An infant born at 24 weeks of gestation has to spend at least the first 3 months of their post-natal life achieving the term infant size, maturation, and developmental milestones outside the womb

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Introducing Solid Foods to Preterm Infants in Developed Countries by D.J. Palmer and M. Makrides

Key insights

This article outlines the challenges faced in balancing the benefits and risks of solid food introduction to preterm infants with the limited evidence available.

Current knowledge

Preterm infants are a heterogeneous population primarily because their gestational age at birth could vary from 23 to 36 weeks and nutritional requirements are increased compared to term infants. In addition to any ongoing medical conditions, developmental readiness is an important factor that should be considered prior to commencing solid foods for both ends of the preterm spectrum. Based on the current evidence, 3 months (13 weeks of corrected age) seems to be an appropriate age to commence high-protein, energy- and nutrient-dense solid foods for otherwise healthy preterm infants.

Practical implications

Individual advice regarding the introduction of solid foods should take into account the infant's gestational age at birth, early nutrition intake, current nutritional status and requirements as well as developmental progress and readiness. Current guidelines for the introduction of solid foods to term infants cannot be directly translated to preterm infants, and further research is needed to provide evidence-based guidelines.

Recommended reading

King C: An evidence-based guide to weaning preterm infants. *Paediatr Child Health* 2009;19:405–414.

Balancing the benefits and risks of introducing solid foods to preterm infants in developed countries. By using the corrected age, both ends of the preterm spectrum would be eating solid foods within the ideal period from a developmental point of view (arrows). The earliest-born infants at 23 weeks of gestation would have an uncorrected age of 7 months, while those infants born closer to term at 36 weeks of gestation would have an uncorrected age of 4 months (see text for details).

Introducing Solid Foods to Preterm Infants in Developed Countries

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Key Messages

- Infants born preterm (<37 weeks of gestation) have increased nutritional requirements.
- The development of good head control is important for the safe eating of solid foods.
- Based on the currently available evidence, 3 months, or 13 weeks of corrected age, seems an appropriate age to commence high-protein, energy- and nutrient-dense solid foods for most preterm infants, while ensuring optimal nutritional intake from birth in the liquid diet.
- Using 3 months corrected age as a guide, the earliest-born infants at 23 weeks of gestation would have an uncorrected age of 7 months, while infants born closer to term at 36 weeks of gestation would have an uncorrected age of 4 months, hence both ends of the preterm spectrum would be eating solid foods within the ideal period from a developmental point of view.
- Further research is required to provide evidence-based guidelines regarding the introduction of solid food for preterm infants in developed countries.

Key Words

Complementary feeding · Developmental readiness · Infant eczema · Preterm infants · Solid food introduction

Abstract

The addition of solid foods to an infant's diet is required to provide adequate nutrition, as eventually an infant will be unable to consume a sufficient volume of breast milk to meet their nutritional needs. The timing of this important dietary change for infants born preterm (<37 weeks of gestation) should take into consideration their delayed early gross motor developmental progress, increased nutritional requirements, organ immaturity, increased gut permeability and increased risk of hospitalization from infections. Good head control is important for safe eating of solid foods: this developmental milestone may be delayed in preterm infants up to 3 months of corrected age. One randomized controlled trial has demonstrated improved nutritional intakes with the introduction of nutrient-dense solid foods from 13 weeks of uncorrected age, resulting in improved nutritional iron status and greater rate of growth during infancy. There is neither current evidence for an increased infection rate with an early introduction of solid foods in developed countries, nor is there evidence that in preterm infants maturation of renal function is reduced. However, one observational study has determined that preterm infants who had 4 or more solid foods introduced prior to 17 weeks of corrected age, or who had any solid foods introduced prior to 10 weeks of corrected age, had an increased risk of eczema development. A compromise is needed to balance the nutritional benefits of commencing solid foods from 13 weeks of uncorrected age with the risks of increased eczema development, along with

ensuring developmental readiness. Based on the current evidence, 3 months (13 weeks) of corrected age seems to be an appropriate age to commence nutrient-dense solid foods for most preterm infants. Further research, with an emphasis on immediate as well as longer-term consequences, would be valuable to provide more specific evidence-based guidelines regarding the introduction of solid food for preterm infants.

