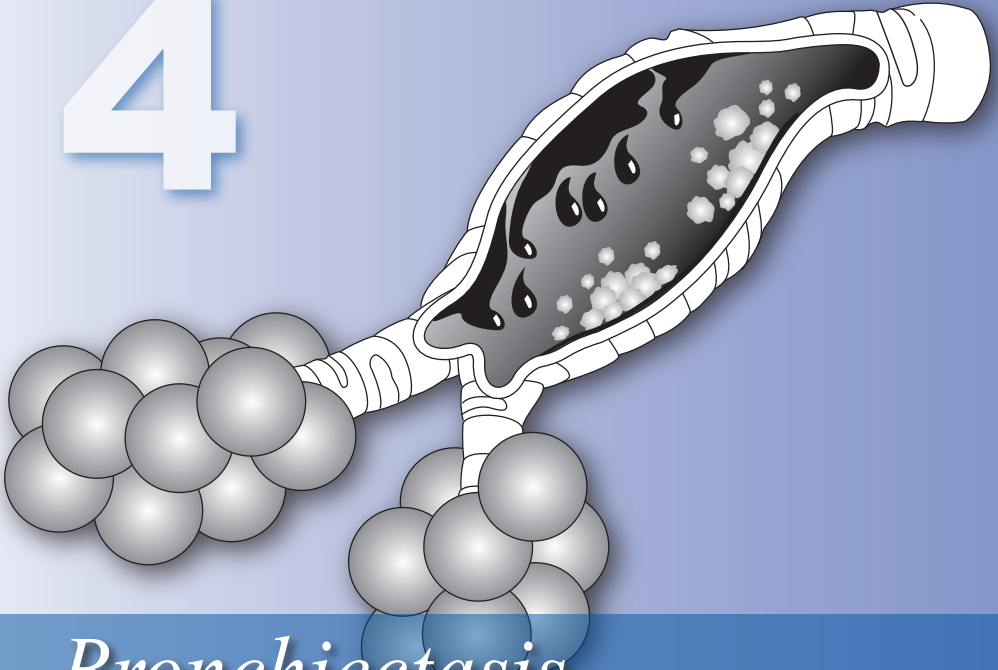


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Bronchiectasis

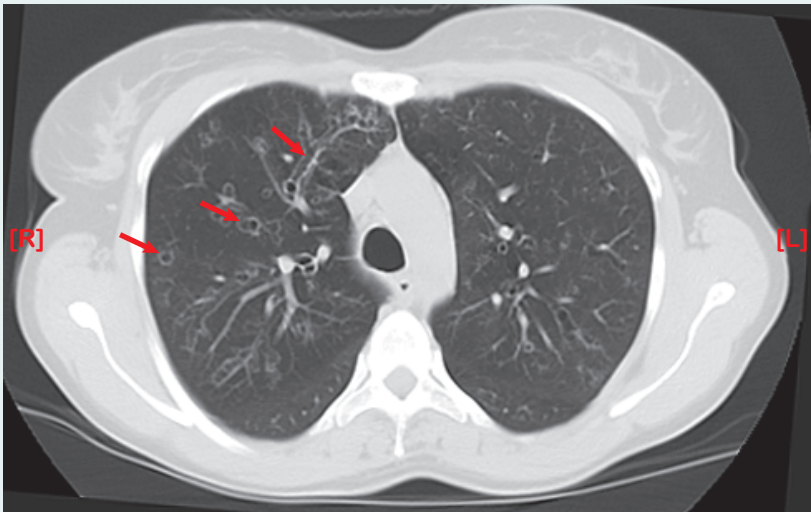
Bronchiectasis is an abnormal, chronic enlargement of the bronchi, the passageways from the trachea to the alveoli that are the air-exchanging parts of the lungs. Bronchiectasis generally occurs as a result of infection, although non-infectious factors may contribute to the development of this condition. Accompanying the enlargement of the bronchi is their decreased ability to clear secretions. Failure to clear secretions allows microbes and particles to collect in them, which leads to more secretions and inflammation that further damage the airways, causing more dilation in a vicious cycle.

Bronchiectasis may occur in a single portion of the lung (localized) or throughout the lungs (diffuse) and is the major lung abnormality of cystic fibrosis. It may have several different contributing factors, such as abnormal cilia, and its course may vary greatly from causing no symptoms to causing death.

