**LUNG ABSCESS**

Lung abscess is defined as necrosis of the pulmonary tissue and formation of cavities containing necrotic debris or fluid caused by microbial infection. The formation of multiple small (<2 cm) abscesses is occasionally referred to as necrotizing pneumonia or lung gangrene. Both lung abscess and necrotizing pneumonia are manifestations of a similar pathologic process. Failure to recognize and treat lung abscess is associated with poor clinical outcome.

Lung abscess was a devastating disease in the preantibiotic era, when one third of the patients died, another one third recovered, and the remainder developed debilitating illnesses such as recurrent abscesses, chronic empyema, bronchiectasis, or other consequences of chronic pyogenic infections. In the early postantibiotic period, sulfonamides did not improve the outcome of patients with lung abscess until the penicillins and tetracyclines were available. Although resectional surgery was often considered a treatment option in the past, the role of surgery has greatly diminished over time because most patients with uncomplicated lung abscess eventually respond to prolonged antibiotic therapy.

**Frequency**

The frequency of lung abscess in the general population is not known.

Mortality/Morbidity. Most patients with primary lung abscess improve with antibiotics, with cure rates documented at 90-95% (Bartlett, 1992). The mortality rate for patients with underlying immunocompromised status or bronchial obstruction who develop lung abscess may be as high as 75% (Pohlson, 1985). A retrospective study (Hirshberg, 1995) reported the overall mortality rate of lung abscesses caused by mixed gram-positive and gram-negative bacteria at approximately 20%.

Age. These conditions occur more commonly in elderly patients because of the increased incidence of periodontal disease and the increased prevalence of microaspiration.

**Classification**

Lung abscesses can be classified based on the duration and the likely etiology.

1. **Acute** abscesses are less than 4-6 weeks old, whereas **chronic** abscesses are of longer duration.

2. Lung abscesses can be further characterized by the responsible pathogen, such as Staphylococcus lung abscess and anaerobic or Aspergillus lung abscess.

3. **Primary abscess** is infectious in origin, caused by aspiration or pneumonia in the healthy host; **secondary abscess** is caused by a preexisting condition (eg, obstruction), spread from an extrapulmonary site, bronchiectasis, and/or an immunocompromised state.

**Causes**

The bacterial infection may reach the lungs in several ways. The most common is aspiration of oropharyngeal contents.

Patients at the highest risk for developing lung abscess have the following risk factors:

* Poor dentition
* Seizure disorder
* Alcohol abuse

Other patients at high risk for developing lung abscess include the following:

* Individuals with an inability to protect their airways because of an absent gag reflex, such as during coma, loss of consciousness, or general anesthesia and sedation
* Patients with primary lung disorders, such as septic emboli from tricuspid endocarditis, vasculitic disorders, cavitating lung malignancies, and pulmonary cystic diseases
* Infrequently, the following infectious etiologies of pneumonia may progress to parenchymal necrosis and lung abscess formation:
  1. Pseudomonas aeruginosa
  2. Klebsiella pneumoniae
  3. Staphylococcus aureus (may result in multiple abscesses)
  4. Streptococcal pneumonia
  5. Nocardia species
  6. Fungal species
* An abscess may develop as an infectious complication of a preexisting bulla or lung cyst.
* An abscess may occur secondary to carcinoma of the bronchus; the bronchial obstruction causes postobstructive pneumonia, which may lead to abscess formation.

**Microbiology**

In lung abscesses, anaerobes are recovered in up to 89% of the patients. In a study by Bartlett et al in 1974, 46% of patients with lung abscesses had only anaerobes isolated from sputum cultures while 43% of patients had a mixture of anaerobes and aerobes. The most common anaerobes are Peptostreptococcus, Bacteroides, Fusobacterium species, and microaerophilic streptococcus.

Other organisms that may infrequently cause lung abscess include Staphylococcus aureus, Streptococcus pyogenes, Streptococcus pneumoniae (rarely), Klebsiella pneumoniae, Haemophilus influenzae, Actinomyces species, Nocardia species, and gram-negative bacilli.

Nonbacterial pathogens may also cause lung abscesses. These microorganisms include parasites (eg, Paragonimus, Entamoeba), fungi (eg, Aspergillus, Cryptococcus, Histoplasma, Blastomyces, Coccidioides), and Mycobacterium.