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Introduction

The introduction of solid food is required by any infant in order to provide adequate nutrition, as eventually they will be unable to consume a sufficient volume of breast milk to meet their nutritional needs. Infants born preterm (<37 weeks of gestation) have increased nutritional requirements, especially for energy [1, 2], protein [2–4], long-chain polyunsaturated fatty acids [5, 6], iron [7, 8], zinc [9, 10], calcium [11] and selenium [12, 13]. As a result of preterm birth, these infants generally have limited nutrient stores because they have missed the crucial last trimester of pregnancy when there is active transfer and accumulation of nutrients to the fetus as well as a rapid rate of growth. The high nutrient demands as well as the organ immaturity of preterm infants combine to render it difficult to achieve dietary intakes that will allow preterm infants to match their in utero growth rates.

At birth, an infant's gestational age will have an influence on its nutritional status. After birth, nutritional progress will be further affected by the amount and type of milk feeding (breast milk/infant formula/both), use of human milk fortifiers and/or preterm infant formula, as well as vitamin and mineral supplementation. Some infants born preterm also have ongoing medical conditions, such as chronic lung disease, which further increase nutritional requirements [14]. Hence, two infants born with the same weight at 28 weeks of gestation could have significant differences in their postnatal nutritional status at 12 weeks uncorrected age (i.e. 0 weeks corrected age).

Hence, two infants born with the same weight at 28 weeks of gestation could have significant differences in their postnatal nutritional status at 12 weeks uncorrected age (i.e. 0 weeks corrected age).

Preterm infants are a heterogeneous population largely because their gestational age at birth could vary between 23 and 36 weeks. During the last trimester of pregnancy, there is significant fetal growth as well as organ maturation and development. An infant born at 24 weeks of gestation has to spend at least the first 3 months of their postnatal life achieving the term infant size, maturation and developmental milestones outside the womb. Thus, clarity is important when describing the current age of an infant as either uncorrected (postnatal age, number of actual weeks since birth) or corrected (postterm age, taking into account gestational age at birth).

Current guidelines for the introduction of solid foods to term infants cannot be directly translated to preterm infants. However, there has been limited research regard-

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ing the optimal age and type of foods to be introduced and whether this period of important dietary change influences later health and development. This review examines the available evidence on benefits and potential harms of the timing of solid food introduction to infants born preterm (<37 weeks of gestation).

Preterm Infants and Developmental Progress

The development of good head control is important for the safe eating of solid foods. Preterm infants have been observed to have delayed early gross motor development when compared with infants born at term, even after correction for prematurity [15]. Therefore, developmental readiness is an important factor that should be considered prior to commencing solid foods. In infant feeding, parents are often advised that if a baby has a reduced tongue thrust (protrusion) reflex, can sit in a stable supported position, can hold their head up well, opens their mouth, and leans forward towards the spoon, then they are developmentally ready for solid food.

Table 1. Introduction of solid food practices: observational studies on low-birth-weight term or preterm infants

Study	Participants	Sample size	Gestational age (GA), weeks Birth weight (BW), kg	Infants with solid food introduced before 5 kg %	Infant age at first solid food introduction weeks	Infants with solid food introduced prior to 4 months (corrected age) %	Type and frequency of first foods introduced
Norris et al. [24], 2002	preterm infants, born Jan 1997 to Dec 1998 UK	n = 253 data on 253 infants (100% completion) (including 34 twins and 3 sets of triplets)	mean GA = 34.4 ± 1.83 (range 28–36) mean BW = 2.34 ± 0.49 (range 0.96–3.60)	21	mean age 17.1 ± 0.23 from birth mean age 11.5 ± 0.21 from term	95	84.6% baby rice 2.8% fruit
Morgan et al. [23], 2006	low-birth-weight infants, born 1996–1998 UK	n = 198 (n = 158, 81.9% singleton births)	median GA = 33 (range 24–42) median BW = 1.80 (range 0.6–2.5)	50	median age 17 (range 8–36) from birth median age 11 (range –1 to 27) from term	not reported	82.4% baby rice
Fanaro et al. [25], 2007	preterm infants, born Jan 2004 to Dec 2005 Italy	n = 230 data on 156 infants (67.8% completion) (including 14 twins and 1 set of triplets)	mean GA = 32.6 ± 0.24 (range 24–36) mean BW = 1.981 ± 0.0541 (range 0.595–4.06)	18.1	mean age 22.2 ± 0.4 from birth mean age 15.1 ± 0.39 from term	61	46.8% fruit 29.1% rice in a vegetable soup

