
CME review article

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Food allergy and the introduction of solid foods to infants: a consensus document

Alessandro Fiocchi, MD*; Amal Assa'ad, MD†; and Sami Bahna, MD‡; for the Adverse Reactions to Foods Committee of the American College of Allergy, Asthma and Immunology§

Objective: To make recommendations based on a critical review of the evidence for the timing of the introduction of solid foods and its possible role in the development of food allergy.

Data Sources: MEDLINE searches using the following search algorithm: [weaning AND infant AND allergy]/[food allergy AND sensitization]/[dietary prevention AND food allergy OR allergens]/[Jan 1980-Feb 2006].

Study Selection: Using the authors' clinical experience and research expertise, 52 studies were retrieved that satisfied the following conditions: English language, journal impact factor above 1 or scientific society, expert, or institutional publication, and appraisable using the World Health Organization categories of evidence.

Results: Available information suggests that early introduction can increase the risk of food allergy, that avoidance of solids can prevent the development of specific food allergies, that some foods are more allergenic than others, and that some food allergies are more persistent than others.

Conclusions: Pediatricians and allergists should cautiously individualize the introduction of solids into the infants' diet. With assessed risk of allergy, the optimal age for the introduction of selected supplemental foods should be 6 months, dairy products 12 months, hen's egg 24 months, and peanut, tree nuts, fish, and seafood at least 36 months. For all infants, complementary feeding can be introduced from the sixth month, and egg, peanut, tree nuts, fish, and seafood introduction require caution. Foods should be introduced one at a time in small amounts. Mixed foods containing various food allergens should not be given unless tolerance to every ingredient has been assessed.

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INTRODUCTION

Whereas parents and pediatricians can be in no doubt regarding the avoidance of cow's milk and dairy products as com-

plementary foods for the primary prevention of allergic disease in at-risk infants,^{1,2} the same degree of confidence cannot be shared regarding the introduction of the child to a solid diet, for which no evidence- or consensus-based guidance is available. To compound the problem, there is no standard schedule for weaning infants who are healthy or at risk for allergy. According to *The Concise Oxford Dictionary*,³ *weaning* is defined as follows: "To accustom an infant or other young mammal to food other than milk." The World Health Organization (WHO)⁴ gives the term *weaning* a more restricted sense to indicate the complete cessation of breastfeeding, but the phrase "introduction of complementary feeding" is increasingly used. This describes the process starting when breast milk alone

* University of Milan Medical School, Milan, Italy.

† Division of Allergy and Immunology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio.

‡ Allergy and Immunology Section, Louisiana State University Health Sciences Center, Shreveport, Louisiana.

§ The members of the Adverse Reactions to Foods Committee are Staffan Ahlstedt, Mercedes Amado, Wesley Burks, William Hark, Sherry Hubbard, Luis Matos, Jennifer Maloney, Binita Mandal, Michael Norvell, James Pollowitz, Mary Catherine Tobin, Diane Wagner, and Brian Wilson.

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ceases to meet the infant's nutritional requirements and when other foods and liquids are needed along with, or in lieu of, breast milk.⁵ The introduction of solid foods, however defined, remains linked to breastfeeding duration and is also determined by adverse reactions. This may explain why "the introduction of solid foods" is not an optimal end point for the focus of research. In the present consensus document, we aim to provide literature-based recommendations on the introduction of solid foods to infants' diets as relates to the development of allergy. For this purpose, a MEDLINE search was performed using the following search algorithm: [weaning and infant and allergy]/[food allergy and sensitization]/[dietary prevention and food allergy or allergens]/[January 1980–February 2006].

INTRODUCTION OF SOLID FOODS

The American Academy of Pediatrics (AAP) recommends exclusive breastfeeding for at least 6 months, followed by the gradual introduction of solid foods in the second half of the first year and continued breastfeeding for up to 12 months or as long as is mutually desired thereafter.⁶ Similar indications are recommended by UNICEF,⁷ and the WHO Expert Consultation recommends exclusive breastfeeding for 6 months, followed by the introduction of complementary foods while breastfeeding is continued.^{8–10} An evidence-based consensus has been reached that 6 months of exclusive breastfeeding is optimal for infant and mother health,¹¹ but few controlled trials support the view that introducing solid foods before 17 weeks of age is harmful in developed countries,¹² and the main perceived risk is that the early introduction of complementary foods may shorten breastfeeding duration.¹³ A large systematic review¹⁴ did not find evidence either in support of or against a departure from the WHO recommendations. In developed countries, it has been hypothesized recently that energy requirements are not fulfilled by exclusive breastfeeding, suggesting that the introduction of complementary feeding may be necessary before 6 months of age.¹⁵ After 6 months of age, however, there is general agreement that it becomes increasingly difficult for breastfed infants to meet all their nutritional needs from human milk alone,⁴ and most infants are by then developmentally ready for other foods.¹⁶

