disease in, the immunosuppressed individual. Although the risk of transmission of the live attenuated vaccine virus is thought to be low, use of the inactivated vaccine is preferred for persons (e.g., health-care personnel) exposed to persons at increased risk of influenza-related complications (947).

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 (948;949). High-risk groups for whom annual vaccination is recommended include persons ≥ 65 years of age; residents of nursing homes and other chronic-care facilities that house persons of any age who have chronic medical

conditions; adults and children who have chronic disorders of the pulmonary or cardiovascular diseases, including asthma; adults and children who have required medical follow-up or hospitalization during the preceding year because of chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies, or immunosuppression (including immunosuppression caused by medications or by HIV infection); children and adolescents (aged 6 months-18 years) who are receiving long-term aspirin therapy and therefore might be at risk for Reye syndrome after influenza infection; and women who will be in the second or third trimester of pregnancy during the influenza season (941;951-954). 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 absenteeism, medical visits, and antibiotic use (941;944;955;956). Because children aged 6-23 months are at substantially increased risk for influenza-related hospitalization, influenza vaccination for all children in this age group is encouraged when feasible (941).

Health-care personnel have been implicated in the transmission of influenza to patients; annual vaccination of health-care personnel, as well as others in close contact with persons at high risk for influenza complications, is recommended (907;908;941;942;944;957). Vaccination of health-care personnel is associated with decreased mortality among nursing home residents (945;946) and reduced health-care personnel illness and absenteeism (944;958).

Influenza vaccine, however, has been underutilized in institutional settings, even after it became a covered benefit of Medicare Part B (959). In order to improve vaccination coverage rates among adults, in March 2000, the ACIP published recommendations for the use of 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 (408). ACIP recommended the use of SOP in LTCFs, inpatient and outpatient facilities, managed-care organizations, assisted living facilities, correctional facilities, pharmacies, adult workplaces, and home health care agencies (408) after SOP programs were shown to be the most effective method of increasing adult vaccination rates (960). To further facilitate the implementation of the SOP to Medicare- and Medicaid-eligible patients, in October 2002, the US Department of Health and Human Services Centers for Medicare and Medicaid Services published an interim final rule that removes the physician-signature requirement for the administration of influenza and pneumococcal vaccines to Medicare and Medicaid patients in hospitals, long-term care facilities, and home health agencies in states where such is allowed (961).

B. Use of Antiviral Drugs

While vaccination of high-risk patients and health-care personnel is the primary focus of efforts to prevent and control influenza in health-care settings, the use of antiviral agents can be an important adjunct (941). 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 (962-964). Amantadine 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 (941). 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 (941). 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 (941). 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 1 day (941;962;963;965-969). 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 (962;964;970). These drugs have been studied extensively as components of influenza-outbreak control programs in nursing homes (916;962;971-973).

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 (974-977). The experience with prophylactic use of these agents in institutional settings or among patients with chronic medical conditions is limited, however (915;977-979).

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 health-care personnel who provide care to high-risk patients; and 5) when vaccine strains do not closely match the epidemic virus strain (941).

The decision about which antiviral agent to use as adjunct to vaccination in the prevention and control of health-care-related influenza is based in part on virologic and epidemiologic surveillance information from the health-care setting and the community. An antiviral agent can limit the spread of influenza in the health-care setting if the drug is administered to all or most patients once influenza illnesses begin in the facility (916;977;980;981). 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 (916;941;980).

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) (964;982). Gastrointestinal side effects occur in approximately 1%-3% of persons taking either drug (964). 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 (972;980). 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 (969;975). A reduction in the dose of oseltamivir is recommended for persons with renal insufficiency (941).

Zanamivir was not associated with significantly different side effects compared to inhaled lactose placebo in clinical trials (966;968;974). 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 (983).

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 (963;984;985). 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 (985-987). This is particularly important if the contacts involve uninfected high-risk persons (986;988).

Development of viral resistance to oseltamivir and zanamivir during their use for patient treatment has been identified but does not appear to be frequent (989-992). 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 (941). 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 (990). 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 (983;992).

D. Isolation Precautions and Other Measures

Measures in addition to vaccination and chemoprophylaxis are recommended for control of influenza outbreaks in health-care 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 upon entering the room or 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 patient movement or transport from the room is necessary, minimizing patient dispersal of droplets by making the patient wear a surgical mask, if possible) are recommended in addition to standard precautions for personnel (i.e., hand decontamination, gloving when handling the patient's respiratory secretions, and gowning when soiling with the patient's respiratory

secretions is likely) (279). The added value of placing patients with influenza in rooms for airborne-infection isolation (i.e., negative-pressure rooms) and using N95 respirators, or of using contact precautions, has not been assessed. In theory, however, contact precautions may be beneficial in infant cases because their secretions are difficult to contain. 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 persons with acute respiratory illnesses from visiting patients; and 4) work restriction for health-care personnel with acute respiratory illness (911;993).

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 (941).

HEALTH-CARE-ASSOCIATED SARS

SARS is an emerging respiratory tract infection apparently linked to a novel corona virus that first appeared in late 2002 in China and spread globally. In several Asian countries, the infection has caused outbreaks in health-care settings with transmission to large numbers of personnel and patients (994-996). Although the most important modes of transmission are by (large) droplet and contact, airborne transmission has not been ruled out. High-risk exposures, such as those associated with aerosolization of respiratory secretions and exposures to “super-shedders” have been associated with transmission of the disease to health-care personnel outside of the USA.

Current infection-control information about SARS is available at <http://www.cdc.gov/ncidod/sars/guidance/index.htm>.

PART II. RECOMMENDATIONS OF THE HEALTHCARE INFECTION CONTROL PRACTICES ADVISORY COMMITTEE

Categorization of Recommendations

In this document, as in previously published HICPAC guidelines, each recommendation is categorized on the basis of existing scientific evidence, theoretical rationale, applicability, and potential economic impact. In addition, a new category accommodates recommendations that are made on the basis of existing national or state 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 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 exists about efficacy.

PREVENTION OF HEALTH-CARE-ASSOCIATED BACTERIAL PNEUMONIA

I. Staff Education and Involvement in Infection Prevention

Educate health-care workers regarding the epidemiology of, and infection control procedures for, preventing health-care-associated bacterial pneumonia to ensure worker competency according to the worker's level of responsibility in the health-care setting, and involve the workers in the implementation of interventions to prevent health-care-associated pneumonia by using performance-improvement tools and techniques (997-1004).

CATEGORY IA

II. Infection and Microbiologic Surveillance

A. Conduct surveillance for bacterial pneumonia in ICU patients who are at high risk for health-care-associated bacterial pneumonia (e.g., patients with mechanically assisted ventilation or selected postoperative patients) to determine trends and help identify outbreaks and other potential infection-control problems (1005;1006). The use of the new NNIS system's surveillance definition of pneumonia is recommended (1007). Include data on the causative microorganisms and their antimicrobial susceptibility patterns (4). 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 (1005;1008;1009). Link monitored rates and prevention efforts and feed data back to appropriate health-care personnel (1010).

CATEGORY IB

B. In the absence of specific clinical, epidemiologic, or infection-control objectives, 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 (1011-1014).

CATEGORY II

III. Prevention 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 (308;310).

CATEGORY IA

b. Whenever possible, use steam sterilization (by autoclaving) or high-level disinfection by wet heat pasteurization at >158°F (>70°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 in Appendix). Use low-temperature sterilization methods (as approved by the Office of Device Evaluation, Center for Devices and Radiologic Health, FDA) for equipment or devices that

are heat- or moisture-sensitive (307;309;310;314;315). After disinfection, proceed with appropriate rinsing, drying, and packaging, taking care not to contaminate the disinfected items in the process (308;310).

