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Practical challenges and considerations for early introduction of potential food allergens for prevention of food allergy

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Abstract: (230 words)

Recent randomized controlled trials aimed at the prevention of food allergy have led to sweeping changes in food allergy prevention guidelines. Emphasis is now on the introduction of potential food allergens, particularly peanut and egg, rather than avoidance. Though guidelines recommend against delaying introduction of other potential allergens there remains little or no evidence of the benefit of their early introduction. Parents and physicians alike report a need for greater guidance and resources on early potential allergen introduction in the complementary feeding period. A thorough understanding of early introduction literature, current prevention

guidelines, and infant nutrition will empower physicians to address patient needs and concerns both when advice is established as effective and where uncertainty remains. We discuss the state of the science, compare recommendations between guidelines, and provide practical options to introduce allergenic foods, alongside other complementary foods, within the first year of life. We include a review of the available literature, including review and suggestions of potential doses of food allergens, and the first published comparison of commercially available products and home-made early introduction foods to help clinicians support their patients. We address the nutritional, dietary and practical considerations of introducing food allergens in the first year of life, while adhering to infant feeding guidelines. Finally, given the limitations of existing guidelines, we review the need for shared decision-making (SDM) between physicians and parents regarding early allergen introduction.

Keywords:

Food allergy

Guidelines

Early introduction

Complementary feeding

Infant nutrition

Prevention

Abbreviations:

- 71 aOR- Adjusted Odds Ratio
- 72 AAAAI- American Academy of Allergy Asthma and Immunology
- 73 AAP- American Academy of Pediatrics
- 74 ASCIA- Australian Society of Clinical Immunology and Allergy
- 75 BSACI- British Society of Allergy and Clinical Immunology
- 76 CF- Complementary foods
- 77 CI- Confidence Interval
- 78 CM- Cow milk
- 79 CMA- Cow milk allergy
- 80 COT- Committee on Toxicity
- 81 CSACI- Canadian Society of Allergy and Clinical Immunology
- 82 DGAC- Dietary Guidelines for Advisory Committee
- 83 EAACI- European Academy of Allergy and Clinical Immunology
- 84 EAT- Enquiring About Tolerance
- 85 HEAP- Hen's Egg Allergy Prevention
- 86 LEAP- Learning Early About Peanut
- 87 NIAID- National Institute of Allergy and Infectious Disease
- 88 PETIT- Prevention of Egg allergy with Tiny amount intake

89 RCT- Randomized Controlled Trial

90 SDM- Shared Decision Making

91 SPADE- Strategy for Prevention of Milk Allergy by Daily Ingestion of Infant Formula in Early

92 Infancy

93 UK- United Kingdom

94 US- United States

95 USD- United States Dollar

96 Word Count- 4554

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Introduction:

Evidence that introduction of peanut in the first year of life prevents peanut allergy has shifted prevention guidelines and clinical practice both in primary care and allergy clinics. Although there are many recommendations about introduction of peanut, less guidance has been provided about introduction of other allergenic foods such as egg despite randomized controlled trials (RCTs) demonstrating benefit of early egg introduction. Furthermore, there are few or no studies to guide the introduction of other potential food allergens. Barriers to early introduction of peanut still exist, with patients and physicians reporting discomfort with feeding peanut containing foods to infants, despite reported awareness of updated guidelines.^{1,2} While gaps exist in our knowledge base, understanding specific ways to introduce potentially allergenic foods as a part of infant complementary feeding may assist clinicians and parents to optimize early introduction of potentially allergenic foods. The time-sensitive nature of food allergy prevention necessitates that the practical aspects early food introduction be addressed.

In this article, we address the real-world aspects of introducing allergenic foods for allergy prevention. We discuss the state of the science, compare recommendations between guidelines and provide practical options to introduce allergenic foods, alongside other complementary foods, within the first year of life. We include the first published comparison of commercially available products and home-made foods for timely introduction of food allergens to help clinicians educate their patients. We address the nutritional and dietary considerations of introducing allergens while adhering to infant feeding guidelines. Finally, given the limitations of existing guidelines, we review the need for shared decision-making (SDM) between physicians and parents regarding early allergen introduction.

What we know: food allergy prevention literature

Multiple prospective RCTs provide evidence that early introduction of peanut and hen's egg decreases the incidence of peanut and egg allergy in infants who are high risk of developing food allergy.³⁻⁸ Studies on the prevention of other food allergens have been less robust, and have shown evidence of safety, but not necessarily efficacy. The EAT trial randomized infants from the general population to an intervention of early introduction of milk, egg, peanut, sesame, fish and wheat beginning at 3 months of age.⁸ Adherence to the protocol was moderate (42.8%) and the ITT analysis indicated a non-statistically significant trend towards prevention of peanut and egg allergy. There was no increased risk of allergy to any of the foods when compared to the "standard" introduction group even with moderate protocol adherence.

The Strategy for Prevention Of Milk Allergy by Daily Ingestion of Infant Formula in Early Infancy (SPADE) study is a RCT by Sakihara et al. that study the effect of daily ingestion of ≥ 10 ml of cow milk (CM) formula plus breastfeeding (N=242) vs use of avoidance of CM while breast feeding using soy formula as needed (N=249) from the ages of 1-2 months old in a general population on rate of cow milk allergy (CMA) at 6 months old.⁹ Participants were able to ingest CM before randomization and the median intake before the study was 80mls per day. CM ingestion challenges done at 6 months found CMA in 2/242 (0.8%) in the cow milk ingestion group and 17/249 (6.8%) in the CM avoidance group (risk ratio 0.12 CI:0.01-0.5 P<0.001) in the ITT analysis. This is the first RCT to demonstrate that early and frequent CM ingestion may be associated with lower rates of CMA with no significant effect on breastfeeding. However, high rates of CMA in the control group and a relatively homogeneous population limit the generalizability of this study. Other prospective observational studies provide a mixed message about whether to introduce CM to prevent CMA.¹⁰⁻¹² Katz et al. showed that introduction of CM between 0-14 days old was associated with a rate of milk anaphylaxis of 0.05% and milk

introduction between 105 and 194 days old had a rate of 1.75% of anaphylaxis to milk.¹¹ With further supportive research, frequent ingestion of low volumes of cow milk in early infancy could potentially be recommended as a strategy to prevent CMA.⁹

In terms of other allergens, the HealthNuts study reported that ingestion of cashew under age 1 (n=140) was associated with no cases of cashew allergy at age 6 years (aOR 0.19, 95% CI, 0.00-1.09; $P = .07$).¹³ There are no available studies on the safety or efficacy of early introduction of other tree nuts, soy, or shellfish.

