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Is it Asthma or is it COPD: The Overlap Syndrome

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A 68 year old female presents with worsening cough, shortness of breath, and occasional wheezing of six months duration. She had a history of childhood asthma and allergic rhinitis, which have not been problematic in years. She has a 15–20 pack year smoking history, but quit 40 years ago. Her mother has a history of exercise induced bronchospasm. Her physical exam is within normal limits and her body mass index (BMI) is 29. In-office spirometry reveals a forced vital capacity (FVC) of 3.2 L (84% predicted), a forced expiratory volume in 1 second (FEV₁) of 2 L (69% predicted), and an FEV₁:FVC ratio of 63%. Because of her age of onset and smoking history, the decision is made to start on therapy for GOLD Group B chronic obstructive pulmonary disease (COPD) with tiotropium. The patient returns a month later with only mild symptom improvement and no change in lung function. A carbon monoxide diffusion capacity (DL_{CO}) assay is performed which is normal. Spirometry after bronchodilator challenge reveals a 12% and 240 mL improvement in FEV₁.

The management of asthma is one of the cornerstones of the allergist's practice. In adult patients, however, the clinical distinction between severe asthma and chronic obstructive pulmonary disease (COPD) is often difficult. In many patients, features of both diseases are seen, and a new clinical entity, the "overlap syndrome", is becoming increasingly recognized and important for a number of reasons¹.

Asthma, by its purest definition, is a disease of reversible airflow obstruction, bronchial hyperresponsiveness, and underlying airway inflammation². Although the majority of patients with asthma have reversible airflow obstruction, a segment of patients with asthma can have severe compromises in lung function, and from the perspective of lung function looks much like COPD. COPD shares features of the components of airflow obstruction, which is often progressive in severity, and elements of airway inflammation, but is historically linked to cigarette smoking. Furthermore, the airflow obstruction in COPD is usually incompletely reversible following the administration of bronchodilator medications. However, as patients with obstructive airway disease age, they often begin to take on characteristics of both diseases. Up to 50% of older patients with obstructive airway disease can be classified as having overlap syndrome, a cross between asthma and COPD^{1,3}.

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Clinically, the overlap syndrome is manifested in patients with symptoms of obstructive airway disease with incomplete bronchodilator reversibility and evidence of bronchial hyperresponsiveness on bronchoprovocation testing¹. These patients often present in different ways. Some patients with asthma show a proportionally greater decline in post-bronchodilator FEV₁ than prebronchodilator FEV₁, indicating a loss of reversibility over time and have pulmonary functions usually associated with COPD⁴. A significant proportion of patients with a diagnosis of COPD, in contrast, have evidence of bronchial hyperresponsiveness as measured by histamine or methacholine bronchoprovocation challenge^{5,6}. Thus, the once prevailing thought that asthma and COPD are distinct clinical entities has given way to the realization that while they do exist in their pure form in many patients, a significant number of patients straddle the line between these diseases. There are important differences between asthma and COPD. In contrast to COPD, those patients with severe asthma and profound obstructive lung disease do not require supplementary oxygen over time. In addition, the primary treatment in COPD is bronchodilator medications whereas those with asthma benefit from anti-inflammatory treatment. The importance of recognizing an overlap syndrome extends beyond the clinic and into the research sphere. Guidelines for treatment of asthma and COPD were developed based on the findings of research studies with strict exclusion criteria. Patients who are current, and often former, smokers are excluded from most asthma trials. Both asthma and COPD trials have set strict limits for bronchodilator reversibility, excluding patients with excessive reversibility from COPD trials and those with minimal reversibility from asthma trials. Thus, patients with overlap syndrome are often treated accordingly to guidelines based on studies that excluded patients with similar presentations to their own. This leads to an emerging diagnostic and therapeutic dilemma, which is only beginning to be approached.

Asthma and COPD also share several important clinical features, including cough and breathlessness, as well as many pathophysiologic mechanisms, including bronchoconstriction, airway inflammation, and excess mucous production. It is no surprise, thus, that patients with one diagnosis can often show signs consistent with the other. One of the strongest risk factors, outside of cigarette smoking, for the future development of COPD remains a diagnosis of childhood asthma, indicating that the link between these diseases is likely a lifelong phenomenon⁷. As our population ages, a larger number of patients with obstructive airway disease will be classified as having overlap syndrome. Further study is certainly warranted at this time to establish diagnostic and therapeutic guidelines that are specifically tailored to this growing subset of patients. Realizing that the overlap syndrome may represent a distinct phenotype of asthma is important for the clinician and ongoing investigation is necessary to more fully define this group of patients and discover what treatments are most effective for them.

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