CATEGORY IA

- c. Preferentially use sterile water for rinsing reusable semicritical respiratory equipment and devices when rinsing is needed after they have been chemically disinfected. If this is not feasible, rinse the device with filtered water (i.e., water that has been through a 0.2 μ filter) or tap water, and then rinse with isopropyl alcohol and dry with forced air or in a drying cabinet (310).

CATEGORY IB

- d. Adhere to provisions in the FDA's enforcement document for single-use devices that are reprocessed by third parties (310;1015).

CATEGORY IC

2. Mechanical ventilators

Do not routinely sterilize or disinfect the internal machinery of mechanical ventilators.

CATEGORY II

3. Breathing circuits, humidifiers, and HMEs

a. Breathing circuits with humidifiers

- (1) Do not change routinely on the basis of duration of use the breathing circuit (i.e., ventilator tubing and exhalation valve and the attached humidifier) that is in use on an individual patient. Change the circuit when it is visibly soiled or mechanically malfunctioning (327-332).

CATEGORY IA

(2) Breathing-circuit-tubing condensate

- (a) 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 (324).

CATEGORY IB

- (b) Wear gloves to perform the above procedure or handle the fluid (269;279).

CATEGORY IB

- (c) Decontaminate hands with soap and water (if hands are visibly soiled) or with an alcohol-based hand rub, after performing the procedure or handling the fluid (269;278).

CATEGORY IA

- (3) *No Recommendation* can be made for placing a filter or trap at the distal end of the expiratory-phase tubing of the

breathing circuit to collect condensate.

UNRESOLVED ISSUE

(4) Humidifier fluids

(a) Use sterile (not distilled, nonsterile) water to fill bubbling humidifiers (146;291;298;299;324).

CATEGORY II

(b) *No recommendation* can be made for the preferential use of a closed, continuous-feed humidification system.

UNRESOLVED ISSUE

b. Ventilator breathing circuits with HMEs

(1) *No recommendation* can be made for the preferential use of either HMEs or heated humidifiers to prevent pneumonia in patients receiving mechanically assisted ventilation (341;343-346;1016).

UNRESOLVED ISSUE

(2) Changing HMEs

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

CATEGORY II

(b) Do not routinely change more frequently than every 48 hours an HME that is in use on a patient (1017-1019).

CATEGORY II

(3) 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 (1020).

CATEGORY II

4. Oxygen humidifiers

a. Follow manufacturers' instructions for use of oxygen humidifiers (1015;1021-1023).

CATEGORIES II and IC

b. Change the humidifier-tubing (including any nasal prongs or mask) that is in use on one patient when it malfunctions or becomes visibly contaminated.

CATEGORY II

5. Small-volume medication nebulizers: in-line and hand-held nebulizers

a. Between treatments on the same patient: clean, disinfect; rinse with sterile water (if rinsing is needed), and dry small-volume in-line or hand-held medication nebulizers (292;306;1024). (See recommendation III-A-1-c if rinsing with sterile water is not feasible.)

CATEGORY IB

- b. Use only sterile fluid for nebulization, and dispense the fluid into the nebulizer aseptically (289;291;298;299;306;316;350).
CATEGORY IA
 - c. Whenever possible, use aerosolized medications in single-dose vials. If multidose medication vials are used, follow manufacturers' instructions for handling, storing, and dispensing the medications (289;350-354;1025).
CATEGORY IB
6. Mist-tents
- a. Between uses on different patients, replace mist tents and their nebulizers, reservoirs, and tubings with those that have been subjected to sterilization or high-level disinfection (1026).
CATEGORY II
 - b. *No Recommendation* can be made about the frequency of routinely changing mist-tent nebulizers, reservoirs, and tubings while in use on one patient.
UNRESOLVED ISSUE
 - c. Subject mist-tent nebulizers, reservoirs and tubings that are used on the same patient to daily low-level disinfection (e.g., with 2% acetic acid) or pasteurization followed by air-drying (1027).
CATEGORY II
7. Other devices used in association with respiratory therapy
- a. **Respirometers and ventilator thermometers**
Between their uses on different patients, sterilize or subject to high-level disinfection portable respirometers, and ventilator thermometers (294;295;305;364;365).
CATEGORY IB
 - b. **Resuscitation bags**
 - (1) Between their uses on different patients, sterilize or subject to high-level disinfection reusable hand-powered resuscitation bags (359-363).
CATEGORY IB
 - (2) *No Recommendation* can be made about the frequency of changing hydrophobic filters placed on the connection port of resuscitation bags.
UNRESOLVED ISSUE
8. **Anesthesia machines and breathing systems or patient circuits**
- a. Do not routinely sterilize or disinfect the internal machinery of anesthesia equipment (368).
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 (310;314).

CATEGORY IB

- c. *No recommendation* can be made about the frequency of routinely cleaning and disinfecting unidirectional valves and carbon dioxide absorber chambers (371).

UNRESOLVED ISSUE

- d. Follow published guidelines and manufacturers' instructions about in-use maintenance, cleaning, and disinfection or sterilization of other components or attachments of the breathing system or patient circuit of anesthesia equipment (369;370).

CATEGORY IB

- e. *No recommendation* can be made for placing a bacterial filter in the breathing system or patient circuit of anesthesia equipment (3;372-378).

UNRESOLVED ISSUE

9. Pulmonary-function testing equipment

- a. Do not routinely sterilize or disinfect the internal machinery of pulmonary-function testing machines between uses on different patients (379;380).

CATEGORY II

- b. Change the mouthpiece of a peak flow meter or the mouthpiece and filter of a spirometer between uses on different patients (379;384).

CATEGORY II

10. 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 (145;288;291).

CATEGORY II

- b. Faucet aerators

- (1) *No recommendation* can be made about the removal of faucet aerators from areas for immunocompetent patients (see also section on Legionnaires Disease, Part II, Section I-C-1-d).

UNRESOLVED ISSUE

- (2) 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 the unit (see also section on Legionnaires Disease, Part II, Section I-C-1-d) (506).

CATEGORY II

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

1. Standard Precautions

a Hand hygiene

Decontaminate hands by washing them with either antimicrobial soap and water or with nonantimicrobial soap and water (if hands are visibly dirty or contaminated with proteinaceous material or are soiled with blood or body fluids) or by using an alcohol-based antiseptic agent (e.g., hand rub) if hands are not visibly soiled after contact with mucous membranes, respiratory secretions, or objects contaminated with respiratory secretions, whether or not gloves are worn.

Decontaminate hands as described previously 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 (278;279).

CATEGORY IA

b. Gloving

(1) Wear gloves for handling respiratory secretions or objects contaminated with respiratory secretions of any patient (279).

CATEGORY IB

(2) Change gloves and decontaminate hands as described previously 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 (278-280;282;283).

CATEGORY IA

c. Gowning

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 (279;280).

CATEGORY IB

2. Care of patients with tracheostomy

a. Perform tracheostomy under aseptic conditions.

CATEGORY II

b. When changing a tracheostomy tube, wear a gown, use aseptic technique, and replace the tube with one that has undergone sterilization or high-level disinfection (279;308;310).

CATEGORY IB

c. No recommendation can be made for the daily application of topical antimicrobial agent(s) at the tracheostoma (1028).

