Pediatric Nutrition in Practice

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The Nestlé Nutrition Institute (NNI) was created to provide healthcare professionals with up-to-date information on nutrition and nutrition-related disorders in order to promote health for children and adults, in particular those who have specific needs, based on the latest medical and scientific breakthroughs.

For more than 60 years the NNI has contributed to the continuing nutrition education of health professionals. NNI’s activities comprise live events (e.g. congresses, workshops), written publications, online programs, audio, video, or other electronic media. The vast majority of information is also available online at www.nestlenutrition-institute.org.

Pediatric Nutrition in Practice is a handbook comprising all relevant, practical reference information for the feeding of generally healthy infants, children and adolescents, and for nutritional care in pediatric diseases. It is intended to be used by pediatricians working in preventive and curative services around the world, including both high- and low-income settings. The content of this book will also be transformed into an accredited e-learning course, available online at www.nestlenutrition-institute.org, which will further increase its utility for pediatricians.

The NNI is deeply indebted to the editor of this book, Prof. Bert Koletzko from the University of Munich, Germany, for his outstanding work in establishing and coordinating the content of Pediatric Nutrition in Practice. We also wish to warmly thank the co-editors, Prof. Peter Cooper, Johannesburg, South Africa; Dr. Maria Makrides, Adelaide, Australia; Prof. Ricardo Uauy, Santiago de Chile, Chile; Prof. Cutberto Garza, Boston, Mass., USA, and Prof. Weiping Wang, Shanghai, China, for their great contribution to the preparation of this book.

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There is no other time in life when the provision of appropriate nutrition is of greater importance than during infancy and childhood. During this phase of life characterized by rapid growth and development, an adequate amount and composition of substrates both in health and disease are of key importance for growth, functional outcomes such as cognition and immune response, and long-term wellbeing. While a number of excellent textbooks on pediatric nutrition are available that provide detailed accounts on the scientific and physiologic basis of nutrition as well as its application, busy physicians and other healthcare professionals often find it difficult to devote sufficient time to study elaborate and extensive books on just one aspect of their practice. Therefore, we decided to develop this compact reference book to provide concise information to readers who seek quick guidance on practical relevant issues in the nutrition of infants, children and adolescents. This book was developed with a truly international perspective to address challenges both in affluent and poorer populations, which could only be achieved with the insightful input of a global editorial board. I wish to thank my co-editors very much indeed for their enthusiastic help and support in developing this project. I am also most grateful to the authors from all parts of the world, who are renowned experts in their fields, for their willingness to dedicate their knowledge, time and effort in preparing their chapters. It has been a great pleasure to work with the editorial production team at Karger Publishers, who did a fantastic and very professional job in producing a book of outstanding quality. Finally, I gratefully acknowledge the generous financial support of the Nestlé Nutrition Institute that covered a large portion of the production costs and will help to widely disseminate this practical guide. With sincere thanks I also wish to highlight the fact that the Nestlé Nutrition Institute and its representatives Petra Klassen-Wigger, Denis Barclay and Ferdinand Haschke supported the editors in making their fully independent choices on content, direction and the authors of this book, and this is greatly appreciated indeed.

It is the sincere hope of the editors that this book will be useful to many healthcare professionals around the world, and that it may contribute to further enhancing the quality of feeding for healthy infants and children, as well as enhancing the standards of nutritional care for sick children. We are very keen to have feedback on this book from you, the readers, including suggestions on which aspects might be improved even further in the future. Thank you very much for your support!

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Introduction

Growth is the main characteristic of childhood, and a sensitive indicator of the child’s nutritional status. Deviations in growth, especially reduced growth, are associated with an increased risk of diseases both in the short- and long-term. Monitoring growth is therefore an important tool for assessing the health and wellbeing of children, especially in countries where other diagnostic tools are scarce. It is also an important tool in advanced clinical settings, but often it is not given the necessary attention, to the detriment of more sophisticated examinations.

1.1 Child Growth

Kim Fleischer Michaelsen

Key Words

Stunting · Wasting · Obesity · Growth monitoring · Insulin-like growth factor-I · Weight · Height · Body mass index · Growth

Key Messages

• Growth is a sensitive marker of health and nutritional status throughout childhood
• Growth monitoring is important both in children with diseases and in healthy children
• Early growth is associated with long-term development and health
• Breastfed infants have a slower growth velocity during infancy, which is likely to have beneficial long-term effects

Growth of the Healthy Child

From conception to adulthood, growth can be divided into periods: intrauterine, infancy, childhood, and adolescence. Each period has its own characteristic pattern and the mechanisms regulating growth differ [1] (fig. 1). Nutrition has its strongest regulatory effect during early life, growth hormone secretion plays an important role during infancy and growth is modified by sex hormones during puberty. Insulin-like growth factor-I (IGF-I) mediates the effect of growth hormone on growth, but IGF-I can also be stimulated directly by nutrients. Linear growth velocity and weight gain is highest during the first few months after birth, with monthly increments of about 4 cm and 1 kg. Then growth velocity declines until the pubertal growth spurt, which is earlier in girls than in boys (fig. 2). Age at puberty differs considerably between populations with later puberty in populations with a poor nutritional status.

Different organs grow at very different rates (fig. 3). The brain and, therefore, head circumference grow mainly during the first 2 years of life, with head circumference reaching about 80% of adult values at the age of 2 years. Body fat mass, expressed as a percentage of body mass, increases from birth to about 6–9 months, then decreases until the age of about 5–6 years, after which there is an increase again. These changes are reflected both in reference curves for body mass index (BMI) and skinfolds (fig. 4).
Regulation of Growth

Many factors influence growth. Genetic influences are strong, but can be modified by many environmental factors. Ethnic differences are likely to be caused more by environmental than genetic factors as preschool children from different parts of the world seem to have the same growth potential, as shown in the new WHO growth standards in which preschool children from different parts of the world have the same growth pattern if they have optimal nutritional and socioeconomic conditions (see Chapter 4.1). Other studies show that the growth patterns of children from families moving to a country with very different dietary and socioeconomic conditions change within one generation, and that the growth pattern in a population can change over time, the so-called secular trend [2].

Nutrition has a marked influence on growth, especially during the first years of life. Breastfed infants have a slower growth with regard to both weight and length than formula-fed infants [3], and it seems that this has beneficial effects in the long-term. It seems that a difference in protein intake may cause these differences. This is in line with evidence suggesting that cow’s milk has a stimulating effect on linear growth, also in well-nourished populations [4]. Nutrition is also a key factor in the development of overweight and obesity as discussed in Chapter 3.4.

Nutritional Problems Affecting Growth

In a global perspective, the most common cause of poor growth is an insufficient diet in which especially a lack of energy and some micronutri-
ents, e.g. zinc, is important. Protein deficiency can also affect growth, but protein deficiency without energy deficiency is not common among malnourished children in developing countries and rare among malnourished patients in industrialized countries. Undernutrition, low weight-for-age, can be caused by low height-for-age (stunting), low weight-for-height (wasting or thinness), or a combination of these. In populations with poor nutrition, stunting is regarded as a result of chronic malnutrition and wasting a result of acute malnutrition, but in the individual this is often a simplification.

Many acute and chronic diseases result in poor appetite and eating difficulties and, consequently, malnutrition. Infections and diseases with inflammation, such as autoimmune diseases and cancers, are associated with anorexia. Psychological problems, such as nonorganic failure to thrive and eating disorders are also associated with anorexia and malnutrition.

Obesity is characterized by an increased body fat mass, but as fat mass is too complicated to measure routinely, the BMI (weight/length$^2$) is commonly used to describe overweight and obesity [5]. Overweight children are often taller than children with normal weight until puberty, which they typically reach earlier than normal weight children. Therefore, there are no major differences in height after puberty.

**Growth and Long-Term Health**

There is strong evidence that marked deviations from the average growth pattern, especially during early life, are associated with impaired development and increased risk of many non-communicable diseases later in life. Examples are increased risk of cardiovascular disease in individuals with low birthweight and increased risk of type-2 diabetes and obesity in individuals with a high growth velocity during early life. Height as an adult is also associated with several diseases; low stature being associated with cardiovascular disease and tall stature being associated with several types of cancer. Early nutrition plays a role as described in Chapter 1.5. However, the mechanisms are not clear and there is only little information about the degree to which the deviations in growth alone or the factors responsible for the deviation in growth are the cause of the increased risk of disease later in life.

**Growth Monitoring**

Regular measurements of weight and height and plotting of weight curves including earlier measurements are important tools in monitoring the health of children in both the primary healthcare system and in hospitals. Weight-for-age curves
are not sufficient. There is a need for both height-for-age and either weight-for-height or BMI curves and calculation of present growth velocity to make a comprehensive evaluation.

With the development of software, easily available on the internet, e.g. www.who.int/childgrowth/software/en/, it has become very easy to enter weight and length data, calculate percentiles and standard deviation scores, and plot the curves on a graph, so that parents will also be able to do the monitoring.

Surveillance, following trends of malnutrition and overweight and obesity in populations, is an important public health tool in monitoring the nutritional status of populations. It is often relevant to perform such surveillances both at the local, regional and national level.

**Conclusions**

- Regular measurements of weight and length/height, and plotting on growth charts, including BMI, are important tools in monitoring the health and nutritional status of both children with diseases and healthy children
- Regular monitoring of growth in healthy children should be performed by the primary healthcare system, including the school health system

**Fig. 4.** Reference charts (percentiles) for subscapular skinfold and body mass index for boys. Modified from Tanner and Whitehouse [9] and Nysom et al. [10].
References


1 General Aspects of Childhood Nutrition

1.2 Nutritional Assessment

1.2.1 Clinical Evaluation and Anthropometry

John W.L. Puntis

Key Words
Nutritional assessment · Feeding history · Anthropometry · Growth · Malnutrition

Key Messages
- Nutritional assessment includes feeding history, clinical examination, and anthropology; basic hematological and biochemical indices should also be included if possible in order to identify specific nutrient deficiencies.
- Careful measurement of growth status and reference to standard growth charts is essential in order to identify those children who are malnourished.
- Addition of skinfold thickness measurements and mid-upper arm circumference allows estimation of body composition; however, this is not often calculated in routine clinical practice.
- There are a number of different ways of defining malnutrition and no definition universally agreed upon.
- Short-term malnutrition affects weight so that the child becomes thin ('wasting').
- Long-term malnutrition leads to poor linear growth so that the child will have a low height for age ('stunting').
- The point at which deteriorating nutritional status demands invasive intervention (tube feeding) in order to prevent adverse outcomes is unclear and will depend on the underlying disease and the overall clinical status of the individual child.
- Serial measurements are required to monitor the effectiveness of nutritional intervention.

Nutritional Assessment

Malnutrition impairs growth, in time leading to multisystem disease. Nutritional status reflects the balance between supply and demand and the consequences of any imbalance. Nutritional assessment is therefore the foundation of nutritional care for children [1]. When judging the need for nutritional support, an assessment must be made both of the underlying reasons for any feeding difficulties, and of current nutritional status. This process includes a detailed dietary history, physical examination, anthropology (weight, length; head circumference in younger children) with reference to standard growth charts [2], and basic laboratory indices (cf. Chapter 1.2.4) if possible. In addition, skinfold thickness and mid-upper arm circumference measurements provide a simple method for estimating body composition [3].

Nutritional Intake

Questions regarding mealtimes, food intake and difficulties with eating should be part of routine history taking, and give a rapid qualitative impression of nutritional intake (cf. Chapter 1.2.2). For a more quantitative assessment a detailed dietary history must be taken which involves recording a food diary or (less commonly) a weighed
food intake. This would usually be undertaken in conjunction with an expert pediatric dietician. Use of compositional food tables or a computer software program allows these data to be analyzed so that a more accurate assessment of the intake of energy and specific nutrients can be made. When considering whether such intakes are sufficient, reference can be made to dietary reference values (DRV) which provide estimates of the range of energy and nutrient requirements in groups of individuals [4]. Many countries have their own values, and international values have been published by the FAO/WHO/UNU. DRV are based on the assumption that individual requirements for a nutrient within a population group are normally distributed and that 95% of the population will have requirements within 2 standard deviations of the mean (cf. Chapter 1.3.1). In a particular individual, intakes above the reference nutrient intake are almost certainly adequate, unless there are very high disease-induced requirements for specific nutrients, while intakes below the lower reference nutrient intake are almost certainly inadequate.

Taking a Feeding History

A careful history is an important component of nutritional assessment. Listed below are some of the questions and ‘cross-checks’ that are integral to an accurate feeding/diet history:

Infant: is the baby being breastfed or formula fed?

For breastfed infants:
- How often is the baby being fed and for how long on each breast? (check positioning and technique)
- Are supplementary bottles or other foods offered?

For formula-fed infants:
- What type of formula? How is the feed made up? (i.e. establish the final energy concentration/100 ml)
- Is each feed freshly prepared?

For older children:
- How many meals and snacks are eaten each day?
- What does the child eat at each meal and snack? (obtain a 1- or 2-day sample meal pattern)
- How do the parents describe their child’s appetite?
- Where does the child eat meals?
- Are there family mealtimes?
- Are these happy and enjoyable situations?
- How much milk does the child drink?
- How much juice does the child drink?
- How often are snacks/snack foods eaten? (Further details are provided in Chapter 1.2.2).

Basic Anthropometry: the Assessment of Body Form

Accurate measurement and charting of weight and height (‘length’ in children <85 cm, or unable to stand) is essential if malnutrition is to be identified; clinical examination without charting anthropometric measurements (‘eye-balling’) has been shown to be very inaccurate [5]. For premature infants up to 2 years of age, it is essential to deduct the number of weeks born early from the actual (‘chronological’) age in order to derive the ‘corrected’ age for plotting on growth charts. Head circumference should be routinely measured and plotted in children less than 2 years. Measurements should be made as follows.