What is advised? National and International Prevention Guidelines

Guidelines regarding introduction of food allergens have evolved over the last two decades, though differing approaches remain. Initial guidance from the United Kingdom (UK) and the United States (US) recommended avoidance of peanut (UK) and other allergens (US) until 3 years of life in children with familial risk for allergy as a means to prevent allergic disease.^{14,15} In 2008, the revised UK and US recommendations on peanut avoidance,¹⁶ rescinded previous recommendations to delay introduction of peanut in high risk children because the advice was being broadly applied by families even if they had no familial risk of allergy, there was no apparent decrease in the incidence of peanut allergy in the UK from 1998-2008, and they suggested there was little evidence to delay food allergen introduction beyond 4-6 months.¹⁷⁻²⁰ The 2013 American Academy of Asthma, Allergy and Immunology (AAAAI) guidance recommended that in all infants, potentially allergenic foods can be given once a few complementary foods have been tolerated, consistent with the Canadian Society of Allergy and Clinical Immunology.^{21,22} The European Academy of Allergy and Clinical Immunology (EAACI) guidelines (2014) made a neutral statement, not recommending to delay or introduce

potential food allergens in the first year of life for all infants.²³ One commonality among the various current early introduction guidelines is that they suggest that 4 months old is an acceptable age for complementary food introduction reflecting historical norms despite current World Health Organization guidance on age of solid food introduction, suggesting introduction of solid foods at 6 months.²⁴

Following the publication of the Learning Early about Peanut (LEAP) study in 2015⁷ and a number of RCTs on egg and multiple allergen introductions,^{3,4,8,25,26} guidelines around the world adapted. The Australian Society of Clinical Immunology and Allergy (ASCIA) guidelines suggested peanut, cooked egg, wheat and dairy foods be introduced into the diets of all infants in the first year of life without screening.²⁷ The National Institute of Allergy and Infectious Disease (NIAID) guidelines (2017) are more prescriptive and suggest different peanut introduction schedules depending on the degree of risk.²⁸ The NIAID guidelines are the only guidelines that recommend allergy testing before introduction of peanut. The 2017 UK COT report suggests peanut and egg should be treated no differently than other complementary foods.²⁹ The British Society of Allergy and Clinical Immunology (BSACI) guidelines suggest that in the general population, egg then peanut can be introduced as part of the family diet, but in high risk infants introduction between 4-6 months is recommended.³⁰ BSACI is the only current guideline to recommend egg introduction before peanut introduction because egg sensitization seems to occur before peanut.³⁰ The AAP Committee on Nutrition and others actively recommend early introduction of peanut in infant safe forms and do not recommend delaying introduction of any specific food after 4-6 months of age.³¹

Unfortunately, this significant recommendation variability can be confusing for families and clinicians alike. With the increasing evidence that early food allergen introduction may induce tolerance, and recommendations by most guidelines not to delay food allergen introduction, physicians and patients desire guidance on how to introduce potentially allergenic foods as a healthy component in the early infant complementary feeding period.³¹

Therefore, when implementing early introduction of potentially allergenic foods in clinical practice, we suggest clinicians place first priority on supporting the introduction of peanut and egg which have evidence of benefit. The order of egg and peanut introduction should be determined based on national guidelines, cultural practices and individual shared decision making between patients and clinicians. Foods which have been evaluated and have been shown not to increase the risk for allergy (milk, wheat, sesame, fish) could be a second priority. Finally, even in the absence of evidence, the early introduction of foods such as tree nuts, soy and shellfish in high risk children should be addressed with families. (Table 1)^{8,32} This discussion is even more important now that commercial products containing various amounts of proteins from these foods are marketed for allergy prevention. (Table 2a)

Barriers to early introduction

Barriers to introduce food allergens may impede opportunities for food allergy prevention. Greenhawt and colleagues surveyed new and expectant parents and found reluctance to feed peanut around 6 months of age.² A survey by Lai and Sicherer reported parental fear of reaction (36%), choking (11%), and lack of infant-safe forms of peanut (6%).¹ Parents also requested additional physician advice (44%), written information (24%), and allergist access (18%). Despite parental awareness of guidelines, peanut-feeding rate was only 37% in infants >6 months of age. In this same survey, only 60% of physicians provided recommendations consistent with

guidelines at the time of the study.¹ Encouragingly, follow up studies from EarlyNuts showed that the rate of peanut introduction in an unscreened Australian population increased from 28.4% during 2007-2011 to 88.6% in 2018.³³ Even when enrolled in clinical trials continued adherence to protocols remains a challenge and adherence is different based on the food. In the largest early introduction trial to date, PreventADALL found that adherence at 26 weeks to introduction of potentially allergenic foods between 13-18 weeks old was 35% for peanut (44% who started peanut), 43% for cow milk (63% who started milk), 44% for wheat (66% who started wheat), and 24% for egg (43% of those who started egg).³⁴ Altogether, data suggests that physicians and families require reassurance and guidance on the practical aspects of early peanut introduction and that written materials may assist implementation. (Table 1)

The Enquiring About Tolerance (EAT) study group also evaluated barriers to early food allergen introduction; nonadherence was associated with three enrollment factors: older maternal age (≥ 33 years old), non-white ethnicity and lower maternal quality of life at enrollment.³⁵ Post-enrollment, parent reporting of infant feeding difficulties by 4 months of age was associated with nonadherence. However, feeding difficulty was reported more frequently in the early introduction group. Because the reported rate of feeding difficulty was similar from 4 months through 12 months of age, the feeding difficulty is likely to have been conflated with the stringent target of allergen consumption, rather than representing developmental issues with consumption.

A qualitative analysis of the parental reporting of problems feeding their infant the allergenic foods identified three main themes: infant refusal (swallowing issues, dislike of the taste and infant illness), concerns about reactions (digestive or skin issues and actual allergy), and

practical problems (lifestyle convenience and food preparation issues).³⁶ Sesame and egg predominated in the parent reporting of feeding problems.

While noted barriers exist, there is patient and clinician interest in safe and practical early introduction of a variety of potential food allergens. In the absence of evidence, food manufacturers are marketing early feeding products containing various potential allergens (Table 2a). The interest in early feeding of multiple potential allergens is outpacing the ability for RCTs to provide evidence for the efficacy, safety, timing, dose and forms of these allergenic foods. This evidence gap leaves many practical questions unanswered for allergists, pediatricians and families.

What form and how much to feed? Clues from the literature

Reviewing previous early introduction studies gives clinicians options for specific recommendations on safe forms and dosing of a food that can be used during early infant feeding. The LEAP study recommended peanut puff snack or smooth diluted peanut butter for younger children and supplied peanut recipes for older children. The participants in LEAP consumed a median peanut protein intake of 7.5 g/week (goal dose was 6g/week, approximately 6 teaspoons) beginning between 4-10 months of age and continuing until 60 months old.⁷ Additionally, early introduction in this form or amount did not affect growth, nutrition or breastfeeding duration.³⁷ To prevent choking in infants thinning of peanut butter with water, milk, or pureed fruit has been recommended. This dilution may be necessary until children are able to safely eat foods with the consistency of peanut butter spread thin which can be after 12 months of age or based on individual developmental abilities.³⁸

The EAT trial attempted introduction of multiple foods in the early complementary feeding period including boiled egg, peanut butter, sesame paste, cow's milk yogurt, white fish and wheat-based cereal.⁸ EAT aimed to introduce at least 2 g of protein from multiple foods, eaten twice per week. Together, the LEAP and EAT studies provide information on effective dosing of peanut for allergy prevention. Infant-safe forms of peanut, in the amount of 2 teaspoons, 3x per week (6 grams peanut protein) is the dose recommended by the NIAID based on the LEAP protocol. A smaller weekly dose is likely effective (4 grams peanut protein per week was used in the EAT trial). Some guidelines simply recommend regular intake.³⁹