INTRODUCTION OF INDIVIDUAL FOODS

Cultural approaches to food in general (and to baby feeding in particular) are the main obstacles against listing suitable solid foods in an introduction schedule acceptable to all families, even in the social context of a single nation. *Dietary Guidelines for Children and Adolescents in Australia*¹⁷ recommends "puréed foods" at 6 to 7 months of age, eg, gluten-free cereals (such as rice) as start-up foods, followed by vegetable (eg, carrot) and fruit (eg, apple and banana) purées, mashed potatoes, and well-cooked puréed liver and meat. Well-cooked fish, minced liver and meat, and mashed cooked vegetables and fruit are suggested for 8- to 12-month-old children. Raw fruit and vegetables, such as banana, melon, and tomato in chopped form, are considered suitable at this age, as are egg yolk, cereals such as wheat and oats, bread, pasta, cheese, custard, and yogurt. Other table foods

and pasteurized milk are deemed acceptable starting at the age of 12 months.

The UK Department of Health has issued qualified advice for the weaning diet¹⁸: "The majority of infants should not be given solid food before 4 months," "cow's milk should not be used as a main drink before one year," and "first weaning foods should be nonwheat cereals and pureed fruit and vegetables." HealthCanada has published nutritional guidelines for healthy infants from birth to the second year of life.¹⁹ These recommendations provide information on, among other topics, the transition to solid foods. A joint document from several government agencies and scientific societies, this statement represents a consensus view based (whenever possible) on scientific evidence. Throughout, the Canadian recommendations strive to distinguish between evidence-based and lay-practice advice.²⁰

In the United States, the AAP recommendations for infants and young children have remained substantially unchanged during the past 4 decades. Exclusive breastfeeding for the first 4 to 6 months of life, the introduction of solid foods at 4 to 6 months of age, the desirability of prolonging nursing to the first birthday and beyond, and infant formula use during the first year of life for infants who are not breastfed remain the backbone of this regimen.²¹ The AAP recommends introducing single-ingredient complementary foods one at a time during a trial lasting several days.²² All these documents, and the European Academy of Allergy and Clinical Immunology and AAP consensus-based guidelines regarding weaning in allergic children,^{23,24} state that the early introduction of solid foods can be associated with the induction of food allergy.

WHICH SOLID FOODS? FACTORS RELEVANT TO INTRODUCTION

The rationale for the timing of the introduction of solid foods should be based on 4 main considerations: (1) the selected foods should provide sufficient energy, protein, and micronutrients in balanced and appropriate-for-age supply to meet the child's growing nutritional needs (nutritional); (2) foods should be hygienically stored and prepared (toxicologic); (3) foods should be supplied in response to the child's signals of appetite and satiety and should be compatible with and promote the development of specific developmental stages vis-à-vis food and feeding skills (behavioral); and (4) foods should be appropriate for current immune development by avoiding exposure of the child to an increased likelihood of sensitization with known allergenic foods (immunoallergologic).

Whereas nutritional and toxicologic considerations may be more relevant to the developing world and behavioral considerations are compatible with current parenting and weaning skills in developed countries, we focus herein on immunoallergologic considerations in the belief that the timing of the introduction of complementary feeding should be predicated mainly on immunoallergologic considerations.

IMMUNOLOGIC ASPECTS OF THE INTRODUCTION OF SOLID FOODS

In the course of evolution, environmental pressure has selected for a mucosal immune system capable of sophisticated adaptive responses to handle these challenges. Oral tolerance is a complex phenomenon^{25,26} and basically depends on apoptosis when intestinal antigen exposure is excessive and on anergy and induction of immune deviation at lower antigen doses.²⁷ Thus, from a theoretical point of view, overexposure to food allergens and avoidance of exposure during vulnerable periods can result in tolerance. The best strategy depends on the answers to 4 crucial questions: (1) Can the early introduction of solid foods cause food allergy? (2) Can the avoidance of solid foods prevent the development of food allergy? (3) Are some foods more allergenic than others? (4) Are some food allergies more persistent than others? In this review, we propose that the rationale for the scheduled introduction of solid foods be based on the issues that these questions raise.