Weight:
- Weigh infants <2 years naked
- Weigh older children only in light clothing (fig. 1)
- Use self-calibrating or regularly calibrated scales.
Length:
- If possible use an infant measuring board, measuring mat (easily rolled and transported) or a measuring rod (see: www.miami-med.com.Height_Measuring_Devices.htm)
- Two people are required to use the measuring board: one person holds the head against the headboard, while the other straightens the knees and holds the feet against the moveable foot board (fig. 2).

Height:
- Use a stadiometer if possible (fig 3), a device for standing height measurement comprising a vertical scale with a sliding horizontal board or arm that is adjusted to rest on the top of the head.

Skinfold thickness:
- Pinch the skin between two fingers and apply specialized skinfold calipers (fig. 6); experience is needed to produce accurate and repeatable measurements (see: http://healthsciences.qmuc.ac.uk/labweb/Equipment/skin_fold_calipers.htm); take triceps skinfold thickness readings at the mid-upper arm using the relaxed non-dominant arm; the layer of skin and subcutaneous tissue is pulled away from the underlying muscle, and readings are taken to 0.5 mm, 3 s after application of the calipers; measurements can also be taken at other sites (see: http://www.cdc.gov/nchs/data/nhans/nhanes3/cdrom/nchs/manuals/anthro.pdf).

Fig. 1. Weigh older children only in light clothing using regularly maintained and calibrated scales.

Fig. 2. An infant measuring board; two people are required for accurate determination of length.
Growth rate in infancy is a continuation of the intrauterine growth curve, and is rapidly decelerating up to 3 years. Growth in childhood is a steady and slowly decelerating growth curve that continues until puberty, a phase of growth lasting from adolescence onwards. During puberty, the major sex differences in height are established, with a final height difference of around 12.5 cm between males and females. Growth charts are derived from measurements

Fig. 3. A stadiometer should be used for accurate assessment of height.

Fig. 4. The mid-upper arm is the point halfway between the acromion of the shoulder and the olecranon of the elbow (marked with a pen).

Fig. 5. To determine mid-upper arm circumference, take the average of three readings made with a non-stretch tape measure at the mid-upper arm point.
of many different children at different ages (cross-sectional data). Data for growth of children are distributed ‘normally’ (i.e. form a ‘bell-shaped’ curve). These data can be expressed mathematically as mean and standard deviations (SD) from the mean. The centile lines delineate data into percentages: the 50th centile represents the mean (average); 25% of children are below the 25th centile. The normal range (approximately ±2 SD from the mean) lies between the 3rd and 97th centile.

Normal Growth – Simple Rules of Thumb

Approximate average expected weight gain for a healthy term infant:

- 200g/week in the first 3 months
- 130 g/week in the second 3 months
- 85 g/week in the third 3 months
- 75 g/week in the fourth 3 months
- Birthweight usually doubles by 4 months and triples by 12 months.

Length:

- Increases by 25 cm in the first year
- Increases by 12 cm in the second year
- By 2 years roughly half of adult height is attained.

Head circumference:

- Increases by 1 cm/month in the first year
- Increases by 2 cm in the whole of the second year
- Will be 80% of adult size by 2 years.

(N.B.: growth rates vary considerably between children; these figures should be used in conjunction with growth charts).

Patterns of Growth

Birthweight/centile is not always a good guide to genetic potential; some infants cross centile lines in the first few months of life (‘catch down’), but from then on continue to follow along a lower centile. The maximum weight centile achieved between 4 and 8 weeks is the best predictor of weight centile at 12 months. Infants born <10th centile for gestational age may have either intrauterine growth retardation (IUGR), or be within the normal 10% of the population who fall below this line. Long-standing IUGR results in low weight, head circumference and length (‘symmetrically’ small); catch-up growth is unlikely. Infants with late IUGR are thin, but may have head circumference and length on higher centile, and subsequently show catch-up in weight. It should be noted that rates of growth vary in young children, and assessments should be based on serial measurements. Short-term energy deficit will make a child thin (low weight for height = wasting). Long-term energy deficit limits height gain (and head/brain growth) causing stunting. Children who are chronically undernourished may be both thin and short.

Assessment of linear growth potential:

- Plot height of both parents at 18-year-old end of centile chart
- Add together parental heights and divide by 2
- Add 7 cm (male child), subtract 7 cm (female) = mid-parental height (MPH); MPH ± 8.5 cm (girl), or ± 10 cm (boy) = target height centile range.

Fig. 6. Triceps skinfold thickness taken with Harpenden calipers at the mid-upper arm allows estimation of fat energy stores and is useful for serial monitoring.
Anthropometric Indices and Definitions of Malnutrition

Weight-for-height compares a child’s weight with the average weight for children of the same height, i.e.: actual weight/weight for height at the 50th centile.

For example, a 2.5-year-old girl: height = 88 cm; weight = 9 kg; 50th centile weight for a child who, at 88 cm, is on the 50th centile for height = 12 kg.

Weight for height is therefore 9/12 = 75% (‘moderate’ malnutrition).

Weight-for-height can be expressed either as percent expected weight, or as ‘z’ score. The z score is commonly used when statistical comparison is being made, as it enables children of different sexes and ages to be compared. A value on the 50th centile would have a z score of 0 whereas values on the 2nd and 98th centiles are −2 and +2 SD, respectively. Mid-upper arm circumference provides a quick population screening tool for malnutrition; reference charts are available [6].

Body mass index is derived from weight in kilograms divided by the square of the height in meters (kg/m²); it is an alternative to ‘weight-for-height’ as an assessment of nutritional status [7].

Classifications of Malnutrition

There is no single, universally agreed on definition of malnutrition in children [8], but the criteria shown in table 1 are commonly used. Classification does not define a specific disease, but rather clinical signs that may have different etiologies. Other nutrients such as iron, zinc and copper may be deficient in addition to protein and energy.

The Wellcome classification of malnutrition is based on the presence or absence of edema and the bodyweight deficit (table 2).

When to Intervene

Malnutrition is a continuum that starts with a nutrient intake inadequate to meet physiological requirements, followed by metabolic and functional alterations and, in due course, by impairment of body composition. Malnutrition is difficult to define and assess because of insensitive assessment tools and the challenges of separating the impact of malnutrition from that of the underlying disease on markers of malnutrition (e.g. hypoalbuminemia is a marker of both malnutrition and severe inflammation) and on outcome. Nutritional

<table>
<thead>
<tr>
<th>Table 1. Criteria for malnutrition</th>
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<td>-----------------------------------</td>
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<tr>
<td>Height for age, %</td>
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<tr>
<td>Weight for height, %</td>
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<tr>
<td>Body mass index</td>
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<tr>
<td></td>
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<tr>
<td>90–100</td>
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<tr>
<td>70–80</td>
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<td>60–70</td>
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<tr>
<td>50–60</td>
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<td>40–50</td>
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<tr>
<td>10–20</td>
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<tr>
<td>0–10</td>
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</table>

<table>
<thead>
<tr>
<th>Table 2. Wellcome classification of malnutrition</th>
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<tr>
<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td>Marasmus</td>
</tr>
<tr>
<td>&lt;60% expected weight for age, no edema</td>
</tr>
<tr>
<td>Marasmic kwashiorkor</td>
</tr>
<tr>
<td>&lt;60% expected weight for age, edema present</td>
</tr>
<tr>
<td>Kwashiorkor</td>
</tr>
<tr>
<td>&lt;60–80% expected weight for age, edema present</td>
</tr>
<tr>
<td>Underweight</td>
</tr>
<tr>
<td>&lt;60–80% expected weight for age, no edema</td>
</tr>
</tbody>
</table>

Clinical Evaluation and Anthropometry 11
intervention may be indicated both to prevent and to reverse malnutrition. In general the simplest intervention should be followed if necessary by those of increasing complexity. For example, energy-dense foods and calorie supplements before progressing to tube feeding (cf. Chapter 3.3). Parenteral nutrition should be reserved for children when nutrient needs cannot be met by enteral feeding (cf. Chapter 3.4). When simple measures aimed at increasing energy intake by mouth are ineffective, tube feeding should be considered [9]; the following are suggested criteria.

- Impaired energy consumption
  Usually 50–60% of recommended daily amount despite high-energy supplements

- Severe and deteriorating wasting
  Weight for height >2 SD below the mean
  Skinfold thickness <3rd centile and/or

- Depressed linear growth
  Fall in height of >0.3 SD/year or
  height velocity <5 cm/year
  or
decrease in height velocity of at least 2 cm from the preceding year during early to mid-puberty

Conclusions

- A detailed feeding history should be part of routine nutritional assessment
- Expert dietetic assistance is required for more objective assessment of nutritional intake, and for appropriate further management
- Accurate assessment of growth by careful measurement and reference to standard growth charts is essential to define and monitor nutritional status
- Malnutrition is a dynamic and complex process without clearly agreed definitions
- The clinical status and particular needs of each individual child require careful evaluation when planning nutritional support

References

4 www.britishnutrition.org.uk.
1 General Aspects of Childhood Nutrition

1.2 Nutritional Assessment

1.2.2 History and Dietary Intake

Roxana Valdes-Ramos

Introduction

Assessment of nutritional status and dietary intake is always related to the patient’s history; history of health and disease and of the family. It is not an easy task to identify all the nutritional risk factors that may be present in a given patient, particularly for the untrained clinician. Some of this history can be obtained from hospital or family physician records, but usually one has to rely on parental information that may vary with educational background and cultural traditions. Cues and questions may be used to prompt patient’s answers. Information from caregivers is essential to evaluate small children, whereas older children and adolescents can provide adequate information in most cases. Dietary intake assessment methods have limited accuracy, but if adequately applied and interpreted can provide useful guidance for identifying inadequate dietary supplies in individuals or populations.

History

A medical history can be obtained from hospital records or the family physician if there is a regular attendance at medical services, but usually the clinician needs to interview the child and caregivers to obtain information on the child and family history. It is important to identify any fact that may affect the child’s nutritional status, such as disease of parents or other family members, course of pregnancy and childbirth, use of medications and nutritional supplements including herbal and traditional remedies. Growth charts should be gathered. Social and economic information should also be obtained in order to establish household food availability (including preparation and distribution within the family), access to health services, cultural and religious habits. The importance of the information will depend on the age of the child and the closeness of the possible effect; for example a grandparent’s history of hypertension may not directly affect an infant, but it is definitely important for an obese adolescent. Table 1 lists the most important historical information relative to nutritional status in children [1, 2].
Table 1. Historical information relative to nutritional status in children

<table>
<thead>
<tr>
<th>Age group</th>
<th>Information requested</th>
</tr>
</thead>
</table>
| Infants (0–12 months)       | Prenatal and postnatal disease history  
|                             | Pattern of lactation or formula feeding  
|                             | (frequency, duration of each session, position, abnormalities and diseases)  
|                             | Use of pacifier or thumb  
|                             | Age and pattern of weaning  
|                             | Unusual or abnormal feeding behaviors  
|                             | Parents’ or infant’s history of food allergies  
|                             | Use of supplements and medications  
|                             | Frequency and appearance of stools and urine  
|                             | Age and condition at birth (preterm, term, post-term; large, appropriate or small for gestational age, low birthweight, Apgar or Silverman)  
|                             | Growth charts (weight and length for age, head circumference)  
|                             | Parents’ psychological status  
|                             | Reflexes (sucking, extrusion, chewing, swallowing, tongue movement)  
|                             | Neurological development  
|                             | (rolling, sitting, crawling, walking, hand-eye-mouth control)  
|                             | Daycare  
|                             | Position among siblings                                                                                                                                          |
| Toddlers (1–3 years)        | Feeding skills  
|                             | Physical activity level                                                                                                                                           |
| and preschoolers (3–5 years)| Food allergies, intolerances, aversion, fads, unusual habits  
|                             | Socioeconomic condition (availability and distribution of food)                                                                                                   |
|                             | Climate and altitude (for iron levels)                                                                                                                            |
|                             | Hunger and satiety cues                                                                                                                                           |
|                             | Pica  
|                             | Number of meals, snacks and daycare feeding  
|                             | Parents’ weight status or body mass index  
|                             | Previous and recurrent diseases  
|                             | Food preparation habits (who, where, how)                                                                                                                        |
| Schoolchildren (6–10 years) | Family history of disease  
|                             | Unusual weight gain or loss  
|                             | Appetite                                                                                                                                                    |
| Adolescents (11–21 years)   | Sexual maturation  
|                             | (development of sexual characteristics, age at menarche in females)                                                                                             |
|                             | Addictions (alcohol, tobacco, drugs)                                                                                                                              |
|                             | Psychological health                                                                                                                                             |
|                             | Body image and perception                                                                                                                                           |
|                             | Physical activity patterns                                                                                                                                          |
|                             | Dieting behavior                                                                                                                                                    |
|                             | Sexual activity                                                                                                                                                    |
|                             | Pregnancy or lactation                                                                                                                                                |

For each age group, the information requested for the previous age group should also be considered.
Dietary Intake

Dietary intake can be evaluated by various methods, depending on the age of the child and the kind of information needed.

Infant’s diets are simple and easy to evaluate through a prospective protocol of all foods consumed over a period of 24 h or 3 days, or a retrospective recall protocol over the last 24 h which the mother or caretaker can fill out on their own, or which can be obtained through questions from the healthcare professional.

