

When asthma and COPD overlap each other

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Learning objectives

After reading this article you should be able to:

- Understand the pathological differences and similarities between asthma and COPD
- Understand the different management strategies for asthma and COPD, and
- Recognise that cases of mixed asthma/COPD may occur and understand the implications for disease management.

Competencies addressed: 3.1.2, 3.1.3, 3.2.2.



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Introduction

Asthma and chronic obstructive pulmonary disease (COPD) are among the top 10 leading chronic conditions in Australia,¹ placing a significant social and economic burden on patients, families and the health care system. More than five million Australians are affected by asthma or COPD, and each year these diseases disrupt the daily lives and productivity of many individuals and contribute to thousands of deaths.²

Asthma and COPD have important similarities and differences. Both are chronic inflammatory diseases that involve the small airways and cause airflow limitation, both result from gene-environment interactions and both are usually characterised by increased mucous production and bronchoconstriction. Differentiation between asthma and COPD is important because the prognosis, treatment goals and several aspects of the guideline-recommended management strategies are different.^{3,4} Once COPD is established, the only interventions that influence life expectancy are smoking cessation and oxygen therapy.³ By contrast, most patients with asthma have a normal life expectancy if they maintain regular preventive anti-inflammatory medication.⁴

Although overlaps exist in the disease characteristics of asthma and COPD, careful history taking, physical examination and lung function testing often reveal information that facilitates distinction between these diseases, allowing better tailoring of therapy. A misdiagnosis of COPD or asthma may lead to inadequate management of patients and escalating healthcare costs. An early and accurate diagnosis can help ensure optimal and cost-effective management. This article focuses on the differences, similarities and overlap of asthma and COPD, and the management of mixed disease.

Asthma

Asthma is a disorder defined by its clinical, physiological and pathological characteristics. The predominant features are episodes of shortness of breath and wheezing. In fact, the word 'asthma' comes from the Greek word *ααζειν* (aazein), which translates as 'to breathe with open mouth or to pant'.⁵ Currently, the Global Initiative for Asthma definition is:

*'Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyper-responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing, particularly at night or early in the morning. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment.'*⁴

For many patients, asthma begins in infancy, and both genetic and environmental factors contribute to its inception and evolution.⁶ The mechanisms whereby these factors influence the development of asthma are complex, and it is likely that genes interact both with other genes and with environmental factors to determine asthma susceptibility.^{7,8} The apparent racial and ethnic differences in the prevalence of asthma

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reflect underlying genetic variances with a significant overlay of socioeconomic and environmental factors.⁹

The symptoms of asthma are caused by airway inflammation and bronchoconstriction. In western medicine, use of bronchodilators for the treatment of asthma started at the beginning of the twentieth century,¹⁰ and it was not until the 1960s that airway inflammation was recognised as an underlying feature.¹¹ This discovery led to the development and use of inhaled corticosteroids (ICS), now the mainstay of asthma therapy.⁴ There is now good evidence that the clinical manifestations of asthma can be controlled with appropriate treatment.¹² When asthma is controlled, there should be no more than the occasional recurrence of symptoms and severe exacerbations should be rare.⁴

Chronic obstructive pulmonary disease

COPD is a disease state characterised by a progressive limitation of airflow in the lungs which, unlike asthma, is not fully reversible by medication.³ The characteristic symptoms of COPD are chronic and progressive dyspnoea, cough and sputum production. The Global Initiative for Chronic Obstructive Lung Disease definition for COPD is:

*'COPD is a preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterised by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases.'*³

It is important to note that the terms chronic bronchitis and emphysema are no longer included in the formal definition of COPD, although they are still used clinically.³ Emphysema is a pathologic term used to describe destruction of the alveolar-capillary membrane, and chronic bronchitis is a clinical term used to describe the presence of cough or sputum production for at least a three-month duration during two consecutive years.¹³