**Pathophysiology**

Most frequently, the lung abscess arises as a complication of aspiration pneumonia caused by mouth anaerobes. The patients who develop lung abscess are predisposed to aspiration and commonly have periodontal disease. A bacterial inoculum from the gingival crevice reaches the lower airways, and infection is initiated because the bacteria are not cleared by the patient's host defense mechanism. This results in aspiration pneumonitis and progression to tissue necrosis 7-14 days later, resulting in formation of lung abscess. Other mechanisms for lung abscess formation include bacteremia or tricuspid valve endocarditis, caused by septic emboli to the lung.

**Histologic Findings**. Lung abscesses begin as small zones of necrosis developing within the consolidated segments in pneumonia. These areas may coalesce to form single or multiple areas of suppuration, which are referred to as lung abscesses. If antibiotics interrupt the natural history at an early stage, the healing results in no residual changes. When the progressive inflammation erodes into the adjacent bronchi, the contents of the abscess are expectorated as malodorous sputum. Subsequently, fibrosis occurs, which causes a dense scar and separates the abscess. The abscess may still occur, and spillage of pus into the bronchial tree may disseminate the infection.

**CLINICAL**

**History.**

Symptoms depend on whether the abscess is caused by anaerobic or other bacterial infection.

* *Anaerobic infection*

Patients often present with indolent symptoms that evolve over a period of weeks to months.

The usual symptoms are

* fever,
* cough with sputum production,
* night sweats,
* anorexia,
* weight loss.

The expectorated sputum characteristically is foul smelling and bad tasting. Patients may develop hemoptysis or pleurisy.

* *Other bacterial pathogens*

These patients generally present with conditions that are more emergent in nature and are usually treated while they have bacterial pneumonia.

Cavitation occurs subsequently as parenchymal necrosis ensues.

Abscesses from fungi, Nocardia, and mycobacteria tend to have an indolent course and gradually progressive symptoms.

**Physical**

The findings on physical examination of a patient with lung abscess are variable. Physical findings may be secondary to associated conditions such as underlying pneumonia or pleural effusion. The physical examination findings may also vary depending on the organisms involved, the severity and extent of the disease, and the patient's health status and comorbidities.

Patients may have low-grade fever in anaerobic infections and temperatures higher than 38.5°C in other infections.

Generally, evidence of gingival disease is present.

Clinical findings of concomitant consolidation may be present (eg, decreased breath sounds, dullness to percussion, bronchial breath sounds, course inspiratory crackles).

The amphoric or cavernous breath sounds are only rarely elicited in modern practice.

Evidence of pleural friction rub and signs of associated pleural effusion, empyema, and pyopneumothorax may be present. Signs include dullness to percussion, contralateral shift of the mediastinum, and absent breath sounds over the effusion.

Digital clubbing may develop rapidly.

**Lab Studies**

A complete white blood cell count with differential may reveal leukocytosis and a left shift.

Obtain sputum for Gram stain, culture, and sensitivity.

If tuberculosis is suspected, acid-fast bacilli stain and mycobacterial culture is requested.

Blood culture may be helpful in establishing the etiology.

Obtain sputum for ova and parasite whenever a parasitic cause for lung abscess is suspected.

**Imaging Studies**

Chest radiograph

A typical chest radiographic appearance of a lung abscess is an irregularly shaped cavity with an air-fluid level inside. Lung abscesses as a result of aspiration most frequently occur in the posterior segments of the upper lobes or the superior segments of the lower lobes.

The wall thickness of a lung abscess progresses from thick to thin and from ill-defined to well-circumscribed as the surrounding lung infection resolves. The cavity wall can be smooth or ragged but is less commonly nodular, which raises the possibility of cavitating carcinoma.

The extent of the air-fluid level within a lung abscess is often the same in posteroanterior or lateral views. The abscess may extend to the pleural surface, in which case it forms acute angles with the pleural surface.

Anaerobic infection may be suggested by cavitation within a dense segmental consolidation in the dependent lung zones.

Lung infection with a virulent organism results in more widespread tissue necrosis, which facilitates progression of underlying infection to pulmonary gangrene.

Up to one third of lung abscesses may be accompanied by an empyema.

**CT scan**

CT scan of the lung may help visualize the anatomy better than the chest radiograph. It is very useful in identification of concomitant empyema or lung infarction.

