

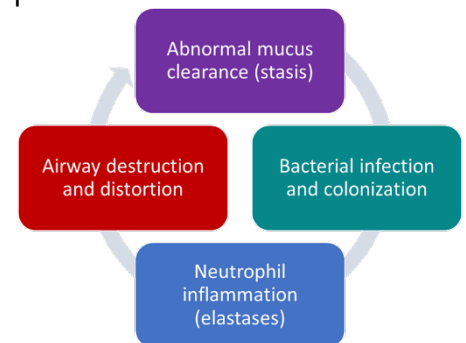


Bronchiectasis UPDATE: Diagnostic Innovations & Therapeutic Frontiers

RAPID RECAP

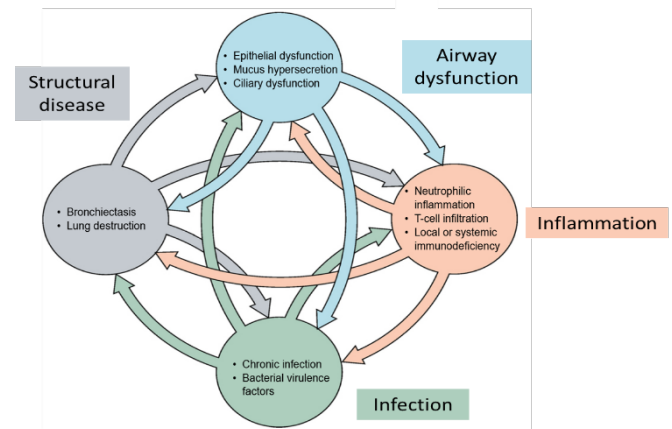
Pathogenesis: Inflammatory Endotypes¹

- Inflammation in bronchiectasis is typically driven by neutrophils
- Compared to eosinophilic inflammation, neutrophilic inflammation is associated with:
 - More severe disease
 - Lower FeNO
 - Weaker bronchodilator response
 - Higher levels of IL-8, lower levels of IL-13
- Neutrophil elastase (NE) is a major inflammatory protease released by neutrophils
 - Present in airways of patients with bronchiectasis
 - Facilitates leukocyte migration to sites of infection
 - Activates inflammation in some chronic airway diseases



Natural History and Risk Factors/Comorbidities²

- Each process contributes to the others, leading to persistent and progressive pathophysiology
- Consequently, interventions that address only one process have modest effects
- Numerous risk factors/comorbidities, including:
 - Infectious processes (eg pneumonia, NTM)
 - Post-inflammatory pneumonitis
 - Genetic (eg, CF, PCD)
 - Connective tissue disease
 - Pulmonary disease (eg, COPD, asthma)
 - Altered immune responses
 - Immunodeficiency





Bronchiectasis UPDATE:

Diagnostic Innovations & Therapeutic Frontiers

RAPID RECAP

Early and Accurate Diagnosis³

- **Confirm diagnosis:** HRCT & Pulmonary Function Testing
- **Basic Work-Up:**
 - CBC, differential (neutrophilic vs eosinophilic inflammation)
 - Immunoglobulins (IgG, IgM, IgA, IgE, IgG sub-classes)
 - Sputum culture (bacterial, mycobacterial, fungal)
 - Alpha-1 antitrypsin
- **Targeted Testing:**
 - ABPA testing (IgE, Aspergillus, eosinophils)
 - Cystic fibrosis (sweat test, CFTR genetics)
 - PCD (nasal nitric oxide, ciliary biopsy, genetics)
 - Autoimmune panel (ANA, RF, ANCA)
 - Gastrointestinal evaluation (if aspiration/reflux suspected)

Emerging Therapies

- New approaches are in development for treating bronchiectasis, including:
 - Use of DPP-1 inhibitors to reduce neutrophil serine protease activity and associated neutrophilic inflammation
 - Brensocatib⁴
 - BI 1291583⁵
 - Combined inhibition of PDE3 and PDE4
 - Ensifentrine⁶
- Brensocatib recently FDA-approved for treatment of non-cystic fibrosis bronchiectasis in adult and pediatric patients 12 years of age and older

Key Takeaways

- Pseudomonas is associated with increased exacerbation frequency and progressive decline in FEV1
- BSI score is helpful in multilobar bronchiectasis predictions for severity
- Nebulized antibiotics are a potential option to decrease exacerbation frequency



Bronchiectasis UPDATE:

Diagnostic Innovations & Therapeutic Frontiers

References

1. McShane PJ, et al. *Am J Respir Crit Care Med*. 2013;188:647-656.
2. Clofent D, et al. *Expert Rev Respir Med*. 2021;15(5):623-634.
3. O'Donnell AE. *N Engl J Med*. 2022;387(6):533-545.
4. Chalmers JD, et al. *N Engl J Med*. 2025;392(16):1569-1581.
5. Chalmers JD, et al. *Eur Respir J*. 2025;65:2401551.
6. Donohue JF, et al. *J Chron Obstruct Pulmon Dis*. 2023;18:1611–1622.