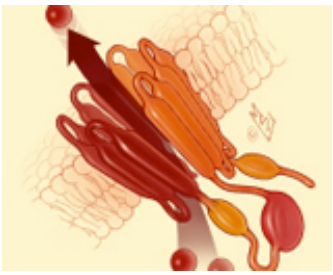
JOHNS HOPKINS MEDICINE
eLITERATURE REVIEW
eCysticFibrosis Review

Presented by the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing

Supported by Educational Grants from Genentech, Inc., Eurand Pharmaceuticals, Inc., Vertex Pharmaceuticals, Incorporated, Axcan Pharma, Inc. and Gilead Sciences Medical Affairs







**August 2010: VOLUME 2, NUMBER 9**

## *Guidelines: State-of-the-Art Treatment for CF Lung Disease*



## In this Issue...

Clinical practice guidelines have become a regular component of health care. The Cystic Fibrosis Foundation has supported the development of several recent clinical practice guidelines to review the evidence that endorses many of the therapies currently in use. Although numerous clinical manifestations of cystic fibrosis (CF) exist, the principal causes of disease-related morbidity and mortality are due to pancreatic insufficiency and chronic airway infection. Recommendations are now available on the assessment and treatment of nutritional disease, use of airway clearance therapies, and use of chronic medications to maintain lung health. Acute complications of CF lung disease include pulmonary exacerbations, hemoptysis, and pneumothorax; guidelines on the management of these complications are currently available as well. Finally, as newborn screening for CF has become standard in all states, we can expect that most patients will be diagnosed in the absence of symptoms. Infant care guidelines should provide primary care physicians with the information needed for appropriate assessment and treatment of newly diagnosed patients.

In this issue, we summarize the clinical practice guidelines for individuals with CF, to aid clinicians in improving the quality and consistency of the care they provide.

## LEARNING OBJECTIVES

After participating in this activity the participant will demonstrate the ability to:

- Understand the cystic fibrosis (CF) pulmonary guidelines, including the use of chronic medications to maintain lung health, airway clearance therapies, treatment of acute pulmonary exacerbations, and management of pulmonary complications.
- Discuss the CF nutritional guidelines, including recommended caloric intake, dosing of pancreatic enzyme supplements, and target goals for nutritional status.
- Examine the CF infant care guidelines, including the recommended evaluation and treatment of infants newly diagnosed with CF.

**Program Information**
CME/CE Info
Accreditation
Credit Designations
Intended Audience
Learning Objectives
Internet CME/CE Policy
Faculty Disclosures
Disclaimer Statement

**Length of Activity**
Physicians
1 hour
Nurses
1 contact hour
Dieticians
1 contact hour
Physical Therapists
1 contact hour

**Release Date**
August 13, 2010

**Expiration Date**
August 12, 2012

**Podcast Release**
September 4, 2010

**Next Newsletter Issue**
October 12, 2010

**TO COMPLETE THE POST-TEST**

**Step 1.**
Please read the newsletter.

**Step 2.**
See the Post-test link at the end of the newsletter.

**Step 3.**
Follow the instructions to access the post-test.

## IMPORTANT CME/CE INFORMATION

▼ Program Begins Below

### ACCREDITATION STATEMENTS

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing . The Johns Hopkins University School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

The Institute for Johns Hopkins Nursing is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation. The Institute for Johns Hopkins Nursing and the American Nurses Credentialing Center do not endorse the use of any commercial products discussed or displayed in conjunction with this educational activity.

### CREDIT DESIGNATIONS

**Physicians**

***Newsletter:*** The Johns Hopkins University School of Medicine designates this educational activity for a maximum of 1.0 *AMA PRA Category 1 Credit(s)*™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

**Nurses**

***Newsletter:*** This 1 contact hour Educational Activity is provided by the Institute for Johns Hopkins Nursing. Each Newsletter carries a maximum of 1 contact hours or a total of 6 contact hours for the six newsletters in this program.

To obtain contact hours, you must complete this Education Activity and post-test before August 9, 2012.

**Dieticians**

***Newsletter:*** The Johns Hopkins University has approved this activity for 1.0 contact hours for non-physicians.

**Physical Therapists**

***Newsletter:*** The Johns Hopkins University has approved this activity for 1.0 contact hours for non-physicians.

**Respiratory Therapists**

**For United States:** Visit this page to confirm that your state will accept the CE Credits gained through this program.

**For Canada:** Visit this page to confirm that your province will accept the CE Credits gained through this program.

### INTENDED AUDIENCE

This activity has been developed for Pulmonologists, Pediatric Pulmonologists, Gastroenterologists, Pediatricians, Infectious disease specialists, Respiratory therapists, Dieticians, Nutritionists, Nurses, and Physical therapists.

