

Cystic Fibrosis Pulmonary Guidelines Pulmonary Complications: Hemoptysis and Pneumothorax

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Rationale: Cystic fibrosis (CF) is a recessive genetic disease characterized by dehydration of the airway surface liquid and impaired mucociliary clearance. As a result, individuals with the disease have difficulty clearing pathogens from the lung and experience chronic pulmonary infections and inflammation. There may be intermittent pulmonary exacerbations or acute worsening of infection and obstruction, which require more intensive therapies. Hemoptysis and pneumothorax are complications commonly reported in patients with cystic fibrosis.

Objectives: This document presents the CF Foundation's Pulmonary Therapies Committee recommendations for the treatment of hemoptysis and pneumothorax.

Methods: The committee recognized that insufficient data exist to develop evidence-based recommendations and so used the Delphi technique to formalize an expert panel's consensus process and develop explicit care recommendations.

Measurements and Main Results: The expert panel completed the survey twice, allowing refinement of recommendations. Numeric responses to the questions were summarized and applied to a priori definitions to determine levels of consensus. Recommendations were then developed to practical treatment questions based upon the median scores and the degree of consensus.

Conclusions: These recommendations for the management of the patient with CF with hemoptysis and pneumothorax are designed for general use in most individuals but should be adapted to meet specific needs as determined by the individuals, their families, and their health care providers. It is hoped that the guidelines provided in this manuscript will facilitate the appropriate application of these treatments to improve and extend the lives of all individuals with cystic fibrosis.

Keywords: cystic fibrosis; hemoptysis; pneumothorax; complications; guidelines

Cystic fibrosis (CF) is a complex genetic disease affecting many organs, although 85% of the mortality results from lung disease (1). The natural history of the lung disease consists of early and persistent infection (2), an exaggerated inflammatory response (3, 4), and progressive airways obstruction, ultimately resulting in respiratory failure. As airways disease worsens, there is an

increased likelihood of respiratory complications, such as hemoptysis and pneumothorax.

Hemoptysis is common in patients with CF; a retrospective review reported 9.1% of patients had hemoptysis in a 5-year period (5). The bleeding, most commonly, is scant to moderate, but massive, life-threatening bleeding can occur. Approximately 4.1% of all patients with CF will suffer massive hemoptysis during their lifetime, and the average annual incidence is 0.87%, or 1 in 115 patients per year (6). The average annual incidence of pneumothorax is 0.64%, or 1 in 167 patients per year (7). Approximately 3.4% of individuals with CF will experience a pneumothorax during their lifetime (7). Both of these complications occur more commonly in older patients with advanced disease (REF).

Appropriate care and management of CF lung disease increase the quality and length of life of individuals with CF. This document represents the Pulmonary Therapies Committee recommendations for the treatment of hemoptysis and pneumothorax. The committee recognized that insufficient data exist to develop an evidence-based document based on a systematic review of the literature. Therefore, the committee chose the Delphi method (8) to formalize an expert panel's consensus opinion and develop explicit care recommendations with a minimum of bias. These guidelines are designed for general use in most individuals with CF but should be adapted to meet specific needs as determined by the individuals, their families, and their health care providers.

METHODS

The guideline development process used a strategy similar to one previously described (9), using the Delphi method to determine and quantify group consensus (10). This method allows for anonymity as there is no face-to-face interaction and participants are blinded to other members of the panel. The panelists responded to questionnaires and the summary of responses was communicated to other participants expressed as a statistical score. The results of the questionnaire are expressed using explicit rules that quantify the level of consensus and the appropriateness of management recommendations (11).

Guideline Development Committee and Expert Panel Members

The CF Foundation Pulmonary Therapies Committee consists of a multidisciplinary group, including representatives of physicians, nursing, respiratory therapy, physical therapy, pharmacy, CF families, and CF Foundation staff. The committee generated the questions for the surveys, but they did not participate in the surveys. The committee selected an expert panel, which consisted of 42 CF clinicians, 6 interventional radiologists, and 7 lung transplantation surgeons (see member list before beginning of the REFERENCES). Because these complications occur in less than 5% of patients, the committee

(Received in original form February 2, 2010; accepted in final form March 17, 2010)

Supported by the Cystic Fibrosis Foundation.

* A complete list of members may be found at the end of the article.

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Am J Respir Crit Care Med Vol 182, pp 298–306, 2010

Originally Published in Press as DOI: 10.1164/rccm.201002-0157OC on March 18, 2010
Internet address: www.atsjournals.org

TABLE 1. QUESTIONNAIRE DEFINITION OF TERMS

Term*	Definition†
Perfect consensus	All respondents agree on an answer
Very good consensus	Median and middle 50% (IQR) of respondents are found at one integer (e.g., median and IQR are both at 8) or 80% of respondents are within one integer of the median (e.g., median is 8, 80% of respondents are from 7–9).
Good consensus	50% of respondents are within one integer of the median (e.g., median is 8, 50% of respondents are from 7–9) or 80% of respondents are within two integers of the median (e.g. median is 7, 80% of respondents are from 5–9).
Some consensus	50% of respondents are within two integers of the median (e.g., median is 7, 50% of respondents are from 5–9) or 80% of respondents are within three integers of the median (e.g., median is 6, 80% of respondents are from 3–9)
No consensus	All other responses

Definition of abbreviation: IQR = interquartile range.

* Derived from Reference 12.

† Definitions refer to Likert scale for responses.

recruited panel members from larger CF centers, as they were more likely to provide care for the greatest number of patients with these complications. Panel members were also selected to achieve a balanced regional distribution.