UNRESOLVED ISSUE

3. Suctioning of respiratory tract secretions
(See also Section IV-B-1-d.)
 - a. *No recommendation* can be made for the preferential use of either the multiuse closed-system suction catheter or the single-use open-system suction catheter for prevention of pneumonia (343;356-358).
UNRESOLVED ISSUE
 - b. *No recommendation* can be made about wearing sterile rather than clean gloves when performing endotracheal suctioning.
UNRESOLVED ISSUE
 - c. *No recommendation* can be made about the frequency of routinely changing the in-line suction catheter of a closed-suction system in use on one patient (355).
UNRESOLVED ISSUE
 - d. If the open-system suction is employed, use a sterile single-use catheter.
CATEGORY II
 - e. Use only sterile 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 II

IV. Modifying Host Risk For Infection

A. Increasing Host Defense Against Infection: Administration of Immune Modulators

1. Pneumococcal vaccination. Vaccinate patients at high risk for severe pneumococcal infections:
 - a. Administer the 23-valent pneumococcal polysaccharide vaccine to persons aged ≥ 65 years; persons aged 5-64 years who have chronic cardiovascular disease (e.g., congestive heart failure or cardiomyopathy), chronic pulmonary disease (e.g., COPD or emphysema, but not asthma), diabetes mellitus, alcoholism, chronic liver disease (cirrhosis), or cerebro-spinal fluid (CSF) leaks; persons aged 5-64 years who have functional or anatomic asplenia; persons aged 5-64 years who are living in special environments or social settings; immunocompromised persons aged ≥ 5 years with HIV infection, leukemia, lymphoma, Hodgkin's disease, multiple myeloma, generalized malignancy, chronic renal failure, nephrotic syndrome, or other conditions associated with immunosuppression (e.g., receipt of HSCT, solid-organ transplant, or immunosuppressive chemotherapy, including long-term systemic

corticosteroids); and persons in long-term care facilities (401;405-407;410;1029).

CATEGORY IA

- b. Administer the 7-valent pneumococcal polysaccharide protein-conjugate vaccine to all children aged <2 years and to children aged 24-59 months who are at increased risk for pneumococcal disease (e.g., children with sickle-cell disease and other hemoglobinopathies or children who are functionally or anatomically asplenic; children with HIV infection; children who have chronic disease, including chronic cardiac or pulmonary disease [except asthma], diabetes mellitus, or CSF leak; and children with immunocompromising conditions including malignancies, chronic renal failure or nephrotic syndrome, receipt of immunosuppressive chemotherapy, including long-term corticosteroids, and receipt of solid-organ transplant). Consider administering the vaccine to all children aged 24-59 months, with priority given to children aged 24-35 months, children who are American Indians/Alaska Natives or black, and children who attend group child-care centers (407).

CATEGORY IB

- c. In nursing homes and other long-term care facilities, establish an SOP for the administration of 23-valent vaccine to persons at high risk of acquiring severe pneumococcal infections, including pneumococcal pneumonia (405;408;409).

CATEGORY IA

- 2. *No recommendation* can be made for the routine administration of preparations of GCSF or intravenous gamma globulin for prophylaxis against health-care-associated pneumonia (411-416).
- 3. *No recommendation* can be made for the routine enteral administration of glutamine for prevention of health-care-associated pneumonia (417;418).

UNRESOLVED ISSUE

B. Precautions for Prevention of Aspiration

As soon as the clinical indications for their use are resolved, remove devices such as endotracheal, tracheostomy, or enteral (i.e., oro- or nasogastric, or jejunal) tubes from patients (13;16;133;218-220).

CATEGORY IB

- 1. Prevention of aspiration associated with endotracheal intubation
 - a. Use of NIV to reduce the need for and duration of endotracheal intubation
 - (1) When feasible and not medically contraindicated, use noninvasive positive-pressure ventilation delivered continuously by face or nose mask, instead of performing endotracheal intubation in patients who are in respiratory

failure and are not needing immediate intubation (e.g., those who are in hypercapnic respiratory failure secondary to acute exacerbation of COPD or cardiogenic pulmonary edema) (254-256;258).

CATEGORY II

- (2) When feasible and not medically contraindicated, use NIV as part of the weaning process (from mechanically assisted ventilation) in order to shorten the period of endotracheal intubation (257).

CATEGORY II

- b. As much as possible, avoid repeat endotracheal intubation in patients who have received mechanically assisted ventilation (149).

CATEGORY II

- c. Unless contraindicated by the patient's condition, perform orotracheal rather than nasotracheal intubation on patients (237;238;343).

CATEGORY IB

- d. If feasible, use an endotracheal tube with a dorsal lumen above the endotracheal cuff to allow drainage (by continuous or frequent intermittent suctioning) of tracheal secretions that accumulate in the patient's subglottic area (245-248;343).

CATEGORY II

- 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 II

2. Prevention of aspiration associated with enteral feeding

- a. In the absence of medical contraindication(s), elevate at an angle of 30-45 degrees the head of the bed of a patient at high risk for aspiration pneumonia (e.g., a person receiving mechanically assisted ventilation or who has an enteral tube in place) (223;227;228).

CATEGORY II

- b. Routinely verify appropriate placement of the feeding tube (1030).

CATEGORY IB

- c. *No recommendation* can be made for the preferential use of small-bore tubes for enteral feeding (229).

UNRESOLVED ISSUE

- d. *No recommendation* can be made for preferentially administering enteral feedings continuously or intermittently (21;210;211;213).

UNRESOLVED ISSUE

- e. *No recommendation* can be made for preferentially placing the feeding tubes (e.g., jejunal tubes) distal to the pylorus (230-236).

UNRESOLVED ISSUE

3. Prevention or modulation of oropharyngeal colonization
 - a. Oropharyngeal cleaning and decontamination with an antiseptic agent
Develop and implement a comprehensive oral-hygiene program (that might include the use of an antiseptic agent) for patients in acute-care settings or residents in long-term care facilities who are at high risk of developing health-care-associated pneumonia (159;160).
CATEGORY II
 - b. Chlorhexidine oral rinse
 - (1) *No recommendation* can be made for the routine use of an oral chlorhexidine rinse for the prevention of health-care-associated pneumonia in all postoperative or critically ill patients or other patients at high risk for pneumonia (161).
UNRESOLVED ISSUE
 - (2) Use an oral chlorhexidine gluconate (0.12%) rinse during the perioperative period on adult patients who undergo cardiac surgery (161).
CATEGORY II
 - c. Oral decontamination with topical antimicrobial agents
No recommendation can be made for the routine use of topical antimicrobial agents for oral decontamination to prevent VAP (140).
UNRESOLVED ISSUE
4. Prevention of gastric colonization
 - a. *No recommendation* can be made for the preferential use of sucralfate, H₂-antagonists, or antacids for stress-bleeding prophylaxis in patients receiving mechanically assisted ventilation (134;197;199;203-205;1031-1033).
UNRESOLVED ISSUE
 - b. *No recommendation* can be made for the routine administration of SDD to all critically ill, mechanically ventilated, or ICU patients (162-194).
UNRESOLVED ISSUE
 - c. *No recommendation* can be made for routine acidification of gastric feeding (208;209).
UNRESOLVED ISSUE

C. Prevention of Postoperative Pneumonia

1. Instruct preoperative patients, especially those at high risk for contracting pneumonia, about taking deep breaths and ambulating as soon as medically indicated in the postoperative period. Patients at high-risk include those who will have abdominal aortic aneurysm repair, thoracic surgery, or emergency surgery; those who will receive general anesthesia; those who

are aged ≥ 60 years; those with totally dependent functional status; those who have had a weight loss $>10\%$; those using steroids for chronic conditions; those with recent history of alcohol use, history of COPD, or smoking during the preceding year; those with impaired sensorium, a history of cerebrovascular accident with residual neurologic deficit, or low ($<8\text{mg/dL}$) or high ($>22\text{ mg/dL}$) blood urea nitrogen level; and those who will have received more than 4 units of blood before surgery (385-387;389).

CATEGORY IB

2. Encourage all postoperative patients to take deep breaths, move about the bed, and ambulate unless these are medically contraindicated (387-389).

CATEGORY IB

3. Use incentive spirometry on postoperative patients at high risk for developing pneumonia (387-389).

CATEGORY IB

4. *No recommendation* can be made about the routine use of chest physiotherapy on all postoperative patients at high risk for pneumonia (387-389).

