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**Infection control recommendations
for patients with cystic fibrosis:
Microbiology, important pathogens, and
infection control practices to prevent
patient-to-patient transmission**

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ABBREVIATIONS USED IN TEXT

- ABPA - allergic bronchopulmonary aspergillosis
AFB - acid-fast bacillus
ATS - American Thoracic Society
BCSA - *Burkholderia cepacia* selective agar
CF - cystic fibrosis
CFF - Cystic Fibrosis Foundation
CFU - colony-forming units
FEV₁ - forced expiratory volume in 1 second
HCW- healthcare worker
HEPA - high efficiency particulate air (filtration)
HICPAC - Healthcare Infection Control Practices Advisory Committee
HIV - human immunodeficiency virus
ICU - intensive care unit
IL-8 - interleukin 8
LPS - lipopolysaccharide
MAC - *Mycobacterium avium* complex
MAI - *Mycobacterium avium-intracellulare*
MDRO - multidrug-resistant organisms
MMWR - *Morbidity and Mortality Weekly Report*
MRSA - methicillin-resistant *Staphylococcus aureus*
MSSA - methicillin-susceptible *Staphylococcus aureus*
NALC-NaOH - *N*-acetyl-L-cysteine and sodium hydroxide
NTM - nontuberculous mycobacteria
OFPBL - oxidative fermentative polymyxin B bacitracin lactose agar
PFGE - pulsed-field gel electrophoresis
PC - *Pseudomonas cepacia* agar
RFLP - restriction fragment length polymorphism
RSV - respiratory syncytial virus
VRE - vancomycin-resistant enterococci

Infection control recommendations for patients with cystic fibrosis: Microbiology, important pathogens, and infection control practices to prevent patient-to-patient transmission

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EXECUTIVE SUMMARY

Infection Control Recommendations for Patients With Cystic Fibrosis: Microbiology, Important Pathogens, and Infection Control Practices to Prevent Patient-to-Patient Transmission updates, expands, and replaces the consensus statement, *Microbiology and Infectious Disease in Cystic Fibrosis* published in 1994.¹ This consensus document presents background data and evidence-based recommendations for practices that are intended to decrease the risk of transmission of respiratory pathogens among CF patients from contaminated respiratory therapy equipment or the contaminated environment and thereby reduce the burden of respiratory illness. Included are recommendations applicable in the acute care hospital, ambulatory, home care, and selected non-healthcare settings. The target audience includes all healthcare workers who provide care to CF patients. Antimicrobial management is beyond the scope of this document.

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The following information set the stage for the development of this guideline:

- (a) Studies published since 1994 that further our understanding of the modes of transmission of pathogens and effective strategies to interrupt transmission among CF patients provide the data needed for evidence-based guidelines.
- (b) Improved microbiology methods provide more accurate detection and further definition of the epidemiology of pathogens in CF patients.
- (c) The publication of the HICPAC/CDC (Healthcare Infection Control Practices Advisory Committee/ Centers for Disease Control and Prevention) *Guideline for Isolation Precautions in Hospitals* in 1996² defined *standard precautions* and recommended universal application to care for all patients at all times to prevent transmission of infectious agents that may not yet have been identified.
- (d) The previously published HICPAC/CDC guidelines for prevention of healthcare-associated infections have not included background information and recommendations for the specific circumstances of patients with CF. Thus, specific guidelines for CF patients are needed.
- (e) The link between acquisition of pathogens and morbidity and mortality is well established. Prevention of acquisition of specific pathogens may further improve the mean survival of CF patients, which has increased to 33.4 years in 2001.³⁻⁹

A multidisciplinary committee consisting of health-care professionals from the United States, Canada, and Europe with experience in CF care and health-care epidemiology/infection control reviewed the relevant literature and developed evidence-based recommendations graded according to the published peer-reviewed supportive data. The participants chose to use the following CDC/HICPAC system for categorizing recommendations based on previous experience in crafting infection control guidelines beyond CF:

- **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 experimental, clinical, or epidemiologic studies and a strong theoretical rationale.
- **Category IC.** Required for implementation, as mandated by federal and/or state regulation or standard.
- **Category II.** Suggested for implementation and supported by suggestive clinical or epidemiologic studies or a theoretical rationale.
- **No recommendation; unresolved issue.** Practices for which insufficient evidence or no consensus regarding efficacy exist.

Category IA and *IB* recommendations are strongly recommended for implementation by all CF centers and considered to be “best practice.” Implementation of *Category II* recommendations is advised by the committee, but individual centers may determine which *Category II* recommendations would be appropriate for their CF centers.

This document integrates knowledge of microbiology laboratory methods, infection control principles, and epidemiology of respiratory pathogens in CF patients. Standardization of infection control practices across CF centers will provide safer environments for patients by reducing the risk of transmission of CF pathogens. In addition to infection control practices that are applicable to all CF patients at all times, specific infection control practices are recommended for inpatient, ambulatory, and non-health-care settings, based on the types of activities and risks associated with the various settings. CF care teams as well as patients and their families must be well educated concerning the known risks and the effective preventive measures to ensure adherence to the evidence-based recommendations in this document. It will be beneficial for each CF center to

evaluate the effectiveness of its infection control program to reduce transmission of pathogens and improve clinical outcomes. Collaboration between the CF care team and the CF center’s infection control team will facilitate effective implementation that takes into consideration the psychosocial impact of these recommendations.

This document was reviewed by the members of HICPAC, and the recommendations were found to be consistent with the principles of infection control that serve as the foundation of HICPAC/CDC guidelines for prevention of healthcare-associated infections. This guideline was formally endorsed by The Society for Healthcare Epidemiology of America and the Association for Professionals in Infection Control and Epidemiology boards in 2002-2003. The National Committee for Clinical Laboratory Standards has endorsed the recommendations for susceptibility testing.

Infection control principles

CF pathogens are transmitted by the droplet and contact routes. Therefore, practices that contain respiratory secretions and prevent transmission of respiratory tract pathogens must be taught to patients and their families as well as to CF healthcare workers. Such practices must be followed with all CF patients and cannot be implemented according to the specific microbiology results of individual CF patients because microbiology methods are not 100% sensitive for the detection of CF pathogens.^{10,11} In addition to washing hands with an antimicrobial-containing soap and water, alcohol-based antiseptic hand rubs are now recommended when hands are not visibly soiled with blood or body fluids because of the improved efficacy of these products in removing microorganisms from the hands.^{12,13} Use of gowns, gloves, and masks follows the recommendations for *standard, contact, and droplet precautions* that have been developed by CDC/HICPAC² to prevent healthcare-associated infections in all patients, ie, both CF and non-CF patients. *Contact precautions* plus *standard precautions* are recommended for all CF patients infected (or colonized) with methicillin-resistant *Staphylococcus aureus* (MRSA), *Burkholderia cepacia* complex, multidrug-resistant *Pseudomonas aeruginosa*, respiratory syncytial virus (RSV), parainfluenza, or vancomycin-resistant enterococci (VRE). Recommendations for room placement, activities outside the hospital room, CF clinic logistics, and adjuvant measures to prevent infections are provided. No recommendation can be made for the routine wearing of masks by CF patients

when leaving an inpatient room or when in the waiting room of a CF clinic.

Specific practices for the use and care of respiratory therapy equipment recommended in this document are based on principles of disinfection and sterilization^{14,15} as well as findings from investigations of outbreaks of infections associated with contaminated respiratory therapy equipment. Cleaning devices, such as nebulizers, with removal of debris as soon as possible and before disinfection, and complete air drying are the critical steps in both healthcare and home settings.

Microbiology, molecular typing, and surveillance

Because aggressive antimicrobial treatment of *P. aeruginosa* at initial acquisition may be associated with a delay in chronic infection and an improved clinical course,¹⁶⁻¹⁸ respiratory tract cultures should be obtained at least quarterly in CF patients with stable pulmonary status as well as at the time of pulmonary exacerbations. Specific recommendations are made for transport and processing of specimens, including the preferred selective media. Agar-based diffusion assays, eg, antibiotic-containing disks or E-tests, rather than automated commercial microbroth dilution systems are recommended for susceptibility testing of *P. aeruginosa* isolates.¹⁹⁻²¹ Molecular typing using appropriate methods, eg, pulsed-field gel electrophoresis (PFGE), rapid amplified polymerase chain reaction (RAPD-PCR), and repetitive DNA sequence PCR (Rep-PCR), are recommended to assess strain relatedness of isolates from different patients when patient-to-patient transmission is suspected.²²⁻²⁵

Recommendations are made to develop surveillance in collaboration with the CF center's infection control team. *S. aureus*, including MRSA, *P. aeruginosa*, and *B. cepacia* complex are always targeted, whereas *Stenotrophomonas maltophilia*, *Achromobacter xylosoxidans*, and nontuberculous mycobacteria (NTM) are included when considered epidemiologically important, eg, patient-to-patient transmission or an outbreak is suspected. Surveillance includes calculation of incidence and prevalence rates and review of antimicrobial susceptibility summaries with trend analysis. Surveillance reports should be shared between the infection control and CF care teams at least annually to evaluate effectiveness of the center's infection control program. Selected *B. cepacia* complex isolates and nonfermenting gram-negative organisms for which species identification

cannot be established after routine analysis should be submitted to the Cystic Fibrosis Foundation (CFF) *Burkholderia cepacia* Research Laboratory and Repository for further study.

Epidemiology of pathogens in CF patients

Studies of the epidemiology of *B. cepacia* complex provide a model for evaluating other pathogens. With the use of more advanced molecular typing systems, eg, PFGE, RAPD, patient-to-patient transmission has been demonstrated in the United States, Canada, and Europe in both healthcare and non-healthcare settings via droplet and contact routes with little evidence for true airborne transmission.²⁶ Transmission has been interrupted successfully by implementing a variety of infection control practices that are based on the principle of containment of respiratory secretions. Although putative virulence factors have been identified in the more common genomovar III strains, there is no one factor that is a sufficient marker of transmissibility.^{22,27} Demonstration of the replacement of *Burkholderia multivorans* with potentially more virulent strains of genomovar III supports the recommendation to segregate patients infected with *B. cepacia* complex from each other and not cohort them together in either the inpatient or ambulatory settings.²⁸⁻³⁰

Patient-to-patient transmission of *P. aeruginosa* has been demonstrated in several different ambulatory settings,^{17,31-37} but not as consistently as has been observed for *B. cepacia* complex. Conditions of crowding, close contact, and failure to observe consistent hand hygiene and other hygienic practices facilitate transmission. Implementation of infection control measures can prevent transmission of *P. aeruginosa* to patients with CF. The role of environmental water sources of *P. aeruginosa* has not been established.

Patient-to-patient transmission of *S. aureus* (including MRSA) occurs among CF patients and therefore mandates adherence to hospital policies established for prevention of transmission of MRSA among non-CF patients. Similarly, because respiratory viral infections in CF patients are associated with clinical deterioration, methods for preventing respiratory viral infections in the general population, eg, *standard plus contact* and/or *droplet precautions*, influenza vaccine, antiviral agents for treatment and prophylaxis, must be used. The clinical impact and epidemiology of *S. maltophilia*, *A. xylosoxidans*, and NTM are continuing to be defined. However, recent studies suggest that infec-

tion control measures to prevent transmission of *S. maltophilia* and *A. xylosoxidans* are beneficial.³⁸⁻⁴⁰ In contrast, the risk of patient-to-patient transmission of NTM and *Aspergillus* spp. is very low. Although *Aspergillus* spp. are ubiquitous in nature, prolonged exposure to high concentrations of *Aspergillus* spores, eg, construction dust, dried water leaks, is best avoided. It is important to verify that recommended dust containment and water leak policies are in place in any facility that provides care for CF patients.

Finally, recommendations based on the above principles of infection control and the epidemiology of pathogens in CF patients are made to assist CF patients and their families in decision-making in non-healthcare settings, eg, homes, schools, CF educational and psychosocial support programs, use of swimming pools and hot tubs, and in selecting and practicing healthcare-related professions.

I. DOCUMENT DEVELOPMENT

A. Rationale for document

During the past two decades, CF patient-to-CF patient transmission of pathogens has been documented with increasing frequency. As a result, infection control policies have been developed within individual CF centers to prevent transmission of infectious agents among patients. However, policies vary from CF center to CF center. These differing policies can generate controversy and anxiety among members of the CF community, including patients, their families, and their medical care team, particularly if care is received at different locations with different practices. Furthermore, there have been many changes in the epidemiology of CF and CF care delivery. Many states have instituted newborn screening for CF with the goal of improving outcomes by initiating CF care, including preventive measures, earlier. The median survival of a CF patient has increased to 33.4 years in 2001,³⁻⁹ and approximately 37% of all CF patients are 18 years of age or older. Most CF centers have separate adult and pediatric clinics. The epidemiology of respiratory tract pathogens in CF patients has become more complex. While *S. aureus*, *Haemophilus influenzae*, and *P. aeruginosa* remain the most common pathogens, *B. cepacia* complex, *S. maltophilia*, *A. xylosoxidans*, *Aspergillus* spp., NTM, and respiratory viruses are isolated from patients with CF and are clinically significant. Often, patients are exposed to numerous broad-spectrum antimicrobials administered orally, by aerosolization, and intravenously. Many of these agents are delivered in the home, in

efforts to preserve pulmonary function and reduce the frequency and duration of hospitalizations. However, this frequent exposure to antibiotics may lead to increasing antimicrobial resistance and potentially the emergence of multidrug-resistant organisms (MDRO).

In 1994, the CFF issued recommendations for infection control practices and appropriate processing of CF specimens as part of the consensus document "Microbiology and Infectious Diseases."¹ However, in the past several years, numerous studies have been published that further our understanding of the modes of transmission of different pathogens and risk factors for acquisition. In May 2001, the CFF convened a multidisciplinary team to develop evidence-based recommendations for standardized clinical microbiology and infection control practices.

B. Participants

A multidisciplinary team was selected by the co-chairpersons. The participants included physicians, nurses, infection control professionals, respiratory therapists, social workers, microbiologists, attorneys, and CF patient representatives from the United States, Canada, and Europe and they had almost 600 years of cumulative experience in CF care. The co-chairpersons set the agenda and assigned individual members the responsibility of presenting the background information and completing a first draft of the recommendations. Infection control consensus recommendations from the United Kingdom, Canada, Germany, and Denmark were presented. The final recommendations set forth in this document have been reviewed by all members of the committee and several expert reviewers who did not attend the conference. Not all members agree with every recommendation, but these recommendations represent an overall consensus.

C. Purpose and goals of document

The purpose of this document is to provide a summary of the relevant data and evidence-based recommendations for infection control practices for CF patients in order to standardize care across CF centers. In the absence of adequate data, some recommendations represent the consensus of the participants and other expert reviewers based on strong theoretical rationale. Preparation of this document therefore has identified areas for future research. Infection control practices are described for inpatient, outpatient, and non-healthcare settings, and

guidelines for one setting may not apply to another. For example, inpatients are generally more symptomatic and produce larger amounts of sputum containing larger quantities of pathogenic microorganisms than patients in non-healthcare settings. The duration and intensity of contact between patients and healthcare workers (HCWs) in an outpatient facility may be increased during a visit to evaluate illness when compared with routine visits. Some non-healthcare settings may provide the opportunity for more intimate and prolonged contact between CF patients. Behaviors may vary in different situations and in children and adults. Newborns attending a screening clinic may be more susceptible to particular pathogens than older patients. Furthermore, every circumstance cannot be anticipated nor can strict rules be crafted for every potential contact.

The background discussion and recommendations that follow provide our current understanding of the routes of pathogen transmission among CF patients. Guiding principles for infection control are presented to support the recommendations for specific CF infection control practices to prevent transmission of potential pathogens and to facilitate decision-making when the CF caregiver is confronted with new situations. The CF and infection control teams of each facility can work together to implement these recommendations within the individual CF center. **The recommendations are graded based on availability of published supportive evidence. Categories 1A and 1B are strongly supported by scientific and/or epidemiologic evidence, and implementation by all CF centers is strongly recommended. When strong evidence is lacking, but there is a consensus based on clinical, epidemiologic, or theoretical rationale, recommendations are graded Category II, and individual centers can decide if specific Category II recommendations are appropriate for their facilities.** An understanding of the guiding principles for infection control presented throughout the document coupled with knowledge of a CF center's specific patient population, individual patient's clinical condition, ongoing surveillance, and available resources will allow each CF center flexibility in implementing Category II recommendations. When relevant, recommendations from guidelines published by the CDC and HICPAC are cited. A glossary with definitions of infection control and microbiology terms is included. A separate infection control document prepared especially for CF patients and families is available on the CF Foundation website (www.cff.org).

II. BACKGROUND

A. GENERAL PRINCIPLES OF INFECTION CONTROL

1. Existing infection control guidelines applicable to CF patients

1.1. CDC/HICPAC guidelines

The components of an effective infection control program include surveillance with feedback to clinicians, prevention of infection, and control of outbreaks.⁴¹⁻⁴⁵ Since 1985, the CDC has published numerous guidelines for prevention of infections in healthcare settings (www.cdc.gov/ncidod/hip). Since 1992, CDC infection prevention guidelines have been developed primarily in collaboration with HICPAC, which is composed of appointed practicing experts in infection control and healthcare epidemiology outside of the CDC, eg, infection control professionals, epidemiologists, physicians, microbiologists, and public health officials. All CDC/HICPAC guidelines are made available for public comment before finalization of recommendations. Guidelines developed before 1998 were written exclusively for acute care hospitals, but those developed in more recent years include recommendations for healthcare settings outside of acute care settings. This change is in response to the shift of health care from acute care hospitals to ambulatory settings, including the home. Hence, the term *healthcare-associated* infection is now preferred over *nosocomial* infection to indicate current guidelines are more inclusive and address all settings. The term “nosocomial” refers to infections acquired in the hospital.

Several HICPAC guidelines have been published or are under development/revision and provide useful background information and graded evidence-based recommendations that are applicable to patients with CF. These include: (1) *Guideline for Isolation Precautions in Hospitals*, which provides recommendations for the use of *standard* and *transmission-based precautions* and management of patients infected or colonized with MDROs and highly transmissible infectious agents (under revision)²; (2) *Guideline for Disinfection and Sterilization in Healthcare Facilities*, which provides methods and indications for sterilization and disinfection of respiratory therapy equipment¹⁵; (3) *Guideline for Hand Hygiene in Health-Care Settings*, which describes the use of alcohol-based antiseptic hand rubs and antimicrobial-containing soap and water for hand hygiene as well as educational programs to enhance adherence to recommended practices¹⁵; (4) *Guideline for Environmental Infection Control in Healthcare*

Table 1. Recommendations for applying standard precautions for the care of all patients in all healthcare settings*

Activity	Recommendation
<ul style="list-style-type: none"> • After touching blood, body fluids, secretions, excretions, contaminated items • Immediately after removing gloves • Between patient contacts 	Hand hygiene
<ul style="list-style-type: none"> • For touching blood, body fluids, secretions, excretions, contaminated items • For touching mucous membranes and nonintact skin 	Gloves
<ul style="list-style-type: none"> • During procedures and patient care activities likely to generate splashes or sprays of blood, body fluids, secretions, excretions 	Mask, eye protection, face shield
<ul style="list-style-type: none"> • During procedures and patient care activities likely to generate splashes or sprays of blood, body fluids, secretions, excretions 	Gown
<ul style="list-style-type: none"> • Handling soiled patient care equipment 	Handle in a manner that prevents contamination or transfer of microorganisms to others and to the environment
<ul style="list-style-type: none"> • Environmental control 	Develop procedures for routine care, cleaning, and disinfection of environmental surfaces
<ul style="list-style-type: none"> • Handling linen 	Handle in a manner to prevent exposures, contamination, and transfer of microorganisms to others and to the environment
<ul style="list-style-type: none"> • Using sharps 	Avoid recapping, bending, breaking, or manipulating used needles Place used sharps in puncture-resistant container Use available safe needle devices whenever possible
<ul style="list-style-type: none"> • Patient resuscitation • Patient placement 	Use mouthpiece, resuscitation bag, or other ventilation devices If patient is likely to contaminate the environment or does not maintain appropriate hygiene, maintain patient in single room, if possible

*Adapted from reference.²

Facilities, which addresses air, water, and surface management to decrease risk of transmission of infectious agents⁴⁴; (5) *Guideline for Prevention of Healthcare-Associated Pneumonia*, which provides recommended *transmission-based precautions* for patients with pneumonia according to the epidemiology of the etiologic agents, care of respiratory therapy equipment, and adjunctive measures to prevent acquisition of healthcare-associated pneumonia (under revision)⁴⁵; and (6) *Guideline for Infection Control in Healthcare Personnel*, which provides recommendations for HCWs with pre-existing or acquired medical conditions that could have implications for transmission of potential pathogens.⁴⁶ Most recently, HICPAC and the CDC are identifying parameters to measure the dissemination, implementation, and impact of the guidelines in changing practice and reducing infection rates. Specific recommendations for CF patients are rarely included in the CDC guidelines, hence the impetus for this document.

1.2. Applicability of *standard precautions* and *transmission-based precautions* to CF patients

Standard precautions were established as the foundation for recommendations to prevent transmission

of infectious agents in healthcare settings in the *1996 Guideline for Isolation Precautions in Hospitals*.² *Standard precautions* combine the principles of *universal precautions* (UP), which were designed to reduce the risk of transmission of blood-borne pathogens, (eg, human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus) and *body substance isolation* (BSI), which was designed to reduce the risk of transmission of pathogens from moist body substances. ***Standard precautions consider all blood, body fluids, secretions including respiratory tract secretions, nonintact skin, mucous membranes, and excretions (except sweat) to potentially contain transmissible infectious agents.*** To prevent person-to-person transmission of infectious agents, HCWs are to observe the appropriate combination of practices and barrier precautions based on the type of exposure anticipated (ie, hand hygiene; gloves; gown; mask, eye protection, face shield; and disinfection, containment of respiratory secretions). *Standard precautions extend to the handling of equipment or items in the patients' environment likely to have been contaminated with infectious secretions or fluids.* Table 1 summarizes the specific components of *standard precautions* according to the type of patient care activity.

Transmission-based precautions are applied to patients with documented or suspected infection with highly transmissible or epidemiologically important infectious agents for which precautions in addition to *standard precautions* are required to prevent transmission. The following categories of precautions are included: *contact*, *droplet*, *airborne infection isolation* and *protective environment*. For CF patients, the use of *contact precautions* is particularly important for preventing transmission of MDROs, eg, MRSA, *B. cepacia* complex, multidrug-resistant *P. aeruginosa*, or respiratory viruses.

