Introduction of Solid Foods

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Introduction

Feeding guidelines for the prevention of allergic diseases follow the view that allergen avoidance leads to a reduction in allergy, which is understood as being mediated by sensitization. The role of early feeding in the development of allergic disorders has been studied widely. Most of these studies have concentrated on the role of breastfeeding and, in the case of children at a high risk of allergies, on the role of hypoallergenic formulas as substitutes for or supplemental to breastfeeding. Less attention has been paid to the role of solid food introduction into the baby’s diet and the conditions under which this has been done. Nevertheless, all guidelines include some recommendations on the introduction of solid food.

According to the joint guidelines of the European Society for Paediatric Allergology and Clinical Immunology (ESPACI), Committee on Hypoallergenic Formulas, and the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN), Committee on Nutrition [1], as well as the German guidelines [2], breastfeeding for the first 4–6 months of life is recommended, with the introduction of solid foods thereafter. The feeding guidelines of the Committee on Nutrition of the American Academy of Pediatrics in general recommend delaying the introduction of solid foods until 6 months of age, but are more stringent with recommendations for certain foods: cow’s milk products should be avoided until 1 year, eggs until 2 years and fish even until 3 years [3]. The guidelines of the WHO recommend the introduction of solids after 6 months of exclusive breastfeeding for all children [4].

The most recent recommendations from an expert group set up by the Section of Pediatrics, European Academy of Allergology and Clinical Immunology, are slightly different, stating that all children should avoid solid foods preferably until 6 months but at least 4 months of age, and that infants
at a high risk of allergic diseases can be nourished like non-high-risk infants after the age of 4 months [5].

**Evidence for Delaying Solid Food Introduction**

The scientific evidence supporting the recommendations to delay solid food introduction until 4–6 months or even longer are scarce. Only a few studies have investigated the effect of early solid food introduction on the development of allergic diseases and their results are inconsistent. The current recommendations are mainly based on 2 older studies.

In 1991, in a prospective, non-randomized trial in children at risk of atopy, eczema and with a history of food allergy, Kajosaari [6], found that allergy was reduced in children in whom solid foods were introduced after 6 months of exclusive breastfeeding compared with children fed solids after 3 months. The effect was seen at 1 year, but had disappeared by the time the children were 5 years old [6]. The second study by Fergusson et al. [7, 8] from 1990, conducted in a large nonselected birth cohort of 1,265 children from New Zealand, has shown that feeding 4 or more diverse solid foods in the first 4 months is associated with a significantly increased risk of eczema (odds ratio (OR) 2.9) in children 2–4 years of age compared to children who had no solids before 4 months of life, and this effect lasted up to age 10 years [7, 8]. From these two studies it seems obvious that the timing and diversity of solid food introduction into the baby’s diet are two crucial factors for the later development of allergic diseases.

**Recent Studies**

However, more recent studies on solid food introduction have looked in more detail into the conditions under which the decision to introduce solid foods into the baby’s diet has been taken, their results adding to the current conflicting data.

In a prospective, observational study following 671 infants from birth to 24 months of age, Forsyth et al. [9] assessed the relationship between the early introduction of solid food and infant weight, gastrointestinal illness and allergic diseases during the first 2 years of life. At 2 years, data from 455 (67.8%) children were available. The timing of solid food introduction was divided into 3 intervals: <8, 8–12, and >12 weeks. 65/671 (9.7%) children were introduced solids at age <8 weeks, and 332/671 (49.5%) between weeks 8 and 12. Infants who received solids early (at <8 weeks and 8–12 weeks) were significantly heavier than those who were fed solids after 12 weeks (p < 0.01) up to 26 weeks of life, thereafter no weight difference between the groups remained. Also, those infants who received solids early were heavier at
their first solid feeding than infants of similar age who had not yet received solids [9].

Apart from a birth weight of ≥4,000 g (n = 66, p = >0.05), the characteristics of children who were fed solid foods early were: male sex (p < 0.005), lower social class, and bottle-fed.