UNRESOLVED ISSUE

D. Other Prophylactic Procedures for Pneumonia

1. Administration of antimicrobial agents other than in SDD

- a. Systemic antimicrobial prophylaxis

No recommendation can be made about the routine administration of systemic antimicrobial agent(s) to prevent pneumonia in critically ill patients and/or in those receiving mechanically-assisted ventilation (193;420).

UNRESOLVED ISSUE

- b. Scheduled changes in the class of antimicrobial agents used for empiric therapy

No recommendation can be made for scheduled changes in the class of antimicrobial agents used routinely for empiric treatment of suspected infections in a particular group of patients (421;422).

UNRESOLVED ISSUE

2. Turning or rotational therapy

No recommendation can be made for the routine use of turning or rotational therapy, either by "kinetic" therapy or by continuous lateral rotational therapy (i.e., placing patients on beds that turn on their longitudinal axes intermittently or continuously) for prevention of health-care-associated pneumonia in critically ill or immobilized patients (343;423;425-427;429;432).

UNRESOLVED ISSUE

**PREVENTION AND CONTROL OF HEALTH-CARE-ASSOCIATED
LEGIONNAIRES DISEASE**

I. Primary Prevention (Preventing health-care-associated Legionnaires disease when no cases have been documented)

A. Staff Education

1. Educate physicians to heighten their suspicion for cases of health-care-associated Legionnaires disease and to use appropriate methods for its diagnosis.

CATEGORY II

2. Educate patient-care, infection-control, and engineering personnel about measures to prevent and control healthcare-associated legionellosis.

CATEGORY II

B. Infection and Environmental Surveillance

1. Maintain a high index of suspicion for the diagnosis of health-care-associated Legionnaires disease and perform laboratory diagnostic tests (both culture of appropriate respiratory specimen and the urine antigen test) 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 aged ≥ 65 years; or patients who have chronic underlying disease such as diabetes mellitus, congestive heart failure, and COPD) (436;452;454-456;461;463;464;517;518).

CATEGORY IA

2. Periodically review the availability and clinicians' use of laboratory diagnostic tests for Legionnaires disease in the facility, and if clinicians do not routinely use the tests on patients with diagnosed or suspected pneumonia, implement measures to enhance clinicians' use of the tests (e.g., by conducting educational programs) (439;457).

CATEGORY II

3. Routine culturing of water systems for *Legionella* spp.

- a. *No recommendation* can be made about routinely culturing water systems for *Legionella* spp. in health-care facilities that do not have patient-care areas (i.e., transplant units) for persons at high risk for *Legionella* infection (317;437;489;494;496;497;499;500;506;525;1034).

UNRESOLVED ISSUE

- b. In facilities with hemopoietic stem-cell- or solid-organ-transplantation programs, periodic culturing for legionellae in water samples from the transplant unit(s) can be performed as part of a comprehensive strategy to prevent Legionnaires disease in transplant recipients (506-508;1035).

CATEGORY II

- c. If such culturing (as in b) is undertaken:
 - (1) *No recommendation* can be made about 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 health-care-associated pneumonia even when environmental surveillance cultures do not yield legionellae (439;456).
CATEGORY IB

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

- 1. Nebulizers and other devices
 - a. Preferentially use sterile water for rinsing nebulization devices and other semicritical respiratory-care equipment after they have been cleaned or disinfected (306;1036). If this is not feasible, rinse the device with filtered water (i.e., water that has been through a 0.2 μ filter) or tap water and then rinse with isopropyl alcohol and dry with forced air or in a drying cabinet (310).
CATEGORY IB
 - b. Use only sterile (not distilled, nonsterile) water to fill reservoirs of devices used for nebulization (291;302;306;317;1036).
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 at least daily and filled only with sterile water (302;1036)
CATEGORY II
 - d. Faucet aerators
 - (1) *No recommendation* can be made for the removal of faucet aerators from areas for immunocompetent patients (see also Bacterial Pneumonia, Part II, section III-A-10-b).
UNRESOLVED ISSUE
 - (2) 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 severely immunocompromised patients (506).
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 (482;483;504;506).

CATEGORIES IB 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 (482;483;504;506).

CATEGORIES IB and IC

3. Water-distribution system

- a. Where practical and allowed by state law, maintain potable water at the outlet at $\geq 51^{\circ}\text{C}$ ($\geq 124^{\circ}\text{F}$) or $< 20^{\circ}\text{C}$ ($< 68^{\circ}\text{F}$), especially in facilities housing organ-transplant recipients or other patients at high risk (504;511;513;514;527). If water is maintained at $\geq 51^{\circ}\text{C}$, use thermostatic mixing valves to prevent scalding (510).

CATEGORY II

- b. *No recommendation* can be made about the treatment of water with chlorine dioxide, heavy-metal ions, ozone, or ultraviolet light (515;529-543;549). (*UNRESOLVED ISSUE*). Hospitals served by municipalities with monochloramine-treated water have had success in controlling legionella (546;548).

4. Health-care facilities with hemopoietic stem-cell or solid-organ transplantation 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)-i to II-B-2-b-3)-a)-v.

CATEGORY IB

- b. Restrict severely immunocompromised patients from taking showers (507;509).

CATEGORY IB

- c. Use water that is not contaminated with *Legionella* spp. for HSCT patients' sponge baths (487;490).

CATEGORY IB

- d. Provide HSCT patients with sterile water for tooth brushing or drinking, or for flushing nasogastric tubes (490;507).

CATEGORY IB

- e. Do not use water from faucets with *Legionella*-contaminated water in patients rooms to avoid creating infectious aerosols (509).

CATEGORY II

II. SECONDARY PREVENTION (Response to identification of laboratory-confirmed health-care-associated Legionellosis)

A. In Facilities with HSCT or Solid-Organ Transplant Recipients:

When one inpatient of an HSCT or solid-organ transplant unit develops a case of laboratory-confirmed definite (i.e., after ≥ 10 days of continuous inpatient stay) or possible (i.e., within 2-9 days of inpatient stay) health-care-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 before 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 II-B-2-b-(5) to determine the source(s) of *Legionella* spp. (506;507). Include but not limit the investigation to such potential sources as showers, water faucets, cooling towers, hot-water tanks, and carpet-cleaner water tanks (457;471;518). On its identification, decontaminate or remove the source of *Legionella* spp.

CATEGORY II

3. If the health-care facility's potable water system is found to be the source of *Legionella* spp., observe the measures outlined in Section I-C-4-b to e about the nonuse of the facility's potable water by recipients of HSCT or solid-organ transplants; and decontaminate the water supply as per Section II-B-2-b-(3)-(a)-i to v.

CATEGORY IB

4. Do not conduct an extensive facility investigation when an isolated case of possible health-care-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 (e.g., HSCT or Solid-Organ Transplant Recipients):

When a single case of laboratory-confirmed definite health-care-associated Legionnaires disease is identified, or when two or more cases of laboratory-confirmed possible health-care-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 through a retrospective review of microbiologic, serologic, and postmortem data to identify previous cases, and begin an intensive prospective surveillance for additional cases of

health-care-associated Legionnaires disease.

CATEGORY II

- a. If no evidence of continued nosocomial transmission exists, continue the intensive prospective surveillance for cases for ≥ 2 months after surveillance is begun.

CATEGORY II

- b. If evidence of continued transmission exists:

- (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 (291;306;482-488;519;521;523;524).

CATEGORY IB

- (2) If a source is not identified, continue surveillance for new cases for ≥ 2 months and, depending on the scope of the outbreak, decide to either defer decontamination pending identification of the source(s) of *Legionella* spp. or proceed 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 the source.

CATEGORY IB

- (a) If the heated water system is implicated:

- i. Decontaminate the heated water system either by superheating or by hyperchlorination. To superheat, raise the hot water temperature to 71°C-77°C (160°F-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; however, the optimal flush time is not known and longer flush times might 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 on which thermal shock treatment is not possible, use shock chlorination as an alternative. Add chlorine,

preferably overnight, to achieve a free chlorine residual of ≥ 2 mg/L (≥ 2 ppm) throughout the system. This might 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 (504;512-514;519;525;526;528).