Both *standard precautions* and *transmission-based precautions* are applicable to CF patients. After a thorough review of the epidemiology of pathogens in CF patients and published reports of transmission of infectious agents among CF patients, summarized in the background section of this document, our group concluded the respiratory secretions of all CF patients potentially could be infected with epidemiologically and clinically important microorganisms for CF patients, even if not yet identified in microbiological cultures. **Therefore, HCWs must all use appropriate precautions when caring for all CF patients to prevent patient-to-patient transmission of pathogens. Contact between CF patients should be limited to avoid transmission of these potential pathogens by either the droplet or direct or indirect contact routes, even if culture results are unavailable or negative for CF pathogens.** For CF patients who live together in the same dwelling, contact cannot be avoided. However, the routine use of recommended precautions will limit contact with each other's respiratory secretions.

1.3. Hand hygiene

The single most important practice for preventing transmission of infectious agents is observation of proper hand hygiene between patient contacts and any time hands are contaminated with respiratory secretions from either direct patient contact or from contact with patient equipment that has become contaminated. Numerous studies have demonstrated greater efficacy for reducing bacterial contamination of hands with alcohol-based hand rubs compared with hand washing using water and plain or antimicrobial-containing soap^{12,13}; therefore, these agents are now the preferred hand hygiene agents in both hospitals and outpatient settings.¹⁵ However, when hands are visibly dirty or contaminated with body fluids, or are visibly soiled with blood, hands must be washed with soap and

water. An antimicrobial-containing soap is preferred when caring for patients with CF.

The care of fingernails and the skin of hands are important components of hand hygiene.¹⁵ Healthcare workers who wear artificial nails are more likely to harbor gram-negative pathogens on their fingertips both before and after hand washing than are HCWs who have natural nails.⁴⁷ Furthermore, artificial nails in HCWs have been associated with transmission of infectious agents, including *P. aeruginosa*, during outbreaks in intensive care unit (ICU) settings.⁴⁸⁻⁵¹ Although there are no studies of the role of artificial nails in transmission of pathogens among CF patients, the experience in ICUs can be applied to CF settings. Therefore, only natural nails are recommended for HCWs who have direct contact with CF patients.

1.4. Care of respiratory therapy equipment

Proper cleaning and sterilization or disinfection of reusable equipment are essential components of a program to prevent infections of CF patients associated with respiratory therapy equipment. Devices used for respiratory therapy (eg, nebulizers) or for diagnostic evaluation (eg, bronchoscopes or spirometers) are potential reservoirs or vehicles for transmission of infectious organisms. Routes of transmission may be from a contaminated device to patient, from one patient to another via a contaminated device, or from one body site to the respiratory tract of the same patient. Reservoirs of aerosol-producing devices (eg, nebulizers) are subject to the overgrowth of bacteria that can be aerosolized during device use. Cleaning and drying home respiratory therapy equipment between uses was found to be associated with a decreased risk of acquiring *B. cepacia* complex in a multicenter survey of patients from 21 CF centers conducted in 1986-1989.⁵² Both in-line and hand-held small-volume nebulizers can produce bacterial aerosols and have been implicated in acquisition of healthcare-associated pneumonia due to contaminated multidose medications vials⁵³⁻⁵⁷ or from contaminated tap water used for rinsing and filling the reservoir.^{44,45} Thus, unit dose medication vials always are preferred. If multidose medication vials are used, the manufacturer's directions for handling, dispensing, and storing must be followed precisely to prevent contamination and transmission of potential pathogens. Furthermore, sterile water is recommended as tap water may harbor NTM, fungi, *Pseudomonas* spp. or *Aeromonas* spp.^{45,58-60} Water that has been processed through a 0.2- μ m filter to remove bacteria also would be

acceptable. Such filtration systems are not readily available or maintainable for home use.

Although there have been no published reports of infections acquired from contaminated equipment during home therapy, bacterial contamination of home nebulizers of CF patients has been documented.^{61,62-64} In a recent study of experimental contamination of nebulizers, hot water and soap effectively removed the majority of bacteria that had been inoculated into the nebulizers.⁶⁵ These experimental conditions may not mimic true use by patients, and there is concern that potential pathogens from environmental sources (eg, tap water) may contaminate equipment inadvertently and potentially infect patients. To prevent this possibility, respiratory therapy equipment should be cleaned and disinfected in the home. Equipment must be cleaned well to remove all organic and inorganic debris before sterilization or disinfection, according to the recommendations of the manufacturer. Dried or baked debris on equipment makes removal more difficult, and the disinfection or sterilization process becomes less effective, or even ineffective.^{65,66} After cleaning, reusable items that touch mucous membranes (eg, nebulizers, tracheostomy tubes) can be disinfected by immersion in one of the following disinfectants that are easily obtained for home use: a 1:50 dilution of 6% sodium hypochlorite (household bleach) for 3 minutes, 70% to 90% ethyl or isopropyl alcohol for 5 minutes, or 3% hydrogen peroxide for 30 minutes.^{14,67} These preparations will lose activity with time, but the optimal storage time is unknown. For example, chlorine preparations have a 50% reduction in activity after 30 days (D. Weber and W. Rutala, personal communication). Acetic acid (vinegar) is NOT recommended because it has inadequate activity against some potential pathogens including gram-positive (eg, *S. aureus*) and gram-negative bacteria (eg, *Escherichia coli*).^{68,69} However, vinegar does kill *P. aeruginosa*. After use of a chemical sterilizing agent or disinfectant, rinsing the equipment with sterile or appropriately filtered water is preferred because tap or locally prepared distilled water may harbor pathogenic organisms. Sterile water can be prepared in the home by achieving a rolling boil for 5 minutes. Sterile water can become contaminated, but the rate at which this occurs is unknown. Boiling water immediately before use minimizes this possibility.

Distilled water should not be used for cleaning or rinsing respiratory therapy equipment because contamination with *B. cepacia* complex can occur during the manufacturing process. The only manu-

facturing regulations for distilled water relate to preventing contamination with coliform bacteria, eg, *E. coli* and *Klebsiella-Enterobacter* spp.⁷⁰

Equipment can be boiled for 5 minutes to disinfect, if permissible by the manufacturer.¹⁵ The dishwasher or microwave oven often is used to disinfect equipment in the home after proper cleaning has occurred. If the equipment is dishwasher safe, a temperature greater than 158°F (70°C) for 30 minutes must be achieved^{69,71,72}; unfortunately, this is higher than the temperature reached by most home dishwashers. If the equipment is microwave safe, the microwaves produced by a home microwave (2.45 Ghz) will completely inactivate microorganisms within 5 minutes.⁷³⁻⁷⁵

In summary, standardized protocols for cleaning to remove organic debris and disinfecting respiratory therapy equipment are important in healthcare settings where equipment is used by more than one patient and in the home where equipment is usually used by only one patient. Sharing equipment by siblings in the home has been associated with transmission of *B. cepacia*.⁷⁶ Home nebulizers can be contaminated with pathogens from CF patients, and tap water is a known source of potentially pathogenic organisms. Thus, care of respiratory therapy equipment in the home should be similar to care of this equipment in the hospital and include cleaning, disinfecting, and drying.

2. Infection control consensus documents from other countries

Infection control recommendations from Canada,^{77,78} the United Kingdom,⁷⁹ Denmark, and Germany/France⁸⁰ were reviewed by the committee. European recommendations differ from those of North America in several ways. European centers emphasize surveillance, with frequent cultures of the respiratory tract and initiation of antimicrobial treatment at first acquisition of *P. aeruginosa*.^{16,18,81} They also recommend cohorting patients by culture status (ie, *B. cepacia* complex negative or positive, and *P. aeruginosa* negative or positive) in both inpatient and outpatient settings. These efforts have been credited with the reduction of patient-to-patient transmission of pathogens in CF.⁸²⁻⁸⁴ The routine wearing of surgical masks by CF patients when in healthcare facilities is not recommended. Differences in the organization of health care and physical structure of health care facilities in different countries may account for some of the variations in recommendations.

Table 2. Host abnormalities that predispose CF patients to chronic lung infections

Abnormality	Proposed impact	Proposed intervention(s)
Abnormal cystic fibrosis transmembrane regulator (CFTR)	Altered secretions (low volume of airway surface fluid and hypertonicity) leads to thick dehydrated mucus, impairment of mucociliary escalator, and impaired defensin-mediated antimicrobial activity	<ul style="list-style-type: none"> • Chest physiotherapy • Inhaled DNase • Gene therapy* • Alter electrolyte and water balance by aerosolized amiloride (block Na⁺ uptake)*, uridine triphosphate (UTP) (increase Cl⁻ efflux),* or provide novel peptides† • Anti-aGMI blocking antibody†
Increased expression of asialoganglioside (aGMI)	Increased <i>P. aeruginosa</i> and <i>S. aureus</i> binding to respiratory epithelial cells	<ul style="list-style-type: none"> • Gene therapy*
Defective CFTR-mediated uptake of <i>P. aeruginosa</i> by respiratory epithelial cells	Decreased clearance of internalized <i>P. aeruginosa</i> with sloughed epithelial cells	<ul style="list-style-type: none"> • Gene therapy*
Abnormal regulation of pro-inflammatory cytokines	<ul style="list-style-type: none"> • Hyperexuberant neutrophil recruitment and release of neutrophil oxidants 	<ul style="list-style-type: none"> • Anti-inflammatory therapy, eg, steroids or ibuprofen beneficial, but associated with side effects such as cataracts, poor growth, or gastrointestinal bleeding • More selective anti-inflammatory agents† • MBL replacement†
Increased IL-8 expression and TNF-alpha	<ul style="list-style-type: none"> • Upregulation of human mucin genes 	<ul style="list-style-type: none"> • More selective anti-inflammatory agents† • MBL replacement†
Variant mannose-binding lectin (MBL)	Polymorphisms may differentially bind bacterial surface carbohydrates	<ul style="list-style-type: none"> • MBL replacement†

*Investigational intervention.

†Theoretic intervention.

3. Overcoming barriers to adherence to infection control guidelines

Despite the evidence to support both clinical and cost effectiveness of proper hand hygiene practices to prevent transmission of infectious agents, adherence by HCWs to these recommended practices has been routinely under 50%, even when caring for the sickest ICU patients.^{12,15} Similarly, efficacy and cost savings of *contact precautions* have been demonstrated for controlling endemic or epidemic MRSA,⁸⁵⁻⁸⁷ VRE,⁸⁸⁻⁹² or RSV^{93,94} in acute care hospitals and in a healthcare region.⁹⁵ Among the reasons cited by HCWs for nonadherence are: (1) inconvenience, time, and the cost of supplies; (2) concern that use of gloves, masks, and gowns impersonalize care, increase patient anxiety, and decrease the frequency of HCW and patient contact; (3) lack of understanding or belief that recommended practices are effective or applicable to every institution; (4) lack of support from healthcare leaders and administrators; and (5) adverse psychosocial impact on patients. Using behavioral theories, investigators have concluded that achieving sustained adherence to recommended infection control precautions is a complex process and requires a combination of education, motivation, and systems change.^{12,13,96,97}

The dynamics of adherence to hand hygiene practices have been studied extensively.^{12,15} Specific educational programs with active support of health-care administrators have been associated with improved rates of adherence to recommended hand hygiene practices and decreased rates of health-care-associated infections caused by MRSA and VRE.^{12,13,96,98} Based on behavioral theory and published experience, recommendations to overcome barriers to adherence to infection control guidelines at CF centers are provided below.^{12,97,99} Ongoing administrative support, monitoring of infection control practices and infection rates, and providing feedback to HCWs are essential components of implementing and sustaining new guidelines. Furthermore, the strong motivation of members of the CF community and proactive approach to embracing preventive programs are important assets to achieving consistent adherence to recommended practices.

B. METHODOLOGIES FOR MICROBIOLOGY, MOLECULAR TYPING, AND SURVEILLANCE

1. Introduction

Delineation of the epidemiology and prevention of transmission of infectious agents in CF patients begins with identification in the clinical microbiol-

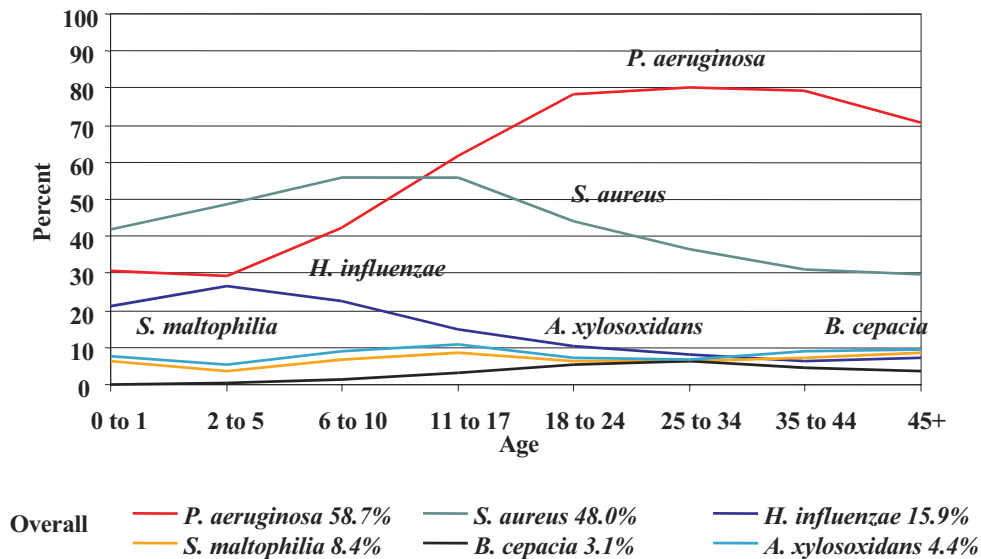


Fig. Age-specific prevalence of respiratory pathogens in CF patients: CFF National Patient Registry Data 2001.⁹

ogy laboratory. Accurate identification of the organisms in the respiratory tract of CF patients has implications for treatment, epidemiology, and infection control. Thus, accurate identification, antimicrobial susceptibility testing, surveillance, molecular typing when appropriate, and awareness of the limitations of currently available methods are the cornerstones for the recommendations provided in this document.

2. Overview of epidemiology of pathogens in CF patients

The unique epidemiology of CF pathogens has been described for decades.¹⁰⁰⁻¹⁰² The predictable cascade of pathogens is universal, generally beginning with nontypable *H. influenzae* and *S. aureus* and progressing to *P. aeruginosa*.¹⁰³ Although a variety of host factors that predispose CF patients to infection have been delineated (Table 2), the precise reasons for this sequence of events are not entirely understood. As reported in the United States CFF Patient Registry annual data report for 2001 (Figure), the prevalence of *S. aureus* in respiratory secretions in CF patients is approximately 40% during the first year of life, rises to 58% during adolescence, and decreases throughout adulthood. *P. aeruginosa* may be the first pathogen recovered from as many as 30% of infants.^{8,9} By 18 years of age, 80% of patients are infected with *P. aeruginosa*. Approximately 3% of CF patients of all ages now harbor *B. cepacia* complex, and 8% of adults are

infected with these organisms. The prevalence and clinical implications of other multidrug-resistant organisms such as *A. xylosoxidans*, *S. maltophilia*, and NTM currently are being elucidated. While the United States CFF Patient Registry is the largest database of its kind, there are limitations to the data due to variations in laboratory methods, reporting, inconsistent laboratory processing, and lack of validation studies.

3. Use of selective media for the isolation of pathogens in CF patients

In CF patients' respiratory tract secretions, the number of pathogens may be numerous, and for certain pathogens, the use of selective media for identification are required.^{104,105} The predominant organism is *P. aeruginosa*, which often is present in large numbers (as much as 10^9 colony-forming units [CFU] per gram of sputum) and may be mucoid; such organisms can overgrow and obscure slower growing and more fastidious organisms (eg, *H. influenzae*).¹⁰⁴ In a recent study of CF patients' respiratory tract microbiology performed in a reference laboratory, the pre-treatment respiratory tract specimens of 595 patients (6 years old or older) from 69 centers contained an average of 2.9 organisms per sample.¹⁰

The first use of selective media for CF specimens was reported by Kilbourn in 1968 to promote the growth of gram-negative bacilli and staphylococ-

Table 3. Recommended media and processing for recovery of CF pathogens

Organism	Recommended media or processing*
<i>S. aureus</i>	Mannitol salt agar Columbia/colistin-nalidixic acid agar
<i>H. influenzae</i>	Horse blood or chocolate agar (supplemented or not with 300 mg/L bacitracin) incubated anaerobically
<i>P. aeruginosa</i>	MacConkey agar
<i>B. cepacia</i> complex	OFPBL agar, PC agar, BCSA
<i>S. maltophilia</i>	MacConkey agar; VIA agar
<i>A. xylosoxidans</i>	DNase agar confirmatory media or biochemical or molecular identification MacConkey agar
Mycobacterial spp.	Biochemical identification assay NALC-NaOH and oxalic acid decontamination step
<i>Aspergillus</i> spp.	<i>Aspergillus</i> spp. and other molds do not grow well on Mycosel, but do grow well (though not selectively) on other media used for CF specimens, especially OFPBL
Other gram-positive organisms	Sheep blood agar supplemented with neomycin and gentamicin (streptococcal selective agar)
Other gram-negative organisms	MacConkey agar

*Detection of some pathogens may be enhanced by prolonging incubation for as long as 4 days to allow slow-growing colonies to become apparent. All media are commercially available.

ci.¹⁰⁶ In 1984, Wong et al. refined processing of CF specimens to include selective agars for *P. aeruginosa* (cetrimide), streptococci (blood agar with neomycin and gentamicin), *H. influenzae* (N-Acetyl-D-glucosamine medium, with anaerobic incubation), staphylococci (mannitol salt agar), and non-lactose fermenting gram-negative bacilli (MacConkey agar).¹⁰⁴ Current recommendations for the use of selective media are summarized in Table 3.

3.1. Selective media for *B. cepacia* complex

With the emergence of *B. cepacia* complex strains as significant pathogens in CF patients, the need for selective media for these organisms became apparent. The first of these, *Pseudomonas cepacia* (PC) agar, was described by Gilligan et al. in 1985 and contained nutrients with crystal violet, bile salts, and ticarcillin and polymyxin as selective agents.¹⁰⁷ In a study of 169 specimens from CF patients, *B. cepacia* complex was isolated from 35 specimens using PC agar and from only 21 using MacConkey agar. Conversely, non-*cepacia* organisms were inhibited by PC agar; 221 potential pathogens were isolated on nonselective media, but only 6 were recovered on PC agar. OFPBL (oxidative-fermentative basal medium with polymyxin B, bacitracin, and lactose) agar, developed by Welch et al., uses oxidative fermentative basal media as an indicator with lactose as the nutrient sugar and bacitracin and polymyxin as selective agents.¹⁰⁸ Using OFPBL, 58 (8%) of 725 specimens yielded *B. cepacia* complex while only 19 (2.6%) were positive using MacConkey and sheep blood agar.

In collaboration with the CDC, a laboratory proficiency study was conducted using simulated CF sputum containing *B. cepacia*.¹⁰⁹ Test 1 evaluated the ability of laboratories to identify *B. cepacia* as a single isolate; 105 (95%) of 111 laboratories did so successfully. Test 2 evaluated the ability of laboratories to isolate *B. cepacia* from simulated sputum containing 10⁵ CFU or greater per mL of *B. cepacia*, *S. aureus*, and *P. aeruginosa*. Overall, 36 (32%) of 115 laboratories detected *B. cepacia*; 14 (95%) of 15 laboratories using OFPBL or PC agar identified *B. cepacia* compared with only 22/100 laboratories not using selective agar. Test 3 evaluated the improved proficiencies of the laboratories that failed to identify *B. cepacia* in Test 2; 97% were successful using selective media. The only failures occurred when selective media were not used. A new *B. cepacia* selective agar (BCSA) has been developed¹¹⁰ and is even more selective when compared with PC agar and OFPBL agar under clinical conditions testing 656 CF specimens.¹¹¹ All 3 of these media are available commercially.

3.2. Selective media for *S. aureus*

Selective media for *S. aureus* have been in use for several decades. Mannitol salt agar, using sodium chloride as a selective agent and phenol red as an indicator of mannitol utilization, is selective for staphylococci and can distinguish between *S. aureus* and nonpathogenic staphylococci.¹¹² Columbia/colistin-nalidixic acid media is selective for staphylococci, but does not distinguish *S. aureus* from other staphylococcal species. Agar containing

oxacillin is used to screen for MRSA in most clinical microbiology laboratories.¹¹⁵

3.3. Selective media for *S. maltophilia*

Several media have been used for the identification and isolation of *S. maltophilia*. DNase agar contains DNA and toluidine blue as an indicator of DNase activity by *S. maltophilia*.¹¹⁴ However, DNase agar does not contain selective agents and thus is a confirmatory media, rather than a selective media. Use of a selective VIA agar (vancomycin, imipenem, amphotericin B) was reported by Denton et al.¹¹⁵ Ingredients include mannitol agar base with bromothymol blue as an indicator and vancomycin, imipenem, and amphotericin B as selective agents. A study of 814 samples from the respiratory tract demonstrated good sensitivity and specificity: 129 (55%) of 235 specimens positive on VIA were negative on bacitracin chocolate agar, while none of the 579 specimens that were negative on VIA were positive on bacitracin chocolate agar.

3.4. Processing sputum for NTM

To improve recovery of NTM and prevent contamination with *P. aeruginosa*, sputum specimens being cultured for NTM from CF patients must be processed differently than specimens from non-CF patients. Whittier et al. demonstrated that if the decontamination step with *N*-acetyl-L-cysteine and sodium hydroxide (NALC-NaOH) was followed by 5% oxalic acid, contamination by *P. aeruginosa* was reduced from 36% to 5%.¹¹⁶ However, in a proficiency study performed by laboratories participating in a natural history study of NTM in CF patients, laboratories failed to detect NTM when present at a low inoculum of 10⁴ CFU per mL.¹¹⁷ Notably, Bange et al. reported a reduction in recovery of NTM from specimens with low concentrations due to killing by oxalic acid.¹¹⁸

4. Antimicrobial susceptibility testing

Accurate antimicrobial susceptibility testing is critical to ensure effective treatment and accurate assessment of the epidemiology of resistance. The 1994 consensus document recommended antibiotic-impregnated disks (Kirby Bauer) be used to determine the antibiotic susceptibility of nonmucoid and mucoid strains of *P. aeruginosa* isolated from patients with CF.¹ In studies to determine the optimal methods for susceptibility testing, 500 multidrug-resistant strains of *P. aeruginosa* from differ-

ent CF patients were tested.¹¹⁹ Commercial automated microbroth dilution assays including Microscan and Vitek were noted to have unacceptably high rates of very major errors (ie, false-susceptibility) and major errors (ie, false-resistance)¹⁹ when compared with a reference microbroth dilution assay.²¹ In contrast, agar-based diffusion assays, such as antibiotic disks or E-tests (antibiotic-impregnated strip) were more accurate and compared favorably with the reference method.¹¹⁹ These studies confirm the 1994 recommendations and have been endorsed by the National Committee for Clinical Laboratory Standards.²⁰ Studies to determine the optimal methods of susceptibility testing for other multidrug-antibiotic resistant organisms, such as *B. cepacia* complex, *S. maltophilia*, or *A. xylosoxidans*, are underway, but results have not yet been reported.