Literature Search

A MEDLINE literature search of English language articles was performed for the period from 1985 to 2009. Searches were conducted using the MeSH headings of “hemoptysis” or “pneumothorax” combined with the terms “randomized controlled trials,” “meta-analysis,” and “guidelines.” Recent review articles were searched for additional randomized controlled trials. A reference list of the retrieved articles was distributed to panel members.

Delphi Questionnaire

The committee organized the questionnaire around key clinical questions facing clinicians in the setting of a patient with CF with hemoptysis or pneumothorax. Panel members were asked to respond to the appropriateness of each statement using a Likert scale ranging from 0 (completely disagree) to 9 (completely agree, pneumothorax) or 10 (completely agree, hemoptysis). The experts were allowed to skip statements by indicating that they did not have sufficient knowledge or experience to respond. Panel members were provided opportunity to comment or cite literature in support of their opinions or to suggest alternate wording for the statement.

Administration of the Questionnaire

The internet-based Delphi questionnaire was submitted to expert panel members, who were requested to complete it within 2 weeks. After the results were analyzed by the committee, the questionnaire was refined and resubmitted to the expert panel. This second questionnaire excluded items for which consensus recommendations were clear. Some items were repeated, accompanied by a summary of the panel members’ original responses (median responses, middle 50% range, and the range for all responses) and a synopsis of the panel members’ comments. Finally, some items that were determined to be ambiguous were refined. The expert panel was again given 2 weeks to complete the questionnaire.

Description of Level of Consensus

Numeric responses to the questionnaire items were summarized and applied to *a priori* definitions to determine levels of consensus (Table 1) (12). Management recommendations were based on the ratings and the degree of consensus (Table 2) (12).

RESULTS

Summaries of the final statements put to the expert panel and the results of their ratings, including the degree of consensus, are shown in Tables 3–6. For these questions we used explicit definitions of complications. The quantity of hemoptysis was defined as scant (<5 ml), mild-to-moderate hemoptysis

(5–240 ml), and massive when more than 240 ml, consistent with previously published guidelines (6, 13, 14). The size of the pneumothorax was defined by the distance between the apex and cupola, and described as either small (≤ 3 cm) or large (> 3 cm), consistent with previously published guidelines (12). However, we appreciate that the size of the pneumothorax may not reflect the pressure under which it resides outside the lung, as CF lungs may not collapse as readily as healthy lungs.

Hemoptysis

When should the patient with hemoptysis contact their health care provider?

Recommendation: The patient with *at least mild* hemoptysis (≥ 5 ml) should contact their health care provider.

Recommendation: The patient with *scant* hemoptysis (<5 ml) should contact their health care provider if it is the first-ever episode or if it is persistent.

Because hemoptysis is a common occurrence in patients with CF, the committee tried to determine the threshold amount of bleeding that should prompt communication with a health care provider. Several panel members believed the bleeding volumes in the definitions were too broad, suggesting they had a higher threshold for the amount of bleeding that should warrant communication with the CF center. Nonetheless, they still believed that 5 ml was a sufficient amount to suggest that an acute problem existed and treatment may be warranted. The panel expressed perfect consensus that all patients with massive hemoptysis should contact their health care provider.

The panel did not report the same concern regarding communication with patients with scant hemoptysis, and no

TABLE 2. MANAGEMENT DEFINITIONS

Management Recommendation	Median* (Middle 50% Range)
Preferred management in most circumstances	7–10 (7–9)
Acceptable management in many circumstances	7–10 (4–9)
Acceptable management in certain circumstances	4–6 (4–9)
Acceptable management in rare circumstances	2 and 3 (1 to ≤ 4)
Inappropriate management	(1–3)
No management recommendation	All other median and range combination, including “no consensus”

Definitions are derived from Reference 12.

* Median scores for responses to questionnaire items asking for ranking of appropriateness are given on a scale of 0 to 9 (pneumothorax) or 0 to 10 (hemoptysis).

TABLE 3. HEMOPTYSIS STATEMENTS AND PANEL RATINGS

Statements	Median	IQR	Consensus
The patient with <i>scant</i> hemoptysis should contact a health care provider.	3	2–7	Some
The patient with <i>a first episode of scant</i> hemoptysis should contact a health care provider.	7	5–9	Some
The patient with <i>persistent scant</i> hemoptysis should contact a health care provider.	7	5–10	Some
The patient with <i>mild-to-moderate</i> hemoptysis should contact a health care provider.	10	8–10	Good
The patient with <i>massive</i> hemoptysis should contact a health care provider.	10	10–10	Perfect
The patient with <i>scant</i> hemoptysis should always be admitted to the hospital.	0	0–1	Very good
The patient with <i>mild-to-moderate</i> hemoptysis should always be admitted to the hospital.	5	3.75–7.25	Some
The patient with <i>massive</i> hemoptysis should always be admitted to the hospital.	10	10–10	Perfect
The patient with <i>scant</i> hemoptysis, but no other features of an acute pulmonary exacerbation, should always be treated with antibiotics.	3	2–5	Good
The patient with <i>mild-to-moderate</i> hemoptysis should always be treated with antibiotics.	9	8–9	Very good
The patient with <i>massive</i> hemoptysis should always be treated with antibiotics.	10	9–10	Very good
The patient with <i>scant</i> hemoptysis should stop NSAIDs.	7	3.75–8	Good
The patient with <i>mild-to-moderate</i> hemoptysis should stop NSAIDs.	9	8–10	Good
The patient with <i>massive</i> hemoptysis should stop NSAIDs.	10	10–10	Very good
The patient who presented with <i>massive</i> hemoptysis and who is <i>clinically stable</i> but is no longer coughing up blood should always be treated with BAE.	4	2–8	None
The patient with <i>massive</i> hemoptysis who is <i>clinically unstable</i> should always be treated with BAE.	9	8–10	Very good
All patients with hemoptysis should have a CT of the chest before BAE.	4	2–6	Some
All patients with hemoptysis should undergo bronchoscopy before BAE.	1	0–2	Very good
For BAE, only the suspected or known bleeding vessel should be embolized.	7	2–8.75	Some
For BAE, all abnormal (dilated and tortuous) vessels should be embolized (bilaterally).	6.5	3–9	None
For the patient with <i>scant</i> hemoptysis and who is using BiPAP as a chronic therapy, the BiPAP should be discontinued as long as there is bleeding.	2	0–2	Good
For the patient with <i>mild-to-moderate</i> hemoptysis and who is using BiPAP as a chronic therapy, the BiPAP should be discontinued as long as there is bleeding.	3	2–4.75	Good
For the patient with <i>massive</i> hemoptysis and who is using BiPAP as a chronic therapy, the BiPAP should be discontinued as long as there is bleeding.	8	4.25–9	Some
The patient with hemoptysis should never undergo lung resection.	2	0.25–3	Good

