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The Spectrum of Obstructive Airway Disease: Clinical and Pathophysiologic Insights

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ABSTRACT

Chronic obstructive pulmonary disease (COPD), asthma, bronchiolitis, bronchiectasis, and cystic fibrosis are types of obstructive airway diseases (OADs), that make it harder for air to flow and make the airways more resistant. This review focuses on the details of these air way diseases including definition, epidemiological trends, clinical features, causes, pathophysiological mechanisms, diagnostic methods, and treatment options. Asthma and COPD are the most common OADs where air pollution, smoking, and genetics making their numbers go up around the world. Bronchiolitis is a common illness in kids, but bronchiectasis and cystic fibrosis can permanently damage the airways and cause infection over and over again. Drugs are selected according to the patient's needs and the severity of the illness. This review highlights on the early diagnosis and treatment modalities available for individual disease conditions which might be helpful to the healthcare community.

Keywords: Cystic Fibrosis, Chronic Obstructive Pulmonary Disease, Inhaled Corticosteroid, Long-Acting Beta Agonist, Obstructive Airway Disease.

INTRODUCTION

Obstructive airway disease is a broad group of chronic respiratory conditions characterized by the presence of airway obstruction causing airflow limitation, affecting millions worldwide and posing a significant public health burden. COPD and asthma are the most prevalent obstructive airway disease with distinct pathophysiological factor but overlap in clinical features such as dyspnea, wheezing, cough, and sputum production[1-3]. OAD also includes bronchiectasis, cystic fibrosis, bronchiolitis and emphysema, often complicating the diagnosis and management[4,5].

The pathogenesis of OAD involves various factors such as genetic predispositions and environmental triggers including allergens, pollutants, infection, and occupational exposure[6]. The genetic and epigenetic factors play an integral role in OAD susceptibility and progression[7,8]. The pathophysiology of COPD involves chronic inflammation driven by neutrophils, macrophages, and CD8+ T cells, leading to irreversible airflow obstruction due to small airway fibrosis, mucus hypersecretion, and emphysematous destruction of alveolar walls[9,10]. Diagnosis of OAD is based on clinical history, spirometry demonstrating airflow obstruction, and in some cases using various imaging techniques and biomarker analysis[11]. Complications of OAD include respiratory failure, pulmonary hypertension, and increased susceptibility to infections[12].

Pharmacological treatment for OAD includes bronchodilators, inhaled corticosteroids and biologics targeting inhaled corticosteroids and biologics targeting specific inflammatory pathway[13]. Despite advances, the heterogenicity of the disease, underdiagnosis, and limited access to care in low-resource settings create various challenges. Therefore, a comprehensive understanding of OAD's mechanism, clinical features and therapeutic options is crucial for optimal patient outcome and future research.

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ASTHMA

Asthma is a chronic inflammatory lung disease that affects individuals of all age groups and it can be a

life-threatening condition in some cases. People with asthma often experience many episodes of breathing difficulty due to persistent inflammation and muscle tightening around the airways. These episodes become more sensitive and gets triggered by various environmental or emotional factors like viruses, allergens, irritants or emotional stress[14-16].

This combination of inflammation, mucus production, and muscle constriction impairs breathing and significantly becomes more life threatening if not detected early[15].

Epidemiology:

Globally, it is ranked 16th among leading causes of years lived with disability and 28th among leading causes of disease burden, as measured by disability-adjusted life years. Approximately 300 million people worldwide have asthma, and this number is expected to increase by an additional 100 million[17].

Etiology and risk factors:

Factors that play a major role in developing asthma are,

- Genetics
- Allergic conditions
- Lifestyle modifications
- Early life events
- Exposure to environmental allergens
- Obesity[16].

Clinical presentation:

Most often the symptoms of asthma worsen at night or during any extensive physical activity. Some common symptoms are,

- Shortness of breath
- Chest pain or tightness
- Wheezing while exhaling
- Persistent cough[14].

Symptoms of asthma worsen when the individual has a cold or there is a change in weather, some of the triggering factors like dust, smoke, fumes, grass and tree pollen, animal fur and feathers, strong soaps and perfume may worsen the symptoms of asthma leading to progression of the condition[16].

Pathophysiology:

Asthma is a chronic inflammatory condition which is mediated by Immunoglobin E (IgE), it get precipitated by an allergic response to an allergen, sensitization occurs during the first exposure which in response produces allergen-specific IgE antibodies leading to the attachment to the mast cell surfaces, which results in the release of inflammatory mediators causing bronchospasm and triggering asthma attack[18].