The age at which solid food is introduced is thought to be crucial for many infants to learn to eat, as during the first year of life most infants transition from suck feeding a liquid diet to chewing more textured foods typical of the family diet. It is not known whether the timing of these feeding-stage progression milestones are preprogrammed or influenced by oral experiences, but infants who lack the opportunity to practice various feeding skills at appropriate ages appear to be at risk of feeding problems later [16]. It is thought that if solids are introduced too late, some infants can develop a resistance to having anything but milk in their mouth. With regard to these considerations, the ideal timing for textured food introduction is thought to be between 6 and 9 months of age [17–19]. Hence, King [16] has concluded that most preterm infants should be offered textured lumpy solid foods before 9 months uncorrected age. There is also the belief that the introduction of solid foods assists speech development through an increased variety of use of tongue and jaw muscles. Taking developmental issues into consideration, King [16] has suggested that most preterm infants may be ready for solid foods between 5 and 8 months of uncorrected age, provided the infant is at least 3 months of corrected age, i.e. when gross motor development should enable safe eating.

Current Guidelines regarding the Introduction of Solid Foods to Preterm Infants

For term infants, guidelines have been changing over the past 40 years regarding the optimal age to introduce solid foods. In the 1970s, the general guideline was to introduce solid foods from about 4 months of age; in the 1980s, it was from 3 to 6 months of age, and in the 1990s it was from 4 to 6 months of age. In 2001, the World Health Organization (WHO) [20] changed its global recommendation to around 6 months of age to encourage exclusive breastfeeding until that time. In 2008, the European Society for Pediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition reviewed current knowledge and practices and concluded that in European industrialized countries, complementary feeding should not be introduced before 17 weeks (4 months) and no later than 26 weeks (6 months) of age [21].

However, for preterm infants such guidelines are lacking. The only guideline relevant to introducing solid foods for preterm infants was the advice from the Department of Health in the United Kingdom published in 1994 [22], which recommended the introduction of solid foods when the preterm infant reaches a weight of 5 kg, has lost the extrusion reflex, and is able to eat from a spoon. Unlike the complementary feeding guidelines for term infants, this guideline does not include an age recommendation.

Introducing Solid Foods to Preterm Infants: Common Practices

With limited guidelines available, observational studies provide information regarding common practices of introducing solid foods to preterm infants. Table 1 summarizes the relevant published studies from the UK [23, 24] and Italy [25] since 1994. Two of the cohorts [24, 25] involved infants born preterm and one investigated infants born with low birth weight (including some infants born at term) [23]. Despite the 1994 UK Department of Health [22] guideline recommending that solid foods commence when the infant born preterm reaches 5 kg, 18% of infants born preterm in the Italian study and 21–50% of the UK infants were introduced to solid foods prior to reaching this target weight. In the Italian cohort [25], there was a direct relationship between weight at birth and weight at weaning ($r = 0.55$; $p < 0.001$). Fanaro et al. [25] also found that extremely- or very-low-birth-weight infants were older but lighter when solid foods were introduced when compared with low- or normal-birth weight infants. In the UK low-birth-weight cohort [23], the age of introducing solid foods was found to be associated with infant birth weight ($r = -0.293$, $p < 0.001$), whereas in the other UK preterm cohort [24] no effect of birth weight on solid food introduction timing was found. Fewtrell et al. [26] has also reported data on a cohort of preterm infants ($n = 228$), born between 1995 and 1997 in the UK, and found that birth weight, weight at 6 weeks, and weight gain between birth and 6 weeks (corrected age) were not predictors of the age at which solid foods were introduced. The lack of a consistent correlation between weight at birth or weight gain progress and age when solid foods are introduced into the diet of preterm infants may be explained by their varied postnatal experiences, including the level of medical intervention required and their individual progress with feeding tolerance.

