

Preventing disease in the 21st century: The importance of maternal and early infant diet and nutrition

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In exploring the ongoing controversy surrounding early diet and nutritional practices and the risk of allergic disease, it is important to begin by considering this in the wider context of increasing rates of many other diseases. Early nutrition has considerable implications for growth trajectory, neurodevelopment, and a microbiome profile that ideally promotes both metabolic and immune homeostasis. It is rapidly becoming clear that all of these factors are interconnected and that early nutrition can underpin the increasing propensity for many modern noncommunicable diseases (NCDs).

Perhaps the greatest challenge of our time is overcoming the pandemic of NCDs, of which allergic disease is arguably one of the most common and the earliest to appear. Within the wider context of this growing burden of cardiovascular disease, obesity, metabolic disease, chronic lung disease, cancers, and so many other NCDs, the debate over the role of allergen exposure in the origins of allergic disease might seem underwhelming. However, as many other disciplines grapple with the maternal and infant dietary strategies to reduce obesity and cardiometabolic diseases, the mounting evidence that delayed complementary feeding might increase allergy risk is becoming a central issue in these interdisciplinary challenges.

Already there is conflict and confusion over what constitutes optimal infant feeding guidelines, and there is an equal lack of clarity in defining dietary recommendations for pregnant and lactating women. Although there have been recommendations on many specific nutrients, some of these are now the subject of scrutiny. Moreover, the dramatic shift in philosophy toward consumption of allergenic foods, such as peanuts in pregnancy, has added to the confusion in both the public and professional domains. Within the space of only 10 years, we have moved from notions of avoidance for the prevention of sensitization to concepts of exposure for promoting immune tolerance. And

although avoidance has been both unsuccessful and difficult to achieve, the merits of early deliberate exposure are also not yet proven and remain the subject of randomized controlled trials.

Concerns over the risk of obesity are often raised in response to the concept that earlier feeding in infants might be important to prevent allergic disease. Similarly, attitudes and practices over maternal nutrition and the consumption of allergenic foods remain in disarray. Most evidence in pregnancy is limited to observational studies, with a natural reticence for undertaking intervention studies using allergens in pregnant mothers. Thus while randomized controlled trials, including our own, will address the role of allergen exposure in the early postnatal period, there are as yet no randomized controlled trials to address this issue in pregnant patients.

In this issue of the *Journal*, Maslova et al¹ focus on the relationship between specific foods in the maternal diet during pregnancy and the subsequent risk of allergic disease in the offspring. They report that regular maternal dietary intake of both peanuts and tree nuts (≥ 1 times per week) during pregnancy was associated with reduced asthma-related outcomes in the children at 7 years of age. Although this is another observational study, the particular strengths of this Danish study include the very large cohort of 61,908 women and the extended period of follow-up to 7 years of age. Although a validated food frequency questionnaire was used, there are acknowledged limitations in how accurately intake of peanuts and tree nuts was determined and whether this included foods containing nuts (including cereals, snack bars, and chocolates) in addition to specific nut products. Given the high proportion (61%) of the women with no reported peanut or tree nut intake, it would have been useful to know whether this was purposeful avoidance or an underestimation of their intake. The authors also acknowledge that it was not possible to measure or exclude associated effects of differences in nut consumption during lactation or in the infant's diet.

The specific relationship between maternal nut consumption and childhood respiratory symptoms reported here by Maslova et al¹ are in apparent contrast to another study by Willers et al,² which indicated that daily maternal consumption of nut products (eg, peanut butter) during pregnancy increased the risk of allergic respiratory disease in children ($n = 2832$) followed up to 8 years of age. However, this relationship was only seen for nut products and not for consumption of whole nuts (peanuts and tree nuts) *per se*.² Other studies have also described frequent (at least once per week) maternal peanut consumption during pregnancy as a risk factor for childhood peanut sensitization, including a cohort study ($n = 503$)³ and a case-control study ($n = 43$).⁴ These studies are limited by retrospective maternal dietary recall of intake during pregnancy, sometimes months or years later. Furthermore, participating families were from highly selected populations with coexisting food sensitization or food allergy (milk, egg, or both), with high potential for reverse causation

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relationships and recall bias. These limitations highlight the need for further research and specific randomized controlled intervention trials in this area.

Although the findings of Maslova et al¹ can be used to support notions that early exposure to allergen was a factor in reducing the risk of disease, specific sensitization and food allergy were not examined. Furthermore, the authors importantly explore a number of other potential explanations for their findings. The consumption of peanuts and tree nuts also provides an important source of specific immunomodulatory nutrients that have been independently associated with allergic risk, including polyunsaturated fatty acids, selenium, zinc, folate, vitamin E, and other antioxidants.⁵⁻⁷ It is also possible that the dietary patterns associated with higher nut consumption could also be associated with higher consumption of vegetables, fruits, and legumes. For example, dietary patterns, such as a Mediterranean diet during pregnancy, have been associated with protection against childhood asthma and wheeze,⁶ in particular higher consumption of vegetables, legumes, and fish.⁸ However, the literature is also unclear and inconsistent, with some studies showing that specific foods (leafy vegetables, fruits, and chocolate) are associated with reduced risk of allergic outcomes^{9,10} and other studies suggesting increased risk effects.¹¹ These inconsistencies are likely to reflect the inherent complexity of the diet, difficulty in accurately measuring it, and interplay with many other segregating environmental and lifestyle factors.