Children may need the help of a parent or caretaker to complete any of the dietary intake methods. Several options for dietary assessment are available [3–6]:

- A 24-hour recall protocol, in which the child is asked to list all the foods and drinks consumed during the 24 h (including approximate weight or size of portions, the number of portions consumed, as well as recipes in the case of homemade products). The validity depends on the child’s memory. A 24-hour recall protocol is particularly useful in assessing larger population groups, whereas in individuals, both day-to-day variations in consumption, as well as errors in recollection often limit the conclusions that can be drawn. The method tends not to be very useful in young children, since their intake usually has large day-to-day variations.

- A prospective 3- or 7-day record of all food and drinks consumed registered by the child and/or caretaker is more informative than the 24-hour recall. It should include one weekend or festive day which may lead to different food choices.

- In a food-frequency protocol the subject reports the number of food and drink portions consumed from a predetermined list of items, during a defined time period, e.g. 1 week, the protocol should define portion sizes or weights. While a food-frequency protocol does not provide precise intake information, it is very useful to identify certain dietary patterns such as the exclusion of specific food groups.

### Table 2. Summary of dietary assessment methods

<table>
<thead>
<tr>
<th>Method</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>24-hour recall</td>
<td>Fast Easy to apply</td>
<td>Not precise</td>
<td>Schoolchildren and adolescents</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gives a snap-shot</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Depends on memory</td>
<td></td>
</tr>
<tr>
<td>Usual diet</td>
<td>Easy to apply</td>
<td>Inaccurate</td>
<td>Toddlers to adolescents</td>
</tr>
<tr>
<td>3- to 7-day record</td>
<td>Accurate Good for habitual diet</td>
<td>Needs good participation Training required</td>
<td>All children</td>
</tr>
<tr>
<td>Food frequency</td>
<td>Gives data over long periods of time</td>
<td>Time-consuming depending on the food list Not very good for specific nutrients Overestimates intake</td>
<td>Schoolchildren and adolescents</td>
</tr>
<tr>
<td>Checklist</td>
<td>Fast Easy to apply</td>
<td>Only for food groups</td>
<td>All children</td>
</tr>
<tr>
<td>Scores/indexes</td>
<td>For very specific purposes and age-groups Need validation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
• A food checklist is similar to the food-frequency protocol but uses a shorter food list and is targeted to specific food groups or nutrients [7–11].

The data obtained from any of these methods need to be interpreted to assess food and nutrient intakes. While the exclusion of certain foods or unbalanced dietary patterns may be quickly detected by an experienced dietician or clinician reviewing the protocol, quantitative assessments and the calculation of nutrient intakes require further calculations based on food composition tables or databases, usually with dedicated software programs [12], and the comparison to reference intake values for age and gender. Such an analysis is time-consuming and should be used with clear questions and indications only.

Table 2 summarizes relevant information on the most common dietary assessment methods.

Conclusions

• Take a detailed history of the patient’s diet and associated factors
• Identify food availability and household distribution patterns
• Evaluate family relationships and attitudes towards food and nutrition
• Use a combination of two or more dietary assessment methods
• Dietary intakes can be assessed by 24-hour recall protocols or by prospective dietary records obtained over 3–7 days, including 1 weekend day
Introduction

Accurate nutritional assessment should be an integral part of pediatric care. Children at risk of malnutrition or who are chronically ill should undergo a detailed nutritional assessment, which sometimes requires technical measures. An important aspect of nutritional assessment is estimating daily energy needs for optimal growth and development. This is especially important in children with health conditions causing undernutrition or obesity. However, the energy needs of such children can be difficult to estimate [1]. Resting energy expenditure (REE) represents a large portion of the energy needed each day. The measurement of REE using indirect calorimetry is the best available method to accurately estimate an individual child’s caloric needs to promote weight gain, loss, or maintenance. The relative and absolute amounts of muscle, fat and bone change during growth [2], but growth during childhood is most commonly assessed by measuring stature and weight rather than specific tissue compartments. The measurement of body composition provides more detailed information about nutritional status than the measurement of stature and weight alone. In addition to anthropometry, the most commonly used clinical method of body composition assessment is dual energy X-ray absorptiometry (DXA). Although mainly used to assess bone health, whole-body DXA scans also provide measurement of three compartments – bone, fat, and lean body mass. DXA-based bone density measurements are increasingly being used to assess bone health in children with chronic diseases. Other body composition methods and bone density measures are mainly research tools that are not readily applicable to the clinical setting.
Estimating daily energy needs is particularly important in caring for children with varying pediatric diagnoses that result in undernutrition or obesity. Their energy needs are difficult to estimate because of variations in metabolic demands of illness, energy expended in physical activity, and the proportion of the body composed of lean tissue. REE accounts for 60–70% of total daily expenditure. REE is used to estimate total energy needs in order to achieve a specific clinical goal – weight maintenance, loss, or gain.

Prediction equations based on the child’s age, sex, weight, and length/height have been developed to estimate REE when direct measurement is not possible. Unfortunately, these equations, derived from measurements of healthy children, do not perform well for children with serious health conditions or altered body composition.

### Table 1. Prediction equations for estimated energy requirements (kcal/day) and physical activity coefficients for healthy children

<table>
<thead>
<tr>
<th>Infants</th>
<th>Prediction equations</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–3 months</td>
<td>89 · weight (kg) – 100 + 175</td>
</tr>
<tr>
<td>3–6 months</td>
<td>89 · weight (kg) – 100 + 56</td>
</tr>
<tr>
<td>6–12 months</td>
<td>89 · weight (kg) – 100 + 22</td>
</tr>
<tr>
<td>12–24 months</td>
<td>89 · weight (kg) – 100 + 20</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Males</th>
<th>General prediction equation&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Sedentary PA coefficient</th>
<th>Low active PA coefficient</th>
<th>Active PA coefficient</th>
<th>Very active PA coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>3–8 years</td>
<td>88.5 – 61.9 · age + PAL · ((26.7 · weight) + 903 · (height)) + 20</td>
<td>1.00</td>
<td>1.13</td>
<td>1.26</td>
<td>1.42</td>
</tr>
<tr>
<td>9–18 years</td>
<td>88.5 – 61.9 · age + PAL · ((26.7 · weight) + 903 · (height)) + 25</td>
<td>1.00</td>
<td>1.13</td>
<td>1.26</td>
<td>1.42</td>
</tr>
<tr>
<td>&gt;18 years</td>
<td>662 – 9.53 · age + PAL · ((15.91 · weight) + 539.6 · (height))</td>
<td>1.00</td>
<td>1.11</td>
<td>1.25</td>
<td>1.48</td>
</tr>
<tr>
<td>Overweight</td>
<td>114 – 50.9 · age + PAL · ((19.5 · weight) + 1,161.4 · (height))</td>
<td>1.00</td>
<td>1.12</td>
<td>1.24</td>
<td>1.45</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Females</th>
<th>General prediction equation&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Sedentary PA coefficient</th>
<th>Low active PA coefficient</th>
<th>Active PA coefficient</th>
<th>Very active PA coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>3–8 years</td>
<td>135.3 – 30.8 · age + PAL · ((10 · weight) + 934 · (height)) + 20</td>
<td>1.00</td>
<td>1.16</td>
<td>1.31</td>
<td>1.56</td>
</tr>
<tr>
<td>9–18 years</td>
<td>135.3 – 30.8 · age + PAL · ((10 · weight) + 934 · (height)) + 25</td>
<td>1.00</td>
<td>1.16</td>
<td>1.31</td>
<td>1.56</td>
</tr>
<tr>
<td>&gt;18 years</td>
<td>354 – 6.91 · age + PAL · ((9.36 · weight) + 726 · (height))</td>
<td>1.00</td>
<td>1.12</td>
<td>1.27</td>
<td>1.45</td>
</tr>
<tr>
<td>Overweight</td>
<td>389 – 41.2 · age + PAL · ((15 · weight) + 701.6 · (height))</td>
<td>1.00</td>
<td>1.18</td>
<td>1.35</td>
<td>1.60</td>
</tr>
</tbody>
</table>

<sup>1</sup> Each prediction equation uses weight (kg) and height (kg), and requires that a physical activity coefficient (PA) be included in the calculation of the estimated energy requirement. The PA categories, based on the physical activity level (PAL, calculated as the ratio of total energy expenditure to resting energy expenditure), are as follows:

- Sedentary: PAL is estimated to be ≥1.0 and <1.4.
- Low active: PAL is estimated to be ≥1.4 and <1.6.
- Active: PAL is estimated to be ≥1.6 and <1.9.
- Very active: PAL is estimated to be ≥1.9 and <2.5.

Adapted from Food and Nutrition Board, Institute of Medicine [5].
The optimal approach is to measure REE using an indirect calorimeter or metabolic cart that measures oxygen consumption and carbon dioxide production.

Accurate REE measurement by indirect calorimetry requires standardized conditions, such as early morning testing after a night of restful sleep and an 8- to 12-hour (or age- or disease-appropriate) fast. A 40- to 60-min test enables initial environmental adjustment and exclusion of measurements during episodes of movement. During the test, the patient should be in a quiet, awake, calm state, in a supine position and not have performed any physical activity or received any medications known to change heart rate (such as bronchodilators). Developmentally normal children who are at least 5 years of age typically do well while watching a movie. Younger children or those with developmental delay often require sedation with a short-acting oral agent.

Energy needed for growth, physical activity, malabsorption, or to support therapeutic growth acceleration must be added to the REE to estimate total energy requirements. Table 1 shows the dietary reference intake prediction equations for estimated energy requirements (kcal/day) and physical activity factors for healthy infants and children. For hospitalized or ill children with less spontaneous physical activity, a factor of 1.3–1.5 × REE is a better estimate of energy needs. Additional corrections are made for disease severity (such as in children with cystic fibrosis) or malabsorption. In patients who require ‘catch-up’ growth, additional energy may need to be factored into the energy requirement estimation to achieve the desired rate of growth.

**Dual Energy X-Ray Absorptiometry**

DXA is a low energy X-ray (radiation exposure less than a day’s background exposure) technique that measures body composition of the total body, and regional bone mass and density. DXA-based bone mineral density (BMD, g/cm²) measurements are increasingly being used in clinical care for children at risk of bone disease. Risk factors for pediatric bone disease include immobility, malabsorption, or use of medications known to affect bone health, such as chronic glucocorticoid exposure [3].

Lumbar spine BMD values should be compared with reference values for healthy children of the same age and sex, and expressed as a z score or standard deviation (SD) score. A z score of 0 is equal to the median value for the reference population of children of the same age and sex; a z score of −1 means the patient’s value is 1 SD below that median value for the reference population. In clinical practice, BMD z scores from −2 to +2 are considered to be in the normal range, with a BMD z score of −1 to −2 being a low normal value [4]. Based on these findings and the patient’s clinical needs, the practitioner decides how best to increase BMD, by optimizing calcium and vitamin D in the diet, supplementing with calcium and/or vitamin D, and prescribing weight-bearing physical activity.

Whole-body DXA scans estimate lean body mass, fat mass, and percent body fat in less than 5 min. DXA body composition assessment is not regularly used in the clinical setting, but it may prove to be useful in the diagnosis and treatment of obesity. In cases where it is difficult to distinguish whether children with high body mass index have excess adiposity, skinfold assessment can be used to make this distinction. However, skinfold measurements by less experienced anthropometrists are subject to measurement error, and DXA assessments are more accurate. As DXA-based reference data become available for children and cutoff points are established for the level of body fat associated with the health risks of obesity, DXA could become a commonly used tool in the diagnosis and treatment of obesity.
Other Techniques for Assessing Body Composition

Other research body composition techniques include air displacement plethysmography (Bod Pod and Pea Pod) and bioelectrical methods such as total body electrical conductivity (TOBEC) and bioelectrical impedance analyzers (BIAs). Bod Pod, Pea Pod and BIAs are currently not used in the clinical care of individual patients who have illnesses that influence body composition and hydration. However, these methods are used in research settings to describe important changes in body composition in groups of subjects. The TOBEC technology is no longer available except in a few research settings, and is not available for clinical care. With further research experience and the necessary healthy infant and child reference data, body composition assessment will likely move into the clinical care setting.

More advanced imaging technologies, CT and MRI, also accurately measure body composition. However, their risk, availability, and cost do not make them useful in clinical practice. Peripheral quantitative computed tomography (pQCT) measures cross-sectional areas for fat and muscle, as well as volumetric bone mineral density of cortical and trabecular bone. However, the pQCT is not available for clinical purposes, as there is no pediatric reference database available for interpretation.

Conclusions

Technical measures in nutritional assessment in the clinical setting:

- Includes indirect calorimetry to directly measure resting energy expenditure. This REE is used to estimate total energy needs in order to achieve weight maintenance, loss, or gain in children
- Includes DXA to measure bone density in children at risk of bone disease and body composition. This may be useful in the diagnosis and treatment of obesity
- Does not include other measures such as Bod Pod, TOBEC, BIA, CT, and MRI, as they are primarily research tools

References

Introduction

Laboratory tests may aid in the diagnosis of primary childhood malnutrition (resulting from inadequate intake) and are invaluable in guiding therapeutic decisions in secondary malnutrition (resulting from conditions of increased need for or losses of substrate). Because nutritional status is an independent predictor of outcome in the sick child, strict attention to indicators of visceral protein stores and vitamin or mineral deficiency is imperative.

Although signs and symptoms of specific nutrient deficiencies commonly overlap and multiple deficiencies are frequently encountered, a judicious approach to ordering laboratory tests is recommended. While a rather comprehensive list of laboratory tests is presented here, clinical suspicion should guide the selection of specific investigations. Depending on the clinical laboratory facilities, turnaround time on certain tests may preclude their usefulness in the acute setting. Familiarity with these limitations will help to avoid ordering tests that do not contribute meaningfully to the management of the child.

