ABPA & Diagnosis

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Allergic bronchopulmonary aspergillosis (ABPA) is a fungal infection of the lung due to a hypersensitivity reaction to antigens of *Aspergillus fumigatus* after colonization into the airways.

Predominantly it affects patients with *bronchial asthma* and those having *cystic fibrosis*.

There are over 100 species of aspergilosis worldwide,

Infection by Aspergillus species causes a broad spectrum of illnesses in humans and depends on the immune status of the host, ranging from hypersensitivity reactions to direct angioinvasion.

Aspergillus fumigatus is the most common airborne fungus causative organism for ABPA.

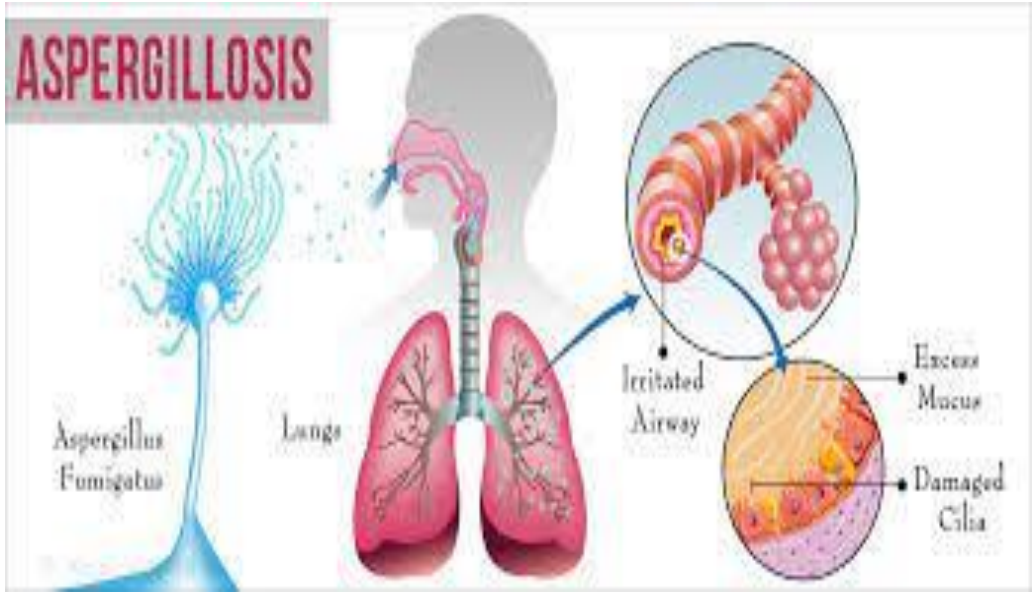

TABLE 1. PULMONARY MANIFESTATIONS OF ASPERGILLUS

Disease	Host
Aspergilloma	Cavity from sarcoid, previous TB, bullae, or bronchiectasis
Allergic bronchopulmonary aspergillosis	Asthma, cystic fibrosis
Chronic necrotizing aspergillosis	COPD, previous TB, corticosteroids, DM
Invasive aspergillosis	Immunocompromised, especially neutropenia
Hypersensitivity pneumonia	Intense or repeated exposure to aspergillus

Definition of abbreviations: COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; TB = tuberculosis.

Epidemiology

Allergic bronchopulmonary aspergillosis commonly presents in the third to fifth decade of life. It is also common in children.

Allergy to Aspergillus, as shown by a positive skin prick test to Aspergillus antigen, is present in almost 25% asthmatics and 50% of cystic fibrosis patients, but ABPA is not that much prevalent.

approximately 2.5% of patients with asthma and 7-10% of CF patients are affected

Pathophysiology

The pathogenesis of allergic bronchopulmonary aspergillosis remains incompletely understood. A. fumigatus spores that get inhaled in sufficient quantities behave as allergens.

- Immunocompetent individuals easily eliminate *Aspergillus* conidia from the airway by the innate immune system mechanisms; therefore, there are no manifestations of pulmonary fungal infections. If isolated in respiratory secretions like sputum or bronchoalveolar lavage, then it only reflects colonization, not an infection.