CATEGORY IB

- ii. Depending on local and state regulations about potable water temperature in public buildings (527), circulate potable water at temperatures not conducive to amplification of *Legionella*: store and distribute cold water at $< 20^{\circ}\text{C}$ ($< 68^{\circ}\text{F}$); and store hot water at $> 60^{\circ}\text{C}$ ($> 140^{\circ}\text{F}$) and circulate it at minimum return temperature of 51°C (124°F) (506;511;513;514;527).

CATEGORY II

- iii. If the methods described in 3a-i and 3a-ii are not successful in decontaminating the hospital's water, seek expert consultation for review of decontamination procedures and assistance with further efforts.

CATEGORY II

- iv. *No recommendation* can be made for the treatment of water with chlorine dioxide, heavy-metal ions, ozone, or ultraviolet light (515;529-543;549). (Hospitals have reported successful decontamination using each of these methods.)

UNRESOLVED ISSUE

- v. Clean hot-water storage tanks and water heaters to remove accumulated scale and sediment (506).

CATEGORY IB

- (b) If cooling towers or evaporative condensers are implicated, decontaminate the cooling-tower system (482;483;504;506).

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 the initial decontamination, or a combination of superheating and hyperchlorination (528).
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 II

PREVENTION AND CONTROL OF HEALTH-CARE-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 (565;567).

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 (565).

CATEGORIES II and IC

B. Conduct active surveillance for cases of pertussis until 42 days after the onset of the last pertussis case (578).

CATEGORY II

C. Notify persons who have had close contact with a case of pertussis in the health-care setting so that they can be monitored for symptoms of pertussis or administered appropriate chemoprophylaxis. Close contact includes face-to-face contact with a 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 (e.g., ≥ 1 hour) with a symptomatic patient; or direct contact with respiratory, oral, or nasal secretions from a symptomatic 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) (578).

CATEGORY II

III. Prevention of Pertussis Transmission

A. Vaccination for Primary Prevention

1. *No recommendation* can be made for routinely vaccinating adults, including health-care workers, with the acellular pertussis vaccine at regular intervals (e.g., every 10 years) (562;578;593;594;1037).

UNRESOLVED ISSUE

2. In LTCFs for children and for children with prolonged stay in acute-care facilities, follow the recommendations of ACIP for vaccinating children according to their chronologic age (578;589).

CATEGORY IB

B. Vaccination for Secondary Prevention

1. *No recommendation* can be made for vaccinating adults, including health-care workers, during an institutional outbreak of pertussis (578;606).

UNRESOLVED ISSUE

2. During an institutional outbreak of pertussis, accelerate scheduled

vaccinations to infants and children aged <7 years who have not completed their primary vaccinations, as follows:

- a. Infants aged <2 months who are receiving their initial vaccination: Administer the first dose of the DTaP vaccine as early as age 6 weeks 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 ≥ 6 months after the third dose (578;588;1038).

CATEGORY II

- b. Other children aged <7 years: Administer DTaP vaccine to all patients who are aged <7 years and are not up-to-date with their pertussis vaccinations, as follows: administer a fourth dose of DtaP vaccine if the child has had 3 doses of DTaP or diphtheria, tetanus and pertussis (DTP) vaccine, is ≥ 12 months old, and >6 months have passed since the third dose of DTaP or DTP vaccine; administer a fifth dose of DTaP vaccine if the child has had four doses of DTaP or DTP vaccine, is aged 4-6 years, and received the fourth vaccine dose before the fourth birthday (567;578;588;589).

CATEGORY IB

3. Vaccination of children with a history of well-documented pertussis disease *No recommendation* can be made for administering additional dose(s) of pertussis vaccine 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) (578;589).

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 (278;578).

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 (278;578).

CATEGORY IB

- b. Perform diagnostic laboratory tests (for confirmation or exclusion of pertussis) on patients who are admitted with or who develop signs

and symptoms of pertussis to allow for the earliest possible downgrading of infection-control precautions to the minimum required for each patient's specific infection(s) (565;569;579;580;582).

CATEGORY IB

D. Management of Symptomatic Health-Care Personnel

1. In conjunction with employee health personnel, perform diagnostic laboratory tests for pertussis in health-care personnel with illness suggestive of pertussis (i.e., unexplained cough illness of >1 week duration, paroxysmal cough) (565;567;569;579;580;582).

CATEGORY IB

2. In conjunction with employee health personnel, treat symptomatic health-care 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-2 (565;566).

CATEGORY IB

3. Restrict symptomatic pertussis-infected health-care workers from work during the first 5 days of their receipt of antimicrobial therapy (566;567;578).

CATEGORY IB

E. Masking

In addition to observing standard precautions, wear a surgical mask when within three feet of a patient with confirmed or suspected pertussis, when performing procedures or patient-care activities that are likely to generate sprays of respiratory secretions, or on entering the room of a patient with confirmed or suspected pertussis (279).

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 (567;595).

CATEGORY IB

- a. With vigilance for IHPS when done in infants aged <2 weeks, use erythromycin (i.e., erythromycin estolate, 40-50 mg/kg day for children and 500 mg four times daily for adults, or erythromycin delayed-release tablets, 333 mg three times daily for adults) for 14 days (567;597; 598;600;601).

CATEGORY IB

- b. For patients who are intolerant to erythromycin, use any of the following regimens: azithromycin for 5-7 days (at 10-12 mg/kg/day) or for 5 days (at 10 mg/kg on day1 followed by four days at 5 mg/kg/day) for infants and young children; or clarithromycin for 10-

14 days (at 500 mg twice a day for adults or 15-20 mg/kg/day in two divided doses for children) (567;578;602;603).

CATEGORY II

2. For chemoprophylaxis of persons who have hypersensitivity or intolerance to erythromycin, use (except in the case of a pregnant woman at term, a nursing mother, or an infant aged <2 months) TMP-SMZ for 14 days (at one double-strength tablet twice a day for adults and 8 mg/kg/day TMP 40 mg/kg/day SMZ in 2 divided doses for children) (578;600;605).

CATEGORY IB

G. Work Exclusion of Asymptomatic Health-Care Workers Exposed to Pertussis

1. Do not exclude from patient care a health-care worker who remains asymptomatic and is 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) (279).

CATEGORY II

2. If mandated by state law or where feasible, exclude an exposed, asymptomatic health-care worker who is unable to receive chemoprophylaxis, from providing care to a child aged <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 (567).

CATEGORIES II and IC

H. Other measures

1. Limiting patient movement or transport
Limit the movement and transport of a patient with diagnosed or suspected pertussis from his room to those for essential purposes only. If the patient is transported out of the room, ensure that precautions are maintained to minimize the risk for disease transmission to other patients and contamination of environmental surfaces or equipment (279).

CATEGORY IB

2. Limiting visitors
Do not allow persons who have symptoms of respiratory infection to visit pediatric, immunosuppressed, or cardiac patients (279;565;1039).

CATEGORY IB

PREVENTION AND CONTROL OF HEALTH-CARE-ASSOCIATED PULMONARY ASPERGILLOSIS

I. Staff Education and Infection Surveillance

A. Staff Education

Educate health-care personnel according to their level of responsibility regarding infection-control procedures to decrease the occurrence of health-care-associated pulmonary aspergillosis.

CATEGORY II

B. Surveillance

1. Maintain a high index of suspicion for health-care-associated pulmonary aspergillosis in severely immunocompromised patients (i.e., patients with severe, prolonged neutropenia [ANC <500/mm³ for 2 weeks or <100/mm³ for 1 week], most notably HSCT recipients and including recipients of solid-organ transplants or patients with hematologic malignancies who are receiving chemotherapy, when they are severely neutropenic as defined previously).and persons receiving prolonged high-dose steroids (614;617;618;625;629;649;673;676).