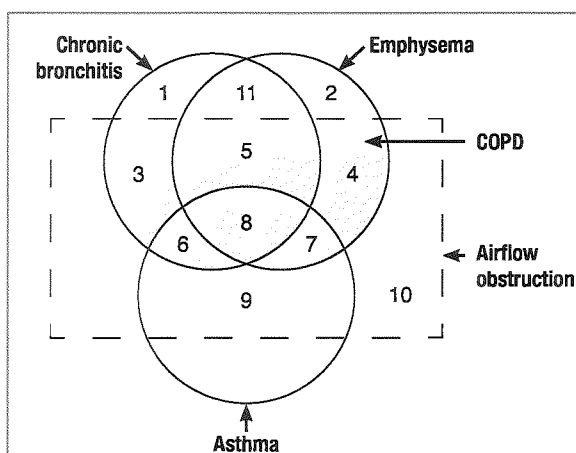
Risk for COPD is related to an interaction between genetic factors and many different environmental exposures.¹⁴ Cigarette smoking is by far the most commonly encountered risk factor for COPD.¹⁴ The population-attributable risk of smoking (smoking and ex-smoking) for COPD is reportedly up to 78%.¹⁵ This population-attributable risk identifies that at least 22% of COPD incidence still needs to be explained by other genetic and environmental risk factors.

The airflow limitation characteristic of COPD progresses slowly, and most patients diagnosed with COPD are aged over 40 years.¹⁶ The aim of COPD management is to reduce symptoms and delay the onset of severe disability.³ Smoking cessation is the only intervention proven to slow the progression of the disease,¹⁷ while pharmacological treatment improves symptoms and reduces the likelihood of exacerbations.¹⁸

Overlap of asthma and COPD

Until recently, the presence or absence of reversible airflow obstruction was thought to be the major distinction between asthma and COPD, with reversibility of airflow obstruction being the hallmark of asthma and irreversible obstruction the hallmark of COPD.¹⁹ In reality asthma and COPD are not single entities; each has a spectrum of reversibility and there is overlap. This is most likely associated with the varying extent and the mix of both structural and inflammatory changes and the predominant anatomic site within the lung at which these changes occur.²⁰ Individual patients commonly share the traits of different obstructive lung diseases.^{21,22} A graphical representation of this relationship was first presented as the non-proportional Venn diagram of chronic airflow obstruction (Figure 1).

Figure 1. Non-proportional Venn diagram of obstructive airways disease developed by the American Thoracic Society.²³



The subsets comprising COPD are shaded. Subset areas are not proportional to the actual relative subset sizes. Asthma is by definition associated with reversible airflow obstruction although, in variant asthma, special manoeuvres may be necessary to make the obstruction evident. Patients with asthma whose airflow obstruction is completely reversible (subset 9) are not considered to have COPD. Because in many cases it is virtually impossible to differentiate patients with asthma whose airflow obstruction does not remit completely from persons with chronic bronchitis and emphysema who have partially reversible airflow obstruction with airway hyper-reactivity, patients with unremitting asthma are classified as having COPD (subsets 6, 7 and 8). Chronic bronchitis and emphysema with airflow obstruction usually occur together (subset 5), and some patients may have asthma associated with these two disorders (subset 8). Individuals with asthma who have been exposed to chronic irritation, as from cigarette smoke, may develop chronic productive cough, which is a feature of chronic bronchitis (subset 6). Persons with chronic bronchitis and/or emphysema without airflow obstruction (subsets 1, 2 and 11) are not classified as having COPD. Patients with airway obstruction due to diseases with known aetiology or specific pathology such as cystic fibrosis or obliterative bronchiolitis (subset 10) are not included in this definition.

It is well established that airway remodelling can occur in long-standing, poorly treated asthma and results in partially reversible airflow obstruction.^{24,25} Therefore, in many patients with long-standing asthma there is a component of irreversible airflow obstruction with reduced lung function and incomplete response to a short-acting bronchodilator or to an oral or inhaled corticosteroid. This makes the diagnosis of obstructive lung disease somewhat challenging in older adults. However, despite similar airflow obstruction, elderly patients with asthma have distinct inflammatory characteristics compared to patients with COPD.²⁶ Long-term asthma has also been associated with an accelerated decline of FEV₁.²⁷ If patients with asthma sometimes show COPD-related phenotypes such as irreversible airflow obstruction and lung function decline, patients with COPD may exhibit airflow functional signs that are characteristic of asthma. Indeed, partial response to a bronchodilator is a common feature in patients with COPD, with almost 50% of patients showing significant improvement in FEV₁ after a bronchodilator.^{28,29} Interestingly, among patients with COPD, reversibility after bronchodilators appears to be associated with other asthma-related phenotypes, such as bronchial hyper-responsiveness.³⁰



Amongst patients with obstructive lung disease, the reported overlap of asthma and COPD ranges from 17 to 55% of patients.

