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SCIENTIFIC OPINION

Scientific Opinion on the appropriate age for introduction of complementary feeding of infants[1]

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)[2, 3]

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ABSTRACT

Following a request from the Commission, the Panel on Dietetic Products, Nutrition and Allergies was asked to deliver a scientific opinion on the appropriate age for the introduction of complementary food for infants in the EU. Many European countries have adopted the WHO recommendation for the duration of exclusive breast-feeding for 6 months, whilst other countries recommend the introduction of complementary feeding between 4 and 6 months. The Panel agrees with WHO and other authoritative national and international bodies that breast-milk is the preferred food for infants, but the focus in this opinion are the factors which determine the appropriate age for the introduction of complementary food into infants' diets. The Panel has evaluated predominantly studies in breast-fed healthy infants born at term for indicators of an appropriate age at which to introduce complementary food irrespective of existing recommendations on breast-feeding duration and on exclusivity of breast-feeding. The Panel has focussed its evaluation on data from developed countries. On the basis of present knowledge, the Panel concludes that the introduction of complementary food into the diet of healthy term infants in the EU between the age of 4 and 6 months is safe and does not pose a risk for adverse health effects (both in the short-term, including infections and retarded or excessive weight gain, and possible long-term effects such as allergy and obesity). Consistent with these conclusions, presently available data on the risk of celiac disease and type 1 diabetes mellitus support also the timing of the introduction of gluten containing food (preferably while still breast-feeding) not later than 6 months of age. Exclusive breast-feeding provides adequate nutrition up to 6 months of age for the majority of infants, while some infants may need complementary foods before 6 months (but not before 4 months) in addition to breast-feeding in order to support optimal growth and development.

KEY WORDS

Complementary food, complementary feeding, infants, nutrition, health.

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SUMMARY

Following a request from the European Commission, the Panel on Dietetic Products, Nutrition and Allergies was asked to deliver a scientific opinion on the appropriate age for the introduction of complementary food for infants in the EU.

The background of the request is an inconsistency within the EU legislation and between the EU legislation and the relevant Codex Standard. The EU legislation (Article 8 of Directive 2006/125/EC) has been based on the opinions of the Scientific Committee for Food on weaning foods (EC, 1989 and 1990) and provides for the following mandatory labelling: 'the stated age shall not be less than four months for any product'. In contrast to this, the labelling provisions in Directive 2006/141/EC concerning follow-on formula require the label to bear a statement saying that it is suitable only for infants over the age of six months. Furthermore, the Codex Standard for processed cereal-based foods for infants and young children (Section 8.6.4) states that 'The label shall indicate clearly from which age the product is recommended for use. This age shall not be less than 6 months for any product'. The Codex Standard is based on recommendations made in the WHO Global Strategy for Infant and Young Child Feeding.

Many European countries have adopted the WHO recommendation for the duration of exclusive breast-feeding for 6 months, whilst other countries recommend the introduction of complementary feeding between 4 and 6 months.

The Panel agrees with WHO and other authoritative national and international bodies that breast milk (mother's milk) is the preferred food for infants, but the focus in this opinion are the factors which determine the appropriate age for the introduction of complementary food into infants' diets. The Panel does not discuss the health consequences of formula feeding compared to breast-feeding. There are numerous publications which discuss the timing of initiating complementary feeding with regard to breast-fed infants whilst the literature on non-breast-fed infants is limited. Therefore, the Panel considers primarily data obtained in exclusively breast-fed infants and, moreover, focuses on data on healthy infants born at term (at or after 37 completed weeks of gestation).

The Panel considers that the appropriate age for starting complementary feeding is determined by the nutritional adequacy of exclusive breast-feeding at different ages, by potential health benefits (or hazards) related to continued exclusive breast-feeding, including effects on development of motor, cognitive and social functions and by the impact of early feeding on risk of diseases in later life, particularly obesity, cardiovascular disease, diabetes mellitus, etc.

The Panel has evaluated predominantly studies in breast-fed healthy infants born at term, for indicators of an appropriate age at which to introduce complementary food irrespective of existing recommendations on breast-feeding duration and on exclusivity of breast-feeding. The Panel has focussed its evaluation on data from developed countries.

Nutritional adequacy of exclusive breast-feeding

The needs for water, energy, protein, calcium and many other nutrients can be met by exclusive breast-feeding for six months. However, breast milk may not provide sufficient iron and zinc for some infants between the age of 4 and 6 months, and these infants will require complementary foods. Iron deficiency in fully breast-fed 6 month old infants is more likely to occur in boys and in infants with a birth weight of 2500-2999 g.

The Panel concludes that it is justified to assume that exclusive breast-feeding by well-nourished mothers for six months can meet a healthy infant's need for energy, protein and most vitamins and minerals. However, nutrient intake and parallel anthropometric data after the age of 6 months are lacking.

Growth

The Panel considers that the age of introduction of complementary feeding seems not to have a strong impact on growth velocity (both weight and length). However, some data suggest that late introduction, after 6 months, could result in a decline in rate of length and weight gain and early introduction, at <4 months, could result in an increased rate of weight gain which could have long term negative consequences with regard to an increased risk for obesity, type 2 diabetes and cardiovascular disease in adult life.

Developmental aspects

The Panel considers that the available data do not permit to define precisely an age when the introduction of complementary food is needed for neuromuscular development or development of food preference. As long as complementary food is introduced after 4 months of life it does not constitute a problem for the digestive system or the renal function of the infant.

Health aspects

Several studies have examined if the age of introduction of complementary food had an effect on risk of obesity in childhood and found no effect, however, a few studies have suggested that early introduction (before 3-4 months) could result in increased risk for obesity. The Panel considers that the age of introduction of complementary food seems not to have a clear impact on the risk of obesity.

The timing of the introduction of complementary foods has rarely been examined as an independent risk factor for atopic disease in breast or formula fed infants. There is no convincing scientific evidence that avoidance or delayed introduction of potentially allergenic foods reduces allergies in infants considered at increased risk for the development of allergy or in those not considered to be at increased risk. The Panel considers that the available data do not permit a conclusion on the appropriate age for introduction of complementary feeding with respect to allergy prevention or reducing the risk of allergy.

The risk of developing celiac disease and type 1 diabetes mellitus (T1DM) has been related to the timing of gluten introduction into the infant's diet. Based on the available data, the Panel notes that the early (< 4 months) introduction of gluten might increase the risk of celiac disease and T1DM, whilst the introduction of gluten between 4 and 6 months while still breast-feeding might decrease the risk of celiac disease and T1DM. The Panel considers that the available data suggest that gluten containing complementary food could be introduced after 4 months in small amounts preferably while the infant is still breast-fed.

The Panel considers that breast-feeding protects against infectious morbidity. This effect is proportional to the length of breast-feeding. The available evidence suggests that early introduction (< 3 months) of complementary feeding may increase the risk of infectious morbidity. There seem to be no effect of introduction of complementary feeding after 4 months on the risk of infectious morbidity.

There is no evidence to suggest a specific age for the introduction of complementary food based on the risk for type 2 diabetes or of caries, or the need for neuromuscular development.

Overall, on the basis of present knowledge the Panel concludes that the introduction of complementary food into the diet of healthy term infants in the EU between the age of 4 and 6 months is safe and does not pose a risk for adverse health effects (both in the short-term, including infections and retarded and excessive weight gain, and possible long-term effects such as allergy and obesity).

Consistent with these conclusions, presently available data on the risk of celiac disease and T1DM support also the timing of the introduction of gluten containing food (preferably while still breast-feeding) not later than 6 months of age.

Exclusive breast-feeding provides adequate nutrition up to 6 months of age for the majority of infants, while some infants may need complementary foods before 6 months (but not before the age of 4 months) in addition to breast-feeding to support optimal growth and development.

TABLE OF CONTENTS

BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

Cereal-based foods and baby foods are foodstuffs for particular nutritional uses[4] (dietetic foods) and are intended for use by infants[5] while they are being weaned and by young children[6] as a supplement to their diet and/or progressive adaptation to normal food. Essential nutritional requirements for the composition of these foodstuffs, as well as specific labelling rules are laid down in Directive 2006/125/EC[7]. This Directive is the consolidated version of Commission Directive 96/5/EC and consequently no substantial changes have been made since that legislation entered into force.

Regarding the labelling rules and in particular the age of introduction of complementary food in an infant's diet, Article 8 of Directive 2006/125/EC provides for the following mandatory particular labelling: '*the stated age shall not be less than four months for any product*' and allows that *'products recommended for use from the age of 4 months may indicate that they are suitable from that age unless independent persons having qualifications in medicine, nutrition or pharmacy, or other professionals responsible for maternal and child care, advise otherwise'*.

These labelling provisions for cereal-based and baby foods have been based on the opinion of the Scientific Committee for Food (SCF) on weaning foods[8], issued in 1989 and 1990.

At international level, the Codex Standard for processed cereal-based foods for infants and young children[9] covers processed cereal-based foods intended for feeding infants as a complementary food generally from the age of 6 months onwards. Section 8.6.4 states that '*The label shall indicate clearly from which age the product is recommended for use. This age shall not be less than 6 months for any product. In addition, the label shall include a statement indicating that the decision when precisely to begin complementary feeding, including any exception to six months of age, should be made in consultation with a health worker, based on the individual infant's specific growth and development needs. Additional requirements in this respect may be made in accordance with the legislation of the country in which the product is sold'*.

It should be added here that labelling provisions laid down in Directive 2006/141/EC[10] concerning follow-on formula, which are products to be used as the liquid part in a diversified diet of infants, should also bear labelling statements to the effect that follow-on formulae are suitable only for particular nutritional use by infants over the age of six months. Any exception to six months of age should be made only on the advice of a professional.

The relevant rule of labelling laid down in the above mentioned Codex Standard takes into account the recommendations made in the Global Strategy for Infant and Young Child Feeding[11], which states that:

"As a global public health recommendation, infants should be exclusively breast-fed for the first six months of life to achieve optimal growth, development and health. Thereafter, to meet their evolving nutritional requirements, infants should receive nutritionally adequate and safe complementary foods while breast-feeding continues for up to two years of age or beyond."

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[4] Directive 2009/39/EC of the European Parliament and of the Council of 6 May 2009 on foodstuffs intended for particular nutritional uses (recast). OJ L 124, 20.5.2009, p. 21–29.