### LAUNCH DATE

This program launched on December 8, 2009, and is published monthly; activities expire two years from the date of publication, ending in December 7, 2011.

### HARDWARE & SOFTWARE REQUIREMENTS

Pentium 800 processor or greater, Windows 98/NT/2000/XP or Mac OS 9/X, Microsoft Internet Explorer 5.5 or later, 56K Modem or better, Windows Media Player 9.0 or later, 128 MB of RAM Monitor settings: High color at 800 x 600 pixels, Sound card and speakers, Adobe Acrobat Reader.

### DISCLAIMER STATEMENT

The opinions and recommendations expressed by faculty and other experts whose input is included in this program are their own. This enduring material is produced for educational purposes only. Use of Johns Hopkins University name implies review of educational format design and approach. Please review the complete prescribing information of specific drugs or combination of drugs, including indications, contraindications, warnings and adverse effects before administering pharmacologic therapy to patients.

### SUCCESSFUL COMPLETION

To take the post-test for eCysticFibrosis Review you will need to visit the Johns Hopkins University School of Medicine's CME website and the Institute for Johns Hopkins Nursing . If you have already registered for other Hopkins CE programs at these sites, simply enter the requested information when prompted. Otherwise, complete the registration form to begin the testing process. A passing grade of 70% or higher on the post-test/evaluation is required to receive CE credit.

### STATEMENT OF RESPONSIBILITY

The Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing take responsibility for the content, quality and scientific integrity of this CME/CE activity.

### INTERNET CME/CE POLICY

The Office of Continuing Medical Education (CME) at the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing are committed to protect the privacy of its members and customers. The Johns Hopkins University maintains its Internet site as an information resource and service for Continuing Medical Education at the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing will keep your personal and credit information confidential when you participate in a CE Internet-based program. Your information will never be given to anyone outside the Johns Hopkins.

### FACULTY DISCLOSURE

As a provider accredited by the Accreditation Council for Continuing Medical Education (ACCME), it is the policy of Johns Hopkins University School of Medicine to require the disclosure of the existence of any relevant financial interest or any other relationship a faculty member or a provider has with the manufacturer(s) of any commercial product(s) discussed in an educational presentation. The presenting faculty reported the following:

- **Michael P. Boyle, MD, FCCP** discloses that he has received grant/research support Vertex Pharmaceuticals, Inc.
- **Peter J. Mogayzel, Jr, MD, PhD** discloses that he has no financial relationship with commercial supporters.
- **Meghan Ramsay, MS, CRNP** discloses that she has no financial relationship with commercial supporters.
- **Donna W. Peeler, RN** discloses that she has no financial relationship with commercial supporters.

Guest Author's Disclosures

## IN THIS ISSUE




Program Directors

**Michael P. Boyle, MD, FCCP**
Associate Professor of Medicine
Director, Adult Cystic Fibrosis Program
The Johns Hopkins University
Baltimore, MD

**Peter J. Mogayzel, Jr., MD, PhD**
Associate Professor of Pediatrics
Director, Cystic Fibrosis Center
The Johns Hopkins University
Baltimore, MD

**Donna W. Peeler, RN, BSN**
Pediatric Clinical Coordinator
Cystic Fibrosis Center
The Johns Hopkins University
Baltimore, MD

**Meghan Ramsay, MS, CRNP**
Adult Clinical Coordinator
Cystic Fibrosis Center
The Johns Hopkins University
Baltimore, MD


## GUEST AUTHOR OF THE MONTH

Commentary & Reviews:


**Patrick A. Flume, MD**
Professor of Medicine and Pediatrics
Medical University of South Carolina
Charleston, South Carolina


***Guest Faculty Disclosures***

**Patrick A. Flume, MD** discloses that he receives grants and research support from Boehringer Ingelheim, Gilead, Mpex, Pharmaxis and Vertex.

***Unlabeled/Unapproved Uses***

The author has indicated that there will be a reference to unlabeled or unapproved uses of azithromycin in the treatment of cystic fibrosis in the presentation.

Program Directors Disclosures

## SEPTEMBER PODCAST

***eCysticFibrosis Review* is happy to offer our accredited PODCASTS, to be sent to you in September.**

The *eCysticFibrosis Review* podcast complements the topic presented in this issue by applying the information to patient scenarios. Our August author, Patrick A. Flume, MD and Robert Busker, eCysticFibrosis Review's Managing Editor discuss the topic: Guidelines: State-of-the-Art Treatment for CF Lung Disease.