Definition of abbreviations: BAE = bronchial artery embolization; BiPAP = bilevel positive airway pressure; CT = computed tomography; IQR = interquartile range; NSAID = nonsteroidal antiinflammatory drugs.

management recommendation could be made. However, comments suggested their opinion might differ in certain circumstances, specifically for a first episode of scant hemoptysis or if scant hemoptysis persists for days. They believed that these

instances represent a significant change in the patient's clinical status and expressed concern that such events might create anxiety in the patient and/or family, and reassurance may be warranted.

TABLE 4. PNEUMOTHORAX STATEMENTS AND PANEL RATINGS

Statements	Median	IQR	Consensus
The patient with <i>small</i> PTX, but clinically stable, may be observed in the outpatient setting.	7	5.5–8	Good
The patient with <i>large</i> PTX should always be admitted to the hospital.	9	9–9	Very good
The patient with <i>small</i> PTX, but clinically <i>stable</i> , should always have chest tube drainage.	1	1–2	Very good
The patient with <i>small</i> PTX, but clinically <i>unstable</i> , should always have chest tube drainage.	8	5.5–9	Good
The patient with <i>large</i> PTX, but clinically <i>stable</i> , should always have chest tube drainage.	9	7–9	Good
The patient with <i>large</i> PTX, but clinically <i>unstable</i> , should always have chest tube drainage.	9	9–9	Very good
The patient with a <i>first small</i> PTX should always undergo pleurodesis to prevent recurrence.	0.5	0–2	Good
The patient with a <i>first large</i> PTX should always undergo pleurodesis to prevent recurrence.	1	0–2	Very good
The patient with <i>recurrent ipsilateral small</i> PTX should always undergo pleurodesis to prevent recurrence.	6	3–7	Good
The patient with <i>recurrent ipsilateral large</i> PTX should always undergo pleurodesis to prevent recurrence.	8	6.25–9	Good
For the patient with PTX who is undergoing pleurodesis the preferred method is surgical pleurodesis.	8	8–8.5	Very good
The patient with PTX should always be treated with antibiotics	4.4	2–8	None
For the patient with <i>small</i> PTX and using BiPAP as a chronic therapy, the BiPAP should be discontinued as long as the PTX is present.	8	5–9	Good
For the patient with <i>large</i> PTX and using BiPAP as a chronic therapy, the BiPAP should be discontinued as long as the PTX is present.	8	6–9	Good
The patient with <i>small</i> PTX should not fly on a plane for 2 wk after it has resolved.	9	8–10	Good
The patient with <i>large</i> PTX should not fly on a plane for 2 wk after it has resolved.	9	8–9	Very good
The patient with <i>small</i> PTX should not lift weights for 2 wk after it has resolved.	7	5.75–9	Good
The patient with <i>large</i> PTX should not lift weights for 2 wk after it has resolved.	8	6–9	Good
The patient with <i>small</i> PTX should not perform vigorous aerobic exercise for 2 wk after it has resolved.	4	2–6	Some
The patient with <i>large</i> PTX should not perform vigorous aerobic exercise for 2 wk after it has resolved.	6.5	6–8.75	Some
The patient with <i>small</i> PTX should not perform spirometry for 2 wk after it has resolved.	9	6–9	Good
The patient with <i>large</i> PTX should not perform spirometry for 2 wk after it has resolved.	9	8–9	Very good
The patient with <i>small</i> PTX and <i>severe lung disease</i> should always be referred for lung transplant evaluation.	2	0–5	Some
The patient with <i>large</i> PTX and <i>severe lung disease</i> should always be referred for lung transplant evaluation.	3	1–7	None
The patient with <i>recurrent</i> PTX and <i>severe lung disease</i> (FEV ₁ < 40% predicted) should always be referred for a lung transplantation evaluation.	5	2–8	None

Definition of abbreviations: BiPAP = bilevel positive airway pressure; IQR = interquartile range; PTX = pneumothorax.