Whom does it affect?

Epidemiology, prevalence, economic burden, vulnerable populations

The prevalence of bronchiectasis is unknown largely because the symptoms are variable and the diagnosis is often not made. In the pre-antibiotic era, it was estimated to be as common as or more common than tuberculosis and to be



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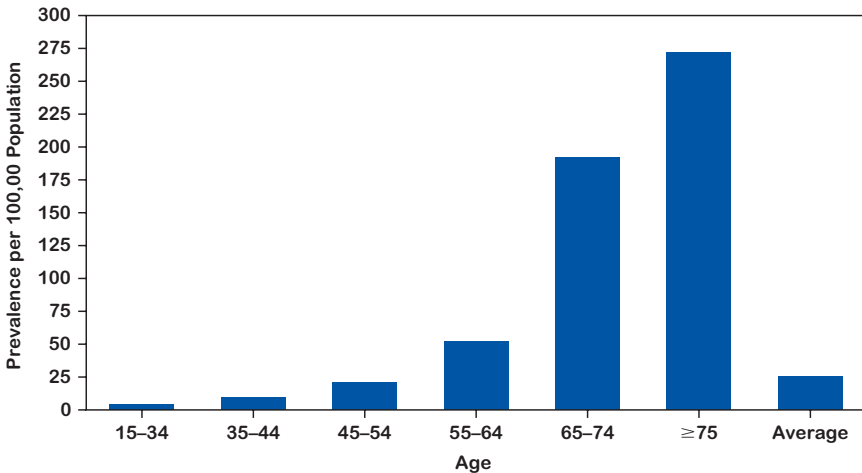
This computed tomographic (CT) image of the lungs shows dilation of the bronchi characteristic of bronchiectasis (arrows). The large white structure in the center is the aorta and the darker areas are normal lung.

present in 92 percent of cases of chronic bronchitis (1). It occurs in every age group and, in the pre-antibiotic era, it most often began in childhood (1). Among all ages, it has been estimated that about 25 people per 100,000 have bronchiectasis, but this number increases to 272 per 100,000 for those over 74 years old (2). However, these statistics were derived from insurance data, which is likely to grossly underestimate its true occurrence. Cases of bronchiectasis are more common in women than men, especially when it is of unknown cause.

A wide range of causes of bronchiectasis has been reported in adults, but for more than half of the cases, there is no known cause or association. It is estimated that between 30 and 35 percent of cases follow a lung infection that damages the bronchi for the first time (3). In addition to bacterial pneumonia, other infections, such as whooping cough (pertussis) or tuberculosis, may cause the bronchial damage. Although the inciting infections are usually severe, bronchiectasis can also occur with minimal or silent infections. This is often the case when the inciting infection is caused by nontuberculous mycobacteria (see Chapter 12).

Individuals with an inadequate immune system are at increased risk for chronic bronchial infections, which can damage airways and set up conditions

Prevalence of Bronchiectasis



Bronchiectasis increases with age. It is likely to be much more common than reported here because it is not usually detected, reported, or treated (2).

for bronchiectasis. Persons who fail to produce antibodies, a condition that can be congenital or acquired, commonly develop bronchiectasis. Other immune deficiency states are also associated with bronchiectasis.

The economic burden attributed to bronchiectasis is great, in part, because it is a chronic disease that may require frequent medical visits, antibiotics, hospitalizations, and chest physiotherapy in order to minimize the risk of recurrent infections and progressive disease. In 2001, it was estimated that the annual medical cost of care for persons in the United States with bronchiectasis was \$13,244, which is greater than the annual cost for many other chronic diseases, such as heart disease (\$12,000) and COPD (\$11,000 to \$13,000) (2). If there are over 110,000 persons in the United States with bronchiectasis, expenditures for medical care are estimated to be greater than \$1.4 billion annually.

For patients who have airway infections resistant to oral antibiotics, the burden is much greater. Intravenous antibiotics complicate care greatly because hospitalization or home monitoring is required. Treatment for these patients includes placement of a central venous catheter, coordination of the doses of drugs that often must be given multiple times per day, regular blood tests to monitor for side effects, and measurement of blood levels of the antibiotic for many days, steps that become expensive and disrupt patients' lives.

