Bronchiectasis, initially considered a rare lung disease, is now being diagnosed with increasing frequency in the developed world. It was initially described by Laennec in 1819 and is defined as an abnormal dilatation of bronchi. The purpose of this update is to review the prevalence, diagnosis, natural history, aetiologies and treatment of non-CF (cystic fibrosis) bronchiectasis.

Prevalence
Weycker et al reported a prevalence in the US of 4.2 per 100,000 persons aged 18 to 34 years and 272 per 100,000 persons among those over 75 years of age. Bronchiectasis is more common in women than in men and, though seen across the age spectrum, is more frequently encountered in middle-aged and elderly persons. Globally, certain demographic groups have been recognised as having an increased risk for the development of bronchiectasis, including individuals with poor access to healthcare or high rates of pulmonary infection in childhood.

Diagnosis
Bronchiectasis should be considered in patients who present with chronic cough productive of mucopurulent sputum. Other features of bronchiectasis include dyspnoea, hemoptysis and nonspecific constitutional complaints like fatigue and weight-loss. Clinical findings may include crackles and wheezes on lung examination and clubbing of the digits. Pulmonary function testing results generally show airflow obstruction ranging from modest to severe. However, bronchiectasis is currently nearly always diagnosed using high-resolution computed tomography (HRCT) scanning. The main diagnostic features are:
- Internal diameter of a bronchus is wider than its adjacent pulmonary artery
- Failure of the bronchi to taper
- Visualisation of bronchi in the outer 1-2cm of the lung fields.

Natural history
One large clinical trial showed a frequency of 1.5 exacerbations per year in patients from North America, the UK and Ireland who were receiving ‘usual’ care for their bronchiectasis. In the past few years, two studies have demonstrated a decline of approximately 50ml/yr in FEV1 in patients with non-CF bronchiectasis. Factors associated with an accelerated rate of decline of lung function include chronic colonisation by Pseudomonas aeruginosa, a history of severe exacerbations and evidence of systemic inflammation.

Aetiology
The aetiologies of bronchiectasis can be categorised as idiopathic, post-infectious, or due to an underlying anatomic or systemic disease. Congenital causes of bronchiectasis include cystic fibrosis (CF), primary ciliary dyskinesia (PCD) and alpha 1-antitrypsin (AAT) deficiency. PCD is a rare genetic disorder also causing bronchiectasis, rhinosinusitis, ear infections and infertility. About one-half of patients with PCD have situs inversus totalis and a smaller percentage have pectus excavatum. Immune deficiencies such as primary hypogammaglobulinaemia can contribute to the onset of bronchiectasis.

IgG subclass deficiencies have been implicated in bronchiectasis, but the evidence is mixed and antibody production deficiency may need to be present in addition to decreased levels. Rarely, immune defects of neutrophil adhesion, respiratory burst and chemotaxis lead to bronchiectasis. Furthermore, HIV/AIDS has been associated with bronchiectasis. Immune-related diseases such as allergic bronchopulmonary aspergillosis (ABPA), collagen vascular diseases and inflammatory bowel diseases all may contribute to the development of bronchiectasis. Bronchiectasis is being noted with increasing frequency in patients with COPD and asthma.

Treatment
The treatment of bronchiectasis may be divided into:
Bronchiectasis is a chronic lung disease characterized by dilated and often infected airways. It can be caused by various factors, including infections, irritants, and genetic predispositions. The chronic inflammation of the airways can lead to recurrent exacerbations, which are episodes of worsening symptoms.

**Antibiotic therapy**
- For both maintenance and treatment of exacerbations
- Anti-inflammatory therapy
- Mobilisation of airway secretions

Furthermore, where an underlying systemic aetiology is identified, it should be addressed, e.g., immunoglobulin replacement for documented deficiency.

**Antibiotic therapy**

It is critical that antimicrobial therapies should be aimed at identified pathogens; hence, sputum cultures need to be obtained frequently and antibiotic sensitivity patterns and antibiotic usage need to be monitored. Gram-negative bacteria are found most commonly, though Staphylococcus aureus and non-tuberculous mycobacteria are encountered also. Up to one-third of patients with bronchiectasis are chronically colonized with P. aeruginosa. This cohort experiences an accelerated decline in lung function and more frequent exacerbations. Notably, the presence of S. aureus raises the suspicion for the presence of cystic fibrosis.

Maintenance antibiotics are commonly used in bronchiectasis although evidence to support them from controlled trials is poor. A retrospective report of 26 patients with bronchiectasis who were treated with cycles of alternating antibiotics, including a quinolone, showed radiographic stability of disease in 77% of patients; the length of therapy was from six to 84 months. Inhaled tobramycin has shown a microbiological benefit in two studies. In the first study, 74 patients were randomised to participate in a four-week trial of inhaled tobramycin, 300mg twice a day, versus placebo, and the treated patients showed decreased P. aeruginosa density in their sputum two weeks after completing therapy.

The second study was an open-label trial of 41 patients who were treated for three cycles of two weeks on/two weeks off with inhaled tobramycin 300mg twice a day, and again a microbiological benefit was demonstrated in addition to improvement in pulmonary symptom scores. An open label trial of colistin in 18 patients showed a reduction in decline in FEV1 and improved quality of life. The greatest concern in using maintenance antibiotics is the possibility of the development of resistance, particularly since the evidence from clinical trials is weak. When bronchiectasis patients experience an exacerbation, it is critical that antibiotic therapy should be tailored to their sputum microbiology results. Mild-to-moderate exacerbations may be treated with therapy with oral antibiotics for two to three weeks, although the optimal duration of therapy is unknown. Severe exacerbations usually require intravenous antibiotics in the home or hospital setting.

**Reduction of airway inflammation**

Treatment with inhaled corticosteroids and oral macrolides may reduce airway inflammation in patients with bronchiectasis. Inhaled fluticasone has been shown to reduce sputum levels of inflammatory markers. Further, the same group has published a 12-month clinical trial that showed clinical improvement in patients who had been treated with 500µg of inhaled fluticasone twice per day compared to placebo.

Macrolide antibiotics are thought to have an anti-inflammatory effect in airways diseases such as panbronchiolitis or bronchiolitis obliterans. In bronchiectasis, the oral macrolide, erythromycin has been shown to reduce the 24-hour sputum volume and improve lung function in a placebo-controlled pilot study. Moreover, a small open-label trial of azithromycin, 500mg twice per week for six months, also suggested a clinical benefit as the patients had a decreased number of exacerbations.

However, one must be cognisant of the possibility of improperly treating unrecognised mycobacterial infections with single-agent macrolide therapy.

**Mobilisation of airway secretions**

There are few studies examining the role of both pharmacological agents and physiotherapy in non-CF bronchiectasis. Bronchodilator therapy with adrenergic and anticholinergic agents are commonly used; however, there have been no randomised controlled trials to support their use. Chest physiotherapy with postural drainage, active cycle of breathing, oscillatory positive expiratory pressure devices, and high-frequency assisted airway clearance also constitute important therapy for patients with bronchiectasis.

**Multimodality treatment plan**

Bronchiectasis is being diagnosed with increasing frequency in developed countries. It is vital that a tailored clinical evaluation is performed on patients where bronchiectasis is suspected, to detect any underlying cause and to initiate an appropriate multimodality treatment plan.

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**References**