PULMONARY DISEASE BOARD REVIEW MANUAL

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The Hospital Physician Pulmonary Disease Board Review Manual is a peer-reviewed study guide for fellows and practicing physicians preparing for board examinations in pulmonary disease. Each manual reviews a topic essential to current practice in the subspecialty of pulmonary disease.

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MANAGEMENT OF PULMONARY EXACERBATIONS AND COMPLICATIONS IN ADULTS WITH CYSTIC FIBROSIS

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NOTE FROM THE PUBLISHER:
This publication has been developed without involvement of or review by the American Board of Internal Medicine.
Management of Pulmonary Exacerbations and Complications in Adults with Cystic Fibrosis

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INTRODUCTION

Cystic fibrosis (CF) is the most common life-shortening autosomal recessive disease among Caucasian populations, with an incidence of 1 in 2000 to 3000 live births and a median survival of 36.8 years (95% confidence interval [CI], 34.7–40.3) in the United States, according to the Cystic Fibrosis Foundation 2011 Registry Report.1 Lung disease remains the most common cause of morbidity and mortality in CF patients, resulting from the progressive loss of lung function due to chronic infection and recurrent exacerbations. Therefore, prevention and appropriate treatment of pulmonary exacerbations are mainstays in the management of patients with CF to prevent morbidity and mortality.2–6

BACKGROUND

DEFINITION OF EXACERBATION

Although pulmonary exacerbation is a common complication in CF patients, a standard definition of what an exacerbation entails has not been established within the CF community. There is significant variation in the diagnosis and management of exacerbations between CF centers in the United States, and even between physicians from the same center. Furthermore, a single physician can demonstrate significant inconsistency in treatment strategies and diagnosis over time.7,8 The European Consensus Group for Cystic Fibrosis defines CF exacerbation as the need to provide additional antibiotic therapy due to a recent change in at least 2 of the following clinical parameters: change in sputum volume or color; increased cough; increased dyspnea; increased malaise, fatigue, or lethargy; anorexia or weight loss; decrease in pulmonary function by at least 10% or radiographic changes.9 This definition is well accepted and is often used in clinical trials. However, it fails to address the degree of symptom severity, which may influence the patient’s perceptions of the event and the type of prescribed therapy as well as the duration and route of administration of therapy.5,10,11

A continually growing area of interest and research in CF is the use of biomarkers of inflammation to define and monitor CF exacerbations. A great variety of biomarkers in the serum, sputum, urine, and breath condensate have been described, but their routine clinical use is still limited.6,8,12–17
IMPACT OF EXACERBATIONS

Pulmonary exacerbations are associated with decreased survival, lung function deterioration, impaired quality of life (poor sleep, missed work/school, family dislocation, impaired neurobehavioral functioning), and increased health care cost.8,18–26 A recent study suggested that 50% of lung function decline in CF patients can be attributed to pulmonary exacerbations.27 Moreover, up to 25% of patients with CF exacerbation do not recover their lung function to baseline levels after 3 months of therapy.25–28

While the frequency of exacerbations contributes directly to declining lung function, it may also be an indicator of an underlying CF genotype and immune dysregulation that predispose patients to persistent infection, lung inflammation, and more rapid decline in lung function compared to other patients. This has been suggested by studies showing that in some patients lung function continues to deteriorate even after the pathogen causing the exacerbation has been eradicated.29 Studies looking at the characteristics of Pseudomonas aeruginosa isolates failed to show any difference between the isolates from patients who were successfully treated with eradication therapy versus those in whom eradication therapy failed. This suggests that the interaction between host immune response and the pathogen may play a major role in the propensity of some CF patients for persistent and recurrent infections.30

PATHOPHYSIOLOGY OF EXACERBATION

The pathogenesis of CF exacerbation has not been completely elucidated. A widely accepted theory hypothesized that exacerbations are caused by the clonal expansion of a single dominant pathogen causing an increase in the load or change in the phenotype of the bacteria colonizing the airways.31–35 This theory has been questioned by recent studies showing discordance between the microbiological susceptibility and the clinical and bacteriological response to antibiotic therapy in CF patients with exacerbations.36,37 Furthermore, there is no significant change in the bacterial load in the sputum prior to and during an exacerbation in some CF patients.37,38 The polymicrobial nature of the airways of patients with CF as well as dynamic interactions within the airways suggests a more complex model is needed to explain the mechanism behind the CF exacerbation.39 The bacterial community colonizing the CF airways, or microbiome, is unique to each patient and can vary spatially and temporally.40–42 A misbalance in the airway microbiome has been hypothesized recently to play a major role in the pathogenesis of CF exacerbations and worsening of the disease.6,8,43–45 However, the relationship between microbiome diversity and lung function is still poorly understood and currently an active area of investigation.