Table 1 provides a summary of the laboratory tests discussed here including their normal values, signs and symptoms of the deficiency state, and pitfalls to avoid in their interpretation.

Protein

Assessment of visceral protein stores is commonly made by measuring serum proteins (table 2), most commonly albumin, prealbumin (trans-thyretin) and retinol-binding protein. Interpretation of serum total protein is predicated on normal globulin levels, limiting its clinical usefulness. Generally, serial measurements of protein status are more meaningful than single values and an understanding of their biological half-lives will dictate the frequency of assessment (table 2). A framework for the investigation of hypalbuminemia is shown in figure 1.
<table>
<thead>
<tr>
<th>Test (specimen)</th>
<th>Normal Range[^1]</th>
<th>Function/Description</th>
<th>Deficiency</th>
<th>Pitfalls to Avoid</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alkaline phosphatase</strong> (serum)</td>
<td>Infants: 150–420 U/l 2–10 years: 100–320 U/l Adolescent boys: 100–390 U/l Adolescent girls: 100–320 U/l Adults: 30–120 U/l</td>
<td>Zinc-dependent metallo-enzyme found in liver, bone, biliary epithelium, kidney and intestine</td>
<td>Low alkaline phosphatase warrants consideration of zinc deficiency</td>
<td></td>
</tr>
<tr>
<td><strong>α1-Antitrypsin</strong> (stool)</td>
<td>&lt;6 months: &lt;4.5 mg/g stool &gt;6 months: &lt;3 mg/g stool[^3]</td>
<td>Measure of protein loss from the gut</td>
<td>Unstable at pH &lt;3, may be unsuitable to assess gastric protein loss[^4]</td>
<td></td>
</tr>
<tr>
<td><strong>Biotin</strong> (serum)</td>
<td>214–246 pmol/l[^5]</td>
<td>Water-soluble vitamin, cofactor for carboxylases</td>
<td>Dermatitis, glossitis, alopecia, poor growth, ataxia, weakness, depression and seizures Anticonvulsants, hemodialysis and parenteral nutrition may give rise to deficiency</td>
<td></td>
</tr>
<tr>
<td><strong>Calcium</strong> (serum)</td>
<td>Preterm: 1.6–2.8 mmol/l Term to 10 days: 1.9–2.6 mmol/l 10 days to 2 years: 2.3–2.8 mmol/l 2–12 years: 2.2–2.7 mmol/l Adults: 2.2–2.5 mmol/l</td>
<td>Skeletal integrity, cofactor in clotting cascade and neuromuscular function</td>
<td>Fatigue, muscular irritability, tetany and seizures Factitious hypocalcemia caused by low albumin (50% is bound to albumin)</td>
<td></td>
</tr>
<tr>
<td><strong>Ceruloplasmin</strong> (serum)</td>
<td>Birth to 3 months: 40–160 mg/l 3–12 months: 290–380 mg/l 1–15 years: 230–490 mg/l[^3]</td>
<td>Carries 90% of serum copper</td>
<td>Positive acute-phase reactant</td>
<td></td>
</tr>
<tr>
<td><strong>Copper</strong> (serum)</td>
<td>Birth to 6 months: 3.1–4.2 μmol/l 6 years: 14.1–29.8 μmol/l 12 years: 12.6–25.1 μmol/l Adults (M): 11–37.7 μmol/l Adults (F): 12.6–24.3 μmol/l</td>
<td>Mineral cofactor for superoxide dismutase and enzymes of connective tissue synthesis</td>
<td>Anemia, neutropenia, depigmentation, characteristic hair changes, weakened bone and connective tissue[^5] Supra-physiologic doses of iron or zinc may impair absorption of copper[^5]</td>
<td></td>
</tr>
<tr>
<td><strong>Creatinine</strong> (serum)</td>
<td>Neonates: 26.5–88.4 μmol/l Infants: 17.7–35.4 μmol/l Children: 26.5–61.9 μmol/l Adolescents: 44.2–88.4 μmol/l Adults (M): 61.9–114.9 μmol/l Adults (F): 53–97.2 μmol/l</td>
<td>Product of muscle creatinine-phosphate metabolism, level parallels muscle mass</td>
<td>Diminished glomerular filtration rate, cimetidine, cephalosporins and trimethoprim may increase serum creatinine[^6]</td>
<td></td>
</tr>
<tr>
<td><strong>Elastase</strong> (stool)</td>
<td>&gt;200 μg/g stool</td>
<td>Indicator of exocrine pancreas sufficiency</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fat</strong> (stool)</td>
<td>&lt;3 years: &gt;85%[^*] &gt;3 years: &gt;95%[^7]</td>
<td>Indicator of fat malabsorption</td>
<td>Classically, a 72-hour stool collection with dietary diary</td>
<td></td>
</tr>
<tr>
<td><strong>Ferritin</strong> (serum)</td>
<td>Neonates: 25–200 μg/l 1 month: 200–600 μg/l 2–5 months: 50–200 μg/l 6 months to 15 years: 7–140 μg/l Adults: 10–250 μg/l</td>
<td>Major storage form of iron, levels mirror body reserves Early and sensitive indicator of iron-deficiency anemia</td>
<td>Positive acute-phase reactant</td>
<td></td>
</tr>
</tbody>
</table>

[^1]: Table 1. Frequently used laboratory tests in the assessment of childhood nutrition
[^2]: Albumin is most abundant serum protein, half-life 20 days
[^3]: Negative acute-phase reactant with hepatic synthetic dysfunction
[^4]: Changes with hydration status and fluid shifts
[^5]: Low alkaline phosphatase warrants consideration of zinc deficiency
[^6]: Unstable at pH <3, may be unsuitable to assess gastric protein loss
[^7]: Water-soluble vitamin, cofactor for carboxylases
[^8]: Carries 90% of serum copper
[^9]: Skeletal integrity, cofactor in clotting cascade and neuromuscular function
[^10]: Fatigue, muscular irritability, tetany and seizures
[^11]: Factitious hypocalcemia caused by low albumin (50% is bound to albumin)
[^12]: Measure of protein loss from the gut
[^13]: Unstable at pH <3, may be unsuitable to assess gastric protein loss
[^14]: Water-soluble vitamin, cofactor for carboxylases
[^15]: Anemia, neutropenia, depigmentation, characteristic hair changes, weakened bone and connective tissue
[^16]: Supra-physiologic doses of iron or zinc may impair absorption of copper
[^17]: Diminished glomerular filtration rate, cimetidine, cephalosporins and trimethoprim may increase serum creatinine
[^18]: Indicator of exocrine pancreas sufficiency
[^19]: Indicator of fat malabsorption
[^20]: Classically, a 72-hour stool collection with dietary diary
[^21]: Positive acute-phase reactant
<table>
<thead>
<tr>
<th>Test (specimen)</th>
<th>Normal Range&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Function/Description</th>
<th>Deficiency</th>
<th>Pitfalls to Avoid</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Folate (serum)</strong></td>
<td>Neonates: 11–147 nmol/l; Infants: 34–125 nmol/l; 2–16 years: 11–48 nmol/l; &gt;16 years: 7–45 nmol/l</td>
<td>Water-soluble vitamin, role in DNA/RNA synthesis and amino acid metabolism</td>
<td>Macrocytic anemia, hypersegmented neutrophils, glossitis, stomatitis, poor growth and fetal neural tube defects</td>
<td>Deficiency may be clinically indistinguishable from that of B&lt;sub&gt;12&lt;/sub&gt; except the neurological signs of the latter Methotrexate, phenytoin and sulfasalazine antagonize folate utilization</td>
</tr>
<tr>
<td><strong>Hemoglobin (whole blood)</strong></td>
<td>0–8 days: 2.06–3.79 mmol/l; 9 days: 1.66–3.33 mmol/l; 3 months: 1.53–2.25 mmol/l; 1 year: 1.38–2.14 mmol/l; 3 years: 1.58–2.31 mmol/l; 11 years: 1.72–2.43 mmol/l; Adults (M): 1.86–2.48 mmol/l; Adults (F): 2.17–2.79 mmol/l</td>
<td>Oxygen-carrying moiety in red blood cell</td>
<td>Microcytic anemia, pallor, weakness, dyspnea</td>
<td>Influenced by hydration status, nutrition, pregnancy</td>
</tr>
<tr>
<td><strong>Iron (serum)</strong></td>
<td>Neonates: 17.9–44.8 μmol/l; Infants: 7.2–17.9 μmol/l; Children: 9–21.5 μmol/l; Adults (M): 11.6–31.3 μmol/l; Adults (F): 9–30.4 μmol/l</td>
<td>Component in heme and cytochrome proteins</td>
<td>Microcytic anemia, pallor, weakness, dyspnea</td>
<td>Transferrin is a sensitive measure of body iron stores, however, it is a negative acute-phase protein</td>
</tr>
<tr>
<td><strong>Lymphocytes (whole blood)</strong></td>
<td>&gt;1,500/mm&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Total lymphocyte count is correlated to degree of malnutrition [6]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Magnesium (serum)</strong></td>
<td>0.65–1 mmol/l</td>
<td>Important for neuromuscular conduction; enzyme cofactor</td>
<td>Arrhythmia, tetany, hypocalcemia, hypokalemia</td>
<td>↓ by low serum albumin ↑ by hemolyzed specimens</td>
</tr>
<tr>
<td><strong>pH (stool)</strong></td>
<td>&gt;5.5</td>
<td>Low fecal pH usually implies carbohydrate malabsorption</td>
<td></td>
<td>Improper specimen processing may lead to false values</td>
</tr>
<tr>
<td><strong>Phosphorus (serum)</strong></td>
<td>Neonates: 1.45–2.91 mmol/l; 10 days to 2 years: 1.45–2.16 mmol/l; 2–12 years: 1.45–1.78 mmol/l; &gt;12 years: 0.87–1.45 mmol/l</td>
<td>Vital for energy transfer at cellular level</td>
<td>Confusion, respiratory distress, tissue hypoxia, bone abnormalities and ↑ alkaline phosphatase</td>
<td>‘refeeding syndrome’ is hypophosphatemia and hypokalemia complicating nutritional rehabilitation of the severely malnourished patient</td>
</tr>
<tr>
<td><strong>Prealbumin (serum)</strong></td>
<td>Neonates: 70–390 mg/l; 1–6 months: 80–340 mg/l; 6 months to 4 years: 20–360 mg/l; 4–6 years: 120–300 mg/l; 6–19 years: 120–420 mg/l</td>
<td>Gauge of visceral protein stores, half-life of 2 days</td>
<td></td>
<td><em>Negative acute-phase reactant</em></td>
</tr>
<tr>
<td><strong>Prothrombin time (plasma)</strong></td>
<td>10.5–15.5 s</td>
<td>Used to assess vitamin K sufficiency</td>
<td>Also prolonged in liver dysfunction, malabsorption syndromes, prolonged antibiotic use and warfarin therapy</td>
<td></td>
</tr>
<tr>
<td><strong>Reducing substances (stool)</strong></td>
<td>Negative</td>
<td>Presence suggests carbohydrate malabsorption</td>
<td>Improper specimen processing may lead to falsely normal values</td>
<td></td>
</tr>
<tr>
<td>Test (specimen)</td>
<td>Normal Range</td>
<td>Function/Description</td>
<td>Deficiency</td>
<td>Pitfalls to Avoid</td>
</tr>
<tr>
<td>-----------------</td>
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<td>----------------------</td>
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<td>------------------</td>
</tr>
</tbody>
</table>
| Selenium (serum) | Preterm: 0.6–1 μmol/l  
Term: 0.8–1.1 μmol/l  
1–5 years: 1.4–1.7 μmol/l  
6–9 years: 1.4–1.8 μmol/l  
>10 years: 1.6–2.1 μmol/l [5] | Water-soluble vitamin essential for glutathione peroxidase | Cardiomyopathy (Keshan disease), myositis and nail dystrophy |  |
| Urea nitrogen (serum) | Preterm (1st week): 1.1–8.9 mmol/l  
Neonates: 1.4–4.3 mmol/l  
Infants/children: 1.8–6.4 mmol/l  
Adults: 2.1–7.1 mmol/l | Produced in liver from protein degradation and is renally excreted | Reversible night blindness (the 1st clinical manifestation) that, uncorrected, is progressive to corneal scarring | ↓ in low protein intake states ↑ in high protein diets but also kidney disease |
| Vitamin A (serum) | Preterm: 0.45–1.6 μmol/l  
Term: 0.63–1.7 μmol/l  
1–6 years: 0.7–1.5 μmol/l  
7–12 years: 0.7–1.7 μmol/l  
13–19 years: 0.91–2.5 μmol/l | Fat-soluble vitamin that functions in vision, maintenance of epithelial tissue and immunity, 90% stored in liver | Beriberi: cardiac failure, peripheral neuropathy, ± edema  
Wernicke encephalopathy, Korsakoff syndrome | ↓ in liver disease, zinc deficiency ↑ with oral contraceptive pill use |
| Vitamin B1 (thiamine, whole blood) | Measure RBC transketolase activity <15% | Water-soluble vitamin with role in oxidative phosphorylation and pentose phosphate pathway | Dermatitis, cheilitis, glossitis and visual impairment |  |
| Vitamin B2 (riboflavin, whole blood) | Measure RBC glutathione reductase activity >1.2 activity coefficients | Water-soluble vitamin that facilitates red/ox reactions | Dermatitis, cheilitis, glossitis and visual impairment |  |
| Vitamin B12 (cobalamin, serum) | Neonates: 118–959 pmol/l  
Infants/children: 147–616 pmol/l | Water-soluble vitamin active in DNA synthesis and branched-chain amino acid metabolism | Megaloblastic anemia, hypersegmented neutrophils and glossitis, stomatitis, weakness, elevated homocysteine and methylmalonic acid | ↓ by phenytoin, proton-pump inhibitors, neomycin and folate deficiency |
| Vitamin C (ascorbate, plasma) | 22.7–85.2 μmol/l | Water-soluble antioxidant vitamin important in collagen synthesis | Scurvy: petechial and gingival hemorrhage, gingivitis and poor wound healing |  |
| Vitamin D (25-hydroxy, plasma) | Summer: 15–80 µg/l  
Winter: 14–42 µg/l [3] | Fat-soluble vitamin involved in calcium and phosphate homeostasis | Deficiency primarily affects bone and is called rickets; ↓ serum calcium, phosphate and ↑ alkaline phosphatase | ↓ with anticonvulsant therapy and cholestyramine |
| Vitamin E (serum) | <11 years: 7–35 μmol/l  
>11 years: 12–46 μmol/l | Fat-soluble antioxidant that protects cell membranes | Diminished deep tendon reflexes, impaired balance and gait | Carried in serum bound to lipid, therefore, hyperlipidemia may mask deficiency  
Vitamin E:lipid ratio useful in these circumstances |
| Zinc (plasma) | 10.7–18.4 μmol/l | Cofactor for >200 enzymes, notably alkaline phosphatase, RNA/DNA polymerase and superoxide dismutase [5] | Acrodermatitis enteropathica, also delayed wound healing, impaired taste, growth failure, delayed puberty and diarrhea | ↑ in hemolyzed specimens ↑ in sickle cell patients, hypoalbuminemia |

