HARRISON'S PRINCIPLES OF INTERNAL MEDICINE — 22nd Edition

Bronchiectasis

Chapter 301 | Part 7: Disorders of the Respiratory System | Part 7 – Respiratory Disorders | DETAILED EDITION

KEY CLINICAL POINTS

1. Bronchiectasis is defined as irreversible airway dilation involving the lung in a focal or diffuse manner, classically categorized as cylindrical/tubular, varicose, or cystic.
2. The 'vicious cycle hypothesis' describes how susceptibility to infection and poor mucociliary clearance lead to microbial colonization, inflammation, and airway wall damage.
3. Chest CT is the imaging modality of choice; findings include 'tram tracks' (parallel dilated airways), 'signet-ring sign' (airway diameter ≥1.5 times adjacent vessel), lack of tapering, and 'tree-in-bud' pattern.
4. Diagnosis requires radiologic criteria (e.g., inner/outer-airway-artery diameter ratio ≥1.5, lack of airway tapering) along with clinical syndrome (cough, sputum, exacerbations).
5. Focal bronchiectasis requires bronchoscopy to exclude airway obstruction by mass or foreign body.
6. NTM (Mycobacterium avium-intracellulare complex) is the most common NTM pathogen; treatment requires macrolide susceptibility testing and ruling out colonization before chronic macrolide therapy.
7. Long-term macrolide therapy (azithromycin/erythromycin) reduces exacerbations and mucus production but carries risks of macrolide-resistant NTM and QT prolongation.
8. Dornase (DNase) is recommended for CF-related bronchiectasis but not for non-CF bronchiectasis due to lack of efficacy and potential harm.
9. Massive hemoptysis management requires intubation, identification of bleeding source, and bronchial artery embolization.
10. Lung function decline in non-CF bronchiectasis is similar to COPD (FEV1 declining 50–55 mL/year), compared to 20–30 mL/year in healthy controls.

FIGURES IN THIS CHAPTER

1. DEFINITION & OVERVIEW

Bronchiectasis refers to an irreversible airway dilation that involves the lung in either a focal or a diffuse manner and that classically has been categorized as cylindrical or tubular (the most common form), varicose,

or cystic. This chapter will focus largely on non–cystic fibrosis (CF) bronchiectasis. The reader is referred to Chapter 302 for a more focused discussion on CF bronchiectasis.

1.1 Classification by Pattern

• Focal bronchiectasis refers to bronchiectatic changes in a localized area of the lung and can be a consequence of obstruction of the airway—either extrinsic (e.g., due to compression by adjacent lymphadenopathy or parenchymal tumor mass) or intrinsic (e.g., due to an airway tumor or aspirated foreign body, a scarred/stenotic airway, or bronchial atresia from congenital underdevelopment).

1.2 Classification by Morphology

• Cylindrical or tubular (most common form).

1.3 Classification by Morphology (Continued)

• Varicose.

1.4 Classification by Morphology (Continued)

• Cystic.

2. EPIDEMIOLOGY

The overall reported prevalence of bronchiectasis in the United States has recently increased, but the epidemiology of bronchiectasis varies greatly with the underlying etiology.

2.1 Age and Sex Distribution

• Patients with CF often develop significant clinical bronchiectasis in late adolescence or early adulthood, although atypical presentations of CF in adults in their thirties and forties also are possible.

2.2 Age and Sex Distribution (Continued)

• Bronchiectasis resulting from MAC infection classically affects nonsmoking women >50 years of age.

2.3 Age and Sex Distribution (Continued)

• In general, the incidence of bronchiectasis increases with age.

2.4 Age and Sex Distribution (Continued)

• Bronchiectasis is more common among women than among men.

2.5 Comorbidities

• Bronchiectasis may also frequently be co-diagnosed with chronic obstructive pulmonary disease (COPD) or asthma.

2.6 Geographic Variation

• In areas where tuberculosis is prevalent, bronchiectasis more frequently occurs as a sequela of granulomatous infection.

2.7 Geographic Variation (Continued)

• Focal bronchiectasis can arise from extrinsic compression of the airway by enlarged granulomatous lymph nodes and/or from development of intrinsic obstruction as a result of erosion of a calcified lymph node through the airway wall (e.g., broncholithiasis).

2.8 Geographic Variation (Continued)

• Apart from cases associated with tuberculosis, an increased incidence of non-CF bronchiectasis with an unclear underlying mechanism has been reported as a significant problem in developing nations.

2.9 Geographic Variation (Continued)

• It has been suggested that the high incidence of malnutrition in certain areas may predispose to immune dysfunction and development of bronchiectasis.

3. ETIOLOGY & PATHOPHYSIOLOGY

Bronchiectasis can arise from infectious or noninfectious causes (Table 301-1). Clues to the underlying etiology often are provided by the pattern of lung involvement.

3.1 Pathogenesis: Infectious Bronchiectasis

• The most widely cited mechanism of infectious bronchiectasis is the 'vicious cycle hypothesis,' in which susceptibility to infection and poor mucociliary clearance result in microbial colonization of the bronchial tree.

3.2 Pathology: Classic Studies

• Classic studies of the pathology of bronchiectasis from the 1950s demonstrated significant small-airway wall inflammation and larger-airway wall destruction as well as dilation, with loss of elastin, smooth muscle, and cartilage.

