

Can a Diet with Low Proinflammatory Potential Help with Asthma?



Augusto A. Litonjua, MD, MPH Rochester, NY

Asthma is a common, complex condition that has its roots in genetics and environmental exposures. Many environmental exposures, or lack thereof, have been implicated in asthma development, and most of these have been related to shifts in lifestyles related to westernization. Diet has been studied for many years as a changing exposure that predated and accompanied the rise in the prevalence of asthma worldwide.¹ Studies of the relationship between diet and asthma have taken different approaches, with many investigating specific nutrients and others investigating diet patterns, such as the Mediterranean diet.² While individual nutrient analyses have shown some associations, it is argued that diet patterns would be more informative because there may be interactions or synergistic effects from nutrients found together in food. Most observational studies of diet patterns, however, have shown null effects on asthma.

Several issues complicate dietary research and have largely been overlooked in asthma and lung diseases. Some of these issues include the changing food production and distribution methods over the last half century, which may affect nutrient content and nutrient availability, organic versus nonorganic food production,³ and the presence of contaminants (eg, antibiotics and chemicals),⁴ albeit in small amounts, in the food supply. These issues make it difficult to compare studies from different regions and countries, and may affect results from large studies in which participants come from a wide area with differential access to local, national, and even international food supplies. Thus, performing observational studies or clinical trials with a more homogeneous supply of foods may be necessary. While there are a few dietary counseling trials in asthma, there is a dearth of clinical trial data of administering a specific diet for asthma with foods from a single source, and these have been published in pilot form only.^{5,6} In contrast, recent trials have shown promise of individual nutrient supplementation, such as vitamins C and D, and omega-3 fatty acids, in abrogating the effects of maternal smoking on infant lung outcomes,⁷

preventing the development of asthma and wheezing in young children,^{8,9} and in aiding in the management of asthma.¹⁰ Clearly, single-nutrient trials are easier to perform than diet trials; however, trials using specific diets as the intervention have shown success with other outcomes,¹¹ and should be encouraged in lung disease outcomes.

There are several methods of collecting information about diets (reviewed in Litonjua¹). Once recorded, the responses of the individual are compared with reference tables that assign calories and nutrients to the specific food items that the individual has reported. The resulting data are then analyzed using different indices and are given a score for how closely the diet adheres to, for example, a Mediterranean diet or a Western diet. In this issue of the *Journal of Allergy and Clinical Immunology: In Practice*, Han et al¹² present their analysis of a novel diet index, the Dietary Inflammatory Index (DII), and its association with asthma, wheeze, and lung function in children and adults from the National Health and Nutrition Examination Survey study. The DII is an index of the proinflammatory nature of an individual's diet that can be applied to any assessment of diet (eg, food records). The index has been validated in multiple populations from different countries against measured levels of inflammatory markers, initially of C-reactive protein,¹³ but subsequently with other inflammatory markers (IL-1 β , IL-6, TNF- α) and anti-inflammatory markers (IL-4 and IL-10).¹⁴ A higher DII score, indicative of a proinflammatory diet, has been associated with a broad range of outcomes.^{15,16} Foods that contribute to a higher DII score are those typical of a Western diet, which are high in saturated fats and trans fats, whereas a diet rich in fruits and vegetables contributes to a lower DII score (ie, anti-inflammatory). Han et al¹² report that among adults, a higher DII score was associated with current wheeze. A higher DII score was also associated with lower indices of lung function, but only in those without asthma or wheezing. In children, the DII was also associated with current wheezing but only in those with high exhaled nitric oxide. There were no significant associations with asthma in either age group. Additional findings from this analysis were that DII scores were higher in non-Hispanic black participants, those with higher body mass index, and those without private health insurance coverage, characteristics that are associated with asthma. Conversely, a higher DII score was associated with higher annual household income, although this may be a function of the low cutoff point for household income (\$20,000) used in this study. The strengths of this study include the large number of children and adults who had information on diet and respiratory outcomes, and the exploration of potential confounders and effect modifiers of diet and the respiratory outcomes. The main limitation remains that this analysis reveals cross-sectional associations, and we must be cautious in invoking causation, despite the valid reasoning of the authors that diet is not easy to change. An

Division of Pediatric Pulmonary Medicine, Golisano Children's Hospital at Strong, University of Rochester Medical Center, Rochester, NY

A.A.L. is funded by the National Institutes of Health (grant nos. R01 HL091528 and UG3 OD023268).