DOES THE EARLY INTRODUCTION OF SOLID FOODS CAUSE FOOD ALLERGY?

Noninterventional studies have found that the introduction of solid foods before the fourth month of life increases the risk of developing atopic dermatitis until the age of 10 years.²⁸ Cow's milk formula supplementation before milk letdown has also been linked to the development of cow's milk allergy.²⁹

To evaluate the relationship between the early introduction of solid foods and infant health during the first 2 years of life, a prospective observational study³⁰ evaluated the effect of different timing of the introduction of foods on weight, gastrointestinal diseases, respiratory illness, nappy rash, and eczema up to 24 months of age. Infants given solid foods at an early age (<8 vs 8–12 weeks) showed a significant increase in respiratory illness at 14 to 26 weeks of age and persistent cough at 14 to 26 and 27 to 39 weeks of age. The incidence of eczema was also increased in infants who received solid foods at 8 to 12 weeks of age.³⁰ However, the magnitude of these differences was not high, and the authors recommend "a more relaxed approach to early feeding."

A prospective, randomized, well-controlled study³¹ of preterm infants followed up to 18 months of age and a prospective study³² of unselected full-term infants followed up to the age of 17 years concurred that introducing solid foods after 6 months of exclusive breastfeeding lowered asthma and eczema risks later in childhood. Conversely, the late introduction of egg has been reported to increase the risk of atopic eczema and wheezing in preschoolers in a cohort of prospectively selected infants.³³ However, because of the retrospective evaluation of this particular item, the authors' conclusion that ". . . results do not support the guidelines for the prevention of asthma and allergy in general populations, stating that the introduction of solids should be delayed for at least 4–6 months" does not exclude reverse causality as the result of design bias. In a different birth cohort study of 2,612 two-year-olds, reverse causation was excluded by stratifying the sample for symptom onset before 6 months of age.³⁴ In view

of the fact that it is impossible to exclude that the parents of infants without early onset of allergic disease may have followed the delayed introduction advice for other reasons, such as a family history of disease or socioeconomic factors, these methods seem open to criticism. Similar considerations may be applied to other noninterventional studies.³⁵

A good example of the effects of the introduction of solid foods early in life is sesame allergy. In Israel, food allergy prevalence was found to be 1.7%, with sesame as the third most common food causing sensitization after egg and cow's milk. Furthermore, sesame was second only to cow's milk as a leading cause of anaphylaxis. This may be due to the increasing use of sesame-containing products among infants in Israel, suggesting that food allergy "is a matter of geography after all."³⁶

DOES THE DELAYED INTRODUCTION OF SOLID FOODS PREVENT THE DEVELOPMENT OF FOOD ALLERGY?

Since the 1980s, prophylaxis of atopic disease has been attempted by intervention in the form of specific food item elimination from the early diet. In a study³⁷ that reported on the effects of late vs early introduction of fish and lemon on allergic sensitization, at 3 years of follow-up, data showed that late exposure to solid foods can postpone but not prevent allergy to these foods. The results of another study³⁸ suggest that total solid food elimination for the first 6 months of life is prophylactic in children at risk for atopy by family history. In a case-controlled epidemiologic study,³⁹ the early introduction of cereals has been associated with grass-triggered asthma, a conclusion that needs confirmation owing to the retrospective data presented.

Many prospective studies have addressed the possibility of food allergy prevention by dietary intervention. Clinical research from Canada,^{40–42} Belgium,^{43,44} the United States,^{45,46} England,^{47–49} Sweden,^{50,51} Denmark,⁵² and Germany⁵³ suggests that the avoidance of cow's milk proteins can reduce sensitization to milk. Recent systematic review of this evidence indicates that dietary prevention of allergy by avoidance of food allergens in early life is effective.^{1,54,55}

WHICH FOODS ARE "ALLERGENIC"?