3.3 Pathophysiology: Small Airway Inflammation

• It has been proposed that inflammatory cells in the small airways release proteases and other mediators, such as reactive oxygen species and proinflammatory cytokines, that damage the larger airway walls.

3.4 Pathophysiology: Airflow Obstruction

• Furthermore, the ongoing inflammatory process in the smaller airways results in airflow obstruction.

3.5 Pathophysiology: Antiproteases

• It is thought that antiproteases, such as α1 antitrypsin, play an important role in neutralizing the damaging effects of neutrophil elastase and in enhancing bacterial killing.

3.6 Pathophysiology: Alpha-1 Antitrypsin Deficiency

• Bronchiectasis and emphysema have been observed in patients with α1 antitrypsin deficiency.

3.7 Pathophysiology: Noninfectious Bronchiectasis

• Proposed mechanisms for noninfectious bronchiectasis include immune-mediated reactions that damage the bronchial wall (e.g., those associated with systemic autoimmune conditions such as Sjögren's syndrome and rheumatoid arthritis).

3.8 Pathophysiology: Noninfectious Bronchiectasis (Continued)

• Recent studies suggest that there might exist a new bronchiectasis endophenotype of patients with sensitization to multiple environmental allergens.

3.9 Pathophysiology: Traction Bronchiectasis

• Traction bronchiectasis refers to dilated airways arising from parenchymal distortion as a result of lung fibrosis (e.g., postradiation fibrosis or idiopathic pulmonary fibrosis).

3.10 Congenital Causes

• More pronounced involvement of the upper lung fields is most common in CF and also is observed in postradiation fibrosis, corresponding to the lung region encompassed by the radiation port.

3.11 Congenital Causes (Continued)

• Bronchiectasis with predominant involvement of the lower lung fields usually has its source in chronic recurrent aspiration (e.g., due to esophageal motility disorders like those in scleroderma), end-stage fibrotic lung disease (e.g., traction bronchiectasis from idiopathic pulmonary fibrosis), or recurrent immunodeficiency-associated infections (e.g., hypogammaglobulinemia).

3.12 Congenital Causes (Continued)

• Bronchiectasis resulting from infection by nontuberculous mycobacteria (NTM), most commonly the Mycobacterium avium-intracellulare complex (MAC), often preferentially affects the midlung fields.

3.13 Congenital Causes (Continued)

• Congenital causes of bronchiectasis with predominant midlung field involvement include the dyskinetic/immotile cilia syndrome.

3.14 Congenital Causes (Continued)

• Finally, predominant involvement of central airways is reported in association with allergic bronchopulmonary aspergillosis (ABPA), in which an immune-mediated reaction to Aspergillus damages the bronchial wall.

3.15 Congenital Causes (Continued)

• Congenital causes of central airway–predominant bronchiectasis resulting from cartilage deficiency include tracheobronchomegaly (Mounier-Kuhn syndrome) and Williams-Campbell syndrome.

3.16 Idiopathic Bronchiectasis

• In many cases, the etiology of bronchiectasis is not determined. In case series, as many as 25–50% of patients referred for bronchiectasis have idiopathic disease.

3.17 Idiopathic Bronchiectasis (Continued)

• There is increasing appreciation for the need to define disease subphenotypes in this heterogeneous group of underlying causes of bronchiectasis, which might permit better targeting of clinical trials and treatment strategies.

4. CLINICAL FEATURES

The evaluation of a patient with bronchiectasis entails elicitation of a clinical history, chest imaging, and a workup to determine the underlying etiology.

4.1 Clinical Presentation

• The most common clinical presentation is a persistent productive cough with ongoing production of thick, tenacious sputum.

4.2 Physical Findings

• Physical findings frequently include crackles and wheezing on lung auscultation, and some patients with bronchiectasis exhibit clubbing of the digits.

4.3 Pulmonary Function Tests

• Mild to moderate airflow obstruction often is detected on pulmonary function tests, overlapping with that seen at presentation with other conditions, such as COPD.

4.4 Acute Exacerbations

• Acute exacerbations of bronchiectasis usually are characterized by changes in the nature of sputum production, with increased volume and purulence.

4.5 Acute Exacerbations (Continued)

• However, typical signs and symptoms of lung infection, such as fever and new infiltrates, may not be present.

4.6 Focal Bronchiectasis Evaluation

• Evaluation of focal bronchiectasis almost always requires bronchoscopy to exclude airway obstruction by an underlying mass or foreign body.

5. DIFFERENTIAL DIAGNOSIS

The diagnosis usually is based on presentation with a persistent chronic cough and sputum production accompanied by consistent radiographic features.

5.1 Radiographic Features

• Although chest radiographs lack sensitivity, the presence of 'tram tracks' indicating dilated airways is consistent with bronchiectasis.

5.2 Radiographic Features (Continued)

• Chest CT is more specific for bronchiectasis and is the imaging modality of choice for confirming the diagnosis.

5.3 Differential Diagnosis by Etiology

• Obstruction (e.g., aspirated foreign body, tumor mass).

5.4 Differential Diagnosis by Etiology (Continued)

• Infection (e.g., bacterial, nontuberculous mycobacterial).

5.5 Differential Diagnosis by Etiology (Continued)

• Immunodeficiency (e.g., hypogammaglobulinemia, HIV infection, bronchiolitis obliterans after lung transplantation).