Conflicts of interest: A.A. Litonjua has received research support from the National Institutes of Health (grant nos. R01 HL091528 and UG3 OD023268), has received consultancy fees from AstraZeneca, and receives royalties from UpToDate.

Received for publication February 22, 2018; accepted for publication February 23, 2018.

Corresponding author: Augusto A. Litonjua, MD, MPH, Division of Pediatric Pulmonary Medicine, Department of Pediatrics, Golisano Children's Hospital at University of Rochester Medical Center, 601 Elmwood Ave, Box 667, Rochester, NY 14642. E-mail: Augusto.Litonjua@URMC.Rochester.edu.

J Allergy Clin Immunol Pract 2018;6:842-3.
2213-2198

© 2018 American Academy of Allergy, Asthma & Immunology
<https://doi.org/10.1016/j.jaip.2018.02.019>

additional limitation is residual confounding by unmeasured variables, such as access to fresh foods and similar food items that have different nutrient and contaminant composition from across the United States, as mentioned earlier. The reason for the null association with asthma is likely due to 1 or a combination of these limitations.

As noted by the authors of the current article, there has been 1 other study that showed an association of DII with asthma and lung function, and thus, it will be a potentially useful tool in studies of diet and asthma. What are the next steps? As I see it, there are a multitude of studies that need to be performed before the DII can be used in the prevention and clinical management of asthma. First, longitudinal studies will need to be performed to get closer to invoking causation. These studies need to be performed in both healthy populations before the development of symptoms of wheezing and also in cohorts of patients with asthma to investigate whether a diet with a low DII can lead to better asthma control. Because wheezing and asthma begin early in life, studies in pregnant women will also be critical. Two studies have shown that a higher DII in pregnancy is associated with markers of maternal systemic inflammation, impaired fetal growth, breast-feeding failure, and the potential for childhood obesity,^{17,18} but no studies relating DII in pregnancy with asthma outcomes in children has been performed. Next, potential mechanisms will need to be elucidated. This is not so easy, because in general, mechanisms of the effects of diet on asthma have remained elusive. Studies have shown that adhering to a Western diet high in fats and processed foods or a diet with a high DII leads to increases in markers of systemic inflammation. However, in asthma and other lung disorders, airway inflammation is critical. Nevertheless, it has been shown that patients with asthma with elevated markers of systemic inflammation have worse outcomes,² and the current study's findings of the association of a higher DII with wheezing only in children with elevated exhaled nitric oxide is consistent with this. In addition, the role of the intestinal microbiome is likely crucial in modulating the effects of a particular diet on the system, and will need to be investigated together with dietary interventions.¹⁹ Third, it remains unclear whether dietary factors are related to the different types of inflammation in asthma and the different asthma phenotypes,²⁰ and more studies with proper phenotyping of asthma are needed. Finally, clinical trials will need to be performed in both pregnant mothers and in established asthmatic patients to determine whether a diet with a low DII can be used to prevent asthma or to help manage asthma, respectively.

There is significant interest in finding dietary interventions that can prevent the development of asthma and help patients with current asthma. While Han et al's study did not find an association with asthma, they did find that symptoms and lung function were improved in subjects who had diets that had low proinflammatory potential. The use of the DII, a more direct measure of the proinflammatory nature of diet compared with other indices, in future studies could help identify dietary

patterns that have low proinflammatory potential that may prove to be useful for clinical recommendations to patients with asthma.