Many forms of egg have been studied for early introduction. EAT is the only trial which used regular unprocessed boiled egg at a dose of 1 small (less than 53g) egg per week. All other early egg introduction trials used various forms of egg such as: egg white vs. whole egg, and boiled vs. pasteurized raw.^{3,4,40} These trials used a wide range of doses per serving and frequencies of ingestion. The PETIT Trial study evaluated a dual intervention of aggressive management of eczema and introduction of tiny doses of egg.⁴ The highest daily dose was 0.075 g egg white protein powder, equivalent to two percent of a 50g egg and reported the greatest reduction of egg allergy in their ITT analysis (9% early egg-group vs 38% placebo-group) (risk ratio 0.22; 95% CI 0.081-0.61, p=0.0012) at 12 months.⁴ It is possible that both interventions contributed to prevention of egg allergy. In contrast, the HEAP trial, which used 2.5g of powdered pasteurized raw egg white protein (approximately 2/3 of a large egg white) eaten three times per week, did not show evidence of allergy prevention and found high rates of reactions on first exposure to the pasteurized raw egg.³ The EAT study found 2g whole egg protein (1.2g egg white protein) eaten once per week had a protective effect in the group that followed the early introduction advice (standard 5.5%, early 1.4%, p=0.009).⁸ Using predictive probability plots in this study, it was

estimated that 4 g of well cooked egg protein (equivalent to 2g of egg white protein) was associated with prevention of egg allergy. These trials also found that pasteurized raw whole egg appears to be less well tolerated with more allergic reactions.⁴⁰ The exact dose and type of egg to prevent egg allergy requires more research. It is clear that raw egg and large doses of egg inconsistent with infant nutrition needs are not required.

Early introduction of other foods in the EAT trial included a 40-60g dose of cow milk yogurt, three teaspoons of sesame paste (1 tablespoon), 25g of white fish and two wheat based cereal biscuits eaten once per week; all equivalent to approximately 2 g protein to be eaten twice per week.⁸

The SPADE study used ≥ 10 ml of CM formula daily for two months starting at 1 month old and found decreased rates of CMA at 6 months.⁹

It is not possible to say if early introduction of fish, sesame or wheat prevents the development of allergy to these foods although it does not in most instances appear to increase the risk.

Complementary Feeding- Potential Allergens Fit!

During the initial complementary feeding period, serving single ingredient foods, one at a time is recommended to observe for symptoms of allergy. Once foods are tolerated they can be combined. There is no evidence guiding how long a food must be fed prior to moving on to the next “new” food, however one new food per day is likely reasonable, especially in terms of the food allergens.⁴¹ Prolonging time between new foods may negatively affect diet diversity, which has been shown to affect food allergy outcomes.^{42,43} Roduit et al. indicated that children with a more diverse early diet had a lower prevalence of food allergy.⁴² This finding was supported by Venter et al. who demonstrated that increased diversity of both food and food allergen intake in

the first year of life was associated with a lower prevalence of food allergy up to 10 years of age.⁴³ For each additional food given by 6 months, the odds of food allergy over 10 years was reduced by 11%. For each additional allergen consumed by 12 months, the odds of food allergy over 10 years was reduced by 33%.

From 6 months of age, it is difficult for infants to meet nutritional needs from breast milk alone, and breastfeeding should continue alongside introduction of nutrient-dense, complementary foods (CF). Based on the 2020 Dietary Guidelines Advisory Committee report (DGAC), fortified infant cereal is an important contribution to meet iron and zinc needs and 0.5 ounces (15g) should be included in the breastfed infant diet.⁴⁴ The DGAC recommends caloric intake ranges from CF based on a percentage of total energy intake. Consumption from CF at 6-9 months of age is 120- 280 kcal/day (20-35% of total energy intake), 56 kcal of which come from a fortified grain for breastfed infants; the remaining CF “budget” is 64-224 calories/day. Therefore, after the introduction of infant grain, other CF in this age group should come from a variety of nutrient-rich foods to help meet the nutritional needs for iron, zinc, potassium, and choline, all of which are nutrients with gaps in the breastfed infant diet. Formula fed infants taking sufficient formula do not benefit from fortified infant cereal to meet iron and zinc requirements and a whole grain is recommended instead to avoid excess dietary iron and zinc intake.⁴⁵ Food group patterns have not been established in the 6-12-month age group, however, recommended infant serving sizes of food groups to meet nutritional goals are listed in Supplement Table S1. Likewise, there are no recommended food group patterns for 4-6-month infant feeding but introducing foods in the amounts found to prevent food allergy (particularly in a high-risk population) are listed in Table 1. The DGAC did not calculate energy levels from CF for 4-6 months because it targeted 6 months as the starting age for CF. Total energy

requirements are lower at 4-6 months than at 6-9 months. If one assumes an average energy need for infants of approximately 600 kcal at 4-6 months, then up to 100 kcal (<20%) from CF is reasonable leaving ample opportunity for early introductions of allergenic foods e.g., 60 kcal from peanut butter or alternatively 20 kcal from peanut flour or powder (2 g protein/2 teaspoons) 26 kcal egg (2 g egg protein/ 1/3 egg); 2-3 times per week. There is no specific need to add a fortified grain to the diet prior to 6 months of age.⁴⁴

The goals of early infant feeding are to introduce foods of varying flavors and textures to encourage future food preference,⁴⁶ and to provide nutrition in a balanced and proportional manner for growth and development. (Supplementary Table S1) The goal and challenge of early complementary feeding of foods thought to be allergenic is to offer these foods without exceeding the needs for calories in the CF period and without displacing other nutrient dense foods such as fruits, vegetables, meats, and whole grain-based foods.

There are a range of commercial products currently available for early allergen introduction. (Table 2a) These products differ by the allergen they contain, the dose of the allergen and the degree of heating of the product. A blinded RCT suggested the tolerability and acceptability of a commercial product containing 13 allergens, although efficacy was not evaluated.⁴⁷ Furthermore, the product protein levels were significantly smaller than doses currently recommended (less than 1 g of total protein) and patients were excluded if they had parent-reported severe eczema or pre-existing food allergy. The nutrient content of the products differ amongst each other and when compared to conventional foods. (Table 2a) Conventional foods (peanut butter, eggs, yogurt) can be purchased at lower cost in the local market and prepared for infant safe feeding. (Table 2b, Table 3) A homemade recipe for mixed tree nut butter is available in the online supplement S3.

Timing of early introduction plays a role in the choice between conventional and commercially available early introduction products. The average age of peanut introduction in LEAP was 6 months old and most children above 6 months old are developmentally ready to introduce various conventionally available forms of peanut, egg, and other potentially allergenic foods.⁷ Therefore after 6 months, there may be limited benefit for most commercially available early introduction products.

Once early introduction has been initiated it then requires maintenance. Most studies of early introduction employed intensive monitoring and encouragement. For example, parents (mostly mothers) were contacted over 100 times over the five years of early peanut introduction.⁷ Continuation rates and frequency of ingestion of these foods in the real world is unknown and likely requires more support from clinicians than is typically offered or is even available. Specialized dietitians were heavily utilized during food-prevention studies and may complement efforts supporting early introduction.

As cited, risk factors for lower adherence to early introduction protocols from the EAT or LEAP studies include non-white ethnicity, older maternal age, and lower maternal quality of life.^{35,36} Food allergy rates are significantly higher in non-white infants making the challenges of early introduction even more relevant in this population.⁴⁸ Patients with these risk factors should be identified and offered support for initiation and continuation of early food introduction. This can involve more frequent monitoring and advice from their primary care specialists and/or dietitians. It also requires identifying affordable sources of potential allergens. Egg and peanut will generally be cheaper than sesame, fish, and tree nuts. This also makes the cost of commercially available products an important factor when implementing early introduction of food.