5. Molecular epidemiology techniques for typing CF bacterial isolates

5.1. Typing methodologies

Methods for typing bacteria from the CF respiratory tract for epidemiologic purposes have evolved over the past decade. While earlier methods were based primarily on comparison of phenotypic (physical) features, current methods are based predominantly on the genetic content of different bacterial isolates. The ideal typing system is one that is reproducible and discriminatory and can differentiate strains that are not epidemiologically related from strains that are essentially identical or derived from the same parent strain. Discriminatory power is the ability to differentiate among unrelated strains and identify isolates of common lineage with minor genetic variation.¹²⁰ Further attributes of the ideal typing system include ease of use, low cost, and unambiguous interpretation.^{80,121}

5.2. Phenotypic changes and typing strategies for *P. aeruginosa*

CF patients usually are infected with the same strain(s) of bacteria for many years.¹²² However, *P. aeruginosa* undergoes substantial phenotypic changes during the process of chronic infection that include: (1) changes in colonial morphology from nonmucoid to mucoid¹²³; (2) changes in lipopolysaccharide (LPS) from smooth to rough¹²⁴; (3) loss of motility¹²⁵; and (4) development of resistance to multiple antimicrobial agents.¹²⁵ These attributes are rarely found in early isolates.¹²⁶

The first systems for *P. aeruginosa* were based on phenotypic characteristics, such as agglutination by antiserum to LPS (O-groups or serotyping), phage susceptibility, pyocin typing, or antimicrobial susceptibility profile (antibiogram). These methods were suitable for typing strains of *P. aeruginosa* from patients with acute infection, such as burn victims or neutropenic hosts. However, a multicenter study of CF patients' respiratory tract isolates demonstrated that these systems were unreliable for CF isolates.²⁵ For example, serotyping may prove unreliable as many CF isolates are polyagglutinable, ie, agglutinated by more than one specific O-serum, or untypable, ie, not agglutinated by any O-serum tested.¹²⁷ In contrast, Speert et al. found that the genetic method, restriction fragment length polymorphisms (RFLP), was highly reproducible and discriminated among epidemiologically unrelated strains of *P. aeruginosa* from CF patients.²⁵

5.3. Molecular typing methods for *P. aeruginosa* and *S. aureus*

RFLP was the first method to be used widely for molecular typing of *P. aeruginosa* strains from CF patients.¹²² In this method, genomic DNA is extracted from the bacterium of interest, digested with a restriction enzyme, and the DNA fragments are separated by electrophoresis. A radiolabelled probe directed to a specific portion of the bacterial genome then is added to hybridize with the DNA fragments. The most discriminatory and informative probes are those that react with a hypervariable portion of the bacterial genome, such as the probe for the region upstream from the gene for *P. aeruginosa* exotoxin A (*exoA*).¹²²

However, RFLP has been largely supplanted by pulsed-field gel electrophoresis (PFGE) and random amplified polymorphic DNA analysis (RAPD). PFGE evaluates genetic polymorphisms within the entire bacterial genome by "macrorestriction." Genomic DNA is extracted and then digested with restriction enzymes, which cleave the DNA into large fragments.¹²⁰ These fragments are separated according to size; small fragments travel faster through the gel than large fragments in a constantly changing electric field. The DNA fragments are stained and the pattern examined by eye or by computer-assisted methods. RAPD analysis is based on polymerase chain reaction (PCR) and takes a "snapshot" of the entire bacterial genome.²⁴ A short PCR primer (usually about 10 bases) is used to amplify random sections of the bac-

terial genome. The amplified DNA segments then are separated by electrophoresis, stained, and analyzed by eye or computer, as for PFGE. Further discrimination among isolates is possible using different PCR primers and/or digesting the PCR amplification products with restriction enzymes. PFGE is used widely for typing *S. aureus* as well.^{128,129}

5.4. Molecular typing for *B. cepacia*

The initial molecular typing system used for *B. cepacia* complex was "ribotyping" in which a radio-labelled ribosomal RNA probe was used to probe digested chromosomal DNA.¹³⁰ This method has been replaced by PFGE and RAPD.^{30,131,132} Another PCR-based method, repetitive DNA sequence PCR (rep-PCR) typing, has been applied to typing of *B. cepacia* complex.²² Furthermore, different specific pairs of PCR primers can be used to differentiate among genomovars.²⁷

Thus, to determine if pathogens have been transmitted among CF patients, a genotypic method must be used. However, most genotyping methods cannot be performed routinely in diagnostic clinical microbiology laboratories. Therefore, research/referral laboratories for molecular typing have been established by CFF in Canada, the United States, Denmark, and the United Kingdom for CF bacterial isolates. These laboratories use a combination of methods to determine if multiple isolates from specific CF centers are the same or different types. These centralized laboratories interact with one another through international networks, such as the International *Burkholderia cepacia* Working Group, and are able to determine whether bacterial strains have been transmitted from one country to another (<http://go.to/cepacia>). Through the efforts of these laboratories, it has been possible to further our understanding of the molecular epidemiology of both *P. aeruginosa* and *B. cepacia* complex.

6. Surveillance by the CF and infection control teams

6.1. Components of general infection control surveillance efforts

Surveillance, defined as the ongoing and systematic collection, analysis, and reporting of data to caregivers, is the foundation of infection prevention. The fundamental goals of surveillance are to monitor colonization/infections by calculating rates, ie, the number of persons with colonization or infection caused by a target pathogen (cases) divided by the number of

Table 4. Clinical and epidemiologic features of selected respiratory pathogens among patients with CF

Organism	Prevalence	Clinical impact	Persistence	Selective media	Route of transmission*	Transmission precautions†	Multidrug resistance	
							Mechanism	Antimicrobial control‡
<i>P. aeruginosa</i>	++++	Significant	Chronic	No	P, E _{rs}	S§	Acquired	+
<i>B. cepacia</i> complex	+	Significant	Chronic	Yes	P>E _s	S, C	Intrinsic	+
MSSA	+++	Significant	Variable	Yes	P>E _s	S	Acquired	+/-
MRSA	+	Variable	Variable	Yes	P>>E _s	S, C	Acquired	+
<i>H. influenzae</i>	++	Variable	Variable	Yes	P	S	Acquired	+/-
<i>S. maltophilia</i>	++	Variable	Variable	Yes	E _s , r>P	S	Intrinsic	+
<i>A. xylosoxidans</i>	+	Variable	Variable	No	E _s >P	S	Intrinsic	+
Respiratory viruses	Seasonal	Variable	No	Yes	P>E _s	S, C; add D for influenza, adenovirus	Acquired	-
<i>Mycobacterium</i> spp.								
Nontuberculous	++	Variable	Variable	Yes	E _r >>P	S	Acquired	-
<i>M. tuberculosis</i>	Rare	Variable	Rare	Yes	P	A	Acquired	-
<i>Aspergillus</i> spp.	++	Variable	Variable	Yes	E _r >>>P¶	S	Intrinsic	-

*P, person-to-person; E, environmental reservoir; E_r, environment may serve as a reservoir eg, water, sinks, soil, etc; or E_s, an environmental surface or patient-care item that has been contaminated with respiratory secretions.

†S, standard precautions; C, contact precautions; D, droplet precautions; A, airborne precautions.

‡Potential prevention strategy.

§Add contact precautions when *P. aeruginosa* is multidrug-resistant.

||Contact precautions when institution has evidence of person-to-person transmission.

¶||Airborne transmission has been documented in setting of high organism burden accompanied by irrigation and debridement of wound.

persons at risk, analyze trends over time, provide feedback to caregivers, develop interventions, and ultimately reduce rates of colonization/infection.⁴⁵ Authoritative infection control textbooks^{41,42,133,134} and review articles^{43,135} provide an excellent overview of surveillance methods applied to the healthcare setting. To benefit patients, there must be on-going interval analysis and feedback reporting of surveillance results to caregivers.

In recent years, targeted surveillance strategies have been used in healthcare settings to focus efforts on high-risk patients, infection sites, or invasive procedures, and to focus on microorganisms of greatest epidemiologic importance.^{41,135} The following factors should be considered when designing a surveillance program: (1) the culturing method; (2) the frequency of acquisition ie, incidence; (3) the duration of carriage; (4) the mode of transmission; (5) the clinical impact of infection, which includes morbidity, mortality, and available therapeutic options; (6) the antimicrobial resistance phenotype; and (7) the impact of prevention strategies such as *transmission-based precautions*, cleaning and disinfecting respiratory equipment, and antimicrobial restriction policies.

6.2. Specific surveillance efforts in CF

Among CF patients, surveillance is based on the detection of potential pathogens in the respiratory

secretions by the clinical microbiology laboratory. General recommendations to detect respiratory pathogens among CF patients have been published.^{10,135} At present, there are no studies defining the optimal interval for sampling the respiratory tract of CF patients. However, increased frequency of obtaining cultures from the respiratory tract can aid in refining our knowledge of the incidence, duration of carriage, prevalence, and route of transmission of respiratory pathogens,¹³⁶ but also increases the cost of care. There is increasing evidence that early detection and treatment of *P. aeruginosa* may preserve lung function.¹⁶⁻¹⁸ Reports from the Epidemiologic Study of Cystic Fibrosis have shown that centers whose patients had pulmonary function in the upper quartile for age had more frequent respiratory tract cultures performed.¹³⁷ Routinely scheduled cultures of the respiratory tract should be performed: (1) for all CF patients, regardless of clinical status; (2) for CF patients who have received a lung or heart-lung transplant; (3) at the time of pulmonary exacerbations; and (4) when indicated epidemiologically, such as when an outbreak is suspected. The relative importance of factors defining clinically and epidemiologically important respiratory pathogens among CF patients is summarized in Table 4.

Individual CF centers should use the data submitted to the CFF Patient Registry to calculate the annual incidence and prevalence rates for their entire CF

patient population as well as for substrata that could include children 10 years of age or younger, adolescents 11 to 17 years of age, and adults 18 years of age or older or substrata that address different care areas, ie, adult and pediatric clinics. This surveillance should be performed at baseline and then following implementation of the recommendations for use of selective media (if not already used) and more frequent culturing to understand the possible contribution of ascertainment bias due to these recommendations. Additionally, review of these data will be essential to assess the effectiveness of new infection control practices.

In summary, surveillance strategies for CF centers include determination of incidence and prevalence rates, antibiotic susceptibility profiles and trend analyses for *B. cepacia* complex,^{25,102,138} *S. aureus*¹²⁸ including MRSA,^{10,129,139,140} and *P. aeruginosa* including multidrug-resistant *P. aeruginosa*.^{31,34,35} Surveillance for other organisms, such as *S. maltophilia* or NTM, should be monitored if clinically or epidemiologically indicated within a center. Surveillance is incomplete until the data are analyzed, rates calculated, and data summarized and disseminated to those who will use the information to prevent and control infections. The frequency of reporting will vary depending on the size of the CF patient population and should be determined by the CF care team following CFF guidelines and in consultation with the hospital infection control committee and the microbiology laboratory. Collaboration with the clinical microbiologists and infection control teams in designing and evaluating the results of CF surveillance programs and infection control interventions is recommended to optimize the accuracy of the surveillance and the effectiveness of the preventive strategies implemented within a center.

7. Use of antimicrobial agents in CF patients

Oral, intravenous, and aerosolized antimicrobial agents are used with great frequency in CF patients in efforts to improve pulmonary function or to delay the progression of pulmonary deterioration.¹⁴¹ The indications for antimicrobial agents are: (1) to treat a pulmonary exacerbation using two or more intravenous antimicrobial agents¹⁴²; (2) to prevent chronic infection with *P. aeruginosa*, by the use of aerosolized and oral agents⁸³; or (3) as maintenance therapy for chronic infection with *P. aeruginosa*, eg, by the use of aerosolized tobramycin.¹⁴³ Despite antibiotic treatment, pathogens are not generally

eradicated from the CF patients' airways, and over time, resistance to antibiotics develops, thereby limiting therapeutic options and mandating the frequent use of broad-spectrum agents that are routinely restricted from use in other groups of patients. To date, there have not been studies of antibiotic control programs in the CF patient population.

Although some small studies of chronic anti-staphylococcal prophylaxis (eg, cephalexin) to prevent the initial infections with *S. aureus* in young children less than 2 years of age had been encouraging, the largest, most recent randomized study of cephalexin prophylaxis for 5 to 7 years demonstrated a significant decrease in colonization with *S. aureus*, but a significant increase in the frequency of infection with *P. aeruginosa* and no clinically significant improvement in major health outcomes.¹⁴⁴ Thus, routine anti-staphylococcal prophylaxis is not recommended for young children with CF.

C. SELECTED PATHOGENS OF IMPORTANCE TO CF PATIENTS AND THEIR EPIDEMIOLOGY

1. *S. aureus*, including MRSA

1.1. Virulence factors of *S. aureus*

S. aureus often is the first pathogen to colonize the respiratory tract of CF patients and may be isolated in three morphologic types: mucoid, nonmucoid, or a small colony variant.¹⁴⁵⁻¹⁴⁷ All three morphologic types, especially the mucoid type, bind to respiratory mucin.¹⁴⁸ CF respiratory epithelial colonization is further promoted by high affinity binding asialoganglioside 1 via the major staphylococcal cell wall component teichoic acid.¹⁴⁹ *S. aureus* may contribute to chronic inflammation of the CF respiratory tract by up-regulation of interleukin-8 (IL-8), leading to neutrophil chemotaxis and dysregulation of B-cell presentation of staphylococcal superantigens.^{29,150}

In the pre-antibiotic era, *S. aureus* and *H. influenzae* were major causes of morbidity and mortality in infants with CF.¹⁵¹ Beginning in 1944, penicillin therapy was associated with increased life expectancy of infants with CF, before the nearly universal acquisition of beta-lactamases by *S. aureus* in the 1950s.¹⁵¹ Today, the adverse clinical impact of *S. aureus* in CF patients is managed relatively effectively by antibiotic treatment. Newly developed *S. aureus* vaccines,^{145,152} one of which has been shown to prevent invasive MSSA and MRSA infections in hemodialysis patients,¹⁵² may have application in CF patients in the future.

1.2. Epidemiology of *S. aureus* in CF patients

S. aureus colonization of the anterior nares is an important risk factor for subsequent disease among both CF and non-CF patients. Nasal colonization and disease-producing isolates typically have the identical genotype.^{129,153-155} Goerke et al. found that CF patients without recent antibiotic treatment had a significantly higher prevalence of nasal colonization with *S. aureus* than did treated CF patients or healthy controls, suggesting an increased susceptibility to colonization among CF patients.¹²⁹ In this study, transmission of *S. aureus* within families and loss or replacement of the strain after 1.5 years was observed frequently in both CF and non-CF groups. CF patients generally harbor the same clone of *S. aureus* in the respiratory tract for at least 1 to 2 years.¹⁵⁶

1.3. Prevalence and impact of MRSA in CF patients

Over the past two decades, the proportion of *S. aureus* strains resistant to methicillin (MRSA) and other β -lactam antimicrobials has increased dramatically.¹⁵⁷ First recognized as a healthcare-associated pathogen acquired most frequently by critically ill hospitalized patients, the onset of MRSA infections outside of healthcare settings has been recognized with increasing frequency in some US communities by patients lacking traditional risk factors.¹⁵⁸⁻¹⁶¹ Community-acquired onset strains in non-CF patients have PFGE types that are distinct from the strains acquired by patients hospitalized in the same geographic location and contain the unique *SCCmecA* type IV gene suggesting a distinct epidemiology.^{162,163} However, many patients with "community-acquired MRSA infection" have received care in a healthcare setting within the recent past, and there is a wide variation in prevalence rates.¹⁶⁴⁻¹⁶⁶ Patient-to-patient spread of MRSA has been well documented in hospitals, particularly ICUs.¹⁶⁷ MRSA can contaminate the surfaces of hospital rooms of patients harboring MRSA and can contaminate the clothing of HCWs.¹⁶⁸

The increase in prevalence of MRSA has been less dramatic among CF patients than among other patient populations, such as patients in ICUs or nursing homes. Seven percent of CF patients in the CFF Registry had MRSA respiratory isolates in 2001 (range, 0 to 22.7% of patients per center). A study of the microbiology from patients at 69 CF centers across the United States found that 18.8% of *S. aureus* were methicillin resistant,¹⁰ whereas rates as high as 51%

have been reported in patients without CF.¹⁵⁸ The proportion of CF inpatients with MRSA isolates is substantially higher (27%) than among nonhospitalized CF patients, likely reflecting differences in age, underlying severity of illness, increased antimicrobial exposure, and increased healthcare-associated acquisition.¹⁶⁹ Patients who may be referred to other CF centers for transplant evaluation or for emergent care without complete medical records may harbor multidrug-resistant pathogens, such as MRSA, and serve as an unrecognized source for transmission to other patients (H.W. Parker, personal communication).

The clinical impact of MRSA among CF patients has been investigated. Miall et al. performed a matched case-control study among pediatric patients with CF to determine the effect on clinical status 1 year after isolation of MRSA.¹⁵⁹ Children with MRSA required significantly more courses of intravenous antibiotics, but had worse baseline chest x-rays, suggesting that matching may not have adequately controlled for differences in underlying severity of illness. MRSA infection did not have a significant effect on growth or lung function. Among a group of adult CF patients, MRSA acquisition was associated with poor lung function, and the duration of colonization was frequently brief, lasting for less than 1 month in 35% of patients.¹⁷⁰ Similarly, Boxerbaum et al. did not note clinical deterioration in 14 patients with MRSA and 10 of 14 had transient colonization.¹⁷¹ In contrast, Givney et al. demonstrated that the same clone of MRSA persisted in an individual CF patient for years.¹⁴⁰ In the study by Thomas et al., MRSA did not adversely affect the clinical course of 2 patients with MRSA at the time of transplantation or of 5 patients who acquired MRSA following transplantation.¹⁷⁰ Thus, current data describing the clinical impact of MRSA on lung function in CF are inconclusive.

1.4. Patient-to-patient transmission of methicillin-susceptible *S. aureus* (MSSA) and MRSA in CF patients

Schlichting et al. described patient-to-patient transmission of MSSA in summer camp.¹²⁸ In this study, 4 typing methods were used to compare MSSA strains before and after attendance at a 4-week summer camp for CF patients. Four of 20 patients acquired a new type that was noted in another camper at the start of camp, suggesting patient-to-patient transmission of this strain.

Healthcare-associated transmission of MRSA from non-CF to CF patients and from CF patient to CF

patient has been reported and may be facilitated by hospitalization of CF patients on general pediatric or adult medical wards.¹⁴⁰ CF patients are likely to be as susceptible to healthcare-associated transmission of MRSA as patients without CF.

In summary, both MSSA and MRSA can be transmitted from CF patient to CF patient and among CF and non-CF patients. Routes of transmission do not differ between MRSA and MSSA strains. However, antibiotic-resistant strains may have an adverse impact on clinical outcome and healthcare costs. Therefore, hospital policies for precautions to prevent patient-to-patient transmission of MRSA among patients without CF must be applied to patients with CF who are colonized or infected with MRSA at any site.²

2. *P. aeruginosa*

2.1. Epidemiology and clinical impact of *P. aeruginosa*

P. aeruginosa is the most important and prevalent pathogen in CF patients. Acquisition is almost universal by adulthood, and this pathogen has an adverse effect on lung function and survival.^{17,172-174} Children with CF infected with *P. aeruginosa* have lower pulmonary function, lower chest radiograph scores, and lower 10-year survival than children uninfected with *P. aeruginosa*.¹⁷³ CF children identified through newborn screening from 1990 through 1992 who became infected with *P. aeruginosa* had a lower National Institutes of Health clinical score, lower % predicted forced expiratory volume in 1 second (FEV₁), and more days of hospitalization.¹⁷ The appearance of the mucoid phenotype has been linked to deterioration in lung function,^{175,176} and early acquisition of mucoid strains has been associated with early mortality.¹⁷ However, aggressive antimicrobial treatment of *P. aeruginosa* at initial acquisition is associated with a delay in chronic infection and an improved clinical course.¹⁶⁻¹⁸ Longitudinal monitoring of *P. aeruginosa* antibody titers in CF patients diagnosed through newborn screening can detect *P. aeruginosa* pulmonary infections 6 to 12 months before isolation of this organism from respiratory tract cultures.¹⁷⁷ Over time, in the CF lung, *P. aeruginosa* becomes increasingly resistant to antimicrobials, making effective therapy progressively difficult.¹⁷⁸

Most CF patients retain the same clone of *P. aeruginosa* throughout their lifetime.^{24,179,180} However, an

individual patient may be infected with more than one clone.⁵⁶ Patients who receive antibiotic therapy to eradicate *P. aeruginosa* may experience recurrent isolation of the initial strain after transient suppression during antimicrobial treatment.¹⁸¹

2.2. Potential sources of *P. aeruginosa*

The initial source of *P. aeruginosa* for most patients remains unknown. The source may be the environment, another CF patient, contaminated respiratory therapy equipment, or medication vials, or other objects that have become contaminated with *P. aeruginosa*.

2.2.1. *P. aeruginosa* in the hospital environment

Many studies have recovered *P. aeruginosa* from the hospital and clinic environment.¹⁸²⁻¹⁸⁴ Studies have shown that *P. aeruginosa* strains of great genetic variability may be widespread in and around water sources including sinks and tap water in a pediatric ward for CF patients.^{184,185} *P. aeruginosa*, suspended in saline, can survive on dry surfaces for 24 hours, whereas mucoid strains can survive for 48 hours or longer.^{182,184} However, *P. aeruginosa* suspended in CF sputum can survive on dry surfaces up to 8 days.¹⁸⁴

Studies by Zimakoff et al. in healthcare settings for CF patients found *P. aeruginosa* in 7% of environmental cultures; sinks, toys, baths, and hand soaps were positive and 12 (60%) of 20 positive cultures shared the same phage types and LPS O-group serotypes as those found in the patients.¹⁸² However, these findings must be questioned because many strains that were considered to be the same were typed with polyclonal sera that identify several different O-types; more recent studies have shown that these strains may be different genotypes. Similarly, Speert and Campbell isolated *P. aeruginosa* from 2 (4%) of 48 pulmonary function test machines and 14 (11%) of 126 hospital drains.¹⁸⁶ Five of 14 sink drain isolates matched the serotype of the patient(s) hospitalized in that room. In this study, the hospital had opened 3 months previously, and over time, contamination of sinks increased from 14% to 66%. Thus, it is possible that the CF patients were the source of the strains isolated from the sink cultures.

