

Allergy and infant feeding guidelines in the context of resource-constrained settings



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Recent discussions about the need for revised infant feeding guidelines in the context of allergy are founded in substantial evidence-based research. Key studies (Table I)¹⁻⁵ undertaken in high-income country settings provide evidence that the introduction of allergenic foods (eg, cow's milk protein, egg, peanuts, fish, sesame, and wheat) to infant diets before the age of 6 months might significantly reduce the risk of food allergy at older ages. Although such a strategy does not promote supplanting breast-feeding with the introduction of a diverse set of foods early on, it will shorten the duration of exclusive breast-feeding [EBF], replacing it with "partial breast-feeding," the combination of breast-feeding with other fluids or solids, and most likely lead to a reduction in overall duration of breast-feeding.

The ongoing discussions after recent evidence could result in the release of official guidelines that recommend introduction of allergenic foods before 6 months of age, leading to discordance with current global infant feeding guidelines that promote EBF for the first 6 months. Of concern is that the recent evidence on the early introduction of allergens and later development of allergy were all conducted in high-income countries, and no data are provided on the medium- to long-term effect of early allergen introduction on maternal and child health outcomes. Research has suggested that the early introduction of solids can increase islet autoimmunity, obesity, adult-onset celiac disease, eczema, anemia and diarrheal disease.⁶

The contribution of EBF to maternal and child health has been the subject of 3 *Lancet* series (*Lancet* breast-feeding series

2016: <http://www.thelancet.com/series/breastfeeding>; *Lancet* maternal and child nutrition series: <http://www.thelancet.com/series/maternal-and-child-nutrition>; and *Lancet* nutrition series 2008: <http://www.thelancet.com/series/maternal-and-child-under-nutrition>) and several systematic and Cochrane reviews. There is indisputable evidence that EBF during the first 6 months of life (ie, delayed introduction of solids and other liquids) is the best nutrition for infants and that EBF significantly reduces the risk of infant otitis media, lower respiratory tract infections, gastroenteritis, and vertical HIV transmission compared with partial (breast-feeding with other fluids or solids) or predominant (breastmilk with nonnutritive liquids) breast-feeding (Table II).⁷⁻⁹ Additionally, EBF has short- and long-term benefits for the mothers and infants from immediately postpartum to adulthood. Some benefits include protection against the development of noncommunicable diseases in adulthood and a possible causal link between predominant breast-feeding and intelligence and income at age 30 years.¹⁰

The World Health Organization and UNICEF advise 6 months of EBF for all infants irrespective of HIV exposure (ie, not introducing complementary feeds before 6 months) based on scientific evidence. Experience from the late 1990s, when early cessation of breast-feeding was recommended to prevent vertical HIV transmission, demonstrated the public health danger associated with this approach because it prioritized feeding patterns/practices to prevent only 1 disease (in this case HIV), ignoring the general benefits of EBF for maternal and child health.

As pediatricians, allergologists, and public health specialists working and interested in optimizing infant health in resource-limited settings, we suggest that international allergy specialists do not normalize guidelines that promote the early introduction of allergens in infants' diets to prevent food allergies. Infants from atopic families can have special needs, necessitating individualized feeding practices, and these infants should be managed appropriately with the evidence summarized in Table I. However, in the absence of long-term data about the early introduction of solids to avoid food allergy and taking note of the proved short-, medium-, and long-term benefits of EBF during the first 6 months of life, which has been demonstrated in all settings (low, middle, and high income), practitioners need to weigh the benefits of early introduction of solids to prevent food allergy against the disadvantages of a shorter duration of EBF, which might be deleterious for maternal and child health (Fig 1).

In settings with a high burden of allergy, HIV/other infectious diseases, and malnutrition, public health advice to introduce complementary foods early might be ill advised. Guidelines regarding early introduction could be less relevant to the populations in which prolonged EBF is most important, given that the overall risk of food allergy is far smaller in those populations. Conversely, the mortality risk of early weaning

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TABLE I. Allergy and infant feeding