On CT scan, an abscess often is a rounded radiolucent lesion with a thick wall and ill-defined irregular margins.

The vessels and bronchi are not displaced by the lesion as they are by an empyema.

The lung abscess is located within the parenchyma compared to loculated empyema, which may be difficult to distinguish on chest radiograph.

The lesion forms acute angles with the pleural surface chest wall.

**Procedures**

To obtain an uncontaminated specimen, transtracheal aspirate or transthoracic needle aspirate are the techniques employed in lung abscess.

Although transtracheal aspirate and transthoracic needle aspiration may provide microbiologic diagnosis, obtaining pleural fluid and blood cultures in patients with lung abscess is easier.

Flexible fiberoptic bronchoscopy is performed to exclude bronchogenic carcinoma whenever bronchial obstruction is suspected. Bronchoscopy using a protected brush to obtain a specimen uncontaminated by the upper airway or quantitative culture of organisms from the bronchoalveolar lavage fluid has been advocated to establish bacteriologic diagnosis in lung abscess. However, the experience with this technique in diagnosis of anaerobic lung infections is limited and the diagnostic yield is uncertain. Furthermore, risk of spillage of infected material into the uninvolved areas of lung exists.

**TREATMENT**

Treatment of lung abscess is guided by the available microbiology and knowledge of the underlying or associated conditions.

**Antibiotic therapy**

Standard treatment of an anaerobic lung infection is clindamycin (600 mg IV q8h followed by 150-300 mg PO qid).

This regimen has been shown to be superior over parenteral penicillin in published trials. Several anaerobes may produce beta-lactamase (eg, various species of Bacteroides and Fusobacterium) and therefore develop resistance to penicillin.

Although metronidazole is an effective drug against anaerobic bacteria, the experience with metronidazole in treating lung abscess has been rather disappointing because these infections are generally polymicrobial. A failure rate of 50% has been reported.

In hospitalized patients who have aspirated and developed a lung abscess, antibiotic therapy should include coverage against S aureus and Enterobacter and Pseudomonas species.

Cefoxitin is a second-generation cephalosporin that has gram-positive, gram-negative, and anaerobic coverage. This agent may be used when a polymicrobial infection is suspected as cause of lung abscess.

**Duration of therapy**

Although the duration of therapy is not well established, most clinicians prescribe antibiotic therapy generally for 4-6 weeks.

Current recommendations are that antibiotic treatment should be continued until the chest radiograph has shown either the resolution of lung abscess or the presence of a small stable lesion.

The rationale for extended treatment maintains that risk of relapse exists with a shorter antibiotic regimen.

**Response to therapy**

Patients with lung abscesses usually show clinical improvement, with improvement of fever, within 3-4 days after initiating the antibiotic therapy. Defervescence is expected in 7-10 days. Persistent fever beyond this time indicates therapeutic failure, and these patients should undergo further diagnostic studies to determine the cause of failure.

Considerations in patients with poor response to antibiotic therapy include bronchial obstruction with a foreign body or neoplasm or infection with a resistant bacteria, mycobacteria, or fungi.

Large cavity size (ie, >6 cm in diameter) usually requires prolonged therapy. Because empyema with an air-fluid level could be mistaken for parenchymal abscess, a CT scan may be used to differentiate this process from lung abscess.

A nonbacterial cause of cavitary lung disease may be present, such as lung infarction, cavitating neoplasm, and vasculitis. The infection of a preexisting sequestration, cyst, or bulla may be the cause of delayed response to antibiotics.

**Surgical Care**

Surgery is very rarely required for patients with uncomplicated lung abscesses. The usual indications for surgery are failure to respond to medical management, suspected neoplasm, or congenital lung malformation. The surgical procedure performed is either lobectomy or pneumonectomy.

**BRONCHIECTASIS**

Bronchiectasis is an abnormal and permanent dilatation of bronchi. It may be either focal, involving airways supplying a limited region of pulmonary parenchyma, or diffuse, involving airways in a more widespread distribution. Although this definition is based on pathologic changes in the bronchi, diagnosis is often suggested by the clinical consequences of chronic or recurrent infection in the dilated airways and the associated secretions that pool within these airways.