[5] 'Infants' means children under the age of 12 months

[6] 'Young children' means children aged between one and three years.

[7] Commission Directive 2006/125/EC of 5 December 2006 on processed cereal-based foods and baby foods for infants and young children (Codified version). *OJ L 339, 6.12.2006, p. 16–35*.

[8] Report of the Scientific Committee for Food concerning the essential requirements for weaning foods (1989-1990): http://ec.europa.eu/food/fs/sc/scf/reports/scf_reports_24.pdf

[9] CODEX STAN 074-1981, revised in 2006: http://www.codexalimentarius.net/download/standards/290/cxs_074e.pdf

[10] Commission Directive 2006/141/EC of 22 December 2006 on infant formulae and follow-on formulae and amending Directive 1999/21/EC.*OJ L 401, 30.12.2006, p. 1–33*.

[11] http://www.who.int/nutrition/topics/global_strategy/en/index.html

However, it should be noted that the above statement is based on the report of an Expert Consultation (WHO) on the optimal duration of exclusive breast-feeding[12] which in summary concluded that:

- Exclusive breast-feeding to six months confers several benefits on the infant and the mother. The most important potential advantage is the protective effect against diarrhoea, particularly in developing-country settings.
- Exclusive breast-feeding to six months can lead to iron deficiency in susceptible infants depending on maternal iron status (this can be a problem both in developing and developed countries).
- The available data are insufficient to exclude several other potential risks with exclusive breast-feeding for six months, including growth faltering and other micronutrient deficiencies.

An important point was made that the timing of the progression of an individual infant from a milk-only based diet to a mixed diet should be established on the basis of the advice of a qualified person responsible for maternal and child care.

It should also be noted that a recently published (Agostini et al., 2008) medical position paper on complementary feeding by the ESPGHAN Committee on Nutrition summarises evidence for health effects of complementary foods. The authors consider full breast-feeding for 6 months as a desirable goal, and conclude that in any case complementary feeding should not be introduced before 17 weeks and not later than 27 weeks[13].

Some Member States and stakeholders have suggested that the Directive 2006/125/EC should be reviewed in the light of the latest scientific evidence.

Before proceeding to the revision of Directive 2006/125/EC on cereal-based foods and baby foods, the Commission would ask EFSA for scientific advice on the appropriate age for the introduction of complementary food for infants in the EU as a first step.

Terms of reference as provided by the European Commission

The Commission requests EFSA to give an opinion on the basis of current scientific knowledge and other available information on the suitable age for the introduction of complementary foods in infants' diets in the EU.

In view of the above and in accordance with Article 29 (1) (a) of Regulation (EC) N°178/2002, the Commission asks EFSA to give an opinion on:

- The appropriate age for the introduction of complementary food for infants in the EU.

Assessment

1. Introduction

The first months of an infant’s life are characterised by a diet which consists of one food only, ideally his/her mother’s milk, which provides both the energy and the nutrients needed by the infant for maintenance, growth and development. Indeed, observed energy and nutrient intakes of healthy exclusively breast-fed infants estimated from measured volumes of consumption and milk nutrient concentration have been used as a method to determine the nutritionally and physiologically adequate intakes of infants during the first six months of life (e.g. IoM, 1997). Breast milk substitutes like infant formula have to fulfil the same condition as human milk, namely that they can satisfy by themselves all nutritional requirements of infants “up to the introduction of appropriate

[12] http://www.who.int/nutrition/publications/infantfeeding/WHO_NHD_01.09/en/index.html
[13] http://www.espghan.med.up.pt/position_papers/con_28.pdf

complementary feeding", as both the Codex Alimentarius Standard[14] and the Commission Directive 2006/141/EC state. Whilst the work on the Codex standard for infant formula was started already in 1967, the first European directive on both infant and follow-on formula is from 1991 and was based on reports from the Scientific Committee on Food (SCF) No. 14 (EC, 1983) and No. 23 (EC, 1989 and 1990). The SCF reports underline that infant formula can substitute, if necessary, for human milk as exclusive food until complementary feeding is started, and is suitable for infant feeding in addition to complementary food until the age of one year, whilst follow-on formula should not be fed without complementary food and is intended to substitute for human milk during the period when the child is weaned from the breast or the bottle.

The age at which it is appropriate to introduce complementary foods depends on a range of factors which include the growth and development of the infant and the readiness of the infant to accept a different feeding mode (e.g. spoon versus suckling). The readiness of the infant is determined both by the stage of development and relationship with caregivers, and by his/her (fine, gross and oral) motor abilities. However, beliefs and cultural habits of the family and socioeconomic factors can play the major role in the decision when complementary feeding is started (Wright et al., 2004).

The "optimal duration of exclusive breast-feeding" has been discussed intensively in the last decades (Kramer and Kakuma, 2002; Reilly and Wells 2005; Morgan et al., 2004). This discussion relates directly to the "appropriate age for the introduction of complementary food" (Agostoni et al., 2008), because the next stage after exclusive breast-feeding may be complementary feeding plus continued breast-feeding. The appropriate age can be determined in different ways: 1) by assessing the nutritional adequacy of exclusive breast-feeding at different ages, 2) by looking for health benefits (or hazards) related to continued exclusive breast-feeding, including effects on development of motor, cognitive and social functions or 3) by considering the impact of early feeding modes on risk of diseases in later life, particularly obesity, cardiovascular disease, diabetes mellitus, etc. However, most of the available studies address the difference in health benefit (or hazard) and in risk for diseases between breast-fed and non-breast-fed infants, which means that they compare the effects of two different types of food or diet and do not address the question of timing of the initiation of complementary food. Moreover, the composition of breast-milk substitutes and of infants' diets has changed considerably during the last century, which may have influenced the outcome particularly in older studies and makes comparisons between studies difficult.

Studies which compare breast-fed and formula-fed infants are never randomised because it is the mothers or the parents who decide on the feeding mode of their infant and it is generally considered to be unethical to use randomisation in view of the recognised advantages of breast-feeding. And studies which compare breast-feeding to not-breast-feeding of infants cannot be double blind, because at least the breast-feeding mother is aware of what she is feeding. Kramer et al. (2001), therefore, have used "cluster randomisation" to circumvent ethical objections in the PROBIT study. They compared outcomes of infants born in regions of Belarus where breast-feeding was supported by propagating the "ten steps to successful breast-feeding" of the WHO/UNICEF Baby-Friendly Hospital Initiative, to outcomes of infants born in regions where no such breast-feeding support was offered. Thereby they created and could compare groups of infants with significantly different rates, durations and intensities of breast-feeding without interfering directly. The start of complementary feeding can, however, be randomised in both breast-fed and formula-fed infants. Two randomised studies in Honduras, one in 141 healthy term infants (Cohen et al., 1994) and the other in 119 healthy small-for-gestational infants (Dewey et al., 1999) who had been exclusively breast-fed for four months assessed the effects of early (at four months) compared to late (at six months) introduction of complementary food in addition to continued breast-feeding on growth and a number of other outcome measures at the age of one year. There was no advantage of early compared to later introduction of complementary food. Mehta et al. (1998) randomised 147 full-term infants predominantly formula-fed at the age of three months to receive complementary food ("solids") either early at 3-4 months of age

[14] Codex STAN 72, 1981. Standard for infant formula and formulas for special medical purposes intended for infants. Amended 1983, 1985, 1987, revised 2007: http://www.codexalimentarius.net/download/standards/288/CXS_072e.pdf

or late at six months of age and followed them until they were one year old for the assessment of growth, body composition and energy and nutrient intake and found no difference. The Panel considers that randomisation of infants to complementary feeding at different ages, as long as it is within the range from 4-6 months, is not unethical considering the need for better scientific evidence for the optimal age of introduction of complementary food as documented in this review. The quality of studies which calculate relative risks as a function of the duration of breast-feeding is impaired by imprecise definitions of the intensity of breast-feeding, the diet of the comparator group or both.

Whilst the Panel agrees with WHO and other authoritative national and international bodies that breast milk (mother's milk) is the preferred food for infants, the Panel focuses in this opinion on the factors which determine the appropriate age for the introduction of complementary food into infants' diets, and does not discuss the health consequences of formula feeding compared to breast-feeding.

There are numerous publications which discuss the timing of initiating complementary feeding with regard to breast-fed infants whilst the literature on non-breast-fed infants is limited. This is reasonable because conceptually different formulae can be composed to satisfy the nutritional requirements which change with the age of infant and that could make complementary feeding superfluous from a purely nutritional point of view, whilst the composition of human milk can not easily be modified intentionally. Therefore, the Panel will consider the question of appropriate timing of complementary feeding initiation primarily in exclusively breast-fed infants and will focus on data on healthy infants born at term (at or after 37 completed weeks of gestation).

1.1. Definitions

Complementary feeding, as defined by WHO in 2002 is "*the process starting when breast milk alone is no longer sufficient to meet the nutritional requirements of infants*" so that "*other foods and liquids are needed, along with breast milk*" (WHO, 2002). In this Opinion "complementary feeding" means the period, when complementary foods are given together with either human milk or a breast-milk substitute. The Panel notes that this definition differs from the definition of "complementary feeding" of WHO where it means breast-feeding in addition to complementary food.

Complementary food in this opinion comprises, therefore, all liquid, semisolid and solid foods other than breast milk and breast milk substitutes which are fed to infants which are being weaned from the breast. Complementary food can be beverages, spoon-fed food, or finger-food.

Weaning in this opinion means the time period of gradual reduction of breast-feeding (or infant formula) both with respect to frequency and to volume of breast milk, which starts with the first introduction of complementary food and which gradually leads to a dietary pattern customary in the infant's family during the second year of life.

Breast-feeding is "*exclusive*" if no other food or liquid is given besides human milk and e.g. vitamin drops. It is "*predominant*" if besides human milk the infant receives non-milk liquids like water or energy-free "teas". Exclusive and predominant breast-feeding together are called "*full*" breast-feeding, whilst "*mixed*" breast-feeding means that besides human milk the infant receives infant formula and *"partial"* breast-feeding is breast-feeding together with complementary food (German National Breast-feeding Committee, 2007). The Panel notes that different definitions may be found in publications.