CATEGORY IA

2. Maintain surveillance for cases of health-care-associated pulmonary aspergillosis by establishing a system by which the facility's infection-control personnel are promptly informed when *Aspergillus* sp. is isolated from cultures of specimens from patient's respiratory tract and by periodically reviewing the hospital's microbiologic, histopathologic, and postmortem data.

CATEGORY II

3. Surveillance cultures

a. Do not perform routine, periodic cultures of the nasopharynx of asymptomatic patients at high risk (1040;1041).

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 (1041).

CATEGORY IB

c. *No recommendation* can be made about routine microbiologic air sampling before, during, or after facility construction or renovation, or before or during occupancy of areas housing immunocompromised patients (506;1042).

UNRESOLVED ISSUE

4. In facilities with PEs, perform surveillance of the ventilation status of these areas either by continuous monitoring or periodic analysis of the following parameters: room air exchanges, pressure relations and filtration efficacy to

ensure that appropriate levels are maintained (506;706).

CATEGORY IB

II. Prevention of Transmission of *Aspergillus* spp. Spores

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

1. 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 accumulation of fungal spores via 1) HEPA filtration of incoming air, 2) directed room airflow, 3) positive air pressure in patient's room in relation to the corridor, 4) well-sealed room, and 5) high (≥ 12) air changes per hour (506;619;700;702;704).
CATEGORIES IB and IC
 - b. Do not use LAF routinely in PE (506;507;681;696;707).
CATEGORY IB
2. Units for autologous HSCT and solid-organ transplant recipients
No recommendation can be made for constructing PE for recipients of autologous HSCTs or solid-organ-transplants (e.g., heart, liver, lung, kidney) (506;705).
UNRESOLVED ISSUE

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

1. Placement of patients in PE
 - a. Place an allogeneic HSCT recipient in a PE that meets the conditions outlined in Section II-A-1.
CATEGORY IB
 - b. *No recommendation* can be made for routinely placing a recipient of autologous HSCT or solid-organ transplant in PE.
UNRESOLVED ISSUE
2. Maintain air-handling systems in PE and other high-risk patient-care areas according to published recommendations (506;702;704).
CATEGORIES IB and IC
3. Develop a water-damage response plan for immediate execution when water leaks, spills, and moisture accumulation occur to prevent fungal growth in the involved areas (506;713).
CATEGORY IB
4. Use proper dusting methods for patient-care areas designated for severely immunocompromised (e.g., HSCT recipients) (506;714).
CATEGORY IB
 - a. Wet-dust horizontal surfaces daily using cloth that has been moistened with an EPA-registered hospital disinfectant (682).
CATEGORY IB

- b. Avoid dusting methods that disperse dust (e.g., feather dusting) (682).
CATEGORY IB
 - c. Keep vacuums in good repair and equip them with HEPA filters for use in areas with patients at high risk (682;714).
CATEGORY IB
- 5. Do not use carpeting in hallways and rooms occupied by severely immunocompromised patients (506;507;1043)
CATEGORY IB
- 6. Avoid using upholstered furniture or furnishings in rooms occupied by severely immunocompromised patients.
CATEGORY II
- 7. Minimize the length of time that immunocompromised patients in PEs are outside their rooms for diagnostic procedures and other activities.
CATEGORY II
 - a. Instruct severely immunocompromised patients to wear a high-efficiency respiratory-protection device (e.g., an N95 respirator) when they leave the PE during periods when construction, renovation, and/or other dust-generating activities are ongoing in and around the health-care facility (715).
CATEGORY II
 - b. *No recommendation* can be made about the specific type of respiratory-protection device (e.g., surgical mask, N95 respirator) for use by a severely 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 health-care facility.
UNRESOLVED ISSUE
- 8. Systematically review and coordinate infection-control strategies with personnel in charge of the facility's engineering, maintenance, central supply and distribution, and catering services (506;507;685).
CATEGORY IB
- 9. When planning construction, demolition, 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, demolition, and renovation sites, and if so, develop a plan to prevent such exposures (506;507;685).
CATEGORY IA
- 10. During construction, demolition, or renovation activities, construct impermeable barriers between patient-care and construction areas to prevent dust from entering the patient-care areas (506;626).
CATEGORY IB
- 11. Direct pedestrian traffic that come from construction areas away from

patient-care areas to limit the opening and closing of doors or other barriers that might cause dust dispersion, entry of contaminated air, or tracking of dust into patient-care areas (506;507;626;679;685).

CATEGORY IB

12. Do not allow fresh or dried flowers or potted plants in patient-care areas for severely immunocompromised patients (695).

CATEGORY II

C. When A Case of Aspergillosis Occurs

1. Assess whether the infection is health-care-related or community-acquired.
 - a. 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; patient's stay at, visit of, or transfer from, other health-care facilities or other locations within the facility; and the period the patient was exposed outside the health-care facility after the onset of immunosuppression and before onset of aspergillosis.

CATEGORY II

- b. Determine, if any ventilation deficiency exists in the PEs (506).
2. If no evidence exists that the patient's aspergillosis is facility-acquired, continue routine maintenance procedures to prevent health-care-associated aspergillosis, as in Section II-B-1 through II-B-12.
3. If evidence of possible facility-acquired infection with *Aspergillus* spp. exists, conduct an epidemiologic investigation and an environmental assessment to determine and eliminate the source of *Aspergillus* spp. (506).
4. Use an antifungal biocide (e.g., copper-8-quinolinolate) that is registered with the Environmental Protection Agency for decontamination of structural materials (506;681;717).

CATEGORY IB

III. CHEMOPROPHYLAXIS

- A. *No recommendation* can be made for the routine administration of antifungal agents such as itraconazole oral solution (5 mg/kg/day) or capsules (500 mg twice a day), low-dose parenteral amphotericin B (0.1 mg/kg/day), lipid-based formulations of amphotericin B (1 mg/kg/day), or nebulized amphotericin B administered by inhalation as prophylaxis for pulmonary aspergillosis in patients at high risk for this infection (507;718-721;723-730).

UNRESOLVED ISSUE

- B. *No recommendation* can be made 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 undergoing hematopoietic stem-cell transplantation who have a history of pulmonary aspergillosis (672;731-736).
UNRESOLVED ISSUE

PREVENTION AND CONTROL OF HEALTH-CARE ASSOCIATED RSV, PARAINFLUENZA VIRUS, AND ADENOVIRUS INFECTIONS

I. Staff Education And Monitoring And Infection Surveillance

A. Staff Education and Monitoring

1. Staff education
 - a. Educate personnel in accordance with their level of responsibility in the health-care setting about the epidemiology, modes of transmission, and means of preventing the transmission of RSV within health-care facilities (817).
CATEGORY IB
 - b. Educate personnel in accordance with their level of responsibility in the health-care setting, about the epidemiology, modes of transmission, and means of preventing the spread of parainfluenza virus and adenovirus within health-care facilities.
CATEGORY II
2. In acute-care facilities, establish mechanisms by which the infection-control staff can monitor personnel compliance with the facility's infection-control policies about these viruses (817).
CATEGORY II

B. Surveillance

1. Establish mechanisms by which the appropriate health-care personnel are promptly alerted to any increase in the activity of RSV, parainfluenza virus, adenovirus, or other respiratory viruses in the local community. Establish mechanisms by which the appropriate health-care personnel can promptly inform the local and state health departments of any increase in the activity of the above-named viruses or of influenza-like illness in their facility.
CATEGORY IB
2. In acute-care facilities during periods of increased prevalence of symptoms of viral respiratory illness in the community or health-care facility, and/or during the RSV and influenza season (i.e., December-March), attempt prompt diagnosis of respiratory infections caused by RSV, influenza, parainfluenza, or other respiratory viruses. Use rapid diagnostic techniques as clinically indicated in patients who are admitted to the health-care facility with respiratory illness and are at high risk for serious complications from viral respiratory infections (e.g., pediatric patients, especially infants, and those with compromised cardiac, pulmonary, or immune function) (749;764;815;817;897).
CATEGORY IA
3. *No recommendation* can be made for routinely conducting surveillance cultures for RSV or other respiratory viruses in respiratory secretions of

patients (including immunocompromised patients, such as recipients of HSCT) (507).