Participants can now receive 0.75 *AMA PRA Category Credits*™ per podcast after completing an online post-test via the links provided on this page.

To learn more about podcasting and how to access this exciting new feature of *eCysticFibrosis Review*, **please visit this page.**.

back to top

## COMMENTARY

Clinical practice guidelines have become a standard component of health care. Such guidelines are defined as "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances."[1] The overall goal of clinical practice guidelines is to improve the quality of patient care.[2] Health outcomes can be enhanced by promoting interventions that have proven benefits and by discouraging the use of ineffective therapies. Such interventions can improve the consistency of care and serve as an impetus for quality improvement; patients with identical problems should not be managed with a wide variety of treatments. Since clinical practice guidelines can empower patients to make well-informed health care decisions, patients should be included in the development of such guidelines. Finally, the systematic process used to create clinical practice guidelines can identify gaps in our knowledge that may establish priorities for clinical research.

The Cystic Fibrosis Foundation (CFF) has supported the development of several recent clinical practice guidelines, including recommendations on the management of nutrition, pulmonary disease, and pulmonary complications among patients with cystic fibrosis (CF). Most recently, infant care guidelines have become available, designed to provide guidance to primary care physicians on the assessment and management of patients newly diagnosed with CF. As newborn screening for CF has become routine practice in all states, we should anticipate that most patients will be asymptomatic at the time of diagnosis. These guidelines should help steer clinicians toward early intervention, which has become an important priority in the management of CF.

Clinical practice guidelines were developed in a manner intended to reduce bias. A systematic review was used whenever possible, and when no publications were available to assess appropriate testing and treatment (eg, hemoptysis and pneumothorax), a survey of experts using the Delphi approach was utilized. The grading of recommendations can be somewhat controversial. The CFF chose the grading system used by the United States Preventive Services Task Force (USPSTF), as it provides a straightforward evaluation of the strength of the evidence and the relative benefits and harms. A common criticism of the USPSTF is that if insufficient evidence is available, no recommendation can be made, as was the case with many of the questions reviewed in these guidelines. However, this also allows us to see where evidence is lacking and where we should consider devoting our time and energy to research.

There are some important caveats to the use of clinical practice guidelines. Although such guidelines demonstrate the strength of evidence of various therapies, the recommendations are derived from the review of studies conducted in populations of patients under ideal conditions. This does not mean that all of these recommendations will be appropriate for all patients, and the clinician must use this information when

RECOMMEND TO A COLLEAGUE

NEWSLETTER ARCHIVE

determining a treatment plan for a particular individual. Additionally, these guidelines are developed from a review of the literature up to a specific time point. Since new information may be published after this date, plans must be made to review the guidelines on a periodic basis. The CFF is committed to reviewing the guidelines for patients with CF every 3 to 5 years.

The reviews in this issue provide many recommendations—too numerous to discuss individually here. What follows are brief summaries of the published CF guidelines on nutrition, chronic therapies to maintain lung health, airway clearance therapies, treatment of acute pulmonary exacerbations, management of pulmonary complications, and infant care guidelines. The reader is encouraged to study the full documents and to incorporate the recommendations into his or her daily practice.

**Commentary References**


1. Field MJ, Lohr KN, eds. Clinical practice guidelines: directions for a new program. Washington, DC: National Academy Press; 1990.
2. Woolf SH, Grol R, Hutchinson A, Eccles M, Grimshaw J. Potential benefits, limitations, and harms of clinical guidelines. *BMJ.* 1999;318(7182):527-530.


## NUTRITION GUIDELINES FOR PATIENTS WITH CF

Stallings VA, Stark LJ, Robinson KA, Feranchak AP, Quinton H; Clinical Practice Guidelines on Growth and Nutrition Subcommittee; Ad Hoc Working Group. **Evidence-based practice recommendations for nutrition-related management of children and adults with cystic fibrosis and pancreatic insufficiency: results of a systematic review.** *J Am Diet Assoc.* 2008;108(5):832-839.

*(For non-subscribers to this journal, an additional fee may apply to obtain full-text articles.)*

View journal abstract View full article

A key manifestation of cystic fibrosis (CF) is pancreatic insufficiency due to obstruction of the pancreatic ducts. Individuals with CF do not produce sufficient enzymes to properly digest their food, resulting in malabsorption of calories and important nutrients. The consequences are profound, with impaired growth, persistent abdominal symptoms, and greater susceptibility to chronic pulmonary infections. Attention to nutrition is a critical part of appropriate CF care, and advances in nutritional management may be a major reason that survival in these patients has improved over time. The Cystic Fibrosis Foundation (CFF) established the Growth and Nutrition Subcommittee to conduct a systematic review of published evidence and develop recommendations on important nutrition-related issues. For this review, the authors also analyzed data from the CFF Patient Registry.