Furthermore, the majority of infants born preterm are introduced to solid foods before the 4 months (corrected) guideline for term infants as recommended by the European Society for Pediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition [21] (table 1). Table 1 also illustrates practice differences between countries in the age of commencement of solid foods, and such

differences have also been observed in a multi-national comparison study by Yee et al. [27]. This comparative study [27] investigated the introduction of complementary foods in preterm infants ($n = 375$) in 3 countries (Chile, $n = 49$; United Kingdom, $n = 51$, and the United States, $n = 275$) and found that by 4 months corrected (postterm) age, 98% of the infants in the UK, 67% in the US and 41% in Chile had been introduced to solid foods. Interestingly, there also appear to be differences between these countries with regard to the type of solid foods first introduced to preterm infants (table 1). With the exception of iron-fortified baby rice, early solid foods are not good sources of the nutrients that preterm infants require, such as energy, protein, long-chain polyunsaturated fatty acids, zinc and calcium.

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With regard to possible influencing factors, younger maternal age [24, 25] and formula feeding have been found to be associated with an earlier introduction of solid foods to preterm infants [24–26]. Only in the study by Norris et al. [24] was an earlier solid food introduction associated with male infants. Fanaro et al. [25] found that female infants were significantly lighter both at birth and at weaning, but no differences in this study were found for weaning age between the sexes. In summary, observational studies in developed countries have found that solid foods are introduced to the majority of preterm infants prior to 4 months of corrected age and that the solid foods introduced were initially low nutrient-dense foods. Observational studies inform us of common practices but intervention trials are required to evaluate the benefits and potential harms associated with the timing and type of solid foods introduced to preterm infants.

Randomized Controlled Trials

To date, there has only been one randomized controlled trial (RCT) conducted in the United Kingdom from 1998 to 1999 that has investigated the timing and nutritional quality of solid foods for preterm infants. This trial included 68 preterm infants who had a mean birth weight of 1.47 ± 0.434 kg and mean gestational age of 31.4 ± 2.9 weeks [28]. Families randomly allocated to the intervention group ($n = 37$) were advised to introduce

solid foods from 13 weeks postnatal age, provided the infant weighed at least 3.5 kg. They were also advised to use high-protein (2.3–5.0 g/100 g), energy-dense (300–450 kJ/100 g) solid foods as well as to use preterm infant formula milk to mix with the solid foods. The control group (n = 31) was advised to introduce solid foods from 17 weeks of postnatal age, provided the infant weighed at least 5.0 kg. They were also advised to use high-protein (1.5–5.0 g/100 g), energy-dense (250–450 kJ/100 g) solid foods, noting that the energy density and the protein content had lower minimum values, 250 kJ/100 g and 1.5 g/100 g, respectively, compared with the intervention group.

The mean postnatal age at which the first solid food was introduced was significantly younger for the intervention group at 14.9 weeks (6.3 weeks of corrected age) compared with 17.8 weeks (9.9 weeks of corrected age) for the control group ($p = 0.003$). They found that at 6 months of gestational corrected age, the mean daily intakes of energy, proteins and carbohydrates were significantly higher for the intervention group while other nutrient intakes were higher without reaching statistical signifi-

The question that arises from these findings is whether the observation of a reduced risk of infection was related to the introduction of formula feeding or the commencement of solid foods.

cance [28]. Other significant findings for the intervention group were the mean hemoglobin concentration increasing between 0 and 6 months (corrected age) and the mean daily iron intake being higher at 12 months (corrected age). In contrast, the mean serum iron for the control group decreased during this time. The infants in the intervention group also had a greater mean rate of growth in length per week (5.1 vs. 4.9 mm; $p = 0.04$) between 0 and 12 months of corrected age. However, there were no significant differences between the two groups at any time point for weight and head circumference measurements [28].