Author	Setting and study population	Prevalence of HIV and malnutrition in this setting	Research design	Main finding	Authors' main conclusion	Critique
Katz et al, 2010 ¹	Israel; newborns born at Assaf-Harofeh hospital over a 2-y period	Not specified; prevalence of both disorders extremely low in Israel	Prospective study of cow's milk allergy; diagnosis by history and skin prick test and/or open food challenge	Of the sample (n = 13,234 infants), 0.5% had an IgE-mediated allergic event to cow's milk; very early introduction of cow's milk (age ≤14 d) protein was associated with lower risk of IgE-mediated cow's milk allergy.	Early complementary feeding of cow's milk proteins along with breast-feeding might promote oral tolerance.	Small sample size for modelling (n = 66); reverse causality (parental atopy) could not be excluded completely. There was neonatal exposure to cow's milk protein.
Koplin et al, 2010 ²	Australia; 11- to 15-month old infants recruited from immunization clinics in Melbourne; timing of egg exposure based on maternal recall	Not specified; prevalence of both disorders extremely low in Australia	Retrospective study of egg allergy; diagnosis by history and skin prick test and/or open food challenge	Introduction of egg at 4-6 mo was associated with lower risk of IgE-mediated egg allergy than introduction after that time.	Data suggest that early introduction of egg might protect against egg allergy. If this finding is confirmed, changes in infant feeding guidelines might reduce the prevalence of egg allergy.	In the adjusted model and in the model stratifying children into low and high risk, a significantly increased allergy risk is only measured when egg introduction is delayed to age 10 mo and later.
Du Toit et al, 2015 ³	UK; infants between ages 4 and 11 mo with severe eczema, egg allergy, or both	Not specified; prevalence of both disorders extremely low in United Kingdom	Prospective interventional study of peanut allergy; diagnosis of peanut allergy at age 5 y by food challenge	Introduction of peanuts between ages 4 and 11 mo was associated with lower risk of IgE-mediated peanut allergy at 5 y than introduction after that time.	Early introduction of peanuts into infants' diets (before 11 mo) leads to immune tolerance, preventing allergy in high-risk sensitized and nonsensitized infants.	Lack of a placebo regimen; exclusion of low-risk infants
Du Toit et al, 2016 ⁴	United Kingdom; infants between the age of 4 and 11 mo with severe eczema, egg allergy, or both (follow-on study to Du Toit et al, 2015)	Not specified; prevalence of both disorders extremely low in United Kingdom	Prospective interventional study of peanut allergy; diagnosis of peanut allergy at age 6 y by food challenge	Introduction of peanuts between the age of 4 and 11 mo was associated with lower risk of IgE-mediated peanut allergy at 6 y than introduction after that time, even 1 y after cessation of exposure.	Early introduction of peanuts in infants' diets leads to a sustained reduced risk of peanut allergy, even if the allergen is withdrawn for 12 mo.	Lack of a placebo regimen and exclusion of low-risk infants
Perkin et al, 2016 ⁵	United Kingdom; infants aged 3 mo	Not specified; prevalence of both disorders extremely low in United Kingdom	Prospective interventional study of allergy to peanut, egg, milk, fish, sesame, and wheat; diagnosis of food allergy by food challenge between 1 and 3 y	Intention-to-treat analysis did not show efficacy of early introduction of allergenic foods. Per-protocol analysis showed lower prevalence of any allergy, peanut allergy, and egg allergy in children aged 1-3 y with early introduction of allergens (3-6 mo of age).	The per-protocol analysis suggests that the protection conferred by early introduction of allergens is dose dependent. Increased exposure (measured by weekly quantity and number of weeks, divided into quartiles) was associated with more protection.	Poor adherence to protocol

strategies might be lower in high-income settings in which child mortality is lower. However, regions of the world that are confronting all 3 child health problems (allergy, HIV, and malnutrition) will experience a significant challenge in weighing infant feeding strategies for specific atopic children that will require an individualized approach. Patient advice will require individualization in low- and high-income countries because there might be subjects in both settings for whom the "general" advice might not be applicable.

With this in mind, we recommend the following:

1. allergy and infant feeding guidelines should be cognizant of the socioeconomic realities in different settings (global consensus would be desirable);
2. allergy and infant feeding guidelines should be contextualized for the setting in which they are to be applied, taking into account the under 5 mortality rate and the contribution of EBF to preserving and optimizing maternal and child health;
3. allergy and infant feeding guidelines should clearly specify target populations for implementation of allergy avoidance strategies;