A strong association exists between energy intake and nutritional status. Prior recommendations had stated that patients should consume up to 200% of the energy needs of a healthy (non-CF) population. This is not easily accomplished, and behavioral intervention may be necessary. The guidelines established target nutritional parameters, as normal growth status was associated with improved lung function and survival. Insufficient information was available to determine a recommended dose of supplemental pancreatic enzymes, so the authors returned to prior recommendations (500 to 2500 units of lipase per kilogram of body weight per meal) developed by an earlier consensus committee. A key recommendation was to utilize body mass index (BMI) as the relevant measure rather than the previously used percent of ideal body weight. For children and adolescents, the target is a BMI >50th percentile; for adults, that target is a BMI of 22 in women and 23 in men.

The current guidelines on nutrition-related care provide greater structure for clinicians and patients on the management of nutritional evaluation and therapies. Clinicians now have specific goals for caloric intake and for enzyme replacement. Although insufficient data are available for defining the optimal dose of enzymes, the guidelines provide practical recommendations for treatment. Finally, there is now a standard measure for the assessment of nutritional health. It is important to recognize that having target BMI values does not mean that these are the optimal nutritional indices for all patients. However, the bar has been raised for measuring the nutritional health of our patients in general.

## Recommendations for Nutritional Guidelines

| | Children birth to < 2 years | Children 2 to 20 years | Adults > 20 years |
|---|---|---|---|
| **Evidence-based recommendations** | | | |
| Routine energy intake as indicated for age and sex | Not reviewed[a] | 110% to 200% standards for healthy population | 110% to 200% standards for healthy population |
| Combined behavioral and nutrition intervention indicated for weight gain | Recommended for children aged 1 to 2 years | Recommended for age 2 to 12 years; insufficient evidence for age 13 – 20 years[a] | Insufficient evidence for adults[a] |
| Nutritional supplementation (oral and enteral) intervention indicated for weight gain | Not reviewed[a] | Recommended | Recommended |
| Optimal ranges of weight-for-age and stature-for-age for children and weight-for-height for adults are indicated to support better $FEV_1$[b] and survival | Not reviewed[a] | Recommended | Recommended |
| Nongeneric, proprietary pancreatic enzyme preparations are required to ensure efficacy in treating cystic fibrosis-related pancreatic insufficuency[c] | Recommended | Recommended | Recommended |
| **Registry data-based recommendations** | | | |
| Discontinue use of percent ideal body weight method and incorporate age-appropriate method of assessment of weight-for-stature | Weight-for-length percentile recommended | BMI[d] percentiles recommended | BMI recommended |
| Maintain growth status for children and weight-for-height status for adults within recommended ranges to support better $FEV_1$ status | Weight-for-length ≥ 50th percentile recommended | BMI ≥ 50th percentile recommended | Women: BMI ≥ 22<br>Men: BMI ≥ 23 |
| Avoid unintentional weight loss to support better $FEV_1$ status in adults | — | — | Recommended |
| After early diagnosis, establish a weight-for-length status of ≥50th percentile by age 2 y to support better $FEV_1$ status during childhood | Recommended | — | — |

[a]If a topic was not reviewed or reviewed and found to have insufficient evidence to make a recommendation, then previous recommendations for children and adults are used for clinical care.
[b]$FEV_1$ – forced expiratory volume in 1 second.
[c]Current recommendations for dose of pancreatic enzymes are 500 to 2,500 units lipase per kilogram body weight per meal, or <10,000 units lipase per kilogram body weight per day, or <4,000 units lipase per gram of dietary fat per day.
[d]BMI – body mass index.

back to top

# PULMONARY GUIDELINES FOR PATIENTS WITH CF: USE OF CHRONIC MEDICATIONS

Flume PA, O'Sullivan BP, Robinson KA, et al; Cystic Fibrosis Foundation; Pulmonary Therapies Committee. **Cystic fibrosis pulmonary guidelines: chronic medications for maintenance of lung health.** *Am J Respir Crit Care Med.* 2007;176(10):957-969.