- In contrast, the thick mucus in the airways of atopic patients makes it difficult to clear up the Aspergillus spores when inhaled and stimulate a chronic allergic inflammatory response then results in the formation of IgE and IgG antibodies.

Th2 cells (Helper T cells) play an essential role in the hypersensitivity reaction caused by the *A. fumigatus* antigen. It manifests as IgE production, eosinophilia, mast cell degranulation, and bronchiectasis.

A. fumigatus proteases release proinflammatory cytokines, such as IL-8, which causes epithelial cell damage and disruption of protective barriers, which triggers the hypersensitivity reaction. It also releases cytokines interleukin (IL)-4, IL-5, and IL-13, which increases blood and airway eosinophils as well as IgE.

Genetic association: HLA-DR molecules DR2, DR5, and possibly DR4 or DR7 contribute to susceptibility; whereas, HLA-DQ2 contributes to resistance, and a combination of these may determine the outcome of ABPA in CF and asthma

History and Physical Ex.

Clinical presentation:

- History of uncontrolled asthma with increased frequency and severity despite optimum asthma medications.
- History of cystic fibrosis.
- History of recurrent episodes of **wheezing** with radiological evidence of patchy fleeting pulmonary infiltrates and bronchiectasis. A presentation of **cough, dyspnea, pleuritic chest pain, blood-stained sputum, or sputum with brown mucus plugs**.
- There are non-specific complaints like **anorexia, fatigue, generalized aches and pains, low-grade fever, and loss of weight**.
- ABPA may occur with allergic fungal sinusitis having symptoms of **chronic sinusitis** with purulent sinus discharge.

Evaluation

The diagnosis is based on:

- classic clinical manifestations,
- radiographic findings,
- immunological findings.

A more current diagnostic criterion was proposed by the International Society for Human and Animal Mycology

Predisposing condition: asthma or cystic fibrosis
ESSENTIAL CRITERIA
1. Type I immediate cutaneous hypersensitivity reaction (wheal and flare) to *Aspergillus fumigatus** or elevated serum IgE against *A. fumigatus* and
2. Elevated total IgE (>1000 IU/mL†)
OTHER CRITERIA (≥2 OF 3 NEEDED)
1. Presence of serum precipitating or IgG against *A. fumigatus*
2. Radiographic pulmonary opacities consistent with ABPA (e.g., pulmonary opacification and/or bronchiectasis)
3. Total eosinophil count >500 cells/μL in patients not on recent corticosteroids

*Although cutaneous skin testing is nearly 100% sensitive and is a useful screening test for ABPA, it is not specific for ABPA.

†Total of IgE <1000 IU/mL may be acceptable if patient meets all other criteria.

ABPA, allergic bronchopulmonary aspergillosis; IgE, immunoglobulin E; IgG, immunoglobulin G.

From Agarwal R, Chakrabarti A, Shah A, et al; ABPA Complicating Asthma ISHAM Working Group. Allergic bronchopulmonary aspergillosis: review of literature and proposal of new diagnostic and classification criteria. *Clin Exp Allergy*. 2013;43:850–873.

However, ***many patients with ABPA do not have all the criteria***, especially with early disease or if taking glucocorticoids.

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- Patients of ABPA with no abnormalities on HRCT chest are labeled as serologic ABPA (ABPA-S) like an early stage of disease.
- Patients with central bronchiectasis on HRCT are labeled as ABPA Central Bronchiectasis (ABPA-CB).