The decision to introduce allergenic foods is complex and families must consider the pros and cons of commercial products versus conventional food. As always, the family's needs and preferences need to be a part of the decision making process. There are a range of commercial products currently available for early food allergen introduction. In order to collaborate with families in shared decision making we suggest that the allergist/dietitian take the following features into account: Cost, Convenience, Additional Ingredients, Nutritional Composition, Dose of allergen, and Degree of Heating. (Table 3) Clinicians should be comfortable guiding the patient through this decision making process.

Shared Decision Making

Shared decision making (SDM) involves a collaborative dialogue between clinicians and patients to reach decisions based on evidence and personal values. Optimization of early food introduction can only be possible if and when a family is willing and able to introduce these foods. As part of the therapeutic relationship with patients and parents, clinicians must ensure that the values and the preferences of patients are incorporated with current scientific understanding to guide the medical decision-making process.⁴⁹ This alignment is especially important when: clinical guidelines change or differ substantially between countries; when there may be significant anxiety surrounding the available approaches; when there is some degree of uncertainty or disagreement regarding the best approach; or there is a lack of practical guidance. Early introduction of foods encompasses all these barriers. Decision aids have been used to help guide decisions about therapies when there is no easy answer. A decision aid for early introduction could be a useful tool however there are currently none available. Therefore, an allied approach using SDM yields the optimal outcome by ensuring that the needs of the patient

remain a priority and that therapeutic decisions incorporate both medical understanding and patient expectations.⁵⁰

Understanding that many food-introduction guideline recommendations have drastically changed from full avoidance to early introduction, and that guidelines will continue to adapt allows clinicians to empathize with patients who distrust new recommendations. Normalizing the initial reluctance of clinicians and patients to incorporate new changes can start an effective conversation about options. Discussion may include addressing mixed messages received from primary care clinicians (or other sources) which may differ from specialist suggestions.⁵¹ The ability to have an open and honest dialogue about this variability in guidance and lack of certainty is crucial in the SDM model.

Early introduction of foods is further complicated when a patient has already developed a food allergy. While the probability of coexistence of other food allergies may be low at a young age, the question of how best to support families with introduction of similar allergens has not yet been formally addressed.⁵² As a result, families are left with few evidence based choices: avoid other allergenic foods; introduce at home without testing; test and then introduce or avoid; or introduce in-office with medical supervision. If families elect to test prior to introduction, careful discussion about the potential for false-positive (and false-negative) testing must occur. In addition, planning how to introduce foods based on testing results should be reviewed prior to any diagnostic evaluation.

Because the efficacy of early food introduction is time sensitive, these challenging conversations may be most effective before complementary food is introduced. The dialogue involved in SDM can take significant time to understand families' perspectives, to discuss limitations of available diagnostic testing and the potential need for oral challenges.⁵²⁻⁵⁴ A significant and practical

barrier to early food introduction is the lack of timely access to clinicians that are knowledgeable and capable of having these detailed conversations, and there is limited access to clinicians who are willing and able to perform food challenges when needed.⁵³ Unfortunately, a recent Canadian survey suggested significant inconsistency in advice regarding introduction of allergenic foods amongst allergists, pediatricians and family practitioners.⁵¹ Ensuring that primary care clinicians are suitably trained and able to have these evidence-based SDM discussions remains the responsibility of allergists and policymakers through education and practical, user-friendly guidelines. The allocation of clinician and allied health experts such as allergy trained dietitians, and the establishment of a triage priority for patients who may benefit from early introduction may help to direct resources more efficiently.

As clinicians we should encourage at-risk infants to be exposed to potentially allergenic foods in a safe manner. In order to prevent various food allergies in as many patients as possible, clinicians should use a SDM approach to incorporate patient desires when creating specific early introduction approaches with families.

Conclusion

As guidelines continue to adapt to developing literature, it is prudent for clinicians to understand that eating certain potential food allergens should be a part of early complementary feeding and other potential food allergens can be part of complementary feeding. Neglecting to engage in discussions around feeding potentially allergenic foods may risk missing the window of opportunity of early introduction. As we venture into a new era of “let the babies eat,” clinicians should be able to discuss available options for introducing home-made or commercially available products containing potential allergens and how these foods might fit in the infant diet. Educational materials will aid clinicians in SDM and provide families with written guidance as

they navigate complementary feeding. A thorough understanding of the early introduction literature, current prevention guidelines, and complementary infant nutrition will empower physicians to address patient needs and concerns both when advice is established as effective and where uncertainty remains.

References

1. Lai M, Sicherer SH. Pediatricians underestimate parent receptiveness to early peanut introduction. *Ann Allergy Asthma Immunol.* 2019;122(6):647-9.
2. Greenhawt M, Chan ES, Fleischer DM, Hicks A, Wilson R, Shaker M, et al. Caregiver and expecting caregiver support for early peanut introduction guidelines. *Ann Allergy Asthma Immunol.* 2018;120(6):620-5.
3. Bellach J, Schwarz V, Ahrens B, Trendelenburg V, Aksunger O, Kalb B, et al. Randomized placebo-controlled trial of hen's egg consumption for primary prevention in infants. *J Allergy Clin Immunol.* 2017;139(5):1591-9 e2.
4. Natsume O, Kabashima S, Nakazato J, Yamamoto-Hanada K, Narita M, Kondo M, et al. Two-step egg introduction for prevention of egg allergy in high-risk infants with eczema (PETIT): a randomised, double-blind, placebo-controlled trial. *Lancet.* 2017;389(10066):276-86.
5. Palmer DJ, Metcalfe J, Makrides M, Gold MS, Quinn P, West CE, et al. Early regular egg exposure in infants with eczema: A randomized controlled trial. *J Allergy Clin Immunol.* 2013;132(2):387-92.e1.
6. Tan JWL, Valerio C, Barnes EH, Turner PJ, Van Asperen PA, Kakakios AM, et al. A randomized trial of egg introduction from 4 months of age in infants at risk for egg allergy. *Journal of Allergy and Clinical Immunology.* 2017;139(5):1621-1628.
7. Du Toit G, Roberts G, Sayre PH, Bahnson HT, Radulovic S, Santos AF, et al. Randomized Trial of Peanut Consumption in Infants at Risk for Peanut Allergy. *N Eng J Med.* 2015;372:803-813.
8. Perkin MR, Logan K, Tseng A, Raji B, Ayis S, Peacock J, et al. Randomized Trial of Introduction of Allergenic Foods in Breast-Fed Infants. *N Engl J Med.* 2016;374(18):1733-43.

9. Sakihara T, Otsuji K, Arakaki Y, Hamada K, Sugiura S, Ito K. Randomized trial of early infant formula introduction to prevent cow's milk allergy. *J Allergy Clin Immunol*. 2020;Online ahead of print.
10. Peters RL, Koplin JJ, Dharmage SC, Tang MLK, McWilliam VL, Gurrin LC, et al. Early Exposure to Cow's Milk Protein Is Associated with a Reduced Risk of Cow's Milk Allergic Outcomes. *J Allergy Clin Immunol Pract*. 2019;7(2):462-470.
11. Katz Y, Rajuan N, Goldberg MR, Eisenberg E, Heyman E, Cohen A, et al. Early exposure to cow's milk protein is protective against IgE-mediated cow's milk protein allergy. *J of All Clin Immunol*. 2010;126(1):77-82.
12. Urashima M, Mezawa H, Okuyama M, Urashima T, Hirano D, Gocho N, et al. Primary Prevention of Cow's Milk Sensitization and Food Allergy by Avoiding Supplementation With Cow's Milk Formula at Birth: A Randomized Clinical Trial. *JAMA Pediatr*. 2019;173(12):1137-1145.
13. Peters RL, Barret DY, Soriano VX, McWilliam V, Lowe AJ, Ponsonby AL, et al. No cashew allergy in infants introduced to cashew by age 1 year. *J Allergy Clin Immunol*. 2020;Online ahead of print.
14. HF W, Kingdom. CoTU. Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment. *Peanut Allergy*. London: Department of Health. 1998.
15. American Academy of Pediatrics. Committee on Nutrition. Hypoallergenic infant formulas. *Pediatrics*. 2000;106(2 Pt 1):346-9.
16. Toxicity Co. COT statement on the review of the 1998 COT recommendations on peanut avoidance 2008 [cited 2020. Available from: <https://cot.food.gov.uk/cotstatements/cotstatementsyrs/cotstatements2008/cot200807peanut>.