*(For non-subscribers to this journal, an additional fee may apply to obtain full-text articles.)*

View journal abstract View full article

The lung disease associated with CF is caused by obstruction of the airways due to dehydrated, thickened secretions; resultant endobronchial infection; and an exaggerated inflammatory response leading to the development of bronchiectasis and progressive obstructive airways disease. Physicians treating patients with CF have a large number of available treatment options for the maintenance of lung health. The CFF established the Pulmonary Therapies Committee to review published evidence and develop recommendations on the use of medications intended to maintain lung health. These guidelines were created using a systematic review of the literature and addressing questions related only to those medications that were believed to be used by patients on a regular basis and for which peer-reviewed literature would be available.

The literature provided evidence to support several recommendations. Aerosolized medications that were recommended for chronic use included dornase alfa, tobramycin, hypertonic saline, and beta-agonist bronchodilators. Oral macrolides were also recommended, as was ibuprofen, at least for adolescents. The use of both oral and inhaled corticosteroids was discouraged as routine therapy, although insufficient evidence was available regarding the use of systemic corticosteroids in adult patients. An important caveat is that corticosteroids may be beneficial in those patients who also have asthma or allergic bronchopulmonary aspergillosis. Oral antistaphylococcal antibiotics intended for use as prophylactic treatment were also discouraged because of a lack of clinical benefit.

For several medications, some of which were used with a reasonably high frequency, no recommendation could be offered because of insufficient information. These included other aerosolized antibiotics (eg, colistin), N-acetylcysteine (Mucomyst®; Bristol-Myers Squibb S.r.l.), anticholinergic bronchodilators, leukotriene modifiers, and cromolyn. This does not mean that these medications are not effective or are harmful, but rather that there is a paucity of published data that demonstrate their clinical effects.

The guidelines on chronic medications for the maintenance of lung health in CF provide a structure from which clinicians and patients can consider a treatment strategy. Although not all patients will benefit from each (or all) of these medications, many patients will benefit from the use of multiple therapies. The clinician must determine when to introduce a new therapy with the intention of chronic use, while at the same time balancing the potential long-term benefits of the agent with the added treatment burden. Since no definitive studies have assessed the appropriate order of treatment for those patients using more than one aerosolized medication, the guidelines offered an intuitive approach —bronchodilators first, followed by dornase alfa or hypertonic saline (or both, but not mixed together), then airway clearance, and finally, aerosolized antibiotics. Pediatricians are often left to decide whether to use medications in their very young patients without the benefit of clinical data. Similarly, as these recommendations were based on evidence from studies conducted in patients >6 years of age, one can ask whether the benefit of such therapies might be observed in even younger patients. Such questions are addressed in the upcoming infant care guidelines.

**View table for Chronic Medications**

back to top

# PULMONARY GUIDELINES FOR PATIENTS WITH CF: AIRWAY CLEARANCE THERAPIES

Flume PA, Robinson KA, O'Sullivan BP, et al; Clinical Practice Guidelines for Pulmonary Therapies Committee. **Cystic fibrosis pulmonary guidelines: airway clearance therapies.** *Respir Care.* 2009;54(4):522-537.

*(For non-subscribers to this journal, an additional fee may apply to obtain full-text articles.)*

View journal abstract View full article

Lester MK, Flume PA. **Airway clearance therapy: guidelines and implementation.** *Respir Care.* 2009;54(6):733-750.

*(For non-subscribers to this journal, an additional fee may apply to obtain full-text articles.)*

View journal abstract View full article

CF lung disease begins early in life with abnormal airway surface fluid, impaired mucociliary clearance, and consequent obstruction of the small airways by mucus. The chronic infection of the airways incites an exaggerated inflammatory response; the material present in the airways of individuals with CF contains pathogenic bacteria and inflammatory cytokines that perpetuate airway injury by recruiting new inflammatory cells. It is intuitive that to maintain lung health, patients with CF must clear their airways of these secretions in order to relieve the obstruction, and reduce infection and inflammation. Airway clearance therapies (ACTs) have thus long been considered the most fundamental strategy for the management of CF airways disease. The CFF established the Pulmonary Therapies Committee to review published evidence and develop recommendations on the use of ACTs to maintain lung health. These guidelines were developed using a systematic review of the literature assessing questions related only to those ACTs that were believed to be used by patients on a regular basis.

Based on this exhaustive review, only 4 recommendations were made. The first is that airway clearance be performed routinely in all patients with CF, including newly diagnosed, asymptomatic infants. The second recommendation is that no ACT has been shown to be superior to another. This is perhaps the most misinterpreted statement, as some may conclude that all therapies are considered to be equal, but this is not what is meant by this recommendation. That is the reason for the third, and perhaps most important, recommendation, which states that the prescribing of therapies must be accomplished on an individual basis for each patient. A strategy for identifying optimal use of ACTs was published in 2009 by Lester and Flume, in which such important factors as age, severity of disease, availability of a parent or partner, observed efficacy, and patient preference are addressed. Finally, the guidelines noted the importance of exercise as an adjunctive therapy for airway clearance, along with its added benefits for overall health.