Children with the early introduction of solids had a significant but less than twofold increased risk of respiratory illnesses at 14–26 weeks of age and persistent cough at 14–26 and 27–39 weeks. These associations persisted even after adjustment for factors that are known to be related to respiratory symptoms in early childhood, such as parental smoking and poor social conditions. However, the follow-up was too short to answer whether these respiratory conditions were the expression of an atopic condition or were due to viral-induced respiratory disorders. The prevalence of eczema in this study was highest in children who had solids introduced at age 8–12 weeks rather than at an earlier (<8 weeks) or later age (>12 weeks). A possible explanation is offered from animal models showing that hypersensitivity reactions caused by a large antigen load are less strong than those caused by small antigen load [10]. As intestinal permeability decreases gradually from birth during the following weeks, it is possible that less antigen crosses the intestinal epithelium between weeks 8 and 12 than in the first 8 weeks.

In preterm infants solid feeding practices in addition to milk feeding patterns and their association with the development of atopic diseases have recently been studied by Morgan et al. [11]. In their prospective study on 257/329 preterm infants they found a rather high prevalence (35.8%) of eczema, and the introduction of 4 or more solid foods before 17 weeks of age was a risk factor for eczema (OR 3.49) at 1 year of age, independent of the family history of atopy. Prematurity in general may be a risk factor for the development of allergic diseases because of the immature immune system. On the other hand, increasing prematurity is known to be associated with a decreasing risk of atopy [12], which could be due to the higher risk of infections in the very preterm children, and to the later introduction of solids than in healthier, less premature infants. However, the results were not adjusted for the different stages of prematurity, and this could well have biased the results [13].

Solid feeding practices were also studied in the German Infant Nutritional Intervention (GINI) study, which is a prospective, randomized birth-cohort study that was conducted to assess the preventive effect of three different hydrolyzed infant formulas in comparison with a standard cow’s milk formula in a double-blind fashion in 2,252 high-risk infants recruited between 1995 and 1998 in two regions of Germany, Munich (n = 1,165) and Wesel (n = 1,087) [14].

Parents received detailed verbal and written recommendations on infant nutrition. Mothers were asked to delay the introduction of solid foods until after the intervention period of 4, better 6, months during which they were
advised to use the randomized study formula as the only milk supplement to breastfeeding. Furthermore, it was recommended that potentially allergenic foods such as cow’s milk and dairy products, eggs, fish, tomatoes, nuts, soy products and citrus fruits should be avoided during the first year.

For the first 24 weeks parents recorded the infant’s nutrition in a weekly diary. They were asked to note the type of milk (breast milk, formula) and the time of weaning, as well as the time of the first introduction and the kind of solid food into the baby’s diet [14].

One GINI sub-study looked at the influence of solid food introduction on specific sensitization at 12 months of age in a subgroup of 170 children from the GINI cohort [15]. Specific IgE to the following food allergens was determined: apple, banana, pear, peanut, hazelnut, carrot, potato, soy, wheat, cow milk, diary products and egg.

According to the parentally recorded questionnaires, children were divided into 2 groups: group BF which was exclusively breastfed during the first 4 months of life, and group SF which received the study formula.

Solid foods in addition to formula or breastfeeding were given in 37/170 (21.8%) before the end of the 16th week, while 30/170 (17.6%) had their first solids between weeks 17 and 20, and 46/170 (21.7%) in weeks 21–24. 53/170 (31.2%) were fed exactly according to the recommendations and received their first solid feeding after the end of 6 months.

Vegetables/juices and cereals were the most common first solids in the first 16 weeks (12.4 and 10.6%, respectively). The most common vegetable was carrots, with 62% of the children consuming them in the first 24 weeks.

By the age of 24 weeks, only 7% of the children had had dairy products, and only 0.7% had had soy. None of the children were reported to have received egg, fish or nuts during the first 24 weeks.