The bronchial dilatation of bronchiectasis is associated with destructive and inflammatory changes in the walls of medium-sized airways, often at the level of segmental or subsegmental bronchi. The normal structural components of the wall, including cartilage, muscle, and elastic tissue, are destroyed and may be replaced by fibrous tissue. The dilated airways frequently contain pools of thick, purulent material, while more peripheral airways are often occluded by secretions or obliterated and replaced by fibrous tissue. Additional microscopic features include bronchial and peribronchial inflammation and fibrosis, ulceration of the bronchial wall, squamous metaplasia, and mucous gland hyperplasia. The parenchyma normally supplied by the affected airways is abnormal, containing varying combinations of fibrosis, emphysema, bronchopneumonia, and atelectasis. As a result of the inflammation, vascularity of the bronchial wall increases, with associated enlargement of the bronchial arteries and anastomoses between the bronchial and pulmonary arterial circulations.

Three different patterns of bronchiectasis were described by Reid in 1950. In cylindrical bronchiectasis the bronchi appear as uniformly dilated tubes that end abruptly at the point that smaller airways are obstructed by secretions. In varicose bronchiectasis the affected bronchi have an irregular or beaded pattern of dilatation resembling varicose veins. In saccular (cystic) bronchiectasis the bronchi have a ballooned appearance at the periphery, ending in blind sacs without recognizable bronchial structures distal to the sacs.

**Infectious Causes**

Adenovirus and influenza virus are the main viruses that cause bronchiectasis in association with lower respiratory tract involvement. Virulent bacterial infections, especially with potentially necrotizing organisms such as Staphylococcus aureus, Klebsiella, and anaerobes, remain important causes of bronchiectasis when antibiotic treatment of a pneumonia is not given or is significantly delayed. Bronchiectasis has been reported in patients with HIV infection, perhaps at least partly due to recurrent bacterial infection. Tuberculosis can produce bronchiectasis by a necrotizing effect on pulmonary parenchyma and airways and indirectly as a consequence of airway obstruction from bronchostenosis or extrinsic compression by lymph nodes. Nontuberculous mycobacteria are frequently cultured from patients with bronchiectasis, often as secondary infections or colonizing organisms. However, it has now also been recognized that these organisms, especially those of the Mycobacterium avium complex, can serve as primary pathogens associated with the development and/or progression of bronchiectasis. Mycoplasmal and necrotizing fungal infections are rare causes of bronchiectasis.

Impaired host defense mechanisms are often involved in the predisposition to recurrent infections. The major cause of localized impairment of host defenses is endobronchial obstruction. Bacteria and secretions cannot be cleared adequately from the obstructed airway, which develops recurrent or chronic infection. Slowly growing endobronchial neoplasms such as carcinoid tumors may be associated with bronchiectasis. Foreign-body aspiration is another important cause of endobronchial obstruction, particularly in children. Airway obstruction can also result from bronchostenosis, from impacted secretions, or from extrinsic compression by enlarged lymph nodes.

Generalized impairment of pulmonary defense mechanisms occurs with immunoglobulin deficiency, primary ciliary disorders, or cystic fibrosis. Infections and bronchiectasis are therefore often more diffuse. With panhypogammaglobulinemia, the best described of the immunoglobulin disorders associated with recurrent infection and bronchiectasis, patients often also have a history of sinus or skin infections. Selective deficiency of an IgG subclass, especially IgG2, has also been described in a small number of patients with bronchiectasis.

The primary disorders associated with ciliary dysfunction, termed primary ciliary dyskinesia, are responsible for 5 to 10% of cases of bronchiectasis. Numerous defects are encompassed under this category, including structural abnormalities of the dynein arms, radial spokes, and microtubules. The cilia become dyskinetic; their coordinated, propulsive action is diminished, and bacterial clearance is impaired. The clinical effects include recurrent upper and lower respiratory tract infections, such as sinusitis, otitis media, and bronchiectasis. Because normal sperm motility also depends on proper ciliary function, males are generally infertile . Approximately half of patients with primary ciliary dyskinesia fall into the subgroup of Kartagener's syndrome, in which situs inversus accompanies bronchiectasis and sinusitis.

In cystic fibrosis, the tenacious secretions in the bronchi are associated with impaired bacterial clearance, resulting in colonization and recurrent infection with a variety of organisms, particularly mucoid strains of P. aeruginosa but also S. aureus, H. influenzae, Escherichia coli, and Burkholderia cepacia.