These guidelines also addressed some important questions that are not answered in the literature, including "Who should educate the patients on ACTs?" Airway clearance is performed in the hospital setting most often by a respiratory or physical therapist. It makes sense that the education of patients and families be carried out by those therapists who have been trained to do so—that is, they have been trained to perform the therapies, as well as to educate patients and families. As for the development of new devices or techniques, they should be consistent with the known pathophysiology, and studies should be powered for either equivalence or superiority to existing therapies using meaningful outcome measures.

| Airway Clearance Therapy |
| --- |
| 1. Airway clearance therapy is recommended for all patients with cystic fibrosis (B). |
| 2. In general, there are no therapies of airway clearance that have been demonstrated to be superior to others (B). |
| 3. For the individual, one form of airway clearance therapy may be superior to others. The prescription of airway clearance therapy should be individualized based on factors such as age, severity of pulmonary disease, patient preference, among others (consensus). |
| 4. Aerobic exercise is recommended for patients with cystic fibrosis as an adjunctive therapy for airway clearance and its additional benefits to overall health (B). |

*Respir Care*. 2009;54(6):733–750.

Recommendation Grade Definitions

A The Committee recommends the service. There is high certainty that the net benefit is substantial.

B The Committee recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.

C The Committee recommends against routinely providing the service. There may be considerations that support providing the service to an individual patient. There is moderate or high certainty that the net benefit is small.

D The Committee recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harm out weighs the benefits.

I The Committee concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.

The guidelines on ACTs make clear the importance of this aspect of routine treatment of patients with CF. The recommendations were based on the quality of the published evidence and the estimate of the net benefit demonstrated within those publications. These recommendations should be viewed as a guideline more than any of the others. The introduction and use of specific ACTs will depend on the individual, his or her social situation, and parental or patient preferences.

back to top

## PULMONARY GUIDELINES FOR PATIENTS WITH CF: PULMONARY EXACERBATIONS

Flume PA, Mogayzel PJ Jr, Robinson KA, et al; Clinical Practice Guidelines for Pulmonary Therapies Committee. **Cystic fibrosis pulmonary guidelines: treatment of pulmonary exacerbations.** *Am J Respir Crit Care Med.* 2009;180(9):802-808.

*(For non-subscribers to this journal, an additional fee may apply to obtain full-text articles.)*

View journal abstract View full article

CF lung disease is characterized by progressive decline in lung function, but there may be episodes of acute worsening of respiratory symptoms, often referred to as "pulmonary exacerbations." Although no generally applicable definition of a pulmonary exacerbation exists, typical clinical features include increased cough, increased sputum production, shortness of breath, chest pain, loss of appetite, loss of weight, and decrease in lung function (eg, forced expiratory volume in 1 second [$FEV_1$]). Pulmonary exacerbations are

associated with considerable morbidity, with an adverse impact on patients' quality of life and a loss of lung function that is not recovered. As many pulmonary exacerbations result in hospitalization, they are associated with a major impact on the overall cost of care as well. The identification of optimal treatment modalities for these events could produce significant improvements in quality and length of life in patients with CF. The CFF established the Pulmonary Therapies Committee to review published evidence and develop recommendations on common treatment methods for exacerbations. These guidelines were created using a systematic review of the literature to evaluate the evidence supporting therapies and approaches for the management of pulmonary exacerbations.

The committee was able to offer only a few specific recommendations. They recommended continuation of chronic medications and ACTs, as most of those studies included patients experiencing an exacerbation, and sufficient evidence was available to suggest that once-daily dosing of aminoglycosides is as safe and effective as is traditional dosing 2 to 3 times daily. The routine use of antibiotic synergy testing against *Pseudomonas* species was not recommended, as no benefit had been demonstrated; however, in certain situations, such information might prove useful, such as in patients who are not responding to conventional treatment or in those who are being evaluated for lung transplantation. The most notable finding of this review, however, is the limited amount of published evidence on other commonly used therapies. For example there are no studies that define the optimal duration of antibiotic therapy. Thus, most of the questions in this review resulted in an "I" recommendation—meaning that insufficient evidence was available from which to make a specific recommendation.

