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

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To the Editor

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 1) undertaken in high income country settings, provide evidence that the introduction of allergenic foods (e.g. cow's milk protein, egg, peanuts, fish, sesame and wheat) to infant diets before the age of six months, may significantly reduce the risk of food allergy at older ages. Whilst 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 breastfeeding, replacing it with "partial breastfeeding", the combination of breastfeeding with other fluids or solids, and most likely lead to a reduction in overall duration of breastfeeding.

The ongoing discussions following recent evidence could result in the release of official guidelines that recommend the introduction of allergenic foods before 6 months of age, leading to discordance with current global infant feeding guidelines that promote exclusive breastfeeding for the first six 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 country settings and no data are provided on the medium to long-term impact of early allergen introduction on maternal and child health outcomes. Research has suggested that the early introduction of solids may increase islet auto-immunity, obesity, adult-onset celiac disease, eczema, anaemia and diarrhoeal disease.⁽¹⁾

The contribution of exclusive breastfeeding to maternal and child health has been the subject of three Lancet series (Lancet Breastfeeding 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-undernutrition>) and several systematic and Cochrane reviews. There is indisputable evidence that exclusive breastfeeding (EBF) during the first 6 months of life (i.e. 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 (LRTI), gastroenteritis (GE), and vertical HIV transmission compared with partial (breastfeeding with other fluids or solids) or predominant breastfeeding (breastmilk with non-nutritive liquids), Table 2. Additionally EBF has short and long-term benefits for the mothers and infants from immediate post-partum to adulthood. Some benefits include protection against the development of non-communicable diseases in adulthood, and a possible causal link between predominant breastfeeding and intelligence and income at age 30 years (10).

The World Health Organisation and UNICEF advise six months of exclusive breastfeeding (EBF) for all infants irrespective of HIV exposure (i.e. not introducing complementary feeds before 6 months) based on scientific evidence.

Experience from the late 1990s, when early cessation of breastfeeding was recommended to prevent vertical HIV transmission, demonstrated the public health danger associated with this approach, as it prioritised feeding patterns / practices to prevent only one disease (in this case HIV), ignoring the general benefits of exclusive breastfeeding for maternal and child health.

As paediatricians, allergologists and public health specialists working and interested in optimising infant health in resource limited settings we suggest that International Allergy Specialists do not normalise guidelines that promote the early introduction of allergens in infants' diets to prevent food allergies. Infants from atopic families may have special needs, necessitating individualised feeding practices, and these infant should be managed appropriately using the evidence summarised in Table 1. However, in the absence of long-term data about the early introduction of solids to avoid food allergy, and taking note of the proven short, medium and long-term benefits of exclusive breastfeeding during the first six months of life, which has been demonstrated in all settings (low, middle and high income), practitioners need to weigh up the benefits of early introduction of solids to prevent food allergy against the disadvantages of a shorter duration of exclusive breastfeeding, which may be deleterious for maternal and child health. Figure 1.

In settings with a high burden of allergy, HIV/other infectious diseases and malnutrition, public health advice to introduce complementary foods early may be ill-advised. Guidelines regarding early introduction may be less relevant to the populations where prolonged exclusive breast feeding is most important, given that that the overall risk of food allergy is far smaller in those populations. Conversely the mortality risk of early weaning strategies may be lower in high income settings where child mortality is lower. However, regions of the world that are confronting all three child health problems (allergy, HIV and malnutrition) will experience a significant challenge in weighing up infant feeding strategies for specific atopic children that will require an individualised approach. Patient advice will require individualisation in low and high income countries as there may be individuals in both settings in which the "general" advice may not be applicable.

With this in mind, we recommend that:

1. Allergy and infant feeding guidelines should be cognizant of the socio-economic realities in different settings; global consensus would be desirable.
2. Allergy and infant feeding guidelines be contextualised for the setting in which they are to be applied, taking into account the under-5 mortality rate and the contribution of exclusive breastfeeding to preserving and optimising maternal and child health.
3. Allergy and infant feeding guidelines should clearly specify target populations for implementation of allergy avoidance strategies.
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.
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 primary health care level or to the public.