TABLE 5. RATINGS OF WITHHOLDING OF AIRWAY CLEARANCE THERAPIES FOR HEMOPTYSIS* AND PNEUMOTHORAX†

Therapy	Mild-to-Moderate Hemoptysis			Massive Hemoptysis			Small Pneumothorax			Large Pneumothorax		
	Median	IQR	Consensus	Median	IQR	Consensus	Median	IQR	Consensus	Median	IQR	Consensus
All	5	3–5	Some	9	8–10	Good	3	2–6	Good	7	4–8.5	Some
P&PD	5	3–6.5	Some	9	8–10	Good	3	2–6	Good	7	3.5–9	Some
ACBT/AD	3	2–4	Good	8	5–9	Some	3	1.5–5.5	Some	6	3–8	None
PEP/oPEP	4	2–6	Some	8.5	7–10	Some	6	4.25–9	None	8	6–9	Good
IPV	5	3–7	Some	9.5	7.75–10	Good	7	5.25–9	Good	9	7–9	Good
HFCC	5	3–7	Some	9	7.5–10	Good	4	2–6	Some	7	3.5–9	Some
Exercise	4	2–5.5	Some	9	7–10	Good	4	2–6	Some	7	4.5–9	Some

Definition of abbreviation: ACBT = active cycle of breathing technique; AD = autogenic drainage; HFCC = high frequency chest compression; IQR = interquartile range; oPEP = oscillating positive expiratory pressure; P&PD = percussion and postural drainage; PEP = positive expiratory pressure.

* In response to the statements: “The patient with (mild-to-moderate or massive) hemoptysis should always stop (all airway clearance techniques or specific airway clearance technique).”

† In response to the statements: “The patient with (small or large) pneumothorax should always stop (all airway clearance techniques or specific airway clearance technique).”

When should the patient with hemoptysis be admitted to the hospital?

Recommendation: The patient with scant hemoptysis may not require admission to the hospital.

Recommendation: The patient with massive hemoptysis should always be admitted to the hospital.

Hemoptysis can be life threatening, and because it may be difficult to predict how much bleeding may occur, the committee wanted to determine the threshold of the volume that would prompt the physician to recommend admission to a health care facility. The panelists rated admission for scant hemoptysis as inappropriate, with comments that many of these patients either do not require treatment or could be managed in the outpatient setting. The panel offered perfect consensus that admission is the preferred management for patients with massive hemoptysis.

The committee was not able to determine adequate consensus on when to recommend admission to a health care facility for patients with mild-to-moderate hemoptysis and ultimately elected not to try to define a specific threshold volume of bleeding for admission of such patients, because panelists themselves offered a broad range varying from 10 to 60 ml. The panelists also commented that some of these patients might be managed comfortably in the home setting, particularly if these patients had had previous bouts of bleeding.

When should the patient with hemoptysis be treated with antibiotics?

Recommendation: The patient with at least mild (≥ 5 ml) hemoptysis should be treated with antibiotics.

Hemoptysis may be considered a result of infection or a manifestation of a pulmonary exacerbation (15, 16). Because antibiotics are typically used in the treatment of a pulmonary exacerbation (17), the committee asked the

panel if hemoptysis alone would warrant treatment with antibiotics. The panel believed strongly that antibiotics should be a part of the treatment regimen in patients with at least mild hemoptysis.

Some members of the panel commented that the presence of scant hemoptysis might represent a manifestation of an acute pulmonary exacerbation, but there was no consensus on this opinion. For those patients with scant hemoptysis but without other features of a pulmonary exacerbation, the panel rated the need for antibiotics as low. However, the responses were too varied to make a management recommendation. Some panelists commented that scant hemoptysis should trigger antibiotic treatment only in the presence of other findings, such as its being a first episode, or the presence of persistent bleeding or a previous history of progressive increase in bleeding.

Should the patient with hemoptysis stop nonsteroidal antiinflammatory drugs?

Recommendation: The patient with at least mild (≥ 5 ml) hemoptysis should stop nonsteroidal antiinflammatory drugs (NSAIDs).

The CF Foundation has recommended the use of NSAIDs as chronic therapy in young patients with CF (18). These medications have the potential risk of contributing to bleeding because of their effect on platelet function (19). Therefore, the committee asked the panel what they would do for the patient with hemoptysis taking chronic NSAIDs. The panel reported that stopping NSAIDs was the preferred management for patients with at least mild (≥ 5 ml) hemoptysis. Comments suggested the medication could be reinstated once the bleeding has stopped. For those patients with scant hemoptysis, the panel was not as concerned. Although they rated moderately high the statement that NSAIDs should be stopped in this setting, the

TABLE 6. RATINGS OF WITHHOLDING AEROSOL THERAPIES FOR HEMOPTYSIS* AND PNEUMOTHORAX†

Therapy	Mild-to-Moderate Hemoptysis			Massive Hemoptysis			Small Pneumothorax			Large Pneumothorax		
	Median	IQR	Consensus	Median	IQR	Consensus	Median	IQR	Consensus	Median	IQR	Consensus
All	2	2–3	Good	5	3–8	None	0	0–1	Very Good	1	0–2.25	Good
Hypertonic saline	5	3–8	Some	8	5–9.5	Some	3	1–6	Some	4	1–7	None
Dornase alfa	4	2–6	Some	6	2–6	Some	1	0–2	Very Good	1.5	0.75–4.25	Some
Bronchodilators	2	1–3	Good	4	1–3	Some	0.5	0–1	Very Good	1	0–2.25	Good
Antibiotics	2	1–3.5	Good	4	2–7	Some	1	0–2	Very Good	1	0–2.25	Good

Definition of abbreviation: IQR = interquartile range.

* In response to the statements, “The patient with (mild-to-moderate or massive) hemoptysis should always stop (all aerosol medications or specific aerosol medication).”

† In response to the statements: “The patient with (small or large) pneumothorax should always stop (all aerosol medications or specific aerosol medication).”

consensus was not sufficient to be able to make a definitive recommendation.

Which patients should undergo bronchial artery embolization?

Recommendation: The patient with *massive* hemoptysis who is clinically unstable should be treated with bronchial artery embolization (BAE).