When children received solids early, that is in the first 16 weeks or in weeks 17–20, sensitization at 12 months to at least one of the 13 allergens tested was low at 5.4 and 6.7%, respectively. In contrast, specific IgE ≥0.35 kU/l to at least one allergen was 17.4% in the children who first had solids in weeks 21–24, and 18.9% when solids were introduced after 24 weeks. Although there was a tendency towards more frequent sensitization with the later introduction of solid foods, this was not significant (p = 0.154).

Data on egg sensitization were available from 111 children. Although 74 children had not received any egg within the first year, 8.1% of them were sensitized to egg at 12 months. Of the other 37 children who had egg in the first year, only 1 child (2.7%) had specific IgE to egg.

Variability of food in the first 24 weeks was divided into 3 categories: 1 = none (n = 53, 31.9%); 2 = 1–2 food groups (n = 66, 39.8%), and 3 = >2 food groups (n = 47, 28.3%). There was an inverse association between the number of foods and sensitization: 20.8% (category 1); 12.1% (category 2), and 8.5% (category 3) [15].
Apart from comparing the 1-year incidence of atopic dermatitis (AD) in children exclusively breastfed during the first 16 weeks of life (BF group) with that of children who were fed with a standard cow's milk formula exclusively or supplemental to breast milk (CMF group), the aim of another GINI sub-study was to examine whether the co-intervention advice of early solid food avoidance has an additional effect on the incidence of atopic eczema [16]. The crude OR of AD for exclusive breastfeeding was 0.60 (95% CI 0.40; 0.91). However mothers in the BF group differ from mothers in the CMF group with regard to several aspects: higher atopic risk level (p = 0.036), higher level of education (p = 0.001), fewer pets in the homes of mothers in the BF group (p = 0.001), and more BF group mothers living in the city of Munich than in the more rural area of Wesel (p = 0.001). After adjustment for the atopic risk factors and confounders, the OR for AD decreased to 0.47 (95% CI 0.30; 0.74).

These differences between the BM and CMF groups have considerably translated into the mothers’ feeding behavior with regard to the infants' age at first introduction of solid foods and solid food diversity in the first months of life. Solid foods were classified according to the types of food (dairy products, eggs, cereals, legume, vegetable, fruit, nuts, meat, fish and others), the diversity of the children’s diet was constructed by summing up the number of different types of solid food that the child had been fed during the first 24 weeks [16]. While only 5.4% of the breastfeeding mothers had introduced solids to the infants’ diet in the first 16 weeks after birth, 30.9% of mothers from the CMF group had done so. No solids had been given at the age of 24 weeks in 49% of the breastfed children compared to 19% of the bottle-fed children. The main factor for delaying solid food introduction beyond the first 6 months of life was the presence of AD in one of the child’s family members.

The results showed an increasing trend in the AD incidence with the later introduction of solid foods and a decreasing trend with food diversity, but no significant effect modification of solid food was found (χ² test, p = 0.89 for the number of food groups).

However, the duration of breastfeeding, age at introduction of solid food and the diversity of solid food are not independent factors because extended breastfeeding is associated with delayed solid food introduction and a reduced diversity of solid food in the diet. On the other hand an extended duration of breastfeeding and consequently delaying the introduction of solid food are associated with parental atopic risk status and educational level.

This study does not confirm the results of the study by Fergusson et al. [7, 8] which showed that a reduced diversity of solid foods in the first 4 months of life, but not breastfeeding itself, had a preventive effect on the incidence of AD. Several reasons for this have been discussed. The main difference was that mothers in the GINI study were provided with detailed recommendations to breastfeed and avoid solid foods for at least 4 months, while parents in the prospective observational development study in New Zealand did not get any
nutritional advice. This resulted in a much lower percentage of children who received solid foods in the first 4 months of life (GINI 5.4% in the breast milk group, 30.9% in the CMF group, compared to 38.3 and 80.1%, respectively, in the New Zealand study). Another important difference is that in the GINI study all children came from atopic families, while the population in the New Zealand study was nonselected.