There is growing evidence of dynamic synergy between different pathogens (virus, bacteria, fungi) of the CF airway microbiome. The interaction between these pathogens is influenced by the CF genotype, patient immunity, and environmental factors. Animal models have shown that when bacteria not pathogenic by themselves (commensal microbiota) are cultured in the presence of Pseudomonas aeruginosa, they act synergistically by increasing inflammation and worsening disease severity without a change in the bacterial load of the pathogenic species.46,47 In addition, the majority of pathogens present in the CF airway microbiome are not readily cultured by standard techniques,43,48 suggesting that we usually underestimate the co-colonization of other important bacteria species.43 These findings would explain
why some CF patients improve with antibiotics in spite of the presence of resistant pathogens in the sputum. Perhaps in these patients the antibiotics exert their action by eradicating unrecognized synergistic bacteria of the microbiome.49,50

**MANAGEMENT**

**PREVENTION OF EXACERBATION**

**Antibiotic Therapy**

The initial *Pseudomonas aeruginosa* colonization/infection of the airways of CF patients eventually results in persistent chronic colonization and infection, which is associated with significant increased risk of exacerbations, more severe lung inflammation, and lung function decline.2,51 Antibiotic eradication therapy (AET) and suppression therapy with inhaled antibiotics are relatively new interventions that have become the standard of care in the management of the CF patients.2,52 Evidence suggests that both AET and suppression therapy decrease the risk of CF exacerbations and delay the decline of lung function.29,53–57 AET consists of treating CF patients with antibiotics for approximately 28 days as soon as they become colonized with *Pseudomonas aeruginosa* in the hope of complete eradication. Several antibiotic regimens have been studied, including inhaled, oral, and intravenous therapy, with similar efficacy (average rate of success of 81.2%).2,58–62 The success rate of AET may decrease if the *Pseudomonas aeruginosa* infection is left untreated for more than 12 weeks.63,64

Once AET fails and chronic *Pseudomonas aeruginosa* infection develops, the risk for pulmonary exacerbations increases and the strategy shifts to suppressive therapies. For those patients in whom AET fails and who develop chronic *Pseudomonas aeruginosa* infection, the CF pulmonary guidelines recommend chronic suppressive antibiotic therapy with inhaled tobramycin or aztreonam (both with formulations that are approved by the US Food and Drug Administration and have more evidence supporting their use).2,52,55–57,65–67 The best schedule for administering this therapy remains unclear: one month-on one month-off schedule versus continuous therapy with one drug or alternating agents.

Chronic therapy with azithromycin in CF patients aged 6 years and older with chronic *Pseudomonas aeruginosa* infection has been shown to be associated with a 50% decrease in the rate of exacerbations.68,69 Due to concerns about an increased rate of nontuberculous mycobacteria (NTM) infection resistance, it is recommended that patients should be screened for NTM before initiating azithromycin therapy, and reassessed at 6- to 12-month intervals. In addition, this monotherapy should be withheld in those infected with NTM.52

**Airway Clearance**

Airway clearance is an integral component of the long-term management of CF patients with or without chronic *Pseudomonas aeruginosa* infection to improve lung function and prevent exacerbations. A variety of pharmacologic and nonpharmacologic methods are available for airway clearance. The CF pulmonary guidelines recommend the long-term use of dornase alfa and inhaled hypertonic saline to improve lung function, improve the quality of life, and reduce exacerbations in CF patients.52 Among the nonpharmacologic methods for promoting airway clearance, some require mechanical devices, while others utilize physical manipulation of the chest (eg, physiotherapy). Conventional chest physiotherapy through the assistance of a caregiver is the current standard of care for achieving airway clearance, particularly in young patients. As patients with CF live longer, there is a need for patients to be able to perform airway clearance independently.
There are at least 3 classes of independent airway clearance devices: positive expiratory pressure devices, airway oscillating devices (either handheld or stationary), and high-frequency chest compression/mechanical percussion devices. Until recently, there was insufficient evidence to suggest superiority between any of the airway clearance techniques. However, a recent prospective multicenter randomized controlled study in Canada showed that positive expiratory pressure may prevent more exacerbations than high-frequency chest wall oscillation via a vest in CF patients ages 6 years and older.