Using the *exoA* probe, Wolz et al. examined isolates from the CF clinic environment. Only two genetically

identical isolates of *P. aeruginosa* were detected, and this strain was not found among patients.¹⁸¹ In contrast, the same strain, as documented by PFGE, had been isolated from sinks and patients including at least one documented new acquisition of *P. aeruginosa* during hospitalization.^{184,187} Similar observations were made in a CF clinic documenting shared clones in the clinic environment (eg, sinks).¹⁸⁷ In contrast, despite documentation of a shared strain of *P. aeruginosa* among adult CF patients, this epidemic strain could not be found in repeated sampling of sinks, drains, toilets, showers, or communal surfaces.³⁵

P. aeruginosa can be recovered from the hands of HCWs and patients. Speert and Campbell demonstrated *P. aeruginosa* on 5 (3%) of 175 patients' hand samples.¹⁸⁶ Zimakoff et al. similarly detected *P. aeruginosa* on 3 (18%) of 16 patients' hands, but not on the hands of 37 staff members.¹⁸² In contrast, Doring et al. used the *exoA* probe and PFGE to demonstrate that sink drains and HCW hands were contaminated with the same genotypes as those harbored by CF patients.¹⁸⁴ These investigators performed studies of experimental hand washing wherein the hands of study participants became contaminated with the same strains of *P. aeruginosa* after washing at sinks with contaminated drains.^{184,188}

The potential for droplet transmission has been demonstrated by placing agar plates within 3 feet of a coughing CF patient; *P. aeruginosa* was recovered from 11 (65%) of 17 plates.¹⁸² In another similar study, growth of *P. aeruginosa* was detected on 1 (17%) of 6 plates held 40 cm (1.25 feet) from the mouths of coughing CF patients.¹⁸⁴

True airborne transmission of *P. aeruginosa* has not been documented. Demonstration of an airborne route of transmission would require isolation of the same strain of *P. aeruginosa* from the sputum of a CF patient and from air samples obtained in the hallway outside that patient's room or in a neighboring room that did not house a CF patient or from 2 patients who shared the same air supply, but did not have contact with each other or with the same medical equipment. Air samples from a CF clinic obtained using a centrifugal air sampler demonstrated that 1% of CFU were *P. aeruginosa*.¹⁸² Similarly, Speert and Campbell demonstrated *P. aeruginosa* in 3 (6%) of 52 air samples from the rooms to which CF patients were admitted.¹⁸⁶ In contrast, Wolz et al. examined the air of the CF clinic and did not recover *P. aeruginosa* from any air samples.¹⁸¹ Survival times of *P. aeruginosa* in aerosols were dependent on strain

characteristics, light, and humidity; the strains' half-life varied from 3 to 76 minutes.¹⁸⁸ It is unlikely that *P. aeruginosa* in CF sputum would remain suspended in the air long enough to be transmitted to other patients who share only the same air supply. Thus, most transmission of *P. aeruginosa* is via the direct and indirect contact or droplet routes.

2.2.2. Colonization of home nebulizers

Studies examining colonization of home nebulizers of CF patients have been performed. Pitchford et al. found that 9 (25%) of 36 patients' home nebulizers were contaminated.⁶² Rosenfeld et al. examined the frequency of colonization of in-use home nebulizers and found that 17 (55%) of 31 nebulizers from 5 different manufacturers were positive for *P. aeruginosa* and 11 (35%) were positive for *S. aureus*.⁶³ In addition, 6 (19%) were positive for *Klebsiella* species, and many were colonized with organisms that are not common pathogens in CF patients. Jakobsson et al. demonstrated *P. aeruginosa* (3 of 41 patients) or *B. cepacia* (1 of 41 patients) in patients' nebulizers.^{61,64} Similarly, Hutchinson et al. found *B. cepacia* complex in home nebulizers.⁶¹

2.2.3. Colonization of whirlpools, hot tubs, swimming pools, and dental equipment

Colonization of whirlpools (ie, hydrotherapy pools), swimming pools, hot tubs, and dental equipment with *P. aeruginosa* has been evaluated. Whirlpools and hot tubs both were found to harbor *P. aeruginosa*, while chlorinated swimming pools did not.¹⁸⁹ Outbreaks of folliculitis, nodular lesions, and more serious infections caused by *P. aeruginosa* have been associated with hot tubs and whirlpool bathtubs in the community and in hospitals.^{190,191} Pools must be well chlorinated according to standard recommendations to prevent *P. aeruginosa* contamination.¹⁹¹ Dental equipment can be colonized with *P. aeruginosa*. Jensen et al. demonstrated that a patient and dental equipment shared the same clone.¹⁹² Standard cleaning and disinfection/sterilization procedures of dental equipment will prevent patient-to-patient transmission of potential pathogens.

2.3. Transmission of *P. aeruginosa* among CF patients

2.3.1. *P. aeruginosa* transmission among siblings

The best documented and most accepted instances of shared strains among CF patients occur among

siblings. Speert and Campbell demonstrated that 3 of 4 sibling pairs shared the same serotype.¹⁸⁶ Thomassen et al. showed that sibling pairs shared the same serotypes.¹⁹³ Using the DNA probe *exoA*, Wolz et al. examined isolates from 12 sibling pairs and found that 7 pairs harbored identical strains.¹⁸¹ Grothues et al. studied 22 siblings from 8 families and demonstrated by PFGE that the siblings in 5 families shared identical clones and in 3 families had closely related clones.¹⁹⁴

2.3.2. *P. aeruginosa* transmission in non-health-care settings among unrelated CF patients

There have been several reports of shared strains of *P. aeruginosa* among CF patients that were linked to non-healthcare settings. Using *exoA*, Wolz et al. examined the isolates of 46 patients before and after a 6-week recreational event.¹⁸¹ Six of 13 previously uninfected patients had acquired *P. aeruginosa*, of whom 1 shared a strain with a previously infected patient. Four previously infected patients shared strains that were identical to strains detected in other patients. Similarly, using PFGE, Ojeniyi et al. examined *P. aeruginosa* obtained from 22 children and adolescents attending a week-long winter camp.³⁶ After camp, 5 previously uninfected children were found to harbor the same clone of *P. aeruginosa* 1 to 14 months later. This same strain was found in 2 previously infected patients. Fluge et al. examined the isolates of 60 patients in Norway and detected a large cluster of the same strain shared by 27 patients and 13 smaller clusters consisting of 2 to 4 patients each.¹⁹⁵ The patients in the large cluster were more likely to have attended summer camp and training courses, but were not more likely to have been hospitalized.

2.3.3. *P. aeruginosa* strains transmission in healthcare settings

There are several studies in different centers around the world that demonstrate patient-to-patient transmission of *P. aeruginosa*. During the 1980s, a Danish CF center reported an epidemic of a multidrug-resistant strain of *P. aeruginosa* that was typed by serotyping and phage typing.³⁷ These same investigators used PFGE to examine 200 isolates from 61 patients attending their clinic and reported 2 strain clusters consisting of 26 and 11 patients each.¹⁷⁹ This Danish CF center found that implementation of infection control measures was associated with a decreased incidence and prevalence of *P. aeruginosa* infection. The measures included establishing separate clinics for patients with or without *P. aeruginosa*

infection, emphasizing good hygiene, especially hand washing for patients and HCWs, and moving to a larger clinic.⁸²⁻⁸⁴

Hunfeld et al. examined the strains isolated from 30 adult CF patients and found that each patient from a center in Germany harbored a unique genotype, and 10 of 12 patients from a center in Israel shared 3 predominant clones.³³ Cheng et al. described the spread of a resistant clone of *P. aeruginosa* in a CF center in the United Kingdom.⁵¹ These investigators were alerted to the possibility of patient-to-patient transmission due to an increase in ceftazidime resistance among patients who had never received this agent during a period when there was extensive use of ceftazidime monotherapy in that center. Using both PFGE and a probe for the flagellin gene of *P. aeruginosa*, it was shown that 55 (85%) of 65 children with strains resistant to β -lactam agents acquired the clone, which had been present in this CF clinic for at least 7 years. The epidemic strain was not recovered from any environmental cultures. In a cohort of 56 children who were identified by newborn screening in Australia who underwent follow up until age 7 years, Nixon et al. identified *P. aeruginosa* in 24 (43%) of 56 children, 4 of whom died. These 4 children were infected by a mucoid, multidrug-resistant strain of *P. aeruginosa* that was shown to have a common PFGE pattern and was shared with older children cared for in the same CF clinic.¹⁷

Farrell et al. examined the acquisition of *P. aeruginosa* in a randomized study of neonatal screening for CF performed in Wisconsin from 1985 to 1996 in Madison (Center A) and Milwaukee (Center B).¹⁹⁶ These investigators found that the prevalence of *P. aeruginosa* was higher at Center B than at Center A (70% vs 48%) and there was a shorter time to acquisition of *P. aeruginosa* at Center B.³² Time to acquisition of *P. aeruginosa* was shorter in infants diagnosed by neonatal screening; the median duration of *P. aeruginosa*-free weeks was 52 weeks among screened infants at Center B versus 289 weeks among unscreened patients at Center A. It was hypothesized that crowded conditions in Center B's clinic before June 1990 contributed to the acquisition of *P. aeruginosa*. A multivariate analysis determined that care in Center B before June 1990 and aerosol use were independent risk factors for acquisition of *P. aeruginosa*, while higher levels of maternal education were protective.¹⁹⁷

Most recently, 2 groups of CF clinicians in the United Kingdom described transmission of *P. aeruginosa*

inosa among adults.^{34,35} In a prospective study of 154 patients, 22 (14%) shared the same clone of multidrug-resistant *P. aeruginosa* as demonstrated by both pyocin typing and PFGE.³⁴ These 22 patients were infected previously with other strains of *P. aeruginosa*. No social contact occurred outside of the CF clinic, but nearly all had been inpatients at least once during the previous 2 years. This clone was not isolated from any of the 24 patients co-infected with *B. cepacia* complex and *P. aeruginosa* who had been segregated for 8 years or from 52 non-CF patients infected with *P. aeruginosa*. The patients infected with *B. cepacia* complex shared outpatient facilities with other CF patients, but visits were scheduled on different days and they were admitted to different inpatient units. The epidemic strain was not isolated from any environmental cultures of the inpatient or outpatient units. McCallum et al. described 5 patients who were superinfected with a multidrug-resistant strain of *P. aeruginosa*.³⁵ No environmental surface cultures were positive for this strain. The investigators concluded that this strain was acquired during hospitalization as CF patients who had never been hospitalized did not acquire this strain.

In contrast, several investigators have failed to detect transmission of *P. aeruginosa* among CF patients. In Vancouver, Speert et al. studied 21 CF patients attending summer camp and found that 5 children who were free of *P. aeruginosa* at the start of camp remained so at the end of camp, 7 days later.¹⁹⁸ Speert and Campbell also studied 27 hospitalized CF patients to examine sharing of strains. Using serotyping, these investigators found that 3 of 7 pairs of patients hospitalized in the same room had transient colonization with shared serotypes that did not persist during the following 2 years.¹⁸⁶ Subsequent analysis revealed isolates that appeared identical by serotyping were actually different when analyzed by molecular methods (D. Speert, personal communication). Mahenthalingam et al. examined 385 sequential isolates from 20 patients and found only one instance of shared RAPD types.²⁴ In the United Kingdom, Williams examined 496 isolates from 69 patients and found no evidence of cross-infection.¹⁹⁹

In a large prospective study of *P. aeruginosa* CF isolates, Speert et al. examined at least 3 isolates from each of 174 patients treated at the CF clinics in Vancouver, British Columbia, Canada, between 1981 and 2000.²⁰⁰ Bacteria were typed by RAPD and by PFGE. For groups of patients who were infected with

the same strain of *P. aeruginosa*, home location, date of acquisition, or any contact with other patients (defined as simultaneous attendance at the hospital's school or playroom while inpatients, contact in CF clinic, or known social interactions) were compared. In all, 157 genetic types of *P. aeruginosa* were identified, 133 of which were unique to individual patients. Twenty-four types were each shared by more than 1 patient; epidemiologic evidence linked these individuals only in the cases of 10 sibships and 1 pair of unrelated patients who were close friends. From these data, the authors concluded that there was an extremely low risk in Vancouver for patients with CF to acquire *P. aeruginosa* from other patients and that prolonged close social contact, such as occurs between siblings, is necessary for patient-to-patient spread.

2.3.4. Transmission of *P. aeruginosa* from a CF patient to non-CF household contacts

To our knowledge, there has been only one case report describing transmission of *P. aeruginosa* from a CF patient to non-CF individuals. In this report, an adult with CF infected with the epidemic strain previously described³⁵ transmitted this strain to her parents who were each carriers of different CF mutations. Both developed pneumonia and subsequent chronic colonization with the epidemic strain.²⁰¹ However, this strain was not recovered from gargle samples obtained from the throats of 31 relatives of 23 other CF patients who were infected with this epidemic *P. aeruginosa* strain. This report suggests that this strain had unique virulence properties that merit further study.

2.4. Summary of transmission of *P. aeruginosa*

In summary, CF patients can share the same strains of *P. aeruginosa*. It is likely that different strains have different potential for transmission as has been noted with strains of *B. cepacia* complex, but close, prolonged contact facilitates transmission. Current data suggest a role for environmental contamination with respiratory secretions as a potential reservoir for *P. aeruginosa*. It is possible that crowded physical conditions and the contaminated hands of HCWs may facilitate transmission. Additional epidemiologic studies using standardized methods are needed to further define the relative contribution of patient-to-patient transmission and potential environmental acquisition of *P. aeruginosa* among CF patients. Environmental cultures should be obtained only as part of an epidemiologic investiga-

Table 5. Members of the *B. cepacia* complex, 2001

Species (Genomovar)	Binomial designation	Reference
I	<i>B. cepacia</i>	388
II	<i>B. multivorans</i>	388
III	Pending	388
IV	<i>B. stabilis</i>	388, 389
V	<i>B. vietnamiensis</i>	388, 390
VI	Pending	202, 391
VII	<i>B. ambifaria</i>	202, 392
VIII	<i>B. anthina</i>	393
IX	<i>B. pyrrocinia</i>	393

tion. Documentation of the distance between CF patients in healthcare settings as well as patient activities within and outside of healthcare settings is necessary to establish the mechanism of patient-to-patient transmission. To date, no studies have evaluated the possibility of transmission of a strain of *P. aeruginosa* among CF patients via shared bathrooms.

3. *B. cepacia* complex

3.1. Taxonomy of *Burkholderia* species

The taxonomy of *Burkholderia* spp. has become very complex due to the realization that isolates of *B. cepacia* are actually members of multiple distinct bacterial species called “genomovars.”²⁰² At present, there are at least 9 distinct species in the *B. cepacia* complex (Table 5) and at least 15 additional species within the genus *Burkholderia*.

3.2. Epidemiology of *Burkholderia* spp. in CF patients

Two research centers in North America have been instrumental in defining the epidemiology of *B. cepacia* complex in CF patients. The United States CFF *B. cepacia* Research Laboratory and Repository was established in 1997.^{26,158} CF caregivers are encouraged to send isolates for confirmatory identification and to assess possible patient-to-patient transmission. Analysis in this laboratory provides identification of specific species within the *B. cepacia* complex. In a study of 606 CF patients from 105 US cities, genomovar III and *B. multivorans* were the most common species encountered, accounting for 50% and 38% of isolates, respectively.²⁷ Nevertheless, all 9 species of the *B. cepacia* complex have been recovered from CF patients.

The Canadian *B. cepacia* Complex Research and Referral Repository was established in Vancouver, British Columbia, in 1994. Since that time, 905 *B. cepacia* complex isolates have been submitted from 447 patients from 8 of the 10 Canadian provinces.²⁰⁵ A total of 80% of the patients were infected with genomovar III strains and approximately 9% with *B. multivorans*. Substantial regional differences were documented.

3.3. Clinical course associated with *B. cepacia* complex

The first reports of *B. cepacia* in CF patients then named *Pseudomonas cepacia*, occurred in the late 1970s and early 1980s and provided the initial descriptions of the virulence of this multidrug-resistant pathogen.^{204,205} The *B. cepacia* syndrome is characterized by high fever, bacteremia, rapid pulmonary deterioration, and death in 62% to nearly 100% of patients. Addition of high-dose intravenous corticosteroids to intensive antimicrobial therapy has been associated with survival in one patient.²⁰⁶ *B. cepacia* complex is found in high concentrations in sputum and has prolonged survival on surfaces.²⁰⁷ Infection with *B. cepacia* complex has been associated with decline in lung function and a markedly shorter median survival.^{205,208-212} There is some evidence that genomovar III, in general, may be more virulent and more likely to be transmitted patient-to-patient, but this needs further study.^{30,213,214}

Although infection with *B. cepacia* complex is generally chronic, in some CF patients infection/colonization may be transient or intermittent. The frequency with which transient infection occurs and the criteria for confirming eradication are not known. It is likely that unidentified host and bacterial factors are determinants, but further study is required. Replacement of one strain with another and association with clinical deterioration was first documented in 5 adults in the United Kingdom.²¹⁵ In a recent study from Vancouver, the replacement of *B. multivorans* by strains of genomovar III was documented.³⁰ Such replacement was associated with deterioration in clinical status in some patients. In an analysis of isolates serially recovered from 347 CF patients chronically infected with *B. cepacia* complex, a change in the infecting strain was noted in 7.4%.²⁸ Thus, CF patients infected with *B. cepacia* must avoid close contact with each other to prevent acquisition of potentially more virulent strains.

Table 6. Factors associated with acquisition of *B. cepacia* complex

Risk factor(s)	Comments
Attendance at CF summer camp ²¹⁶ <ul style="list-style-type: none"> • Sleeping in same cabin • Sharing a personal item (eg, eating utensils) • Dancing or hugging <i>B. cepacia</i> infected camper 	Risk of acquisition increased with time spent at camp and prevalence of <i>B. cepacia</i> at the camp
Attendance at summer educational program ²³	3 (20%) of 15 patients acquired same ribotype
Participation in adult CF group ³³²	Disbanded meetings and extensive social contact
Social contact ^{102,332} <ul style="list-style-type: none"> • Kissing • Intimate contact • Prolonged car rides • Fitness class • Sharing drinking utensils 	
Sibling with <i>B. cepacia</i> complex ²⁰⁵	
Handshaking ^{102,184,217,222}	<ul style="list-style-type: none"> • 2 of 68 cultures positive; 1 from patient and 1 from investigator²¹⁷ • Patients' hands became contaminated after coughing¹⁰² • Risk of acquisition increased if hospitalized within 3 months and if hospitalized longer • Interviews with healthcare workers indicated poor adherence to <i>contact precautions</i>
Inpatient exposures <ul style="list-style-type: none"> • Recent hospitalization^{205,217} • Use of specific shower • Sharing hospital room with another patient infected with <i>B. cepacia</i>²¹⁷ • Cared for by a medical student 	
Respiratory therapy equipment <ul style="list-style-type: none"> • Sharing equipment • Hospital nebulizers²²⁷ • Spirometer²⁰⁴ • Mouthpiece filters¹⁰² 	Reservoirs of large volume nebulizers grew <i>B. cepacia</i>

3.4. Transmission of *B. cepacia* complex among CF patients

For more than a decade, it has been recognized that *B. cepacia* complex can be transmitted from patient-to-patient in both healthcare and non-healthcare settings. Both indirect and direct contact with infected secretions and droplet spread have been implicated in transmission; the risk factors associated with transmission of *B. cepacia* complex are summarized in Table 6.^{26,76,102,205,216,217} Ribotyping was the first typing method used to provide evidence of patient-to-patient transmission among CF patients.²¹⁸ In some instances, detection of transmitted strains of *B. cepacia* complex by conventional culture methods occurred 2 years after exposure in a non-healthcare setting.²⁵ Similar studies were performed in the United States; Edinburgh, Scotland; Manchester, England; and Ontario, Canada, and led to the disbanding of CF summer camps worldwide.^{102,219} In a recent study, both inter-city spread of a genomovar III strain and the 20-year persistence of this epidemic strain in a large CF center were documented, using molecular typing.²²

Contact with healthcare settings has been identified as a risk factor in several studies.^{193,217} Recent hos-

pitalization,²¹⁷ poor adherence to hand washing,^{217,220} contaminated respiratory therapy equipment,^{220,221} and possibly contaminated hospital showers^{217,222} have been associated with transmission of *B. cepacia* complex. In contrast, dental care is unlikely to be associated with acquisition of *B. cepacia*. During aerosol-generating dental treatments of four CF patients infected with *B. cepacia*, *B. cepacia* was not recovered from any of the samples from the dental environment nor from the dentist.²²³

True airborne transmission of *B. cepacia* complex is less certain. Ensor et al. studied 8 adult CF patients chronically colonized with *B. cepacia* before and after chest physiotherapy.²²⁴ Before physiotherapy, 16% of air samples were positive for *B. cepacia*, but during and after chest physiotherapy as coughing was induced, 47% and 44% of air samples were positive; no air samples were positive for 3 of 8 patients. Of note, air samplers were positioned 100 cm (39 inches) from the patients, which is approximately the 3-foot range defined for droplet transmission. *B. cepacia* was detected in air samples obtained 15 to 45 minutes after the patients left the room. All samples obtained at 60 minutes were negative.²²⁵ In a CF clinic, *B. cepacia* was detected at very low counts (1 CFU/mm³) in only 2 of 29 air

samples obtained approximately 39 inches from patients.²²⁶ Other air sampling studies did not recover *B. cepacia* from air samples obtained from rooms in which patients chronically infected with *B. cepacia* were coughing and talking²²⁷ or within 39 inches of patients undergoing chest physiotherapy or in the waiting room.^{102,217} While *B. cepacia* has been detected with air sampling, most studies obtained samples within approximately 3 feet of infected patients, indicating a droplet route of transmission. There have been no reports of patient-to-patient transmission of *B. cepacia* among CF patients who have shared only the same air supply. The same criteria to establish an airborne route of transmission of *P. aeruginosa* described above (Section 2.2.1) are applicable to *B. cepacia*. Thus, similar to *P. aeruginosa*, most transmission of *B. cepacia* complex is via the direct and indirect contact or droplet routes.

3.4.1. Bacterial virulence factors associated with transmission of *B. cepacia* complex

Patient-to-patient transmission of genomovar III strains has been associated with two markers: cable pili (*cbIA*)²²⁸ and the *B. cepacia* epidemic strain marker (BCESM).¹⁵¹ The *cbIA*-encoded cable pili is expressed by the ET12 clone, a specific genomovar III strain that has caused outbreaks in Ontario, Canada, and the United Kingdom. In Canada, there was only evidence of patient-to-patient spread of genomovar III strains, which harbored either the cable pili or the BCESM,²⁰⁵ and only genomovar III strains harbored these transmissibility markers.⁵⁰ However, the ET12 strain has rarely been found among strains recovered from CF patients in the United States, and patient-to-patient transmission of strains without the cable pili or BCESM has occurred.^{22,27} Thus, neither the cable pili nor BCESM is a sufficient marker of strain transmissibility.