5.6 Differential Diagnosis by Etiology (Continued)

• Genetic causes (e.g., cystic fibrosis, Kartagener's syndrome, α1 antitrypsin deficiency).

5.7 Differential Diagnosis by Etiology (Continued)

• Autoimmune or rheumatologic causes (e.g., rheumatoid arthritis, Sjögren's syndrome, inflammatory bowel disease).

5.8 Differential Diagnosis by Etiology (Continued)

• Immune-mediated disease (e.g., allergic bronchopulmonary aspergillosis).

5.9 Differential Diagnosis by Etiology (Continued)

• Recurrent aspiration.

5.10 Differential Diagnosis by Etiology (Continued)

• Miscellaneous (e.g., yellow nail syndrome, traction bronchiectasis from postradiation fibrosis or idiopathic pulmonary fibrosis).

5.11 Differential Diagnosis by Etiology (Continued)

• Idiopathic (Exclusion of other causes).

6. INVESTIGATIONS & DIAGNOSIS

A workup for diffuse bronchiectasis includes analysis for the major etiologies (Table 301-1), with an initial focus on excluding CF. Pulmonary function testing is an important component of a functional assessment of the patient.

6.1 Chest Imaging

• Chest imaging (chest x-ray and/or chest CT) is included in the general workup for all etiologies of bronchiectasis.

6.2 Bronchoscopy

• Chest imaging (chest x-ray and/or chest CT) and bronchoscopy are used for focal bronchiectasis workup.

6.3 Sputum Analysis

• Sputum Gram's stain/cultures for acid-fast bacilli and fungi.

6.4 Sputum Analysis (Continued)

• If no pathogen is identified, consider bronchoscopy with bronchoalveolar lavage.

6.5 Laboratory Tests

• Complete blood count with differential; immunoglobulin measurement; HIV testing.

6.6 Laboratory Tests (Continued)

• Measurement of chloride levels in sweat (for cystic fibrosis).

6.7 Laboratory Tests (Continued)

• α1 antitrypsin levels; nasal or respiratory tract brush/biopsy (for dyskinetic/immotile cilia syndrome); genetic testing.

6.8 Laboratory Tests (Continued)

• Clinical examination with careful joint exam, serologic testing (e.g., for rheumatoid factor).

6.9 Laboratory Tests (Continued)

• Consider workup for underlying allergic bronchopulmonary aspergillosis.

6.10 Laboratory Tests (Continued)

• Test of swallowing function and general neuromuscular strength.

6.11 Diagnostic Criteria

• Recently, a group of international experts put forth consensus guidelines for clinical and radiologic diagnosis of bronchiectasis, proposing that a diagnosis of bronchiectasis should require radiologic criteria (at least one of the following on chest CT: [1] inner- or [2] outer-airway-artery diameter ratio ≥1.5; [3] lack of airway tapering; and, [4] visibility of airways in the periphery) along with the clinical syndrome (at least two of the following: [1] cough most days of the week; [2] sputum production most days of the week; and [3] history of exacerbations).

6.12 NTM Diagnostic Criteria

• Decisions about treatment of NTM infection can be difficult, given that these organisms can be colonizers as well as pathogens, and the prolonged treatment course often is not well tolerated.

6.13 NTM Diagnostic Criteria (Continued)

• Consensus guidelines have advised that diagnostic criteria for true clinical infection with NTM should be considered in patients with symptoms and radiographic findings of lung disease who have at least two sputum samples positive on culture; at least one bronchoalveolar lavage (BAL) fluid sample positive on culture; a biopsy sample displaying histopathologic features of NTM infection (e.g., granuloma or a positive stain for acid-fast bacilli) along with one positive sputum culture; or a pleural fluid sample (or a sample from another sterile extrapulmonary site) positive on culture.

6.14 NTM Diagnostic Criteria (Continued)

• MAC strains are the most common NTM pathogens, and the recommended regimen for HIV-negative patients infected with macrolide-sensitive MAC includes a macrolide combined with rifampin and ethambutol.

6.15 NTM Diagnostic Criteria (Continued)

• Consensus guidelines recommend macrolide susceptibility testing for MAC isolates.

7. MANAGEMENT & TREATMENT

Treatment of infectious bronchiectasis is directed at the control of active infection and improvements in secretion clearance and bronchial hygiene so as to decrease the microbial load within the airways and minimize the risk of repeated infections.

7.1 Antibiotic Treatment

• Antibiotics targeting the causative or presumptive pathogen (with Haemophilus influenzae and P. aeruginosa isolated commonly) should be administered in acute exacerbations, usually for a minimum of 7–10 days and perhaps for as long as 14 days.

7.2 NTM Treatment

• Decisions about treatment of NTM infection can be difficult, given that these organisms can be colonizers as well as pathogens, and the prolonged treatment course often is not well tolerated.

7.3 NTM Treatment (Continued)

• Consensus guidelines have advised that diagnostic criteria for true clinical infection with NTM should be considered in patients with symptoms and radiographic findings of lung disease who have at least two

sputum samples positive on culture; at least one bronchoalveolar lavage (BAL) fluid sample positive on culture; a biopsy sample displaying histopathologic features of NTM infection (e.g., granuloma or a positive stain for acid-fast bacilli) along with one positive sputum culture; or a pleural fluid sample (or a sample from another sterile extrapulmonary site) positive on culture.