1.2. Current recommendations and practices in European countries

Many European countries have adopted the WHO recommendation for the duration of exclusive breast-feeding, sometimes with qualifications, whilst other countries continue to recommend the introduction of complementary feeding between 4[15] and 6 months (Table 1). However, there has been disagreement between advisory bodies even within the same country. This reflects the limited

[15] In this opinion 4 months means completed 4 months = 17 weeks = 120 days. The 5th month starts the day after the 4 completed months.

scientific evidence from industrialised countries and practices in many countries, with a large proportion of children receiving complementary foods before 6 months and some before 4 months. Since the WHO recommendation is not directly applicable to formula-fed infants, some countries have adopted different recommendations regarding the introduction of complementary foods in these infants.

Table 1: Recommendation from different institutions in Member States (and EEA countries) on the age for introduction of complementary food (Source: Members of the working group on dietetic food, European Commission).

Member state	Year	Institution	Recommended age
Belgium	2006	The federal authority	Between 4 and 6 months
Czech Republic			No general advice. On a case by case basis each advice depends on the health and development of the infant and his/her specific needs
Cyprus			Around 6 months but not earlier than 4 months
Denmark	2009	Danish National Board of Health	About 6 months. If complementary foods are introduced earlier, it should not be before 4 months
Estonia	2006	National Institute for Health Development. Estonian Nutrition and Food Recommendations (2006)	After 6 months, before that only if there is a medicinal need
Finland	2004	Ministry of Social Affairs and Health	Individually, but not later than six months
Germany		National Breast-feeding Committee at the BfR and Forschungsinstitut für Kinderernährung Dortmund	Not before the beginning of the 5th and not after the beginning of the 7th month of life
Greece		Professionals responsible for maternal and child care	Not before 4 months and not after 6 months
Hungary	2009	Ministry of Health	About 6 months of age, but in lack of breast feeding the age of 4 months earliest
Ireland	2008, 1999	Nutrition Sub-Committee of the Food Safety Authority of Ireland	Infants fed on formula food should start not before 17 weeks (approx 4 months) and not after 26 weeks (approx 6 months)
Italy	2009	Ministry of Labour, Health and social policies	The starting age has to be discussed with the paediatrician
Latvia	2003	Ministry of Health	After 6 months
Lithuania	2005	Ministry of Health	From 6 months

Member state	Year	Institution	Recommended age
Malta			Around 6 months
Netherlands		Nutrition Centre, on behalf of the Ministry of Health	Start from the age of 6 months
Norway			After 6 months for breast-fed infants; if needed, earliest at 4 months. Infants who are not breast-fed between 4 and 6 months
Poland		National Consultant for Paediatrics	Not breast-fed: from 4 months. Breast-fed: gruel or cereal mash from 4 months, meals from 6 months
Romania		Paediatric nutrition authorities	When infants are developmentally ready, for most infants between 4 and 6 months of age. Optimal age is 5.5 to 6 months
Slovak Republic	2008	Public Health Authority	About 6 months, not before 4 months
Slovenia		Ministry of Health	Not before 17 weeks (119 days) and not later than 26 weeks of age (182 days)
Spain		Spanish Society of Paediatric and Paediatrics of the Regional Health Systems	From 4-6 months of age
Sweden	2003	National Food Administration	About 6 months
United Kingdom	2008	Department of Health, Scientific advisory committee on nutrition	Around 6 months

Even though there are differences in the wording of the recommendations the Member States give, all mention 6 months as the upper age and none recommend complementary food before 4 months.

The observed time of introduction of complementary feeding in healthy infants in 5 European countries (Belgium, Germany, Italy, Poland, Spain) within a multicentre trial on the effects of different protein intakes on later growth have been recently published (Schiess et al., 2009). According to this report, complementary foods were introduced earlier in formula-fed infants (median 19 weeks, interquartile range 17-21) than breast-fed infants (median 21 weeks, interquartile range 19-24). Some 37.2% of formula-fed infants and 17.2% of breast-fed infants received complementary food earlier than at 4 months. At 5 months, more than 75% of formula-fed infants, and more than 50% of breast-fed infants, had received complementary food. At 6 completed months 96.2% of formula-fed infants and 87.1% of breast-fed infants had already received complementary foods. Complementary food had been introduced at 7 months in 99.3% of formula-fed infants and 97.7% of breast-fed infants, respectively. There were also relevant between-country differences.

In the WHO Multicentre Growth Reference Study which was conducted from 1997 to 2003 in six countries (8440 children from Brazil, Ghana, India, Norway, Oman and the USA) the introduction of complementary food occurred at mean ages between 4.8 (Oman) and 5.8 months (Ghana) (WHO MGRS, 2006b). Criteria for inclusion into the longitudinal component of the study were 1) exclusive or predominant breast-feeding for at least four months, 2) introduction of complementary foods between the ages of 120 and 180 days and 3) partial breast-feeding until at least twelve months.

The Panel considers that actual feeding practices in the complementary feeding period are the results of family beliefs, country traditions and scant scientific information, with unpredictable influence of medical and paediatric advice.

2. Criteria for setting the appropriate age of introduction of complementary food

2.1. Nutritional aspects and nutrient deficiencies

The assessment of the time span for which human milk is nutritionally adequate as the sole food of term infants can be based on the comparison of estimated nutrient intakes at defined ages of the exclusively breast-fed infant (provided by measurements of milk volume consumed multiplied by the nutrient concentration in human milk) with defined nutrient requirements of infants. Determining nutrient requirements of infants is performed either a) by dietary surveys of healthy populations, b) by factorial approaches which add the needs for maintenance to the needs for growth and c) by balance methods in which the input and the output of nutrients is determined. For some nutrients, e.g. for vitamin A, vitamin D, iron and zinc, the physiological needs are met by human milk intake and availability from stores which have been transferred from the mother to the infant during pregnancy. In those instances the dietary requirement varies with the magnitude of these stores. To avoid the circular argumentation inherent with method a), assessment of growth or indicators of nutrient deficiency are added as important functional outcomes of nutritional adequacy in infants. Assessment of the (normal) progression of growth can, however, only be done when an appropriate growth standard is available.

2.1.1 Nutrient adequacy of exclusive breast-feeding for the term infant during the first months of life

Butte et al., (2002) reviewed the available data relevant to the evaluation of the nutritional adequacy of exclusive breast-feeding over six months as a background paper for the WHO expert consultation on the optimal duration of exclusive breast-feeding held at Geneva on 28-30 March 2001. This report compiles the then available data on measured human milk volume intakes of both exclusively and partially breast-fed infants in each month of the first year of life, separated for developed and developing countries and calculates mean daily intakes weighted for the respective sample sizes and pooled standard deviations. The mean human milk intakes of exclusively breast-fed infants in developed countries at the age of 1, 2, 3, 4, 5, 6, 7, 8, 9 and 11 months are 699, 731, 751, 780, 796, 854, 867, 815, 890 and 910 mL/day. However, whilst the sample sizes are 131 to 376 for ages up to five months which may be considered to be moderately informative, only 34, 27, 16 and 10 samples have been available for the ages 7, 8, 9 and 11 months. This limits the usefulness of combining such intake values with nutrient concentrations in human milk to calculate the total daily nutrient intakes, compare them with dietary reference values for infants and estimate the proportion of infants at risk for particular nutrient deficiency using either the “probability approach” (NRC, 1986) or the estimated average requirement (AR) cut-point method (Beaton, 1994). The Panel notes that the intake of human milk in 13 fully breast-fed infants increased only slowly after one month from about 700 mL/day to about 800 mL/day (range 710-936 mL) at six months and 848, 818 and 817 mL/day (ranges 796-945, 720-1002, 681-871) at seven, eight and nine months, respectively, see figure 1 (Neville et al., 1988). The same observation was made in another longitudinal study in which 36 from 198 healthy full-term infants were still fully breast-fed at the age of nine months (Salmenperä et al., 1985). It is likely that it is the child who regulates the milk intake, as most mothers will be able to produce more milk (e.g. feed twins). The reason why the child does not up-regulate the milk volume is not known.

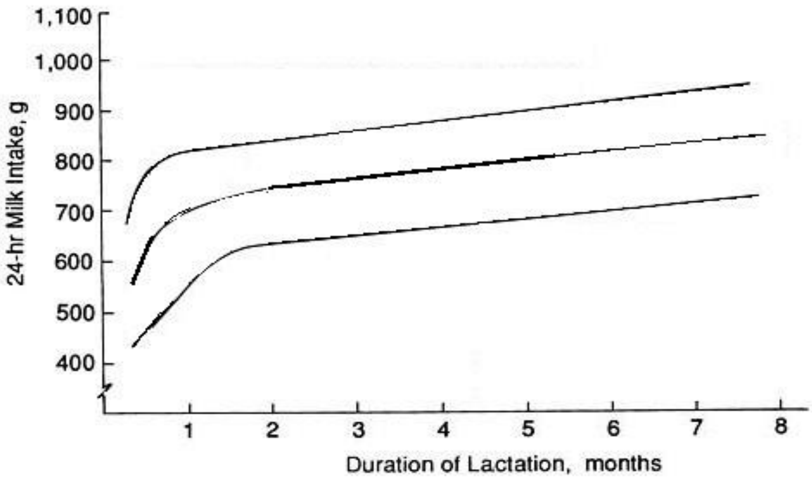

Fig 1: Milk intake obtained by test-weighing of fully breast-fed infants. The lines are the smoothed means plus/minus 1 standard deviation from 16 different studies (modified from Neville et al., 1988).

The energy content of human milk varies within a meal, with lactational stage and between individuals. Assuming an average energy content of human milk of 0.67 kcal/g, applied to age specific volume intakes corrected for insensible water losses and relating the total energy intake from breast milk to data on total energy expenditure and energy deposition related to growth and accretion of fat and protein, Butte et al. (2002) conclude that mean energy requirements are met by exclusive breast-feeding during the first six months of life and possibly longer. The metabolisable energy content of human milk was recently, however, calculated to be only about 0.62 kcal/g in a review of available data from Europe, North America, Australia and New Zealand (Reilly et al., 2005). The authors conclude that the mean metabolisable energy intake from exclusive breast-feeding at six months of age is 525-574 kcal/day which is below the estimated requirement of 632-649 kcal/day of UK infants at six months based on the data for energy requirement by FAO/WHO/UNU (2004), and that, therefore, six months of exclusive breast-feeding should not be considered to be the norm for all infants and might lead to insufficient growth in some (Reilly and Wells, 2005). The postulated gap between mean energy intake in exclusively breast-fed infants at 6 months and mean energy requirements demonstrated by an indirect evaluation (Reilly and Wells, 2005) almost disappears when simultaneous measurements of breast-milk consumption and body weight in the same subjects are used and in particular when the sexes are evaluated separately (Kersting et al., 2006). The Panel notes that the age at which exclusive breast-feeding provides insufficient energy can not be defined by the available data and that the introduction of complementary food needs to be decided individually.