Most episodes of major bleeding will stop spontaneously. If the bleeding persists, BAE can be performed to stop the bleeding (13, 20). Because there are currently no guidelines to determine which patients should undergo BAE, questions were designed to identify indications for the procedure. Although the question was asked in several ways, there was consensus only for those patients with massive hemoptysis who are clinically unstable. There was not sufficient consensus for those patients who were deemed clinically stable despite massive hemoptysis. Some panelists believe that there are some patients who are best treated with BAE even in the absence of further bleeding. Others expressed concern about the potential complications of BAE and required additional bleeding to prompt them to recommend BAE.

Which studies should be performed in patients before bronchial artery embolization?

Recommendation: The patient with *massive* hemoptysis should not undergo bronchoscopy before BAE.

Some clinicians have recommended specific procedures (i.e., computed tomography [CT] of the chest or bronchoscopy) to assist in the localization of the bleeding sites in patients without CF with hemoptysis (21, 22). When asked about their strategy in evaluating the patient with CF before performance of the BAE, the panel expressed low enthusiasm for pre-BAE testing. There was not sufficient consensus regarding performance of a CT of the chest before BAE to make a recommendation. Some suggested it would be useful, but not essential. Others suggested that performance of a CT of the chest might waste valuable time, delaying the BAE.

The panel determined that bronchoscopy was inappropriate management before performance of BAE. Panelists commented that there was little evidence that bronchoscopy could effectively localize bleeding and that performing the procedure lost valuable time.

Which is the preferred strategy for BAE in patients with CF and massive hemoptysis?

Although the primary goal of BAE is to embolize the culprit vessel, some have advocated that all large and suspicious bronchial arteries should be embolized because of the high recurrence rate (6, 23, 24). The panel was asked separately if the preferred strategy was to embolize only the suspected or known bleeding vessel or to embolize all abnormal (dilated and tortuous) vessels bilaterally. No matter how this question was asked, there was not a sufficient consensus to make a management recommendation. The panel was split in their preference of strategy. Those who preferred embolization of all abnormal vessels believed this was useful in the prevention of future bleeding, whereas those who preferred embolization of only the suspect vessels focused on the potential complications of BAE (e.g., embolization of a spinal artery).

Should bilevel positive airway pressure be continued in patients with hemoptysis?

Recommendation: Bilevel positive airway pressure (BiPAP) should not be withheld from patients with *scant* hemoptysis.

Recommendation: BiPAP should be withheld from patients with *massive* hemoptysis.

Patients who suffer massive hemoptysis more commonly have severe obstructive airways disease. Some of these patients

will also be using noninvasive ventilatory support, specifically bilevel positive airway pressure (BiPAP) (25). The panel was asked whether BiPAP should be withheld from patients with hemoptysis. The panel believed that the risks of continuing BiPAP in the patients with scant hemoptysis did not outweigh its benefit and that it was inappropriate to withhold this therapy from these patients. For those patients with mild-to-moderate hemoptysis there were low ratings with good consensus, but not sufficient to make a management recommendation. However, for patients with massive hemoptysis, withholding BiPAP was rated highly, showing it to be an acceptable management strategy in many circumstances.

Is lung resection contraindicated for patients with CF and massive hemoptysis?

Recommendation: Lung resection should be performed for patients with CF with *massive* hemoptysis only as a final therapeutic option.

Some patients without CF with massive hemoptysis are treated with resection of the affected lung (26). The panel was asked whether resection was contraindicated in patients with CF with hemoptysis. When confronted with the statement that patients with CF should never undergo lung resection, the panel believed that this statement was an inappropriate recommendation. Some panelists were uncomfortable with the term "never" and suggested that resection could be life saving. Others suggested that resection of lung was a procedure of last resort, and only after other measures (e.g., BAE) had failed.

Should the patient with hemoptysis stop airway clearance therapies?

Recommendation: The patient with *scant* hemoptysis should not stop airway clearance therapies.

Recommendation: The patient with *massive* hemoptysis should stop all airway clearance therapies.

The formation of a clot at the site of bleeding is believed to be important in the cessation of hemoptysis. Some have expressed concern that airway clearance therapies may impair clot formation and adherence resulting in more bleeding (27). The committee asked the panel whether they shared these concerns and whether their choice of airway clearance therapy varied by the volume of hemoptysis. The panel reported that stopping airway clearance therapies was inappropriate for the patient with scant hemoptysis (median score, 1; interquartile range [IQR], 0–2; good consensus).

Conversely, the panel rated stopping airway clearance therapies as the preferred management for patients with massive hemoptysis, independent of type of therapy. There was increased concern about the continuance of airway clearance in patients with mild-to-moderate hemoptysis, but there was not sufficient consensus to make a recommendation. Several members of the panel suggested that hemoptysis at this volume was not life threatening and that successful clearance of airway phlegm was critical in the resolution of the underlying process.

The specific type of airway clearance did not influence the recommendations of the panel. However, it should be noted that the panelists had the least concern with the techniques of active cycle of breathing and autogenic drainage in patients with hemoptysis.

Should the patient with hemoptysis stop aerosol therapies?

Recommendation: The patient with *scant* hemoptysis should not stop aerosol therapies.

Recommendation: The patient with *massive* hemoptysis should stop aerosolized hypertonic saline.

Patients with CF are commonly treated with inhaled medications (18). Because these therapies may be irritating to the

airways and induce bronchospasm or cough in some patients (28), the committee asked the panel whether all aerosol therapies should be withheld from patients with hemoptysis. The panel reported that stopping aerosol therapies was inappropriate for the patient with scant hemoptysis (median score, 0; IQR, 0–2; consensus good). The panel expressed a similar opinion for patients with mild-to-moderate hemoptysis; the rating displayed their belief that aerosol therapies should be withheld in only rare circumstances. The ratings were higher for patients with massive hemoptysis, but there was not sufficient consensus to make a general recommendation regarding all aerosol therapies for these patients.