Guidelines typically demonstrate what we know from clinical studies, but there is value in making evident that which we do not know. This allows a determination of what studies should be conducted. Ultimately, some questions will not be answered, but others are so important that studies should be conducted to determine the optimal treatment strategy. From this review, important questions regarding pulmonary exacerbations remain unanswered, such as whether a patient should be treated in the hospital or at home, which combination of antibiotics is the most effective, and what is the optimal duration of antibiotic therapy. Given the frequency at which pulmonary exacerbations are diagnosed, these are questions for which answers should be available.

The committee did not attempt to define a pulmonary exacerbation, nor was there any discussion of the severity of such exacerbations. Perhaps the most important conclusion to be drawn from this review is the fact that a great need exists for a validated and accepted definition of a pulmonary exacerbation. Only then can we move forward with determining the optimal treatment for patients with CF.

| Treatment of Pulmonary Exacerbations | |
|---|---|
| Site of treatment (home vs. hospital) | I |
| Chronic medications | B* |
| Inhaled plus IV tobramycin | I |
| Airway clearance | B* |
| 1 vs. 2 antibiotics for *Pseudomonas* | I |
| Aminoglycosides: once daily vs. multidose | C |
| Continuous infusion ß-lactam antibiotics | I |
| Duration of antibiotics | I |
| Routine synergy testing | D |
| Corticosteroids | I |

Recommendation Grade Definitions

A The Committee recommends the service. There is high certainty that the net benefit is substantial.

B The Committee recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.

C The Committee recommends against routinely providing the service. There may be considerations that support providing the service to an individual patient. There is moderate or high certainty that the net benefit is small.

D The Committee recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harm out weighs the benefits.

I The Committee concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.

*Consensus recommendation (see previous guidelines)

back to top

## PULMONARY GUIDELINES FOR PATIENTS WITH CF: RESPIRATORY COMPLICATIONS

Flume PA, Mogayzel PJ Jr, Robinson KA, Rosenblatt RL, Quittell L, Marshall BC; Clinical Practice Guidelines for Pulmonary Therapies Committee. **Cystic fibrosis pulmonary guidelines: pulmonary complications: hemoptysis and pneumothorax.** *Am J Respir Crit Care Med.* 2010 Mar 18. [Epub ahead of print]

*(For non-subscribers to this journal, an additional fee may apply to obtain full-text articles.)*

View journal abstract View full article

As the airways disease associated with CF worsens, there is an increased likelihood of respiratory complications, particularly hemoptysis and pneumothorax. Hemoptysis is a common event in patients with CF and can vary in severity. Although the bleeding is typically scant, massive, life-threatening bleeding occurs in approximately 4% of all patients with CF. Approximately 3.5% of individuals with CF will experience a pneumothorax during their lifetime. The development of a pneumothorax is more common among older patients with advanced stages of pulmonary disease. The CFF established the Pulmonary Therapies Committee to review published evidence and develop recommendations on the treatment of patients with hemoptysis and pneumothorax. As there are no controlled trials to guide the treatment of either complication, the committee used the Delphi method to systematically determine the consensus opinions. The recommendations were developed using expert opinion from a panel of clinicians with broad experience treating patients with CF. Since there was no face-to-face interaction, the participants were blinded to other members of the panel, thus reducing the bias that

might be introduced into consensus guidelines. The panelists responded to questionnaires, and the summary of their responses was expressed as a statistical score so the clinician could see the degree of consensus for each recommendation.

The guidelines addressed practical considerations faced by clinicians who are treating patients with these CF-related complications. Important issues, such as who should be admitted to the hospital and when antibiotic therapy should be initiated, were addressed, as well as which diagnostic tests should be considered (bronchoscopy is not necessary for hemoptysis). Practical questions were addressed, including whether to continue ACTs and aerosolized medications—in summation, it depends. The patient with mild hemoptysis can continue with regular therapies, but if there is extensive bleeding, then some ACTs (eg, high-frequency chest compression) and aerosol medications (eg, hypertonic saline) should be withheld.

In patients experiencing hemoptysis, the increased amount of bleeding was more likely to invoke recommendations for hospital admission, use of antibiotics, and alteration of chronic therapies (eg, discontinuation of nonsteroidal anti-inflammatory drugs). For those in whom a pneumothorax developed, there was a strong tendency toward hospital admission and placement of a chest tube, with the exception being when a very small pneumothorax developed in a stable patient. Several therapies or activities should be avoided following a pneumothorax, such as bilevel positive airway pressure (BiPAP) ventilation, spirometry, air travel, and heavy exertion.

Although a strong consensus could be determined for many of the questions (eg, the patient with massive hemoptysis should be admitted to the hospital), for some questions a broad range of response existed, suggesting considerable disagreement (eg, the patient with a pneumothorax should be treated with antibiotics).