CASE STUDY

A 57-year-old woman was referred to a pulmonologist for worsening cough and sputum production over nearly two years. A nonsmoker, she appeared thin but not in distress and had no other significant medical problems. Additional symptoms included shortness of breath and fatigue. Her primary care physician had treated her with antibiotics for bronchitis six times over the previous 18 months. She had no heartburn, acid reflux, choking, or sinus symptoms. There was no systemic inflammatory disease, history of tuberculosis, or other chest infections, such as whooping cough. She had no family history of lung disease. A chest radiograph showed dilated airways in several areas that were confirmed by a chest computed tomography (CT) scan. Blood tests, including antibody (immunoglobulin) levels, were normal. Pulmonary function testing demonstrated a decrease in lung capacity with mild airflow obstruction that significantly improved with an inhaled bronchodilator. Sputum collected for bacterial culture grew the bacteria *Pseudomonas aeruginosa*. Bronchiectasis was diagnosed, and the patient began a treatment program that included a bronchodilator, a mucus-clearance device, chest physiotherapy, antibiotics, and a regular exercise program. Over the next 12 months, her symptoms improved dramatically, although they did not resolve completely. She regained her energy and was able to resume her normal lifestyle that included recreational activities, such as golfing, while continuing with her pulmonary treatment program.

Comment

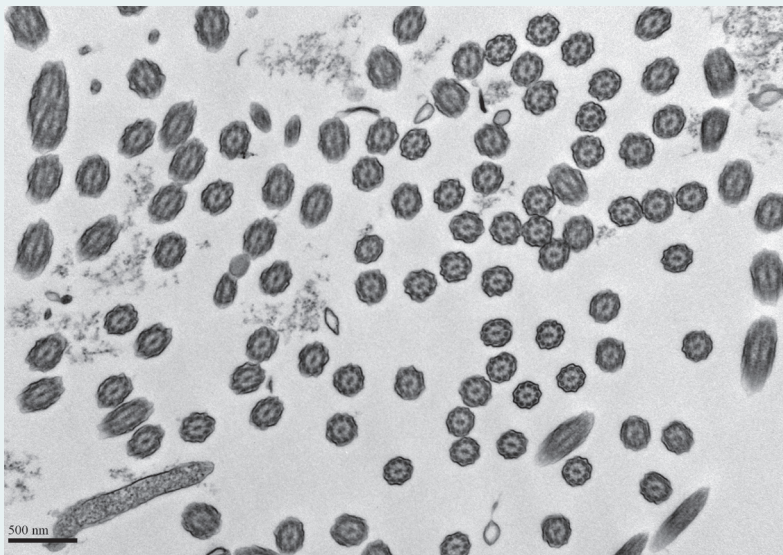
This case study represents several common features of bronchiectasis. The diagnosis of bronchiectasis is frequently delayed for months or years, often with symptoms misdiagnosed as bronchitis, asthma, or recurrent pneumonia. Symptoms are often downplayed by both the patient and physician. Once diagnosed, bronchiectasis requires a health maintenance program with intermittent treatment of airway infections. This program is usually tailored to the patient's symptoms and can range from occasional follow-up to frequent hospitalizations for intensive treatment. Chest radiographs or CT scans allow visualization of the dilated bronchi and can also diagnose pneumonia, which is a recognized complication. Pulmonary function tests demonstrate impairment of lung function when present.

What are we learning about the disease?

Pathophysiology, causes: genetic, environment, microbes

The respiratory tract is lined with cells that contain cilia, hair-like structures that stick into the mucous layer that lines the airways and beat to propel the mucus out of the lungs. Mucus traps bacteria and particles, and mucociliary clearance is an important defense mechanism for the bronchial tubes. It is not surprising that a variety of problems of cilia are associated with bronchiectasis. Ciliated cells also line the inner surface of the nose and sinuses, which are part of the respiratory tract. Ciliary disorders usually, therefore, also are associated with sinus infections. Sinus disease is common in bronchiectasis even when a ciliary defect is not known.