Radiological manifestations of ABPA

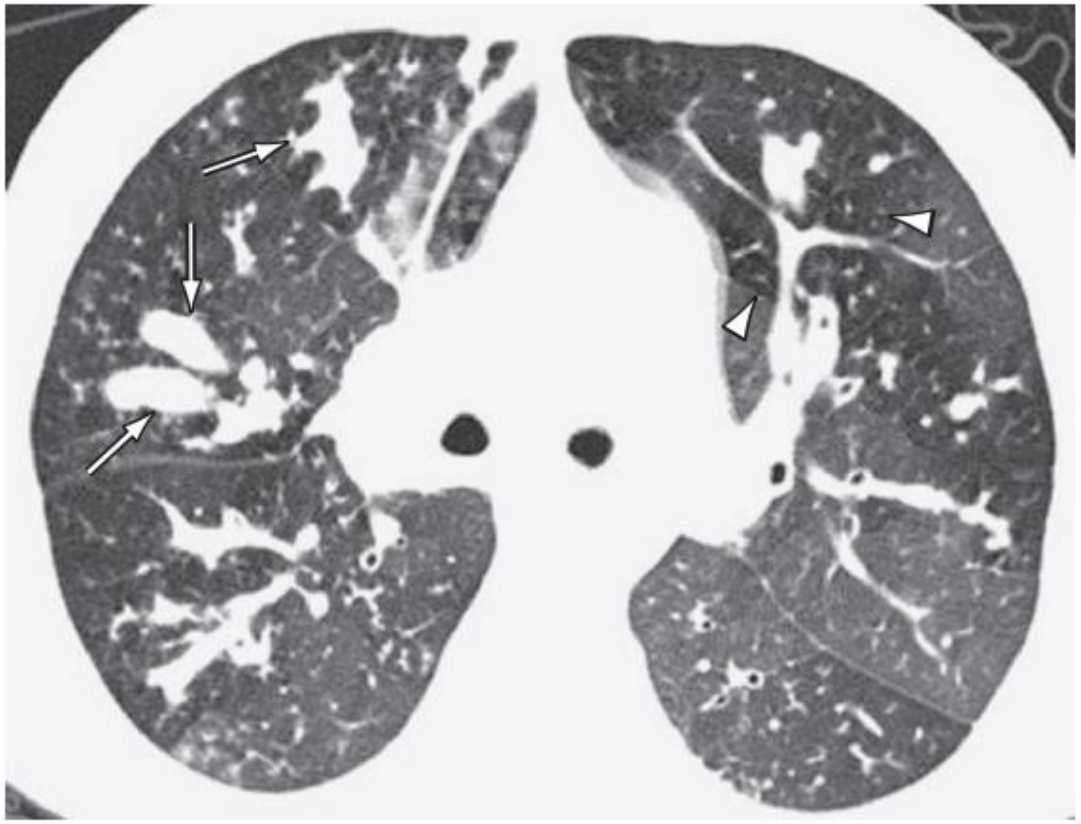
- Chest X-ray has 50% sensitivity for the diagnosis of ABPA. It can show parenchymal infiltrate and bronchiectasis changes
- HRCT Chest is the investigation of choice to detect bronchiectasis distribution and other abnormalities, such as centrilobular nodules and tree-in-bud appearance.