**Noninfectious Causes**

Some cases of bronchiectasis are associated with exposure to a toxic substance that incites a severe inflammatory response. Examples include inhalation of a toxic gas such as ammonia or aspiration of acidic gastric contents, though the latter problem is often also complicated by aspiration of bacteria. An immune response in the airway may also trigger inflammation, destructive changes, and bronchial dilatation. This mechanism is presumably important for bronchiectasis with allergic bronchopulmonary aspergillosis (ABPA), which is due at least in part to an immune response to Aspergillus organisms that have colonized the airway. Bronchiectasis accompanying ABPA often involves proximal airways and is associated with mucoid impaction. Bronchiectasis also occurs rarely in ulcerative colitis, rheumatoid arthritis, and Sjögren's syndrome, but it is not known whether an immune response triggers airway inflammation in these patients.

In α1-antitrypsin deficiency, the usual respiratory complication is the early development of panacinar emphysema, but affected individuals may occasionally have bronchiectasis. In the yellow nail syndrome, which is due to hypoplastic lymphatics, the triad of lymphedema, pleural effusion, and yellow discoloration of the nails is accompanied by bronchiectasis in approximately 40% of patients.

**Etiology and pathogenesis**

Bronchiectasis is a consequence of inflammation and destruction of the structural components of the bronchial wall. Infection is the usual cause of the inflammation; microorganisms such as Pseudomonas aeruginosa and Haemophilus influenzae produce pigments, proteases, and other toxins that injure the respiratory epithelium and impair mucociliary clearance. The host inflammatory response induces epithelial injury, largely as a result of mediators released from neutrophils. As protection against infection is compromised, the dilated airways become more susceptible to colonization and growth of bacteria. Thus, a reinforcing cycle can result, with inflammation producing airway damage, impaired clearance of microorganisms, and further infection, which then completes the cycle by inciting more inflammation.

**CLINICAL**

Patients typically present with persistent or recurrent cough and purulent sputum production. Hemoptysis occurs in 50 to 70% of cases and can be due to bleeding from friable, inflamed airway mucosa. More significant, even massive bleeding is often a consequence of bleeding from hypertrophied bronchial arteries.

When a specific infectious episode initiates bronchiectasis, patients may describe a severe pneumonia followed by chronic cough and sputum production.

Alternatively, patients without a dramatic initiating event often describe the insidious onset of symptoms. In some cases, patients are either asymptomatic or have a nonproductive cough, often associated with “dry” bronchiectasis in an upper lobe.

Dyspnea or wheezing generally reflects either widespread bronchiectasis or underlying chronic obstructive pulmonary disease. With exacerbations of infection, the amount of sputum increases, it becomes more purulent and often more bloody, and patients may become febrile. Such episodes may be due solely to exacerbations of the airway infection, but associated parenchymal infiltrates sometimes reflect an adjacent pneumonia.

**Physical examination**

Physical examination of the chest overlying an area of bronchiectasis is quite variable. Any combination of crackles, rhonchi, and wheezes may be heard, all of which reflect the damaged airways containing significant secretions. As with other types of chronic intrathoracic infection, clubbing may be present. Patients with severe, diffuse disease, particularly those with chronic hypoxemia, may have associated cor pulmonale and right ventricular failure. Amyloidosis can result from chronic infection and inflammation but is now seldom seen.

**Radiographic and laboratory findings**

Though the chest radiograph is important in the evaluation of suspected bronchiectasis, the findings are often nonspecific. At one extreme, the radiograph may be normal with mild disease. Alternatively, patients with saccular bronchiectasis may have prominent cystic spaces, either with or without air-liquid levels, corresponding to the dilated airways. These may be difficult to distinguish from enlarged airspaces due to bullous emphysema or from regions of honeycombing in patients with severe interstitial lung disease. Other findings are due to dilated airways with thickened walls, which result from peribronchial inflammation. Because of decreased aeration and atelectasis of the associated pulmonary parenchyma, these dilated airways are often crowded together in parallel. When seen longitudinally, the airways appear as “tram tracks”; when seen in cross-section, they produce “ring shadows.” Because the dilated airways may be filled with secretions, the lumen may appear dense rather than radiolucent, producing an opaque tubular or branched tubular structure.

