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Diet and Asthma: Nutrition Implications from Prevention to Treatment

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ABSTRACT

Asthma is characterized by lung airway inflammation initiated and perpetuated by an inappropriate immune response, increased airway responsiveness, and variable airflow obstruction. In Western countries there has been a marked increase in asthma prevalence such that it has become a public health concern. It has been hypothesized that the increase may be due to changing antioxidant intake, increasing dietary ratio of n-6:n-3 polyunsaturated fatty acids (PUFA), and vitamin D deficiency (and supplementation). Observational studies have reported associations between asthma and dietary antioxidants (vitamin E, vitamin C, carotenoids, selenium, polyphenols, and fruit), PUFA, and vitamin D. However, supplementing the diets of adults with asthma with antioxidants and n-3 PUFA has minimal, if any, clinical benefit. Currently there is insufficient evidence to support the use of nutrient supplements to complement conventional treatment; however, results of ongoing studies are awaited, and additional research is required, particularly in children. Interest in the potential of dietary intervention during pregnancy to reduce the likelihood of childhood asthma has increased. A small number of cohort studies have highlighted associations between childhood asthma and reduced maternal intake of some nutrients (vitamin E, vitamin D, selenium, zinc, and PUFA) during pregnancy. Although vitamin D intervention studies during pregnancy are ongoing and two intervention studies suggest that dietary PUFA manipulation during pregnancy may be advantageous, further trials are needed to establish if modification of maternal nutrient intake during pregnancy can be used as a healthy, low cost, public health measure to reduce the prevalence of childhood asthma.

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Asthma is a chronic disorder of the lung airways associated with increased airway responsiveness and variable airflow obstruction. Typical symptoms include periodic wheezing, breathlessness, paroxysmal cough, and chest tightness, and severity ranges from occasional symptoms to disabling persistent symptoms and/or frequent life-threatening exacerbations. Asthma and the allergic diseases of atopic dermatitis (eczema), allergic rhinitis (hayfever), and immunoglobulin E–mediated food allergy are closely associated, the likelihood of developing asthma being increased by a personal or family history of allergic disease. Asthma and allergic diseases are characterized by inflammatory processes with T-helper (Th) cell responses of the Th2 phenotype being considered crucial for the initiation and perpetuation of the inflammatory responses (1). Cytokines such as interleukin (IL)-4, IL-5, and IL-13 secreted by Th2 cells are important mediators of asthmatic and allergic inflammation that is characterized by elevated immunoglobulin E, mast-cell degranulation, and eosinophilic inflammation (1,2). There is increasing interest in the role of regulatory T (Treg)-cells in the pathogenesis of asthma and allergic disease because of their ability to directly inhibit both Th1 and Th2 responses (3).

Asthma is one of the world's most common chronic diseases, with a conservative estimate of 300 million people being affected by it. It is associated with Western urban communities, and it is estimated that by 2025 there could be an additional 100 million people with the disease. Asthma is a common and costly disease globally, accounting for the loss of approximately 15 million disability-adjusted life years, being the 25th greatest cause of disability-adjusted life years lost in 2001 (4). North America (the United States and Canada) has a high prev-

alence of asthma at 11.2%, representing 35.5 million people with asthma in a population of 316.9 million, with the United States having a prevalence rate of 10.9%, which in 1994 cost the economy an estimated $12 billion (4). Between 2001 and 2003 there were an average of 20 million people with asthma living in the United States each year, with 6.2 million of them being children (5). Access to drugs essential to control the condition tends to be good, with more than 95% of people able to acquire them. This may be reflected in the relatively low fatality rate of 5.2 per 100,000 people with asthma (4). In the absence of curative treatments, clinical management of asthma aims to control symptoms using bronchodilator and anti-inflammatory therapies. Given the high prevalence of asthma and its affect on individuals and society there is a need to identify interventions that can be used to complement conventional asthma therapy and more importantly, interventions to reduce the likelihood of children developing asthma.