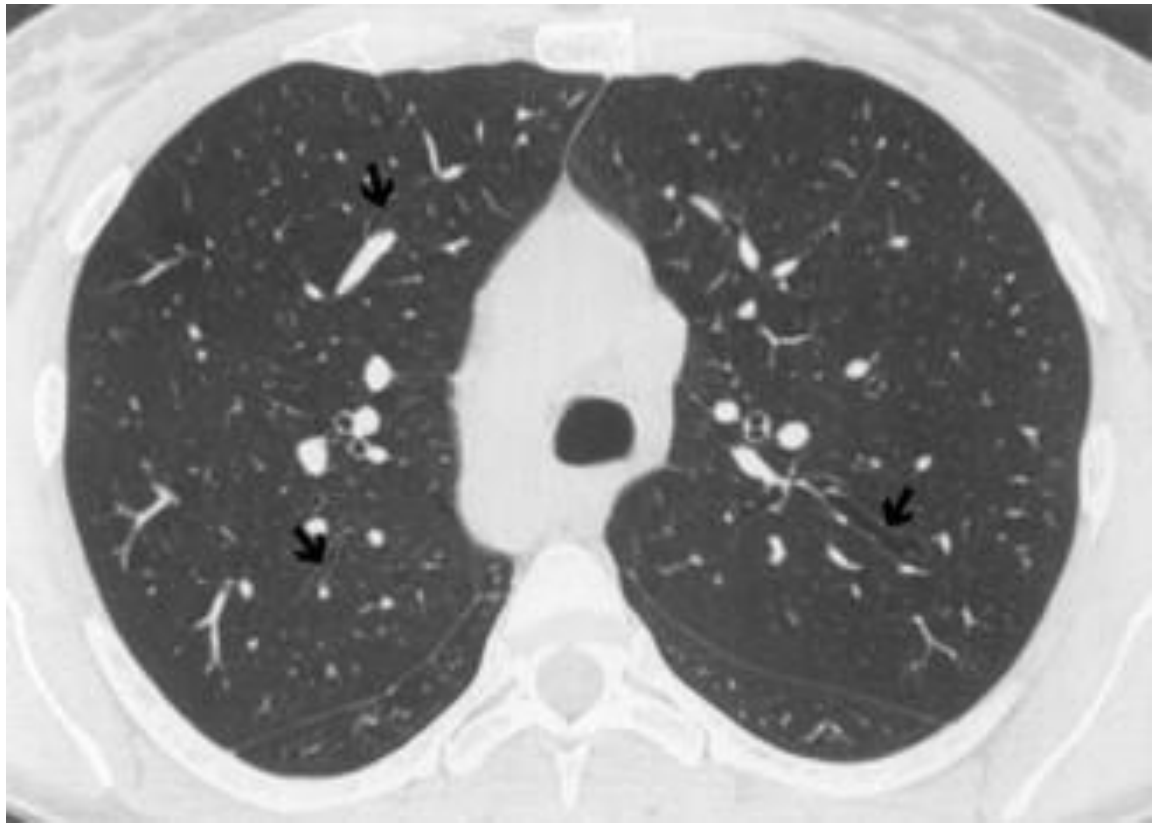
The following shadows may present radiologically:

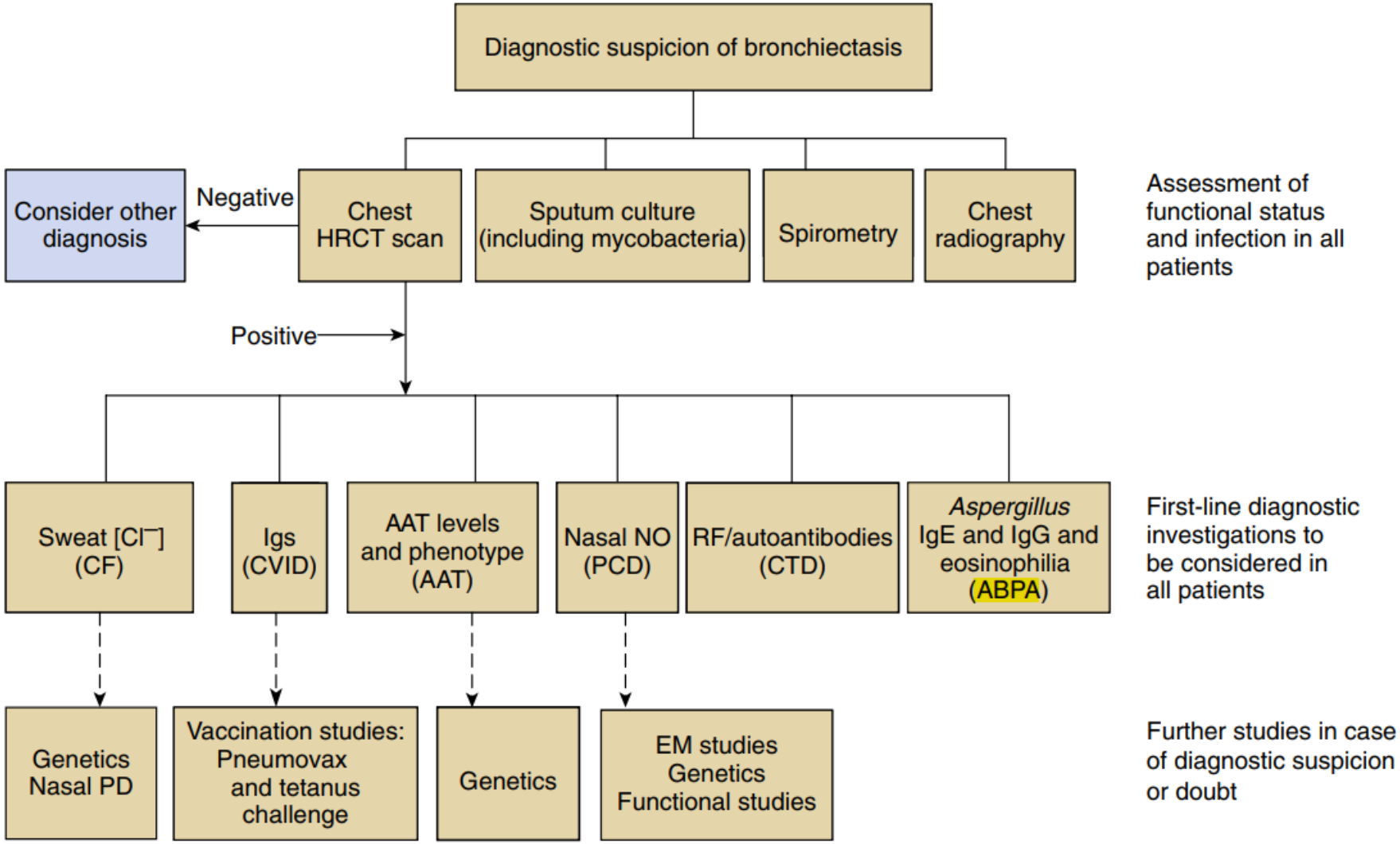
- “Finger in glove” opacity: suggestive of mucoid impaction in dilated bronchi.
- “Tramline shadows”: suggestive of parallel linear shadows extending from the hilum in bronchial distribution and reflecting longitudinal views of inflamed, edematous bronchi
- “Toothpaste shadows”: representing mucoid impaction of the bronchi
- “Ring shadows”: reflecting dilated bronchi with inflamed bronchial walls