UNRESOLVED ISSUE

4. In LTCFs, establish mechanism(s) for continuing surveillance to allow rapid identification of a potential outbreak in the facility.

CATEGORY II

II. Prevention Of Transmission Of RSV, Parainfluenza Virus, Or Adenovirus

A. Prevention of Person-to-Person Transmission

1. Standard and contact precautions for RSV and parainfluenza virus; and standard, contact, and droplet precautions for adenovirus

a. Hand hygiene

Decontaminate hands after contact with a patient or after touching respiratory secretions or fomites potentially contaminated with respiratory secretions, whether or not gloves are worn. Use soap and water when hands are visibly dirty or contaminated with proteinaceous material or are visibly soiled with blood or other body fluids, and use an alcohol-based hand rub if hands are not visibly soiled (271;279;284;782;802-804;813;817).

CATEGORY IA

b. Gloving

- (1) Wear gloves when entering the room of patients with confirmed or suspected RSV, parainfluenza, or adenovirus infection, and/or before handling the patients, their respiratory secretions, or fomites potentially contaminated with the patients' secretions (279;280;782;802;803;810;815;817;819).

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 (279;280;282;817). Decontaminate hands after removing gloves (see II-A-1-a).

CATEGORY IA

- (3) After glove removal and hand decontamination, do not touch potentially contaminated environmental surfaces or items in the patient's room (279).

CATEGORY IB

c. Gowning

Wear a gown when entering the room of a patient suspected or proven to have RSV, parainfluenza virus, or adenovirus infection, and when soiling with respiratory secretions from a patient is anticipated (e.g., when handling infants with suspected or proven RSV, parainfluenza, or adenovirus infection). Change the gown after

such contact and before giving care to another patient or when leaving the patient's room. After gown removal, ensure that clothing does not come into contact with potentially contaminated environmental surfaces (279;280).

CATEGORY IB

d. Masking and wearing eye protection

(1) Wear a surgical mask and eye protection or a face shield when performing procedures or patient-care activities that might generate sprays of respiratory secretions from any patient whether or not the patient has confirmed or suspected viral respiratory tract infection (279).

CATEGORY IB

(2) Wear a surgical mask and eye protection or a face shield when within 3 feet of a patient with suspected or confirmed adenovirus infection (279).

CATEGORY IB

e. Patient placement in acute-care facilities

(1) Place a patient with 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 and no other infection (279;749;810;813;815;819).

CATEGORY IB

(2) Place a patient with suspected RSV, parainfluenza, adenovirus, or other viral respiratory tract infection in a private room.

CATEGORY II

(a) Promptly perform rapid diagnostic laboratory tests on patients who are admitted with or who have symptoms of RSV infection after admission to the health-care facility to facilitate early downgrading of infection-control precautions to the minimum required for each patient's specific viral infection (817;819).

CATEGORY IB

(b) Promptly perform rapid diagnostic laboratory tests on patients who are admitted with or who have symptoms of parainfluenza or adenovirus infection after admission to the health-care facility to facilitate early downgrading of infection-control precautions to the minimum required for each patient's specific viral

infection and early initiation of treatment when indicated.

CATEGORY II

- f. Limiting patient movement or transport in acute-care facilities
 - (1) Limit to essential purposes only the movement or transport of patients from their rooms when they are diagnosed or suspected to be infected with RSV, parainfluenza virus, or adenovirus (279).

CATEGORY IB

- (2) If transport or movement from the room is necessary
 - (a) For a patient with diagnosed or suspected RSV or parainfluenza virus infection, ensure that precautions are maintained to minimize the risk for transmission of the virus to other patients and contamination of environmental surfaces or equipment by ensuring that the patient does not touch other persons' hands or environmental surfaces with hands that have been contaminated with his/her respiratory secretions (279).

CATEGORY IB

- (b) For a patient with diagnosed or suspected adenovirus infection, minimize patient dispersal of droplets by having the patient wear a surgical mask, and ensure that contact precautions are maintained to minimize the risk of transmission of the virus to other patients and contamination of environmental surfaces or equipment (279).

CATEGORY IB

2. Other measures in acute-care facilities

a. Staffing

- (1) Restrict health-care personnel in the acute stages of an upper respiratory tract infection from caring for 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) (279;507;813;815;817).

CATEGORY II

- (2) When feasible, perform rapid diagnostic testing on health-care personnel with symptoms of respiratory tract infection, especially those who provide care to patients at high-risk for acquiring and/or developing severe complications from RSV, parainfluenza, or adenovirus 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, immunocompromised, or cardiac patients (279;507;810;817;819).

CATEGORY IB

c. Use of monoclonal antibody (palivizumab) for attenuation of RSV infection

Follow the recommendations of the American Academy of Pediatrics to consider monthly administration of palivizumab, an RSV monoclonal-antibody preparation, to the following infants and children aged <24 months: 1) those born prematurely at ≤ 32 weeks of gestational age and have bronchopulmonary dysplasia, and those born prematurely at <32 weeks gestation without chronic lung disease who will be aged <6 months at the beginning of the RSV season, and (2) those born at 32-35 weeks gestation, if two or more of the following risk factors are present: child-care attendance, school-aged siblings, exposure to environmental pollutants, congenital abnormalities of the airways, or severe neuromuscular disease (820;822-824).

CATEGORY II

3. Control of outbreaks in acute-care facilities

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. Promptly cohort the patients (according to their specific infections) as soon as the results of the screening tests are available (749;764;810;813;815;817;819). In the interim, when possible, admit patients with symptoms of viral respiratory infections to private rooms.

CATEGORY IB

b. Personnel cohorting

(1) During an outbreak of health-care-associated RSV infection, cohort personnel as much as practical (e.g., restrict personnel who give care to infected patients from giving care to uninfected patients) (810;813;815).

CATEGORY II

(2) *No recommendation* can be made for routinely cohorting personnel during an outbreak of health-care-associated adenovirus or parainfluenza virus infection.

UNRESOLVED ISSUE

c. Use of RSV immune globulin or monoclonal antibody

No recommendation can be made for the use of RSV immune globulin or monoclonal antibody to control outbreaks of RSV infection in the health-care setting (820-825;827-829).

UNRESOLVED ISSUE

PREVENTION AND CONTROL OF HEALTH-CARE-ASSOCIATED INFLUENZA

I. Staff Education

Provide health-care 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 health-care-associated influenza (1029;1044-1046).

CATEGORY II

II. Surveillance

A. Establish mechanisms 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 (942).

CATEGORY II

2. Arrange for laboratory tests to be available to clinicians for prompt diagnosis of influenza, especially during November-April (936-939).

CATEGORY II

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 (410;941;1047;1048). Groups at high risk for influenza-related complications include those aged ≥ 65 years; residents of nursing homes and other chronic-care facilities that house persons of any age who have chronic medical conditions; adults and children aged >6 months who have chronic disorders of the pulmonary or cardiovascular system, including asthma; adults and children who have required regular medical follow-up or hospitalization during the preceding year because of chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies; or immunosuppression (including immunosuppression caused by medications or HIV); children and adolescents (aged 6 months-18 years) who are receiving long-term aspirin therapy; and women who will be in the second or third trimester of pregnancy during the influenza season (941;950-954;957). In addition, offer annual influenza vaccination to all

persons aged 50-64 years, close contacts of children aged <24 months, and healthy children aged 6-23 months (941).