The strength of this RCT is that it included a number of nutritional outcomes, including weight, length, head circumference measurements, dietary intake assessments of energy, protein and minerals, and levels of hemoglobin, serum iron and serum ferritin. A major limitation of the study is that more infants ($p = 0.02$) in the intervention group had received breast milk fortifier than in the

control group, hence providing these infants with increased nutrients in their early liquid diet also. Other limitations of this study include the small sample size and the fact that there are no outcome data on possible short- or long-term harms of early solid food introduction, as discussed further below.

Possible Harms of an Early Introduction of Solid Foods

Risk of Infection

In certain countries or communities, the risk of infection from the introduction of solid foods is high due to exposure to contaminated water, foods or feeding equipment. Although food safety issues must be given a priority, they can be of varying importance depending on the environment. The PROBIT study [29], conducted in Belarus, involved 17,046 term infants and found decreased gastrointestinal infection in infants exclusively breastfed for 6 months compared to infants exclusively breastfed for 3 months. More recently, in Greece, Ladomenou et al. [30] followed 926 term infants up to 12 months of age and found that infants who had been exclusively breastfed for 6 months had fewer infectious episodes of acute respiratory infection, acute otitis media and thrush than their partially breastfed or non-breastfed peers. The question that arises from these findings is whether the observation of a reduced risk of infection was related to the introduction of formula feeding or the commencement of solid foods. A study in the United Kingdom [31] involving 15,980 term infants found an increased risk of hospitalization due to diarrhea or lower respiratory tract infection in formula-fed infants, with no effect of the age of solid food introduction on the risk of hospitalization. This result suggests that it is the cessation of breastfeeding that is the predictor of infection risk. It should be noted that all three studies described above studied term infants. These data may not directly extrapolate to preterm infants, who are more vulnerable and more likely to be hospitalized with infections than their term-born counterparts.

With specific regard to preterm infants, Morgan et al. [32] collated data from two infant formula interventional trials, involving preterm infants (total $n = 467$), which were conducted between 1993 and 1997 in the United Kingdom. In a combined analysis from these two trials, there was no evidence for an association between the introduction of solid foods ≤ 12 or >12 weeks corrected (postterm) age and the number of episodes of gastroen-

Hence, the majority of infants born preterm should have sufficient renal function to process the increased renal solute load of nutrient-dense solid foods.

teritis (diarrhea plus vomiting) or lower respiratory tract infections. Thus, the available data do not support an association between the timing of solid food introduction for preterm infants and the incidence of common infant infections in developed countries.

Maturation of Renal Function

Another important consideration is possible immature kidney function as a result of preterm birth. This is relevant as the recommendation to use nutrient-dense solid foods in the RCT by Marriott et al. [28] would result in a higher protein intake and hence an increased renal solute load. However, it has been found that renal function maturation occurs after birth regardless of whether an infant is born term or preterm [33]. D'Souza et al. [34] investigated the serum biochemistry levels of 50 preterm infants (born at 28–32 weeks of gestation with birth weight <1,501 g) after leaving hospital and found no differences between those infants (n = 26) who had solid foods introduced between 2 weeks and 4 months (corrected age) compared to those infants (n = 24) with solid foods introduced at 4–6 months (corrected age). Hence, the majority of infants born preterm should have sufficient renal function to process the increased renal solute load of nutrient-dense solid foods.

Development of Allergies

As preterm infants are known to have increased gut permeability [35], it has been proposed that they may be at higher risk of developing food allergy due to increased exposure to foreign food proteins associated with the early introduction of solid foods. Liem et al. [36] have reported on the 1995 Manitoba Birth Cohort in Canada, of which 881/13,980 (6.3%) infants were born preterm (gestational age <37 weeks). The overall rate of food allergy in this cohort was 4.2%, and no significantly increased risks were found for food allergy development from birth to 7 years of age for either prematurity or low birth weight. In Norway, Kvenshagen et al. [37] found that there was no difference in the prevalence of eczema/atopic dermatitis at 2 years of age between 32/161 (19.9%) children born

preterm and 63/351 (17.9%) born at term. Adverse reactions to food were found in 15.8% of children with atopic dermatitis, with a similar prevalence in children born preterm (15.6%) compared with those born at term (15.9%). There was also no difference in the prevalence of IgE-mediated food allergy in children with atopic dermatitis between infants born preterm (2/32, 6.2%) and term (6/63, 9.5%). In both studies, the lack of a difference in food allergy between term and preterm infants may be explained by another study reporting that infant gut permeability appears to rapidly adapt after birth, regardless of gestational age or birth weight [38].