REFERENCES

1. Litonjua AA. Dietary factors and the development of asthma. *Immunol Allergy Clin North Am* 2008;28:603-29.
2. Guilleminault L, Williams EJ, Scott HA, Berthon BS, Jensen M, Wood LG. Diet and asthma: is it time to adapt our message? *Nutrients* 2017;9:E1227.
3. Zalecka A, Bugel S, Paoletti F, Kahl J, Bonanno A, Dostalova A, et al. The influence of organic production on food quality—research findings, gaps and future challenges. *J Sci Food Agric* 2014;94:2600-4.
4. Chiesa LM, Nobile M, Panzeri S, Arioli F. Antibiotic use in heavy pigs: comparison between urine and muscle samples from food chain animals analysed by HPLC-MS/MS. *Food Chem* 2017;235:111-8.
5. Brigham EP, Matsui EC, Appel LJ, Bull DA, Curtin-Brosnan J, Zhai S, et al. A pilot feeding study for adults with asthma: the healthy eating better breathing trial. *PLoS One* 2017;12:e0180068.
6. Clark J, Craig L, McNeill G, Smith N, Norrie J, Devereux G. A novel dietary intervention to optimize vitamin E intake of pregnant women to 15 mg/day. *J Acad Nutr Diet* 2012;112:297-301.
7. McEvoy CT, Schilling D, Clay N, Jackson K, Go MD, Spitale P, et al. Vitamin C supplementation for pregnant smoking women and pulmonary function in their newborn infants: a randomized clinical trial. *JAMA* 2014;311:2074-82.
8. Bisgaard H, Bonnelykke K. Fish oil in pregnancy and asthma in offspring. *N Engl J Med* 2017;376:1191-2.
9. Wolsk HM, Chawes BL, Litonjua AA, Hollis BW, Waage J, Stokholm J, et al. Prenatal vitamin D supplementation reduces risk of asthma/recurrent wheeze in early childhood: a combined analysis of two randomized controlled trials. *PLoS One* 2017;12:e0186657.
10. Jolliffe DA, Greenberg L, Hooper RL, Griffiths CJ, Camargo CA Jr, Kerley CP, et al. Vitamin D supplementation to prevent asthma exacerbations: a systematic review and meta-analysis of individual participant data. *Lancet Respir Med* 2017;5:881-90.
11. Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *N Engl J Med* 1997;336:1117-24.
12. Han Y, Forno E, Shivappa N, Wirth MD, Hebert JR, Celedon JC. The dietary inflammatory index and current wheeze among children and adults in the United States. *J Allergy Clin Immunol* 2018;6:834-41.
13. Cavicchia PP, Steck SE, Hurley TG, Hussey JR, Ma Y, Ockene IS, et al. A new dietary inflammatory index predicts interval changes in serum high-sensitivity C-reactive protein. *J Nutr* 2009;139:2365-72.
14. Shivappa N, Steck SE, Hurley TG, Hussey JR, Hebert JR. Designing and developing a literature-derived, population-based dietary inflammatory index. *Public Health Nutr* 2014;17:1689-96.
15. Fowler ME, Akinyemiju TF. Meta-analysis of the association between dietary inflammatory index (DII) and cancer outcomes. *Int J Cancer* 2017;141:2215-27.
16. Ruiz-Canela M, Bes-Rastrollo M, Martinez-Gonzalez MA. The role of dietary inflammatory index in cardiovascular disease, metabolic syndrome and mortality. *Int J Mol Sci* 2016;17:E1265.
17. Sen S, Rifas-Shiman SL, Shivappa N, Wirth MD, Hebert JR, Gold DR, et al. Dietary inflammatory potential during pregnancy is associated with lower fetal growth and breastfeeding failure: results from Project Viva. *J Nutr* 2016;146:728-36.
18. Sen S, Rifas-Shiman SL, Shivappa N, Wirth MD, Hebert JR, Gold DR, et al. Associations of prenatal and early life dietary inflammatory potential with childhood adiposity and cardiometabolic risk in Project Viva [published online ahead of print May 10, 2017]. *Pediatr Obes*. <https://doi.org/10.1111/ijpo.12221>.
19. Clemente JC, Manasson J, Scher JU. The role of the gut microbiome in systemic inflammatory disease. *BMJ* 2018;360:j5145.
20. Wood LG, Baines KJ, Fu J, Scott HA, Gibson PG. The neutrophilic inflammatory phenotype is associated with systemic inflammation in asthma. *Chest* 2012;142:86-93.

Reproduced with permission of copyright owner. Further reproduction prohibited without permission.