Bronchiectasis

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Bronchiectasis is a chronic respiratory disease with distinctive radiographic findings characterized by irreversible dilatation of small- and medium-sized bronchi from recurrent and prolonged infections or inflammation. The most common complaint is a chronic wet cough from impaired mucus clearance and subsequent airway plugging, but symptoms can also include hemoptysis, weight loss, wheezing, and difficulty breathing. Patients may also have concurrent moderate or severe persistent asthma, gastroesophageal reflux disease, or snoring secondary to sleep apnea. Broadly, the underlying etiology of bronchiectasis is cystic fibrosis (CF) or a non-CF process such as allergic bronchopulmonary aspergillosis (ABPA), immunodeficiencies, airway obstruction secondary to tumor or foreign body, neuromuscular disorders with poor cough and airway clearance, or genetic diseases such as primary ciliary dyskinesia (PCD) or alpha-1 antitrypsin deficiency. Those diagnosed as having bronchiectasis before age 6 months often have histories of chronic lung disease, prematurity, poor weight gain, and failure to thrive. When patients with bronchiectasis present after 6 months, their histories often show recurrent pulmonary and sinus infections beyond the limits of normal, along with a frequent need for antibiotics and corticosteroids to control respiratory symptoms.

The general presentation to arouse suspicion for bronchiectasis is an unremitting productive cough with evidence of decreased pulmonary function during an exacerbation. Physical examination is extremely variable depending on whether the patient is in a state of relative wellness or experiencing a flare of symptoms. Chest expansion can range from normal to hyperexpanded, and pulmonary findings can include crackles, crepitus, or rhonchi or be entirely clear on auscultation. Pulmonary function tests show nonreversible obstructive defects. If a patient presents in a period of health, one should not be dissuaded from beginning an evaluation for bronchiectasis and initiating a possible referral to an appropriate specialist.

Subspecialty referrals can be made depending on local resources and the history and clinical course of symptoms. For distinctive pulmonary symptoms, a pulmonologist would be appropriate, but for patients with recurrent sinusitis, otitis, and bronchitis, referral to allergy/immunology allows for immunodeficiency evaluation in the context of repeated bouts of infection. If ABPA is suspected, an immunoglobulin E level can be helpful. Although further laboratory studies performed in conjunction with an allergist/immunologist, such as lymphocyte subset enumeration, memory B-cell panel, and mitogen proliferation studies, can elucidate specific immune vulnerabilities, the general goal is to first rule out PCD. Otolaryngology referral can be made to obtain the ciliary biopsies required to make the PCD diagnosis but can also clarify any airway anatomy contributing to the symptoms.

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the illness. Sinus imaging can detect underlying sinus disease or aberrant sinus anatomy.

The diagnosis of bronchiectasis is confirmed by evidence of airway dilatation on high-resolution noncontrast computed tomography. Chest computed tomography will note specific findings of airway dilatation, particularly pronounced compared with the adjacent pulmonary artery diameter. There can be central or peripheral airway dilatation, with or without scarring of the pulmonary parenchyma. In addition, there is an anatomical correlation between distribution of bronchiectasis and pathology; bronchiectasis from CF tends to occur in the upper lobes, whereas postinfectious bronchiectasis preferentially appears in the lower lobes. Based on the level of suspicion for chronic colonization, sputum, tracheal aspirate, and bronchial cultures can be obtained by bronchoscopy and early-morning gastric lavage. Early diagnosis of bronchiectasis is important because prompt treatment can help preserve remaining lung function.