In conclusion, the guidelines on the management of common respiratory complications in patients with CF—that is, hemoptysis and pneumothorax—were developed by an expert panel using an approach that limited bias, as there are otherwise no controlled trials to guide treatment. These are practical recommendations that address the common issues faced by the clinician treating patients with CF.

**View table for Hemoptysis Statements and Panel Ratings**

**View table for Pneumothorax Statements and Panel Ratings**

**View table for Ratings of Withholding of Airway Clearance Therapies for Hemoptysis* and Pneumothorax****

**View table for Ratings of Withholding Aerosol Therapies for Hemoptysis* and Pneumothorax****

back to top

## GUIDELINES FOR THE MANAGEMENT OF INFANTS WITH CF

Borowitz D, Robinson KA, Rosenfeld M, et al. **Cystic Fibrosis Foundation evidence-based guidelines for management of infants with cystic fibrosis.** *J Pediatr.* 2009;155(6 suppl):S73-S93.

*(For non-subscribers to this journal, an additional fee may apply to obtain full-text articles.)*

View journal abstract View full article

CF has been added to the panel of diagnoses assessed as part of newborn screening. Therefore, it is expected that there will be a growing number of infants with CF who will be asymptomatic at the time of diagnosis, creating an opportunity for early intervention in the hopes of improved outcomes later in life. The CFF convened a committee of experts to provide a set of guidelines for the evaluation and treatment of infants with CF. As there are few controlled trials involving infants, these recommendations are derived from a consensus of experts.

A critical recommendation is that newly diagnosed infants should be evaluated and treated at an accredited CF care center, with the initial visit taking place within 72 hours of diagnosis. It is expected that this first visit would include comprehensive education regarding CF care, so the visit may involve up to 2 hours of direct interaction between the care team and the family. A strong association exists between nutritional health at 2 years of age and pulmonary function later in childhood, suggesting that improving the nutritional status of young children will result in better pulmonary outcomes. Thus, it is not surprising that most of the recommendations are related to nutritional assessment and treatment. These include an evaluation for pancreatic insufficiency and appropriate dosing recommendations on supplemental digestive enzymes and vitamins. A key recommendation is that the supplementation of table salt be initiated at diagnosis. As is often the case, there were some therapies for which insufficient evidence was available from which to derive a recommendation, such as supplementation with linoleic acid and docosahexaenoic acid.

Although many recommendations with respect to nutritional therapies were offered, there were fewer recommendations for pulmonary therapies. The recognition that lung disease can be present in the absence of symptoms has led to exploration of diagnostic testing, such as computed tomography (CT) chest scans and bronchoscopy with lavage. Although the guidelines did not support the routine use of these diagnostic tests, they nonetheless may prove useful in infants with symptoms or signs of lung disease who fail to respond to appropriate interventions. New acquisition of *Pseudomonas aeruginosa* should be treated with antibiotics regardless of the presence or absence of symptoms. Whereas evidence supports attempts to eradicate *Pseudomonas* species, no information is available on whether to take the same approach with methicillin-resistant *Staphylococcus aureus* (MRSA).

Some recommendations were consistent with the treatment of patients with CF of any age. These include annual influenza vaccination and the use of appropriate infection control measures, along with the additional recommendation that newly diagnosed patients should be separated from other patients treated in CF clinics until adequate infection control education has been provided to and is understood by the caregivers.

As suggested in an accompanying editorial, these guidelines will serve as a core component of quality improvement in CF centers, reducing the variability in practice patterns. An important addition to these guidelines is a section dedicated to primary care physicians, with the very important statement that life expectancy is steadily increasing as long as patients are receiving daily therapy. The recommendations were presented with a care grid that should function as an important instrument for both primary care physicians and CF specialists involved in the management of infants with CF.

**View table for Treatment Recommendations for Infants with Cystic Fibrosis**

back to top



Presented by JHUSOM and IJHN in collaboration with DKBmed.

**COMPLETE THE POST-TEST**

**Step 1.**
Click on the appropriate link below. This will take you to the post-test.

**Step 2.**
If you have participated in a Johns Hopkins on-line course, login. Otherwise, please register.

**Step 3.**
Complete the post-test and course evaluation.

**Step 4.**
Print out your certificate.

PHYSICIAN POST-TEST

NURSE POST-TEST

DIETICIAN POST-TEST

PHYSICAL THERAPIST POST-TEST

* (The post-test for the newsletter is 1 credit hour.)

**Respiratory Therapists**
Visit this page to confirm that your state will accept the CE Credits gained through this program or click on the link below to go directly to the post-test.

RESPIRATORY THERAPIST POST-TEST