# Approach to management of chronic cough and chronic airway diseases: “Treatable traits” or correct diagnosis?

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**Editorial**

# Treatable traits or correct diagnosis? Thoughts on chronic cough and chronic airway diseases

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Treatable traits are a recently introduced and important concept in the management of chronic airway diseases such as chronic obstructive pulmonary disease (COPD) and asthma [1]. Recently, this concept of treatable traits has been introduced in the management of chronic cough. The management of chronic persistent cough has improved significantly by following an anatomical diagnostic protocol. The diagnosis of underlying diseases such as cough-variant asthma and gastroesophageal reflux has advanced the understanding of pathology and the management of chronic cough. Conversely, cough hypersensitivity that may reflect a complex interplay between peripheral (cough sensory nerves) and central (brain stem and higher centers) nervous system has been proposed more than 15 years ago and has now found acceptance, particularly in Europe, as an important concept encompassing cough with various etiologies [2]. The most recent guidelines on the diagnosis and treatment of chronic cough published by the European Respiratory Society emphasize the potential role of cough hypersensitivity in adult patients with chronic cough [3] who respond to an exposure to low levels of thermal, chemical, or mechanical stimulation [4]. In these guidelines, the diagnostic labels for chronic cough are replaced with treatable traits or phenotypes of chronic cough, described as asthmatic cough, reflux cough, and upper airways cough syndrome. The Japanese Respiratory Society guidelines for the management of cough and sputum have also introduced cough hypersensitivity syndrome as an emerging concept [5]. Although there remains some room for debate, cough hypersensitivity can be included in the management of chronic cough based on promising results with potential new treatments including purinergic P2X3 receptor antagonists [6]. In addition, every effort should be made to identify the underlying conditions that augment the sensitivity of peripheral nervous system, whichever terms of treatable traits or diagnosis

are used.

In contrast to chronic cough, the re-emphasis appears to be on “correct diagnosis” in COPD and asthma. One of the major treatable traits in obstructive airway diseases is elevated blood eosinophil counts. In both asthma and COPD, the risk of exacerbation increases by about 1.2–1.3 in patients with blood eosinophil counts above 300 cells/μL [7] [8]. Blood eosinophilia is a useful parameter for managing patients with COPD because the addition of inhaled corticosteroids may decrease the exacerbation frequency in this population, even though it may also increase the risks of pneumonia [9]. In contrast, blood eosinophil counts have been reported not to be very informative regarding the induction of anti-interleukin-5 class biologics in patients with COPD [10] [11] when compared with its efficacy in eosinophilic asthma. This difference might be due to the relatively smaller percentage of patients with severe eosinophilia within the overall COPD population compared to those with asthma; however, a recent study may provide a clue to the discrepant roles of blood eosinophil count between eosinophilic COPD and eosinophilic asthma [12]. In this study, despite having similar elevated blood eosinophil counts (>200 cells/μL) and elevated serum total IgE levels, only *CST1* gene, a gene encoding cystatin-SN that belongs to type 2 cystatin family, was correlated with blood eosinophil counts in both eosinophilic COPD and eosinophilic asthma. This finding suggests that eosinophilic COPD and eosinophilic asthma share the treatable trait of blood eosinophilia, but molecular mechanisms underlying this trait in two diseases are substantially different. In conclusion, the recognition of treatable traits is clearly important in clinical practice; however, correct diagnosis and efforts to identify the underlying mechanisms should be a continuous priority.

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