**Exercise**

Exercise has become an important component in the chronic management of CF patients. Exercise intolerance is well established in this population. It is mainly related to impaired lung function (especially those with severe disease) as well as poor nutritional status and low muscle mass, although other factors such as muscle dysfunction, CF genotype, and physical activity (which is influenced by a variety of psychosocial factors, such as gender and parental involvement) may also influence exercise capacity in CF patients. Exercise intolerance is dependent on the progression of the disease and may have a significant role as a prognostic indicator of lung function decline, quality of life, and survival in CF patients. Exercise training programs may be a useful therapeutic strategy to improve not only physical fitness and exercise capacity in CF patients, but also to improve airway clearance, quality of life, and lung function preservation and decrease the rate of hospitalization. Exercise training is thought to have a positive impact on nonpulmonary complications from CF, such as bone mineral density and CF-related diabetes.

Despite the evidence suggesting that exercise may be beneficial in CF patients, there are no studies showing that exercise training prolongs survival in this population. There is also no consensus about the best exercise training modality: aerobic versus anaerobic or a combination thereof. Unfortunately, there have not been any successful strategies to increase participation of CF patients in exercise training and maintain their adherence to it (the adherence rate of CF patients to exercise training ranges between 24% and 57%). The recommendations for exercise training in CF patients at this time are based on extrapolations from small studies as well as an understanding of the physiological mechanism of exercise and clinical reasoning. The incorporation of exercising training as part of the chronic management of CF patients should be individualized and take into consideration the patient's age, physical fitness, nutritional status, disease severity, and potential barriers to adherence such as burden of therapy, lack of information about the benefits of exercise, and lack of parental involvement.

**TREATMENT OF EXACERBATION**

The management of CF exacerbations should include the participation of the CF multidisciplinary team including physicians, nurses, respiratory therapists, social workers, pharmacists, and dietitians. In addition to appropriate antibiotic therapy, the therapeutic strategy should focus on airway clearance, nutrition support, drug monitoring, physical therapy, and detection and management of other complications such as CF-related diabetes.

The Cystic Fibrosis Foundation recommends that CF patients receiving chronic treatment with dornase alfa and hypertonic saline, macrolide therapy, and bronchodilators should continue and intensify these therapies during the course of an exacerbation. With regard to the chronic inhaled antibiotic therapy, there is no evidence that continuing inhaled antibiotics in addition to systemic
antibiotic therapy offers any benefit during CF exacerbations.102 Despite the lack of evidence, physicians usually prescribe and continue inhaled antibiotics in up to 25% of CF exacerbations, often to maintain the therapeutic routine for the patient.2,103 Nevertheless, caution must be taken with this strategy since some inhaled antibiotics can be absorbed systemically, leading to an increase in the levels of the systemically administered drugs. This increase in drug levels can result in an increased risk of drug toxicity and affects the interpretation of the serum drug monitoring levels. This is particularly relevant with aminoglycosides, as described by Stenbit and colleagues,104 where up to 45% of trough tobramycin concentrations were significantly influenced by the timing of administration of the inhaled dose, leading to either the under dosing of the systemically administered drug or changing the administration interval.

Setting: Inpatient or Outpatient?

Once the diagnosis of CF exacerbation is established, the next step in the management of these patients is to select the setting in which the treatment will be administered. Studies addressing clinical and quality of life outcomes based on the setting of treatment have shown conflicting results, with some favoring in-hospital therapy versus home therapy,105–109 while others showed no difference between settings.110 The decision should be individualized, and it should take into consideration the severity of the exacerbation, the need for intravenous therapy, the patient’s adherence, need for drug monitoring and diabetes control, as well as the social and logistical support of the patient at home. The Cystic Fibrosis Foundation guidelines recommend against the nonhospital setting unless the resources and support at home are equivalent to those in the hospital setting.6,10

Route of Antibiotics: Inhaled versus Systemic (Oral and Intravenous)

During an exacerbation, there is increased inflammation along with increased vascular permeability and production of mucus plugs, often causing obstruction of the small airways. Because of this airway obstruction, inhaled antibiotic therapy would only be delivered to the large airways without reaching the distal portions of the bronchial tree. Based on this rationale, systemic administration (either oral or parenteral) is preferred. The use of inhaled antibiotics as adjuvant to systemic therapy is still controversial since it has not been shown to improve outcomes.102