Regarding specific aerosol medications, the panel expressed good consensus for the continuation of inhaled bronchodilators in patients with mild-to-moderate hemoptysis. There was a similar opinion for inhaled antibiotics, but there was not a sufficient consensus to make a specific recommendation. The ratings for the discontinuance of dornase alfa and hypertonic saline in patients with mild-to-moderate hemoptysis were slightly higher but were not sufficient to make a specific recommendation. For the patient with massive hemoptysis, the panel rated it appropriate to withhold hypertonic saline in many circumstances; however, no recommendations could be made for the other inhaled therapies. The panel stressed the greater likelihood of hypertonic saline to induce cough and possibly exacerbate hemoptysis. Panel comments suggested that the benefits of continuing other therapies outweighed the risks, and therefore that they be withheld only if they seemed to exaggerate or provoke bleeding.

PNEUMOTHORAX

When should the patient with pneumothorax be admitted to the hospital?

Recommendation: The patient with a large pneumothorax should always be admitted to the hospital.

Recommendation: The patient with a small pneumothorax, but otherwise clinically stable, may be closely observed in the outpatient setting.

There was no disagreement on the preferred management for patients with a large pneumothorax; the consensus was very good that these patients should be admitted to the hospital. For the patient with a small pneumothorax but otherwise clinically stable, close observation in the outpatient setting was considered acceptable management in many circumstances. The panel expressed concern for the potential of progression of a small pneumothorax. Some panelists suggested symptomatic patients should be admitted, whereas those who have a small pneumothorax found incidentally on chest radiograph could be observed. Circumstances that may factor into the decision for hospitalization included the reliability of the patient and family and the ease of access to health care if the pneumothorax worsened.

When should a chest tube be placed in a patient with CF with pneumothorax?

Recommendation: The patient with a large pneumothorax should have a chest tube placed.

Recommendation: The patient with a small pneumothorax should have a chest tube placed if there is clinical instability.

The panel rated that the placement of a chest tube was the preferred management of a large pneumothorax. Neither the clinical stability of the patient nor the severity of pulmonary impairment influenced their rating of this statement.

However, the panel believed that the decision to place a chest tube in patients with a small pneumothorax depended on the clinical stability of the patient. The panel rated that it

was inappropriate management to routinely place a chest tube in patients with a small pneumothorax who are clinically stable. The severity of the patient's underlying pulmonary impairment did not significantly influence the ratings of the panel. There were several comments that the pain associated with a chest tube may outweigh the benefits in these patients and that observation might be more appropriate. For the patient with a small pneumothorax who is clinically unstable, the placement of a chest tube was considered acceptable management in many circumstances. Some panelists did not rate this statement higher as there was doubt that the small pneumothorax would be the cause of clinical instability and that treatment of a pulmonary exacerbation (17) would be more appropriate.

When should pleurodesis be performed to prevent recurrence of a pneumothorax?

Recommendation: The patient with a first pneumothorax should not undergo pleurodesis to prevent recurrence.

Recommendation: The patient with a recurrent large pneumothorax should undergo pleurodesis to prevent recurrence.

Many patients (estimated 50–90%) may suffer a recurrence of pneumothorax after its resolution (29). Because there is high morbidity (e.g., pain, dyspnea) and high health care cost (7) associated with a pneumothorax, more definitive treatment (i.e., pleurodesis) aimed at preventing a recurrence is a consideration for some patients. The committee wished to learn what factors influenced the decision to perform pleurodesis. This excludes those patients whose pneumothorax is refractory to chest tube drainage alone.

The panel demonstrated consensus in their ratings that pleurodesis is inappropriate management for the first occurrence of a pneumothorax, whether large or small. Some expressed concern about the effect that pleurodesis may have on future candidacy for lung transplantation.

The panel rated pleurodesis of a recurrent large ipsilateral pneumothorax as appropriate in many circumstances. The panel expressed interest in pleurodesis for recurrent small pneumothoraces, even achieving the criteria for good consensus. Yet the range of responses was still broad enough to prevent making a definitive management recommendation.

Which method of pleurodesis is preferred for patients with pneumothorax?

Recommendation: For the patient with CF with a pneumothorax who is undergoing pleurodesis, the preferred method is surgical pleurodesis.

The literature contains retrospective reports of outcomes after various methods of pleurodesis (29), but there are no controlled trials that have compared these strategies (30). Chemical pleurodesis was defined as intrapleural instillation of a sclerosing agent through a chest tube or percutaneous catheter. Surgical pleurodesis was defined as a pleurodesis performed with a thoracoscope or through a limited or full thoracotomy.

The committee had originally asked whether either strategy should always be performed. The ratings for chemical pleurodesis (median, 1.5; IQR, 0–3; some consensus) and for surgical pleurodesis (median, 7; IQR, 6–8; good consensus) suggested that surgical pleurodesis was the preferred management in many circumstances. However, there appeared to be a bimodal rating of the latter statement with panelists either completely agreeing or disagreeing.

Because there appeared to be greater preference for surgical pleurodesis, the committee refined the statement to see if there was consensus on this point. The results indicated that surgical

pleurodesis was the preferred management option, with very good consensus.

Should patients with pneumothorax be treated with antibiotics?

Because pneumothoraces typically occur in patients with more advanced obstructive airways disease, it may be that worsening infection and resultant obstruction contributes to this complication. The committee asked the panel whether antibiotics should be used in all patients with a pneumothorax. There was a broad range of responses from which the committee could not gain a consensus or deliver a recommendation for management. Although some panelists suggested a pneumothorax was a manifestation of a pulmonary exacerbation, others required additional evidence of a pulmonary exacerbation before treating the patient with antibiotics.