Asthma if untreated, results in migration of eosinophils, T-helper cells and mast cells into the airways leading to in excessive mucus production by goblet cells, plugging the airway along with increased airway tone and airway hyperresponsiveness, causing narrowing of the airway and exacerbation[19].

Diagnosis:

- Physical examination
- Chest x-ray
- Spirometry test
- Peak flow meter test
- Allergy testing
- Nitric oxide test
- Bronchoprovocation testing
- Sputum eosinophil examination[20].

Treatment:

Most commonly used treatment is inhaled drug therapy, allowing the medication to reach the lungs directly. Two main types of inhaled drug therapy used are, bronchodilators and steroids which is used to alleviating the symptoms by opening the air passages and reducing the inflammation in the airways[16].

Long-term asthma control medications taken daily are the cornerstone of asthma management. Inhaled corticosteroids like budesonide, which helps in reducing the airway inflammation by decreasing the overactive immune system's inflammatory response. Oral medications include leukotriene modifiers like montelukast, helps in relieving the initial symptoms of asthma. Combination in inhalers containing long-acting beta agonist along with corticosteroids like fluticasone-salmeterol, are used to manage the symptoms. FDA has issued a black-box warning for the occurrence of severe exacerbation of asthma if fluticasone-salmeterol given as a monotherapy[21].

Short-acting inhaled beta agonist like albuterol and levalbuterol, offer quick-relief by relaxing the bronchus during an asthma attack. Oral and intravenous corticosteroids like prednisone and methylprednisolone cause serious side effects when used long term, so these drugs are used only on a short-term basis to treat severe asthma symptoms[21,22].

Individuals with severe asthma remain uncontrolled despite being treated with medications, for such patients, biological therapy like omalizumab, mepolizumab is recommended[20].

Mechanical ventilation can be used to treat severe asthma and acute exacerbations lead to respiratory failure. Intubation and non-invasive ventilation are employed in case of slowing of the respiratory rate, depressed mental status, inability to maintain respiratory effort and to cooperate with administration of inhaled medications, worsening hypercapnia and associated respiratory acidosis[14].

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

COPD is a common heterogeneous lung disease characterized by progressive airflow limitation and tissue destruction due to prolonged exposure to noxious particles or gases such as cigarette smoke[23]. The British Thoracic Society (BTS) defines COPD as "a slowly progressive disorder characterized by airflow obstruction that does not vary markedly over several months". It is considered to be the leading cause of morbidity and mortality in developed countries and an emerging disease in developing countries[24].

Epidemiology:

According to the WHO, COPD is considered tenth leading cause of global mortality. It also estimates COPD to be third leading cause of death worldwide by 2030. COPD by gender variations revealed a higher prevalence of about 15.47% in men compared to 8.79% in women[25]. Higher prevalence was noticed in urban areas (11.6%) than in rural areas (5.6%)[26].

Etiology and risk factors:

COPD is a heterogenous progressive multifactorial disease induced by inhalation of noxious particles or gases such as

- Tobacco smoke
- Indoor and outdoor air pollution
- Occupational exposure to dust and gases
- Ambient ozone pollution
- Second-hand smoking
- Lead exposure.

Other factors such as

- Genetic predisposition
- Maternal diet and drug use
- Preterm birth
- Abnormal lung development
- Accelerated ageing
- Childhood obesity
- High-fat diet

- Pulmonary infections
- Low socioeconomic status and
- Poverty increases the risk of developing diseases[27-29].

Symptoms:

- Chronic and progressive dyspnea
- Productive cough, with or without sputum production
- Chest tightness
- Fatigue
- Swelling of feet, ankles or legs
- Weight loss
- Frequent cold, flu or other respiratory infections[30].

Pathophysiology:

Primary pathological features include airway luminal cellular inflammation, fibrosis, and obliteration of small airways. The airway lining undergoes changes like squamous metaplasia, goblet cell hyperplasia, and excess mucus production, leading to airway thickening, narrowing and reduced airflow[29]. These are caused due to exposure to various triggers such as infection, pollutants worsening the inflammation and bronchoconstriction manifesting as hypoxemia, respiratory muscle fatigue and progresses to cor pulmonale. These structural changes are driven by the oxidative stress, epithelial injury and chronic immune activation[31].