"The ability of a given food to elicit specific IgE sensitization and to cause allergic reactions in a given population" varies according to the characteristics of the food and of the population in which it is consumed.⁵⁶ Data from European surveys^{57,58} indicate that the most allergenic solid foods are egg, fish, seafood, peanut, soybean, and tree nuts. In the Swedish adult population, among patients reporting symptoms of "food intolerance," 26% developed elevated IgE levels in response to egg white, peanut, soybean, milk, fish, and wheat.⁵⁹ In France, the most frequent allergenic foods are fruits from the Rosaceae family (apple, cherry, and peach; 14%), followed by vegetables (9%); milk (8%); crustaceans (8%); shellfish (7%); the latex-cross-reactive avocado, kiwifruit, banana, and chestnut (5%); hen's egg (4%); tree nuts (3%); and peanut (1%).⁶⁰ In a study of Danish 3-year-olds, 0.6% reacted to cow's milk, 1.6% to hen's

egg, and 0.2% to peanut.⁶¹ In Germany, foods often implicated in food allergy include nuts and fruits (77.6%), vegetables (54.4%), wheat flour (14.9%), milk (4.5%), and egg (2.9%).⁶² It has been reported that shellfish constitutes the primary cause of food allergy in adults in some areas of the United States.⁶³ Consequently, the implicated foods have been designated for explicit labeling in the case of processed food products.^{64–66} In this section, we focus first on the foods that trigger the more severe reactions and then continue to the foods that are likely to cause persistent allergies.

Hen's Egg

Exquisitely small amounts of egg allergen have been reported to trigger reactions after inhalation in adults^{67,68} and children.^{69,70} Patients allergic to egg can experience reactions to fowl. Chicken serum albumin (α -livetin) has been implicated in the bird-egg syndrome. However, IgE reactivity to chicken albumin was reduced by 88% after heating at 90°C for 30 minutes.⁷¹ Thus, it seems that homogenized, rather than fresh, poultry products should be preferred in introducing the infant to these nutritionally useful animal proteins.

Peanut

Peanut allergy has increased in prevalence,^{72–74} but the magnitude of the rise remains to be ascertained.⁷⁵ Whether this is linked to increased peanut consumption, ubiquitous peanut-containing nonfood products,^{76,77} consuming peanuts while breastfeeding,⁷⁸ or other factors is also unclear. An intriguing observation is that peanut allergy is rare in China,⁷⁹ where consumption of the legume is not different from that in the United States. Although the frequency of atopic disease is generally lower in China, preparation methods differ. In China, peanut is boiled or fried, whereas it is dry roasted in the United States. Roasting seems to enhance the allergenicity of peanut.^{80,81} Another relatively thermostable allergen belonging to the Leguminosae family is soybean. Its behavior can be modified by technological treatments,⁸² but the effects of cooking on these proteins are not uniformly interpreted.^{83,84} One study⁸⁵ found remarkably thermostable antigenicity using home technology, with cooking at 100°C for 2 hours decreasing IgE binding to soy proteins, whereas cooking at 80°C to 120°C for 60 minutes did not. In another study, however, cooking at 80°C to 120°C for 60 minutes decreased IgE binding.⁸⁶ To our knowledge, no *in vivo* study has evaluated the effects of cooking soy proteins, and neither have large studies been performed on soybean proteins. Soy hydrolysates have had the same scant attention.⁸⁷ Legumes exhibit an extensive degree of cross-sensitization, which does not always translate into clinical reactivity. Up to 94% of skin prick tests have yielded false-positive results for soybean,^{88,89} and sensitization to carob seeds does not translate to cross-reactivity in children allergic to peanut.⁹⁰ These observations have important clinical correlates; for example, carob may be acceptable as an additive in processed foods, antiregurgitation formulas, and weaning formulas because avoidance of its

proteins cannot be recommended on the basis of cross-reactivity, which is considered low between Leguminosae.⁹⁰

Tree Nuts

Allergic reactions to tree nuts can be life threatening. Some nut allergens have been identified and characterized, and some of their IgE-reactive epitopes have been described.^{91,92} Allergens such as lipid transfer proteins, profilins, and members of the Bet v 1-related family are considered panallergens. Others, such as legumins, vicilins, and 2S albumins, represent major seed storage protein constituents of the nuts.⁹³ Cross-reactions frequently occur among hazelnut, walnut, cashew, almond, chestnut, Brazil nut, pine nut, macadamia nut, and pistachio nut (and even coconut). Thus, avoidance of all kernels is recommended to patients responsive to a single nut.⁹⁴ The roasting of hazelnuts may reduce their allergenicity.⁹⁵