**Bronchography**, which involves coating the airways with a radiopaque, iodinated lipid dye instilled through a catheter or bronchoscope, can provide excellent visualization of bronchiectatic airways. However, this technique has now been replaced by computed tomography (CT), which also provides an excellent view of dilated airways as seen in cross-sectional images. With the advent of high-resolution CT scanning, in which the images are 1.0 to 1.5 mm thick, the sensitivity for detecting bronchiectasis has improved even further. Other features on high-resolution CT scanning can suggest a specific etiology of the bronchiectasis. For example, bronchiectasis of relatively proximal airways suggests ABPA, whereas the presence of multiple small pulmonary nodules (nodular bronchiectasis) suggests infection with M. avium complex.

**Examination of sputum** often reveals an abundance of neutrophils and colonization or infection with a variety of possible organisms. Appropriate staining and culturing of sputum often provide a guide to antibiotic therapy.

Additional evaluation is aimed at diagnosing the cause for the bronchiectasis. When bronchiectasis is focal, fiberoptic bronchoscopy may reveal an underlying endobronchial obstruction. In other cases, upper lobe involvement may be suggestive of either tuberculosis or ABPA. With more widespread disease, measurement of sweat chloride levels for cystic fibrosis, structural or functional assessment of nasal or bronchial cilia or sperm for primary ciliary dyskinesia, and quantitative assessment of immunoglobulins may explain recurrent airway infection. In an asthmatic person with proximal bronchiectasis or other historical features to suggest ABPA, skin testing, serology, and sputum culture for Aspergillus are helpful in confirming the diagnosis.

Pulmonary function tests may demonstrate airflow obstruction as a consequence of diffuse bronchiectasis or associated chronic obstructive lung disease. Bronchial hyperreactivity, e.g., to methacholine challenge, and some reversibility of the airflow obstruction with inhaled bronchodilators are relatively common.

**TREATMENT**

Therapy has four major goals:

1) elimination of an identifiable underlying problem;

2) improved clearance of tracheobronchial secretions;

3) control of infection, particularly during acute exacerbations;

4) reversal of airflow obstruction.

Appropriate treatment should be instituted when a treatable cause is found, for example, treatment of hypogammaglobulinemia with immunoglobulin replacement, tuberculosis with antituberculous agents, and ABPA with glucocorticoids.

Secretions are typically copious and thick and contribute to the symptoms. A variety of mechanical methods and devices accompanied by appropriate positioning can facilitate drainage in patients with copious secretions. Mucolytic agents to thin secretions and allow better clearance are controversial. Aerosolized recombinant DNase, which decreases viscosity of sputum by breaking down DNA released from neutrophils, has been shown to improve pulmonary function in cystic fibrosis, but similar benefits have not been found with bronchiectasis due to other etiologies.

Antibiotics have an important role in management. For patients with infrequent exacerbations characterized by an increase in quantity and purulence of the sputum, antibiotics are commonly used only during acute episodes. Although choice of an antibiotic may be guided by Gram's stain and culture of sputum, empiric coverage (e.g., with ampicillin, amoxicillin, trimethoprim-sulfamethoxazole, or cefaclor) is often given initially. When P. aeruginosa is present, oral therapy with a quinolone or parenteral therapy with an aminoglycoside or third-generation cephalosporin may be appropriate. In patients with chronic purulent sputum despite short courses of antibiotics, more prolonged courses, e.g., with an oral antibiotic or inhaled aminoglycosides, or intermittent but regular courses of single or rotating antibiotics have been used.

Bronchodilators to improve obstruction and aid clearance of secretions are particularly useful in patients with airway hyperreactivity and reversible airflow obstruction. Although surgical therapy was common in the past, more effective antibiotic and supportive therapy has largely replaced surgery. However, when bronchiectasis is localized and the morbidity is substantial despite adequate medical therapy, surgical resection of the involved region of lung should be considered.

When massive hemoptysis, often originating from the hypertrophied bronchial circulation, does not resolve with conservative therapy, including rest and antibiotics, therapeutic options are either surgical resection or bronchial arterial embolization. Although resection may be successful if disease is localized, embolization is preferable with widespread disease. In patients with extensive disease, chronic hypoxemia and cor pulmonale may indicate the need for long-term supplemental oxygen. For selected patients who are disabled despite maximal therapy, lung transplantation is a therapeutic option.