Protein content of human milk changes with lactational stage and is on average 13 g/L in the second week, 9 g/L in the second month and 8 g/L in the fourth month until weaning. The method of determination plays a significant role and needs to be considered. Estimating true protein intakes from breast milk is difficult because of the non-protein nitrogen fraction that accounts to about 25% of total nitrogen in human milk. Nutritionally available protein in mature human milk provides about 5-6% of the energy content. The safe level of protein intake for infants has been evaluated to be 1.77 g/kg body weight at 1 month and progressively decrease to 1.14 g/kg body weight at 6 months (FAO/WHO/UNU, 2007). Protein requirements of young infants during the first six months of life are assumed to be equal and met by the protein provided by human milk and this conclusion is also supported by evidence of factorial estimates of requirements for maintenance and deposition (Dewey et al., 1996; EC, 2003; FAO/WHO/UNU, 2007). This conclusion is supported by studies which relate the protein intake from human milk to infant growth (Dewey et al., 1992; Heinig et al., 1993) but not by another study with exclusively breast-fed infants in Houston (Butte and Garza, 1985), with protein intakes of 1.6 +/- 0.3 g/kg b.w. per day and 0.9 +/- 0.2 g/kg b.w. per day at the age of one and four months, respectively and whose Z-scores for weight and length above zero at baseline (based on the

WHO pooled breast-fed data set) decreased below zero thereafter. On the other hand, the growth (both weight and length) of infants between four and eight months who had received formula with varying protein concentrations (13, 15, and 18 g/L) and who at six months had significantly higher protein intakes than breast-fed infants from the DARLING study (Dewey et al., 1992) did not differ from breast-fed infants (Akeson et al., 1998). Exclusively breast-fed healthy term infants in Honduras who received a protein supplement from four to six months of age in addition to breast-milk did not differ in growth rates from a control group exclusively breast-fed for six months (Dewey et al, 1996b).

The iron content of human milk is low (0.4-0.8 mg/L in colostrum and 0.2-0.4 mg/L in mature milk) and decreases with the length of lactation and is unaffected by maternal iron status and diet. The term infant of a well-nourished mother is born with a store of iron (body content about 75 mg/kg body weight, Widdowson and Spray, 1951), which can be increased by about 30-35 mg of iron by late cord clamping (at least two minutes) of the umbilical cord (Hutton and Hassan, 2007). This amount of iron is sufficient to supply the iron needed for the formation of haemoglobin and myoglobin concomitant with growth until about six months of age in fully breast-fed infants (Chaparro et al., 2008). With data pooled from 404 fully breast-fed infants from 6 studies from 4 different countries (Ghana, Honduras, Mexico, Sweden), predictors of iron deficiency anaemia (IDA) at 6 months were reported as male sex (Adjusted Odds Ratio [AOR]: 7.6; 95% CI: 2.5, 23.0), birth weight of 2500-2999 g (AOR: 3.4; 1.5, 7.5), and weight gain above the median since birth (AOR: 3.4; 95% CI: 1.3, 8.6). The percentage of infants with iron deficiency (ID) (ferritin <12 µg/L) was 6% and the percentage of infants with IDA (haemoglobin <105 g/L) was 2% in Sweden. It was concluded that among fully breast-fed infants with a birth weight >2500 g, IDA is uncommon before 6 months, but male infants and those with a birth weight of 2500-2999 g are at higher risk of ID and IDA (Yang et al 2009). Infants (n=36) exclusively breast-fed for nine months (Salmenperä et al., 1985) showed significantly lower serum iron and ferritin levels than infants weaned at 3.5 months whilst haemoglobin levels did not differ (Siimes et al., 1984). The need for dietary iron increases from about 4 months after depletion of the iron stores. Iron requirement as determined by factorial, balance and stable isotope methods has been estimated to be 0.5 mg/day and 0.9 mg/day at 0-6 months and 6-12 months of age, respectively (Butte et al., 2002). Other authors have estimated an Average Requirement (AR) of 6.9 and a Population Reference Intake (PRI) of 11 mg/day for iron for the age 7-12 months (IoM, 2001). This requirement cannot be met by human milk after the first six months of life. Breast-fed infants who do not receive iron from supplements or complementary foods are at risk of iron deficiency during the second half of the first year of life (Butte et al., 2002).

The infant is born with stores of prenatally acquired zinc which may help to meet the zinc requirement that cannot be met by the zinc in human milk, which decreases rapidly between early (4-5 mg/L) and mature milk (1-2 mg/L and about 0.5 mg/L at three and six months, respectively) regardless of maternal zinc intake or supplementation (Krebs et al., 1995, Hannan et al 2009). The zinc Adequate Intake (AI) of infants has been estimated to be 2 mg/day at 0-6 months of age based on the zinc intake of 780 mL of human milk with a zinc concentration of 2.5 mg/L, whilst the AR is 2.5 mg/day and the PRI is 3 mg/day at 7-12 months of age based on a factorial estimation (IoM, 2001). Exclusive breast-feeding for six months and longer bears a certain risk of zinc deficiency, and a negative zinc balance has been found in 33% of infants at the age of 4 months without clinical signs of a deficiency (Butte et al., 2002). The risk of zinc deficiency which increases at about the age of 6 months (Krebs and Hambidge, 2007) and is associated with decreased growth velocity in some fully breast-fed infants (Michaelsen et al., 1994) may be considered as a determinant for the timing of the introduction of complementary food with bioavailable zinc.

Vitamin D is low in breast milk of mothers with low serum 25(OH)D levels, which will occur in mothers delivering in autumn and winter and who live at or above 40ºN latitude (or at or below 40ºS latitude) due to limited sun exposure and vitamin D synthesis. Infants living at such latitudes require at least 2.5 µg/day to prevent rickets and 5 µg/day is the recommended intake level for infants between 0 and 6 months (IoM, 1997). The vitamin D concentration in milk from well-nourished women was found to be less than 1 µg/L and is, therefore, insufficient to cover the needs of an infant without sun exposure. Rickets was observed in one of the three infants who after being exclusively breast-fed until the age of nine months without a vitamin D supplement participated in an experiment of self-selection of complementary foods in late infancy (Davis, 1928). Low 25(OH)D levels are observed in the serum of such infants (Butte et al., 2002). The adequacy or inadequacy of the vitamin D content of human milk is not a determinant for the need to introduce complementary foods, because infants in the EU are routinely supplemented with vitamin D.

The vitamin A requirement of infants is covered by both moderate liver stores of retinyl esters acquired *in utero* and by vitamin A content in human milk which is dependent on the maternal vitamin A status. The vitamin A content in human milk which is about 1.7 µmol/L in well-nourished women decreases with prolonged lactation, particularly in countries with endemic vitamin A deficiency. The recommended intake level for infants between 0 and 6 months of age is 400 µg Retinol Equivalents (RE)/day and 500 µg RE/day for infants 7-12 months of age (IoM, 2001). The content in human milk is adequate to meet the infant’s requirement in well-nourished populations and indices for vitamin A insufficiency in breast-fed infants are absent in such populations (Butte et al., 2002). In well-nourished populations, the vitamin A content of human milk is not a determinant for the timing of the introduction of complementary food.

The composition of mature human milk is fairly constant and varies only slightly with lactational stage for most components. Some constituents like long-chain poly-unsaturated fatty acids vary with maternal status and habitual diet whilst most B vitamins and selenium are directly influenced by current maternal intake. Low vitamin B6 status of exclusively breast-fed infants was associated with a decrease in length growth reversible on supplementation (Butte et al., 2002). Vitamin B12 is actively transported via the placenta to the foetus and the content in human milk is related to maternal status. Infants of mothers who have been following a strict vegan diet for three years are at risk to develop signs of vitamin B12 deficiency at age 2-14 months (Specker et al., 1990). Vitamin K is poorly transported to the foetus via the placenta and human milk is, as a rule, poor in vitamin K, (but can be raised by pharmacological doses of vitamin K), which can lead to haemorrhagic disease of the newborn which typically manifests itself at 3-8 weeks of life. In most European countries this is prevented with neonatal administration of vitamin K.

Because there are not sufficient data available on volume intakes of exclusively breast-fed infants above the age of six months which in combination with data on nutrient concentrations could serve to estimate the nutrient intake of such infants, and because for most nutrients, with the exception of iron and zinc, the Dietary Reference Values are based on observed intakes from human milk and complementary foods or on extrapolation from other age groups, calculations of the nutritional adequacy of human milk during the second half of the first year of life are circular and hampered by numerous default assumptions.

In conclusion, it is justified to assume that exclusive breast-feeding by well-nourished mothers for six months can meet a healthy infant’s need for energy, protein and for most vitamins and minerals. However, nutrient intake and parallel anthropometric data after the age of 6 months are lacking.

2.2 Growth

2.2.1. Growth in breast-fed infants and the WHO Growth Standard

Many studies have shown that breast-fed infants have a different growth pattern, when compared to infants fed infant formula (Dewey et al., 1995; Agostoni et al., 1999; Kramer et al., 2004). The growth pattern in breast-fed infants, compared to formula fed infants, is a higher weight gain during the first months, and thereafter a gradual decline in weight gain during the remaining part of infancy. A similar pattern, but not so pronounced, is seen for length. Therefore, children being breast-fed also tend to be leaner in late infancy (Dewey et al., 1993; Dewey et al., 1995; Burke et al., 2005). The reason for this difference in growth pattern is not completely understood, but it is likely that differences in milk protein content between breast milk and infant formula play a role (Nielsen et al., 1998; Hoppe et al., 2004; Koletzko et al., 2009; Ong et al., 2009; Savino et al., 2009).