There is no longer any doubt that both maternal and infant nutrition play a critical role in determining the subsequent risk of not only allergic diseases but also many other NCDs. However, it is increasingly unlikely that allergen exposure is a driving risk factor. As suggested by Maslova et al,¹ dietary allergen restriction is neither justified nor likely to be effective in reducing allergic disease. Rather, our focus should be on understanding the complex changes in dietary composition that have occurred with progressive modernization. In addition to direct nutrient effects, modern dietary patterns appear to promote adverse gut microbiome patterns that lead to low-grade systemic inflammation, metabolic dysregulation, and associated chronic diseases.^{12,13} We need to urgently develop effective strategies to restore traditional dietary patterns, which clearly have many properties that protect not only against allergic disease but also against cardiovascular disease, obesity, diabetes, and many other NCDs.

Although the concept of promoting a healthy balanced diet appears both simple and logical, it is naive not to recognize the many complex social, cultural, and economic barriers to achieving this. For this reason, more than ever, it is important that we move toward more interdisciplinary collaboration and more multisectorial engagement to understand and address the complex determinants of health and disease in the modern world.

REFERENCES

1. Maslova E, Granström C, Hansen S, Petersen SB, Strøm M, Willett WC, et al. Peanut and tree nut consumption during pregnancy and allergic disease in children—should mothers decrease their intake? Longitudinal evidence from the Danish National Birth Cohort. *J Allergy Clin Immunol* ■■■■■■■■.
2. Willers SM, Wijga AH, Brunekreef B, Kerkhof M, Gerritsen J, Hoekstra MO, et al. Maternal food consumption during pregnancy and the longitudinal development of childhood asthma. *Am J Respir Crit Care Med* 2008;178:124-31.
3. Sicherer SH, Wood RA, Stablein D, Lindblad R, Burks AW, Liu AH, et al. Maternal consumption of peanut during pregnancy is associated with peanut sensitization in atopic infants. *J Allergy Clin Immunol* 2010;126:1191-7.
4. Frank L, Marian A, Visser M, Weinberg E, Potter PC. Exposure to peanuts in utero and in infancy and the development of sensitization to peanut allergens in young children. *Pediatr Allergy Immunol* 1999;10:27-32.
5. Allan K, Devereux G. Diet and asthma: nutrition implications from prevention to treatment. *J Am Diet Assoc* 2011;111:258-68.
6. Nurmatov U, Devereux G, Sheikh A. Nutrients and foods for the primary prevention of asthma and allergy: systematic review and meta-analysis. *J Allergy Clin Immunol* 2011;127:724-33, e1-30.
7. Patelarou E, Giourgouli G, Lykeridou A, Vrioni E, Fotos N, Siamaga E, et al. Association between biomarker-quantified antioxidant status during pregnancy and infancy and allergic disease during early childhood: a systematic review. *Nutr Rev* 2011;69:627-41.
8. Chatzi L, Torrent M, Romieu I, Garcia-Esteban R, Ferrer C, Vioque J, et al. Mediterranean diet in pregnancy is protective for wheeze and atopy in childhood. *Thorax* 2008;63:507-13.
9. Erkkola M, Nwaru BI, Kaila M, Kronberg-Kippila C, Ilonen J, Simell O, et al. Risk of asthma and allergic outcomes in the offspring in relation to maternal food consumption during pregnancy: a Finnish birth cohort study. *Pediatr Allergy Immunol* 2012;23:186-94.
10. Willers SM, Devereux G, Craig LC, McNeill G, Wijga AH, Abou El-Magd W, et al. Maternal food consumption during pregnancy and asthma, respiratory and atopic symptoms in 5-year-old children. *Thorax* 2007;62:773-9.
11. Sausenthaler S, Koletzko S, Schaaf B, Lehmann I, Borte M, Herbarth O, et al. Maternal diet during pregnancy in relation to eczema and allergic sensitization in the offspring at 2 y of age. *Am J Clin Nutr* 2007;85:530-7.
12. Ley RE, Turnbaugh PJ, Klein S, Gordon JI. Microbial ecology: human gut microbes associated with obesity. *Nature* 2006;444:1022-3.
13. Turnbaugh PJ, Ley RE, Mahowald MA, Magrini V, Mardis ER, Gordon JI. An obesity-associated gut microbiome with increased capacity for energy harvest. *Nature* 2006;444:1027-31.