3.5. *B. cepacia* complex transmission among non-CF patients

Common source outbreaks of *B. cepacia* infections related to contamination of antiseptic products during the manufacturing process have been well described.⁷⁰ Holmes et al. reported transmission among non-CF and CF patients in an intensive care unit.²²⁰ Recent studies in non-CF patients have demonstrated epidemic strains of *B. cepacia* complex associated with hospital-acquired infection. Siddiqui et al. described a 2-year outbreak of a strain

of genomovar III that was found in 17 (85%) of 20 non-CF patients and 2 (1%) of 200 environmental cultures including a bottle of hand lotion and a drain.²²⁹ None of the CF patients cared for at other healthcare institutions in the area was infected with this clone. Infection control interventions that led to the termination of the outbreak included: contact isolation for all patients infected or colonized with *B. cepacia* complex, education for nurses and respiratory therapists, and temporary removal of hand lotions. Another outbreak of *B. cepacia* complex infection/colonization among 9 mechanically ventilated patients was thought to be due to contamination of multidose albuterol vials.⁵⁶ Case-patients were more likely to have been cared for by a specific respiratory therapist. Of note, multidose vials were not always discarded within 24 hours and nebulizers were noted to be inadequately dried after each treatment. These investigators postulated that the multidose vial dropper became contaminated by contact with an incompletely dried nebulizer that was contaminated with *B. cepacia* complex.

To assess transmission of *B. cepacia* from infected CF patients to HCWs without CF, 7 HCWs with repeated contact with 3 to 5 infected patients in a CF clinic were studied.²⁵⁰ During the 3-month study period, *B. cepacia* was not recovered from any of the 73 throat cultures that were obtained from the HCWs.

3.6. Environmental reservoirs of *B. cepacia* complex

Because implementation of infection control measures has reduced, but not eliminated new acquisition of *B. cepacia* complex by CF patients, several studies have examined strains recovered from various environmental sources in an attempt to identify possible reservoirs for these species.^{231,232} Mortensen et al. cultured numerous sites within the homes of 14 CF patients and 13 controls to look for possible reservoirs.²³¹ *B. cepacia* complex strains were found in 5 of 916 cultures: 3 from the homes of CF patients and 2 from the homes of controls.

B. cepacia complex are soil and plant commensal bacteria. It is likely that the various species of the *B. cepacia* complex occupy different niches in the natural environment. This distribution, however, requires further elucidation. Genomovar III strains have been recovered from agricultural soil^{233,234} and from maize rhizosphere.²³⁵ Recently, a strain known to infect persons with CF was identified from among isolates recovered from fields planted

Table 7. Infection control interventions that have been associated with decreased patient-to-patient transmission of *B. cepacia* complex among CF patients

Intervention	Reference
Emphasize hand hygiene for CF patients and HCWs	182, 193, 238
Educate patients, families, and HCWs about risk factors for transmission of <i>B. cepacia</i> complex	22, 193, 238, 239
Use single patient rooms with separate showers for hospitalized patients with <i>B. cepacia</i> complex*	22, 102, 193, 216, 238, 239, 212
Place hospitalized patients with <i>B. cepacia</i> complex on contact precautions	217, 238
Eliminate socializing between CF patients infected with <i>B. cepacia</i> and other CF patients while in hospital	193
No CF patients share rooms	238
Inpatients and outpatients wear mask	22
Inpatients wear gloves	22
Improve microbiological detection	193, 238
Segregate outpatient clinics, ie, <i>B. cepacia</i> complex patients attend different clinic or different clinic day	22, 102, 238, 239
Decontaminate environment including respiratory equipment	22, 182, 193, 238, 239
Monitor environmental decontamination (eg, drains, showers, exercise equipment, and physiotherapy equipment)	182, 238
Reduce social contact between patients infected with <i>B. cepacia</i> complex and other CF patients in non-healthcare facilities	102, 193, 238, 239
Separate summer camps for CF patients with <i>B. cepacia</i> complex†	193
Ban patients with <i>B. cepacia</i> complex from attending CF conferences	212, 394

*Thomassen et al. admitted patients with *B. cepacia* complex to a different hospital ward.

†It is recommended that CF summer camps be discontinued.

with onions.²⁵⁶ However, genomovar III was infrequently recovered from soil samples from urban settings.²⁵⁷ To date, *B. multivorans* has not been found in soil samples. Further studies are needed to more clearly define the preferred niche that species of the *B. cepacia* complex reside. Thus, the risk to CF patients posed by strains residing in the natural environment has yet to be defined.

3.7. Misidentification of *B. cepacia* complex

B. cepacia complex bacteria are frequently misidentified. In a study of 1,051 isolates referred from 608 patients receiving care in 91 US cities, 88 (11%) of 770 isolates identified by referring laboratories as *B. cepacia* were found to be other genus or species. In addition, of the 281 isolates referred as other species, 101 (36%) were identified as *B. cepacia* complex based on genotypic testing.¹¹ Such misidentification of *B. cepacia* complex isolates can thwart infection control efforts.

3.8. Successful infection control interventions

Successful infection control interventions to prevent patient-to-patient transmission of *B. cepacia* complex have been described (Table 7). In general, multiple interventions were introduced simultaneously, making it difficult to assess the relative impact of individual interventions. These have included segregating patients with *B. cepacia* complex from other CF patients; discouraging CF patients from visiting each other while hospitalized; emphasizing hand hygiene;

discouraging socializing in non-healthcare settings; educating staff, patients, and families; hospitalizing patients harboring *B. cepacia* in single rooms with separate showers; monitoring environmental decontamination by culturing water samples from showers and drains; and obtaining cultures from exercise and physiotherapy equipment.^{22,193,238,239} Clinics that have failed to practice segregation have documented ongoing transmission of epidemic clones.^{22,238,239} If all patients with *B. cepacia* are grouped together on a separate clinic day, they must still avoid contact with each other because of the risk of replacement of less virulent genomovars by newly acquired virulent genomovars.^{22,28,30,215}

At present, there are no studies demonstrating the efficacy of placement of surgical masks on CF patients in preventing patient-to-patient transmission of potential pathogens, but this intervention has proven useful in preventing droplet transmission of certain infectious agents, such as influenza, *Bordetella pertussis*, or adenovirus, from non-CF patients to HCWs.^{2,45} Several centers have reduced the incidence of *B. cepacia* complex without requiring patients to wear masks,¹⁹⁵ but the efficacy of mask use has not been studied for other pathogens acquired by CF patients.

3.9. Summary of transmission of *B. cepacia*

In summary, the potential for transmission of *Burkholderia* species from CF patient to CF patient has been well established in both healthcare and

non-healthcare settings. Transmission is facilitated by prolonged close contact between CF patients, sharing of equipment, and intrinsic bacterial factors that are poorly understood at present. A reference laboratory can provide accurate identification to species level and molecular typing. Numerous interventions have been implemented successfully to prevent transmission, but the relative contributions of individual interventions cannot be measured as they have been employed in combination.

4. Emerging pathogens

To develop rational infection control guidelines for emerging pathogens, such as *S. maltophilia*, *A. xylosoxidans*, and NTM, in CF patients, it is critical to establish prevalence in CF patients, pathogenicity in CF lung disease, and transmissibility among CF patients.

4.1. *S. maltophilia* and *A. xylosoxidans*

4.1.1. Epidemiology of *S. maltophilia*

S. maltophilia is an intrinsically multidrug-resistant pathogen and is well known to cause healthcare-associated infections including sepsis and pneumonia, particularly in ICU patients.²⁴⁰⁻²⁴² Broad-spectrum antimicrobial use, eg, the carbapenems imipenem and meropenem and extended spectrum cephalosporins, has been shown to be a risk factor for acquisition of *S. maltophilia*.^{241,243} Based on the most recently available data,⁹ the overall prevalence of *S. maltophilia* in American CF patients was 8.4%. There were significant differences among CF care centers; 11 (9%) of 117 centers reported no patients with *S. maltophilia*, while other centers reported a prevalence as high as 25%. In single CF center studies of *S. maltophilia*, prevalence rates were much higher than generally reported to the CFF Registry; 10% to 25% of patients harbored this organism.^{244,245} Furthermore, Burns et al. compared the prevalence of *S. maltophilia* among patients 6 years old or older reported to the registry with the prevalence among similarly aged participants enrolled in aerosolized tobramycin trials; in 1996 and 1997, 2.9% and 3.9% of patients, respectively, in the registry harbored this organism. This contrasts with 10.7% of study participants.¹⁰ These differences may be due to the selective media and special culture techniques used in the clinical trials.¹ Thus, the CFF Patient Registry may underestimate the prevalence of *S. maltophilia* colonization/infection.

It is unclear whether the prevalence of *S. maltophilia* in CF patients is increasing. Talmaciu et al. exam-

ined 58 patients who acquired *S. maltophilia* from 1993 to 1997 and found that the annual incidence increased from 2.8% to 6.2%.²⁴⁶ These investigators found that chronic treatment with antibiotics, including oral, aerosol, and intravenous agents, and the number of days of intravenous antibiotics were risk factors for acquisition of *S. maltophilia*. Misidentification of *S. maltophilia* as *B. cepacia* may account, in part, for the lower prevalence in the earlier years.²⁴⁷ The United States *B. cepacia* Reference Laboratory can provide genotypic confirmatory testing of *S. maltophilia* using PCR.²⁴⁸

4.1.2. Clinical impact of *S. maltophilia*

Investigators have used several definitions of pathogenicity to determine whether newly emerging organisms are true pathogens in CF patients. These definitions include the association of the organisms with: (1) acute pulmonary exacerbations; (2) chronic decline in pulmonary function; and (3) increased mortality. Saiman and Edwards examined the CFF Registry between 1990 and 1997 and reported increased rates of pulmonary exacerbations (defined as the use of intravenous antibiotics) among patients with *S. maltophilia* compared with patients infected with *H. influenzae* or *S. aureus*.²⁴⁹ The rates were comparable to those noted in children and adolescents 6 to 17 years old infected with *P. aeruginosa* and comparable to the rates of pulmonary exacerbations in patients 18 years of age or older infected with *B. cepacia*.

Numerous investigators have attempted to identify an association between *S. maltophilia* and chronic decline in lung function and/or mortality. Gladman et al. used 13 patients with *S. maltophilia* as a control group to examine the virulence of *B. cepacia* and noted no deaths or unexpected decline in pulmonary function in the *S. maltophilia* group.²⁵⁰ Karpati et al. studied 12 patients who harbored *S. maltophilia* for longer than 6 months.²⁵¹ No difference in lung function was identified after 2 years, but lung function decreased 2 to 7 years after acquisition. Demko et al. compared the survival of 211 patients with *S. maltophilia* with 471 patients whose cultures were negative for *S. maltophilia*.²⁴⁴ There was no significant difference in survival after 2 years, but among patients who initially had severe lung disease, survival after 5 years was 40% in *S. maltophilia* patients compared with 72% among patients without *S. maltophilia*. Of note, 50% of patients had transient colonization with *S. maltophilia*; no subsequent cultures were positive for

this organism. The study by Saiman et al. did not demonstrate a difference in pulmonary function associated with the presence of *S. maltophilia* compared with *P. aeruginosa*, but did suggest an increase in mortality.²⁴⁹ Goss et al. also examined the impact of *S. maltophilia* using CFF Registry data from 1991 to 1997 and found after stratifying for age and lung function, there was no significant difference in mortality due to *S. maltophilia*.²⁵²

4.1.3. Epidemiology of *A. xylosoxidans* in CF patients

In 1997, the prevalence of *A. xylosoxidans* in the CFF Patient Registry was only 2.7%. However, the baseline data from inhaled tobramycin trials found a prevalence of 8.7% in patients 6 years of age or older, while the registry data reported 0.5% and 1.9% prevalence in this age group in 1996 and 1997, respectively.^{4,5,10} Saiman et al. examined isolates sent to the CF Referral Center for susceptibility and synergy testing. Of 114 isolates identified as *Alcaligenes* spp., 12 were misidentified by referring laboratories and found to be *P. aeruginosa* (n = 10), *B. cepacia* (n = 1), or *S. maltophilia* (n = 1).²⁵³ The United States *B. cepacia* Reference Laboratory can provide confirmatory genetic testing of *A. xylosoxidans* using PCR.²⁵⁴

4.1.4. Clinical impact of *A. xylosoxidans* in CF patients

The pathogenicity of *A. xylosoxidans* in CF is poorly defined. An association of *A. xylosoxidans* with pulmonary exacerbation has been reported, although most patients were co-infected with *P. aeruginosa*.^{255,256} However, studies examining the effects of *A. xylosoxidans* on lung function and mortality in CF have not been performed.

4.1.5. Potential transmissibility of *S. maltophilia* and *A. xylosoxidans*

The transmissibility of *S. maltophilia* has been investigated in several studies. The majority of these have typed isolates with PFGE and PCR-based methodologies to examine a single CF center or hospital setting or sequential isolates from an individual patient.^{39,40,244,245,256,257} In 2 studies, patient isolates were unique, but the same genotype generally persisted in an individual patient.^{40,257} Denton et al. isolated numerous strains of *S. maltophilia* from the homes of both colonized (20 sites, 36% positive) and noncolonized CF patients (25 sites, 42% positive), the hospital ward (18 sites, 32% positive), and CF

clinic (4 sites, 17% positive).²⁴⁵ For a year, the sites within the hospital were colonized with same clone of *S. maltophilia* and 1 patient harbored the same genotype as a strain isolated from a hospital sink, but that patient was never hospitalized. Krzewinski et al. examined *S. maltophilia* recovered from patients at 61 CF centers participating in aerosolized tobramycin trials.³⁸ Six centers had 5 or more patients who harbored *S. maltophilia*. Three centers had patients with shared isolates (1 sibling pair and 2 pairs who did not have a known epidemiologic link). Similarly, Valdezate et al. demonstrated that 3 patients shared the same strain of *S. maltophilia*.⁴⁰

Relatively few studies have addressed the molecular epidemiology of *A. xylosoxidans*. Two studies did not identify shared isolates among CF patients.^{256,257} However, another study found that 2 of 8 chronically infected patients shared a single genotype of *A. xylosoxidans*. Although no environmental source was identified, the patients had been hospitalized at the same time.⁵⁹ Krzewinski et al. examined the molecular epidemiology of *A. xylosoxidans* isolates from patients at 46 CF centers.³⁸ These investigators found that 5 of 7 centers with more than 4 patients harboring *A. xylosoxidans* had pairs of patients with shared isolates. Of these, 2 pairs were siblings, 1 pair was friends who had been hospitalized at the same time, and 2 pairs did not have a known epidemiologic link.

4.1.6. Summary of transmission of *S. maltophilia* and *A. xylosoxidans*

In summary, the prevalence of *S. maltophilia* and *A. xylosoxidans* in CF patients is likely to be underestimated by the CFF Registry data. Current data suggest that these organisms may be pathogenic in CF patients and there is evidence of some patient-to-patient transmission. Well-designed epidemiologic studies of the risk of transmission, risk factors for acquisition, and the impact of colonization/infection have not been conducted. It is particularly important to determine whether increased exposure to broad-spectrum antimicrobial agents is associated with infection caused by these organisms.

4.2. Nontuberculous mycobacteria

4.2.1. Impact of NTM in non-CF and CF patients

The epidemiology of NTM in the general population has been reviewed.^{258,259} NTM predominantly caus-

es four clinical syndromes: pulmonary disease, lymphadenitis, skin and soft-tissue disease, or disseminated disease in persons with acquired immune deficiency syndrome²⁶⁰ or with rare gamma interferon receptor defects.²⁶¹ All four clinical syndromes are increasing in frequency, especially in immunocompromised hosts. A consensus statement has defined the criteria for the diagnosis of pulmonary disease caused by NTM and provided recommendations for treatment.²⁶² Multiple nosocomial outbreaks of NTM in non-CF patients have been reported due to either inadequate disinfection/sterilization of medical devices or environmental contamination of medications or medical devices.²⁶³ Patient-to-patient transmission of NTM has not been described except via inadequately cleaned and disinfected medical devices.²⁶³ An outbreak of NTM furunculosis that resulted from inadequate cleaning of whirlpool footbaths has been reported recently in a non-healthcare setting.²⁶⁴

During the past 15 years, it has been increasingly appreciated that CF patients may become infected/colonized with mycobacterial species. Smith et al. reported that 7 (3%) of 223 patients observed for a 6-year period had positive sputum cultures for mycobacteria including 3 with *Mycobacterium tuberculosis* and 3 with NTM.²⁶⁵ Kilby et al. reported that from 1981 to 1990, 17 (20%) of 87 adult CF patients had at least 1 positive culture for NTM, 11 had *Mycobacterium avium-intracellulare* (MAI), 2 had both MAI and *Mycobacterium chelonae*, 3 had *M. chelonae*, and 1 had *Mycobacterium fortuitum*.²⁶⁶ Another single CF center study conducted by Aitken et al. found that 8 (13%) of 64 adult CF patients harbored NTM.²⁶⁷ From 1988 to 1989, Hjelt et al. found that 7 patients at their center had more than 1 culture positive for mycobacteria, while an additional 6 had only 1 positive culture consistent with transient colonization.²⁶⁸ From 1990 to 1994, 8 North American and European CF centers reported a series in which patients were prospectively screened for mycobacteria; the combined rate for NTM was 13% (range among centers, 2.3% to 28.2%).²⁶⁹ From 1992 to 1998, Olivier and colleagues conducted a multicenter study of 986 American CF patients 10 years of age or older and found that the prevalence of NTM (defined as the proportion of patients with more than 1 positive culture for NTM) was 12.5%.²⁷⁰ Among these 21 sites, the prevalence ranged from 5% to 31%. *M. avium* complex (MAC) was the most common species isolated (72%) followed by *Mycobacterium abscessus* (16%).

4.2.2. Risk factors for NTM in CF patients

Risk factors for NTM colonization/infection in CF patients have been assessed. Torrens et al. found that intravenous and aerosolized antibiotics were risk factors for NTM in their center.²⁷¹ In the multicenter prevalence study performed by Olivier et al., patients with NTM compared to patients without NTM were significantly older (3.9 years), had a 5.8% higher percent predicted FEV₁, an 11.6% higher frequency of *S. aureus*, and a 10.4% lower frequency of *P. aeruginosa*.²⁷⁰ These data have been interpreted to be consistent with a “healthy survivor” effect.

4.2.3. Clinical impact of NTM in CF patients

There are reports of NTM causing clinical lung disease in CF patients who responded to antimycobacterial therapy.²⁷²⁻²⁷⁴ Biopsy and autopsy studies have demonstrated caseating granulomas in patients with clinical disease caused by NTM.^{275,276} However, there also are reports of patients with positive sputum cultures for NTM who were not treated and showed no adverse clinical consequences.²⁷⁴ In the multicenter study reported by Olivier et al., the demographic and clinical characteristics of patients who did (n = 25) or did not (n = 103) meet the American Thoracic Society's²⁶² criteria for NTM disease were compared; no differences, including pulmonary function, were noted between the two groups. Culture-positive patients (n = 59) have been matched to culture-negative patients (n = 100) and are undergoing follow up to evaluate the effect of NTM colonization/infection on their clinical course.²⁷⁰

4.2.4. Transmission of NTM

To date, there are very few studies that have used molecular typing of NTM isolates in CF patients to examine the possibility of patient-to-patient transmission. In the analysis of a large number of NTM isolates from the multicenter study by Olivier and colleagues, all NTM strains were unique with the exception of single pairs of isolates from two centers.²⁷⁷ In both cases, the matched pairs were obtained on the same day and collection or laboratory cross-contamination could have accounted for this matching. Unfortunately, at least one member of each pair failed to yield an additional isolate of NTM at later sampling, making it impossible to confirm cross-contamination. Thus, this study does not support patient-to-patient transmission or common

source acquisition of NTM. Furthermore, NTM colonization/infection did not correlate with the number of outpatient clinic visits or hospitalization, suggesting that acquisition in a healthcare setting was less likely. Bange et al. analyzed NTM strains from five patients at a single CF center and reported that all strains had unique genotypes, indicating that patient-to-patient transmission had not occurred.²⁷⁸

4.2.5. Summary of transmission of NTM

In summary, CF patients are at risk of acquiring mycobacteria species, the vast majority of which are NTM. However, there are reports of *M. tuberculosis* in CF patients. Thus, acid-fast bacilli must be identified to the species level to prevent patient-to-patient spread of *M. tuberculosis* and to direct appropriate treatment. The role of antimycobacterial therapy in CF patients harboring NTM is unclear, and the risk of patient-to-patient transmission of NTM is very low. Treatment decisions must be made on a case-by-case basis.

5. Fungi and molds

5.1. Epidemiology and clinical impact in CF patients

It is well known that *Aspergillus* spp. can colonize the lungs of CF patients and in some patients can cause allergic bronchopulmonary aspergillosis (ABPA). In addition, there have been rare case reports of aspergilloma and invasive aspergillosis in CF patients who were not lung transplant recipients.^{279,280}

Most isolates from CF patients are *Aspergillus fumigatus*, although some patients harbor other *Aspergillus* spp. and, rarely, other molds. The CFF Patient Registry data indicate an annual prevalence of 10.6%, but data from an aerosolized tobramycin study demonstrated that 114 (25%) of 465 patients 6 years of age or older were colonized with *Aspergillus* spp., 108 (95%) of which were *A. fumigatus*.¹⁰ During the trial, more frequent acquisition of *Aspergillus* spp. occurred among patients treated with aerosolized tobramycin (18%) compared with those patients in the placebo group (8%), but this was not associated with ABPA or fungal pneumonia.²⁸¹ The clinical significance of these findings associated with long-term use of aerosolized tobramycin remains to be determined. Bargon et al. found that prophylactic antibiotics (both oral and aerosolized agents) were risk factors for colonization with *Aspergillus* spp. among adult CF patients,

but there was no difference in lung function between patients with and without colonization.²⁸²

Saprophytic fungi other than *Aspergillus* spp. were detected in only 2.4% of patients in a tobramycin trial.¹⁰ A recent European study, however, reported an 8.6% incidence of *Scedosporium apiospermum* in sputum samples from 128 CF patients who underwent prospective follow up over a 5-year period, suggesting that the frequency of colonization with this organism may be underestimated.²⁸³ The significance of *Scedosporium* spp. as a pulmonary pathogen in CF is unknown.

The presence of *A. fumigatus* in the airway may trigger an immunologic response that results in ABPA. The prevalence of ABPA in CF is poorly defined, in part due to the vagaries in making the diagnosis of ABPA. However, prevalence rates reported from large multi-center databases of CF patients in North America and Europe were 2% and 7.8%, respectively,^{284,285} with regional variations noted in both studies.