The increased public awareness in the last 1–2 decades regarding the association between the development of allergic diseases in the child and the family history, on the one hand, and the possibility for allergy prevention by certain dietary interventions, on the other hand, has led to behavioral changes [16, 17]. Parents in the GINI study, who were recruited for the study 15 years later than the parents in the New Zealand study, may have been much more prepared to breastfeed longer and to introduce solid foods later because they were atopic themselves. Therefore, one explanation for the results of the GINI study may be reverse causality, that is, cause and effect are reversed.

Reverse causality is also considered as one reason for the results in a population-based prospective birth cohort study by Zutavern et al. [17]. They followed 642 children prospectively from birth to 5 years of age and looked into the association between the development of preschool wheezing, transient wheezing, atopy or eczema and solid foods. They could not find a protective effect of late solid food introduction, but instead a statistically increased risk of eczema in relation to the late introduction of egg (adjusted OR 1.6, 95% CI 1.1–2.4) and milk (adjusted OR 1.7, 95% CI 1.1–2.5). The risk of preschool wheezing was also, though not significantly, increased when egg was introduced late (adjusted OR 1.5, 95% CI 0.92–2.4).

From more recent studies [9, 11, 15–17] it seems that evidence for the preventive effect of the late introduction of solid foods and low diversity as recommended in feeding guidelines is rather weak when confounding factors like reverse causality are considered. This is not surprising since the dose of allergen is only one factor in the complex mechanism for the development of allergic disorders and the induction of oral tolerance which protects the individual from food hypersensitivity. In a recent review by Chehade and Mayer [18] factors involved in oral tolerance were discussed, some of which are related to the antigen and antigen handling, and some to the host, where the genetic background, age and intestinal microflora are important players in the complex scenario of allergy development or tolerance.

**Conclusion**

Although all feeding guidelines for the prevention of allergic diseases recommend the late introduction of solid foods to the infant’s diet, the scientific evidence for this is scarce and mainly based on two studies. More recent studies on the association between solid food introduction and the development
of allergic diseases have looked in more detail into the conditions under which solids were introduced. The increasing public awareness of an association between genetic background and the development of childhood allergic diseases, and the possibilities for nutritional preventive interventions has led to changes in feeding behaviors which may explain the conflicting data of older and more recent studies. When the reverse of cause and effect (reverse causality) is considered, early solid food introduction seems to be less harmful than previously thought.

References

Discussion

Dr. Zeiger: With respect to your last report, what are your recommendations with regard to the more recent data that are available?

Dr. von Berg: First of all it is almost impossible to do randomized controlled studies in the area of solid food introduction. But on the basis of what we see here in the latest studies, I think that there is evidence that allows us to be a little less rigid with our recommendations. For example I think the American recommendations on solid food introduction are far too strict. I would say that the introduction of solid foods should be postponed to after the 4th month, but I would not say that the children should not have eggs until 2 years and milk until 1 year of age, I think that is too much.

Dr. Klish: The natural way to feed infants is not only to breastfeed but to share solid foods. In most ancient cultures, not only did infants receive antigens of a broad variety through breast milk but mothers tended to share whatever they were eating with their infants by pre-masticating the food and spitting it into the mouths of their babies. So from a teleological point of view it makes sense that exposure to antigens early is good for infants. However, in saying that, one of the recent issues has to do with weight gain of infants who have solid foods introduced to them early and what role this plays in the obesity epidemic. I wonder if you have any comments on either of these points?

Dr. von Berg: Yes, as we heard yesterday, I think nobody argues against recommendations to breastfeed for 4–6 months, and what we saw here in this study is that breastfeeding mothers don't give solids early. The normal way of feeding babies is breastfeeding, they don't need to get solid foods in the first 4 or 6 months, and probably by that we reduce the risk of early weight gain.