There are currently no evidence-based criteria or treatment guidelines for pediatric bronchiectasis, necessitating that some recommendations for children be derived from adult studies. Because bronchiectasis is a dynamic disease process that can regress and recur, management generally focuses on airway clearance to evacuate mucus and on antimicrobials to eliminate infection. When asymptomatic, patients should practice chest percussion therapy at some baseline frequency to facilitate mucociliary clearance, with increased frequency and duration of these airway clearance techniques when they get sick. Data on pharmacologic airway clearance with inhaled mucoactive drugs is indeterminate; hypertonic saline is efficacious in children with CF and adults with non-CF bronchiectasis, whereas recombinant DNase did not show benefit to adults with non-CF bronchiectasis in some case reports. Likewise, bronchodilators and inhaled corticosteroids such as fluticasone were promising therapies in bronchiectasis patients with symptomatic comorbid asthma but has limited applicability to nonasthmatic children. With each treatment comes an added layer of complexity to an increasingly lengthy medication regimen, making adherence a challenge as well. Preventive therapies are universally recommended, with influenza vaccine yearly and a complete primary series of *Haemophilus influenzae* and pneumococcal (13-valent pneumococcal conjugate vaccine) vaccines, with an additional 23-valent pneumococcal polysaccharide vaccine in childhood. To minimize susceptibility to future exacerbations, patients should continue all therapies for concurrent asthma, allergies, and rhinitis when relevant and strive to optimize their nutritional status by increasing dietary intake or increasing caloric content via gastrostomy feeds if needed.

Recently, macrolides have come to attention due to their immunomodulating and anti-inflammatory effects. Their benefit in treating organisms such as *Staphylococcus aureus*, streptococcus, and *H influenza* make them useful in treating the usual suspects of childhood infection and giving them promise as long-term chronic treatment for bronchiectasis exacerbations unrelated to CF. A limited randomized controlled study in 2013 (Bronchiectasis Intervention Study) determined weekly azithromycin therapy to be effective in decreasing pulmonary exacerbations in children with confirmed or suspected non-CF bronchiectasis, and a 2018 review suggests similar results with long-term azithromycin therapy in adults. Evidence on macrolides remains inconclusive because their cardiovascular effect of QT prolongation must be considered in the context of bacterial resistance and patient adherence. Inhaled nonsteroidal anti-inflammatory drugs have been posited to reduce chronic airway inflammation in bronchiectasis, but not proven, and as such are not recommended.

Of the limited data on antibiotic therapy in acute exacerbations of pediatric non-CF-related bronchiectasis, 2 international bronchiectasis exacerbation studies (BEST-1 and BEST-2) are precedent randomized controlled trials specifically evaluating acute treatment. The Australian BEST-1 study found that 14 days of amoxicillin-clavulanate therapy was superior first-line treatment for acute bronchiectasis exacerbations, and BEST-2 determined that 21 days of azithromycin therapy was non-inferior to amoxicillin-clavulanate, especially in clinical situations involving penicillin allergy or noncompliance. Ultimately, the specific antimicrobial agent is selected based on the organism grown from a respiratory sample obtained on the day of presentation, or it can be selected empirically based on cultures from previous bronchiectasis episodes.

Bronchiectasis is an underdiagnosed condition with significant associated morbidity. The most important differentiation is whether the bronchiectasis is CF-related because this makes a difference in methods of airway clearance and in treatment of acute and chronic infection. When faced with suspected non-CF bronchiectasis, the primary etiology may be difficult to determine and requires a comprehensive evaluation, usually with subspecialty support. Most research on bronchiectasis encompasses other comorbidities, such as CF or immune deficiencies, which differ in management and outcomes. Adult studies have moderate evidence at best and may not be generalizable to children.

Many challenges still exist with bronchiectasis, including vague clinical diagnostic criteria, a limited research population, and lack of formal universal management guidelines. Therefore, general pediatricians must be vigilant in
recognizing bronchiectasis by using a longitudinal history, close follow-up, and a high index of suspicion.

COMMENTS: Bronchiectasis can be challenging to diagnose, as this In Brief reviews. Yet it is prudent to diagnose both to determine whether there is an underlying etiology such as an immunodeficiency disorder that has treatment options of its own and to provide the best preventive treatments because the pulmonary effects are irreversible and future exacerbations can cause more damage. Hence, earlier diagnosis may help prevent further morbidity and preserve lung function. The actions of pediatricians are essential to help patients improve their future lung function, improve their quality of life, and minimize morbidity and mortality because this chronic diagnosis will continue to be problematic along the life course. As noted in this In Brief, there has been a paucity of research especially in children, and randomized controlled trials are needed to provide best options for therapy. An international bronchiectasis network has been set up linking researchers and patients from the United States, Europe, Australia, and Asia. These types of international networks are essential to gather epidemiological information, facilitate the collaboration of research expertise in designing studies, and include patients from different geographic regions to provide sufficient sample sizes needed to develop best practice guidelines.

–Janet Serwint, MD
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