17. Turke J, Venter C, Dean T. Maternal experiences of peanut avoidance during pregnancy/lactation: an in-depth qualitative study. *Pediatr Allergy Immunol*. 2005;16(6):512-8.
18. Dean T, Venter C, Pereira B, Grundy J, Clayton CB, Higgins B. Government advice on peanut avoidance during pregnancy--is it followed correctly and what is the impact on sensitization? *J Hum Nutr Diet*. 2007;20(2):95-9.
19. Venter C, Hasan Arshad S, Grundy J, Pereira B, Bernie Clayton C, Voigt K, et al. Time trends in the prevalence of peanut allergy: three cohorts of children from the same geographical location in the UK. *Allergy*. 2010;65(1):103-8.
20. Greer FR, Sicherer SH, Burks AW, American Academy of Pediatrics Committee on N, American Academy of Pediatrics Section on A, Immunology. Effects of early nutritional interventions on the development of atopic disease in infants and children: the role of maternal dietary restriction, breastfeeding, timing of introduction of complementary foods, and hydrolyzed formulas. *Pediatrics*. 2008;121(1):183-91.
21. Fleischer DM, Spergel JM, Assa'ad AH, Pongracic JA. Primary prevention of allergic disease through nutritional interventions. *J Allergy Clin Immunol Pract*. 2013;1(1):29-36.
22. Chan ES, Cummings C, Atkinson A, Chad Z, Francoeur MJ, Kirste L, et al. Dietary exposures and allergy prevention in high-risk infants: a joint position statement of the Canadian Society of Allergy and Clinical Immunology and the Canadian Paediatric Society. *Allergy Asthma Clin Immunology*. 2014;10(1):45.
23. Muraro A, Halken S, Arshad SH, Beyer K, Dubois AE, Du Toit G, et al. EAACI food allergy and anaphylaxis guidelines. Primary prevention of food allergy. *Allergy*. 2014;69(5):590-601.

24. Kramer MS, Kakuma R. Optimal duration of exclusive breastfeeding. *Cochrane Database Syst Rev.* 2002(1):CD003517.
25. Hua MC, Yao TC, Chen CC, Tsai MH, Liao SL, Lai SH, et al. Introduction of various allergenic foods during infancy reduces risk of IgE sensitization at 12 months of age: a birth cohort study. *Pediatr Res.* 2017;82(5):733-40.
26. Wei-Liang Tan J, Valerio C, Barnes EH, Turner PJ, Van Asperen PA, Kakakios AM, et al. A randomized trial of egg introduction from 4 months of age in infants at risk for egg allergy. *J Allergy Clin Immunol.* 2017;139(5):1621-1628.
27. Netting MJ, Campbell DE, Koplin JJ, Beck KM, McWilliam V, Dharmage SC, et al. An Australian Consensus on Infant Feeding Guidelines to Prevent Food Allergy: Outcomes From the Australian Infant Feeding Summit. *J Allergy Clin Immunol Pract.* 2017;5(6):1617-1624.
28. Togias A, Cooper SF, Acebal ML, Assa'ad A, Baker JR, Jr., Beck LA, et al. Addendum guidelines for the prevention of peanut allergy in the United States: Report of the National Institute of Allergy and Infectious Diseases-sponsored expert panel. *J Allergy Clin Immunol.* 2017;139(1):29-44.
29. Assessing the health benefits and risks of the introduction of peanut and hen's egg into the infant diet before six months of age in the UK: A Joint Statement from the Scientific Advisory Committee on Nutrition and the committee on Toxicity of Chemicals in food, Consumer products and the Environment. In: Scientific Advisory Committee on Nutrition CoT, editor. 2017. p. 1-22.
30. Turner PJ, Feeney M, Meyer R, Perkin MR, Fox AT. Implementing primary prevention of food allergy in infants: New BSACI guidance published. *Clin Exp Allergy.* 2018;48(8):912-915.

31. Greer FR, Sicherer SH, Burks AW, Committee On N, Section On A, Immunology. The Effects of Early Nutritional Interventions on the Development of Atopic Disease in Infants and Children: The Role of Maternal Dietary Restriction, Breastfeeding, Hydrolyzed Formulas, and Timing of Introduction of Allergenic Complementary Foods. *Pediatrics*. 2019;143(4):1-11.
32. FDA. FDA Acknowledges Qualified Health Claim Linking Early Peanut Introduction and Reduced Risk of Developing Peanut Allergy Washington, DC2017 [Available from: <https://www.fda.gov/food/cfsan-constituent-updates/fda-acknowledges-qualified-health-claim-linking-early-peanut-introduction-and-reduced-risk>.
33. Soriano VX, Peters RL, Ponsonby A, Dharmage SC, Perrett KP, Field MJ, et al. Earlier ingestion of peanut following changes to infant feeding guidelines: The EarlyNuts Study. *J Allergy Clin Immunol* 2019;144(5):1327-1335.
34. Skjerven HO, Reh binder EM, Vettukattil R, LeBlanc M, Granum B, Haugen G, et al. Skin emollient and early complementary feeding to prevent infant atopic dermatitis (PreventADALL): a factorial multicenter, cluster-randomized trial. *Lancet*. 2020;395(10228):951-961.
35. Perkin MR, Bahnson HT, Logan K, Marrs T, Radulovic S, Knibb R, et al. Factors influencing adherence in a trial of early introduction of allergenic food. *J Allergy Clin Immunol*. 2019;144(6):1595-1605.
36. Voorheis P, Bell S, Cornelsen L, Quaife M, Logan K, Marrs T, et al. Challenges experienced with early introduction and sustained consumption of allergenic foods in the Enquiring About Tolerance (EAT) study: A qualitative analysis. *J Allergy Clin Immunol*. 2019;144(6):1615-1623.