7.4 NTM Treatment (Continued)

• MAC strains are the most common NTM pathogens, and the recommended regimen for HIV-negative patients infected with macrolide-sensitive MAC includes a macrolide combined with rifampin and ethambutol.

7.5 NTM Treatment (Continued)

• Consensus guidelines recommend macrolide susceptibility testing for MAC isolates.

7.6 Bronchial Hygiene

• The numerous approaches used to enhance secretion clearance in bronchiectasis include hydration and mucolytic administration, aerosolization of bronchodilators and hyperosmolar agents (e.g., hypertonic saline), and chest physiotherapy (e.g., postural drainage, traditional mechanical chest percussion via hand clapping to the chest, or use of devices such as an oscillatory positive expiratory pressure flutter valve or a high-frequency chest wall oscillation vest).

7.7 Bronchial Hygiene (Continued)

• Pulmonary rehabilitation and a regular exercise program may assist with secretion clearance as well as with other aspects of bronchiectasis, including improved exercise capacity and quality of life.

7.8 Mucolytics

• The mucolytic dornase (DNase) is recommended routinely in CF-related bronchiectasis but not in non-CF bronchiectasis, given concerns about lack of efficacy and potential harm in the non-CF population.

7.9 Anti-Inflammatory Therapy

• It has been proposed that control of the inflammatory response may be of benefit in bronchiectasis, and relatively small-scale trials have yielded evidence of alleviated dyspnea, decreased need for inhaled β-agonists, and reduced sputum production with inhaled glucocorticoids.

7.10 Anti-Inflammatory Therapy (Continued)

• However, no significant differences in lung function or bronchiectasis exacerbation rates have been observed.

7.11 Anti-Inflammatory Therapy (Continued)

• Risks of immunosuppression and adrenal suppression must be carefully considered with use of anti-inflammatory therapy in infectious bronchiectasis.

7.12 Anti-Inflammatory Therapy (Continued)

• Nevertheless, administration of oral/systemic glucocorticoids may be important in treatment of bronchiectasis due to certain etiologies, such as ABPA, or of noninfectious bronchiectasis due to underlying conditions, especially that in which an autoimmune condition is believed to be active (e.g., rheumatoid arthritis or Sjögren's syndrome).

7.13 Anti-Inflammatory Therapy (Continued)

• Patients with ABPA also may benefit from a prolonged course of treatment with an oral antifungal agent such as itraconazole.

7.14 Refractory Cases

• In select cases, surgery can be considered, with resection of a focal area of suppuration.

7.15 Refractory Cases (Continued)

• In advanced cases, lung transplantation can be considered.

7.16 Suppressive Antibiotics

• After resolution of an acute infection in patients with recurrences (e.g., ≥3 episodes per year), the use of suppressive antibiotics to minimize the microbial load and reduce the frequency of exacerbations has been proposed.

7.17 Suppressive Antibiotics (Continued)

• Although there is less consensus about this approach in non-CF-associated bronchiectasis than in CF-related bronchiectasis, small studies have supported benefits of selected therapies, though with concerns for development of antibiotic resistance over time.

7.18 Suppressive Antibiotics (Continued)

• Possible suppressive treatments include (1) administration of an oral antibiotic (e.g., ciprofloxacin) daily for 1–2 weeks per month; (2) use of a rotating schedule of oral antibiotics (to minimize the risk of development of drug resistance); (3) administration of a macrolide antibiotic (see below) daily or three times per week (with mechanisms of possible benefit related to non-antimicrobial properties, such as anti-inflammatory effects and reduction of gram-negative bacillary biofilms); (4) inhalation of aerosolized antibiotics (e.g., tobramycin inhalation solution) for select patients on a rotating schedule (e.g., 30 days on, 30 days off), with the goal of decreasing the microbial load without eliciting the side effects of systemic drug administration; other studies examining inhaled aztreonam and inhaled ciprofloxacin formulations have shown conflicting results, suggesting there might be subpopulations of patients with bronchiectasis who might benefit from specific therapies; and (5) intermittent administration of IV antibiotics (e.g., 'clean-outs') for patients with more severe bronchiectasis and/or resistant pathogens.

7.19 Macrolide Therapy

• In relation to macrolide therapy (point 3 above), a number of double-blind, placebo-controlled, randomized trials have been published in non-CF bronchiectasis and support a benefit of long-term macrolides (6–12 months of azithromycin or erythromycin) in decreasing rates of bronchiectasis exacerbation, mucus production, and decline in lung function.

7.20 Macrolide Therapy (Continued)

• However, two of these studies and a meta-analysis also reported increased macrolide resistance in commensal pathogens, dampening enthusiasm for universal use of macrolides in this setting and raising the question of whether there might be select non-CF bronchiectasis patients with higher morbidity for whom benefits of long-term macrolides might outweigh the risks of emergence of antibiotic resistance.

7.21 Macrolide Therapy (Continued)

• In particular, development of macrolide-resistant NTM is a potential concern, making treatment of those pathogens much more difficult.

7.22 Macrolide Therapy (Continued)

• Furthermore, patients with different patterns of microbial colonization may not all experience similar benefits with macrolide therapy.

7.23 Macrolide Therapy (Continued)

• Therefore, before chronic macrolide therapy is considered, it is advisable to rule out NTM infection and carefully consider each patient's scenario closely, obtaining an electrocardiogram to rule out a prolonged QT interval that might place the patient at increased risk of arrhythmias.