5.2. Transmission of *Aspergillus* spp.

Aspergillus spp. are ubiquitous in nature and therefore it is not possible to completely prevent exposure to these fungi. Large concentrations of fungal spores may become aerosolized during some activities, such as construction or renovation within healthcare facilities, or gardening and lawn cutting. Water leaks that are not dried within 72 hours are an important source of *Aspergillus* spp. within the healthcare environment.⁴⁴ Specific recommendations for dust containment during construction and renovation must be followed to minimize exposure of vulnerable patients to *Aspergillus* spores.^{44,286}

Patient-to-patient transmission of *Aspergillus* spp. has been reported only once. This occurred when a non-CF patient hospitalized in an ICU had undergone liver transplant and developed a deep abdominal wound infection with *A. fumigatus*. The extensive infection, a large burden of organisms, subsequent deep debridement, and frequent dressing changes resulted in aerosolization of spores as documented by positive air sampling cultures and transmission to other patients in distal locations (>6 feet) in a multi-bed ICU.²⁸⁷

6. Respiratory viruses

Most respiratory tract illnesses are viral, and most viral illnesses have a seasonal pattern. The incidence

varies inversely with age, and young children can have as many as eight episodes of respiratory viral illnesses per year. Most viral illnesses are acute, relatively mild events, but severe illness can occur in young infants, the chronically ill and immunocompromised hosts. RSV, influenza, parainfluenza, adenovirus and rhinoviruses are the most frequent viruses that cause respiratory tract infections. These viruses have relatively short incubation periods (< 1 week), and transmission occurs primarily via direct contact with infected persons and items handled by them. Droplet transmission of infective respiratory secretions onto the mucous membranes of uninfected individuals within 3 feet is an important mode of transmission for influenza and adenoviruses. Viral particles are introduced through the mucous membranes of the eyes and nose of susceptible individuals and multiply in the respiratory epithelium, subsequently interfering with normal ciliary movement and mucus production.^{2,45}

Patients with CF are not more susceptible to viral respiratory tract infections than non-CF individuals. In a 2-year prospective study, Ramsey et al. found no difference in the rate of respiratory viral infections in school-aged CF patients when compared with their non-CF siblings.²⁸⁸ Similarly, Hiatt et al. found no difference in the number of respiratory illnesses in CF infants when compared with age-matched controls.²⁸⁹

However, the outcome of respiratory viral illnesses can be more severe in CF patients than non-CF patients. Viral illnesses are more likely to result in acute infection of the lower respiratory tract, impaired pulmonary function, and hospitalization,^{172,289-291} and decreased pulmonary function may persist for several months in young infants.^{172,289} Viral respiratory infections may predispose the CF lung to bacterial infection, although the pathophysiology of this process is not well understood.^{289,292,293} There is a direct relationship between the number of annual viral infections and the progression of pulmonary disease in CF patients.²⁹¹

6.1. Respiratory syncytial virus

RSV infection is most frequent in infants and young children, but causes acute respiratory illness in people of all ages.²⁹⁴ Children of any age with pulmonary or cardiac disease or who are immunocompromised can develop severe lower respiratory tract disease associated with substantial morbidity and mortality. A severe giant cell pneumonia with pro-

longed shedding of the virus occurs in immunocompromised patients.²⁹⁵ RSV infection provides only limited immunity; therefore, repeated infections may occur throughout life. Each year an estimated 90,000 hospitalizations and 4,500 deaths are attributed to RSV lower respiratory tract disease in both infants and young children in the United States.²⁹⁶

RSV can cause severe acute illness and residual impairment in lung function in CF patients. Abman et al. studied 48 infants with CF who developed RSV infection; 7 infants required prolonged hospitalization, including 3 who were mechanically ventilated for respiratory failure.²⁹⁷ Upon follow up (mean, 26 months after RSV infection), the 7 hospitalized children had persistent chronic respiratory symptoms and lower Brasfield chest x-ray scores than the 41 children who had not been hospitalized. Hiatt et al. compared CF infants with normal age-matched controls and found that 7 of 30 CF infants acquired RSV infection and 3 were hospitalized for a mean of 9 days.²⁸⁹ None of the controls were hospitalized. After 3.2 months, the CF infants with RSV infection continued to have decreased pulmonary function. A similar increase in morbidity associated with RSV infection in CF infants has been reported by Armstrong et al.²⁹⁵

RSV immune globulin intravenous (RSV-IGIV) and palivizumab, an RSV monoclonal antibody administered intramuscularly monthly during the RSV season, have been approved and are recommended for prevention of RSV disease in children younger than 24 months of age with bronchopulmonary dysplasia or with a history of premature birth.²⁹⁸ Several investigators have suggested that infants with CF should be considered prime candidates for RSV prevention trials using RSV immune globulin or palivizumab.^{289,293,299} A safety trial of palivizumab was conducted in approximately 106 infants with CF, but these results are pending (P. Campbell, personal communication). Studies using an investigational RSV subunit vaccine in CF patients are being performed.³⁰⁰

Cost-effective infection control strategies shown to reduce the incidence of healthcare-acquired RSV infection include laboratory confirmation of RSV using rapid diagnostic testing, patient placement in a single room or cohorting RSV-infected non-CF patients together with dedicated staff, consistent adherence to *standard plus contact precautions*, screening visitors for signs and symptoms of respiratory tract infection, and infection surveillance.⁹⁵

6.2. Influenza

Influenza viral infections can exacerbate underlying medical conditions and lead to secondary bacterial pneumonia or primary influenza pneumonia.³⁰¹ Rates of infection are highest among children. Hospitalization rates among children 4 years of age or younger without high-risk conditions are 100 per 100,000 population and increase to 500 per 100,000 population for those with high-risk conditions.³⁰¹

Influenza infection has been associated with respiratory deterioration and increased hospitalization among patients with CF.^{290,302} Pribble et al. demonstrated that 29% of pulmonary exacerbations in 54 CF patients between the ages of 10 months and 32 years (mean, 15.4 years) were due to nonbacterial infection and influenza was associated with greater deterioration in lung function than other nonbacterial infections.²⁹⁰ Conway et al. observed similar respiratory deterioration among CF patients with influenza.³⁰³ Influenza vaccine has been shown to be safe and effective in preventing influenza in CF patients^{304,305} and is recommended annually for all patients with CF who are 6 months of age or older and their close contacts.³⁰¹ The antiviral agents rimantidine, oseltamivir, and zanamivir are effective agents for treatment of influenza infections and for postexposure prophylaxis of unimmunized patients exposed to influenza.

6.3. Other respiratory viruses

Adenovirus, rhinovirus and parainfluenza viruses have been identified as causes of pulmonary disease in children with CF.^{172,289,292} Hiatt et al. found that adenovirus infection was significantly associated with worsening lung function and increased airway obstruction beyond the acute phase of illness.²⁸⁹ Rhinoviruses are the most common cause of respiratory infection and cause the majority of common colds. However, rhinoviruses also can infect the lower airway and cause a local inflammatory response. Rhinoviruses are associated with exacerbations of asthma, including severe episodes requiring hospitalization, but the impact of rhinoviruses on CF patients has not been studied.³⁰⁶

D. LUNG OR HEART-LUNG TRANSPLANT RECIPIENTS

Lung or heart-lung transplants are performed in selected severely ill CF patients to provide intermediate-term survival as the 1-, 3-, and 5-year survival

of transplant recipients is 70%, 53% and 48%, respectively.³⁰⁷ After transplant, CF patients are at risk of colonization or infection of the transplanted lungs with pretransplant pathogens retained in the upper airways or at risk of acquisition of new pathogens.³⁰⁸

1. *B. cepacia* complex in CF transplant recipients

Posttransplantation complications due to *B. cepacia* complex have been described.³⁰⁹ Snell et al. examined the clinical course of 22 patients undergoing lung transplantation and found that *B. cepacia* caused significant morbidity and mortality.³¹⁰ Ten patients had infection with *B. cepacia* pretransplant and 5 patients acquired *B. cepacia* posttransplantation. Seven of 15 died with infectious complications due to this pathogen, and the median survival of the 15 patients with *B. cepacia* infection posttransplantation was 28 days. Steinbach et al. evaluated 5 CF patients infected with *B. cepacia* before transplant and noted that posttransplant, 3 of 5 patients became infected with the same clones that were present before transplant and 2 remained free of *B. cepacia* infection.³¹¹

More recently, the outcome of infection with specific genomovars following transplantation has been described. Aris et al. found that 5 of 12 patients infected with genomovar III had mortality related to *B. cepacia* complex while 0 of 8 patients infected with other species of *Burkholderia* died.²¹⁵ DeSoyza et al. reported significantly improved survival rates for non-genomovar III-infected patients compared with genomovar III-infected patients.²¹⁴ Reduced mortality in genomovar III lung transplant recipients has been reported with the use of triple antibiotic regimens.³¹² Thus, infection with *B. cepacia* has not been an absolute contraindication to lung transplantation.³⁰⁷

2. *Pseudomonas* and other pathogens in CF transplant recipients

Posttransplant complications due to other pathogens have been described. Walter et al. typed *P. aeruginosa* isolates by PFGE from 11 CF patients undergoing lung transplantation from 1988 to 1994 and found that all patients became colonized or infected posttransplant with the same clone detected pretransplantation.³¹³ Kanj et al. reported 12 of 21 patients had infectious complications after transplantation.³¹⁴ One patient died within 24 hours of transplantation from *S. maltophilia* sepsis and 3 of 21 died

with *P. aeruginosa* pneumonia. Of the 17 patients who survived, 8 had infectious complications including bacteremia with *B. cepacia* or *Burkholderia gladioli* (all of which were present preoperatively), MRSA, *P. aeruginosa*, or *Pseudomonas fluorescens*. Similar observations were made by Nunley et al. who compared the outcome of CF patients and non-CF patients undergoing lung transplantation and found that CF patients were more likely to develop earlier infections with *P. aeruginosa*. However, the mortality was not increased in CF patients; 9 (28%) of 32 CF patients and 4 (19%) of 21 non-CF patients died with *P. aeruginosa* pneumonia.³¹⁵

3. Invasive aspergillosis in CF transplant recipients

CF patients undergoing lung transplantation are at risk of invasive aspergillosis, although the incidence is low despite high pre- and posttransplant colonization rates.^{314,316} Paradowski reported one center's experience with saprophytic fungal infections in 126 lung transplant recipients, of whom 65 had CF.³¹⁷ Before transplant, 52% of the CF patients were colonized with *Aspergillus* spp., and after transplant, 40% were colonized; 7% were colonized both pre- and posttransplant. None of the CF patients received prophylactic antifungal therapy, and none developed infection with *Aspergillus* spp. In all, 5 of 126 patients died from invasive mold infection after lung transplantation; 1 CF patient died of a brain abscess and ventriculitis due to *S. apiospermum*, which was not identified in pre- or posttransplant sputum cultures, and 4 non-CF patients died of invasive aspergillosis.³¹⁷

Nunley et al. compared the prevalence of colonization and infection with *Aspergillus* spp. in lung transplant recipients with and without CF. Seven (22%) of 31 CF recipients had *Aspergillus* spp. colonization before transplant, and 15 (48%) of 31 had *Aspergillus* spp. isolated from sputum or bronchial alveolar lavage posttransplant, including 4 of 7 colonized before transplant. In contrast, none of 53 non-CF recipients were colonized before transplant, but 21 (40%) of 53 had *Aspergillus* spp. isolated from the lower respiratory tract after transplantation. A 40% acquisition rate in non-CF patients suggests a nosocomial source of *Aspergillus* spp. Serious *Aspergillus* infections occurred in 3 (14%) of 21 non-CF patients and 4 (27%) of 15 CF patients, of whom 3 of 4 were known to be colonized with *Aspergillus* spp. before transplantation.³¹⁶ No typing studies were per-

formed to determine if the pre- and posttransplant strains were the same genotype or if patients shared the same type.

Based on published reports of efficacy, the CDC now recommends placing allogeneic hematopoietic stem cell transplant recipients in a protective environment during the period of highest risk for the prevention of invasive aspergillosis.^{44,318} These same recommendations have not been made for patients undergoing solid organ transplantation, including lung transplantation in CF patients, because there are no published data to support efficacy of a protective environment in these other groups of patients.

4. Summary of transmission of pathogens after transplantation in CF patients

In summary, morbidity and mortality can occur in CF patients after lung transplantation due to pretransplant pathogens. CF patients undergoing transplantation are usually infected with multidrug-resistant bacteria and are a potential reservoir for other CF and non-CF patients in the hospital. Although there are no data to support routine placement of CF patients in a protective environment posttransplant, it is important to ensure that proper dust containment and water leak protocols are in place in the facility performing the transplants. Transplant centers with high rates of new *Aspergillus* infections acquired posttransplant should evaluate potential environmental sources of *Aspergillus* and consider placing patients in a protective environment during the period of greatest risk.

E. PSYCHOSOCIAL IMPLICATIONS OF INFECTION CONTROL GUIDELINES

1. Studies among CF patients

It is critical to acknowledge the psychosocial impact of infection control guidelines for CF patients, but at present, there is a paucity of studies in this area. Acceptance of recommendations to segregate CF patients from each other has led to a shift among CF patients in their friendship and support groups away from other CF patients to non-CF patients.^{238,319} Because families are limiting social interactions with other CF patients, similar limitations set within the healthcare environment are most likely expected and accepted.

Physicians at the Danish CF center acknowledged the psychosocial consequences of *isolation precautions*, but stated that reducing the risk of chronic

infection outweighed the negative impact of social isolation.⁸⁵ In addition, changes in pathogen status can be associated with adverse psychosocial consequences (N. Hoiby, personal communication). Stern noted that isolation of patients infected with *B. cepacia* was associated with adverse psychosocial effects, but similar effects were observed in CF patients without *B. cepacia* infection (R. Stern, personal communication). These effects included separation from friends, loss of familiar hospital surroundings, guilt, depression regarding worsening prognosis, paranoia about acquiring *B. cepacia*, and change in social activities among patients with CF.

2. Studies among non-CF patients

While there are limited studies in CF populations, there are studies examining the impact of isolation among non-CF patients with MRSA, tuberculosis, and cancer. There are obvious differences between these illnesses and CF and the isolation requirements, but there are similarities that can be extrapolated to CF patients. Several studies concluded that significant psychological effects result from isolation.³²⁰⁻³²⁶ These included feelings of confinement, abandonment, neglect, frustration, anxiety, depression, low self-esteem, stigmatization, and boredom.

The impact of isolation on family members has been explored as well. Powazek et al. evaluated the emotional reactions of the mothers of 123 hospitalized children who required *isolation precautions* and found that both mothers and children experienced anxiety and depression.³²⁷ Casey reported that young children in respiratory isolation demonstrated behaviors ranging from irritability to sadness and from misery to withdrawal.³²⁸ These children were very demanding of parents and nurses as they sought human contact and security.

In contrast to these examples, single patient rooms are recommended for CF patients, but in most instances, patients are allowed to leave their rooms and visit other common areas of the hospital as long as no other CF patient is present at the same time. The ability to leave the room reduces the feelings of social isolation. Additionally, by observing *standard precautions* for all CF patients, singling out patients because of their pathogen status is minimized.

Not all of the psychosocial effects of *isolation precautions* are negative. Ward found that patients isolated in single rooms felt the rooms were quiet, private, and relaxed.³²⁹

3. Interventions to minimize impact of *Isolation precautions*

Many studies have emphasized that some negative effects of *isolation precautions* can be ameliorated by implementing interventions to improve communication and physical facilities. Oncology patients wanted to receive information about *isolation precautions* along with information about their disease, treatment, and prognosis.³³⁰ To be useful, this information was provided at the patient's cognitive level. Ward stressed that both written and verbal forms of communication should be used.³²⁹ Many authors have emphasized that patients in isolation require frequent contact with other humans through visitors (family and friends), other patients (if appropriate), and healthcare professionals to prevent boredom and loneliness.^{321,329,330} Communication can be enhanced by human touch and humor displayed by healthcare professionals, especially nurses.

The physical facilities of a patient's isolation area can be altered to decrease the impact of isolation. Gammon described the need to provide children with opportunities for exploration with play and to provide familiar surroundings with television, music, and computers.³²² Familiar items from home, such as pictures, personal belongings, a clock, and radio, can decrease the impact of isolation. Other studies reiterated these findings and emphasized the importance of providing facilities that connect patients to the outside world with windows that have a view of the ward or a view of the outdoors.^{329,330}

4. Organized CF social and educational activities

There are many educational and fund-raising activities that take place in the CF community. To date, there have been no reports of transmission of CF pathogens at CF Education Day or at Great Strides Walks. Great Strides is an outdoor activity, and CF patients can easily maintain a minimal distance of 3 feet between each other. It is imperative that patients and families anticipate and avoid social situations with a risk for acquisition of CF specific pathogens that could arise as a result of attending CF Education Day (eg, sharing car rides, meals, or hotel rooms).

5. Summary of psychosocial implications of infection control guidelines

In summary, while infection control guidelines for patients with CF serve to protect them from

acquiring pathogens, it is imperative to protect their autonomy and to alleviate the negative psychosocial effects of isolation. Awareness and early recognition of the potential adverse psychological effects of isolation should prompt the healthcare team to implement measures that will alleviate these effects and improve adherence to infection control guidelines and the quality of the hospital stay or clinic visit. Education of patients and their families about the importance of infection control will enhance adherence. Encouraging patients and families to express their feelings and to obtain counseling, if indicated, may be important interventions.

F. THE HEALTHCARE WORKER WITH CF

HCWs with CF present special challenges for infection control. A survey of CF patients performed in the United Kingdom in 1995 found that 6.6% of respondents were working in healthcare professions.⁵³¹ Informal discussions with CF center directors in the United States support the conclusion that a small but significant number of people with CF are employed in healthcare professions. There are no published studies that systematically evaluate the risk of transmission of pathogens from HCWs with CF to either the CF and non-CF patients they serve or from patients to the HCW with CF.

Employment laws that govern the protections and procedures for HCWs with CF include the Americans With Disabilities Act (ADA) and Section 504 of the Rehabilitation Act as described in the Appendix.

In the absence of specific data on which to base recommendations for HCWs with CF, the committee reviewed transmission of pathogens among CF patients and concluded: (1) CF patients considering entering the healthcare profession should be counseled about the potential risks and the options within the healthcare profession available to them; (2) the modes of prevention and modes of transfer of infectious agents between a HCW with CF and a CF patient are the same as between any two individuals with CF; (3) a HCW with CF should know his or her *B. cepacia* complex status; (4) each HCW with CF must be evaluated on an individual basis and the following factors should be considered when making patient care assignments: frequency and severity of coughing episodes, quantity of sputum production during these episodes, ability to contain res-

piratory tract secretions, and known colonization/infection with epidemiologically important pathogens; and (5) the occupational (employee) health service should be aware if a HCW has CF to assist in preventing exposures to potential pathogens. A similar approach has been recommended by Walters in the United Kingdom (personal communication, 2001).

III. RECOMMENDATIONS FOR INFECTION CONTROL GUIDELINES FOR CF PATIENTS

A. GRADING OF THE EVIDENCE

Each recommendation was categorized by the participants on the basis of existing scientific data and theoretical rationale. Grading of evidence assists clinicians to understand the importance of following those recommendations with strong supporting data (*Category IA* and *IB*) and to prioritize the implementation of such recommendations. Recommendations are graded *Category II* when strong evidence is lacking, but there is consensus based on theoretical, epidemiologic, or clinical rationale, allowing individual choices according to local circumstances and experience. Applicability and economic impact are additional considerations for those recommendations lacking sufficient supportive evidence (*Category II*). When there were insufficient or inconsistent data, or no consensus could be reached, recommendations were not graded and categorized as *no recommendation; unresolved issue*. The participants chose to use the following CDC/HICPAC system for categorizing recommendations based on previous experience in crafting infection control guidelines beyond CF:

- **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 experimental, clinical, or epidemiologic studies and a strong theoretical rationale.
- **Category IC.** Required for implementation, as mandated by federal and/or state regulation or standard.
- **Category II.** Suggested for implementation and supported by suggestive clinical or epidemiologic studies or a theoretical rationale.
- **No recommendation; unresolved issue.** Practices for which insufficient or conflicting evidence exists and no consensus regarding efficacy has been reached.