37. Feeney M, Du Toit G, Roberts G, Sayre PH, Lawson K, Bahnson HT, et al. Impact of peanut consumption in the LEAP Study: Feasibility, growth, and nutrition. *J Allergy Clin Immunol*. 2016;138(4):1108-1118.
38. Choking Hazards: Centers for Disease Control and Prevention; 3/30/2020 [<https://www.cdc.gov/nutrition/infantandtoddlernutrition/foods-and-drinks/choking-hazards.html>]. Last Accessed 10/5/2020.
39. Joshi PA, Smith J, Vale S, Campbell DE. The Australasian Society of Clinical Immunology and Allergy infant feeding for allergy prevention guidelines. *Medical J Aust*. 2019;210(2):89-93.
40. Palmer DJ, Sullivan TR, Gold MS, Prescott SL, Makrides M. Randomized controlled trial of early regular egg intake to prevent egg allergy. *J Allergy Clin Immunol*. 2017;139(5):1600-1607.
41. Samady W, Campbell E, Aktas ON, Jiang J, Bozen A, Fierstein JL, et al. Recommendations on Complementary Food Introduction Among Pediatric Practitioners. *JAMA Netw Open*. 2020;3(8):e2013070.
42. Roduit C, Frei R, Depner M, Schaub B, Loss G, Genuneit J, et al. Increased food diversity in the first year of life is inversely associated with allergic diseases. *J Allergy Clin Immunol*. 2014;133(4):1056-1064.
43. Venter C, Maslin K, Holloway JW, Silveira LJ, Fleischer DM, Dean T, et al. Different Measures of Diet Diversity During Infancy and the Association with Childhood Food Allergy in a UK Birth Cohort Study. *J Allergy Clin Immunol Pract*. 2020;8(6):2017-2026.
44. Scientific Report of the 2020 Dietary Guidelines Advisory Committee Advisory Report to the Secretary of Agriculture and Secretary of Health and Human Services.

- 598 <https://www.dietaryguidelines.gov/sites/default/files/2020->
599 [07/ScientificReport_of_the_2020DietaryGuidelinesAdvisoryCommittee_first-print.pdf](https://www.dietaryguidelines.gov/sites/default/files/2020-07/ScientificReport_of_the_2020DietaryGuidelinesAdvisoryCommittee_first-print.pdf) First
600 Print: July 2020; Last access: 9/29/2020
- 601 45. Dube K, Schwartz J, Mueller MJ, Kalhoff H, Kersting M. Iron intake and iron status in
602 breastfed infants during the first year of life. *Clin Nutr.* 2010;29(6):773-778.
- 603 46. Maier A, Chabanet C, Schaal B, Leathwood P, Issanchou S. Food-related sensory
604 experience from birth through weaning: contrasted patterns in two nearby European regions.
605 *Appetite.* 2007;49(2):429-440.
- 606 47. Holl JL, Bilaver LA, Finn DJ, Savio K. A randomized trial of the acceptability of a daily
607 multi-allergen food supplement for infants. *Pediatr Allergy Immunol.* 2020;31(4):418-20.
- 608 48. Keet CA, Savage JH, Seopaul S, Peng RD, Wood RA, Matsui EC. Temporal trends and
609 racial/ethnic disparity in self-reported pediatric food allergy in the United States. *Ann Allergy*
610 *Asthma Immunol.* 2014;112(3):222-229.
- 611 49. Anagnostou A, Hourihane JO, Greenhawt M. The Role of Shared Decision Making in
612 Pediatric Food Allergy Management. *J Allergy Clin Immunol Pract.* 2020;8(1):46-51.
- 613 50. Blaiss MS, Steven GC, Bender B, Bukstein DA, Meltzer EO, Winders T. Shared decision
614 making for the allergist. *Ann Allergy Asthma Immunol.* 2019;122(5):463-470.
- 615 51. Abrams EM, Singer AG, Soller L, Chan ES. Knowledge gaps and barriers to early peanut
616 introduction among allergists, pediatricians, and family physicians. *J Allergy Clin Immunol*
617 *Pract.* 2019;7(2):681-684.
- 618 52. Schroer B, Bjelac J. Moving Past "Avoid All Nuts": Individualizing Management of
619 Children with Peanut/Tree Nut Allergies. *Immunol Allergy Clin North Am.* 2019;39(4):495-506.

- 620 53. Abrams EM, Soller L, Singer AG, Fleischer DM, Greenhawt M, Chan ES. Comparison
621 of practice patterns among Canadian allergists before and after NIAID guideline
622 recommendations. *J Allergy Clin Immunol.* 2019;7(8):2901-2903.
- 623 54. Pieterse AH, Stiggelbout AM, Montori VM. Shared Decision Making and the Importance
624 of Time. *JAMA.* 2019;322(1):25-26.

625 **Table 1- Including potential allergens for allergy prevention and/or healthy infant feeding during the first year of life**

Food	Choose healthy infant foods*	How much/how often As part of the infant's complementary diet
BENEFICIAL for prevention When developmentally ready** around 6 months of age or between 4-6 months of age if advised by your doctor due to high risk of allergy (severe eczema or egg allergy)***		
Peanut^	Choose peanut flour or thinned peanut butter that has no added ingredients (salt, sugar, oils) for healthier options! Peanut butter should be thinned with breastmilk, water or formula or mixed into a pureed food e.g., 2 teaspoons of peanut butter mixed with 2-3 teaspoons liquid.	About 1-2 teaspoons peanut butter/powder per serving, served 2-3 times per week as tolerated
BENEFICIAL for prevention but effective dose requires further research When developmentally ready after 4-6 months of age**		
Egg	Serve <u>well-cooked</u> egg mashed with pureed foods or chopped and served as finger food.	About 1/3 of a well-cooked egg, 2-3 times per week
HAVE NOT BEEN STUDIED SUFFICIENTLY to know if early introduction decreases risk of allergy therefore doses are based on healthy feeding# There is currently no evidence of benefit to delay introduction of highly allergenic foods after 4-6 months of age and developmentally ready**		
Wheat	Infant wheat cereals (iron-fortified for the breastfed infant); whole wheat toast, pasta or crackers for older infants	½-1 ounce total grains per day. ½ ounce wheat serving includes: ¼ cup fortified infant wheat cereal; ¼ cup pasta, ½ slice bread
Milk	Plain, full-fat yogurt can be mixed into pureed fruit or vegetable; cow's milk should not substitute for breast milk or infant formula	2-4 fluid ounces per day
Sesame^	Tahini is sesame paste typically served as an ingredient in hummus or as tahini dipping sauce for finger foods like vegetables (blended with water, lemon juice, olive oil, and herbs for flavoring).	> or = ½ ounce seeds/any nuts per week (or 3 teaspoons)
Seafood	Low mercury finfish https://www.fda.gov/media/102331/download	1 ounce per serving, 3 times per week (See FDA link for frequency and type of fish)
HAVE NOT BEEN STUDIED to know if early introduction decreases allergy risk therefore doses are based on healthy feeding# There is currently no evidence of benefit to delay introduction of highly allergenic foods after 4-6 months of age and developmentally ready**		
Tree nuts^	Smooth, thinned nut butters e.g., almond, cashew, hazelnut, pistachio, walnut, pecan	> or = ½ ounce seeds/any nut per week (or 3 teaspoons)
Soy	Soft tofu	2 Tablespoons per serving

* When beginning complementary feeding, offer single ingredient foods one at a time initially to determine tolerance.
There is no prescribed number of days or feedings required to determine tolerance but we recommend only one new food per meal.

**How do I know if my infant is developmentally ready? Here are some signs:

- Holds head upright
- Closes mouth around a spoon can open mouth and lean forward to accept a spoon
- Can sit with some assistance.

Offer your baby 1-2 foods prior to offering potentially allergenic foods to ensure they are developmentally ready to eat complementary foods.

***For most infants with severe eczema and/or egg allergy who are already eating solid foods, introducing foods containing ground peanuts between 4 and 10 months of age and continuing consumption may reduce the risk of developing peanut allergy by 5 years of age. The FDA has determined, however, that the evidence supporting this claim is limited to one study. If your infant has severe eczema and/or egg allergy, check with your infant's healthcare provider before feeding foods containing ground peanuts.³²

Infant feeding

- Protein foods, modified for texture, such as peanut, tree nuts, egg, sesame, fish, and soy can be fed as healthy additions in the infant diet within this recommended framework.
- We recommend introducing potential allergenic foods early and feeding them regularly rather than a prescribed amount as long as it is within the context of healthy infant feeding.
- See Online Supplement S1 for further infant feeding guidance.