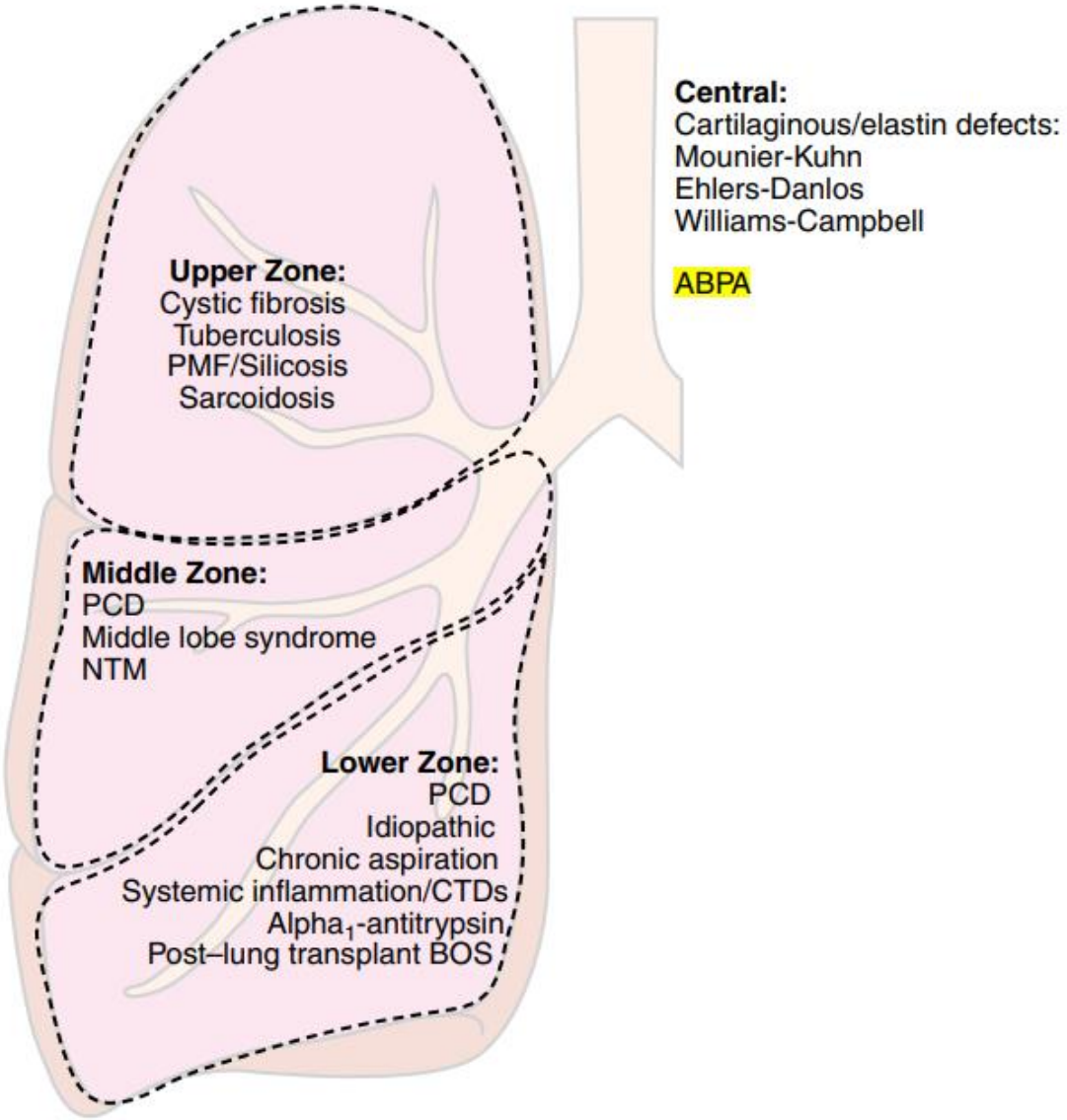
Revised radiologic classification of allergic bronchopulmonary aspergillosis based on findings on a high-resolution computed tomography of the chest.