TABLE II. General child health and infant feeding

Author	Setting and study population	Prevalence of HIV and malnutrition in this setting	Research design	Main finding	Authors' main conclusion	Critique
Coovadia et al, 2007 ⁷	KwaZulu-Natal province, South Africa; infants aged ≤26 wk born to HIV-infected and uninfected mothers recruited antenatally	Antenatal HIV prevalence was approximately 36.5%. During this time, infant HIV/AIDS contributed to 40.3% of childhood deaths, and protein energy malnutrition contributed to 4.3%.	Nonrandomized intervention cohort study to assess the HIV transmission risks and survival associated with infant feeding patterns	In the absence of maternal antiretroviral therapy, breast-fed infants who also received solids were significantly more likely to acquire infection than exclusively breast-fed children (HR, 10.87 [1.51-78.00], <i>P</i> = .018), as were infants who at 12 wk received both breastmilk and formula milk (HR, 1.82 [0.98-3.36], <i>P</i> = .057).	Promote EBF for the first 6 months to reduce vertical HIV transmission	Conducted in the time of single-dose nevirapine antiretroviral interventions; the effect of early introduction of solids when HIV-positive mothers received lifelong antiretroviral therapy is not known.
Black et al, 2008 ⁸	Random effects meta-analysis of data from India, Bangladesh, Ghana, and Peru	It is not specified in the article, but adult HIV prevalence ranges from <0.1% to 2.5%, and infectious disease and malnutrition prevalence is high.	Secondary analysis of data from observational studies and randomized controlled trials	During the first 6 mo of life predominant, breast-feeding increased the risk of all-cause mortality and pneumonia incidence compared with EBF during the first 6 mo (RR, 1.48 [1.13-1.92] and 1.79 [1.29-2.48], respectively), and partial breast-feeding significantly increased the risk of all-cause mortality (RR, 2.85 [1.59-5.10]), diarrhea-related mortality (RR, 4.62 [1.81-11.77]), pneumonia mortality (RR, 2.49 [1.03-6.04]), and diarrhea incidence (RR, 3.04 [1.32-7.00]), respectively.	EBF protects against childhood morbidity and mortality in the first 6 mo of life compared with predominant and partial breast-feeding. Early introduction of solids is not advised.	Data only from 4 countries
Sankar et al, 2015 ⁹	Systematic review; studies from Africa (n = 6), Latin America (n = 2), South-East Asia (n = 5), the Eastern Mediterranean (n = 1), and the Western Pacific (n = 1)	It was not specified, but many of these settings have a high prevalence of malnutrition and HIV.	Secondary analysis of data from 13 studies meeting inclusion criteria	Three studies demonstrated that in the first 6 mo of life, predominant and partial breast-feeding significantly increased all-cause and infection-related mortality compared with EBF (RR, 1.48 [1.13-1.92] and 2.84 [1.63-4.97], respectively) for all-cause mortality and for infection-related mortality (RR, 1.7 [1.18-2.45] and 4.56 [2.93-7.11]).	The review underscored the importance of optimal breast-feeding practices (EBF during the first 6 mo).	A small number of studies exist, and thus only 13 were included in the review.

HR, Hazard ratio; RR, risk ratio.

4. contraindications for implementation of allergy avoidance strategies should be clearly specified in such guidelines;
5. efforts should be made to combine feeding guidelines for allergy prevention and for child mortality prevention in a unified protocol; and

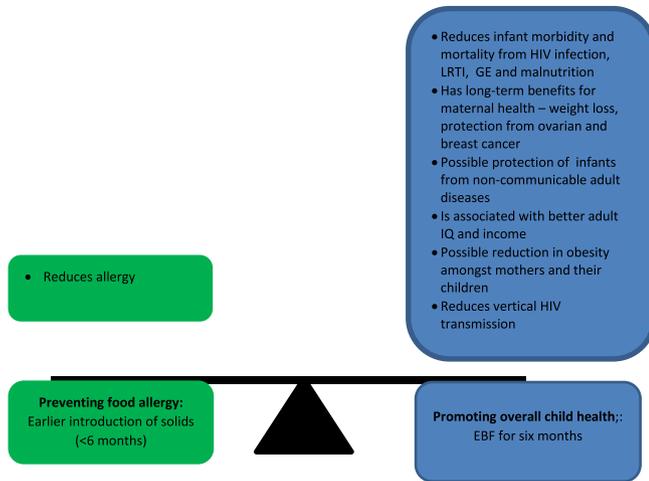


FIG 1. Feeding strategies to balance preventing food allergy with promoting overall child health.

6. in countries with high child mortality and low food allergy, guidelines recommending the option of earlier introduction of solids to high-risk infants should be circulated cautiously and should not be freely distributed at the primary health care level or to the public.

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