

Asthma–Chronic Obstructive Pulmonary Disease Overlap Syndrome

Nothing New Under the Sun



Nirupama Putcha, MD, MHS*, Robert A. Wise, MD

KEYWORDS

• Asthma • COPD • Overlap • Subtypes • ACOS

KEY POINTS

- It is increasingly recognized that there is a group of individuals having characteristics of both chronic obstructive pulmonary disease (COPD) and asthma.
- This group is thought to have characteristics of both diseases and might be at higher risk for respiratory events, exacerbations, and heightened symptoms.
- Understanding this subgroup is important in understanding the mechanisms for adverse outcomes and determining if specialized treatments have utility.
- Patients with asthma–COPD overlap syndrome include patients with COPD and eosinophilia, smoking asthmatics, long-standing asthmatics with airway remodeling, and steroid-resistant asthmatics with neutrophilic inflammation.

INTRODUCTION

The debate about the relationship between asthma and chronic obstructive pulmonary disease (COPD) on the spectrum of obstructive lung disease is far from new. The earliest and most famous example of such a debate can be found in the juxtaposition of the “Dutch” and the “British” hypotheses. Orié and colleagues from the Netherlands first described their hypothesis in 1961 that one disease termed “Chronic Nonspecific Lung Disease (CNSLD)” existed, which described all individuals with asthma, chronic bronchitis, and emphysema. They hypothesized that all of these individuals had shared endogenous and exogenous factors (now called gene–environment interaction) that contributed to the development of the disease. Host factors included allergic disease and bronchial hyperresponsiveness, and environmental factors included

Division of Pulmonary and Critical Care Medicine, Johns Hopkins University School of Medicine, 5501 Hopkins Bayview Circle, JHAAC 4B.74, Baltimore, MD 21224, USA

* Corresponding author.

E-mail address: Nputcha1@jhmi.edu

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cigarette smoke and pollution.^{1,2} Conflicting with this position was the “British” hypothesis, which distinguished a syndrome of chronic, irreversible airflow obstruction resulting from, most notably, exposure to smoking in susceptible individuals.³ This was thought to be separate from asthma, which was related to allergic disease and airways hyperreactivity. Patients with chronic airflow obstruction were considered to differ from those with asthma based on clinical course and pathogenesis.

Studies such as those reported by Burrows and colleagues⁴ in 1987, which demonstrated in a large, longitudinal epidemiologic study that nonsmoking individuals with a more asthmatic, atopic phenotype had significantly less decline in forced expiratory volume in 1 second (FEV₁) over time as well as much lower mortality rate than the group of nonatopic former and current smokers, seemed to lend substantial weight to the British hypothesis of 2 distinct clinical syndromes. Beyond outcome measures, other important evidence pointing to 2 distinct clinical syndromes drew from work that describes asthma and COPD as having distinct physiologic, inflammatory, and radiologic patterns. Asthma has been described to involve more eosinophilic inflammation⁵ as opposed to the neutrophilic inflammation thought to be more dominant in individuals with COPD. Fabbri and colleagues⁵ also showed that, in individuals with a history of asthma with a similar degree of fixed airflow obstruction and airway hyperreactivity as a group of individuals with COPD, those with asthma had less emphysema on computed tomography scans, lower residual volume, and higher diffusing capacity on pulmonary function testing. Patients with a history of asthma also showed more eosinophilic inflammation in blood, sputum, airway histology, and higher levels of expired nitric oxide. With regard to describing a distinct COPD diagnosis, in an early paper on the subject, Vermeire and Pride⁶ proposed a COPD phenotype comprising individuals with airflow obstruction, bronchial hypersecretion, and alveolar destruction. In contrast with asthma patients, this group of patients with smoking-related airflow obstruction has neutrophil-predominant airways inflammation.⁷

Research endeavors, drug development, and clinical guidelines about COPD and asthma in the past few decades have focused on the diseases as distinct entities. However, it has always been recognized by clinicians, as evidenced by the Dutch versus British hypothesis debate, that the distinctions between COPD and asthma are less clear, with a spectrum of disease. In recent years, there has been a resurgence of thought about the presence of a significant group of individuals that have attributes of both asthma and COPD, recently termed the asthma-COPD overlap syndrome (ACOS). Understanding this historical context of the Dutch versus British debate is a reminder that the idea of asthma and COPD as potentially overlapping entities is not an entirely novel perspective, but also highlights the importance of this topic given its implications for our understanding of obstructive airways disease and treatment strategies. The resurgent interest in ACOS has been kindled by the recognition by both the Global Initiative for Asthma (GINA; in asthma) and Global Initiative of Chronic Obstructive Lung Disease (GOLD; in COPD) expert panels that many patients were not adequately addressed by either group, and the acronym ACOS was put forth.

PREVALENCE AND EPIDEMIOLOGY OF ASTHMA-CHRONIC OBSTRUCTIVE PULMONARY DISEASE OVERLAP SYNDROME

Recent studies have focused on understanding the scope, characteristics and epidemiology of individuals with ACOS.⁸ The estimated prevalence of the syndrome seems to vary based on the population studied and the definitions used to describe the

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