^ Peanut and Tree nuts and Sesame

- Peanut, tree nuts and sesame are protein foods with higher fat and calorie content therefore, a smaller serving size is more appropriate.
- Balance these higher fat/protein foods with lower fat foods such as fish, soy, and other proteins not considered highly allergenic such as lean meats, poultry, legumes, etc.
- Doses for tree nut prevention are not known.
- It may not fit within healthy infant feeding regimens to aim for 1-2 teaspoons of each tree nut per week.
- See mixed nut butter recipe in online Supplement S2.

Goal doses of food protein per week from EAT study- 2 g of each allergenic food protein twice each week (4 g of allergen protein per food per week). The full weekly amount for the allergenic foods consisted of 2 small 40- to 60-g portions of cow's milk yogurt, 3 rounded teaspoons of peanut butter, 1 small hard-boiled egg (<53 g), 3 rounded teaspoons of sesame paste, 25 g of whitefish, and 2 wheat-based cereal biscuits (e.g. Weetabix).⁸

662 Table 2 a. Early Allergen Introduction: Commercial Products

Product	Recommended Weekly Dose (maintenance)	Allergens: Type and Protein Dose	Form	Ingredients	Instructions	Cost per 4 weeks (USD)	Nutrition/Serving Peanut Products
Hello, Peanut!	Up to 3g peanut protein	Peanut: <u>Introduction Packets:</u> Gradually increasing dose <u>Maintenance Packets:</u> 1 gram/packet	Powder	Organic blend of peanut and sprouted oat flakes	<u>Day 1-7 (Introduction):</u> Mix 1 packet into baby food daily. <u>Days 8+ (Maintenance):</u> Mix 1 packet into baby food up to 3x per week.	Introduction Kit: \$25 Maintenance Kit: \$20 28 day cost 3x/week= \$30 Combination Kit: \$40	10 calories 1 g protein 2 g carbohydrate 0 g fat 0 mg sodium 0g added sugar
Lil Mixins	4-6 g Egg white protein (2 g egg white protein, 2-3 times) 6 g peanut protein (2 g peanut protein, 3 times) 6 g Tree nut protein-mixed (2 g mixed tree nut powder, 3 times)	Egg white: 2 grams in 2 scoops (5g) Peanut: 2 grams in 2 scoops (5g) Tree nut: (Almond, Pistachio, Hazelnut, Walnut): 2 grams mixed tree nut protein in 2 scoops (5g)	Powder	<u>Egg:</u> Baked egg whites and tapioca starch <u>Peanut:</u> Organic ground peanuts <u>Tree nut:</u> Almonds, walnuts, hazelnuts, pistachios	Add 2 scoops (5g) of Peanut Powder Mix into any baby food. Mix well to blend into food.	<u>Egg:</u> Single Serve 1 month \$16.66 240g Jar 1 month = \$8.74 <u>Peanut:</u> Single Serve 1 month \$16.66 240g Jar 1 month = \$8.74 <u>Tree nut:</u> Single Serve 1 month \$16.66 240g Jar 1 month = \$8.74	<u>Egg</u> 20 calories 2 g protein Fat content not available 30 mg sodium 0 g added sugar <u>Peanut</u> 20 kcal 2 g protein 0.5 g fat Sodium content not available 2 g carbohydrate 0 g added sugar <u>Tree nuts</u> 20 calories 2 g protein Fat content not available 30 mg sodium 3 g carbohydrate 0 g added sugar
MightyMe	6 g Peanut protein (1 full pouch)	Peanut: 1 gram per serving	Puff; Melt-able Solid	Organic Rice Flour, Organic ground peanuts, Organic Peanut Oil, Sea Salt, Calcium Carbonate	1 pouch per week	\$17.60 per month	30 calories 1 g protein 1.5g fat 20 mg sodium 3 g carbohydrate 0 g added sugar
Ready, Set, Food!	3 g Milk protein 0.88 g Egg protein 3 g Peanut protein	Milk: 0.43 grams per maintenance packet Egg White: 0.125 grams per maintenance packet Peanut: 0.43 grams per maintenance packet	Powder	Organic cow's milk Organic peanut Organic cooked egg white	Add a daily packet to the child's breast milk, formula, or food. Start with Stage 1 packets (Days 1-11), then offer daily Stage 2 (Maintenance) packets.	Individual intro box from Amazon: \$18 1 month supply: \$49/month 3 month supply: \$39/month 6 month supply: \$29/month	10 calories 1 g protein Fat content not available 10 mg sodium 1 g carbohydrate 0 g added sugar

Spoonfulone	210 mg of each allergen protein	30 mg per day of each of the following: Milk, Egg, Wheat, Soy, Sesame, Peanut, Tree Nuts: Almond, Cashew, Pistachio, Hazelnut, Walnut, Pecan, Fish: Salmon, Cod, Shellfish: Shrimp	Mix-in Powder Puffs Oat Crackers	All products contain a blend of the following ingredients: peanuts, milk, shellfish (shrimp), tree nuts (almond, cashew, hazelnut, pecan, pistachio, and walnut), pasteurized egg white, fish (cod and salmon), grains (wheat and oat), soy, and sesame. <u>Mix-Ins:</u> Rosemary extract, salt, organic cane sugar, natural flavors <u>Puffs:</u> Organic white rice flour, salt, rosemary extract, organic invert sugar syrup, organic strawberry powder (organic strawberry, organic maltodextrin, organic corn starch), natural flavors, calcium carbonate, mixed tocopherols. <u>Oat Crackers:</u> Organic whole oat flour, organic sugar, organic palm oil, salt, rosemary extract, organic invert sugar syrup, organic vanilla extract, natural flavors, organic dried blueberries, baking soda, organic sunflower lecithin, salt, cinnamon, mixed tocopherols	Mix 1 packet into your baby's food daily.	1x Purchase: 7 pack: \$19.00 14 pack: \$34.95 28 pack= \$67.95 Subscription: 14 pack: \$33.20 28 pack: \$59.50/month	<u>Mix-Ins</u> 10 calories <1 g protein 0 g fat 0 mg sodium 1 g carbohydrate < 1 g sugar <u>Puffs</u> 30 calories 1 g protein 0 g fat 0 mg sodium 6 g carbohydrate 1g sugar <u>Oat Crackers</u> 50 calories 1 g protein 1.5 g fat 35 mg sodium 7g carbohydrate 2 g sugar
Gerber Organic Baby Pops Peanut	No dose recommended	Peanut protein content unknown. 1 g <i>total</i> protein per serving (18 pieces or 1/3 cup) Also available in Tomato flavor and Banana flavor with 0g protein per serving (peanut listed as last ingredient)	Puffs	Organic corn flour, organic de-fatted peanut flour, organic whole grain oat flour (contains wheat), organic high oleic sunflower oil, calcium carbonate, mixed tocopherols (to maintain freshness), vitamin b1 (thiamin mononitrate).	No instruction on how much or frequency to feed for allergy prevention.	\$2.29/5 servings Cost per month for 3 servings per week: \$5.50	30 calories 1 g protein 1 g fat 5 mg sodium 5 g carbohydrate 0 g added sugar
Happy Baby Organics Nutty Blends	3 g Walnut protein 3 g Peanut protein 3 g Cashew protein 3 g Almond protein	Apple Walnut with 1 teaspoon walnut butter = 1g walnut protein Banana Peanut with ½ teaspoon peanut butter = 1 g peanut protein Pear Cashew with 1 teaspoon cashew butter = 1 g cashew protein Banana Almond with ½ teaspoon almond butter = 1 g almond protein	Fruit pouches (each 3 ounces or 85g)	<u>Apple Walnut:</u> Organic apple puree, organic walnuts, organic lemon juice concentrate, mixed tocopherols (vitamin E), ascorbic acid (vitamin C) to preserve freshness. <u>Banana Almond:</u> Organic banana puree, organic almonds, organic lemon juice concentrate, mixed tocopherols (vitamin E), ascorbic acid (vitamin C) to preserve freshness. <u>Banana Peanut:</u> Organic banana puree, organic peanuts, organic lemon juice concentrate, mixed tocopherols (vitamin E), ascorbic acid (vitamin C) to preserve freshness. <u>Pear Cashew:</u> Organic pear puree, organic cashews, organic lemon juice concentrate, mixed tocopherols (vitamin E), ascorbic acid (vitamin C) to preserve freshness.	Feed “several times per week” for allergy prevention.	\$1.99 per pouch 23.88/month per allergen	<u>Apple Walnut</u> 100 calories 1 g protein 4.5 g fat 0 mg sodium 13 g carbohydrate 0 g added sugar <u>Banana Almond</u> 100 calories 2 g protein 3 g fat 0 mg sodium 19 g carbohydrate 0 g added sugar <u>Banana Peanut</u> 90 calories 2 g protein 1 g fat 0 mg sodium 19 g carbohydrate 0 g added sugar <u>Pear Cashew</u> 80 calories 1 g protein 2.5 g fat 0 mg sodium 13 g carbohydrate 0 g added sugar

