Asthma is an extremely common illness which affects an estimated 300 million people of all ages and ethnic backgrounds worldwide with significant costs for healthcare systems. The clinical course of the disease is characterised by acute episodes of worsening of symptoms and decrease in lung function known as exacerbations. Prevention of exacerbations has been the goal of most therapeutic interventions developed so far because exacerbations seriously affect the quality of life of patients and their families. The clinical presentation of asthma exacerbations may be extremely heterogeneous; they can be rapid in onset or occur more gradually. The severity of asthma exacerbations is also extremely variable, ranging from mild episodes to severe attacks which result in respiratory failure and may ultimately lead to death.

Airway inflammation is a characteristic feature consistently present in patients with asthma from the early stages in children to elderly people. The inflammatory process has been extensively investigated in stable conditions, showing an increased infiltration of eosinophils, mast cells and CD4 T lymphocytes characterised by a Th2 profile, with release of cytokines such as interleukin (IL)-4, IL-5, IL-13, eotaxin and RANTES. Conversely, little is known about the cellular mechanisms activated during exacerbations and, in particular, in severe exacerbations.

In this issue of Thorax (see p 475), Qiu et al investigated the inflammatory response in bronchial biopsy specimens taken from patients admitted to hospital with a severe exacerbation of asthma and who required intubation for respiratory failure. They found that, during severe exacerbations, there was an increase in eosinophils and an even greater increase in neutrophils, resulting in similar final numbers of the two granulocyte subtypes infiltrating the airways. These results confirm previous observations on sputum and bronchoalveolar lavage fluid in acute severe asthma. A unique quality of the study by Qiu et al is that, unlike the other studies, it examined bronchial biopsy specimens obtained during exacerbations. This provides direct information on the airway tissue where inflammatory responses take place and interact with smooth muscle and mucus-secreting cells, thus contributing to airway narrowing.

Tissue inflammation in severe exacerbations of asthma has been evaluated previously, but only at post mortem examination. The pathological abnormalities observed in the airways of subjects who suffered a fatal asthma attack included both eosinophil and neutrophil infiltration. In particular, neutrophils predominated in those patients who died suddenly after onset of the attack, while eosinophils were more frequent in fatal events with a slow onset. It has been proposed that these differences in the inflammatory profile may reflect the dynamics of inflammatory cell recruitment in the airways, with the neutrophil being the predominant cell in the early phase following an inflammatory stimulus and the eosinophil being the predominant cell in the late phase. However, it was unclear whether these observations truly reflected the cellular mechanisms underlying the severe exacerbation or were rather due to death-related events.

The study by Qiu et al sheds some light on this issue by confirming that infiltration of neutrophils and eosinophils are indeed characteristic features of severe exacerbations of asthma.

Interestingly, in a previous paper the same authors reported that both granulocyte subtypes were increased even in stable asthma compared with those observed in exacerbations. Moreover, the subjects examined were not well matched with those in previous studies. Perhaps more importantly, this is a cross-sectional rather than a longitudinal study, so the possibility that neutrophilia was already present in those subjects before occurrence of severe exacerbations cannot be ruled out. Indeed, most of the patients with an asthma exacerbation had severe disease treated with high doses of inhaled or oral corticosteroids, while patients with stable asthma had mild disease controlled only with β2-agonists on an as needed basis. This difference in the degree of severity may have influenced the inflammatory cell profile in the patients with stable asthma since there was a significant increase in neutrophils compared with stable exacerbations.
is evidence that tissue neutrophilia is more frequent in severe asthma.22

Despite these unavoidable limitations, the report by Qiu et al is important because it promotes a better understanding of the events contributing to the development of severe exacerbations. Indeed, this study provides the framework for the cellular changes occurring in the airway tissue and the molecular mechanisms responsible for inflammatory cell recruitment. As a consequence, these observations will encourage new research into therapeutic strategies to prevent exacerbations, one of the most important aims of asthma management.


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**Dietary supplements and asthma**

**Dietary supplements and asthma: another one bites the dust**

**Johanna Feary, John Britton**

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**No effect of selenium supplementation on symptoms of asthma**

Throughout history, clinical observation and clinical trials have identified links between nutritional deficiency and disease. For example, scurvy was described by Hippocrates over 2000 years ago, and native cultures have known its cause and cure for centuries. The first intervention study to demonstrate the successful treatment of scurvy with citrus fruits was published in 1753 by Captain James Lind in “A Treatise of the Scurvy”. Moving forward to the 20th century, one of the resounding achievements in this field has been identification of the importance of folic acid supplements in the prevention of spina bifida, leading to an overall reduction in incidence in the Western world. The possibility that nutritional factors may play a similarly important role in the aetiology of chronic respiratory disease is therefore intriguing and has recently attracted a great deal of interest.

The aetiology of asthma remains unclear, but it is widely accepted that environmental factors play a major role, and, of these, diet is a potentially important contender. Evidence for this arises from the observations that the prevalence of asthma increases as societies move towards Western lifestyle; this is associated, among other factors, with a change in dietary pattern including adoption of a dietary pattern including adoption of a more processed and “convenience-orientated” diet. The result of this dietary change is an overall increase in the intake of refined sugars, fats and additives, and a relative reduction in the intake of complex carbohydrates and micronutrients. This change is a relatively modern phenomenon, occurring in the UK since the end of wartime rationing and also resulting from increased industrialisation of the food supply chain.

There is now an extensive literature on the relationship between diet and respiratory disease.1,2 In asthma, observational studies have shown encouraging evidence of a protective effect of several nutrients on disease prevalence and symptoms, including vitamin C,3 vitamin E,4 selenium5 and magnesium.6 However, and disappointingly in view of early promise with vitamin C,3 these findings have not generally translated into consistently positive outcomes in intervention studies. For example, in a recent randomised placebo-controlled trial of vitamin C, magnesium or placebo in 300 patients, we found no effect of either supplement on clinical asthma control.7 Similarly, an intervention study of vitamin E in adults with asthma also showed no evidence of a benefit.8 While fish oil supplements have been...
The laws of attraction: chemokines, neutrophils and eosinophils in severe exacerbations of asthma
Graziella Turato, Simonetta Baraldo, Renzo Zuin and Marina Saetta

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