The initial insult primarily affects the airway epithelium, by triggering the immune system causing activation of macrophages, dendritic cells, neutrophils, CD8+ cytotoxic T lymphocytes and B cells. The inflammatory cells release various pro-inflammatory cytokines such as TNF-α, IL-8, IL-1β and various proteolytic enzyme such as matrix metalloproteinases (MMPs) and neutrophil elastase, which degrades extracellular matrix components, causing alveolar wall destruction and emphysema[32,33].

A central mechanism of COPD is oxidative and nitrosative stress, caused by both external insult such as cigarette smoking and internal insult such as immune cell derived reactive oxygen species (ROS). This chronic stress overtakes the antioxidant defence mechanisms due to Nrf2 and heme oxygenase-1 (HO-1) causing lung tissue damage[31]. Increased level of nitric oxide reacts with superoxide to form peroxynitrite which is toxic enough to damage the protein structures of epithelial cells leading to cell death. This damage in turn lowers the histone deacetylase 2 (HDAC2) level, a protein that reduces inflammation, leading to chronic inflammation[33].

Diagnosis:

Diagnosis of COPD is confirmed by using spirometry, a post-bronchodilator FEV1/FVC ratio < 0.70 or below the lower limit of normal.

- Chest x-ray
- Chest CT
- Peak expiratory flow (PEF) test
- Fractional exhaled nitric oxide (FeNO) test
- Arterial blood gas test[34].

Treatment:

The main drug classes include long-acting β_2-agonists (LABAs), long-acting muscarinic antagonists (LAMAs), and inhaled corticosteroids (ICS), with selection based on the patient's clinical condition, response to the medication, and patient preference. Treatment initiation is guided by the GOLD guidelines, which uses the ABCD assessment to tailor therapy according to symptom severity and exacerbation risk[35].

According to the GOLD guidelines, the initiation therapy includes bronchodilators, and dual-acting bronchodilators combination (LABA + LAMA). For patients with blood eosinophil count ≥ 300 cells/µl, a triple therapy with LABA + LAMA + ICS is recommended. The triple therapy with LABA + LAMA + ICS has shown superiority over LABA + ICS.

For patients continuing to have exacerbations (with/without dyspnea), who are on bronchodilator monotherapy, a start-up to LABA + LAMA is recommended and for those with blood eosinophilic ≥ 300 cells/µl LABA + LAMA + ICS is recommended. If this does not improve symptoms then a triple therapy is recommended for patients with eosinophilic levels of 100 cells/µl. An addition of roflumilast or a macrolide is considered in patients with eosinophilic count 100/µl, who continue to exacerbate, despite taking the triple therapy[36].

Nonpharmacological management includes smoking cessation, guideline-recommended vaccinations and individualized physical activity. Long-term oxygen therapy is indicated in chronic or exertional hypoxemia, noninvasive ventilation support for patients with persistent hypercapnia. Lung transplantation is reserved for end-stage COPD patients with preserved rehabilitation potential and no major comorbidities[37].

BRONCHIOLITIS

Bronchiolitis is a common lung infection in young adults[38]. Bronchioles (small airways) connect the airways (bronchi) to the tiny air sacs of the lungs. When these bronchioles become swollen and filled with mucus causing swelling of these small airways making it difficult for the air to get into the lungs leading to breathing difficulties, such a condition is bronchiolitis. Bronchiolitis becomes more severe in infants those who are premature or having any airway disease condition, while it is generally self-limiting in healthy children. Whereas, Bronchiolitis obliterans is a rare as well as dangerous condition which is primarily seen in the adult population, it is chronic and progressive condition which requires long term management and in some severe cases requiring lung transplantation[39].

Epidemiology:

Bronchiolitis is most common in children under 2 years of age, particularly those under 6 months. Approximately 11% to 15% of infants experience bronchiolitis in their first year of life. Bronchiolitis typically exhibits a seasonal pattern, with peaks during the autumn and winter months, reflecting its association with seasonal respiratory viruses[38].

Etiology:

- Infection
- Collagen vascular disease
- Post lung and stem cell transplant
- Toxic exposure
- Idiopathic.

Acute Bronchiolitis: This is primarily caused by viral infections, especially in young children. The most common viruses involved are:

- Respiratory Syncytial Virus (RSV)
- Rhinoviruses
- Enteroviruses
- Other viruses: Adenovirus, Influenza virus, Parainfluenza virus.
- Bacterial: Legionella pneumophila, Mycoplasma pneumoniae

Subacute and Chronic Bronchiolitis: These can sometimes be associated with other pathogens, including:

- Mycobacterial infections**:** Such as tuberculosis, can cause chronic respiratory symptoms and sometimes bronchiolitis in a subacute or chronic form[40-42].

