

Eosinophilic Endotype of Asthma



Fernando Aleman, MD^a, Hui Fang Lim, MBBS, MRCP(UK)^b,
Parameswaran Nair, MD, PhD, FRCP, FRCPC^{c,*}

KEYWORDS

• Asthma • Eosinophil • Sputum • Airway inflammation • Endotype

KEY POINTS

- Eosinophilic asthma is an endotype whereby eosinophils play a central effector role in the pathophysiology of the condition rather than being just one of many cells that may be present in the airway.
- Although there is no general consensus, a diagnosis of eosinophilic asthma may be made if the absolute eosinophil count is 400/ μ L or greater in blood or 3% or greater in sputum on more than one occasion, particularly during exacerbations.
- At the moment, sputum examination is the most reliable and valid method to identify the eosinophilic endotype and can be effectively used to monitor asthma control and guide therapeutic decisions.
- When persistently elevated ($\geq 400/\mu$ L), blood eosinophil counts may also be used to identify eosinophilic asthma and predict the response to corticosteroids. However, there is still insufficient evidence to recommend the use of fraction of exhaled nitric oxide (FeNO), immunoglobulin E, or periostin to guide decisions in clinical practice.
- Inflammatory phenotyping of severe asthmatic patients is essential for therapy optimization. Identification of eosinophilic asthma allows provision of targeted therapies to suppress eosinophilic inflammation, which effectively improve lung function and reduce symptoms and exacerbations.

Asthma is a chronic disorder characterized by variable airflow limitation and airway hyperresponsiveness and an associated chronic inflammation of the airways. As our understanding of the pathophysiological mechanisms that lead to these processes advances, we recognize several clinical endotypes, particularly depending on the type of airway inflammation, severity, and response to treatment.¹ The most predominant and clearly described endotype is eosinophilic asthma, which accounts for

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^a Division of Respiriology, St Joseph's Healthcare Hamilton, McMaster University, Hamilton, Ontario, Canada; ^b Department of Respiratory Medicine, National University of Singapore, Singapore, Singapore; ^c Division of Respiriology, St Joseph's Healthcare Hamilton, McMaster University, 50 Charlton Avenue East, Hamilton, Ontario L8N 4A6, Canada

* Corresponding author.

E-mail address: parames@mcmaster.ca

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approximately 50% to 60% of the total asthma population. Most of these patients can be controlled on moderate to high doses of inhaled corticosteroids (ICS), but 5% to 10% have severe disease that requires oral corticosteroids to control the eosinophilic airway inflammation.¹ This article is a brief overview of the definition, identification, natural history, and implications of treatment of eosinophilic asthma. The mechanisms that contribute to airway eosinophilia are not discussed in detail in this article.

DEFINITION OF EOSINOPHILIC ASTHMA

The definition is arbitrary. It is probably best considered as an endotype whereby eosinophils play a central effector role in the development of the physiological abnormalities that characterize the condition rather than being just one of many cells that may be present in the airway. It may be difficult to establish this; the main indication that eosinophils are the dominant cells responsible for the pathophysiological changes of the disease in a particular patient may be the demonstration that eosinophils are persistently increased and activated in the blood and airway (sputum, bronchoalveolar lavage, or bronchial mucosa or submucosa) when asthma is severe or uncontrolled² and that treatments aimed at decreasing the number and activity of eosinophils in the airways improve lung function and reduce symptoms and exacerbations.³ There is no general consensus on what defines *persistence* and what the appropriate cutoff levels are in various body compartments. It seems reasonable to consider a demonstration of an absolute eosinophil count of 400/ μ L or greater in blood or 3% or greater in sputum on more than one occasion, particularly at the time of an exacerbation, to consider an eosinophilic endotype of asthma. It is logical that these numbers that represent the upper-limit-of-normal values are determined by the dose of corticosteroids that these patients are on at the time of assessment.

DIAGNOSIS OF EOSINOPHILIC ASTHMA

Demonstration of eosinophils in the airways would be the most direct evidence of an eosinophilic endotype of asthma. This presence can be demonstrated in the tissue (bronchial mucosa or submucosa) or in the lumen (in bronchial wash, bronchoalveolar lavage, or in sputum).

Bronchial Mucosal and BAL Eosinophils

The histopathologic examination of a bronchial-biopsy specimen would perhaps be the most accurate method to demonstrate the presence of eosinophils in the airway epithelium and submucosa. However, because this involves an invasive procedure, it is impractical in routine clinical practice for monitoring over periods of time and to evaluate patients at the time of exacerbations. The correlation between eosinophils in the various airway compartments is poor.⁴ This poor correlation is not surprising given that BAL samples the peripheral airways, whereas bronchial wash and sputum represent a mixture of small and more proximal larger airways. Further, the quantification of eosinophils in BAL and in bronchial submucosa is not standardized and, therefore, difficult to compare between laboratories. More or less, if the BAL and tissue show abundant eosinophil numbers, they are likely to be increased in sputum as well. The converse may not be true.⁵ More importantly, sputum (airway luminal) eosinophil numbers correlated more with clinical parameters of asthma control, for example, the number of exacerbations, than tissue eosinophil numbers.⁵ This correlation is perhaps not surprising, given that eosinophils are activated when they move from one compartment to another and are more activated in the airway lumen than in tissue (or in circulation).⁶

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