7.24 Prevention

• Reversal of an underlying immunodeficient state (e.g., by administration of gamma globulin for immunoglobulin-deficient patients) and vaccination of patients with chronic respiratory conditions (e.g., influenza, pneumococcal, COVID, and RSV vaccines) can decrease the risk of recurrent infections.

7.25 Prevention (Continued)

• Patients who smoke should be counseled about smoking cessation.

8. PROGNOSIS & COMPLICATIONS

Outcomes of bronchiectasis can vary widely with the underlying etiology and comorbid conditions and may also be influenced by the frequency of exacerbations and (in infectious cases) the specific pathogens involved (with worse outcomes associated with P. aeruginosa colonization).

8.1 Lung Function Decline

• Increasing attention is being given to defining clinical subphenotypes of bronchiectasis in light of heterogeneous clinical, radiographic, and microbial features and to developing screening tools for the assessment of quality of life and disease severity.

8.2 Lung Function Decline (Continued)

• In one study, the decline of lung function in patients with non-CF bronchiectasis was similar to that in patients with COPD, with the forced expiratory volume in 1 s (FEV1) declining by 50–55 mL per year as opposed to 20–30 mL per year for healthy controls.

8.3 Complications: Microbial Resistance

• In more severe cases of infectious bronchiectasis, recurrent infections and repeated courses of antibiotics can lead to microbial resistance to antibiotics.

8.4 Complications: Hemoptysis

• In certain cases, combinations of antibiotics that have independent toxicity profiles may be necessary to treat resistant organisms.

8.5 Complications: Hemoptysis (Continued)

• Recurrent infections can result in injury to superficial mucosal vessels, with bleeding and, in severe cases, life-threatening hemoptysis.

8.6 Complications: Hemoptysis (Continued)

• Management of massive hemoptysis usually requires intubation to stabilize the patient, identification of the source of bleeding, and protection of the nonbleeding lung.

8.7 Complications: Hemoptysis (Continued)

• Control of bleeding often necessitates bronchial artery embolization and, in severe cases, surgery.

9. SPECIAL CONSIDERATIONS

• Reversal of an underlying immunodeficient state (e.g., by administration of gamma globulin for immunoglobulin-deficient patients) and vaccination of patients with chronic respiratory conditions (e.g., influenza, pneumococcal, COVID, and RSV vaccines) can decrease the risk of recurrent infections.

9.1 Immunodeficiency

• Reversal of an underlying immunodeficient state (e.g., by administration of gamma globulin for immunoglobulin-deficient patients).

9.2 Smoking

• Patients who smoke should be counseled about smoking cessation.

9.3 HIV

• Immunodeficiency (e.g., hypogammaglobulinemia, HIV infection, bronchiolitis obliterans after lung transplantation).

10. KEY PEARLS & CLINICAL TRAPS

• Bronchiectasis can arise from infectious or noninfectious causes (Table 301-1).

10.1 Clinical Pearls

• Clues to the underlying etiology often are provided by the pattern of lung involvement.

10.2 Clinical Pearls (Continued)

• The most widely cited mechanism of infectious bronchiectasis is the 'vicious cycle hypothesis,' in which susceptibility to infection and poor mucociliary clearance result in microbial colonization of the bronchial tree.

10.3 Clinical Pearls (Continued)

• Some organisms, such as Pseudomonas aeruginosa, exhibit a particular propensity for colonizing damaged airways and evading host defense mechanisms.

10.4 Clinical Pearls (Continued)

• Impaired mucociliary clearance can result from inherited conditions such as CF or dyskinetic cilia syndrome.

10.5 Clinical Pearls (Continued)

• It has been proposed that a single severe infection (e.g., pneumonia caused by Bordetella pertussis or Mycoplasma pneumoniae) can result in significant airway damage and poor secretion clearance.

10.6 Clinical Pearls (Continued)

• The presence of the microbes incites continued chronic inflammation, with consequent damage to the airway wall, continued impairment of secretions and microbial clearance, and ongoing propagation of the infectious/inflammatory cycle.

10.7 Clinical Pearls (Continued)

• Moreover, it has been proposed that mediators released directly from bacteria can interfere with mucociliary clearance.

10.8 Clinical Pearls (Continued)

• A recent study suggested that there exist molecular endotypes of bronchiectasis with differential inflammatory markers and microbiome signatures that correlate with risk of exacerbations.

10.9 Clinical Pearls (Continued)

• Classic studies of the pathology of bronchiectasis from the 1950s demonstrated significant small-airway wall inflammation and larger-airway wall destruction as well as dilation, with loss of elastin, smooth muscle, and cartilage.

10.10 Clinical Pearls (Continued)

• It has been proposed that inflammatory cells in the small airways release proteases and other mediators, such as reactive oxygen species and proinflammatory cytokines, that damage the larger airway walls.

10.11 Clinical Pearls (Continued)

• Furthermore, the ongoing inflammatory process in the smaller airways results in airflow obstruction.

10.12 Clinical Pearls (Continued)

• It is thought that antiproteases, such as α1 antitrypsin, play an important role in neutralizing the damaging effects of neutrophil elastase and in enhancing bacterial killing.

10.13 Clinical Pearls (Continued)

• Bronchiectasis and emphysema have been observed in patients with α1 antitrypsin deficiency.