Figure legend

Figure 1: Feeding strategies to balance preventing food allergy with promoting overall child health

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Table 1: 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
Allergy and Infant feeding						
Katz et al 2010(2)	Israel. Newborns born at Assaf-Harofeh hospital over a 2 year 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.	0.5% of the sample (n=13 234 infants) had an IgE mediated allergic event to cows milk. Very early introduction of cow's milk (age≤14 days) protein associated with lower risk of IgE mediated cow's milk allergy.	Early complementary feeding of cow's milk proteins along with breastfeeding may promote oral tolerance	Small sample size for modelling (n=66); reverse causality (parental atopy) could not be excluded completely. Neonatal exposure to cow's milk protein.
Koplin et al 2010(3)	Australia. 11 to 15 month infants recruited from immunisation 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 months associated with lower risk of IgE mediated egg allergy than introduction after that time.	Data suggests 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 months and above
Du Toit et al 2015(4)	UK. Infants between the age of 4 and 11 months with severe eczema, egg allergy or both.	Not specified. Prevalence of both disorders extremely low in UK.	Prospective interventional study of peanut allergy. Diagnosis of peanut allergy at age 5 years by food challenge.	Introduction of peanuts between the age of 4 – 11 months associated with lower risk of IgE mediated peanut allergy at 5 years than introduction after that time.	Early introduction of peanuts into infants' diets (before 11 months) leads to immune tolerance, preventing allergy in high-risk sensitised and non-sensitised infants.	Lack of a placebo regimen. Exclusion of low risk infants.
Du Toit et al 2016(5)	UK. Infants between the age of 4 and 11 months with severe eczema, egg allergy or both (follow-on study to Du Toit 2015).	Not specified. Prevalence of both disorders extremely low in UK.	Prospective interventional study of peanut allergy. Diagnosis of peanut allergy at age 6 years by food challenge.	Introduction of peanuts between the age of 4 – 11 months associated with lower risk of IgE mediated peanut allergy at 6 years than introduction after that time even 1 year 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 months.	Lack of a placebo regimen. Exclusion of low risk infants.
Perkin et al 2016(6)	UK. Infants aged 3 months.	Not specified. Prevalence of both disorders extremely low in UK.	Prospective interventional study of allergy to peanut, egg, milk, fish, sesame and wheat. Diagnosis of food allergy by food challenge between 1 and 3 years.	Intention to treat analysis did not show efficacy of early introduction of allergenic foods. Per protocol analysis showed lower prevalence of any allergy, peanut and egg allergy in children aged 1-3 years, with early introduction of allergens (3-6 months 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.

Table 2: 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)	Kwa Zulu Natal province, South Africa. Infants aged ≤26 weeks 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 to 4.3%	Non-randomised intervention cohort study to assess the HIV transmission risks and survival associated with infant feeding patterns	In the absence of maternal antiretroviral therapy, breastfed infants who also received solids were significantly more likely to acquire infection than were exclusively breastfed children (Hazard ratio (HR) 10.87, 1.51–78.00, $p=0.018$), as were infants who at 12 weeks received both breastmilk and formula milk (1.82, 0.98–3.36, $p=0.057$).	Promote exclusive breastfeeding for the first six 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	Not specified in paper 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 randomised controlled trials	During the 1 st 6 months of life predominant, breastfeeding increased the risk of all-cause mortality and pneumonia incidence compared with exclusive breastfeeding during the first 6 months (Risk Ratio (RR) 1.48, 1.13-1.92 and 1.79, 1.29- 2.48, respectively); and partial breastfeeding significantly increased the risk of all-cause mortality (RR 2.85, 1.59-5.10) , diarrhoea mortality (4.62, 1.81-11.77), pneumonia mortality (2.49; 1.03-6.04) and diarrhoea incidence (3.04, 1.32-7.00), respectively.	Exclusive breastfeeding protects against childhood morbidity and mortality in the first 6 months of life compared with predominant and partial breastfeeding. Early introduction of solids is not advised.	Data only from 4 countries
Sankar et al 2016(9)	Systematic Review. Studies from Africa (n=6), Latin America (n = 2), South-East Asia (n = 5), Eastern Mediterranean (n = 1) and the Western Pacific (n = 1)	Not specified but many of these settings have high prevalence of malnutrition and HIV.	Secondary analysis of data from 13 studies meeting inclusion criteria	Three studies demonstrated that in the first 6 months of life predominant (PredBF) and partial breastfeeding (ParBF) significantly increased all-cause and infection-related mortality compared with exclusive breastfeeding [RR 1.48 (1.13–1.92) and 2.84 (1.63–4.97), respectively for all-cause mortality and RR 1.7 (1.18–2.45) 3 and 4.56 (2.93–7.11) for infection-related mortality.	The review underscored the importance of optimal breastfeeding practices (exclusive breastfeeding during the first 6 months)	Small number of studies exist; thus only 13 were included in the review

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