This difference in growth pattern was the reason that WHO decided to develop a new growth standard, based on breast-fed infants. This standard was to replace the growth reference values for infants (WHO, 1983), which were based on the United States National Center for Health Statistics growth curves (NCHS, 1977) derived for the major part from the Fels Longitudinal Study and which included data from 1929 of infants who were primarily bottle fed. The study was undertaken between 1997 and 2003 with the aim to collect growth related data from breast-fed infants born at term to non-smoking mothers from widely different countries (Brazil, Ghana, India, Norway, Oman, USA) (de Onis et al., 2004). The study comprised a longitudinal component from birth to 24 months of age, and a cross-sectional study performed in children between 18 to 71 months of age. The study was carried out in affluent surroundings of the respective countries. Overall, 74.7% of the children were exclusively or predominantly breast-fed for at least four months, 68.3% were partially breast-fed for at least 12 months and average duration of breast-feeding was 14.3 months. Complementary feeding was started at a mean age of 5.4 (range among the six sites: 4.8-5.8) months, while 99.5% had been started on complementary feeding at the age of six months (WHO MGRS Group, 2006a and b). There was a striking similarity in linear growth of the children of all six investigation sites (WHO MGRS group, 2006c).

The growth pattern of breast-fed infants, with slower growth velocity during infancy, is considered a more healthy growth pattern, as many studies have shown that a high growth velocity during infancy is associated with an increased risk of non-communicable diseases such as obesity, type 2 diabetes and cardiovascular disease later in life (Ong and Loos, 2006; Ekelund et al., 2006; Chomto et al., 2008, Leunissen et al., 2009).

2.2.2. Growth and introduction of complementary feeding

A number of studies have analysed the effect of age of introduction of complementary foods or duration of exclusive breast-feeding on growth.

In a randomised study of timing of introduction of complementary food, infants (N=165) were randomised to start complementary foods at 3 or 6 months. None of the infants were breast-fed at the start of the study at 3 months. There were no differences in length, weight or body composition (DEXA scan) at 6 or 12 months (Mehta et al., 1998).

Kramer and Kakuma have performed a large Cochrane review of the effects of duration of exclusive breast-feeding which was last updated in 2009 (Kramer and Kakuma, 2002, updated 2009). The overall conclusion was that neither controlled clinical trials, nor observational studies from developing or developed countries show deficits in weight or length gain for those who continued to be exclusively breast-fed for 6 months. However, they also concluded that the data were insufficient to rule out a modest increase in risk of under-nutrition in children exclusively breast-fed for 6 months and also that the data were grossly inadequate to reach conclusions about the effect of exclusive breast-feeding beyond 6 months. In a sub-analysis of studies from developed countries comparing exclusive and partially breast-feeding for the period from 3 to 7 months, they found a small but significant difference in weight gain during the period from 4 to 8 months, with those being exclusively breast-fed having a slight but significant lower weight gain (-12 g/month). They also found that those being exclusively breast-fed had a small but significant lower length gain (-1.1 mm/months) from 4 to 8 months, compared to those being partially breast-fed. Interestingly, from 8 to 12 months there was a small but significant catch-up in linear growth among those being exclusively breast-fed.

In a large cohort of Danish children born 1996 early introduction of complementary feeding (before 16 weeks) was positively associated with infant weight gain, but only in those breast-fed for less than 20 weeks (Baker et al., 2004).

In a study from Finland the growth of infants breast-fed exclusively beyond the age of 6 months was analysed (Salmenperä et al., 1985). There was a progressive decline in linear growth and by the age of 9 months 45% of the infants had decreased > 1 SD in relative length, using a current Finnish reference. Interestingly, there was no decrease in relative weight and therefore an increase in body mass index. Some of these infants showed catch-up in linear growth when complementary foods were introduced, suggesting that they had been malnourished.

Interpreting studies on the effect of age of introduction of complementary food on growth can be difficult for several reasons. First, most studies are observational. In observational studies introduction of complementary foods could be influenced by factors associated with the weight of the infant. A mother might introduce complementary foods earlier, because she is not satisfied with the weight gain of the infant (reverse causation), or a heavy infant might signal interest in complementary food earlier, because breast feeding might not be sufficient at an earlier age. Second, the composition of the complementary foods can influence growth. The amount of milk protein in the diet seems to have a stimulating effect on IGF-I, linear growth and weight gain (Ziegler et al., 2003; Hoppe et al., 2004; Koletzko et al., 2009; Ong et al., 2009), at least in some studies. Therefore, a change in milk protein intake associated with introduction of complementary feeding is likely to also influence growth. Finally, there is uncertainty about the ideal growth pattern of infants. Many studies suggest that a high growth velocity during infancy is associated with a higher risk of non-communicable diseases later in life as suggested by the growth acceleration hypothesis (Singhal and Lucas, 2004). However, some of these studies, which have analysed the associations for different age periods during infancy and young childhood, found significant positive associations with early growth 0-3 months (Chomto et al., 2008; Leunissen et al., 2009) or 0-6 months (Ekelund et al., 2006; Wells et al., 2005), but none found significant associations with growth from 6-12 months. Among the two studies which examined growth during the 3-6 month period, which is relevant for the effects of introducing complementary foods, one found a positive association with later fat mass (Chomto et al., 2008) and one found no association with risk markers of type 2 diabetes and cardiovascular disease (Leunissen et al., 2009). The issue about optimal growth is further complicated by the fact that some studies suggest that the slightly slower linear growth in breast-fed compared to formula fed infants seems to be compensated later in childhood, most likely because of a programming of the IGF-I axis (Martin et al., 2002; Larnkjær et al., 2009).

The Panel considers that the age of introduction of complementary feeding seems not to have a strong impact on growth velocity (both weight and length). However, some data suggest that late introduction in fully breast-fed infants, after 6 months, could result in a decline of length and weight gain and that early introduction from 3 to 4 months, could result in increased weight gain which could have long term negative consequences with regard to an increased risk for obesity, type 2 diabetes and cardiovascular disease in adult life.

2.3. Developmental aspects

2.3.1. Neuromuscular coordination

At term, normal infants are able to coordinate efficient sucking, swallowing and respiration (Bu'Lock et al., 1990). However, mandibular movements remain rudimentary and further maturation will consist in the gradual acquisition of new movement components and response patterns. As early as four months, the infant gains more stability in the jaw, neck and shoulders and the primitive sucking pattern begins to modify (Meyer, 2000). Labial closure represents a landmark in mature swallowing development, with labial closing pressure increasing steadily from 5 months to 3 years (Ayano et al., 2000). A pronounced shift in oromotor functions occurs with the transition from sucking to chewing, which typically occurs between 5 and 8 months of age (Sheppard & Mysak, 1984). By that time, new feeding behaviours also develop: 5-6 months old infants reach for a spoon when hungry; by 8-9 months, they use their fingers to rake food; by 12 months, they chew and swallow firmer foods without chocking (Carruth & Skinner, 2002). There may be a critical window for introducing lumpy solid foods (Illigworth & Lister, 1964) and if they are not introduced before 10 months of age, it may increase the risk of feeding difficulties (Illigworth & Lister, 1964; Northstone et al., 2001) which may have an impact on dietary habits later in life.

The Panel considers that the available data do not permit to define precisely an age when the introduction of complementary food is needed for further neuromuscular development. However, many infants will have matured their neuromuscular coordination enough at about 5 months to be spoon fed.

2.3.2. Food preferences

Preference for flavour compounds, particularly those detected by the sense of smell, is highly influenced by learning early in life. For instance, prenatal experience with food flavours, transmitted from the mother's diet to amniotic fluid, leads to a greater acceptance of these foods at the time of introduction of complementary foods (Mennella et al., 2001). Flavour learning continues after birth, as a consequence of exposure to mother's milk. As in the case with amniotic fluid, breast milk does influence infants' liking and acceptance of food flavours (Forestell and Mennella, 2007). Of course, food preferences are also affected by the introduction of complementary feeding. Repeated exposures to such foods promote their acceptance (Sullivan & Birch, 1994). There are some indications that a progression in texture complexity may also play a positive role in infants' food preferences (Lundy et al., 1998). Similarly, providing infants with a variety of flavours when complementary foods are first introduced greatly facilitates the subsequent acceptance of foods that are new for the infants (Maier et al., 2008), which may have an impact on dietary habits later in life.

The Panel considers that the available data do not permit a precise conclusion on the appropriate age of introduction of complementary feeding for all infants based on the available literature on food preference.

2.3.3. Digestion and absorption

The secretion of gastric and pancreatic enzymes is not developed to adult levels at birth. Nevertheless, the infant is able to fully digest and absorb the nutrients in human milk, partly because breast milk also provides enzymes which contribute to digestion. In infants, secretion outputs and enzyme activity levels mature at very different rates: gastric lipase activity already reaches adult levels by 3 months (Ménard et al., 1995), whereas pancreatic α-amylase only does so after 3 years of age (Zoppi et al., 1972). In contrast, the small intestine of human infants is mature at birth and can handle the various nutrients (Shmerling, 1976). Despite the slow maturation of pancreatic amylase, most cooked starches are digested and absorbed almost completely (De Vizia et al., 1975). As in the adult, the colonic microbiota contributes to the final digestion of incompletely processed starches. Indeed, its role seems to grow with the increase in carbohydrate complexity (Christian et al., 1999). By about 4 months, gastric acid and pepsin secretion are able to process proteins. Whereas breast milk proteins are fully digested, complete casein absorption is less than 6 g/day at 10 days but about 20 g/day at 5 months of age (Hirata et al., 1965). Similarly, the coefficient of absorption of triglycerides is about 96% from human milk at 1.5 month, whereas it is only 70-85% from formulae at 3 months (Manson et al., 1999). If complementary food is introduced after 4 months of age, the digestive system will be mature enough to digest and absorb starches, proteins and fats provided by a non-milk diet. However, infants' functional gastric capacity is quite limited. It ranges from 38 to 76 mL in term neonates (Zangen et al., 2001) to about 20 mL/kg body weight in toddlers (Zangen et al., 2003), which amounts to about 160-200 g/meal for a 6-8 months infant.

The Panel considers that the available data do not indicate the need for the introduction of complementary food at a certain age, however, if complementary food is introduced after 4 months of life it does not constitute a problem for the digestive system of the infant.