Oral therapy for CF exacerbations can avoid hospitalization and cost less than intravenous therapy, and may cause less impairment of the patient’s quality of life. Some studies suggest that CF patients with mild exacerbations caused by methicillin-resistant Staphylococcus aureus (MRSA),111–113 Pseudomonas,114,115 and other bacteria like Haemophilus influenzae116–119 can be successfully treated with oral regimens, avoiding the need for intravenous antibiotics in up to 73.8% of patients.120 However, the evidence supporting the use of oral antibiotics in mild CF exacerbations is still scarce.121 Unfortunately, the difference between mild and severe exacerbation has yet to be clearly defined. Thus, the decision to use oral antibiotics should be individualized on a case-by-case basis and take into consideration the severity of the exacerbation, the underlying lung function, microbiological susceptibility patterns, nutritional status and oral tolerance, patient’s adherence, and the logistical support at home to provide the other essential components of the CF exacerbation management (eg, airways clearance, diabetes control).6 If symptoms worsen or new symptoms develop while undergoing oral therapy, intravenous antibiotic administration should be promptly considered.
Choice of Antibiotic: Microbiology and Role of Antibiotic Susceptibility Testing

For many years a group of bacteria including *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Haemophilus influenzae*, *Burkholderia* species like *B. cenocepacia*, *Stenotrophomonas maltophilia*, and *Achromobacter xylosoxidans* were thought to be the main etiologic pathogens causing CF exacerbations. As our understanding of the pathogenesis of CF exacerbation and airway microbiome continues to improve, we have learned that CF exacerbations can also be caused by other pathogens such as virus (eg, influenza A and B, rhinovirus, respiratory syncytial virus), NTM, fungus (mainly *Aspergillus*), and bacteria other than the organisms described above, including the normal oral flora. Also, rather than one predominant pathogen causing the exacerbation, it seems that the complex interaction between the host immunity, environmental factors, and multiple organisms acting synergistically cause a misbalance of the CF airway microbiome, resulting in a CF exacerbation.43

Traditionally, the selection of antibiotic therapy for CF exacerbations was based on the results of antibiotic susceptibility testing from the CF airway microbiome. However, there are 2 caveats to this approach. First, several studies have shown poor correlation between in vitro susceptibility data and clinical outcome after systemic antibiotic therapy for CF exacerbation.122,123 Parkins and colleagues described a rate of success of 57% in treating CF exacerbations, even when the *Pseudomonas aeruginosa* from the airway cultures were resistant to the antibiotic administered.124 Second, most of the standard culture methods utilized in hospitals are unable to cultivate a significant number of pathogens present in the CF airway microbiome.43,48 These findings have challenged the previous practice of selecting antibiotics based on the results from in vitro microbiological susceptibility. The Cystic Fibrosis Foundation guidelines recommend selecting antibiotics based on previously successful response to antibiotics during CF exacerbations. It is still reasonable to perform an airway culture to select the spectrum of bacteria to be covered. Microbiological antibiotic susceptibility testing is still advised when patients fail to improve while on antibiotic therapy and a change in the antibiotic regimen is required.6,10

For the treatment of *P. aeruginosa*, the Cystic Fibrosis Foundation guidelines recommend double therapy, since there is not sufficient evidence showing that monotherapy is equivalent to dual therapy for this pathogen. If aminoglycosides are chosen, once-daily dosing is preferable to 3-times daily dosing.10 In general, the first line of treatment is a beta-lactam antibiotic in addition to an aminoglycoside. Often when this combination is no longer effective a carbapenem can be substituted for the beta-lactam, or alternatively an extended-spectrum penicillin such as piperacillin/tazobactam can be used.

The Cystic Fibrosis Foundation guidelines recommend against synergy testing as part of the routine evaluation of patients with CF exacerbation.10

Duration of Antibiotic Therapy

There are no clear guidelines on the optimum duration of antibiotic therapy for CF exacerbations. The average duration of therapy in CF exacerbation is 10 to 14 days. Although shorter duration of therapy would improve quality of life and compliance as well as reduce the incidence of side effects and the cost, it may also be insufficient to clear the infection and may cause early recurrences.125 The CF pulmonary guidelines recommend that the duration of therapy should be decided based on clini-
cal response rather than microbiology data. Ideally, therapy should be continued until patients achieve resolution of symptoms and restoration of lung function, but therapy should not exceed 3 weeks.\textsuperscript{2,10} Collaco and colleagues demonstrated that the improvement of forced expiratory volume in 1 second (FEV1) in patients with CF exacerbations usually plateaus after 6 to 10 days of therapy,\textsuperscript{110} although often patients, their parents, and treating physicians feel that a third week of therapy would be beneficial.\textsuperscript{126}