Risk factors:

- Infants who are under 3 months old, as their lungs and immune system are not fully developed, are at greater risk of developing bronchiolitis.
- Children who are younger than 2 years
- History of prematurity (less than 32 to 34 weeks gestational age)
- Neuromuscular disease
- Congenital heart disease

- Chronic lung illness
- Immunodeficiency[38].

Clinical presentation:

Fever, cough, rhinorrhea, loss of appetite, these are the initial signs of infection, the symptoms may worsen after a day of infection, developing

- Shortness of breath
- Wheezing
- Worsening of cough
- Respiratory distress
- Some infants may have mild disease with only tachypnea, but others may show severe retractions, grunting, and cyanosis.
- Some symptoms like blue lips or skin, breathing difficulty or respiratory failure may also occur[7,9].

Pathophysiology:

Bronchiolitis is due to the obstruction of airways in the lungs and results in diminished lung function. Once the epithelial cells in the airways of the lungs are infected by the virus, it induces an inflammatory reaction that may cause ciliary dysfunction and cell death leading to accumulation of debris causing edema and narrowing of the airways, leading to air trapping, increased mucus production, atelectasis, labored breathing and decreased ventilation.

During expiration, dynamic narrowing of airways results in decreased airflow and air trapping. This leads to increase end-expiratory lung volume and decrease lung function. The pulmonary epithelial cells recover after 3-4 days, but cilia do not regenerate for approximately two weeks and the debris is cleared by macrophages[43,44].

Diagnosis:

- Chest X-ray
- Blood test (WBC)
- Nasopharyngeal swab
- Pulmonary function test
- Pulse oximetry
- Bacterial cultures including urine, blood and cerebrospinal fluid[45,46].

Treatment:

There is no vaccine or specific treatment, common cold medicines and antibiotics are not effective for treating bronchiolitis. Symptomatic care is the essential step to be taken care of in the management of bronchiolitis. Mild to moderate symptoms can be treated with nasal saline, antipyretics, and a cool-mist humidifier. Some patients need immediate excessive hydration and should be provided with humidified oxygen and nebulized hypertonic saline. Saturation of above 90% is adequate when the patients are given oxygen therapy. Patients who develop severe signs of respiratory distress may sometimes develop respiratory failure. In such conditions, intensive care with mechanical ventilation or non-invasive support may be required[38,47].

BRONCHIECTASIS:

Bronchiectasis is a chronic respiratory disease clinically characterized by chronic cough, sputum production, and recurrent pulmonary exacerbations associated with radiological features such as an increased ratio of airway–artery diameter, lack of airway tapering, and visibility of airways in the periphery of the lungs[34].

Bronchiectasis is still a challenging chronic lung disease in developing countries, which is marked by permanent dilation and abnormal widening of the bronchi that usually occurs in the context of airway inflammation[48].

Epidemiology:

Worldwide, bronchiectasis is a health issue that has been linked to up to 566 cases per 100,000 adults in the United Kingdom, 701 cases per 100,000 Medicare recipients in the United States of America, and more than 1000 cases per 100,000 persons in China and

1250 per 100,000 in India according to the European Multicentric Bronchiectasis Audit and Research Collaboration and the Indian Bronchiectasis Registry (EMBARC-India) [49].

Etiology:

Bronchiectasis is a highly heterogeneous disorder that can develop due to various causes like infections, inflammatory, autoimmune, and genetic conditions, severe infections such as tuberculosis (TB) and pneumonia are believed to be the leading causes of bronchiectasis worldwide[49].

Risk factor:

The most common causes of childhood bronchiectasis are immune system abnormalities, Cystic Fibrosis (CF), and Primary Ciliary Dyskinesia (PCD), which undermine the body's natural defensive mechanism. Adult bronchiectasis is a rare consequence of these diseases.

Asthma, GERD (gastric reflux disease), rheumatoid arthritis, inflammatory bowel disease, chronic obstructive pulmonary disease (COPD), and others can increase an adult's risk of developing bronchiectasis. Nontuberculous mycobacteria (NTM) external link infections (organisms found in soil, dust, and water) have also been linked to bronchiectasis[50].

Clinical presentation:

Symptoms of bronchiectasis are

- Productive cough
- Hemoptysis
- Sputum expectoration
- Respiratory distress
- Growth retardation
- Night sweats
- Malaise
- Fever
- Weight loss
- Diarrhoea[51].