664 **Table 2 b. Early Allergen Introduction Foods**

Food	Serving	Calories	Protein (g)	Fat (g)	Added Sugar (g)	Sodium (mg)	Cost per 4 weeks (USD)
Egg- hard boiled, well-cooked scrambled	1/3 egg	24.8	2.08	1.67	0	21.6	Large organic eggs \$3.49 Conventional eggs \$1.18 Based on using portions of 3 eggs/week/4weeks
Peanut butter national brand	1 teaspoon	32	1.17	2.67	0.5	23	\$0.44 Based on 3 teaspoons per week/4 weeks
Peanut butter “healthy” brand (just ground peanuts)	1 teaspoon	33	1.33	2.67	0	15	\$0.52 Based on 3 teaspoons per week/4 weeks
Powdered peanut butters (e.g., PB2)	1 teaspoon	10	1.0	<0.5	<0.5	15	\$0.86 Based on 3 teaspoons per week/4 weeks
Bamba	0.35 ounce (about 10 sticks)	55 calories	1.0	3.5	0.5 g	40	\$5.25 Based on 3 servings per week/4 weeks

665 Based on:

666 Organic eggs dozen-\$3.49; Conventional eggs dozen \$1.18; Peanut butter-16 ounce-\$3.49; Peanut butter “healthy”-16 ounce- \$4.19;

667 PB2-6.5ounce-\$5.99; Bamba 8 pack of 0.7 ounce-\$6.99

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Table 3: Commercial products for early introduction of food allergens compared to conventional foods

There is a range of commercial products currently available for early food allergen introduction. These products differ by the allergen they contain, the dose of the allergen and the degree of heating of the product. Cost of commercial products are significantly higher than conventional foods and the nutrient content of the products differ amongst each other and also when compared to conventional foods. It is a complex decision to make about whether to use the commercial products vs. conventional foods. As always, the families needs and preferences need to be a part of the decision making process. However, in order to collaborate with families in decision making we suggest that the allergist/dietitian take the following features into account:

Features	Commercial	Conventional
Cost	More expensive	Less expensive
Convenience	More convenient for families spending little time preparing foods	Can be convenient to families, cooking and preparing most of their meals
Additional ingredients	These foods can act as food allergens too	Ability to use a pure source of the food allergen only
Nutritional composition	Generally low in calories and lacking a wider nutritional profile	Rich sources of other nutrients: see online e-supplement S1
Dose of food allergen	Some products contain far less food allergen compared to doses used in research and those recommended by international guidelines	A desired dose can be chosen from allergen containing foods
Degree of heating	Degree of heating/cooking of the allergen may be not similar to those used in research and those recommended by international guidelines	A desired degree of cooking/heating can be chosen from allergen containing foods

Online supplement S1: Recommended Daily Infant Portions 6-12 months

	Smaller portions for younger infants	Sample infant safe forms
Fruits	2-8 Tablespoons	Smooth puree or soft cooked and chopped
Vegetables Include red, orange, and dark green vegetables	2-8 Tablespoons	Smooth puree or soft cooked and chopped
Grains* Choose a variety whole grains including wheat grains	½– 1 ounce (This includes ½ ounce per day or fortified grains for the breast-fed infant)	Whole wheat or fortified infant cereal (or farina or cream of wheat), whole grain pasta or pastina, toast or crackers
Protein foods** Meat, fish, poultry, eggs, nuts, seeds	¾ - 3 ounces	Smooth diluted peanut or tree nut butters or powders or butters/powders mixed into pureed foods Hard boiled, well-scrambled eggs blended into pureed foods or chopped for finger foods Tahini (sesame)
Dairy	¼ – ½ cup	Yogurt, cheese
Breast milk or formula	3-5 feedings 24-32 ounces/day (and as low as 16-20 ounces as infant approaches 12 months of age)	

*1 ounce protein foods = 50g egg; 28.35gram lean meat or seafood; ¼ cup tofu;

1 Tablespoon peanut butter, tree nut butters, or seed butter (diluted for infant safe feeding);

For vegetarian diets the recommendation for protein foods increases to 4 ounces per day of nuts, seeds, legumes.

**1 ounce grain = 1/2 cup pasta, 1 slice bread, or 4 Tablespoons for infant cereal

Online Supplement S2 Recipe:**Mixed nut butter recipe:**

Place all ingredients in a food processor and process until completely smooth (including any added nuts).
Serve spread on whole-wheat toast or as a dip for soft cooked

Nut (Total g wt per nut)	Gram of protein per nut	2 grams protein per serving
Almond (1.2 g)	0.254	8 nuts (2.032 g)
Peanut (0.9g)	0.219	9 kernels (1.917)
Cashew (app. 1.5 g)	0.273	8 (Whole nuts 2.1 g)
Pistachio (0.7 g)	0.141	14 nuts (1.974 g)
Macadamia (2.6 g)	0.202	10 nuts (2.02 g)
Brazil (5 g)	0.716	3 nuts (2.139 g)
Walnut (4g whole = 2 halves)	0.609	3.5 whole or 7 halves (2.13 g)
Pecan (4 g whole = 2 halves)	0.348	6 whole or 7 halves (2.088)
Hazelnut (app 1.4 g)	0.234	9 nuts (2.11 g)
https://ndb.usda.gov		
4 types of nuts (approx. 1/3 cup) plus 2 tablespoons of oil – grind and mix with blender 9 types of nuts (almost 1 cup) plus 4 tablespoons of oil - grind and mix with blender Keep in fridge and eat as is or mix with any preferred food such as apple sauce or yogurt. Oil will separate from nut butter during storage, mix well before using.		