1 All reference ranges from the Harriet Lane Handbook [1], unless otherwise noted.
The most important limitation to measurement of serum proteins is their function in the acute phase response (Table 3). Appreciating the positive and negative acute phase reactants will help avoid misinterpretation of data. Another limitation of measuring serum proteins is that their manufacture is tied to hepatic synthetic function. Therefore, in the child with advanced liver disease a low serum protein may not necessarily reflect a lack of substrate but rather a lack of synthetic function. Finally, their concentrations are also susceptible to changes in hydration status and fluid shifts, and these changes may occur rapidly (e.g., increased vascular permeability associated with sepsis or trauma).

**Vitamins and Minerals**

Evaluating vitamin and mineral stores should take into account suspected underlying pathology (e.g., measurement of fat-soluble vitamins in conditions associated with fat malabsorption such as celiac disease or cystic fibrosis). Frequently, signs and symptoms of nutrient deficiency overlap with one another underscoring the importance of an informed approach to laboratory investigation.

<table>
<thead>
<tr>
<th>Protein Half-life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin 20 days</td>
</tr>
<tr>
<td>Prealbumin (transthyretin) 2 days</td>
</tr>
<tr>
<td>Retinol-binding protein 12 h</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Protein</th>
<th>Half-life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td>20 days</td>
</tr>
<tr>
<td>Prealbumin (transthyretin)</td>
<td>2 days</td>
</tr>
<tr>
<td>Retinol-binding protein</td>
<td>12 h</td>
</tr>
</tbody>
</table>

**Table 3. Serum proteins used in the acute-phase response**

<table>
<thead>
<tr>
<th>Positive acute-phase reactants</th>
<th>Negative acute-phase reactants</th>
</tr>
</thead>
<tbody>
<tr>
<td>α1-Antitrypsin</td>
<td>Albumin</td>
</tr>
<tr>
<td>C3 complement</td>
<td>Prealbumin (transthyretin)</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>Retinol-binding protein</td>
</tr>
<tr>
<td>Ferritin</td>
<td>Transferrin</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>Thyroxin-binding globulin</td>
</tr>
</tbody>
</table>

An often overlooked class of patients prone to malnutrition are those with absent (surgically resected) or diseased (Crohn’s disease, small bowel bacterial overgrowth) terminal ilea. Deficiencies of vitamins B₁₂ and K and zinc are prevalent in these patients.
Finally, the effects of drugs, particularly therapeutic agents, are important considerations. An exhaustive list of these interactions is beyond the scope of this text, however, some important nutrient-specific examples are shown in table 1.

Tests of Malabsorption

Analysis of the stool is a logical starting point for the investigation of malabsorption.

1. Enteric protein loss: Stool $\alpha_1$-antitrypsin, unlike albumin, passes into the stool undegraded.

2. Fat malabsorption: Fecal fat as assessed by 72-hour collection with diet record is an accurate, albeit cumbersome tool (for patients and laboratory technicians) to document malabsorption. A fecal smear with Sudan staining gives a rough qualitative estimate of steatorrhea and may be useful for screening purposes. Fecal elastase is a specific gauge of exocrine pancreatic sufficiency. Its level is not affected by pancreatic enzyme supplementation.

3. Carbohydrate malabsorption: Fecal pH and reducing substances are indicators of unabsorbed carbohydrate. Testing should be done on the most liquid portion of the stool and can be done at the bedside using Clinitest strips. Hydrogen breath testing is a sensitive method of detecting carbohydrate malabsorption. Breath hydrogen is measured at baseline and after the patient is given an oral load of the carbohydrate of interest (e.g. lactose): a rise in hydrogen $>10$ ppm above baseline is diagnostic. False-negative tests may be obtained in patients recently administered antibiotics. Additionally, a positive test does not always correlate with symptoms of intolerance.

Small bowel bacterial overgrowth may be assessed in an analogous manner using lactulose or glucose. A peak within 15–30 min or elevated baseline breath hydrogen ($>40$ ppm) is indicative of bacterial overgrowth.

Conclusions

- Serial measurement of visceral protein status helps guide nutritional therapy
- Evaluation of hypoalbuminemia must take into account potential deficient intake, potential losses, the inflammatory response (acute phase) and the volume status of the patient

References

1 General Aspects of Childhood Nutrition

1.3 Nutritional Needs

1.3.1 Nutrient Intake Values: Concepts and Applications

Berthold Koletzko

Key Words
Nutrient requirements • Recommended intakes • Dietary requirements • Recommended dietary allowances • Extrapolation

Key Messages
• Nutrient intake values (NIV) provide estimates on appropriate dietary substrate supply for populations of healthy people
• The average nutrient requirement is the estimated median requirement for a particular age- and sex-specific group
• The population reference intake is the intake meeting the known nutrient needs of practically all healthy individuals in a particular population
• Major uncertainties exist in the establishment of NIV for infants, children and adolescents due to limited scientific data. Deriving NIV from observed nutrient intakes (e.g. the supply with breast milk) or extrapolation from other age groups has considerable limitations

Introduction

Nutrient intake values (NIV) comprise a set of recommendations on dietary substrate supply for populations of healthy people. NIV are used to assess intake data from dietary surveys and food statistics, to provide guidance on appropriate dietary composition, meal provision, and food-based dietary guidelines; they serve as the basis for national or regional nutrition policies, nutritional education programs, food regulations and provide reference points for the labeling of food products if nutrient contents are expressed as a percentage of an NIV. The term NIV has been agreed upon by a recent expert consultation convened by the United Nations University’s Food and Nutrition Programme, in collaboration with the Food and Agriculture Organization (FAO), the World Health Organization (WHO), and UNICEF, rather than the terms nutrient reference values (NRV) previously used in Australia and New Zealand, reference values for nutrient supply in Germany/Austria/Switzerland, dietary reference values in the United Kingdom, and dietary reference intakes or previously recommended dietary allowances by the United States and Canada. Conceptually NIV are based on physiological requirements, which are defined as the amounts and chemical forms of nutrients needed systematically to maintain normal health and development, without disturbance of the metabolism of any other nutrient and without extreme homeostatic processes and excessive depletion or surplus in bodily depots. The dietary requirement of a nutrient is the intake sufficient to meet the physiological requirement, considering nutrient bioavailability from foodstuffs. NIV reflect the estimated distributions of nutrient intakes required to achieve a specific outcome in a
defined population considered healthy, but for many nutrients this distribution of requirements and the modifying biological and environmental factors are not well known, which results in considerable uncertainty in NIV. Therefore, NIV should be considered approximations that reflect the often limited data available. NIV are even more uncertain for infants and young children where original data are particularly scarce, and hence NIV are often derived from interpolation of data from other age groups which must be expected to yield inaccurate values. It is important to remember NIV refer to populations, but not to individuals. NIV do not allow determination of an insufficient nutrient intake or a nutrient deficiency in an individual, or accurate determination of nutrient needs in disease states.

Definitions of NIV

NIV for populations are generally estimated based on the concept that individual requirements follow a statistical distribution (bell-shaped curve; fig. 1). The average nutrient requirement (ANR; also called estimated average requirement [EAR]) is the estimated average of median requirement of a specific nutrient in the population derived from a statistical distribution of requirement criterion and for a particular age- and sex-specific group based on a specific biological endpoint or biochemical measure. The population reference intake (PRI; also called individual nutrient level 97% [INL97], reference nutrient intake [RNI], or recommended dietary allowance [RDA]) is the nutrient intake considered adequate to meet the known nutrient needs of practically all healthy individuals in a particular age- and sex-specific group. Based on the assumed statistical distribution of requirements, the PRI is set at a level of intake that meets the needs of 97% of the population (mean + 2 SD; fig. 1). The PRI value is generally used as the target for provision of essential nutrients to populations and as the reference point for nutrient labeling of foods, with the exception of energy where the average nutrient requirement is used because the provision of energy equivalent to the PRI would result in overfeeding and induction of obesity in about one half of the population. The upper nutrient level (UNL; or upper tolerable intake level) is the highest level of daily nutrient intake that is likely to pose no risk of adverse health effects for almost all individuals of a particular age- and sex-specific group. Ideally, the UNL is based on an analysis of the statistical distribution of risk for high nutrient intakes. The UNL is generally set at a level where the risk of excessive intakes is practically nonexistent. A nutrient intake equal to or higher than the UNL should be avoided on a chronic basis.

Examples of NIV for children and adolescents are provided in Annex 4.2.

Limitations in the Estimation of NIV

The concept of a near normal, symmetrical distribution of nutrient requirements (fig. 1) is known not to be correct for a number of nutrients. Examples are the nutrient needs for iron, vitamin D and polyunsaturated fatty acids. Iron requirements are not normally distributed, with higher needs in menstruating women, particularly in those with large blood losses. Vitamin D requirements depend on endogenous synthesis in the skin and hence on variation of UV light exposure with geographic location and time of the year, but also on biological determinants such as degree of skin pigmentation and genetic variations in vitamin D receptor. The dietary needs of essential fatty acids vary considerably with genetic polymorphisms for the fatty acid desaturation enzymes Δ⁶- and Δ⁵-desaturases that determine the relative turnover of polyunsaturated fatty acids [3].

The establishment of NIV for infants, children and adolescents is further hampered by severe limitations in the available scientific data ob-
tained in healthy children [4]. This is unfortunate because infants, children and adolescents have relatively large nutrient needs due to their growth and development, and adequate substrate is of utmost importance to support their short- and long-term health, wellbeing, and performance [5]. Current reference values for nutrient intakes vary considerably (see Annex 4.2), partly due the limitations of the available scientific database and partly due to major differences in underlying concepts, definitions, and terminology [4].

Due to the lack of adequate scientific studies, NIV for children are often based on observed nutrient intakes of groups of children in apparent good health. However, this approach is weak, because it assumes that the children in these surveys are in good health and are achieving their full genetic potential and that their diets are quantitatively and qualitatively appropriate and free from adverse long-term effects [1]. The concerns with respect to this approach are strengthened by recent evidence on the long-term effects of early nutrition on metabolic programming and the subsequent risk of hypertension, obesity, diabetes mellitus, and cardiovascular disease in adult life [6].

The derivation of NIV from observed intakes is a standard approach for infants during the first 6 months of life, when the intakes of breastfed babies are considered an appropriate guide to optimal nutritional supply. However, this approach has major limitations because the actual metabolizable substrate intakes of breastfed infants have not been well determined. The volume of milk consumed varies between about 550 and 1,100 ml/day, and milk composition differs between women and changes during the course of lactation, during the day and even during a single feeding [1]. Moreover, the bioavailability of substrates and their metabolism differs between infants fed human milk and those fed infant formula and complementary feeds, which can result in differences in requirements. Therefore, human milk composition and the nutrient supply to breastfed infants may not always provide useful guidance for infants that are not exclusively breastfed.
Due to the paucity of original research data for estimating nutrient requirements in the pediatric age group, very often NIV are extrapolated from data for other age groups. Frequently, this involves extrapolation from adults to children and adolescents. Examples of extrapolation methods that are used include body size (weight or metabolic weight), energy intakes for age, or factorial estimates of requirements for growth [4]. However, there is no truly correct method for extrapolation that would result in physiologically adequate NIV for infants, children and adolescents. It is important that the rationale or scientific basis for the method chosen should be completely transparent and thoroughly described for each nutrient and life-stage group. Extrapolation is always the second choice, and the use of innovative, noninvasive methods or of existing methods (e.g., stable isotopes) is encouraged to determine nutrient requirements of infants, children, and adolescents [4].

Conclusions

- Nutrient intake values (NIV) provide an estimate for adequate nutrient provision to populations considered healthy, but do not determine the optimal nutrient supply for an individual
- Population reference intakes (PRI; also reference nutrient intakes [RNI], or recommended dietary allowances [RDA]) are the levels of intake that meet the needs of almost all healthy individuals of a given age and sex group
- The diet for healthy children should generally provide nutrient intakes matching the PRI, except for energy where average nutrient requirements provide guidance on appropriate intakes for groups
- Children affected by disease, malnutrition or those in whom catch-up growth is desired may have nutrient needs that differ markedly from PRI

Acknowledgment

The author’s work in this area is carried out with partial financial support from the Commission of the European Communities specific RTD Program, ‘Food Quality and Safety – Integrating and Strengthening the European Research Area’, within the 6th Framework Program, research contract No. FP6-036196-2 (Aligning nutrient recommendations across Europe with special focus on vulnerable groups and consumer understanding). This paper does not necessarily reflect the views of the Commission and in no way anticipates future policy in this area.