CATEGORY IA

2. In nursing homes and other long-term care facilities, establish an SOP for timely administration of the inactivated influenza vaccine to high-risk persons as identified in Section III-A-1 (408;409;941;1029).

CATEGORY IA

- a. Obtain consent for influenza vaccination (if such is required by local or state law) from every resident (or his/her guardian) at the time the resident is admitted to the facility or anytime afterwards, before the next influenza season (941;1029;1049).

CATEGORY IB

- b. Routinely vaccinate all residents, except those with medical contraindication(s) to receipt of influenza vaccine, (under an SOP or with the concurrence of the residents' respective 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 (941;957;1049;1050).

CATEGORY IA

- c. In settings not included in sections III-A-1 and -2, where health care is given (e.g., in homes visited by personnel from home health-care agencies), vaccinate patients for whom vaccination is indicated, as listed in section III-A-1, and refer patient's household members and care givers for vaccination, before the influenza season (941).

CATEGORY IA

3. Personnel

- a. Beginning in October each year, provide inactivated influenza vaccine for all personnel including night and weekend staff (941;944-946;956;958). Throughout the influenza season, continue to make the 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 III-A-1 above (941).

CATEGORY IA

- b. Educate health-care personnel regarding the benefits of vaccination and the potential health consequences of influenza illness for themselves and their patients (941).

CATEGORY IB

- c. Take measures to provide all health-care personnel convenient access to inactivated influenza vaccine at the work site, free of

charge, as part of employee health program (941).

CATEGORY IB

B. Use of Antiviral Agents (See Section V-C)

IV. PREVENTION OF PERSON-TO-PERSON TRANSMISSION

A. Droplet Precautions

1. Place a patient who is diagnosed to have influenza in a private room or in a room with other patients with confirmed influenza, unless there are medical contraindications to doing so (279).

CATEGORY IB

2. Place a patient suspected to have influenza in a private room and promptly perform rapid diagnostic laboratory tests to facilitate early downgrading of infection-control precautions to the minimum required for the patient's infection (279).

CATEGORY II

3. Wear a surgical mask upon entering the patient's room or when working within 3 feet of the patient (279).

CATEGORY IB

4. Limit the movement and transport of the patient from the room to those for essential purposes only. If patient movement or transport is necessary, have the patient wear a surgical mask, if possible, to minimize droplet dispersal by the patient (279).

CATEGORY II

B. Eye Protection

No recommendation can be made for wearing eye-protective device upon entering the room of a patient with confirmed or suspected influenza or when working within 3 feet of the patient.

UNRESOLVED ISSUE

C. Contact Precautions

No recommendation can be made for observance of contact precautions (in addition to droplet precautions) for patients with confirmed or suspected influenza (279;921).

UNRESOLVED ISSUE

D. Standard Precautions

1. Decontaminate hands before and after giving care to and/or touching a patient or after touching a patient's respiratory secretions, whether or not gloves are worn: if hands are visibly dirty or contaminated with proteinaceous material or are visibly soiled with blood or body fluids, wash them with either a nonantimicrobial soap and water or an antimicrobial soap and water; and if hands are not visibly soiled, use an alcohol-based hand rub for their decontamination (278).

CATEGORY IA

2. Wear gloves if hand contact with patient's respiratory secretions is expected (279;921).

CATEGORY II

3. Wear a gown if soiling of clothes with patient's respiratory secretions is expected (279).

CATEGORY II

E. Air Handling

No recommendation can be made 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 (909;922;924).

UNRESOLVED ISSUE

F. Personnel Restrictions

In acute-care facilities, utilize the facility's employee health service or its equivalent to evaluate personnel with influenza-like illness and determine whether they should be removed from duties that involve direct patient contact. Use more stringent criteria for personnel who work in certain patient-care areas (e.g., ICUs, nurseries, and organ-transplant [especially HSCT] units) where patients who are most susceptible to influenza-related complications are located (920;993;1051).

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 (936-939).

CATEGORY IB

B. Vaccination of Patients and Personnel

Administer current inactivated influenza vaccine to unvaccinated patients and healthcare personnel (941;945;946;957).

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 (regardless of whether they received influenza vaccinations during the previous fall) for a minimum of 2 weeks or until approximately 1 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 12-24 hours after specimen collection (931;941;964;1050).

CATEGORY IA

- b. Administer amantadine, rimantadine, oseltamivir, or zanamivir to patients acutely ill with influenza, within 48 hours of illness onset.

Choose the agent appropriate for the type of influenza virus circulating in the community (931;941;964;967;1050;1052).

CATEGORY IA

- c. Offer antiviral agent(s) (amantadine, rimantadine, or oseltamivir) for prophylaxis to unvaccinated personnel for whom the antiviral agent is not contraindicated and who are in the involved unit or taking care of patients at high-risk (931;941;964;975;1050).

CATEGORY IB

- d. Consider prophylaxis for all healthcare personnel, regardless of their vaccination status, if the outbreak is caused by a variant of influenza that is not well matched by the vaccine (941).

CATEGORY IB

- e. *No recommendation* can be made about the prophylactic administration of zanamivir to patients or personnel (915;941;974;977).

UNRESOLVED ISSUE

- f. 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 (962).

CATEGORY IA

- g. 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 (941;1053).

CATEGORY IB

- 2. 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 (963;984;985;987;988).

CATEGORY IB

D. Other Measures in Acute-Care Facilities:

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 (993).

CATEGORY II

- 2. Restrict cardiovascular and pulmonary surgery to emergency cases only (993).

CATEGORY II

- 3. Restrict persons with influenza or influenza-like illness from visiting patients in the health-care facility (993).

CATEGORY II

4. Restrict personnel with influenza or influenza-like illness from patient care (993).
CATEGORY IB

HEALTH-CARE-ASSOCIATED SARS

Updated information about prevention and control of SARS in health-care facilities is available in a separate document, *Public Health Guidance for Community-Level Preparedness and Response to SARS, Version 2. Supplement I: Infection Control in Healthcare Home and Community Settings*, available at (<http://www.cdc.gov/ncidod/sars/guidance/index.htm>).

PART III. PERFORMANCE INDICATORS

1. Monitor rates of VAP; can use established benchmarks and definitions of pneumonia (e.g., NNIS definitions and rates) . Provide feedback to the staff about the facility's VAP rates and reminders about the need for personnel to adhere to infection-control practices that reduce the incidence of VAP.
- 2.. Establish an SOP for influenza vaccination and monitor the percentage of eligible patients in acute-care settings or patients or residents in long-term care settings who receive the vaccine.
3. Before and during the influenza season, monitor and record the number of eligible health-care personnel who receive the influenza vaccine and determine the desired unit- and facility-specific vaccination rates as recommended by ACIP.
4. Monitor the number of cases of health-care-associated RSV infections by geographic location within the facility and give prompt feedback to appropriate staff members to improve adherence to recommended infection-control precautions.
5. Periodically review clinicians' use of laboratory diagnostic tests (both culture of appropriate respiratory specimen and the urine antigen test) for legionellosis, especially in patients who are at high risk of acquiring the disease (e.g., patients who are immunosuppressed, including recipients of HSCT or solid-organ transplant or are receiving systemic steroids; patients aged ≥ 65 years; or patients who have chronic underlying disease such as diabetes mellitus, congestive heart failure, and COPD). Provide feedback on the utilization of these tests to clinicians.
6. During construction or renovation activities in the facility, monitor personnel adherence to infection-control measures (e.g., use of barriers, maintenance of negative room pressure) that are aimed at minimizing dust dispersion in patient-care areas. Review all cases of health-care-associated aspergillosis to determine the presence of remediable environmental risks.
7. Periodically monitor the frequency of diagnostic testing for pertussis and the time interval between suspicion of the infection and initiation of isolation precautions for patients in whom pertussis is suspected.

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APPENDIX

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 CO₂ 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.