B. APPLICABILITY OF STANDARD PRECAUTIONS AND TRANSMISSION-BASED PRECAUTIONS FOR CF PATIENTS IN HEALTHCARE SETTINGS

1. General principles for healthcare settings

- Assume that ALL CF patients could have transmissible pathogens in respiratory tract secretions. *Category IA*^{10,11}
- Apply *standard precautions* to ALL CF patients to contain their secretions and to minimize the potential for CF patients to come into contact with the secretions of other CF patients. *Category IA*²
- Implement *standard plus transmission-based precautions* according to CDC/HICPAC published recommendations for use of *contact*, *droplet*, or *airborne precautions* as defined by special circumstances, eg, *B. cepacia* complex, multidrug-resistant *P. aeruginosa*, MRSA, or *M. tuberculosis*. *Category IA*²
- Avoid activities and risk factors that have been associated with transmission of pathogens in CF patients as shown in Table 6. *Category IA*^{23,102,184,205,216,217,222,332}
- *No recommendation* for criteria to discontinue *contact precautions* for patients who have been historically culture positive for multidrug-resistant organisms, eg, MRSA, *B. cepacia*, and multidrug-resistant *P. aeruginosa*, but are currently culture negative. *Unresolved issue*

2. Use of specific barrier precautions

2.1. Hand hygiene for HCWs (the following recommendations are supported by evidence summarized in^{12,13})

- When hands are visibly dirty, contaminated with proteinaceous material, or visibly soiled with blood or other body fluids, including respiratory tract secretions, wash hands with an antimicrobial soap and water. *Category IA*
- If hands are not visibly soiled, use an alcohol-based hand rub or wash hands with an antimicrobial soap and water to routinely decontaminate hands in all clinical situations. *Category IA*
- Use proper hand hygiene whether or not gloves are worn. *Category IA*
- Perform hand hygiene in the following clinical situations:
 - After removing gloves. *Category IB*
 - Before and after contact with any patient. *Category IB*

- After contact with personal or patient's:
 - Mucous membranes. *Category IA*
 - Respiratory secretions. *Category IA*
 - Objects contaminated with respiratory secretions. *Category IA*
 - Respiratory device after use. *Category IA*
- Ensure ready availability of waterless antiseptic, eg, alcohol-based hand rubs, or similar dispenser, or similar FDA-approved product, in all patient rooms, pulmonary function testing rooms, and in waiting area for patients and families. *Category IA*
- Only natural nails are permitted for HCWs with direct patient contact. *Category II*⁴⁹⁻⁵¹
- *No recommendation* on wearing rings by HCWs in healthcare settings. *Unresolved issue*

2.2. Gloves for HCWs (the following recommendations are supported by evidence summarized in^{12,13})

- Wear gloves when caring for patients who require *contact* or *droplet precautions*. *Category IA*²
- Wear gloves for handling respiratory secretions or objects contaminated with respiratory secretions of any patient. *Category IA*²
- Change gloves: *Category IB*³³³
 - After handling respiratory secretions or after handling objects contaminated with secretions from one patient and before contact with another patient, object, or environmental surface.
 - When moving from a contaminated body site to a clean body site or to the respiratory tract or to a respiratory device on the same patient.
 - Before and after contact with a patient.
- Do not wash gloves and then reuse. *Category IB*^{333,334}

2.3. Gowns for HCWs

- Wear gown as defined by *standard precautions*. *Category IB*²/*IC*³³⁵
- Wear gowns for patients who require *contact* or *droplet precautions* when close contact with the patient or patient's immediate environment is anticipated. *Category IB*^{2,88}
- When soiling with respiratory secretions from a patient is anticipated, eg, during chest physiotherapy, suctioning or examining a patient known to have coughing spasms, wear a gown and remove the gown after such contact and

before providing care to another patient. *Category IB² Category IC³⁵⁵*

2.4. Use of masks and eye protection for HCWs

- Wear mask and eye protection or a face shield to protect mucous membranes of the nose, mouth, and eyes from becoming contaminated when splashes or sprays of secretions, body fluids, blood, or excretions are anticipated during procedures or patient care activities. *Category IB²*

3. Environmental infection control

3.1. General measures for sterilization/disinfection and care of equipment

- Follow published recommendations for sterilization and disinfection of patient care equipment, particularly respiratory therapy and dental equipment. *Category IA^{14,15}*
- Clean patient care equipment and devices of visible organic residue (eg, blood, respiratory tract secretions, or tissue) as soon as practical with a detergent or enzymatic cleaner and water before high-level disinfection or sterilization. Soiled materials that become dried onto instruments cause disinfection or sterilization to be less effective or even ineffective. *Category IA^{15,65,66,336-341}*
- Following high-level disinfection of semicritical equipment and devices (eg, nebulizers and humidifiers) used on the respiratory tract, use one of the following rinse methods: tap water followed by 70% to 90% ethyl or isopropyl alcohol with forced air drying, or sterile water, or 0.2- μ m filtered water. Do not use tap, bottled, or distilled water only to rinse equipment. Air dry the equipment completely after rinsing. *Category IB^{45,58-60,336,342}*
- Dedicate noncritical patient care equipment to patients on *contact precautions* and disinfect before use by another patient or use disposable equipment. *Category IB²*
- Disinfect environmental surfaces that have become contaminated with respiratory tract secretions, eg, during pulmonary function testing, body plethysmography, and in hospital activity rooms. *Category IB²⁰⁷*

3.1.1. Indications for sterilization, high-level disinfection, and low-level disinfection

- Sterilize critical medical and surgical devices and instruments that enter normally sterile tissue or the vascular system, or through which a

sterile body fluid flows (eg, blood) before each patient use. *Category IA^{15,337,339,343}*

- At a minimum, high-level disinfect semicritical patient care equipment that touches mucous membranes (eg, respiratory therapy equipment, bronchoscopes) or nonintact skin. Follow disinfection with appropriate rinsing with tap water followed by 70% to 90% ethyl or isopropyl alcohol with forced air drying, or sterile water, or 0.2- μ m filtered water. Following rinsing, dry and store the device, taking care not to contaminate the item(s) in the process. *Category IA^{15,336,344-346}*
- Low-level disinfect noncritical patient care equipment that touches intact skin. *Category II³⁴⁷⁻³⁵⁰*

3.2. Wall humidifiers

- Follow manufacturers' instructions for use and maintenance of wall oxygen humidifiers. *Category IB^{45,351-355}*
- Change the tubing, including any nasal prongs or mask, used to deliver oxygen from a wall outlet before and after each new patient's use. *Category IB⁴⁵*
- Discard disposable items between patients as these are intended for single patient use. *Category IC³⁵⁴*

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

- Follow the manufacturers' recommendations on the proper use and care of all equipment including nebulizers and air compressors. *Category IB^{45,355}*
- Use air compressor for the duration recommended by the manufacturer and maintain machine parts. *Category IB³⁵⁵*
- Between treatments on the same patient, disinfect, rinse with sterile or filtered water (0.2 μ m), and air-dry small-volume in-line or hand-held medication nebulizers. *Category IB^{45,61-64,356}*
- Ensure proper cleaning, drying, and storage of patient's mask used to deliver aerosol therapy according to manufacturers' recommendations. *Category II*
- Use only sterile fluid for nebulization and dispense the fluid into nebulizer aseptically. *Category IA^{55,57,357}*
- Use single-dose vials for aerosolized medications whenever possible. If multidose medication vials are used, handle, dispense, and store

them according to manufacturers' instructions. *Category IA*^{45,53-57,358,359}

- Do not share nebulizers (eg, between siblings). *Category IA*^{61,62,76,205,216}

3.4. Other devices used in association with respiratory therapy

- Sterilize or high-level disinfect portable respirometers and other respiratory devices between uses on different patients. *Category IB*^{45,360,361}

3.5. Pulmonary function testing equipment

- Do not sterilize or disinfect the internal machinery of pulmonary function testing machines between use on different patients. *Category II*^{45,362,363}
- Use a disposable in-line bacterial filter for each patient performing a pulmonary function test. *Category II*
- Disposable mouthpieces are preferred. *Category II*
- Sterilize, or high-level disinfect, reusable mouthpieces, tubing, and connectors between uses on different patients or follow manufacturers' recommendations for reprocessing. *Category IB*³⁶⁴

3.6. Disinfection in ambulatory care settings

3.6.1. Equipment

- Follow the same classifications for patient care equipment used in ambulatory care settings (eg, outpatient medical/surgical facilities) and home care as used in the hospital setting^{14,336}:
 - Critical devices require sterilization.
 - Semicritical devices require at a minimum high-level disinfection.
 - Noncritical equipment requires low-level disinfection.

3.6.2. Environmental surfaces

- Use a one-step process and an EPA-registered hospital grade disinfectant/detergent designed for housekeeping purposes in patient care areas. *Category IB*^{15,44}
- Clean surfaces in examining room and around equipment according to hospital policy and after room is vacated if contaminated with respiratory tract secretions, eg, from patient with productive cough. *Category IB*⁴⁴
- Clean housekeeping surfaces (eg, floors, walls, and tabletops) on a regular basis and as spills

occur or when visibly soiled. *Category IB*^{15,44,365}

- Follow manufacturers' instruction for proper use of disinfecting products, especially the recommended use dilution. *Category IB*^{44,366,367}
- Promptly clean and decontaminate spills of blood and other potentially contaminated materials. *Category IC*³³⁵
- Use EPA-registered phenolic or quaternary ammonium compound for disinfecting noncritical surfaces, eg, blood pressure cuffs, therapy vests, bedpans, and furniture. An alternative is to use 1:100 to 1:500 diluted household bleach (chlorine preparation). *Category II*³⁶⁸
- Disinfect noncritical medical equipment with disinfectant at the use dilution and contact time of at least 30 seconds. *Category IB*¹⁵
- Implement regular disinfection schedule for sinks in examining rooms and waiting area bathrooms. *Category II*

C. MICROBIOLOGY, MOLECULAR TYPING, AND SURVEILLANCE

1. Perform respiratory tract cultures in CF patients: *Category IB*^{10,16-18,22,81,136,369}

- At least quarterly in patients who are clinically stable and not having pulmonary exacerbations, including those who have received a lung or heart-lung transplant.
- At the time of pulmonary exacerbations.
- With change in clinical status.
- When hospitalized.
- When epidemiologically indicated.

2. Respiratory tract specimen processing

- Ensure that respiratory specimen type and handling adhere to CFF standard practice guidelines, which include: *Category IB*¹⁰
 - Rapid transport and processing of specimens after collection. If immediate processing is not done, store specimens at 4°C (on ice, do not freeze specimens) for no more than 24 hours before processing.
 - Inoculate respiratory tract specimens (throat, sputum, and bronchoalveolar lavage fluid) on selective media described below and incubate for at least 48 hours. Slower growing organisms may require up to 4 days.
 - Determine susceptibility of isolates of *P. aeruginosa* with distinctive colony morphology.
 - Use biochemical panels or molecular testing to identify non-*P. aeruginosa*, gram-negative nonlactose fermenters.

3. Use of selective media

- Use the following selective media to improve the rate of recovery of clinically and epidemiologically important CF pathogens including: *Category IA*^{10,104}
 - *P. aeruginosa* - MacConkey agar.
 - *S. aureus* - mannitol salt agar or Columbia/colistin-nalidixic acid.¹⁰⁵
 - *B. cepacia* complex - BCSA, OFPBL, or PC agar are acceptable, but BCSA has superior specificity.^{107,108,110,111}
- Use selective media for *H. influenzae* (horse blood or chocolate agar with or without the addition of bacitracin, incubated anaerobically), fungal pathogens, and other nonlactose fermenting gram-negative bacilli as clinically or epidemiologically indicated. *Category IB*³⁷⁰
- Identify and report *S. maltophilia* using DNase agar or molecular methods for identification. *Category IB*¹¹⁴
- Identify and report *A. xylosoxidans* using biochemical or molecular methods for identification. *Category IB*^{253,254}
- Use special processing techniques for AFB to prevent overgrowth by *P. aeruginosa*: NALC-NaOH decontamination followed by 5% oxalic acid. *Category IB*^{116,117}

4. Antimicrobial susceptibility testing

- Use agar-based diffusion assays, such as antibiotic disks or E-tests, rather than automated commercial microbroth dilution systems for susceptibility testing of nonmucoid and mucoid *P. aeruginosa*. *Category IB*^{19-21,119}

5. Other diagnostic and identification testing

- Perform diagnostic tests for respiratory viral pathogens (eg, influenza A and B,³⁷¹ parainfluenza,³⁷² RSV,³⁷³ and adenovirus³⁷⁴) by rapid antigen detection test, direct fluorescent antibody, or viral culture, when clinically or epidemiologically indicated. *Category IB*^{288,289}
- Identify gram-negative bacteria by standard biochemical testing or molecular methods, not by rapid or automated methods. *Category IB*^{11,248,253,254,375-377}

6. Use of the CFF *B. cepacia* Research Laboratory and Repository

- Send the following CF isolates of *Burkholderia* spp. to the laboratory at the University of Michigan for confirmation of identification, speciation, and molecular typing: *Category IB*²²

- All initial isolates from every patient.
- At least one isolate per patient per year.
- Any isolates suspected of being associated with transmission or an outbreak.²²
- Any nonfermenting gram-negative organism for which species identification remains equivocal after routine analysis.^{11,377}

CFF *Burkholderia cepacia* Research Laboratory and Repository

University of Michigan

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1150 West Medical Center Drive

Ann Arbor, MI 48109-0646

Telephone: (734) 936-9767

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7. Surveillance strategies

- Collaborate with the CF center's infection control team when developing surveillance strategies and when analyzing and reporting data related to infection. *Category II*
- Target *B. cepacia* complex, *S. aureus* including MRSA, and *P. aeruginosa*, including multidrug-resistant and mucoid *P. aeruginosa* for surveillance. *Category IB*^{10,31,102,129,140,218}
- Target other potential pathogens including *S. maltophilia*, *A. xylosoxidans*, or NTM if epidemiologically or clinically indicated (eg, patient-to-patient transmission or an outbreak suspected). *Category II*
- Report the prevalence of *A. xylosoxidans* to the CFF Patient Registry. *Category II*
- Survey CF patients who have undergone lung transplantation separately from other CF patients and as part of hospital-wide surveillance for transplant recipients. *Category IB*^{508,310}
- Target *Aspergillus* spp. and multidrug-resistant pathogens, such as *B. cepacia* complex, MRSA, or *P. aeruginosa*, in CF transplant recipients. *Category IB*^{287,314-316}
- Calculate the incidence and prevalence rates of target organisms and summarize antimicrobial susceptibility profiles. *Category IB*^{41-43,134}
- Share reports of surveillance summaries of targeted organisms between the Infection Control Team and CF Care Team at least annually. *Category IB*^{43,134}

- Perform epidemiologically directed environmental cultures in consultation with infection control team if an environmental reservoir is suspected to be associated with transmission of pathogens in CF patients. *Category IB*⁴⁴

8. Molecular typing

- Use the *B. cepacia* Research Laboratory and Repository or another reference laboratory for molecular typing. *Category IA*²²
- Perform molecular typing of *B. cepacia* complex isolates and other organisms when epidemiologically indicated. *Category IA*^{22,26,218}
- Perform molecular typing using an appropriate genotyping method (eg, PFGE, RAPD-PCR, or Rep-PCR). *Category IA*²²⁻²⁵

It is anticipated that selective media, increased frequency of obtaining respiratory tract specimens for culture, use of reference laboratories, and enhancing surveillance will increase the prevalence of some pathogens due to improved ascertainment.

D. INPATIENT SETTINGS

1. Transmission precautions

- All HCWs must observe *standard precautions* when caring for patients with CF. *Category IA*²
- Place CF patients who are infected (or colonized) with MRSA, *B. cepacia* complex, multidrug-resistant *P. aeruginosa*, RSV, parainfluenza virus, or VRE on *contact precautions* in addition to *standard precautions*. *Category IA*²
- Place CF patients who are infected with adenovirus on *contact* and *droplet precautions* in addition to *standard precautions*. *Category IA*^{2,45}
- Place CF patients who are infected with influenza on *droplet precautions* in addition to *standard precautions*. *Category IA*^{2,45}

2. Room placement

- Place all CF patients who are colonized or infected with *B. cepacia* complex, MRSA, or VRE in a single patient room that does not share common facilities (eg, bathroom or shower) with other patients. *Category IA*^{2,22,193,238}
- Admit CF patients who are not colonized or infected with *B. cepacia* complex, MRSA, or VRE to a single patient room whenever possible or to a room shared with a patient without CF and at low risk for infection. *Category II*
- CF patients who sleep in the same room at home may share a hospital room. *Category II*

- Place all CF patients who are lung, heart-lung, or liver transplant recipients in a single patient room in accordance with hospital policy. Positive pressure and HEPA filtration are not required. *Category II*
- Ensure that proper dust containment and water leak policies are followed in areas where CF patients are hospitalized, especially those patients who have received lung, heart-lung, or liver transplants. *Category IB*,⁴⁴ *IC*³⁷⁸

3. CF patient activity outside hospital room

- Evaluate CF patient activity outside of hospital room in accordance with hospital policies for specific pathogens (eg, MRSA or *B. cepacia*). *Category II*
- Evaluate CF patients not on transmission-based precautions on a case-by-case basis in accordance with hospital policy. Considerations include capability of a patient for containing his or her respiratory tract secretions, age, ability to use proper hygiene, endemic levels of pathogen in individual center, and adherence to the following practices: *Category II*
 - Perform proper hand hygiene immediately before leaving the room.
 - Avoid direct contact between CF patients in the hospital unless they are co-habitants (eg, sleep in the same room at home).
 - Use the hospital activity rooms (eg, playroom, exercise room, or schoolroom) only when no other CF patient is present.
 - Go to public places in the hospital (eg, cafeteria, lobby) but remain at least 3 feet from other CF patients in such places.
- After a CF patient has left the hospital activity room, clean surfaces and items handled by the patient with a disinfectant/detergent. *Category IB*^{44,207}
- *No recommendation* for CF patients to routinely wear a mask when leaving the patient room unless on *droplet precautions*. *Unresolved issue*

4. Respiratory therapy

- Assume that ALL CF patients could have transmissible pathogens in respiratory tract secretions even if not yet identified by culture or if culture results are unknown. *Category IA*^{10,23}
- Perform all respiratory interventions, including aerosol therapy, airway clearance and sputum collection, in the patient's room. *Category IB*²²⁴
- Adhere to *standard precautions* (using the appropriate combination of hand hygiene, gloves,

gown, mask, and eye protection) when performing cough-inducing procedures. *Category IA*^{2,224}

- Dedicate airway clearance devices (eg, flutter, acapella, pep device, and therapy vest) to single patient use during inpatient hospitalization. *Category II*
- Encourage patients to use their own home airway clearance devices (eg, flutter, acapella, pep device, and therapy vest) during inpatient hospitalization in addition to professional chest physiotherapy. *Category II*
- Dispose of sputum/soiled tissues into covered, no-touch receptacles. *Category II*

E. AMBULATORY SETTINGS

1. Clinic logistics

- Develop a reliable method, eg, computerized access, to ensure ready availability of each patient's most recent respiratory secretion culture and antimicrobial susceptibility results. *Category IB*¹⁰
- Alert other diagnostic areas (eg, radiology or pulmonary function test laboratory) of patients' transmission precautions, especially if they harbor organisms that are a threat to non-CF patients, eg, MRSA or VRE. *Category IB*²
- Schedule and manage patients to minimize time in common waiting areas. Strategies include: a staggered clinic schedule, placement of patients in an examining room immediately on arrival at the clinic, use of a pager system whereby patients are summoned when an examining room is available, and keeping the patient in one examining room while the CF team rotates through the rooms. *Category II*
- *No recommendation* for restricting the use of common bathrooms in the clinic. *Unresolved issue*

2. Waiting area behaviors

- Instruct patients and family members to observe proper hand hygiene on arrival at the clinic and when leaving the clinic. *Category IB*^{102,184,217,222}
- Ensure ready availability of dispensers containing a waterless antiseptic, eg, alcohol-based hand rub or similar FDA-approved product, in the waiting area for use by patients and families. *Category IA*¹³
- Instruct patients to cough into a tissue and immediately discard tissue into a covered, no-touch receptacle or toilet and perform hand hygiene after coughing. *Category II*

- Discourage handshaking and physical contact between CF patients to prevent direct and indirect contact with respiratory secretions. *Category IA*^{182,184,193}
- Maintain a minimal distance of 3 feet between patients in the waiting area to prevent droplet transmission of respiratory pathogens. *Category IB*¹⁸²
- Discourage patient use of common items, eg, the clinic's computer and toys in the waiting area, that cannot be cleaned between patients. *Category II*
- *No recommendation* for CF patients to routinely wear masks while in the waiting room in a CF clinic. *Unresolved issue*

3. Organism-specific circumstances

- Observe *contact plus standard precautions* when caring for a CF patient who is coughing and infected with epidemiologically important pathogens (eg, *B. cepacia*, MRSA, or multidrug-resistant *P. aeruginosa*). *Category IA*²
- ***B. cepacia* complex**: observe the following for patients infected with *B. cepacia* complex: *Category IB*^{2,17,22,238,239}
 - Segregate from other CF patients.
 - Segregate from other CF patients infected with *B. cepacia* complex to prevent replacement of one strain with another potentially more virulent strain.
 - Schedule on a separate day or schedule at the end of the clinic session.
 - Place in examining room immediately.
- **Multidrug-resistant *P. aeruginosa***: place in examining room immediately. *Category IB*^{17,34,35,82-84,197}
- **Other multidrug-resistant bacteria**: manage CF patients harboring other multidrug-resistant organisms, such as *S. maltophilia* or *A. xylosoxidans*, according to hospital policy. *Category II*
- **Acid-fast bacilli**: observe the following:
 - Place CF patients who are AFB smear positive in *airborne infection isolation* until *M. tuberculosis* disease has been excluded. *Category IA*³⁷⁹
 - Use *standard precautions* for patients with NTM. *Category IB*^{2,277,278}
 - Place patients with documented *M. tuberculosis* in *airborne infection isolation* until clinically improved and three AFB sputum specimens obtained at 8-hour or longer intervals are smear negative. *Category IA*³⁷⁹

4. Adjunctive measures to prevent respiratory infections

- Administer all vaccines, especially pneumococcal, measles and pertussis, to CF patients and their

close contacts according to the Advisory Committee on Immunization Practices (ACIP)/American Academy of Pediatrics/American Academy of Family Physicians recommendations. *Category IA*^{380,381}

- Administer annual influenza immunization to CF patients who are 6 months of age or older and to close contacts of all CF patients according to ACIP recommendations. *Category IA*³⁰¹
- Use amantadine/rimantadine/oseltamivir according to ACIP recommendations for the prevention of influenza in exposed, unimmunized patients. *Category IA*³⁰¹
- *No recommendation* for routine administration of palivizumab to CF patients who do not meet criteria established for non-CF patients to prevent RSV infections. *Unresolved issue*

F. NON-HEALTHCARE SETTINGS

1. Multipatient family

- Co-inhabitants who live together in the same house:
 - Do not share items that come into contact with mucous membranes (eg, toothbrush, utensils, and respiratory therapy equipment). *Category IB*^{76,205,216}
 - Perform home physiotherapy in different rooms and at different times whenever possible with only one patient in the room at the time of treatment. *Category II*²²⁴
- At family gatherings at which there are multiple family members with CF who do not live together, instruct them to avoid activities associated with transmission of pathogens, including handshaking, and to maintain a distance of greater than 3 feet between each other. *Category II*
- Emphasize hand hygiene and containment of respiratory secretions for CF patients while in non-healthcare settings. *Category II*^{2,13}

2. Care of nebulizers and other therapy equipment in the home

- Manage all respiratory therapy equipment, eg, handheld nebulizers and tracheostomy tubes, used in the home setting according to the same principles applied in the hospital setting. *Category IB*^{61,62}
- First, Clean by removing all respiratory tract secretions from reusable objects that touch mucous membranes (semicritical items, eg, nebulizers and tracheostomy tubes) by washing

with soap and water as soon as possible and prior to disinfecting. *Category II*^{14,67}

- Then, Disinfect these reusable items with one of the following methods if acceptable according to manufacturers' recommendations:
 - Boil in water for 5 minutes. *Category IB*¹⁵
 - Immerse* in one of the following:
 - 1:50 dilution of 5.25% to 6.15% sodium hypochlorite (household bleach) for 3 minutes.
 - 70% to 90% ethyl or isopropyl alcohol for 5 minutes.
 - 3% hydrogen peroxide for 30 minutes.
- *If immersed in one of the above, rinse with sterile or filtered water (0.2 µm). Do not rinse with tap, bottled, or distilled water. An alternative is to rinse equipment with tap water, then 70% to 90% ethyl or isopropyl alcohol. *Category II*^{44,45,342}
- Use a standard cycle dishwasher, if the water temperature is 70°C (158°F) or higher and maintained for at least 30 minutes. *Category IB*³⁸²
- Microwave for 5 minutes. *Category IB*^{73-75,383}
- Do not use acetic acid (vinegar) to disinfect reusable objects that touch mucous membranes. *Category IB*^{68,69}
- Finally, air dry all equipment.
- Clean noncritical items (eg, therapy vest) with a detergent. *Category II*¹⁴

3. CF-specific camps and overnight CF education retreats

- Discontinue all CF-specific camps and overnight CF education retreats. *Category IB*^{36,181,195,218,219}
- Encourage CF patients to participate in camps and sports with non-CF individuals. *Category II*

4. Schools

- Maintain the diagnosis of CF and the results of respiratory tract cultures as confidential medical information unless the family chooses to make this information known to the school. *Category II*
- CF patients may attend the same school. *Category II*
- When it is known that CF patients attend the same school, do not place CF patients in the same classroom, whenever possible. If in the same classroom or other communal areas in the school (eg, lunchroom), separate by greater than 3 feet. *Category II*

