

EDITORIAL

Clinical & Experimental Allergy

Asthma in children and nutritional selenium get another look

This editorial discusses the findings of the paper in this issue by Thomson et al. [8], pp. 560–567.

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Asthma is a multifactorial disease characterized by airway hyper-reactivity (AHR), episodic wheezing, airway inflammation, and mucus secretion [1]. The incidence of allergic asthma has been globally increasing, leaving clinicians and researchers searching for genetic, environmental, or nutritional factors that may be contributing factors to the rise in this disease. Maternal diet during pregnancy and nutritional status in early childhood have been suggested as important factors that dramatically influence the developing immune system and allergic sensitization, thereby impacting the incidence of childhood allergic disease [2]. In particular, the antioxidant status of pregnant women and their children during the first years of life is believed to impact the development of allergic disease during childhood. That said, it remains unclear whether intake of nutritional antioxidants at levels that are too little, too much, or somewhere between contributes to a higher susceptibility to asthma [3].

The most common form of asthma in children is allergic asthma, which starts early in life and is characterized by AHR, airway inflammation, and atopy [1, 4]. The development of T helper (Th)-2 responses against allergic antigens (allergens) is a hallmark feature of this disease and Th2 cells have been implicated in human and animal models of allergic asthma. Exactly how or why Th2 responses against otherwise harmless allergens arise in some children and not others are issues that have been at the center of dec-

ades of clinical and basic science research. Yet, the answers remain elusive and clinicians are largely resigned to treating the symptoms of this costly disease instead of treating the causes. One nutrient that has been suggested to influence the development of allergic asthma is selenium. As a potent antioxidant, selenium may provide protection from the higher levels of pulmonary oxidative stress that accompany allergic asthma. In addition, selenium has been shown in cell culture and mouse models to influence the development of T helper (Th)-2 responses, which play a critical role in driving allergic asthma [5, 6].

New Zealand is one country in which associations between low selenium status and asthma have been found [7]. In the study by Thomson et al. included in this issue [8], a New Zealand birth cohort was assessed after 6 years ($n = 635$) for associations between plasma selenium and allergy-related health outcomes including asthma, wheeze, hayfever, rhinitis, eczema, and rash. No significant associations were found after adjusting for location and subject factors, arguing against a correlation between selenium status and the high incidence of asthma in New Zealand. Selenium status by itself seems to not contribute strongly enough to the development of asthma to produce a consistent association in studies such as that conducted by the New Zealand team. Importantly, this study did not include selenium supplementation at pharmacological levels, and the promising results from animal models showing diminished Th2 responses and allergic asthma were obtained with pharmacological levels of selenium intake. In addition, further follow-up of the children may reveal allergic asthma cases that emerge after the age of 6 in the study subjects. Regardless, the negative results of this study emphasize the complexity of asthma and the difficulties of directly correlating one nutritional factor with disease outcome.

One interesting finding in the study by Thomson et al. involved data supporting the role of dietary

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selenium as a protective factor in the development of asthma associated with cigarette exposure. The notion of selenium acting to offset the effects of cigarette smoke seems to make sense. Selenium levels promote T-cell proliferation, while cigarette smoke decreases proliferative capacity [9]. Also, higher levels of selenium skew immune responses toward Th1/T_{reg} and away from Th2 [6, 10], while prenatal secondhand cigarette smoke has been shown to promote Th2-type responses [11]. It is important to consider the possibility that high selenium intake may counteract the allergic immune effects of maternal or childhood exposure to cigarette smoke. This is especially the case given that gestational or childhood exposure to cigarette smoke is a strong risk factor for pulmonary dysfunction, including asthma and chronic obstructive pulmonary disease (COPD) [12, 13].

It must be considered that other antioxidants compensate for mild deficiencies in selenium intake, and overall nutritional antioxidant intake may be a more valid parameter to consider when interrogating oxidative stress, nutrition, and allergic asthma. In fact, studies and meta-analyses of maternal and infant nutrition have implicated several antioxidants along with selenium in the etiology of allergic asthma, including vitamin E, flavonoids, vitamin C, and zinc [14]. Thus, the redox status of T cells and other immune cells that drive allergic asthma most likely are affected by a number of different nutritional factors. Overall, there still appears to be no clear picture for the relationship between dietary selenium levels and asthma, and the impact of nutritional antioxidants during childhood development on the development of this multi-factorial disease also remains unclear.

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