Approximately 25% of patients do not improve in spite of adequate antibiotic therapy. In these cases, multidrug-resistant \textit{Pseudomonas} and MRSA,\textsuperscript{112} NTM, and allergic bronchopulmonary aspergillosis should be suspected and aggressively treated if confirmed. These patients usually need longer periods of antibiotic therapy. Other factors associated with treatment failure include very advance airway disease, the use of enteric feed, presence of CF-related diabetes and liver disease, low socioeconomic status, and elevated markers of inflammation.\textsuperscript{120,124}

\textbf{Nutrition and Glucose Control}

CF patients with a pulmonary exacerbation have an increase in energy expenditure and consequently increased nutritional need.\textsuperscript{127} The lack of appetite due to worsening dyspnea and other symptoms like nausea, vomiting, and abdominal discomfort can further complicate the ability of patients to meet their nutritional requirements. In addition, patients with CF-related diabetes have an increase in insulin demand during an exacerbation,\textsuperscript{128} and even those with normoglycemia showed impaired glucose tolerance during exacerbations.\textsuperscript{129} Nutritional support and good blood glucose management are essential components in the treatment of a CF exacerbation.

\textbf{Oxygen Therapy and Noninvasive Ventilation}

There are no well-designed studies to guide the prescription of chronic oxygen supplementation in CF patients with advanced lung disease. According to a recent systematic review, short-term oxygen therapy during sleep and exercise improve oxygenation, although it may be associated with mild hypercapnia. Short-term oxygen improves exercise duration, time to fall asleep, and regular attendance at school or work. However, it remains unclear what the best schedule for oxygen supplementation therapy is: continuous versus during exercise or sleep or both.\textsuperscript{130}

Another modality that is used in advanced lung disease is noninvasive ventilation. The impact of noninvasive ventilation on pulmonary exacerbations and disease progression has not been clearly defined. Noninvasive ventilation may be a useful adjunct to other airway clearance techniques, particularly in CF patients who have difficulty expectorating sputum. When used in addition to oxygen, noninvasive ventilation may improve gas exchange during sleep to a greater extent than oxygen therapy alone in CF patients with moderate to severe disease.\textsuperscript{131}

\textbf{Exercise and Physical Therapy}

Even though exercise has become an essential component of the chronic management of CF patients, little is known about exercise as part of the therapy in acute exacerbations. In a randomized controlled study involving children admitted to the hospital due to a pulmonary exacerbation, children who underwent in-hospital aerobic and anaerobic exercise training had significantly better aerobic capacity, activity levels, quality of life, weight gain, lung function, and muscle strength than children in the placebo control group at the time of discharge and for at least 1 month after discharge.\textsuperscript{132} Physi-
cians should be aware that CF patients have much higher energy expenditure and nutritional requirement at rest and during exercise compared to normal patients. Moreover, due to the high sodium and chloride concentration in the sweat and abnormal thirst stimulus, CF patients are more prone to dehydration during exercise and heat stress. Thus, adequate nutrition and fluid electrolyte replacement should be guaranteed for CF patients undergoing exercise training programs, especially during acute exacerbations.

OTHER PULMONARY COMPLICATIONS

PNEUMOTHORAX

Spontaneous pneumothorax is a pulmonary complication in the CF population, with up to 3.4% of CF patients experiencing an episode of spontaneous pneumothorax during their lifetime. The incidence of spontaneous pneumothorax increases as lung function declines, with 75% of events occurring in patients with FEV1 less than 40% predicted. After an episode of pneumothorax, the risk of a subsequent unilateral and contralateral pneumothorax is approximately 50% to 90% and 46%, respectively. Given the correlation of spontaneous pneumothorax with poor lung function, it is not surprising that 72.4% of spontaneous pneumothorax cases occur in adult patients. The occurrence of spontaneous pneumothorax remains a prognostic factor of poor outcome, with a 2-year mortality rate of 48.6%.

The most likely mechanism underlying the pathogenesis of spontaneous pneumothorax appears to be air trapping within alveoli due to mucus plugging in the airways. When the alveolar pressure exceeds the interstitial pressure, air moves into the interstitium, traveling to the hilum (pneumomediastinum), and eventually rupturing into the mediastinal pleura. Spontaneous pneumothorax arising from the rupture of blebs in the visceral pleural are a less common mechanism of pneumothorax, evidenced by the poor correlation between blebs or cysts and the incidence of spontaneous pneumothorax in CF patients.