Seafood

The causes of seafood allergenicity are of a chemophysical nature. Codfish includes one of the most heat-stable major allergens, Gad c 1, which not only withstands cooking but also becomes airborne in steam without undergoing denaturation.⁹⁶ It is also resistant to chemical detergents⁹⁷ and is minimally affected by various cooking methods when protein bands at sodium dodecyl sulfate–polyacrylamide gel electrophoresis are compared with raw and cooked codfish.⁹⁸ The major allergens responsible for cross-reactivity among distinct species of fish and amphibians are parvalbumins, and the major shellfish allergen has been identified as tropomyosin.⁹⁹ These allergens are responsible for cross-reactions between mites and snails^{100,101} and among insects, shrimps, and cockroaches.¹⁰² In the literature, reports of extensive clinical cross-reactivity between fish species are common.¹⁰³

Fresh Fruits and Vegetables

Plant food panallergens are so sensitive to heat that they cannot be reliably preserved in reagents for skin testing.¹⁰⁴ For this reason, they are conceived of as a nonoffending food and are, therefore, introduced early in the weaning process. However, early exposure may result in allergy, and reactions to kiwifruit are increasing with its popularity among children.¹⁰⁵ A heat-treated homogenized kiwifruit preparation was tolerated by children with challenge-confirmed allergy to fresh kiwifruit.¹⁰⁶ Industrial treatment in this case may be sufficient but perhaps not necessary, given the lability of fruit allergens, to destroy kiwifruit allergenicity.

Cross-reactivities between different types of fruits may be different in children and adults.^{107–109} Despite this possibility, patients allergic to raw fruits and vegetables do not generally react to the cooked food. The fact that some vegetables (such as potatoes) are always consumed cooked can account for this, despite the known allergenicity of solanaceous proteins.^{110,111} A notable exception to the suitability of cooked greens is celery. This plant (in both its root vegetable and aerial stem varieties) retained its allergenicity after cooking at 110°C for 15 minutes.¹¹²

Cereals

A Western diet staple, wheat, is responsible for causing food allergies in children and has been linked to food-dependent, exercise-induced anaphylaxis in recent years.¹¹³ Sensitization patterns show a great degree of individual variation, and the presence of IgE to purified ω -5 gliadin in children was highly predictive of immediate clinical symptoms on oral wheat challenge in one study.¹¹⁴ Most of these allergens seem to be heat stable, and most symptoms can be related to the ingestion of bakery products. Thus, it seems that the relatively long baking time and high temperature do not suppress the allergenicity of wheat proteins.¹¹⁵ Because celiac disease is far more frequent than wheat allergy, at least in certain countries, the timing of the introduction of wheat is generally more often dictated by the latter than the former.¹¹⁶ In Western countries, the frequency of allergic reactions to rice does not reach 1% of atopic patients,^{117,118} and anaphylaxis to rice in children has been described only occasionally.^{119,120} In contrast, rice is an important allergen in Asia, where a hypoallergenic rice has been marketed with clinical success.¹²¹

Meat

Beef represents a special case in that exposure to bovine serum albumin, the major beef allergen, is more likely to have occurred before the introduction of solid foods through milk supplementation. Cooking can alter the reactivity of beef,¹²² and homogenized and freeze-dried beef baby food preparations lose their ability to elicit a positive skin prick test reaction.^{123,124} In children allergic to beef, lamb and turkey have been proposed as substitute sources of animal protein,¹²⁵ but little is known about their allergenicity. Lamb is not as hypoallergenic as is often believed, as bovine and ovine serum albumins share 552 of their 607 amino acid sequences^{126,127} and are close enough biochemical relatives for cross-reactivity, as demonstrated by means of serologic analysis in beef-allergic children.¹²⁸

These and other data indicate a wide cross-sensitization potential between the meats of different and related animal species. Tropomyosin¹²⁹ and bovine IgG¹³⁰ have also been indicated as cross-reactive allergens in patients allergic to beef and other meats. The use of alternative meats in beef-allergic children, therefore, must be carefully evaluated for the individual patient, and no meat should be presumed to be "hypoallergenic." Well-cooked beef¹³¹ can be recommended in weaning for its reduced allergenicity.

WHICH FOOD ALLERGIES ARE LIKELY TO BE MORE PERSISTENT?