10.14 Clinical Pearls (Continued)

• Proposed mechanisms for noninfectious bronchiectasis include immune-mediated reactions that damage the bronchial wall (e.g., those associated with systemic autoimmune conditions such as Sjögren's syndrome and rheumatoid arthritis).

10.15 Clinical Pearls (Continued)

• Recent studies suggest that there might exist a new bronchiectasis endophenotype of patients with sensitization to multiple environmental allergens.

10.16 Clinical Pearls (Continued)

• Traction bronchiectasis refers to dilated airways arising from parenchymal distortion as a result of lung fibrosis (e.g., postradiation fibrosis or idiopathic pulmonary fibrosis).

10.17 Clinical Pearls (Continued)

• More pronounced involvement of the upper lung fields is most common in CF and also is observed in postradiation fibrosis, corresponding to the lung region encompassed by the radiation port.

10.18 Clinical Pearls (Continued)

• Bronchiectasis with predominant involvement of the lower lung fields usually has its source in chronic recurrent aspiration (e.g., due to esophageal motility disorders like those in scleroderma), end-stage fibrotic lung disease (e.g., traction bronchiectasis from idiopathic pulmonary fibrosis), or recurrent immunodeficiency-associated infections (e.g., hypogammaglobulinemia).

10.19 Clinical Pearls (Continued)

• Bronchiectasis resulting from infection by nontuberculous mycobacteria (NTM), most commonly the Mycobacterium avium-intracellulare complex (MAC), often preferentially affects the midlung fields.

10.20 Clinical Pearls (Continued)

• Congenital causes of bronchiectasis with predominant midlung field involvement include the dyskinetic/immotile cilia syndrome.

10.21 Clinical Pearls (Continued)

• Finally, predominant involvement of central airways is reported in association with allergic bronchopulmonary aspergillosis (ABPA), in which an immune-mediated reaction to Aspergillus damages the bronchial wall.

10.22 Clinical Pearls (Continued)

• Congenital causes of central airway–predominant bronchiectasis resulting from cartilage deficiency include tracheobronchomegaly (Mounier-Kuhn syndrome) and Williams-Campbell syndrome.

10.23 Clinical Pearls (Continued)

• In many cases, the etiology of bronchiectasis is not determined. In case series, as many as 25–50% of patients referred for bronchiectasis have idiopathic disease.

10.24 Clinical Pearls (Continued)

• There is increasing appreciation for the need to define disease subphenotypes in this heterogeneous group of underlying causes of bronchiectasis, which might permit better targeting of clinical trials and treatment strategies.

10.25 Clinical Pearls (Continued)

• The most common clinical presentation is a persistent productive cough with ongoing production of thick, tenacious sputum.

10.26 Clinical Pearls (Continued)

• Physical findings frequently include crackles and wheezing on lung auscultation, and some patients with bronchiectasis exhibit clubbing of the digits.

10.27 Clinical Pearls (Continued)

• Mild to moderate airflow obstruction often is detected on pulmonary function tests, overlapping with that seen at presentation with other conditions, such as COPD.

10.28 Clinical Pearls (Continued)

• Acute exacerbations of bronchiectasis usually are characterized by changes in the nature of sputum production, with increased volume and purulence.

10.29 Clinical Pearls (Continued)

• However, typical signs and symptoms of lung infection, such as fever and new infiltrates, may not be present.

10.30 Clinical Pearls (Continued)

• Evaluation of focal bronchiectasis almost always requires bronchoscopy to exclude airway obstruction by an underlying mass or foreign body.

10.31 Clinical Pearls (Continued)

• Although chest radiographs lack sensitivity, the presence of 'tram tracks' indicating dilated airways is consistent with bronchiectasis.

10.32 Clinical Pearls (Continued)

• Chest CT is more specific for bronchiectasis and is the imaging modality of choice for confirming the diagnosis.

10.33 Clinical Pearls (Continued)

• Recently, a group of international experts put forth consensus guidelines for clinical and radiologic diagnosis of bronchiectasis, proposing that a diagnosis of bronchiectasis should require radiologic criteria (at least one of the following on chest CT: [1] inner- or [2] outer-airway-artery diameter ratio ≥1.5; [3] lack of airway tapering; and, [4] visibility of airways in the periphery) along with the clinical syndrome (at least two of the following: [1] cough most days of the week; [2] sputum production most days of the week; and [3] history of exacerbations).

10.34 Clinical Pearls (Continued)

• Antibiotics targeting the causative or presumptive pathogen (with Haemophilus influenzae and P. aeruginosa isolated commonly) should be administered in acute exacerbations, usually for a minimum of 7–10 days and perhaps for as long as 14 days.

10.35 Clinical Pearls (Continued)

• Decisions about treatment of NTM infection can be difficult, given that these organisms can be colonizers as well as pathogens, and the prolonged treatment course often is not well tolerated.

10.36 Clinical Pearls (Continued)

• Consensus guidelines have advised that diagnostic criteria for true clinical infection with NTM should be considered in patients with symptoms and radiographic findings of lung disease who have at least two sputum samples positive on culture; at least one bronchoalveolar lavage (BAL) fluid sample positive on culture; a biopsy sample displaying histopathologic features of NTM infection (e.g., granuloma or a positive stain for acid-fast bacilli) along with one positive sputum culture; or a pleural fluid sample (or a sample from another sterile extrapulmonary site) positive on culture.