Should BiPAP be continued in patients with pneumothorax?

Recommendation: BiPAP should be withheld from patients with pneumothorax as long as the pneumothorax is present.

Patients who suffer a pneumothorax are more commonly those with severe obstructive airways disease (7) who may also be on noninvasive ventilatory support, specifically BiPAP (25). The committee asked the panel whether BiPAP should be withheld from patients with pneumothorax for fear that it may cause progression of the complication. The panel reported that withholding BiPAP from patients with pneumothorax, independent of its size, was acceptable management in many circumstances. Several panelists expressed concern that withholding BiPAP may be a problem, as the patient may need the support, and suggested that observation of the patient in the intensive care unit may be appropriate when withholding BiPAP.

Are there any activities that the patient should avoid after treatment for a pneumothorax?

Recommendation: The patient with pneumothorax should not fly on a plane for 2 weeks after the pneumothorax has resolved.

Recommendation: The patient with pneumothorax should not lift weights (>5 pounds) for 2 weeks after the pneumothorax has resolved.

Recommendation: The patient with pneumothorax should not perform spirometry for 2 weeks after the pneumothorax has resolved.

There are several activities that have been suggested that could exacerbate a recurrence of a pneumothorax including air travel, lifting weights, and exercise (31, 32). Likewise, performance of spirometry requires generation of high intrathoracic pressures and could exacerbate a recently healed pneumothorax. The committee asked the panel whether the patient should avoid these activities for a period after resolution of the pneumothorax and chose an arbitrary date of 2 weeks. The panel reported that avoidance of flying on a plane after resolution of a pneumothorax, both small and large, was the preferred management in most circumstances. Several panelists suggested this time should be extended to 4 to 6 weeks. Similarly, the panelists rated lifting weights as an activity to be avoided in many circumstances, again for both small and large pneumothoraces.

The results were indeterminate for a recommendation regarding exercise after resolution of a pneumothorax, irrespective of the size of the pneumothorax. They rated that performance of spirometry should be withheld for 2 weeks after resolution of both small (acceptable in many circumstances) and large (preferred management) pneumothorax.

Should the occurrence of pneumothorax influence the decision to refer for lung transplantation?

The occurrence of a pneumothorax is more frequent in patients with severe pulmonary impairment, and there is an attributable mortality to the complication (7). Pneumothoraces are discussed in guidelines for referral of patients with CF to lung transplant centers (33). The committee asked the panel whether the occurrence of a pneumothorax should influence the decision to consider evaluation for lung transplantation. There was no consensus in the responses for the committee to be able to make a recommendation. It did not matter whether it was a single occurrence or a recurrent pneumothorax. The lack of consensus may be because the statements used the term “always”; the committee chose not to pursue this question in greater depth because many of the comments reflected that because pneumothorax is more common in patients with severe disease, the complication did not further influence their decision regarding the evaluation of the patient for lung transplantation.

Should the patient with pneumothorax stop airway clearance therapies?

Recommendation: Some airway clearance therapies, specifically positive expiratory pressure and intrapulmonary percussive ventilation, should not be used in patients with pneumothorax.

Airway clearance therapies are a standard component of the treatment of patients with CF (34). The committee asked whether some airway clearance therapies should be discontinued in patients with a pneumothorax for fear that they would contribute to progression of the complication. The panel did not recommend stopping airway clearance therapy, in general, for the patient with a small pneumothorax. Some panelists expressed concern that airways obstruction by phlegm might contribute to worsening of the complication. The panel gave a higher rating to withholding airway clearance therapies for the patient with a large pneumothorax, suggesting this may be the appropriate approach in many circumstances. Some panelists commented that withholding therapies is not necessary if there is a chest tube present.

The committee also asked the panel to rate the use of specific types of airway clearance therapies. For most therapies, no recommendation could be made for the patient with a small pneumothorax. However, the panel rated positive expiratory pressure/oscillating positive expiratory pressure (PEP/oPEP) and intrapulmonary percussive ventilation high enough to suggest it may be appropriate to withhold these specific therapies in certain circumstances, although there was not sufficient consensus to make a recommendation or suggestion for PEP/oPEP.

Similarly, the panel suggested, with good consensus, that it would be appropriate to withhold PEP/oPEP, intrapulmonary percussive ventilation, and exercise in patients with a large pneumothorax in many circumstances. No management recommendation could be made for any of the other therapies in patients with a large pneumothorax.

Should the patient with pneumothorax stop aerosol therapies?

Recommendation: The patient with pneumothorax should not stop aerosol therapies.

Because inhaled therapies can be irritating to the airways and induce cough and bronchospasm in some patients (28), the committee asked the panel whether aerosol therapies should be withheld from patients with a pneumothorax. The panel reported that stopping aerosol therapies was inappropriate for the patient with pneumothorax. Neither the size of the pneumothorax nor the type of aerosol therapy influenced their

rating. Although there were higher ratings for hypertonic saline, they were not so high as to change the recommendation. Several panelists suggested they would stop aerosol therapies only if they promoted cough in a patient.

CONCLUSION

The CF Foundation Pulmonary Therapies Committee has made recommendations on how to manage various aspects of the complication of hemoptysis and pneumothorax in patients with CF. As there are no controlled trials to guide treatment, the committee sought expert opinion from a panel of clinicians with broad experience with patients with CF. The committee used the Delphi method to systematically determine the consensus opinions. These recommendations should be helpful to the CF community in their care of patients with CF.