In designing a solid food introduction diet for the infant, not only should the risk of sensitization to any food be taken into account, but the risk of developing persistent allergies should be evaluated on a case-by-case basis. In general, there is a relationship between symptom severity after ingestion and the likelihood of outgrowing the problem.^{132,133} Other factors, such as specific IgE antibody level and age at diagnosis,¹³⁴ have also been associated

with prognosis of food allergy, although these associations are not consistent among studies.¹³⁵⁻¹³⁷

To indicate the persistence of food allergies to solid foods, an estimate of the persistence of allergies can be drawn from the duration of food allergy. For example, 50% of children lose their cow's milk allergy by 1 year of age.¹³⁸ In a limited sample of children with egg allergy (median age, 17 months), tolerance reached 44% of cases at 2½ years of age.¹³⁹ Other studies found that 31% to 51% of children allergic to egg overcame the problem.¹⁴⁰ However, it is difficult to compare the results of earlier studies because of widely varying study designs. A more recent study¹⁴¹ found persistence of egg allergy in 50% of the patients at 35 months of follow-up. This means that half the children allergic to egg will tolerate the food when they are 4 to 4½ years old.¹⁴¹ The proportion of tolerant children was 66% after 5 years. Thus, egg allergy persistence should be considered 3 times greater than cow's milk allergy persistence.

Peanut allergy was once considered to be a lifelong condition,¹⁴² but peanut-allergic infants sometimes outgrow their allergy.¹⁴³⁻¹⁴⁶ Taking the results of the various studies together, it seems that approximately 20% of young children outgrow peanut allergy.¹⁴⁷ In rare cases, patients may become susceptible again to these allergens, but further studies are needed to clarify this point.^{148,149} Thus, it is not possible to establish an average duration of peanut allergy. Similarly, fish allergy is usually a long-lasting condition, and reports of recovery are rare,¹⁵⁰ with possible re-sensitization.¹⁵¹ However, no study has evaluated the natural history of fish allergy in infants, and fish should also be regarded as causing persistent allergies.

Whereas it is known that peanut, tree nut, fish, and seafood allergies are mostly persistent conditions, little is known about the natural history of allergy to staples such as fruits, vegetables, cereals, and meat. Because young children with milk (or egg) allergy likely have other food allergies, it is often recommended that major food allergens, such as peanuts, tree nuts, fish, and shellfish, be avoided until the child is at least 3 years of age.⁵³ Although this recommendation seems reasonable, there is no evidence to demonstrate that an avoidance strategy will be successful in preventing future allergy.

An important observation is that older children¹⁵² and adults¹⁵³ lose their reactivity to foods if the responsible food allergen is identified and strictly eliminated from the diet.¹⁵⁴ Relevantly, the severity of the initial reaction does not seem to correlate with the likelihood of clinical reactivity loss, but the degree of compliance with the allergen avoidance diet and the food responsible for the reaction affect the outcome. Thus, it seems a good precaution to introduce weaning foods later during infancy in children at risk of persistent allergy.

OPTIMAL TIMING OF SOLID FOODS

Although it would be difficult to propose an optimal feeding schedule for infants in general, studies measuring the effect of dietary intervention in children at risk of food allergy may circumstantially provide practical suggestions. Two issues should be considered in introducing individual foods: (1)

avoiding interference with any prescribed dietary intervention, such as special formula, and (2) evaluating the effects of delayed solid food introduction on allergic sensitization and atopic disease. The definition of allergy risk, however, was not universal in all the studies. Some studies considered as “at risk” children with atopic parent(s) or relatives, whereas others used predictors such as cord blood IgE levels and specific questionnaires (Table 1).

In all these studies, schedules recommend the introduction of solid foods between the ages of 4 and 6 months for at-risk children (similar to that for children who are not candidates for intervention). The timing of the introduction of specific foods varies widely, but most researchers consider it prudent to introduce hen’s eggs between 9 and 12 months of age and fish, peanut, and nuts after the age of 12 months. However, such recommendations are not evidence based. The effect of the late introduction of solid foods on sensitization is not reported for specific foods.