Just how commonly do asthma and COPD co-exist? A number of studies have attempted to answer this question by analysing health surveys, Medicaid data, general practice databases or by classifying patients according to respiratory characteristics derived from international consensus guidelines. Amongst patients with obstructive lung disease, the reported overlap of asthma and COPD ranges from 17 to 55% of patients.^{21,31,32} Variations in the rates of overlap seem to stem from different methods of disease classification and differing study populations. Furthermore, diagnostic confusion between asthma and COPD appears commonly in the primary care setting.³³ The proportion of patients with mixed disease seems to increase with age,²¹ and the burden of the concomitant diseases is reportedly much higher than the combined burden of each individually.³²

Implications for management

Asthma and COPD tend to be treated with the same medications, with variations on emphasis (Table 1). Asthma is optimally treated with regular anti-inflammatory medications (preferably ICS), and short-acting bronchodilators are used when needed.⁴ COPD is usually treated with long-acting bronchodilators, which provide symptomatic benefits, and ICS to reduce the frequency of exacerbations.³ Whilst chronic inflammation underlies both asthma and COPD, the nature of the inflammation differs, as does the response to anti-inflammatory medications.^{34,35}

Table 1. Major differences between asthma and COPD management in adults³⁶

Asthma	COPD
Regular ICS treatment is recommended for patients of all ages with persistent asthma.	ICS are generally reserved for patients with severe disease and frequent exacerbations, or those who have shown improvement with ICS therapy.
Anticholinergic agents (e.g. tiotropium, ipratropium) are not used.	Tiotropium 18 mcg once daily improves dyspnoea, exacerbation rates, exercise capacity and health status.
Antibiotics are rarely indicated to manage exacerbations.	The use of antibiotics is often appropriate in the management of exacerbations.

Differences in these diseases can also be found in the goals of treatment. In asthma, treatment should be aimed at primarily achieving normal or near-normal lung function and preventing symptoms, which allows patients to live a relatively normal life.⁴ In COPD, the goal of therapy is to reduce the progressive nature of the disease with a focus on reducing symptoms and exacerbations while improving physical functioning and quality of life.³ Basically, the pharmacological treatment of asthma is driven by the need to suppress the chronic inflammation, whereas in COPD, pharmacological treatment is driven by the need to reduce symptoms.¹⁹

While consensus-based management guidelines for asthma and COPD acknowledge that the two diseases may co-exist, succinct treatment recommendations for mixed cases are lacking. Management should therefore be tailored to the individual's symptoms, physical functioning and frequency of exacerbations. Future research is required to determine whether patients with coexisting signs of asthma and COPD may benefit from management strategies that are based on multiple functional, morphologic and immunologic assessments rather than a categorisation into rigid diagnostic labels of either asthma or COPD.³⁷

Tailoring treatment to individual patients and assessing its benefits carefully should maximise quality of life, reduce adverse effects of medication, optimise physical function and better prepare patients for exacerbations.³⁸ Adapting management strategies to meet individual patients' needs should be the overriding consideration in achieving better outcomes for patients with obstructive airways disease.

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Questions

1. In patients with COPD, which ONE of the following interventions has been shown to slow disease progression?
 - a) Ipratropium therapy
 - b) Tiotropium therapy
 - c) Inhaled corticosteroid therapy
 - d) Smoking cessation.
2. The population-attributable risk of smoking for COPD is approximately:
 - a) 40%
 - b) 60%
 - c) 80%
 - d) 100%
3. Which ONE of the following characteristics is NOT included in the current Global Initiative for Asthma definition?
 - a) Chronic inflammation
 - b) Airway hyper-responsiveness
 - c) Progressive airflow limitation
 - d) Widespread, reversible airway obstruction
4. The proportion of patients with obstructive lung disease who have mixed asthma/COPD may be as high as:
 - a) 10%
 - b) 30%
 - c) 55%
 - d) 80%
5. Which ONE of the following statements is FALSE?
 - a) In patients with COPD, inhaled corticosteroids are reserved for those with severe disease and frequent exacerbations.
 - b) The pharmacological treatment of asthma is driven by a need to reduce existing symptoms.
 - c) In patients with COPD, antibiotics are frequently used to manage exacerbations.
 - d) Management of mixed asthma/COPD should be tailored to the individual's symptoms, physical functioning and frequency of exacerbations.

(A score of 4 out of 5 attracts 1 credit point.)