Almost any cause of significant bronchial injury can lead to bronchiectasis. Several auto-immune diseases, such as rheumatoid arthritis or Sjögren's syndrome, can cause bronchiectasis. Aspiration of oral contents can be particularly damaging. Gastroesophageal reflux disease (GERD) with gastric aspiration may contribute as well. Even obstruction of the airway by an inhaled peanut or other



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This electron microscopic image shows cilia, small hair-like structures on the surface of cells in the airways. Ciliary defects are associated with bronchiectasis. Cilia move mucus out of the lung. About 200 cilia are present on the surface of each cell, and more than 250 genes are responsible for their proper functioning.

foreign body can set up conditions for bronchiectasis by blocking drainage of normal mucus. Other impairments in the bronchial structure or mucociliary clearance can also cause it. For example, thick mucus can be retained in bronchi in patients with asthma. If the mucus becomes infected by a common fungus, *Aspergillus*, an intense inflammation can ensue. The inflammation can damage the airway and result in bronchiectasis.

In addition to cystic fibrosis, inherited conditions like immotile ciliary syndrome and alpha-1 antitrypsin deficiency may lead to bronchiectasis. A rare condition called *Ehlers-Danlos syndrome* causes lax supporting tissue in and around the airway that, under certain circumstances, can be associated with bronchiectasis. Bronchiectasis can also occur in a variety of rare genetic defects of the immune system.

Infection by environmental nontuberculous mycobacteria (see Chapter 12) is also being recognized and treated, with significant improvement in patients' quality of life. These ubiquitous bacteria are in the same family as *Mycobacterium tuberculosis* but are not contagious. They have a propensity to live in the secretions of patients with bronchiectasis. Most mycobacterial infections can be treated, but they require many months or even years of medication. Certain bacteria such as *Pseudomonas* and other drug-resistant organisms may be difficult to treat and require inhaled or intravenous antibiotics.

How is it prevented, treated, and managed?

Prevention, treatment, staying healthy, prognosis

Prevention of bronchiectasis is difficult because the risk for developing it is generally not known before the diagnosis. However, if a cause is known and can be corrected, that becomes the highest priority in managing bronchiectasis. For example, correcting a lack of antibodies (agammaglobulinemia) or removing a bronchial obstruction may “cure” the bronchiectasis. If other causative or aggravating conditions are present, they should be treated. For example, aspiration should be prevented, and infectious and other associated inflammatory disorders generally should be treated.

Bronchiectasis is treatable but rarely curable. In the majority of patients with bronchiectasis, there are strategies for preventing or slowing its progression. The two most important elements of these strategies are clearance of airway secretions and prompt treatment of lung infections. Retained secretions in the airway

make a favorable environment for bacteria to flourish, resulting in the cycle of infection, airway inflammation, airway injury with further enlargement, and more retained secretions. Untreated, this cycle of infection, inflammation, and injury often results in progressive symptoms and loss of lung function. In one study, poor prognosis was correlated with decreased activity and quality of life, chronic *Pseudomonas aeruginosa* infection, and poor pulmonary function tests (4).

General self-care techniques are an important part of bronchiectasis treatment. These techniques include such infection prevention methods as proper hand washing, covering the mouth when coughing, and appropriate vaccinations. Regular aerobic activity, a balanced diet, and avoidance of all tobacco products are also important.

As bronchiectasis advances, symptoms are more frequent and severe, and eradication of the infection and secretions becomes more difficult. The goal of therapy remains to minimize symptoms, prevent loss of lung function, and preserve quality of life.

Keeping airways clear of secretions helps break the infection, inflammation, and injury cycle and is a key for successful management of patients with bronchiectasis. For those patients that do not produce sputum (“dry bronchiectasis”), little is needed to do to keep airways clear. In these patients, chronic infection is uncommon.

Most patients with bronchiectasis produce from a teaspoon to over a cup of sputum per day. Techniques for clearing retained secretions vary greatly. In some instances, regular exercise is sufficient to mobilize and clear them. Chest percussion with or without postural drainage is often first tried to raise sputum. Several medical devices are marketed for this purpose. These may be simple handheld instruments that vibrate air in the airway or more complicated chest-wall vibrating devices. The vibration may “shake loose” thick mucus, but not all techniques work for every patient, and a trial-and-error approach is usually required to find the most effective regimen for a specific patient. Lack of hydration may thicken sputum, so drinking plenty of fluids is generally recommended.