In addition to poor lung function, other factors associated with an increased risk of the development of a spontaneous pneumothorax are airway infection by Pseudomonas (odds ratio [OR], 2.27; 95% CI, 2.07–2.49) and Burkholderia (OR, 1.78; 95% CI, 1.52–2.10); allergic bronchopulmonary aspergillosis (OR, 1.48; 95% CI, 1.20–1.81); chronic therapy with dornase alfa (OR, 2.05; 95% CI, 1.48–2.85) and inhaled tobramycin (OR, 1.60; 95% CI, 1.20–2.14); pancreatic insufficiency (OR, 1.39; 95% CI, 1.17–1.65); and tube feeds (OR, 1.68; 95% CI, 1.49–1.90).

The clinical presentation and diagnosis of spontaneous pneumothorax are similar in CF patients and in non-CF patients. However, physicians should be aware that in some CF patients the chest radiograph fails to provide the diagnosis of spontaneous pneumothorax because of the presence of pleural adhesions, which prevents collapse of the lung. In these cases, chest computed tomography will demonstrate a loculated pneumothorax.

In 2010, the Cystic Fibrosis Foundation published guidelines for the management of CF patients with spontaneous pneumothorax. It is recommended that patients with a small pneumothorax (<5 cm) and without significant clinical compromise can be managed by outpatient observation or small catheter aspiration. Therapy with dornase alfa and inhaled tobramycin, as well as airway clearance techniques, should not be discontinued, with the exception of positive pressure ventilation and intrapulmonary percussive ventilation. CF patients with
a large pneumothorax (>5 cm) or significant clinical compromise should be hospitalized and managed with chest tube placement. The guidelines do not recommend withholding dornase alfa and inhaled tobramycin in these patients, but recommend discontinuing airway clearance therapy. Pleurodesis should be reserved for patients who fail to improve with chest tube placement (around 37%) or those with recurrent large pneumothorax. Surgical pleurodesis is preferred over chemical medical, unless the patient is unable to tolerate surgery.

HEMOPTYSIS

The expectoration of blood is a common pulmonary complication in CF patients. Most patients will have a scant (<5 mL) or mild episode (≥5 mL), but up to 4.1% of CF patients will have an episode of massive hemoptysis (≥500 mL of expectorated blood over a 24-hour period or bleeding at a rate ≥100 mL/hour) during their lifetime. The 2010 Cystic Fibrosis Foundation guidelines also included recommendations for the management of CF patients with hemoptysis. The guidelines recommend that CF patients should contact their health care provider even with scant episodes of hemoptysis. Those with massive hemoptysis should always be hospitalized as this complication could be life-threatening. Because hemoptysis should be considered a result of infection and a manifestation of pulmonary exacerbation, the guidelines recommend that CF patients with at least mild hemoptysis should receive antibiotics. For episodes of scant hemoptysis, there is no consensus about the need to start antibiotic therapy.

Because of the concern that airway clearance therapy can impair the ability to stabilize clot formation, the guidelines recommend withholding these techniques during massive hemoptysis. They can be continued in patients with scant hemoptysis, however. For those with mild hemoptysis, there is no consensus for an official recommendation. The guideline recommends withholding the use of hypertonic saline in cases of massive hemoptysis. There was no consensus to make an official recommendation in relation to the therapy with dornase alfa and inhaled antibiotics in these patients, nor about the need to withhold inhaled therapy in patients with mild to moderate hemoptysis. For those with scant hemoptysis, the guideline recommends continuing inhaled therapy.

While most episodes of hemoptysis in CF patients will stop spontaneously, some patients will have persistent bleeding. These patients should be evaluated for bronchial artery embolization therapy. Bronchoscopy is not mandatory prior to this therapy.

CONCLUSION

Pulmonary exacerbations are common events during the course of CF, and they are associated with progressive lung function decline, poor nutritional status, impaired quality of life, and increased health care cost. However, there is a lack of consensus in how to define a CF exacerbation and determine its severity. The pathogenesis of CF exacerbation is also still poorly understood. The management of CF exacerbations should include the participation of the CF multidisciplinary team. The therapeutic strategy should take into consideration the severity of the exacerbation, the need for intravenous therapy, patient’s adherence, drug monitoring, diabetes control, as well as the social and logistical support of patients at home. Specific recommendations have been published by the Cystic Fibrosis Foundation about the management of other pulmonary complications in CF patients, such as spontaneous pneumothorax and hemoptysis.
Pulmonary Exacerbations and Complications in Cystic Fibrosis

BOARD REVIEW QUESTIONS
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