- Minimize CF patient exposure to other CF patients by scheduling common activities at different times (eg, lunch or gym). *Category II*
- Emphasize hand hygiene and containment of respiratory secretions for CF patients while in school. *Category II*^{2,13}

5. Family education days and great strides

- Educate CF patients to avoid contact with each other's respiratory secretions and to observe frequent hand hygiene while attending these events. *Category II*
- CF patients who are not infected with *B. cepacia* complex may attend CF Family Education Days or Great Strides Walks. *Category II*
- Develop alternative CF education programs, eg, videotapes, video-conferencing, and CD-ROM web-based learning, that do not require face-to-face meetings among all CF patients. *Category II*
- Emphasize hand hygiene and containment of respiratory secretions for CF patients while at such events. *Category II*^{2,13}

6. Construction, renovation, gardening, and lawn cutting

- Avoid areas of construction, renovation, gardening, and lawn cutting to decrease prolonged exposure to large concentrations of *Aspergillus* spp. *Category II*

7. Swimming pools, hot tubs, and whirlpool spas used by CF patients

- Ensure adequate chlorination. *Category IB*^{190,191}
- For CF patients with central venous catheters in place: do not submerge the catheter under water. Showering may be permitted if precautions can be taken to reduce the likelihood of introducing organisms into the catheter, eg, the catheter and connecting device should be protected with an impermeable cover during the shower. *Category II*³⁸⁴⁻³⁸⁶

G. PSYCHOSOCIAL IMPACT OF INFECTION CONTROL GUIDELINES

- Educate HCWs, CF patients, their families, and when appropriate, friends, teachers, employers, and coworkers about the rationale and the potential psychosocial impact of infection control guidelines. *Category II*
- Identify CF center specific issues for potential psychosocial impact of guidelines for CF patients in the hospital, clinic, community, school, and home. *Category II*

- Develop age- and culture-specific educational tools in written, audiovisual, and audio format in lay person's language. *Category II*
- Inform patients, family members (when applicable), and HCWs of the microbiological status of patients. *Category II*
- Monitor adherence to infection control guidelines by HCWs, patients, and family members and provide feedback of adherence to the CF care team. *Category IB*¹³
- Ensure that a counselor is available to address psychosocial issues that may be induced by implementation of the infection control guidelines. *Category II*
- Collaborate with child life staff to ensure individualized programs consistent with the recommended infection control guidelines. *Category II*
- Make accommodations, eg, providing entertainment, enhancing communication with the outside world, facilitating visits with non-CF individuals, and adapting child life programs, to relieve the psychosocial stress of inpatient and outpatient infection control guidelines without placing the patient at risk of transmission or acquisition of pathogens. *Category II*

H. HEALTHCARE WORKERS WITH CF

- Provide career counseling to CF patients considering careers in health care and include:
 - Education about the modes of transmission of infectious agents
 - Examples of specialty areas (eg, radiology, pathology, primary care, and social work) where the job duties minimize the risk of transmission or acquisition of potential pathogens. *Category II*
- Educate HCWs with CF about the modes of transmission of infectious agents and the importance of observing *standard precautions* at all times for the protection of both HCWs and patients. *Category IA/IC*^{2,335}
- Avoid direct or indirect contact (eg, within 3 feet) with patients who have CF. *Category IB*^{84,102,193,216,332}
- When it is known that a HCW with CF is infected/colonized with *B. cepacia* complex, segregate the HCW from patients with CF. *Category IB*^{22,26,193,238,239}
- When it is known that a HCW is infected/colonized with MRSA, make work assignments according to hospital policy. *Category II*
- Make assignments for the care of patients who do not have CF on a case-by-case basis, consid-

ering the following health-related factors:
Category II

- Frequency and severity of coughing episodes, quantity of sputum production during these episodes, and ability to contain respiratory tract secretions.
- Known colonization/infection with epidemiologically important pathogens.
- A HCW's ability to use barrier precautions and adhere to infection control guidelines, institutional guidelines, Centers for Medicare and Medicaid Services (CMS, formerly Health Care Financing Administration or HCFA), HICPAC, and CDC Guidelines.
- Evaluate risk of transmission of pathogens between patients by HCW in the context of the specific job.
- Advise HCWs with CF to seek guidance concerning patient care assignments from their CF physician and/or occupational (employee) health service, if their health status changes. *Category II*

IV. DISSEMINATION AND EDUCATION FOR CF INFECTION CONTROL GUIDELINES

A. MEASURES TO ACHIEVE SUSTAINED ADHERENCE TO INFECTION CONTROL GUIDELINES

- Define clearly the rationale and specific interventions using language and beliefs that are consistent with the culture of the local medical and CF community. *Category IA*^{2,97,387}
- Stage the interventions. *Category II*
- Choose interventions to implement those that are compatible with the healthcare facility's existing physical structure. *Category II*
- Optimize acceptance of interventions by involving the infection control team, CF team, residents, medical staff, and administrative/organizational leaders. *Category II*
- Identify and use internal and external reinforcers (eg, rewarding adherence to recommended infection control practices). *Category II*
- Use the term *adherence* rather than *compliance* to promote a feeling of active participation. *Category II*³⁸⁷

B. EDUCATION OF PATIENTS, FAMILIES, AND HCWS

- Educate patients, families, and HCWs about the routes of transmission of infectious agents and methods to prevent patient-to-patient spread, using the following strategies: *Category II*

- Disseminate this document to all CF centers, infection control professionals, pulmonologists, and infectious disease specialists, in collaboration with appropriate professional societies.
- Place information about the document on the CFF Website and publish the document in professional journals.
- Within a center, educate all members of the medical, nursing, respiratory therapy, and support staff who care for CF patients in the principles of infection control to prevent transmission of pathogens among CF patients.
- Distribute a summary document approved by the consensus committee to CF patients and their families written in lay person's language, including a guide for care of CF respiratory therapy equipment.
- Place patient/family summary document on CFF Website and local institutional Website.
- Distribute a PowerPoint presentation to CF care providers and CF center infection control departments to facilitate implementation of these infection control guidelines.

C. AMERICAN SOCIETY OF MICROBIOLOGY ENDORSEMENT

- Seek the endorsement of the American Society for Microbiology (ASM) for these guidelines for processing clinical specimens from CF patients to achieve national standards for processing such specimens. *Category II*

V. PROPOSED RESEARCH PROJECTS

A. HOST FACTORS

Evaluation of differences in CF hosts including genetic, treatment, and environmental exposures in determining rates of infection.

B. PATHOGENS IN PATIENTS WITH CF

1. *P. aeruginosa*: patient-to-patient transmission using improved molecular typing studies to compare environmental to clinical isolates, particularly in outpatient settings.
2. *B. cepacia* complex: delineation of natural history of colonization, assessment of virulence and clinical outcomes according to specific genomovars, replacement of one strain by another, and assessment of natural reservoirs.
3. *S. maltophilia*, *A. xylosoxidans*, and NTM: pathogenic role and transmissibility.

4. *Aspergillus* spp.: predictors and risk factors for development of ABPA and invasive *aspergillosis*, especially environmental factors.
5. Validation of CFF Registry microbiology database.

C. ROLE OF ANTIMICROBIAL AGENTS

1. Impact of antimicrobial control programs on rates of emerging pathogens and antibiotic resistance.
2. Quantification of the selective pressure of aerosolized antibiotics on antimicrobial resistance patterns in hospitals and outpatient clinics.

D. ENVIRONMENT

1. Determination of the optimal duration of use of hospital nebulizers for individual patients.
2. Surveillance of the healthcare environment of CF patients in the ambulatory setting to ascertain possible sources and routes of transmission of potential pathogens.

E. HCWS WITH CF

1. Determination of the number of HCWs with CF, career counseling received, nature of patient care assignments, and their microbiological and clinical status.
2. Obtain cultures from the environment of HCWs with CF to examine the risk of contamination with their respiratory tract flora.

F. INFECTION CONTROL PRACTICES

1. Validation of recommendations; the relative contributions of specific recommendations (eg, masks and different clinic days for *P. aeruginosa* positive and negative patients) in preventing transmission of pathogens should be assessed.
2. Comparison of infection control practices at centers with ongoing patient-to-patient transmission of *B. cepacia* complex with practices at centers without transmission.
3. Evaluation of dissemination of these infection control recommendations.
4. Evaluation of implementation of these guidelines, HCW adherence to recommended infection control practices and their impact on outcome, using measures including quantification of infection rates, antimicrobial utilization rates, hospitalization rates, and cost analysis of infection control strategies. Identification of needed modifications to guidelines.
5. Psychosocial aspects of infection control practices:
 - Acceptance of recommended *isolation precautions* by parents and patients according to age groups, evaluation of rates of adher-

ence to recommended precautions, and attitudes of CF team members and other HCWs.

- The impact of interventions to counterbalance the negative impact of *isolation precautions*.
- Understanding the beliefs systems that motivate CF team members.
- Suggestions on alternative means of educating patients and effectiveness of non-face to face interventions for education and support of patients.

GLOSSARY

Airborne transmission/airborne infection isolation: transmission of infectious agents by dissemination of either airborne droplet nuclei (small-particle residue $\leq 5 \mu\text{m}$ in size of evaporated droplets containing microorganisms that remain suspended in the air for long periods of time) or dust particles containing the infectious agent. Microorganisms carried in this manner can be dispersed widely by air currents and may be inhaled by susceptible hosts within the same room or over a longer distance from the source-patient, depending on environmental factors. Therefore, special air handling and ventilation, eg, negative pressure relative to the corridor, high efficiency particulate exhaust to the outside, and 12 air changes or more per hour are required to prevent airborne transmission. Microorganisms spread by airborne transmission include *M. tuberculosis*, measles, and varicella-zoster (chickenpox/shingles) viruses.

American Thoracic Society (ATS) diagnostic criteria for disease caused by NTM: (1) three AFB smear negative specimens that are culture positive for NTM; or (2) two positive cultures for NTM with at least one positive AFB smear.

Antiseptic agents: antimicrobial substances that are applied to the skin to reduce the amount or level of microbial flora. Examples include alcohols, chlorine, chlorhexidine, hexachlorophene, iodine, quaternary ammonium compounds, disinfectants, parachlorometaxyleneol, and triclosan.

Antiseptic hand rub: applying a waterless antiseptic agent to all surfaces of the hands to reduce the number of microorganisms present. Alcohol-based products are the most frequently used.

Antiseptic hand wash: washing hands with water and soap or other detergents containing an antiseptic agent.

Clone: strains of microorganisms (bacteria or fungi) that are derived from the same parent as defined by genotyping.

Colonization: presence of a microorganism, eg, bacteria or fungi, on a mucosal surface without active replication, evidence of clinical signs or symptoms, or histologic evidence of disease.

Contact transmission/precautions: there are two types of contact transmission:

- (1) *Direct contact transmission:* direct body surface-to-body surface physical transfer of an infectious agent(s) between a susceptible host and an infected or colonized person, eg, kissing or touching hands contaminated with secretions, patient-care activities that require direct patient contact.
- (2) *Indirect contact transmission:* contact of a susceptible host with an intermediate object that has been contaminated with secretions containing an infectious agent, eg, eating utensils, respiratory therapy equipment, toys, gloves that have not been changed between patients. *Contact precautions* require the use of gown and gloves by HCWs caring for patients colonized or infected with epidemiologically and/or clinically important infectious agents or when handling objects or environmental surfaces that have been touched by the patient or contaminated with infected patient secretions to prevent transmission to patients or HCWs. A single patient room is preferred.

Critical item: any medical device that enters sterile tissue or the vascular system must be sterile, because of the high risk of infection if such an item is contaminated with any microorganism, including bacterial spores. This category includes surgical instruments, intravascular and urinary catheters, and implants.

Discriminatory power: for genotyping, differentiates between unrelated strains, but varies as species vary in genetic stability under the influence of selective pressure.

Disinfectant: a chemical or physical agent that destroys infectious pathogens on environmental surfaces or medical devices, but may not kill bacterial spores; thus, disinfectant refers to substances applied to inanimate objects. The EPA categorizes disinfectants by product label claims as “limited,” “general,” or “hospital” disinfection.

Disinfection: the destruction of pathogenic and other kinds of microorganisms by thermal or chemical means. Disinfection is a less lethal process than sterilization because it destroys most recognized pathogenic microorganisms, but not necessarily all microbial forms, such as bacterial spores. Organic matter, eg, blood, must first be removed from the object for disinfectants to be effective. Other factors that can adversely affect disinfection efficacy are: (1) the type and level of microbial contamination; (2) the concentration of and exposure time to the germicide; (3) the nature of the object (eg, crevices, hinges, lumens); (4) the presence of biofilms; and (5) the temperature and pH of the disinfection process.

Droplet transmission/precautions: person-to-person spread of infectious agents by large particle ($> 5 \mu\text{m}$) droplets generated primarily during coughing, sneezing, or talking, and during the performance of certain procedures such as suctioning or bronchoscopy. Transmission occurs when infectious droplets are propelled a short distance (≤ 3 feet) through the air and are deposited on the conjunctivae, nasal mucosa, or mouth of a susceptible host (or in the environment). Special air handling and ventilation are NOT required to prevent droplet transmission. Standard surgical masks (with or without face shield) are required for those working within three feet of a patient placed on *droplet precautions* to prevent transmission (\pm face shield).

Ease of interpretation: for genotyping, multiple users of the typing system obtain the same results and reach the same conclusions. Ideally, guidelines exist for interpretation.

Ease of performance: for genotyping, the rapidity, convenience, cost of equipment, and personnel needed to perform a technique.

Environment: can refer to a reservoir, eg, water, sinks, soil, etc. (E_r), or an environmental surface or patient care item that can be contaminated with infectious materials (E_s).

Epidemiologically important microorganisms: highly transmissible infectious agents that have a proclivity toward causing outbreaks, are associated with a severe clinical outcome, or are especially difficult to treat.

Genomovars: species of a genus that are distinguished genetically.

Hand hygiene: a general term that applies to either hand washing, antiseptic hand wash, antiseptic hand rub, or surgical hand antisepsis.

Hand washing: washing hands with plain (nonantimicrobial) soap and water.

High-level disinfectant: an agent capable of killing bacterial spores when used in sufficient concentration under suitable conditions. It is therefore expected to kill all microorganisms.

Incidence: the number of new cases that occur in a defined population at risk during a specified period of time. The incidence rate is calculated by dividing the number of new cases (eg, patients with the respiratory pathogen) in a given period by the number of patients at risk during that period.

Incidence density: the instantaneous rate at which disease is occurring, relative to the size of the disease-free population, calculated as the number of new cases per 1,000 patient-days.

Intervention: A change(s) in practice implemented in response to identification of a clinical problem that is associated with an undesirable patient outcome. Interventions are identified from evidence in the medical literature or strong theoretical rationale. Ongoing surveillance is essential to ascertain the safety and effectiveness of the newly implemented intervention.

Low-level disinfectant: an agent that destroys all vegetative bacteria (except tubercle bacilli), lipid viruses, some nonlipid viruses, and some fungi, but not bacterial spores.

Multidrug-resistant organism: an organism (eg, MRSA, VRE, *P. aeruginosa*, *B. cepacia* complex, *S. maltophilia*, *A. xylosoxidans*) resistant to all of the agents in two or more classes of antibiotics (eg, β -lactam agents, aminoglycosides, quinolones).

Noncritical item: medical equipment that comes in contact with intact skin, but not mucous membranes. Intact skin acts as an effective barrier to most microorganisms and sterility is “not critical.” Examples of noncritical items are bedpans, therapy vests, crutches, bed rails, linens, some food utensils, bedside tables, patient furniture, and floors. In contrast to critical and some semicritical items, most noncritical reusable items may be cleaned where they are used and do not need to be transported to a central processing area.

Noncritical patient care items occasionally serve as vectors for transmitting pathogens between patients. Environmental surfaces such as walls and floors are rarely, if ever, involved in patient-to-patient transmission of pathogens. However, noncritical surfaces in direct contact with patients (eg, bed rails) potentially contribute to transmission by contaminating the hands of healthcare workers or other equipment.³⁹⁵ However, noncritical items could potentially contribute to secondary transmission by contaminating the hands of healthcare workers or other medical equipment that will contact patients.

Period prevalence: prevalence, or total number of cases present, is calculated during a specified time period.

Personal protective equipment: materials used to protect healthcare workers from acquiring infection when exposed to blood or body fluids during patient care activities and to prevent transmission of pathogens to others, ie, gloves, gowns, masks, goggles, or face shields.

Phage typing: phage are viruses for bacteria that kill certain strains and spare others and can be used as a phenotypic method of distinguishing bacterial isolates.

Point prevalence: prevalence calculated at a specified point in time.

Prevalence: the total number of active (existing) patients with the respiratory pathogen divided by the number of patients cultured during a period or interval.

Protective environment: designed for allogeneic hematopoietic stem cell transplant (HSCT) patients or other high-risk immunocompromised patients to minimize fungal spore counts in air by maintaining: (1) filtration of incoming air by HEPA filters; (2) directed room airflow with supply on one side of the room, across the patient, and out through exhaust on the other side of the room (ie, laminar flow); (3) positive room air pressure relative to the corridor; (4) well-sealed rooms to prevent infiltration from the outside; and (5) 12 air changes or more per hour for new construction. Laminar air flow is unnecessary to maintain a protective environment. Wearing N95 respirators is advised when patients leave the protective environment for diagnostic tests or treatments to prevent inhalation of respirable particles and reaerosolization of exhaled

particles, but clinical efficacy in preventing aspergillosis has not been fully evaluated. A protective environment is not recommended routinely for solid organ transplant patients.

Pyocin typing: technique based on the production of antibiotic-like bacteriocins by *P. aeruginosa*. Strains are typed by their spectrum of inhibition patterns and each unique pyocin typing pattern is assigned a number. More than 100 pyocin types of *P. aeruginosa* have been recognized.

Reproducibility: the same result is obtained when the same strain is tested repeatedly and may be influenced by technical factors (day-to-day variation) and biological factors (variation in the stability of the characteristic).

Restriction endonucleases: enzymes that cleave DNA at known base sequences.

Segregation: separation of patients from one another.

Semicritical item: medical device that comes in contact with mucous membranes or nonintact skin. They should be free of all microorganisms, although small numbers of bacterial spores may be present. Intact mucous membranes are generally resistant to infection by common bacterial spores, but susceptible to other organisms, such as bacteria, mycobacteria, and viruses. Respiratory therapy and anesthesia equipment, endoscopes, laryngoscope blades, esophageal manometry probes, anorectal manometry catheters, and diaphragm fitting rings are included in this category.

Serotyping of gram-negative bacilli: use of antiserum raised against specific lipopolysaccharide O-groups to agglutinate bacteria; can be used as a phenotypic method of distinguishing bacterial isolates of the same genus and species from each other.

Standard precautions: apply to ALL patients, regardless of diagnosis or presumed infection status. *Standard precautions* combine the principles of *universal precautions* and *body substance isolation* and consider all blood, body fluids, secretions, excretions except sweat, non-intact skin, and mucous membranes to have the potential for containing transmissible infectious agents. To prevent person-to-person transmission of infectious agents when an HCW anticipates contact or has contact

with potentially infectious body substances, the HCW must observe the appropriate combination of the following: hand hygiene, gloves, mask, eye protection, face shield, gown, handling patient equipment or items likely to have been contaminated with infectious fluids in a manner to prevent transmission of infectious agents.

Sterilization: the complete destruction of ALL forms of microbial life, including fungal and bacterial spores. Sterilization is accomplished in health-care settings by either physical or chemical processes. Chemicals (ie, ethylene oxide) used for this purpose are referred to as “chemical sterilants” and prolonged exposure times (6-10 hours) are required to kill spores.

Surveillance: the ongoing, systematic collection, analysis, and interpretation of health data essential to the planning, implementation, and evaluation of health practices, closely integrated with the timely dissemination of these data to those who need to know (eg, caregivers, program evaluators).

Transmission-based precautions: apply to patients with documented or suspected infection with highly transmissible or epidemiologically important infectious agents for which precautions in addition to *standard precautions* are required to interrupt transmission. Categories include: *contact*, *droplet*, *airborne*, and *protective environment* or a combination when a disease has multiple routes of transmission.

Typability: for genotyping, likelihood of obtaining an unambiguous result for each isolate analyzed. Nontypable isolates give a null or uninterpretable result.

APPENDIX

Employment laws relevant to the HCW with CF

Employment laws that govern the protections and procedures for HCWs with CF include the Americans With Disabilities Act (ADA) and Section 504 of the Rehabilitation Act. These laws require that (1) medical inquiries in a job interview be limited to those which are job related; (2) individuals with disabilities be evaluated on a case-by-case basis based on their job qualifications and their individual skills for that job; and (3) reasonable accom-

modations be provided by employers in certain circumstances.

An employer cannot inquire about an individual's health in a job interview, but can ask how an individual will perform a job. An employer may conduct a medical examination after an offer of employment is made providing such an examination is required of all job applicants. The offer of employment can only be withdrawn if it is determined that the HCW poses a direct threat to the health of patients and there is no accommodation that would reduce or eliminate the risk to an acceptable level. However, a diagnosis of CF alone is insufficient to interfere with the hiring of HCWs with CF.

For institutions employing HCWs with CF, the institution must individually assess the risks that the HCW with CF poses to others. The assessment should include the ability of the individual to do the job with or without a reasonable accommodation that would reduce or eliminate the risk. Examples of reasonable accommodations are: regular training in infection control guidelines, strict adherence to infection control guidelines, regular screening of infectious status, or assignment of the HCW to areas of the hospital with less risk for infection control problems.

Institutions should already have policies in place that monitor and assess all HCWs for their continued ability to safely and effectively perform their jobs. Monitoring and assessing a HCW with CF is not unique or different from the policies already in place at most institutions, and HCWs with CF should not be treated differently from other HCWs with conditions that may potentially pose risks to patients (eg, HIV, tuberculosis, hepatitis C, hepatitis B) or other conditions that may place the HCW at risk (eg, pregnancy).

A medical examination given during the course of employment is permitted if it is job-related and consistent with business necessity. The most common reasons for postemployment examinations are (1) to assess the worker's continued ability to safely perform the essential functions of the job; and (2) to assess the need, scope, and nature of a requested reasonable accommodation. Otherwise, there is generally no legitimate reason to conduct a medical examination during the course of employment. An example of a job-related examination would be an examination that is given to all HCWs,

including an HCW with CF, to test for the presence of harmful microbiological organisms. When harmful microbiological organisms are found to be present, an HCW could request a reasonable accommodation, which could include a modification in the job to reduce or eliminate risks caused by the presence of the organism. Another possible reasonable accommodation could be a reassignment of the HCW's duties to areas of the institution where the HCW does not pose a risk. If no reasonable accommodation is possible to reduce or eliminate the risk to patients, it is possible the individual could be dismissed from employment.

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