Pathophysiology:

Four core factors of the pathophysiology of bronchiectasis are shared by all the patient subgroups irrespective of the origin of the condition. These elements include lung injury due to structural issues, inflammation, infection, and impaired mucociliary clearance, which are independent of the cause, age, race, or gender of the patient. The "vicious cycle theory" describes the harmful impact of persistent airway infections, explaining how compromised airways are vulnerable to long-term colonization, leading to inflammation and more damage, causing the weakening of immunity[52]. The main type of inflammation in bronchiectasis is neutrophilic mediated, which is related to a long-term bacterial infection. Breakdown of airway elastin and high frequency of exacerbations are associated with excessive neutrophilic inflammation. T-cells and cell-mediated immunity plays a major role in the pathophysiology of bronchiectasis[53]. Airway dehydration, excess mucus volume, viscosity, and structural bronchiectasis have adverse effect on the mucociliary clearance. In addition to small airway illness and emphysema, structural alteration in the lungs is linked to bronchial dilatation, bronchial wall thickening, and mucus plugging. The causes of breathlessness include airway blockage, poor gas transfer, deconditioning from exercise, and additional comorbidities[54].

Diagnosis:

When the broncho-arterial ratio is > 1, it indicates that the bronchial width is higher than the surrounding vessel's. However, age may affect the broncho-arterial ratio; studies indicate that 20–40% of healthy adults over 65 have ratios that are too high. To detect ongoing dilation of the airways, a high-resolution computed tomography (HRCT) scan is necessary[55].

Treatment:

Antibiotics, anti-inflammatory, and mucolytic drugs make up the majority of the pharmaceutical treatment. The goal of treatment is to avoid mucus stasis and the subsequent mucus clogging, airway blockage, and lung damage[56].

Only minimal evidence shows that ICSs are beneficial in bronchiectasis, which is likely because of bacterial infections in the bronchi and neutrophilic inflammation. Although ICSs are overused, their indication in patients with bronchiectasis is not advised due to their limited action in the presence of predominantly neutrophilic inflammation, and also due to their immunosuppressive properties.

CYSTIC FIBROSIS

Cystic fibrosis (CF) is an autosomal recessive, monogenic disease resulting in shortness of life. A mutation, or change in the chemistry of the CF gene, which is also known as the cystic fibrosis transmembrane conductance regulator (CFTR) protein which regulates the chloride channel, essential for effective mucus transport. Mutations in CFTR cause hyper concentration of mucus and a reduction in mucociliary clearance by interfering with the production of chloride, sodium reabsorption, and water transport[57]. Chronic bronchitis, bronchiectasis, chronic sinusitis, gastroesophageal reflux disease, constipation, diarrhea, diabetes, chronic pancreatitis, malnourishment, delayed development, male infertility, osteoporosis, asthma, and nasal polyposis are frequent conditions that affect people with cystic fibrosis (CF) [58].

Epidemiology:

Over 72,000 patients worldwide suffer with cystic fibrosis. There are between 1 in 2000 and 100,000 people who have CF. The reported prevalence of cystic fibrosis (CF) in India was between 1/10,000 and 1/40,000, according to immigrants from the United States and the United Kingdom.

F508del is the most prevalent causal mutation (>85%) among European ancestries and accounting for 27% of CF patients of South Asian ancestry. More specifically, it appears that non-European groups have a lower allele frequency[59].

Etiology:

A gene on chromosome 7 that is genetically altered to induce cystic fibrosis (CF) encodes the transmembrane conductance regulator (CFTR) protein, which functions as a transmembrane AMP-activated chloride channel. Mutations in both copies of the gene result in clinical disease.

There are about 2000 different mutations in the CFTR gene that might cause disease.

Classification:

1. Impaired protein synthesis

2. Impaired protein processing

3. Disorganized regulation

4. Impaired chloride conductance

5. A quicker turnover of channels[60].

Risk factors:

Chronic inflammation, a defining feature of cystic fibrosis, has also been connected to increased cardiac risk in other inflammatory conditions such HIV, rheumatoid arthritis, and systemic lupus erythematosus (SLE). Diabetes, excessive salt consumption, and chronic kidney illness are risk factors for heart disease that patients with EMBARC-India CF may have[61].