2.3.4. Renal function

The renal control of water balance is not fully developed at birth. The rate of water renal excretion is influenced by the solute load to be excreted. As the renal concentrating capacity is limited in the neonatal period (Joppich, 1977), a high solute load could result in a rapid and profound alteration in water balance. Renal solute load is derived from exogenous and endogenous sources. The former comes mainly from electrolyte intake, while the latter results from metabolism, particularly nitrogenous end-products related to protein metabolism. The potential renal solute load refers to solute of dietary and endogenous origin that would have to be excreted in urine if none were diverted into the synthesis of new tissue or lost through non-renal routes. It is defined as the sum of four electrolytes (sodium, potassium, chloride and phosphorus) plus the solutes derived from protein metabolism, which usually contributes more than 50% to the potential renal solute load (PRSL) (Fomon, 2000). For instance, the PRSL of human milk is about 97 mOsm/L whereas that of cow's milk is about 307 mOsm/L (EFSA, 2008). Thus, PRSL is primarily a concern for non-breast-fed infants, particularly during illness. After 4 months, renal function has matured considerably and infants can handle higher PRSL.

The Panel considers that the available data do not indicate the need for the introduction of complementary food at a certain age, however, if complementary food is introduced after 4 months of life it does not constitute a problem for the renal function of the infant.

2.4. Health aspects

2.4.1. Obesity and type 2 diabetes

Obesity

There is quite some evidence that breast-feeding reduces the risk of obesity (Owen et al., 2005; Arenz et al., 2004; WHO, 2007). In one meta-analysis the odds ratio (OR) was 0.78 (95% confidence interval **(**CI): 0.72-0.84) (WHO, 2007). Some of these studies have also shown a dose-response effect of duration of breast feeding (Arenz et al., 2004; Harder et al., 2005; WHO 2007). Other studies show no effect of breast-feeding (Nelson et al., 2005; Michels et al., 2007). The mechanism responsible for the protective role of breast-feeding on obesity is not clear. Influence on eating behaviour, including an effect on appetite has been suggested as well as an effect of a higher protein intake, if complementary food is introduced early (Lucas et al., 1980; Salmenperä et al., 1988; Baur et al., 1998; Koletzko et al., 2009; van Dijk, 2009). Hormones contained in mothers' milk could also be involved (Savino et al., 2009).

Several studies have examined if age at introduction of complementary food had an effect on risk of obesity in childhood and found no effect (Burdette et al., 2006; Kramer, 1981; Zive et al., 1992; Maffeis et al., 1994; Lanigan et al. 2001). However, one prospective study from Scotland found that those who were introduced to complementary foods before 15 weeks had higher weight and body fat at age 7 years (Forsyth et al., 1993; Wilson et al., 1998). There were no effects at age 2 years suggesting that there was a programming[16] effect. In a Danish study with 5068 individuals born 1951-61 there was no effect of age at introduction of complementary food on the risk of obesity during childhood, but at follow-up at 42 years, those who were introduced to complementary feeding late had a lower risk of obesity as adults. The range of age at introduction was from 3-6 months (Schack-Nielsen et al., in press).

The effect of early introduction of complementary food on measures of adiposity at 6.5 years was examined in the large randomised PROBIT study from Belarus. In an intention-to-treat analysis taking advantage of the cluster randomisation, there was no effect of duration or exclusivity of breast-feeding (Kramer et al., 2007, 2009**)** However, when data were analysed with children grouped

[16] The term ''programming'' refers to the concept that an insult or stimulus applied at a critical or sensitive period may have long term or lifetime effects on the structure or function of an organism (Lucas, 1991)

according to duration of exclusive breast-feeding it was found that children breast-fed exclusively for more than 6 months had significantly higher BMI, skinfold thickness and hip circumference, compared to infants exclusively breast-fed for three months, but continued to be partially breast-fed up to 6 months (Kramer et al., 2009). However, the authors interpret these results as being due to reverse causation. Reverse causation would mean that mothers with infants with a high growth velocity waited longer to introduce complementary feeding.

In the study of children from Scotland followed up at 7 years, those receiving complementary foods before the age of 15 weeks were heavier and had a higher body fat percentage measured by skinfolds and impedance (Wilson et al., 1998). In an analysis where the age of introduction of complementary foods was included as a continuous variable, a positive association between body fat and age at introduction of complementary foods was also found.

There are many studies which have found highly significant positive associations between growth during infancy and the risk of being overweight or obese later in life (Ekelund et al., 2005; Vogels et al., 2006; Chomto et al., 2008). The studies of the effect of age at introduction of complementary food on infant growth (section 2.2.2) have therefore also some relevance for the question if age of introduction of complementary foods has an effect on the risk of later obesity.

The Panel considers that the evidence is insufficient to show that the age of introduction of complementary food has an impact on the risk of obesity irrespective of breast-feeding. A few studies have suggested that early introduction (before 3 to 4 months) could result in increased obesity.

Type 2 diabetes

There is evidence that breast-feeding protects against type 2 diabetes in later life. A large review, including 76,744 subjects found that the OR of developing type 2 diabetes was 0.61 (95% CI: 0.41-0.85) in those breast-fed compared to those not breast-fed (Owen et al., 2006). In the meta-analysis by Owen et al. (2006) they also found evidence that breast-fed infants had lower glucose and insulin levels during infancy and that insulin levels in breast-fed infants were marginally lower later in life suggesting a programming effect on insulin metabolism which could influence the risk of acquiring type 2 diabetes later in life. Introduction of complementary feeding is likely to have an effect on current insulin levels but there is no evidence that there are any long term effects of the age of introduction of complementary feeding on insulin levels.

The Panel considers that there is no evidence that the age of introduction of complementary food has an effect on the risk for type 2 diabetes.

2.4.2. Allergy

It is impossible to exclude contact to food allergens in exclusively breast-fed infants. E.g. severe allergic reactions can occur from exposure to minute quantities of food allergens even during breast-feeding in infants at high risk for allergy (Tan et al., 2001). Animal models suggest that for induction of tolerance, oral exposure to an allergen may be necessary (Strobel and Movat, 2006). The “dual allergen-hypothesis” proposes that allergic sensitisation to food can occur through low-dose cutaneous sensitisation, and that early consumption of food protein induces oral tolerance (Lack et al., 2008).

The timing of the introduction of complementary foods has rarely been examined as an independent risk factor for atopic disease in breast or formula fed infants. Statistical adjustment for covariates, e.g. for atopic family history, cannot exclude “reverse causality” related to delayed introduction in infants with early symptoms of food allergy (Bergmann et al., 2002; Zutavern et al., 2004; Lowe et al., 2006). On the other hand, when in some studies infants, who develop atopic symptoms while being breast-fed, are excluded from the analysis to avoid reverse causality, the early, most severe cases of atopic disease may be missed (Kull et al., 2005; Snijders et al., 2008).

One of the first prospective observational studies on infant feeding and eczema reported a seven times higher prevalence of infantile eczema in bottle fed versus breast-fed infants in Chicago (Grulée and

Sanford, 1936). But all infants in this study had received orange juice from 4 weeks, cod liver oil from 6 weeks, cereal at 5 months and vegetables at 6 months of age (Grulee et al., 1934).

As long as the elimination of allergenic foods was a cornerstone in policies for the prevention of food allergies, studies favouring breast-feeding and the late introduction of solid foods were popular. A prospective non randomised cohort study in Helsinki on 135 exclusively breast-fed infants with an atopic family history observed atopic eczema and a history of food allergy to be significantly reduced, when solid foods were introduced after 6 months of age compared to 3 months (Kajosaari and Saarinen, 1983; Kajosaari, 1994). In a prospective birth cohort study on 1265 infants born in 1977 in New Zealand, a relationship was observed between the diversity of complementary foods introduced during the first 4 months of age and the occurrence of chronic eczema until the age of 10 years ($p < 0.05$), no matter if they had been breast or bottle fed (Fergusson et al., 1981, 1990).

More recent studies on the introduction of complementary food after 4 months of age usually observed no benefits of a delayed introduction. In the German Infant Nutritional Intervention (GINI) study on the allergy preventive effect of different formulas, infants exclusively breast-fed for 16 weeks had less atopic eczema than those receiving cow's milk formula, while the timing of complementary food introduction was less important (Schoetzau, 2002). But if complementary food was introduced between 17 and 24 weeks, the OR for atopic eczema was 0.48 (95% CI: 0.26-0.91) in breast-fed compared to bottle fed infants receiving cow's milk formula. Earlier (< 17 weeks) or later introduction (> 24 weeks) of complementary food did not result in such a risk reduction by breast feeding. The follow-up at age 4 years did not find an evidence for a protective effect of delaying the introduction of complementary food beyond 4 months or of potentially higher allergenic food beyond 6 months, even after adjusting for the type of milk received during the first 4 months of age (Filipiak et al., 2007). This is in line with the results of a prospective cohort study in Kent, where no evidence for a protective effect on an atopic manifestation at age 5 1/2 years was observed by the introduction of vegetables before 4 months compared to after 4 months even after adjusting for breast feeding and other confounders (Zutavern et al., 2004). At the age of 6 1/2 years in children who had been breast-fed exclusively for 3 months compared to those exclusively breast-fed for 6 months in the PROBIT study, there was no statistically significant difference in the prevalence of atopic symptoms or diagnoses according to the ISAAC questionnaire nor in skin prick test results (Kramer et al., 2009).

In a systematic review of early introduction of complementary food, it was concluded that there is insufficient evidence to suggest that, on its own, the early introduction of complementary food to infants is associated with an increased risk of food allergy (Tarini et al., 2006).

In recent years the advice on the timing of the introduction of complementary foods was changed by the Committee on Nutrition, Section on Allergy and Immunology of the American Academy of Pediatrics (Greer et al., 2008), the Section on Pediatrics of the European Academy of Allergology and Clinical Immunology (Høst et al., 2008) and the ESPGHAN Committee on Nutrition (Agostoni et al., 2008). These all agree that there is no convincing scientific evidence that avoidance or delayed introduction of potentially allergenic foods beyond 4-6 months reduces allergies in infants considered at increased risk for the development of allergy or in those not considered to be at increased risk.

The Panel considers that the available data do not permit a conclusion on the appropriate age for introduction of complementary feeding with respect to allergy prevention or reducing the risk of allergy.