However, of particular significance are the results of Morgan et al. [39], whose observational study investigated 257 preterm infants born in the UK and found that those infants who had 4 or more solid foods introduced at ≤ 17 weeks of corrected age had an increased risk (odds ratio 3.49) of developing eczema by 12 months of corrected age. This study also reported that the introduction of solid foods prior to 10 weeks of corrected age was associated with an increased risk (odds ratio 2.94) of eczema development. This study had a high prevalence of eczema (35.8% of the infants at 12 months, postterm age) and a high withdrawal rate (21.9%), suggesting possible participation and completion bias. In contrast to this finding, another paper by the same group published in

Given these contrasting reports, RCTs specifically designed to assess the benefits and risks of age when and the way in which solid foods are introduced to preterm infants are needed.

the same year [32] collated data from two UK infant formula interventional trials involving preterm infants (total n = 467). This latter paper [32] found no evidence of an association between the age of introducing solids (≤ 12 or >12 weeks, postterm age) and the incidence of eczema, with a total of 21% of the preterm infants reported to have developed eczema by 9 months (corrected age). Given these contrasting reports, RCTs specifically designed to assess the benefits and risks of age when and the way in which solid foods are introduced to preterm infants are needed.

Conclusion

With limited evidence available and the heterogeneity of the infant population born preterm, individual advice regarding the introduction of solid foods should take into account the infant's gestational age at birth, early nutritional intake, current nutritional status and requirements as well as developmental progress and readiness. The only published guidelines specifically for infants born preterm [22] recommend that the introduction of solid foods be advised when the infant reaches a weight of 5 kg, has lost the extrusion reflex and is able to eat from a spoon. However, we were unable to find any evidence to support the 5-kg weight recommendation. Some infants whose weight gain and growth have slowed may benefit from energy-dense solid foods (as introduced in the RCT by Marriott et al. [28]) prior to reaching 5 kg in weight.

In her review on this topic, King [16] also highlighted that the preterm infants born at the shortest gestations could be as old as 10 months of uncorrected age before they reach 5 kg and, thus, may be resistant to having anything but milk in their mouth. Taking developmental issues into consideration, King suggests that most preterm infants may be ready for solid foods between 5 and 8 months of uncorrected age, provided that the infant is at least 3 months of corrected age, i.e. when gross motor development should enable safe eating. Based on the limited available evidence, it could be concluded that a corrected age of 3 months (13 weeks) may be an appropriate age to commence the introduction of solid foods for most pre-

The advice to use high-protein, energy- and nutrient-dense solid foods once solid foods are introduced is important for infants born preterm.

term infants. The earliest-born infants at 23 weeks of gestation would have an uncorrected age of 7 months, while those infants born closer to term at 36 weeks of gestation would have an uncorrected age of 4 months. By using

the uncorrected age, both ends of the preterm spectrum would be eating solid foods within the ideal period from a developmental point of view. Solid food introduction from a corrected age of 3 months (13 weeks) would also reduce the potentially increased risk of eczema development observed by Morgan et al. [39]. Three months of corrected age is later than recommended in the RCT by Marriott et al. [28]; however, ensuring optimal nutritional intake from birth in the liquid diet until solid foods are introduced will improve nutritional status. The advice to use high-protein, energy- and nutrient-dense solid foods once solid foods are introduced is important for infants born preterm. Further research is required to provide evidence-based guidelines specifically for preterm infants and studies should investigate immediate as well as longer-term consequences of the pattern and timing of introducing solid foods on later health and developmental outcomes.

Disclosure Statement

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