References

1 General Aspects of Childhood Nutrition

1.3 Nutritional Needs

1.3.2 Energy Requirements of Infants, Children and Adolescents

Nancy Butte

Introduction

The energy requirements of infants, children and adolescents are defined as the amount of energy needed to balance total energy expenditure (TEE) at a desirable level of physical activity, and to support optimal growth and development consistent with long-term health [1]. Unlike recommendations for other nutrients which meet or exceed the requirements of practically all individuals in the population, recommendations for energy intake are based on the average requirement of the population to avoid energy intakes that exceed requirements. Recommendations for energy intake and physical activity are intended to support and maintain the growth and development of well-nourished and healthy infants, children and adolescents. The 2004 FAO/WHO/UNU recommendations for energy intake are based upon estimates of TEE and an allowance for growth [1].

For infants, TEE is predicted from measurements of TEE by the stable isotope method, doubly labeled water (DLW). For children and adolescents, heart rate monitoring and the DLW method were used to predict TEE. The energy cost of growth was derived from average velocities and the composition of weight gain.

Energy requirements during growth and development can be partitioned into components of basal metabolism, thermogenesis, physical activity, and energy cost of growth [2]. Basal metabolism is defined as that energy expended to maintain cellular and tissue processes fundamental to the organism. The Schofield equations [3] to predict basal metabolic rate (BMR) are presented in table 1. The thermic effect of feeding (TEF) refers to the energy required for the ingestion and digestion of food and for the absorption, transport and utilization of nutrients. TEF amounts to about 10% of the daily energy expenditure.
moregulation can constitute an additional energy cost when exposed to temperatures below and above thermoneutrality, however, clothing and behavior usually counteract such environmental influences. Physical activity is the most variable component of energy requirements, and entails both obligatory and discretionary physical activities. The energy cost of growth as a percentage of total energy requirements decreases from around 35% at 1 month to 3% at 12 months of age, and remains low until the pubertal growth spurt, at which time it increases to about 4% [2].

**Approaches to Estimating Energy Requirements**

Energy requirements are derived from TEE based on the factorial approach or measurements using the DLW method or heart rate monitoring. DLW is a stable (nonradioactive) isotope method that provides an estimate of TEE in free-living individuals [4]. In the heart rate method, TEE is predicted from heart rate based on the nearly linear relationship between heart rate and oxygen consumption during submaximal muscular work [5].

**Energy Requirements of Infants**

In the recent FAO/WHO/UNU recommendations [1], the average energy requirements of infants were based upon the TEE and growth rates of healthy, well-nourished infants (table 2; figs. 1, 2). In the FAO/WHO/UNU report, the median weight-for-age and monthly rates of weight gain of the WHO pooled breastfed data set were used to calculate energy requirements [6]. A prediction equation (eq. 1) for TEE was developed based on longitudinal data on 76 healthy infants studied at 3-month intervals for the first 2 years of life [2, 7].

\[
\text{TEE (MJ/day)} = -0.416 + 0.371 \text{ weight (kg)} \quad \text{SEE} = 0.456 \\
\text{TEE (kcal/day)} = -99.4 + 88.6 \text{ weight (kg)} \quad \text{SEE} = 109, \quad (eq. 1)
\]

in which SEE is the standard error of estimation.

Assuming energy equivalents of protein (23.6 kJ/g or 5.65 kcal/g) and fat (38.7 kJ/g or 9.25 kcal/g), and body composition changes during infancy [8, 9], energy deposition changes substantially during the first year of life from approximately 730 kJ/day (175 kcal/day) at 0–3 months, to 250 kJ/day (60 kcal/day) at 4–6 months and 85 kJ/day (20 kcal/day) for 1–12 months of age.

---

**Table 1.** Schofield equations for estimating basal metabolic rate (BMR) from weight (kg) in children [3]

<table>
<thead>
<tr>
<th>Age</th>
<th>Males</th>
<th>Females</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 3 years</td>
<td>BMR (MJ/day) = 0.249 weight – 0.127 SEE = 0.293</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BMR (MJ/day) = 0.244 weight – 0.130 SEE = 0.246</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BMR (MJ/day) = 59.5 weight – 30.4 SEE = 70</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BMR (MJ/day) = 58.3 weight – 31.1 SEE = 59</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3–10 years</td>
<td>BMR (MJ/day) = 0.095 weight + 2.110 SEE = 0.280</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BMR (MJ/day) = 0.085 weight + 2.033 SEE = 0.292</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BMR (MJ/day) = 22.7 weight + 504.3 SEE = 67</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BMR (MJ/day) = 20.3 weight + 485.9 SEE = 70</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–18 years</td>
<td>BMR (MJ/day) = 0.074 weight + 2.754 SEE = 0.440</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>BMR (MJ/day) = 0.056 weight + 2.898 SEE = 0.466</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BMR (MJ/day) = 17.7 weight + 658.2 SEE = 105</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BMR (MJ/day) = 13.4 weight + 692.6 SEE = 111</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SEE = Standard error of estimation.
### Table 2. Energy requirements of boys during the first year of life

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td></td>
<td>kJ/kg/day</td>
<td>kcal/day</td>
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<tr>
<td></td>
<td>MJ/day</td>
<td>kcal/kg/day</td>
</tr>
<tr>
<td>0–1</td>
<td>519 2.166</td>
<td>518 473</td>
</tr>
<tr>
<td>1–2</td>
<td>485 2.387</td>
<td>570 434</td>
</tr>
<tr>
<td>2–3</td>
<td>456 2.494</td>
<td>596 397</td>
</tr>
<tr>
<td>3–4</td>
<td>431 2.38</td>
<td>569 343</td>
</tr>
<tr>
<td>4–5</td>
<td>414 2.546</td>
<td>608 340</td>
</tr>
<tr>
<td>5–6</td>
<td>404 2.674</td>
<td>639 337</td>
</tr>
<tr>
<td>6–7</td>
<td>397 2.73</td>
<td>653 329</td>
</tr>
<tr>
<td>7–8</td>
<td>395 2.845</td>
<td>680 330</td>
</tr>
<tr>
<td>8–9</td>
<td>397 2.936</td>
<td>702 330</td>
</tr>
<tr>
<td>9–10</td>
<td>414 3.058</td>
<td>731 335</td>
</tr>
<tr>
<td>10–11</td>
<td>418 3.145</td>
<td>752 336</td>
</tr>
<tr>
<td>11–12</td>
<td>437 3.243</td>
<td>775 337</td>
</tr>
</tbody>
</table>

### Table 3. Energy requirements of girls during the first year of life

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td></td>
<td>kJ/kg/day</td>
<td>kcal/day</td>
</tr>
<tr>
<td></td>
<td>MJ/day</td>
<td>kcal/kg/day</td>
</tr>
<tr>
<td>0–1</td>
<td>519 1.942</td>
<td>464 447</td>
</tr>
<tr>
<td>1–2</td>
<td>485 2.162</td>
<td>517 421</td>
</tr>
<tr>
<td>2–3</td>
<td>456 2.301</td>
<td>550 395</td>
</tr>
<tr>
<td>3–4</td>
<td>431 2.245</td>
<td>537 350</td>
</tr>
<tr>
<td>4–5</td>
<td>414 2.389</td>
<td>571 345</td>
</tr>
<tr>
<td>5–6</td>
<td>404 2.507</td>
<td>599 341</td>
</tr>
<tr>
<td>6–7</td>
<td>397 2.525</td>
<td>604 328</td>
</tr>
<tr>
<td>7–8</td>
<td>395 2.63</td>
<td>629 328</td>
</tr>
<tr>
<td>8–9</td>
<td>397 2.728</td>
<td>652 328</td>
</tr>
<tr>
<td>9–10</td>
<td>414 2.828</td>
<td>676 331</td>
</tr>
<tr>
<td>10–11</td>
<td>418 2.902</td>
<td>694 331</td>
</tr>
<tr>
<td>11–12</td>
<td>437 2.981</td>
<td>712 331</td>
</tr>
</tbody>
</table>

### Table 4. Energy requirements of boys at 0–18 years of age, computed for a moderate level of physical activity

<table>
<thead>
<tr>
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<tbody>
<tr>
<td></td>
<td>kJ/kg/day</td>
<td>kcal/day</td>
</tr>
<tr>
<td></td>
<td>MJ/day</td>
<td>kcal/kg/day</td>
</tr>
<tr>
<td>1–2</td>
<td>439 4.0</td>
<td>950 345</td>
</tr>
<tr>
<td>2–3</td>
<td>418 4.7</td>
<td>1,125 350</td>
</tr>
<tr>
<td>3–4</td>
<td>397 5.2</td>
<td>1,250 334</td>
</tr>
<tr>
<td>4–5</td>
<td>397 5.7</td>
<td>1,350 322</td>
</tr>
<tr>
<td>5–6</td>
<td>377 6.1</td>
<td>1,475 312</td>
</tr>
<tr>
<td>6–7</td>
<td>377 6.6</td>
<td>1,575 303</td>
</tr>
<tr>
<td>7–8</td>
<td>326 7.1</td>
<td>1,700 295</td>
</tr>
<tr>
<td>8–9</td>
<td>326 7.7</td>
<td>1,825 287</td>
</tr>
<tr>
<td>9–10</td>
<td>326 8.3</td>
<td>1,975 279</td>
</tr>
<tr>
<td>10–11</td>
<td>267 9.0</td>
<td>2,150 270</td>
</tr>
<tr>
<td>11–12</td>
<td>267 9.8</td>
<td>2,350 261</td>
</tr>
<tr>
<td>12–13</td>
<td>228 10.7</td>
<td>2,550 252</td>
</tr>
<tr>
<td>13–14</td>
<td>228 11.6</td>
<td>2,775 242</td>
</tr>
<tr>
<td>14–15</td>
<td>200 12.5</td>
<td>3,000 233</td>
</tr>
<tr>
<td>15–16</td>
<td>200 13.3</td>
<td>3,175 224</td>
</tr>
<tr>
<td>16–17</td>
<td>186 13.9</td>
<td>3,325 216</td>
</tr>
<tr>
<td>17–18</td>
<td>186 14.3</td>
<td>3,400 210</td>
</tr>
</tbody>
</table>

### Table 5. Energy requirements of girls at 0–18 years of age, computed for a moderate level of physical activity

<table>
<thead>
<tr>
<th></th>
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<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>kJ/kg/day</td>
<td>kcal/day</td>
</tr>
<tr>
<td></td>
<td>MJ/day</td>
<td>kcal/kg/day</td>
</tr>
<tr>
<td>1–2</td>
<td>439 3.6</td>
<td>850 335</td>
</tr>
<tr>
<td>2–3</td>
<td>418 4.4</td>
<td>1,050 339</td>
</tr>
<tr>
<td>3–4</td>
<td>397 4.8</td>
<td>1,150 322</td>
</tr>
<tr>
<td>4–5</td>
<td>397 5.2</td>
<td>1,250 310</td>
</tr>
<tr>
<td>5–6</td>
<td>356 5.6</td>
<td>1,325 301</td>
</tr>
<tr>
<td>6–7</td>
<td>356 6.0</td>
<td>1,425 289</td>
</tr>
<tr>
<td>7–8</td>
<td>280 6.5</td>
<td>1,550 280</td>
</tr>
<tr>
<td>8–9</td>
<td>280 7.1</td>
<td>1,700 268</td>
</tr>
<tr>
<td>9–10</td>
<td>280 7.7</td>
<td>1,850 255</td>
</tr>
<tr>
<td>10–11</td>
<td>227 8.4</td>
<td>2,000 243</td>
</tr>
<tr>
<td>11–12</td>
<td>227 9.0</td>
<td>2,150 230</td>
</tr>
<tr>
<td>12–13</td>
<td>189 9.5</td>
<td>2,275 218</td>
</tr>
<tr>
<td>13–14</td>
<td>189 10.0</td>
<td>2,375 205</td>
</tr>
<tr>
<td>14–15</td>
<td>173 10.2</td>
<td>2,450 197</td>
</tr>
<tr>
<td>15–16</td>
<td>173 10.4</td>
<td>2,500 188</td>
</tr>
<tr>
<td>16–17</td>
<td>167 10.5</td>
<td>2,500 184</td>
</tr>
<tr>
<td>17–18</td>
<td>167 10.5</td>
<td>2,500 184</td>
</tr>
</tbody>
</table>
Energy Requirements of Children and Adolescents

In the 2004 FAO/WHO/UNU report [1], DLW and heart rate monitoring were used to predict the TEE of children and adolescents. TEE data of 801 boys and 808 girls aged 1–18 years were compiled from Canada, Denmark, Italy, Sweden, the Netherlands, Brazil, Chile, Columbia, Guatemala, and Mexico, from which prediction equations for TEE were developed for boys and girls [10].

For boys:
TEE (MJ/day) = 1.298 + 0.265 weight (kg) – 0.0011 weight\(^2\) (kg\(^2\)) SEE = 0.518
(\text{eq. 2})
TEE (kcal/day) = 310.2 + 63.3 weight (kg) – 0.263 weight\(^2\) (kg\(^2\)) SEE = 124

For girls:
TEE (MJ/day) = 1.102 + 0.273 weight (kg) – 0.0019 weight\(^2\) (kg\(^2\)) SEE = 0.650
(\text{eq. 3})
TEE (kcal/day) = 263.4 + 65.3 weight (kg) – 0.454 weight\(^2\) (kg\(^2\)) SEE = 155

During adolescence, gender differences in body size and composition are attenuated [12]. The energy cost of growth was based on mean rates of weight gain calculated from the WHO
weight-for-age standards [11]. The composition of weight gained was assumed to be 10% fat with energy content of 38.7 kJ/g (9.25 kcal/g), 20% protein with an energy content of 23.6 kJ/g (5.65 kcal/g), or equivalent to 8.6 kJ/g (2.1 kcal/g).