2.4.3. Autoimmune diseases. Celiac disease and type 1 diabetes mellitus (T1DM)

Celiac disease is an autoimmune condition caused by the intake of wheat gluten and related proteins from barley and rye in genetically predisposed subjects. The majority of individuals with celiac disease (95%) carry the HLA-DQ2 or DQ8 haplotype, as do about 30% of the general population (Myléus et al., 2009); these genetic factors are necessary but not sufficient for disease development. An epidemic of celiac disease was observed in Swedish children between 1984 and 1996, increasing the annual incidence rate 4-fold in children below 2 years of age (Ivarsson et al., 2000). This was mainly attributed to changes in feeding habits: introduction of gluten was delayed from 4 to 6 months, when breast feeding was often discontinued, and the gluten content of commercially available foods and drinks was increased (Ivarsson et al., 2000). A further study on the prevalence of celiac disease in 12 year-old children born during the epidemic (1993) indicated that the real prevalence was 3% (29/1000; 95% CI: 25-33), which is much higher than that generally reported (1%) (Myleus et al., 2009). A Swedish population based case-control study showed that the risk was reduced in children below 2 years of age when they were still breast-fed while dietary gluten was introduced (OR: 0.59; 95% CI: 0.42-0.83) or even lower when breast feeding was continued beyond the month when gluten had been introduced (OR: 0.36; 95% CI: 0.26-0.51). When gluten was consumed in an amount higher or equivalent to 16 g flour/day two weeks after a first portion of 7 g flour had been introduced the risk was increased by 50% (OR: 1.5; 95% CI: 1.1-2.1) compared to lower consumption (Ivarsson et al., 2002). The effect of age at the time of gluten introduction (from 1-4, 5-6 to 7-12 months) was not conclusive.

A decline of symptomatic cases was observed after new dietary recommendations were introduced in Sweden in 1996, stressing a slow introduction of gluten at 4 instead of 6 months while the infant is still breast-fed (Carlsson et al., 2006). A systematic review and meta-analysis of qualified retrospective studies published between 1966 and 2004 showed, that breast-feeding during the introduction to gluten (pooled OR 0.48; 95% CI:0.40-0.59) and increasing duration of breast-feeding were both associated with a reduced risk of developing celiac disease in children (Akobeng et al., 2006).

The only prospective observational study (DAISY) so far, was conducted in Denver from 1994-2004 on 1560 4.8-year old children at increased risk for celiac disease or T1DM according to the possession of either HLA-DR3 (now called HLA-DR17) or DR4 alleles, or having a first degree relative with type 1 diabetes (Norris et al., 2005). Children exposed to wheat, barley or rye had a 5-fold higher risk for tissue transglutaminase (tTG) antibodies after the data were adjusted by the HLA-DR3 status, when these gluten containing cereals were introduced in the first 3 months of life compared to 4-6 months (hazard ratio (HR): 5.17; 95% CI: 1.44-18.57), and a slightly (but significantly) increased risk if introduction occurred in the 7th month or later (HR: 1.87; 95% CI: 0.97-3.60). This risk calculation was independent of the timing for the introduction of other complementary foods. When the case group was restricted to the 25 children who had biopsy-diagnosed celiac disease, initial exposure to gluten-containing foods in the first 3 months of life or in the 7th month or later significantly increased the risk of celiac disease autoimmunity compared with exposure at 4 to 6 months (HR: 22.97; 95% CI: 4.55-115.93, and HR: 3.98; 95% CI: 1.18-13.46, respectively). There seems to be a time effect of gluten introduction in this selected population at risk of the disease.

T1DM is a hyperglycaemia caused by a destructive autoimmune process targeting the insulin-producing pancreatic islet cells. Some studies have found an association between T1DM and short duration of breast feeding and introduction of solid food, soy milk formulas, gluten and wheat consumption at young age (Borch-Johnsen et al., 1984; Mayer et al., 1988; Kostraba et al., 1993; Strotmeyer et al., 2004; Frisk et al., 2008). The risk of T1DM has also been related to the time of gluten introduction into the infant’s diet. Auto-antibodies to islet cells can be found years prior to the diagnosis of T1DM. A large prospective study (DAISY study) including first degree relatives with T1DM and increased T1DM risk infants based on the HLA genotype was conducted in Denver. In this study, T1DM antibodies appeared in a significantly higher proportion of children, if cereals (rice, oats, wheat, barley and rye) were introduced in the first 3 months or at 7 months or older compared to introduction at 4-6 months (HR: 4.32; 95% CI: 2.0-9.35 and HR: 5.36; 95% CI: 2.08-13.8, respectively) (Norris et al., 2003). When cereals were introduced while the infant was still being breast-fed the risk was slightly but significantly reduced (HR: 0.50; 95% CI: 0.25-0.99) (Norris et al., 2003). In the prospective study BABYDIAB conducted in Germany that followed 1610 newborns of parents with T1DM up to 5 years of age, the risk of developing T1DM auto-antibodies was increased when gluten containing foods were introduced in the first 3 months compared to those only breast-fed (HR: 4.0; 95% CI: 1.4-11.5), but not if gluten was introduced after 6 months (Ziegler et al., 2003). In the All Babies Southeast Sweden cohort comprising 657 children, representative of the general population, the combination of an introduction of cow's milk formula before 2 months and of gluten containing foods after 6 months increased the risk significantly (OR: 5.8; 95% CI: 1.3-25.5) for at least one T1DM autoantibody at 1 and at 2 ½ years of age (Wahlberg et al., 2006). An association between T1DM and introduction of solid food gluten and wheat consumption at young age is not observed in all the studies (Nigro et al., 1985; Kyvik et al., 1992; Samuelsson et al., 1993; Meloni et al., 1997).

The Panel notes that the early (< 4 months) introduction of gluten might increase the risk of celiac disease and T1DM, whilst the progressive introduction of gluten between 4 and 6 months, preferably while the infant is still breast-fed might decrease the risk of these diseases.

2.4.4. Infections

Breast-feeding contributes both to passive protection and to the development of the immune system of the infant, reducing infectious morbidity (Chantry et al., 2006; Chirico et al., 2008).

The recommendation of the WHO (2001) mainly relies on the data of the PROBIT study, which compared 2862 infants exclusively breast-fed for 3 months (with continued mixed breast-feeding through ≥6 months) with 621 infants who were exclusively breast-fed for ≥ 6 months. The infants that were breast-fed exclusively for 6 months, experienced less morbidity from gastrointestinal infections than infants who were mixed breast-fed after 3-4 months of age, during the period from 3 to 6 month (adjusted incidence density ratio [IDR]: 0.35 [95% CI: 0.13-0.96]) but the protective effect did not persist at 6-12 months (adjusted IDR: 0.90 [95% CI: 0.46-1.78]); no differences were detected on the risk of respiratory infections between the two groups (Kramer et al., 2003). Studies in US and Europe have also shown that exclusive breast-feeding for at least 6 months decreases the risk of infections (Chantry et al., 2006; Paricio Talayero et al., 2006; Quigley et al., 2007; Rebhan et al., 2009). A population-based cross-sectional survey of children enrolled at ≥ 2 months of age in the US revealed a reduced risk of respiratory tract infection, showing the strongest evidence for recurrent otitis media (≥ 3 episodes) in children who were fully breast-fed for ≥ 6 months in comparison with those fully breast-fed for 4 to < 6 months at < 12 months of age (OR: 4.27; 95% CI: 1.27-14.35 and OR: 1.95; 95% CI: 1.06-3.59) (Chantry et al., 2006). An evaluation of the effect of duration of full breast-feeding (up to 6 months) on the probability of hospitalisation as a result of infectious processes (respiratory and gastrointestinal) during the first year of life in 1385 infants in Spain revealed that for every month without full breast-feeding the risk for hospitalisation was multiplied by 1.43 (95% CI: 1.27-1.59, P < 0.0001) (Paricio Talayero et al., 2006). Another population-based survey (the Millennium Cohort Study with 15,890 healthy term infants) also concluded that prolonged (more than 6 months) breast-feeding protects against severe infectious morbidity (Quigley et al., 2007). Infants were divided into: (1) non breast-fed; (2) partially breast-fed; and (3) exclusively breast-fed. Infants who were exclusively breast-fed had a significant reduction in risk of hospitalisation for diarrhoea (adjusted OR: 0.37; 95% CI: 0.18-0.78) and lower respiratory tract infections (adjusted OR: 0.66; 95% CI: 0.47-0.92) than those who were not breast-fed. The effect of partial breast-feeding was weaker and not significant. A recent "Bavarian Breast-feeding study" recruited prospectively a cohort of 1901 healthy infants and comparisons were done between infants (475) who were exclusively breast-fed for ≥ 6 months, infants (879) who were fully breast-fed ≥ 4 months but not for ≥ 6 months and infants (619) not breast-fed or breast-fed < 4 months (Rebhan et al., 2009). Data regarding infections were recorded retrospectively by asking about infections diagnosed by a physician from birth till 9 months of age. In multivariate analysis, ≥ 6 months of exclusive breast-feeding reduced significantly the risk for > or =1 episode of gastrointestinal infection(s) during months 1-9 compared to not breast-feeding or < 4 months breast-feeding (adjusted OR: 0.60; 95% CI: 0.44-0.82).

In summary, these data support that full breast feeding for up to 6 months provides greater protection than partial breast feeding or shorter breast feeding against the risk of infectious morbidity. The Panel notes that the effects of introduction of complementary food are not specifically addressed.

Studies designed to assess the association between infection rates and the age of introduction of complementary food in both formula and breast-fed infants are scarce. A prospective observational study of 671 infants in Dundee revealed a significant increase in respiratory illness and persistent cough between 14 and 39 weeks of age among the infants given complementary food early (at < 8 weeks or 8-12 weeks) in comparison with those given complementary food later (> 12 weeks of age). No effects were detected on the incidence of gastrointestinal illness, with or without adjustment for milk feeding (Forsyth et al., 1993). In a prospective cohort study (Millennium Baby Study) of 604 term infants recruited in UK and followed up to 13 months of age, early introduction of complementary food (< 3 months versus > 4 months) was associated with an increased rate of infectious morbidity (diarrhoea; OR: 1.65; 95% CI: 1.09-2.5) between 6 weeks and 4 months after adjusting or not for feeding mode (breast-fed versus non breast-fed at 4 month) (Wright et al., 2004). There was no influence of age of weaning on illness rates between 4 and 8 months of age (Wright et al., 2004). By contrast, a review which included the data of 1694 infants from five prospective randomised dietary trials to investigate the effects of early introduction of complementary food (before 12 weeks) versus later introduction of complementary food (after 12 weeks) on infant’s health up to the age of 18 months did not reveal any effect on the proportion of infants developing lower respiratory tract infection or gastroenteritis after adjusting for type of milk feeding (human milk or formula) (Morgan et al., 2004). Most recently, the Millennium Cohort Study (15,980 term infants in the UK) has assessed the effects of complementary food and feeding either human milk or formula on the risk for infection during the first 8 months of life. The breast-feeding rates of this cohort of infants were low with 17.5% exclusively breast-fed infants at 4 months and 1.2% at 6 months. The monthly risk of hospitalisation, for both diarrhoea and lower respiratory tract infection, was significantly lower only in those infants receiving breast milk compared with those receiving formula, but this was independent of whether or not the infants received complementary food. The results were the same when considering all infants (aged 8 months) as when considering younger infants (aged ≤ 4 months), in which the effects of complementary food could be stronger (Quigley et al., 2009). The results of this study confirm that there is a protective effect of breast feeding on infectious diseases but no effects from the age of introduction of complementary food.