10.37 Clinical Pearls (Continued)

• MAC strains are the most common NTM pathogens, and the recommended regimen for HIV-negative patients infected with macrolide-sensitive MAC includes a macrolide combined with rifampin and ethambutol.

10.38 Clinical Pearls (Continued)

• Consensus guidelines recommend macrolide susceptibility testing for MAC isolates.

10.39 Clinical Pearls (Continued)

• The numerous approaches used to enhance secretion clearance in bronchiectasis include hydration and mucolytic administration, aerosolization of bronchodilators and hyperosmolar agents (e.g., hypertonic saline), and chest physiotherapy (e.g., postural drainage, traditional mechanical chest percussion via hand clapping to the chest, or use of devices such as an oscillatory positive expiratory pressure flutter valve or a high-frequency chest wall oscillation vest).

10.40 Clinical Pearls (Continued)

• Pulmonary rehabilitation and a regular exercise program may assist with secretion clearance as well as with other aspects of bronchiectasis, including improved exercise capacity and quality of life.

10.41 Clinical Pearls (Continued)

• The mucolytic dornase (DNase) is recommended routinely in CF-related bronchiectasis but not in non-CF bronchiectasis, given concerns about lack of efficacy and potential harm in the non-CF population.

10.42 Clinical Pearls (Continued)

• It has been proposed that control of the inflammatory response may be of benefit in bronchiectasis, and relatively small-scale trials have yielded evidence of alleviated dyspnea, decreased need for inhaled β-agonists, and reduced sputum production with inhaled glucocorticoids.

10.43 Clinical Pearls (Continued)

• However, no significant differences in lung function or bronchiectasis exacerbation rates have been observed.

10.44 Clinical Pearls (Continued)

• Risks of immunosuppression and adrenal suppression must be carefully considered with use of anti-inflammatory therapy in infectious bronchiectasis.

10.45 Clinical Pearls (Continued)

• Nevertheless, administration of oral/systemic glucocorticoids may be important in treatment of bronchiectasis due to certain etiologies, such as ABPA, or of noninfectious bronchiectasis due to underlying conditions, especially that in which an autoimmune condition is believed to be active (e.g., rheumatoid arthritis or Sjögren's syndrome).

10.46 Clinical Pearls (Continued)

• Patients with ABPA also may benefit from a prolonged course of treatment with an oral antifungal agent such as itraconazole.

10.47 Clinical Pearls (Continued)

• In select cases, surgery can be considered, with resection of a focal area of suppuration.

10.48 Clinical Pearls (Continued)

• In advanced cases, lung transplantation can be considered.

10.49 Clinical Pearls (Continued)

• After resolution of an acute infection in patients with recurrences (e.g., ≥3 episodes per year), the use of suppressive antibiotics to minimize the microbial load and reduce the frequency of exacerbations has been proposed.

10.50 Clinical Pearls (Continued)

• Although there is less consensus about this approach in non-CF-associated bronchiectasis than in CF-related bronchiectasis, small studies have supported benefits of selected therapies, though with concerns for development of antibiotic resistance over time.

10.51 Clinical Pearls (Continued)

• Possible suppressive treatments include (1) administration of an oral antibiotic (e.g., ciprofloxacin) daily for 1–2 weeks per month; (2) use of a rotating schedule of oral antibiotics (to minimize the risk of development of drug resistance); (3) administration of a macrolide antibiotic (see below) daily or three times per week (with mechanisms of possible benefit related to non-antimicrobial properties, such as anti-inflammatory effects and reduction of gram-negative bacillary biofilms); (4) inhalation of aerosolized

antibiotics (e.g., tobramycin inhalation solution) for select patients on a rotating schedule (e.g., 30 days on, 30 days off), with the goal of decreasing the microbial load without eliciting the side effects of systemic drug administration; other studies examining inhaled aztreonam and inhaled ciprofloxacin formulations have shown conflicting results, suggesting there might be subpopulations of patients with bronchiectasis who might benefit from specific therapies; and (5) intermittent administration of IV antibiotics (e.g., 'clean-outs') for patients with more severe bronchiectasis and/or resistant pathogens.

10.52 Clinical Pearls (Continued)

• In relation to macrolide therapy (point 3 above), a number of double-blind, placebo-controlled, randomized trials have been published in non-CF bronchiectasis and support a benefit of long-term macrolides (6–12 months of azithromycin or erythromycin) in decreasing rates of bronchiectasis exacerbation, mucus production, and decline in lung function.

10.53 Clinical Pearls (Continued)

• However, two of these studies and a meta-analysis also reported increased macrolide resistance in commensal pathogens, dampening enthusiasm for universal use of macrolides in this setting and raising the question of whether there might be select non-CF bronchiectasis patients with higher morbidity for whom benefits of long-term macrolides might outweigh the risks of emergence of antibiotic resistance.

10.54 Clinical Pearls (Continued)

• In particular, development of macrolide-resistant NTM is a potential concern, making treatment of those pathogens much more difficult.

10.55 Clinical Pearls (Continued)

• Furthermore, patients with different patterns of microbial colonization may not all experience similar benefits with macrolide therapy.

10.56 Clinical Pearls (Continued)

• Therefore, before chronic macrolide therapy is considered, it is advisable to rule out NTM infection and carefully consider each patient's scenario closely, obtaining an electrocardiogram to rule out a prolonged QT interval that might place the patient at increased risk of arrhythmias.