Author Disclosure: P.A.F. received lecture fees from AstraZeneca (\$1,001–\$5,000). He received grant support from MPex, Novartis (more than \$100,001), Pharmaxis (\$10,001–\$50,000), Gilead, and Vertex (more than \$100,001). P.J.M. received grant support (more than \$100,001) and served on the Board or Advisory Board for the Cystic Fibrosis Foundation (\$10,001–\$50,000). K.A.R. received grant support from the Cystic Fibrosis Foundation to facilitate development of evidence-based guidelines (more than \$100,001). R.L.R. received honorarium for giving Grand Rounds from Monmouth medical center (\$1,001–\$5,000) and served on the Board or Advisory Board for the Cystic Fibrosis Foundation (\$1,001–\$5,000). L.Q. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. B.C.M. is employed by the Cystic Fibrosis Foundation.

Acknowledgment: Members of the Clinical Practice Guidelines for Pulmonary Therapies Committee, including representatives from internal medicine, pediatrics, nursing, respiratory therapy, pharmacy, systematic review procedures, and the CF Foundation: Patrick A. Flume, M.D., co-chair, Medical University of South Carolina, Charleston, SC; Peter Mogayzel, M.D., Ph.D., co-chair, Johns Hopkins University, Baltimore, MD; James Cunningham, M.D., Cook Children's Medical Center, Fort Worth, TX; Anne Downs, P.T., University of Indianapolis, Indianapolis, IN; Jill Fleige, R.N., L.N.C., University of Nebraska Medical Center, Omaha, NE; Chris Goss, M.D., University of Washington, Seattle, WA; Hector Gutierrez, M.D., University of Alabama-Birmingham, Birmingham, AL; Leslie Hazle, R.N., Cystic Fibrosis Foundation, Bethesda, MD; Robert Kuhn, Pharm.D., University of Kentucky, Lexington, KY; Mary Lester, R.R.T., Medical University of South Carolina, Charleston, SC; Bruce Marshall, M.D., Cystic Fibrosis Foundation, Bethesda, MD; Lynne Quittell, M.D., Columbia University, New York, NY; Karen A. Robinson, Ph.D., Johns Hopkins University, Baltimore, MD; Randall Rosenblatt, M.D., University of Texas Southwestern Medical School, Dallas, TX; Kathryn Sabadosa, M.P.H., Dartmouth-Hitchcock Medical Center, Lebanon, NH; Robert L. Vender, M.D., Penn State Milton S. Hershey Medical Center, Hershey, PA; Terry B. White, Ph.D., Cystic Fibrosis Foundation, Bethesda, MD; Donna Beth Willey-Courand, M.D., University of Texas Health Science Center at San Antonio, San Antonio, TX. Cystic Fibrosis Foundation Representatives: Melissa Chin, Clinical Programs Project Assistant. Expert Panel: Pediatric CF Program Directors: Carlos E. Milla, M.D., Stanford University; Jeff Wagener, M.D., University of Colorado; Christopher M. Oermann, M.D., Texas Children's Hospital; Thomas Ferkol, Jr., M.D., Washington University; Wyn Hoover, MD, University of Alabama-Birmingham; Michelle S. Howenstine, M.D., University of Indiana; Michael J. Rock, M.D., University of Wisconsin; George Retsch-Bogart, M.D., University of North Carolina at Chapel Hill; Ronald Rubenstein, M.D., Ph.D., Children's Hospital of Philadelphia; Michael Schechter, M.D., M.P.H., Emory University; David M. Orenstein, M.D., University of Pittsburgh; John L. Colombo, M.D., University of Nebraska Medical Center; Beryl Rosenstein, M.D., Johns Hopkins University; Henry L. Dorkin, M.D., Harvard University; James D. Acton, M.D., University of Cincinnati; Susanna A. McColley, M.D., Children's Memorial Hospital; Felix Ratjen, M.D., The Hospital for Sick Children, Toronto, Canada; Adult CF Program Directors: Moira L. Aitken, M.D., University of Washington; Paul Mohabir, M.D., Stanford University; Jerry A. Nick, M.D., B.S., University of Colorado; Marcia Katz, M.D., Baylor College of Medicine; Daniel Rosenbluth, M.D., Washington University; Randall K. Young, M.D., University of Alabama Birmingham; Aruna Sannuti, M.D., B.S., University of Indiana; Guillermo A. doPico, M.D., University of Wisconsin-Madison; James R. Yankaskas, M.D., University of North Carolina at Chapel Hill; Douglas Holsclaw, M.D., University of Pennsylvania; Linda L. Wolfenden, M.D., Emory University; Joseph M. Pilewski, M.D., University of Pittsburgh; Peter (Jim) J. Murphy, M.D., University of Nebraska; Michael P. Boyle, M.D., Johns Hopkins University; Ahmet Uluer, D.O., Brigham and Women's Hospital; Steven D. Strausbaugh, M.D., University Hospitals of Cleveland; Patricia (Trish) M. Joseph, M.D., University of Cincinnati; Manu Jain, M.D., Northwestern University; Elizabeth Tullis, M.D., St. Michael's Hospital, Toronto, Canada; Interventional Radiologists: Souheil Saddekni, M.D., University of Alabama Birmingham; Patricia Burrows, M.D., Texas Children's Hospital; Mark Wholey, M.D., University of Pittsburgh; Charles Burke, M.D., University of North Carolina at Chapel Hill; Mark Sands, M.D., Cleveland Clinic

Foundation; Sally Mitchell, M.D., Johns Hopkins University; Cardiothoracic Surgeons: R. Duane Davis, M.D., Duke University; Thomas M. Egan, M.D., University of North Carolina at Chapel Hill; Charles B. Huddleston, M.D., Washington University; Mike Mulligan, M.D., University of Washington; David McGiffin, M.D., University of Alabama Birmingham; Wicki Vigneswaran, M.D., University of Chicago; Craig Lillehei, M.D., Harvard University.

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