INCREASING PREVALENCE OF ASTHMA

The prevalence of asthma has been rapidly increasing within Westernized countries, with increases of between 25% and 75% per decade being observed since 1960 (4). A recent survey by Moorman and colleagues (5) reported that the prevalence of self-reported asthma in the United States increased from 3.1% in 1980 to 5.6% in 1995, being more marked in children (an increase from 3.5% to 7.5%) than adults (an increase from 2.9% to 5.0%). The increase in asthma has probably been greater in the United Kingdom; for example, serial cross-sectional surveys of Aberdeen schoolchildren aged 9 to 12 years have demonstrated that the prevalence of asthma increased from 4.1% in 1964 to 28.4% in 2004 (6). The rate of increase in asthma prevalence appears to have slowed, with studies from some Westernized countries reporting that asthma prevalence may have plateaued; for example, in the United States the prevalence of asthma did not significantly change between 2001 and 2004 (5).

The rapid increase in asthma is most likely to be a consequence of changing environmental/lifestyle rather than genetic influences. In the past 15 years, several dietary hypotheses have been proposed and, somewhat surprisingly, changing diet has emerged as a promising candidate as a contributory environmental factor to the increase in asthma. In this narrative review, the rationale for investigating associations between diet and asthma is outlined, the potential for dietary intervention to complement conventional asthma treatment is then discussed, and finally the recent data suggesting that diet may influence the development of asthma are summarized. In each section, to reflect the focus of recent studies, nutrients are discussed in three groups: antioxidants (vitamins A, C, E, selenium, and antioxidant-rich foods), polyunsaturated fatty acids (PUFA), and vitamin D. To identify relevant articles, a set of 117 search terms relevant to asthma and diet were developed. These included symptoms of asthma (eg, wheeze), physiological parameters (Forced expiratory volume in 1 second), broad dietary terms, and specific nutrients (eg, vitamin E and PUFA). Included studies were all those relevant to adults and children (ie, mothers during pregnancy, infants, and children) that investigated the association between nutrients and foods and asthma (ie, cohort, case-controlled, cross-sectional, and all intervention studies). Three international databases were searched: Cochrane Library, MEDLINE, and EMBASE. The literature search encompassed studies from 1950 to December 2009. All references of published studies were hand searched. Of the 1,457 identified studies, 329 were considered to be directly relevant and were categorized into systematic reviews, intervention, and observational studies. While this review emphasizes published systematic reviews and clinical trials, such studies are relatively few, limited to adults, and focus on a few specific nutrients (eg, vitamin C). In the absence of systematic reviews and interventional study data, illustrative examples of the best available observational studies are presented.

Antioxidants

Two hypotheses relate the increase in asthma to changing dietary antioxidant intake.

The first proposes that the increase is a consequence of declining dietary antioxidant intake (7). This was based on the observation that in the United Kingdom asthma had increased concurrently with marked changes in the diet. The changes highlighted were those associated with the transition from a traditional diet comprising foods produced and marketed locally and eaten shortly after harvesting to the modern diet dominated by foods that have been processed, stored, and transported great distances. There is some evidence that the nutrient content of food may also have changed; for example, in the United Kingdom it has been suggested that the mineral content of vegetables, fruit, and meat has declined (8). Temporal changes in dietary habits and food nutrient content appear to have resulted in changes in antioxidant intake. Unfortunately, longitudinal data are very limited for antioxidants highlighted in studies of asthma. European selenium intake and blood selenium concentrations have declined, probably because of declining use of North American grain and changes in bread-making technology (9). In the United Kingdom, average selenium intake has fallen from 60 mg/day in 1975 to 30 to 40 mg/day currently (9-11). The limited data on United Kingdom vitamin E intake suggest little change from 10.82 mg/day in 1994 to 10.66 mg/day in 2004-2005 (12). However, extrapolation of the 2000-2001 UK National Diet and Nutrition Survey using the UK National Food Surveys suggests that vitamin E intake in the early 1950s was probably higher, at about 13 to 15 mg/day, perhaps because of increased consumption of green vegetables and bread/whole grains/cereals (13,14).

The second antioxidant hypothesis proposes that the increase in asthma and allergic disease is a consequence of increased antioxidant intake because of the increased availability of functional and antioxidant-enriched foods (15). This hypothesis was based on in vitro observations that some antioxidant rich foods and extracts of traditional Vietnamese and Chinese herbal medicines suppress secretion of the Th1 cytokine interferon-γ (15). It is postulated that increased antioxidant intake by suppressing Th1 differentiation promotes Th2 differentiation because of inherent cross-regulatory mechanisms. Whilst this hypothesis is primarily based on in vitro immunological observations, there is some evidence that the intake