During adolescence, gender differences in body size and composition are accentuated [12]. The energy cost of growth was based on mean rates of weight gain calculated from the WHO weight-for-age standards [11]. The composition of weight gained was assumed to be 10% fat with energy content of 38.7 kJ/g (9.25 kcal/g), 20% protein with an energy content of 23.6 kJ/g (5.65 kcal/g), or equivalent to 8.6 kJ/g (2.1 kcal/g).

The energy requirements of boys and girls aged 0–18 years are summarized in tables 4, 5 and figures 3, 4.

**Recommendations for Physical Activity**

A minimum of 60 min/day of moderate-intensity physical activity is recommended for children and adolescents [1], although there is no direct experimental or epidemiological evidence on the
minimal or optimal frequency, duration or intensity of exercise that promotes the health and well-being of children and adolescents [13]. Regular physical activity is often associated with decreased body fat in both genders and, sometimes, increased fat-free mass at least in males. Physical activity is associated with greater skeletal mineralization, bone density, and bone mass.

Energy requirements must be adjusted in accordance with habitual physical activity. Torun [14] compiled 42 studies on the activity patterns of 6,400 children living in urban, rural, industrialized and developed settings from around the world. The TEE of rural boys and girls was 10, 15 and 25% higher at 5–9, 10–14 and 15–19 years of age, respectively, than their urban counterparts. As part of the compilation of TEE values described above, physical activity level (PAL) values were estimated by using measured or predicted BMR [10]. The Schofield equations for BMR [3] were used to predict PAL for children and adolescents, if not provided in the original publication. The average PAL (1.7) from these studies reflects a moderate level of activity. To estimate the energy requirements of children with different levels of habitual physical activity, a 15% allowance was subtracted or added to the average PAL to estimate light (PAL = 1.5) and vigorous (PAL = 2.0) levels of activity in the 2004 FAO/WHO/UNU report.

Conclusions

The energy requirements of infants, children and adolescents are defined as the amount of energy needed to balance TEE at a desirable level of physical activity, and to support optimal growth and development consistent with long-term health [1]. Even though energy requirements also are presented for varying levels of physical activity, moderately active lifestyles are strongly encouraged for children and adolescents to maintain fitness and health and to reduce the risk of overnutrition.

References

5 Berggren G, Christensen EH: Heart rate and body temperature as indices of metabolic rate during work. Arbeitsphysiologie 1950;14:255–260.
Introduction

Protein, derived from the Greek word proteos which means ‘primary’ or ‘taking first place’, is the major structural component of all cells in the body.

Proteins also function as enzymes, transport carriers, and as hormones; and their component amino acids are required for the synthesis of nucleic acids, hormones, vitamins and other important molecules.

The nutritional importance of proteins is due to their constituent amino acids. The 20 α-amino acids which are part of proteins are classified based on their nutritional importance into indispensable (essential) amino acids, conditionally indispensable (essential) amino acids and dispensable (nonessential) amino acids (table 1).

Protein in the body is in a dynamic state referred to as protein turnover, which involves continuous degradation to free amino acids, and resynthesis of new proteins. The free amino acids are also constantly degraded and oxidized to carbon dioxide and nitrogenous end products, principally urea and ammonia.

Dietary protein is necessary to replenish these losses of amino acids to maintain protein homeostasis. Furthermore, in children, there is an increased need for dietary protein to allow new tissue growth.

The requirement of dietary protein is therefore composed of two components: maintenance and growth.

The requirement of protein in children and adults was analyzed in detail earlier [1, 2], and recently by the Institute of Medicine, Food and Nutrition Board, US National Academy of Science in the Dietary Reference Intakes [3].

Protein Requirement

Protein requirement is defined as the minimum intake of high quality dietary protein (see Protein Quality, below) that will provide the needs for maintenance at an appropriate body composition, and will permit growth at the normal rate for age, assuming energy balance and normal physical activity.
Expression of Requirement

Protein requirement is expressed as the estimated average requirement (EAR), or the average requirement of the population.

Due to the lack of conclusive data from empirical studies, the EAR is calculated by a factorial method which includes (1) requirement for maintenance, estimated from Nitrogen Balance studies in children, and (2) requirement for growth, estimated from rates of protein deposition which are derived from body composition analysis [4, 5], and the efficiency of protein utilization for each age group.

The recommended dietary allowance (RDA) is the safe level of intake which will satisfy the protein needs of nearly all individuals (97.5%) in the population. The RDA for protein is the EAR + two times the standard deviation of the EAR of each age group.

Protein Requirements for Infants and Children

Infants: 0–6 Months
Human milk is the optimal source of nutrients for normal, full-term infants throughout the first year of life and is recommended as the sole nutritional source for infants during the first 4–6 months of life. The recommended intakes of protein are based on an adequate intake (AI) that reflects the mean protein intake of infants fed human milk. For infants at 0–6 months of age the average milk intake is 0.78 liters/day and the average protein content of human milk is 11.7 g/l. Therefore, the AI for protein in infants at 0–6 months is 9.1 g/day or 1.52 g/kg per day.

Infants: 7–12 Months
During the second 6 months of life, solid foods become a more important part of the diet of infants and add a significant amount of protein to the diet. The recommendation is for continued feeding of human milk for infants between 9 and 12 months of age with appropriate introduction of solid foods. The EAR and RDA are 1.0 and 1.2 g protein/kg body weight per day, respectively (table 2).

Children: 1–18 Years
Protein requirements for older children are calculated and recommended based on life stage groups representing different velocities of growth and endocrine status: toddlers (1–3 years), early childhood (4–8 years), puberty (9–13 years), and adolescence (14–18 years; table 2). During these stages, there is a continuing but slow decline in protein needs relative to weight. The EAR determined by the factorial method is set at the average for boys and girls in each age group except adolescence (table 2).

Amino Acid Requirement for Infants and Children

The 9 indispensable amino acids (IAA; table 1) need to be obtained from the diet and, therefore, requirements have been defined for them. The amino acid requirements (AI) for young infants (0–6 months) are based on average human milk feeding of human milk for infants between 9 and 12 months of age with appropriate introduction of solid foods. The EAR and RDA are 1.0 and 1.2 g protein/kg body weight per day, respectively (table 2).

<table>
<thead>
<tr>
<th>Indispensable</th>
<th>Conditionally indispensable</th>
<th>dispensable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histidine</td>
<td>Arginine</td>
<td>Alanine</td>
</tr>
<tr>
<td>Isoleucine</td>
<td>Cysteine</td>
<td>Aspartic acid</td>
</tr>
<tr>
<td>Leucine</td>
<td>Glutamine</td>
<td>Asparagine</td>
</tr>
<tr>
<td>Lysine</td>
<td>Glycine</td>
<td>Glutamic acid</td>
</tr>
<tr>
<td>Methionine</td>
<td>Proline</td>
<td>Serine</td>
</tr>
<tr>
<td>Phenylalanine</td>
<td>Tyrosine</td>
<td></td>
</tr>
<tr>
<td>Threonine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tryptophan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valine</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
intake of 0.78 liters/day and the mean content of each indispensable amino acid in human milk (table 3).

The EAR for IAA in older infants (7–12 months) and children (1–18 years) are calculated using the factorial method (table 4). The method assumes that the maintenance requirement for each IAA is similar to adults and the requirements differ in children only by the growth needs. The requirement for growth is estimated from the rate of protein deposition, amino acid composition of whole body protein and the efficiency of protein utilization.

Recently we provided evidence that the maintenance requirements for adults and children are similar [6–8]. For a detailed review on the methods to determine amino acid requirements refer to Pencharz and Ball [9].

The conditionally indispensable amino acids (table 1) are those that the infant or child is unable to produce in sufficient amounts and hence all or part of the daily needs for those amino acids must be provided by the diet.

---

**Table 2.** Protein requirement for infants, children and adolescents

<table>
<thead>
<tr>
<th>Age</th>
<th>Average requirement (EAR) g protein/kg body weight per day</th>
<th>Safe level of intake (RDA) g protein/kg body weight per day</th>
<th>Intake per day g/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>7–12 months</td>
<td>1.0</td>
<td>1.2</td>
<td>11</td>
</tr>
<tr>
<td>1–3 years</td>
<td>0.87</td>
<td>1.05</td>
<td>13</td>
</tr>
<tr>
<td>4–8 years</td>
<td>0.76</td>
<td>0.95</td>
<td>19</td>
</tr>
<tr>
<td>9–13 years</td>
<td>0.76</td>
<td>0.95</td>
<td>34</td>
</tr>
<tr>
<td>14–18 years, boys</td>
<td>0.73</td>
<td>0.85</td>
<td>52</td>
</tr>
<tr>
<td>14–18 years, girls</td>
<td>0.71</td>
<td>0.85</td>
<td>46</td>
</tr>
</tbody>
</table>

Data from Dietary Reference Intakes 2002/2005 [3].

**Table 3.** Indispensable amino acid requirements for young infants at 0–6 months of age

<table>
<thead>
<tr>
<th>Amino Acid</th>
<th>Adequate intake mg/kg per day</th>
<th>Intake per day mg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histidine</td>
<td>36</td>
<td>214</td>
</tr>
<tr>
<td>Isoleucine</td>
<td>88</td>
<td>529</td>
</tr>
<tr>
<td>Leucine</td>
<td>156</td>
<td>938</td>
</tr>
<tr>
<td>Lysine</td>
<td>107</td>
<td>640</td>
</tr>
<tr>
<td>Methionine + cysteine</td>
<td>59</td>
<td>353</td>
</tr>
<tr>
<td>Phenylalanine + tyrosine</td>
<td>135</td>
<td>807</td>
</tr>
<tr>
<td>Threonine</td>
<td>73</td>
<td>436</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>28</td>
<td>167</td>
</tr>
<tr>
<td>Valine</td>
<td>87</td>
<td>519</td>
</tr>
</tbody>
</table>

Data from Dietary Reference Intakes 2002/2005 [3].

**Protein Quality**

The requirement of protein is affected by not only the quantity but also by the quality of the protein source. Different sources of protein vary widely in their chemical composition and nutritional value. The protein quality is determined principally by digestibility and the amino acid composition of the protein. The most important factor of the two is the relative content and metabolic availability of the individual IAA.

If the content of a single IAA in the diet is less than the individual’s requirements, then it will limit the utilization of other amino acids and thus prevent normal rates of protein synthesis even when the total nitrogen intake is adequate. Thus, the ‘limiting amino acid’ will determine the nutritional value of the total nitrogen or protein in the diet.
### Table 4. Indispensable amino acid requirement for older infants, children and adolescents

<table>
<thead>
<tr>
<th>Age</th>
<th>Average requirement (EAR) mg/kg per day</th>
<th>Safe level of intake (RDA) mg/kg per day</th>
<th>Age</th>
<th>Average requirement (EAR) mg/kg per day</th>
<th>Safe level of intake (RDA) mg/kg per day</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>7–12 months</strong></td>
<td></td>
<td></td>
<td><strong>9–13 years, girls</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Histidine</td>
<td>22</td>
<td>32</td>
<td>Histidine</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>Isoleucine</td>
<td>30</td>
<td>43</td>
<td>Isoleucine</td>
<td>17</td>
<td>21</td>
</tr>
<tr>
<td>Leucine</td>
<td>65</td>
<td>93</td>
<td>Leucine</td>
<td>38</td>
<td>47</td>
</tr>
<tr>
<td>Lysine</td>
<td>62</td>
<td>89</td>
<td>Lysine</td>
<td>35</td>
<td>43</td>
</tr>
<tr>
<td>Methionine + cysteine</td>
<td>30</td>
<td>43</td>
<td>Methionine + cysteine</td>
<td>17</td>
<td>21</td>
</tr>
<tr>
<td>Phenylalanine + tyrosine</td>
<td>58</td>
<td>84</td>
<td>Phenylalanine + tyrosine</td>
<td>31</td>
<td>38</td>
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<td>49</td>
<td>Threonine</td>
<td>18</td>
<td>22</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>9</td>
<td>13</td>
<td>Tryptophan</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Valine</td>
<td>39</td>
<td>58</td>
<td>Valine</td>
<td>22</td>
<td>27</td>
</tr>
<tr>
<td><strong>1–3 years</strong></td>
<td></td>
<td></td>
<td><strong>14–18 years, boys</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Histidine</td>
<td>16</td>
<td>21</td>
<td>Histidine</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>Isoleucine</td>
<td>22</td>
<td>28</td>
<td>Isoleucine</td>
<td>17</td>
<td>21</td>
</tr>
<tr>
<td>Leucine</td>
<td>48</td>
<td>63</td>
<td>Leucine</td>
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<td>47</td>
</tr>
<tr>
<td>Lysine</td>
<td>45</td>
<td>58</td>
<td>Lysine</td>
<td>35</td>
<td>43</td>
</tr>
<tr>
<td>Methionine + cysteine</td>
<td>22</td>
<td>28</td>
<td>Methionine + cysteine</td>
<td>17</td>
<td>21</td>
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<tr>
<td>Phenylalanine + tyrosine</td>
<td>41</td>
<td>54</td>
<td>Phenylalanine + tyrosine</td>
<td>31</td>
<td>38</td>
</tr>
<tr>
<td>Threonine</td>
<td>24</td>
<td>32</td>
<td>Threonine</td>
<td>18</td>
<td>22</td>
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<tr>
<td>Tryptophan</td>
<td>6</td>
<td>8</td>
<td>Tryptophan</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Valine</td>
<td>28</td>
<td>37</td>
<td>Valine</td>
<td>22</td>
<td>27</td>
</tr>
<tr>
<td><strong>4–8 years</strong></td>
<td></td>
<td></td>
<td><strong>14–18 years, girls</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Histidine</td>
<td>13</td>
<td>16</td>
<td>Histidine</td>
<td>12</td>
<td>14</td>
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<tr>
<td>Isoleucine</td>
<td>18</td>
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<td>Leucine</td>
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<td>Lysine</td>
<td>37</td>
<td>46</td>
<td>Lysine</td>
<td>32</td>
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</tr>
<tr>
<td>Methionine + cysteine</td>
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<td>19</td>
</tr>
<tr>
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<td>Phenylalanine + tyrosine</td>
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<tr>
<td>Threonine</td>
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<td>Threonine</td>
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</tr>
<tr>
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<td>5</td>
<td>6</td>
<td>Tryptophan</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Valine</td>
<td>23</td>
<td>28</td>
<td>Valine</td>
<td>20</td>
<td>24</td>
</tr>
</tbody>
</table>

Data from Dietary Reference Intakes 2002/2005 [3].