The 2000 AAP Committee on Nutrition²³ and the 1999 European Society of Pediatric Allergy and Clinical Immunology together with the European Society of Pediatric Gastroenterology, Hepatology, and Nutrition (ESPACI-ESPGHAN)²⁴ recommendations for the prevention of food allergy concur that solid foods should be introduced between 5 and 6 months of age in infants with a family history of allergy (Table 2). The guidelines differ only in that the AAP specifies several solid food classes and the ESPACI-ESPGHAN document indicates optimal breastfeeding duration and avoidance of generic supplementary food before the fifth month of life. The American College of Allergy, Asthma and Immunology food allergy 2006 practice parameter¹⁵⁵ recommends “avoidance of solids at a young age” for primary prevention of food allergy.

Table 2. Timing of the Introduction of Foods in Children at Risk for Allergy

Recommendation	Age at introduction, mo	
	AAP ²⁴	ESPACI-ESPGHAN ²⁵
Breastfeeding	≤12	≤4–6
Solid foods	≥6	≥5
Hypoallergenic diet	6	NA
Dairy products	12	NA
Egg	24	NA
Peanut, tree nuts	36	NA
Fish	36	NA

Abbreviations: AAP, American Academy of Pediatrics; ESPACI-ESPGHAN, European Society of Pediatric Allergy and Clinical Immunology–European Society of Pediatric Gastroenterology, Hepatology, and Nutrition; NA, not applicable.

EVIDENCE-BASED TIMING OF THE INTRODUCTION OF SOLID FOODS

Currently, evidence as to an optimal time for the introduction of any individual solid food in the infant’s diet is lacking, and it may be better to think in terms of individual schedules toward which broad categories of patients may be addressed on an experimental basis. This would also be in keeping with the etymologic meaning of the verb *to wean* (from Old English *wenian*, to accustom³). Optimizing introduction schedules characterizes the allergist’s earliest intervention to influence the process of tolerance induction beyond milk and dairy products. Because this is geared toward reducing the incidence or delaying the onset of allergic symptoms, this area is in need of practice guidelines based on special epidemiologic and clinical studies.

Table 1. Evaluation of Allergic Risk and Timing of the Introduction of Solid Foods and Single Specific Foods in Studies on the Prevention of Food Allergy

Source	Risk factor for atopy	Specific IgE	Age introduced, mo			
			Solids	Egg	Nuts	Fish
Chandra et al ⁴⁰	≥1 first-degree relative	Yes	NA	NA	NA	NA
Chandra et al ⁴¹	≥1 first-degree relative	Yes	>6	18	36	18
Vandenplas et al ⁴³	≥2 first-degree relatives	No (yes to egg on 5th day)	>4 (apple)	>6	NA	>6
Zeiger et al ⁴⁵	1 parent (SPT/RAST)	Yes	>6	24	24	24
Zeiger et al ⁴⁶	≥1 parent	No	>6	24	36	36
Arshad et al ⁴⁷	2 first-degree relatives or 1 first-degree relative and CB IgE >0.5 kU/L	Yes	? (wheat 10 mo)	11	>12	>12
Hide et al ⁴⁸	2 first-degree relatives or 1 first-degree relative and CB IgE >0.5 kU/L	Yes	?	>9	>9	>9
Hide et al ⁴⁹	2 first-degree relatives or 1 first-degree relative and CB IgE >0.5 kU/L	Yes	?	>9	>9	>9
Oldaeus et al ⁵¹	2 first-degree relatives or 1 first-degree relative and CB IgE >0.5 kU/L	Yes	>4	>12	?	>12
Halken et al ⁵²	Both parents or 1 first-degree relative and CB IgE >0.5 kU/L	Yes	>4	?	?	?
Von Berg et al ⁵³	1 first-degree relative with allergy according to a questionnaire	No	Left to the mother	>12	>12	>12

Abbreviations: CB, cord blood; RAST, radioallergosorbent test; SPT, skin prick test.

The introduction of solid foods is not an ideal research end point because its full benefit depends on the duration of breastfeeding. It should not be forgotten that the timing of the introduction of solid foods into the diet of infants has only recently become a field of study in its own right. The practical lesson from clinical studies may be biased by outcome misclassification because of the diverse methods used.³⁵ Attempts at systematic review of prospective and retrospective works together with randomized, well-controlled evidence may well depict the evidence of a link between the early introduction of solid foods and the onset of atopy as conflicting and inconsistent.¹⁵⁶

Thus, devising a timetable leading to the definition and minimization of clinical risk in a defined population of likely candidates remains among the achievable goals of food allergy prevention. Faced with a parent asking “which food” and “when,” the pediatrician has to integrate a reasonable schedule for the introduction of solid foods based on biochemical, immunologic, and epidemiologic data. Choosing the food to be introduced depends on its “allergenicity index,” which depends on several factors: (1) sensitization risk (how many children become sensitized to that food when exposed), (2) allergy risk (how many children sensitized to that food develop clinically relevant symptoms), (3) allergy persistence risk (the half-life of a diagnosis of allergy), and (4) personal risk (familial recurrence of allergic diseases).