Clinical presentation:

- Feeling dry or coughing up mucus
- Recurring cold
- Wheezing or shortness of breath
- Recurrent sinus infections
- Very salty skin tone

In addition to the patient's genetic component, the symptoms may vary depending on their age at diagnosis. Chloride levels exceeding 60 mmol/l are known to cause these symptoms in patients.

The disorders commonly observed in adults and adolescents are growth retardation, male sterility with azoospermia, digital clubbing, recurrent stomach discomfort, pancreatitis, distal intestine obstruction syndrome, liver cirrhosis, and portal hypertension[62].

Pathophysiology:

The CFTR protein is distinct from the other members of the PwCF binding cassette protein superfamily, it is a transmembrane glycoprotein made up of two specular halves, each of which consists of six membrane-spanning domains and a nucleotide-binding domain, joined by a regulatory domain. The traditional roles of CFTR are associated with its function as a bicarbonate and chloride ion channel, which is involved in the appropriate hydration of airway surface liquid (ASL). Due to CFTR's tonic inhibitory impact on the Epithelial sodium channel (ENaC), causing it to become hyperactivated and aid in liquid hypersorption from the airways, CFTR is also implicated in the concentration of sodium ions in the ASL. These early occurrences eventually result in decreased mucociliary clearance (MCC), mucus buildup, airway clogging, bacterial colonization, inflammation, gradual tissue damage, and a reduction in lung function[63].

Diagnosis:

- Sweat test: The sweat test relies on the CFTR protein's ability to reabsorb chloride ions from perspiration back into the cells of the sweat duct. Higher levels of chloride values are found in sweat when the CFTR protein is not functioning properly.

- Genetic examination is the next step in the diagnostic process, which looks for abnormalities in the CFTR gene responsible for the dysfunction or cessation of the CFTR protein. Polymerase chain reaction (PCR) analysis is also employed to determine the pathogenic variant[64].

Treatment:

Antibiotics, airway clearance, and the use of mucus thinners are all part of the treatment for CF lung disease. To hydrate heavy mucus in the airways of CF patients, inhalation therapy with hypertonic saline is used to thin mucus. The common method for clearing secretions is chest physiotherapy based on postural drainage and percussion, with bronchoscopic lavage in CF patients who have retained purulent secretions that impede airflow and damage airways.

Patients with long-term CF-related diabetes, are now known to have microvascular complications such as retinopathy, peripheral neuropathy, and chronic kidney disease. Additionally, individuals with CF-related low bone mineral density in childhood or early adulthood are more vulnerable to fractures from age-related bone loss, especially after menopause[65].

ABBREVIATIONS

ABCD - Airway, Breathing, Circulation, Defibrillation

AMP- Adenosine Monophosphate

ASL- Airway Surface Liquid

ATP - Adenosine Triphosphate

BTS - British Thoracic Society

CD8+ T cells - Cluster of Differentiation 8 T helper cells

CF - Cystic Fibrosis

CFTR - Cystic Fibrosis Transmembrane Conductance Regulator protein

COPD - Chronic Obstructive Pulmonary Disease

EMBARC-India - European Multicentric Bronchiectasis Audit and Research Collaboration and the Indian Bronchiectasis Registry

ENaC - Epithelial sodium channel

FDA - Food and Drug Administration

FeNO - Fractional Exhaled Nitric Oxide

FEV1/FVC - Forced Expiratory Volume / Forced Vital Capacity

GERD - Gastroesophageal Reflux Disease

GOLD - Global Initiative for Chronic Obstructive Lung Disease

HIV - Human Immunodeficiency Viruses

HO-1 - Heme Oxygenase-1

HDAC2 - Histone deacetylase 2

HRCT - High-Resolution Computed Tomography

IgE - Immunoglobin E

ICS - Inhaled Corticosteroid

IL-8, IL-1β - Interleukin-8, Interleukin-1 beta

LABA - Long-Acting Beta Agonist

LAMA - Long-Acting Muscarinic Antagonist

MCC - Mucociliary Clearance

MMPs - Matrix Metalloproteinases

NO - Nitric Oxide

NRF2 - Nuclear factor erythroid related factor 2

NTM - Nontuberculous Mycobacteria

OAD - Obstructive Airway Disease

PCD - Primary Ciliary Dyskinesia

PCR - Polymerase Chain Reaction

PEF - Peak Expiratory Flow

ROS - Reactive Oxygen Species

RSV - Respiratory Syncytial Virus

SLE- Systemic Lupus Erythematosus

TNF-α - Tumor Necrosis Factor alpha

TB - Tuberculosis

WBC - White Blood Cells.

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