In summary, specific evidence on the possible independent effects of early introduction of complementary food on the risk of infections in young infants is limited. One observational study finds that introduction of complementary food at < 3 months of age increases the risk of gastrointestinal diseases and another study reports that introduction of complementary food at < 12 weeks increases the risk of respiratory illness, but two other studies did not show any effect of introducing complementary food before 4 months of age on the risk of hospitalisation by infection.

The Panel considers that breast-feeding protects against infectious morbidity. This effect is proportional to the length of breast-feeding. The available evidence suggests that early introduction (< 3 months) of complementary feeding may increase the risk of infectious morbidity. There seems to be no effect of introduction of complementary feeding after 4 months on the risk of infectious morbidity.

2.4.5. Dental health

Data on the possible association between the age of introduction of complementary foods and the risk of caries are very scant and poor. One observational study has identified the odds of having caries increased for each incremental increase in age at introduction of complementary food (Bray et al., 2003). The PROBIT study, based on an intention to treat analysis, was not able to identify differences between 3 or 6 month exclusive breast-feeding in dental caries at 6.5 years of age (Kramer et al., 2009).

The Panel notes that the risk of having caries cannot be connected to the age of introduction of complementary food.

CONCLUSIONS

The Panel has evaluated predominantly studies in breast-fed healthy infants born at term for indicators of an appropriate age at which to introduce complementary food irrespective of existing recommendations on breast-feeding duration and on exclusivity of breast-feeding. The Panel has focussed its evaluation on data from developed countries. The Panel takes note of the fact that other than scientific factors and factors not discussed in this opinion may determine the age of introduction of complementary foods.

1. Nutritional adequacy of exclusive breast-feeding

The needs for water, energy, protein, calcium and many other nutrients can be met by exclusive breast-feeding for six months. However, breast milk may not provide sufficient iron and zinc in some infants after the age of 4-6 months, and these infants require complementary foods. Iron deficiency in fully breast-fed 6 months old infants is more likely to occur in male infants and in infants with a birth weight of 2500-2999 g.

The Panel concludes that it is justified to assume that exclusive breast-feeding by well-nourished mothers for six months can meet a healthy infant's need for energy, protein and for most vitamins and minerals. However, nutrient intake and parallel anthropometric data after the age of 6 months are lacking.

2. Growth

Studies have shown that breast-fed infants have a different growth pattern, when compared to infants fed infant formula. Neither controlled clinical trials, nor observational studies from developing or developed countries show deficits in weight or length gain for those who continued to be exclusively breast-fed for 6 months. The data are insufficient to rule out a modest reduction in growth in children predominantly breast-fed for 6 months. However, there is no indication that a small reduction in growth has negative effects. The data were grossly inadequate to reach conclusions about the effect of exclusive breast-feeding beyond 6 months.

The Panel considers that the age of introduction of complementary feeding seems not to have a strong impact on growth velocity (both weight and length). However, some data suggest that late introduction, after 6 months, could result in a decline in rate of length and weight gain and early introduction, before 4 months, could result in an increased rate of weight gain which could have long term negative consequences with regard to an increased risk for obesity, type 2 diabetes and cardiovascular disease in adult life.

3. Developmental aspects

3.1. Neuromuscular coordination

The Panel finds that the introduction of complementary food with different feeding modes (spoon, cup, self-feeding with fingers) marks important developmental milestones in motor and coordinative abilities which appear at individually variable ages but which follow a constant pattern. The biological variability in the attainment of developmental stages does not allow, however, to establish a certain age. Both too early and too late introduction of new feeding modes might hamper the normal development as well. The Panel considers that the available data do not permit to define precisely an age when the introduction of complementary food is needed for further neuromuscular development. However, many infants will have matured their neuromuscular coordination enough at about 5 months to be spoon fed.

3.2. Food preferences

Breast milk does influence infants' liking and acceptance of food flavours. Food preferences are also affected by the introduction of complementary feeding. The Panel considers that the available data do not permit a precise conclusion on the appropriate age of introduction of complementary feeding for all infants based on food preference.

3.3. Digestion and absorption

If complementary food is introduced after 4 months of age, the digestive system will be mature enough to digest and absorb starches, proteins and fats provided by a non-milk diet. The Panel considers that if complementary food is introduced after 4 months of life it does not constitute a problem for the digestive system of the infant.

3.4. Renal function

The renal control of water balance is not fully developed at birth. After 4 months, renal function has matured considerably and infants can handle higher potential renal solute load. The Panel considers that if complementary food is introduced after 4 months of life it does not constitute a problem for the renal function of the infant.

4. Health aspects

4.1. Obesity and type 2 diabetes

Obesity
Several studies have examined if age of introduction of complementary food had an effect on risk of obesity in childhood and found no effect. However, one prospective study from Scotland found that those who were introduced to complementary foods before 15 weeks had higher weight and body fat at age 7 years. In a Danish study there was no effect of age at introduction of complementary food on the risk of obesity during childhood, but at follow-up at 42 years, those who were introduced to complementary feeding late had a lower risk of obesity as adults. The range of age at introduction was from 3-6 months.

The Panel considers that the age of introduction of complementary food seems not to have a clear impact on the risk of obesity. A few studies have suggested that early introduction (before 4 months) could result in increased risk for obesity.

Type 2 diabetes
There is evidence that breast-feeding protects against type 2 diabetes in later life. A large review, found that the risk of developing type 2 diabetes was reduced by 39% in breast-fed infants compared to not breast-fed infants. The Panel considers that there is no evidence that the age of introduction of complementary food has an effect on the risk for type 2 diabetes.

4.2. Allergy

The timing of the introduction of complementary foods has rarely been examined as an independent risk factor for atopic disease in breast or formula fed infants. More recent studies on the introduction of complementary food after 4 months of age usually observed no benefits of a delayed introduction. In a systematic review on early introduction of complementary food it was concluded that there is insufficient evidence to suggest that, on its own, the early introduction of complementary food to infants is associated with an increased risk of food allergy. There is no convincing scientific evidence that avoidance or delayed introduction of potentially allergenic foods reduces allergies in infants considered at increased risk for the development of allergy or in those not considered to be at increased risk. The Panel considers that the available data do not permit a conclusion on the appropriate age for introduction of complementary feeding with respect to allergy prevention or reducing the risk of allergy.

4.3. Autoimmune diseases. Celiac disease and type 1 diabetes mellitus

Observational studies indicate that the timing of gluten introduction, the amount of gluten introduced and the continuation of breast-feeding while gluten is introduced into the infant's diet may influence the risk of developing celiac disease. The risk of T1DM has also been related to the timing of gluten introduction into the infant's diet. The risk was also slightly reduced when cereals were introduced while the infant was still being breast-fed

Based on the available data on autoimmune diseases the Panel notes that the early (<4 months) introduction of gluten might increase the risk of celiac disease and T1DM, whilst the introduction of gluten between 4 and 6 months while still breast-feeding might decrease the risk of celiac disease and T1DM.

4.4. Infections

Studies in US and Europe have found that exclusive breast-feeding for at least 6 months decreases the risk of infectious morbidity. Data support that full breast feeding for up to 6 months provides greater protection than partial breast feeding or shorter breast feeding against the risk of respiratory and gastrointestinal infections. Specific evidence on the possible independent effects of early introduction of complementary food on the risk of infections in young infants is limited.

The Panel considers that breast-feeding protects against infectious morbidity. This effect is proportional to the length of breast-feeding. The available evidence suggests that early introduction (< 3 months) of complementary feeding may increase the risk of infectious morbidity. In the EU there seem to be no effect of introduction of complementary feeding after 4 months on the risk of infectious morbidity.

4.5. Dental health

There is no evidence to suggest a specific age for the introduction of complementary food based on the risk of caries.

5. Overall conclusion

In response to a request of the Commission to give an Opinion on the appropriate time for the introduction of complementary food into infants' diet in the EU, the Panel concludes the following:

On the basis of present knowledge the Panel concludes that the introduction of complementary food into the diet of healthy term infants in the EU between the age of 4 and 6 months is safe and does not pose a risk for adverse health effects (both in the short-term, including infections and retarded and excessive weight gain, and possible long-term effects such as allergy and obesity).

Consistent with these conclusions, presently available data on the risk of celiac disease and T1DM support also the timing of the introduction of gluten containing food (preferably while still breast-feeding) not later than 6 months of age.

Exclusive breast-feeding is nutritionally adequate up to 6 months for the majority of infants, while some infants may need complementary foods before 6 months (but not before the age of 4 months) in addition to breast-feeding to support optimal growth and development.

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Glossary / Abbreviations

25(OH)D	25-hydroxy vitamin D
AOR	Adjusted Odds Ratio
AR	Average Requirement
BMI	Body Mass Index
CI	Confidence Interval
DEXA	Dual Energy X-ray Absorptiometry
EC	European Commission
EEA	European Economic Area
ESPGHAN	European Society for Paediatric Gastroenterology Hepatology and Nutrition
EU	European Union
FAO	Food and Agriculture Organization
HLA	Human Leukocyte Antigens
HR	Hazard Ratio
ID	Iron Deficiency
IDA	Iron Deficiency Anaemia
IDR	Incidence Density Ratio
IGF-1	Insulin-like Growth Factor 1
IoM	Institute of Medicine
NCHS	National Center of Health Statistics
NRC	National Research Council
OR	Odds Ratio
PRI	Population Reference Intake
PRSL	Potential Renal Solute Load
RE	Retinol Equivalents
SCF	Scientific Committee on Food
SD	Standard Deviation
T1DM	Type 1 Diabetes Mellitus
Ttg	Tissue Transglutaminase
UNICEF	The United Nations Children's Fund
UNU	United Nations University
WHO	World Health Organization