Dr. Björkstén: My comment is actually similar to that of Dr. Klish. There is traditionally no such thing as exclusive breastfeeding. In every culture there has always been early introduction of solids. Exclusive breastfeeding with no solids is a novel situation. Suppose that the introduction of solid foods affects the gut microbiota, you mentioned apples, carrots, potatoes, fibers which all would affect the gut microbiota but are poorly antigenic. There is a difference in time between the New Zealand study and the GINI study and things have changed. The New Zealand diet in the 1980s and late 1970s when this study population was collected was different from a modern diet, and there have been changes in the gut microbiota. I think that your own data fit more nicely into an ecological effect and it has nothing to do with the immunology that we have been searching for years. Is this very provocative to you?

Dr. von Berg: No, it is not provocative at all. In all nutritional intervention studies, for example the studies by Halken et al. [1] and Kalliomaki et al. [2], there was hardly any difference in sensitization regardless of what the children were fed. But what was interesting I think, if we look at exposure and sensitization here, the highest sensitization was to egg, and this is probably not because these children got so much egg, but because they are very susceptible for producing IgE antibodies.

Dr. Björkstén: Many years ago some studies showed that it is an excellent predictor for allergic disease as the children were followed up to age 15, but it is not the atopic march on which we based many of our studies. It only indicates that you have the propensity for IgE antibody formation as egg is a more common antigen to be exposed to.

Dr. von Berg: Yes, and perhaps a very aggressive antigen. One question is if, by manipulations with hydrolysates, for example, we could avoid sensitization to hen's egg, whether we could then avoid asthma, because we know from these epidemiological studies that the early sensitization to hen's egg is almost a predictor for later asthma. I just wanted to add one thing. In the GINI study at 1 year we looked at those children who had hen's egg-associated atopic dermatitis, and saw that the only hydrolysate that actually reduced this atopic dermatitis was the extensively hydrolyzed casein formula. In following these children we will see whether the extensively hydrolyzed casein
formula does something on the development from hen’s egg-associated atopic dermatitis to asthma.

**Dr. Björkstén:** That is based on the assumption that hen’s egg exposure is subsequently a risk factor for respiratory allergies. I think there is absolutely no evidence for that. What it shows is that the person who is prone to make IgE antibodies relieves his propensity to egg and milk, because we know this natural story from the inhalant allergens and we know that the person who develops asthma is often sensitized at an early age, but there is absolutely no evidence that the avoidance of these antigens early in life actually prevents the sensitization. Indeed it is the other way around, it seems to be promoting tolerance, the early exposure, so what I think is that, yes, if you avoid development of IgE antibodies to egg you have a marker but it is a marker for the constitution rather than having anything to do with risk factor.

**Dr. von Berg:** At least this analysis nicely shows that early introduction of vegetables is not a risk factor of sensitization.

**Dr. Hanson:** With due respect to my colleagues I would like to protest against the claim that the procedures from traditional societies are to be accepted as useful and positive, because we are now in the age of evidence-based medicine and I have rather extensive experience of procedures, of handling newborns in rural Pakistan, where we could define a number of these practices as being very dangerous. This includes giving a plant extract that was kept between the delivery of each child and was heavily contaminated, and was given the first day. Furthermore, the start of breastfeeding was delayed for 1–3 days by giving this and other infected material and so on. So I would like to remain with our modern medicine.

**Dr. Sampson:** I just want to ask you, how good an indicator is sensitization? In other words, we know from the food allergy data, for example, that of all the positive skin tests we see, the minority really reflect clinical disease, and I would suspect if we were to do the same thing with aero allergens we would see the same thing. So by simply looking at sensitization, is it even a useful marker?

**Dr. von Berg:** Sensitization in general is not enough. Probably, as you did in food allergy, we should look at the degree of sensitization. We defined sensitization as positive when it was just measurable, and this is probably not enough. But the results were not much different when we took CAP class 2, this is 0.7 kU/l, but what we have not done up to now is to correlate the CAP class with the severity and the course of disease. I think actually sensitization might be a marker or predictor for whether atopic dermatitis is transient or persistent. We have many children with atopic dermatitis in the study who are not sensitized, and these are probably the ones who have transient atopic dermatitis, and we are going to look at that.