Airway inflammation with asthmatic-like reactions is often present in bronchiectatic airways and most often should be treated with asthma medications, such as inhaled bronchodilators or inhaled corticosteroids. Bronchodilators relax airway muscles and may enhance mucous clearance. Inhaled corticosteroids reduce inflammation and may be beneficial in select patients. Nebulized concentrated salt solution (hypertonic saline) affords enhanced secretion clearance

in cystic fibrosis patients, but its benefit to other patients with bronchiectasis remains unproven.

Finally, a small subgroup of patients with localized bronchiectasis may benefit from surgical resection of the affected area of the lung. This procedure is most often done if the lung segment is a site of substantial bleeding, bronchial obstruction, or recurrent infection.

Are we making a difference?

Research past, present, and future

Since the first description of bronchiectasis by René Laënnec in the early 1800s, knowledge has been gained about the natural history, the characteristics of different bacteria, and the structure and physiology of the cells of the airways. Antibiotics have transformed bronchiectasis from a common sequela of pneumonia to an uncommon condition. They have also greatly improved the quality of life of these patients.

The discovery of the gene that causes cystic fibrosis in 1989 allowed more detailed knowledge of the biology of the cells of the airway, the transport of water and salts into the mucus, and the character of the sputum, although treatments for cystic fibrosis do not necessarily translate into the care of patients with bronchiectasis without cystic fibrosis.

Bronchiectasis is associated with cellular and molecular defects and adverse events that result in airway injury, mucus stagnation, and infection. Research has advanced the knowledge of each of these areas. More is being learned about who gets bronchiectasis. The complexity of ciliated cells and other bronchial lining cells is being recognized.

The slimy material that collects at the bottom of standing water is called a biofilm. Biofilms are usually made up of a community of many different bacteria; some bacteria produce the slimy material and other bacteria use it for their advantage. In humans, dental plaque is an example of a biofilm. Biofilms also occur in the airways of patients with bronchiectasis. If one species of bacteria produces a substance that inactivates an antibiotic, all the other organisms in the biofilm benefit.

Biofilm material forms a submicroscopic netlike mesh that may prevent the body's immune cells from engulfing and destroying the bacteria. The bacteria of the biofilm communicate to inform each other about the concentration of bacteria. The communications may signal the bacteria to grow if conditions are favorable, or to reduce activity if conditions are not. A change in activity of the bacteria

could irritate the bronchial lining cells and set off an episode of cough, sputum, and breathlessness.

As more is being learned about biofilms, new agents are being developed that can block the inter-bacterial communication. Although antibiotics and secretion clearance have led to stabilization of bronchiectasis in most patients, better antibiotics are being developed to allow oral medications and nebulized solutions to replace intravenous medicines to treat exacerbations of bronchiectasis.

A national non-cystic fibrosis bronchiectasis registry has been established to better define the patients and the infections they get. This registry has been modeled after the one for cystic fibrosis patients that was established many years ago. Genetic studies, which would investigate predisposing factors, should open new doors to study the cells and molecules that fail to protect against bronchiectasis as well as to alert persons who might be at increased risk for the disease.

What we need to cure and eliminate bronchiectasis

Bronchiectasis is almost certainly less frequent and severe today than it was in the preantibiotic era. Treatment of pneumonia with antibiotics has reduced cases of bronchiectasis, a common sequela. Development of antibiotics that are easier to deliver and more effective should further reduce its burden. The next steps toward eliminating bronchiectasis require better understanding of the basic mechanisms of the disease, the organisms involved, biofilms, and how the lung damage is perpetuated. Research on nontuberculous mycobacteria, their relation to the mucus layer, and susceptibility to new antibiotics will likely help control this group of pathogens. Clinical trials need to be done to determine when, which, and how long antibiotics should be given. Lastly, awareness leading to more prompt diagnosis and treatment of both bronchiectasis and its underlying conditions is essential to reduce and control this disease.

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Web sites of interest

Bronchiectasis Research Registry
www.csc.unc.edu/bron

National Heart, Lung, and Blood Institute
Diseases and Conditions Index
www.nhlbi.nih.gov/health/dci/index.html

Nontuberculous Mycobacteria Info & Research, Inc.
<http://ntminfo.org>

Cystic Fibrosis Foundation
www.cff.org