- ABPA-S (Serological ABPA): Fulfills the diagnostic criteria of ABPA with an absence of any radiological finding of ABPA on HRCT of the thorax.
- ABPA-B (Bronchiectasis ABPA): Satisfies the diagnostic requirements of ABPA along with the presence of bronchiectasis.
- ABPA-HAM (ABPA- High attenuation mucus): ABPA, along with the presence of high attenuation mucus on HRCT of the thorax.
- ABPA-CPF (ABPA-Chronic pleuropulmonary fibrosis): Fulfills the diagnostic criteria of ABPA with at least two radiological features suggestive of fibrosis (including fibrocavitary lesions, pulmonary fibrosis, pleural thickening) without the presence of mucoid impaction (or HAM).






Diagnostic suspicion of bronchiectasis
Consider other diagnosis
Negative
Chest HRCT scan
Sputum culture (including mycobacteria)
Spirometry
Chest radiography
Assessment of functional status and infection in all patients
Positive
Sweat [Cl⁻] (CF)
Igs (CVID)
AAT levels and phenotype (AAT)
Nasal NO (PCD)
RF/autoantibodies (CTD)
Aspergillus IgE and IgG and eosinophilia (ABPA)
First-line diagnostic investigations to be considered in all patients
Genetics Nasal PD
Vaccination studies: Pneumovax and tetanus challenge
Genetics
EM studies Genetics Functional studies
Further studies in case of diagnostic suspicion or doubt


Central:
Cartilaginous/elastin defects:
Mounier-Kuhn
Ehlers-Danlos
Williams-Campbell
ABPA
Upper Zone:
Cystic fibrosis
Tuberculosis
PMF/Silicosis
Sarcoidosis
Middle Zone:
PCD
Middle lobe syndrome
NTM
Lower Zone:
PCD
Idiopathic
Chronic aspiration
Systemic inflammation/CTDs
Alpha1-antitrypsin
Post–lung transplant BOS

Early diagnosis and rapid implementation of proper management are critical to prevent complications and/or disease progression