10.57 Clinical Pearls (Continued)

• Outcomes of bronchiectasis can vary widely with the underlying etiology and comorbid conditions and may also be influenced by the frequency of exacerbations and (in infectious cases) the specific pathogens involved (with worse outcomes associated with P. aeruginosa colonization).

10.58 Clinical Pearls (Continued)

• Increasing attention is being given to defining clinical subphenotypes of bronchiectasis in light of heterogeneous clinical, radiographic, and microbial features and to developing screening tools for the assessment of quality of life and disease severity.

10.59 Clinical Pearls (Continued)

• In one study, the decline of lung function in patients with non-CF bronchiectasis was similar to that in patients with COPD, with the forced expiratory volume in 1 s (FEV1) declining by 50–55 mL per year as opposed to 20–30 mL per year for healthy controls.

10.60 Clinical Pearls (Continued)

• In more severe cases of infectious bronchiectasis, recurrent infections and repeated courses of antibiotics can lead to microbial resistance to antibiotics.

10.61 Clinical Pearls (Continued)

• In certain cases, combinations of antibiotics that have independent toxicity profiles may be necessary to treat resistant organisms.

10.62 Clinical Pearls (Continued)

• Recurrent infections can result in injury to superficial mucosal vessels, with bleeding and, in severe cases, life-threatening hemoptysis.

10.63 Clinical Pearls (Continued)

• Management of massive hemoptysis usually requires intubation to stabilize the patient, identification of the source of bleeding, and protection of the nonbleeding lung.

10.64 Clinical Pearls (Continued)

• Control of bleeding often necessitates bronchial artery embolization and, in severe cases, surgery.

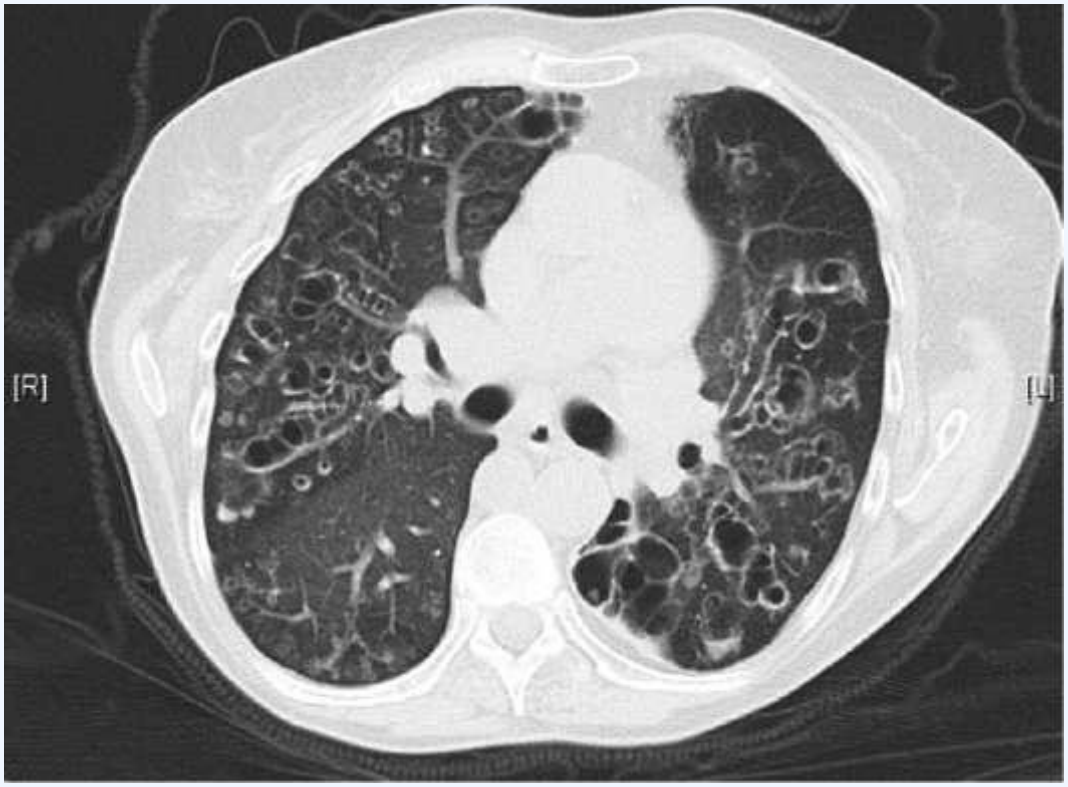
10.65 Clinical Pearls (Continued)

• Reversal of an underlying immunodeficient state (e.g., by administration of gamma globulin for immunoglobulin-deficient patients) and vaccination of patients with chronic respiratory conditions (e.g., influenza, pneumococcal, COVID, and RSV vaccines) can decrease the risk of recurrent infections.

10.66 Clinical Pearls (Continued)

• Patients who smoke should be counseled about smoking cessation.

FIGURES & ILLUSTRATIONS — FROM HARRISON'S



Harrison's 22e · Figure 1

in FIGURE 301-1 Representative chest CT image of severe bronchiectasis. This 2 patient’s CT demonstrates many severely dilated airways, seen both longitudinally (arrowhead) and in cross-section (arrow). — Figure 301-1 Representative chest CT image of severe bronchiectasis. This patient's CT demonstrates many severely dilated airways, seen both longitudinally (arrowhead) and in cross-section (arrow).