RECOMMENDATIONS

1. Exclusive breastfeeding, with the exclusion of cow’s milk formulas and any supplemental foods, is indicated during the first 6 months of life because it has a preventive effect against the onset of allergic symptoms extending far beyond the period of breastfeeding.

2. The introduction of supplemental foods during the first 4 months of life has been associated with a higher risk of allergic diseases up to the age of 10 years. This confirms current WHO recommendations, and complementary feeding can be introduced starting at the sixth month of life.

3. Exposure avoidance is an effective means of preventing cow’s milk allergy, and there seems to be no reason why delayed exposure to solid foods should not prove similarly useful in the prevention of food allergies.

4. The main foods posing an allergy risk in the developed world are bovine milk, egg, peanut, tree nuts, fish, and seafood. Other foods can become clinically significant allergens if introduced early. It also seems reasonable that foods should be introduced individually and gradually.

5. Mixed foods containing various food allergens should not be given unless tolerance to every ingredient has been evaluated.

6. Cooked, homogenized foods should be preferred to their fresh counterparts when a reduction of allergenicity has been clinically demonstrated for that processed food (eg, beef and kiwifruit).

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Requests for reprints should be addressed to:
 Alessandro Fiocchi, MD
 Chairman, Adverse Reactions to Foods Committee
 American College of Allergy, Asthma and Immunology
 Melloni Paediatrics
 University of Milan Medical School at the Melloni Hospital
 Via Melloni 52
 20129 - Milan, Italy
 E-mail: allerg@tin.it

Objectives: After reading this article, participants should be able to demonstrate an increased understanding of their knowledge of allergy/asthma/immunology clinical treatment and how this new information can be applied to their own practices.

Participants: This program is designed for physicians who are involved in providing patient care and who wish to advance their current knowledge in the field of allergy/asthma/immunology.

Credits: ACAAI designates each Annals CME Review Article for a maximum of 2 category 1 credits toward the AMA Physician's Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity. The American College of Allergy, Asthma and Immunology is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians.

CME Examination

1–7, Fiocchi A. 2006;97:10–21.

CME Test Questions

1. What is the optimal age of introduction of solid foods according to the American Academy of Pediatrics recommendations?
 - a. 3 months
 - b. 4 months
 - c. 5 months
 - d. 6 months
 - e. “soon after the cessation of breastfeeding”
2. Which is the optimal age of introduction of egg in children at no allergic risk according to the National Institutes of Health guidelines?
 - a. 6 months
 - b. 8 months
 - c. 10 months
 - d. 12 months
 - e. none of the above
3. All of the following have been reported in noninterventional studies about the effects of the early introduction of solid foods except
 - a. the introduction of solid foods before 4 months of age correlates with the risk of atopic dermatitis
 - b. solid foods before 1 month of age are associated with perineal rash and atopic dermatitis
 - c. solid foods at an early age are associated with an increased incidence of eczema
 - d. introducing solid foods after 6 months of exclusive breastfeeding reduces asthma and eczema risks later in childhood
 - e. the late introduction of egg increases the risk of atopic eczema
4. All the following are subject to the Food and Drug Administration allergenic foods requirements except
 - a. crustacean
 - b. shellfish
 - c. celery
 - d. wheat
 - e. soybeans
5. Which of the following foods can be introduced freely in infants’ diets because of low allergenicity?
 - a. fish
 - b. seafood
 - c. egg
 - d. rice
 - e. none of the predicted
6. Half the infants allergic to egg will tolerate the food when they are
 - a. 2 years old
 - b. 3 years old
 - c. 4 years old
 - d. 5 years old
 - e. none of the above
7. The average duration of fish allergy is
 - a. 2 years
 - b. 5 years
 - c. 10 years
 - d. lifelong
 - e. none of the above

Answers found on page 77.