**Dr. Lake:** As pediatricians we are asked to delay the introduction of shellfish and peanut until after 15–18 months, even in the absence of a family history of food allergy. Do you have any data, now out 3 years, to support this recommendation?

**Dr. von Berg:** No, not yet.

**Dr. Björkstén:** I would again reiterate this sort of sensitization. I think that we really have to look at the data that there is no causal relationship. One of the things we are learning from the traditional societies, in this case Estonia again, is that over 60% of an unselected cohort of healthy newborn babies have circulating IgE antibodies to foods, which means that we have done something wrong in the laboratory although it is the same people and we actually retested it. In Estonia there is no relationship to disease and it tells us that IgE development is an immunological phenomenon which is part of the development of immune responses and tolerance. So by avoiding egg sensitization, not even today is it reasonable to suspect that it would prevent respiratory allergies or that it obviously can play a role in food allergy in infants.

**Dr. von Berg:** Actually we looked at ‘sensitization’ at CAP class 0.5 and found a lot of so-called sensitization which had no implication at all, so this is what you found as well?
**Dr. Björkstén:** No, I am not talking about the borderline, that was one of the Hattevig studies. No, these were actually clearly positive CAP 1 and CAP 2, but we didn’t see all 4 classes, but the 1 and 2 are there and they are not related to disease in Estonia, while in Sweden it is beautifully related.

**Dr. Wang:** We see a lot of patients with atopic dermatitis and they are breastfeeding. Do you think the food allergen goes through the breast milk and the infants get these allergens? Did you have this kind of situation in your studies? If so it might have affected your results. On the other hand, we should make sure the mothers aren’t giving solid food especially hen’s egg and cow’s milk.

**Dr. von Berg:** We saw in the GINI study that there were some children who actually developed atopic dermatitis while they were being exclusively breastfed. But whether that comes through the mother or whether that comes, as discussed before, through some dermal sensitization, for example, is not known. In such cases when the child develops atopic dermatitis we tell the mother to stop breastfeeding for a while, but that she should extract the milk by breast pump. If the child got better then of course she should stop breastfeeding altogether, otherwise she could go back. We had many cases where it was not the breast milk to which the child reacted although the atopic dermatitis started while it was being breastfed.

**Dr. Sorensen:** Do you think that eventually there will be different recommendations regarding the introduction of solid foods depending on breastfeeding versus formula feeding or even different types of formula, and that the single recommendation that we presently have from the various regulatory organisms is no longer justified?

**Dr. von Berg:** No, I would say breastfeeding of course for 4–6 months and no different recommendations for breastfed or formula-fed children with regard to solid food introduction. From our studies we don’t have any evidence that solid food introduction other than egg has any effect on outcome. Therefore I would at least say that we should not be that rigid anymore.

**Dr. Tjesic-Drinkovic:** The recommendation for exclusive breastfeeding for 4–6 months gives us a rather long 2-month period to start with solids. According to your data and other knowledge, i.e., on inducing tolerance, would you be in favor of earlier introduction of solid foods, say closer to 4 months than 6 months?

**Dr. von Berg:** If a child is hungry he has to have something and that is more often after 4 than after 6 months, and from our data that doesn’t make a difference. As you see from our data it depends probably on what you give. If you give carrots and potatoes you should not have any problems.

**Dr. Klish:** It is my impression that the rigidity of the recommendations from the American Academy of Pediatrics has come primarily from the Breast Feeding Task Force of the academy, and they feel that the early introduction of solids (4 months of age) somehow interferes with the continuation of breastfeeding itself. That is why these recommendations have become more rigid. Would you care to comment on that relationship?

**Dr. von Berg:** I can’t talk for the Americans here but it sounds logical that if you have a strong breastfeeding task force within the academy they will try to influence the recommendations in order to improve breastfeeding.

**References**