EAR = Estimated average requirement, calculated from maintenance + growth (rate of protein deposition × efficiency of protein utilization); RDA = recommended dietary allowance, calculated from EAR + 2 × SD of EAR.
Protein Sources

Protein from animal sources such as meat, poultry, fish, eggs, milk, cheese, and yogurt provide all 9 IAA, and are called ‘high quality’ or ‘complete proteins’. Protein from plants, legumes, grains, nuts, seeds, and vegetables tend to be deficient in one or more of the IAA and are called ‘incomplete proteins’. Specifically, cereal grains are deficient in lysine and legumes are deficient in methionine. Thus, for children who are actively growing, it is recommended to ensure sufficient intake of ‘high quality’ protein. Children who restrict their diet to plant proteins should consume a varied diet containing complementary mixtures of protein (e.g. rice with beans) to ensure adequate protein intake.

Conclusions

• For infants 0–6 months human milk is considered the ideal food and the protein intake must be sufficient to maintain growth and meet other needs
• The protein requirement for children is affected by both the quantity and quality of the protein source
• All indispensable amino acid requirements must be met by the diet to ensure normal rates of protein synthesis in healthy children
• Therefore, consumption of ‘high quality’ proteins rich in the 9 indispensable amino acids, principally animal sources such as meat, poultry, eggs, milk products and complementary mixtures of plant protein, is recommended

References

Introduction

Dietary carbohydrates may be categorized as potentially digestible by enzymes present in the saliva, stomach, or intestine (or absorbable without digestion), and indigestible. Examples of the former are lactose, sucrose, human milk oligosaccharides, and vegetable starch. Dietary fibers found in cereals, vegetables, and fruit and fructooligosaccharides such as inulin, present in certain vegetables and processed foods (e.g. pastry), are indigestible. Lactose may be only partially digestible in preterm and, to some extent, in term infants and older children and adults who are not of northern European descent. Human milk oligosaccharides undergo little digestion and only about 10% of vegetable starch is not digested. Carbohydrates which are not digested and reach the colon undergo bacterial fermentation to partially absorbed gases such as hydrogen and methane and to short-chain fatty acids (SCFA) such as butyrate, which are efficiently absorbed in the colon. Butyrate has been reported to have many effects on mammalian cell gene transcription, protein synthesis, and both cellular proliferation and apoptosis. Besides being a source of substrate for the production of compounds like butyrate, fermentable carbohydrates may also alter the composition of the colonic microflora (prebiotic effects), which can alter the risk of disease as well as having many potential effects on mammalian cell function via the largely unstudied properties of bacterial proteins. Certain carbohydrates, such as dietary fiber, human milk oligosaccharides, and inulin, have effects on mammalian functions
Carbohydrate Assimilation by the Small Intestine and Colon

Overview
Dietary carbohydrate is assimilated via intestinal digestion and absorption, and via bacterial fermentation in the colon [1]. Fermentation may have both beneficial and adverse effects on the infant [1]. SCFA produced via bacterial fermentation are almost entirely absorbed in the colon and then partially (e.g. acetic acid) or more completely (e.g. butyric acid) metabolized by the colonic mucosa. SCFA then enter the liver where further metabolism occurs. There is controversy over whether lactose fermentation in the preterm newborn enhances the risk of necrotizing enterocolitis [1].

Digestible and Absorbable Carbohydrates
Monosaccharides (such as glucose and fructose), disaccharides (lactose, sucrose, maltose), and plant starch are digestible and/or absorbable. However, lactose digestion diminishes progressively in older children, especially those who are not of northern European descent [2]. Mobile animals store most of their energy as fat because glycogen is hydrated and very heavy per unit kilocalorie. Plants store energy as starch, a mixture of amylose (a polymer of maltose) and amylopectin, which has a structure similar to glycogen. Plant starch exists in the form of small granules which generally escape milling; the crystalline structure of these granules determines their relative susceptibility to digestion by mammalian enzymes [3].

Absorption of galactose and glucose per se increases the circulating concentration of glucose with its attendant metabolic effects (via insulin secretion) [1]. Lactose digestion facilitates calcium absorption [4]. Glucose is an important source of energy for brain and other tissues [1].
Indigestible Carbohydrates: Fiber, Oligosaccharides and Prebiotics

‘Dietary Fiber’
In their cell walls, plants contain constituents not digestible by mammalian enzymes; these are collectively known as dietary fiber (cellulose, hemicellulose, lignin, pectin, and gums) [3].

Oligosaccharides and Prebiotics
Besides lactose, human milk contains a complex mixture of oligosaccharides, which are almost entirely fermented in the colon (fig. 1) [4]. Fiber and oligosaccharides have been added to both formulas and infant foods [5]. Beyond infancy, humans consume both glucooligosaccharides, and fructooligosaccharides (FOS) such as inulin. FOS are consumed mainly in pastry, confectionery, and dairy products and also are found naturally in such foods as onion [6]. The term ‘prebiotic’ has been applied to indigestible carbohydrates, especially FOS such as inulin, which are almost quantitatively fermented in the colon and which tend to be selectively fermented by certain bacteria, thus leading to changes in the colonic flora (such as ‘beneficial’ increases in bifidobacteria) [6]. Inulin also might alter colonic cell proliferation and modify the diarrhea caused by lactulose [7].

Functional and ‘Dysfunctional’ Carbohydrate Foods: Foods May Have Functions Independent of Their Nutrient Content (table 1)

Carbohydrates and the Risk of Diabetes [8, 9]
Type-2 diabetes develops, usually in insulin-resistant people, when pancreatic β-cell function is insufficient to maintain euglycemia. The glycemic response to various carbohydrate-containing foods has been characterized as the glycemic index [3, 8]. Low glycemic index foods, such as breakfast cereal, whole wheat bread, pasta, barley, parboiled rice, and legumes, tend to lessen the risk of type-2 diabetes [8]. Initial research emphasized the potential metabolic effects of certain SCFA (e.g. propionate) and the effects of physical properties of fiber on slowing gastric emptying and delaying or moderating glycemic

Table 1. Carbohydrates as functional foods

<table>
<thead>
<tr>
<th>Carbohydrate</th>
<th>Putative functional effect</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fiber/low glycemic index foods</td>
<td>Improved glucose tolerance/insulin secretion</td>
<td>Mechanism unknown</td>
</tr>
<tr>
<td>Fructose</td>
<td>? Increased obesity/insulin resistance</td>
<td>Low intakes from fruit not harmful; more human studies needed</td>
</tr>
<tr>
<td>Fiber (bran)</td>
<td>Decreased risk of colon cancer</td>
<td>Fermentation may increase colon cell proliferation and increase risk</td>
</tr>
<tr>
<td>Fiber, lactulose</td>
<td>Decreased constipation</td>
<td>Diarrhea with excessive intake</td>
</tr>
<tr>
<td>Prebiotics</td>
<td>Decreased inflammatory disease and enteric infection of the bowel; ? Effects of bacterial proteins on obesity</td>
<td>Effects on cell proliferation appear variable</td>
</tr>
<tr>
<td>Human milk oligosaccharides</td>
<td>Reduced intestinal bacterial adhesion</td>
<td>Are there other oligosaccharides in food with similar effects?</td>
</tr>
</tbody>
</table>
responses [3]. More recently it has been shown that low glycemic index foods improve insulin secretion by an unknown mechanism [8]. Independent of the caloric content per se, a high fructose intake, derived from the combined ingestion of sucrose and high-fructose corn syrup (sweetened beverages and foods), may increase the risk of obesity and insulin resistance because of the metabolic effects of fructose [9].

**Fiber and Colon Cancer**
For over 30 years, there has been controversy over whether higher intakes of fiber lower or increase the risk of colonic neoplasms [3, 10]. One hypothesized mechanism for a benefit of fiber relates to the dilution effect of water adsorbed to non-fermentable fibers, which would dilute or ‘flush out’ carcinogens [3]. Another theoretical mechanism for reduced colon cancer development is the inhibition of cell proliferation by butyrate [1, 7]. In cultured neoplastic cells of colonic origin, butyrate generally causes a suppression of the cell cycle, but in vivo, butyrate may have the opposite effect [7]. Thus, highly fermentable fibers could actually be detrimental [1, 3].

**Indigestible Carbohydrates Including Fiber and Constipation**
Dietary fiber reduces constipation [11]. Inulin also might increase the frequency of loose stools [7]. Interestingly, preterm infants, who may have lactase deficiency at birth, thrive and seldom manifest diarrhea in response to human milk or formulas containing lactose as the sole carbohydrate [1].

**Prebiotics**
FOS may alter the bacterial colonization of the colon in favor of less clostridia, but the results of studies in humans are inconsistent [3, 5, 6]. Similarly, inulin has been shown to have both stimulatory and inhibitory effects on colonic cell proliferation [7]. Both prebiotics and probiotics seem to have potential value in the treatment of inflammatory bowel disease [12]. Finally, there is emerging evidence that different bacterial species or strains may, via their protein products, affect mammalian gene expression and thus the risk of health disorders such as obesity [7, 13].

**Human Milk Oligosaccharides**
Human milk oligosaccharides may prevent bacterial adhesion by interfering with the docking of bacteria on the intestinal cell surface and with the expression of certain enzymes in the intestine required for bacterial adhesion [14].

**Conclusions**
- Supplementation of infant formula or infant solid foods with fiber or inulin (prebiotics) may be warranted in some patients, but the overall benefits to health are not clear.
- High intakes of foods and beverages containing fructose or high-fructose corn syrup may increase the risk of obesity, insulin resistance, and ultimately type-2 diabetes.
- Despite the controversy over the specific health benefits of fiber, a generous intake of whole grains, fruits, and vegetables is recommended because of their nutrient content and because such foods replace saturated, trans, and polyunsaturated fat, and contain other compounds with potentially advantageous effects on health (e.g. tomato and lycopene).
References

**Key Words**

Lipids • Essential fatty acids • Linoleic acid • α-Linolenic acid • Long-chain polyunsaturated fatty acids • Arachidonic acid • Docosahexaenoic acid • Saturated fatty acid • Trans fatty acid

**Key Messages**

- Optimal lipid nutrition begins in fetal life with adequate n-3 to n-6 fatty acids and preformed long-chain polyunsaturated fatty acid (LCPUFA) supply through the maternal diet.
- Breast milk from mothers consuming a balanced diet provides the best source of bioavailable lipids for term neonates.
- Linoleic and α-linolenic acids are essential fatty acids, in addition LCPUFAs are important for lifelong health.
- LCPUFAs in the diet during the first months of life are important for visual and cognitive development, after that they contribute to lifelong health.
- Trans fatty acids interfere with LCPUFA metabolism, affect lipoprotein cholesterol regulation and promote cardiovascular disease.
- The balance between dietary n-3 and n-6 is important to promote lifelong health, reducing disease risk linked to allergic and inflammatory responses.

**Introduction**

Fats are the main source of energy for infants and young children, and n-6 and n-3 fatty acids (FAs) are essential for normal growth and development. Fat-soluble vitamins (A, D, E, K) require dietary lipids for absorption. Fats provide flavor and texture to foods and thus affect taste and acceptability of diets. Membrane lipid composition defines in part the functional properties of membranes (fluidity, transport properties, receptor activity, uptake and release of substances, signal transduction and conduction and ion flows). FAs can also have a direct effect on gene expression or by regulating transcription factors that affect the expression of multiple other genes (i.e. peroxisome proliferator-activated receptors). Dietary lipids provide structural components for brain and retinal structure, cell membranes, transport of lipid components in plasma and form the only true body energy store (adipose tissue). Fats and oils are key dietary factors affecting cardiovascular risk, obesity and diabetes. Linoleic acid (LA, C18:2n-6) and α-linolenic acid (LNA, C18:3n-3) are essential, they serve as precursors for the long-chain polyunsaturated FAs (LCPUFAs), such as arachidonic acid (AA, C20:4n-6) and docosahexaenoic acid (DHA, C22:6n-3). Neural cell phospholipids in the retina and brain cortex are rich in DHA while vascular endothelia are rich in AA. LCPUFAs are precursors for eicosanoids (C20) and docosanoids (C22), which act as local and systemic mediators for clotting, immune, allergic and inflammatory responses; they also affect blood pressure, vessel and bronchial relaxation and constriction. The dietary balance of n-6 and n-3 FAs can have profound influences.
in these responses, modulating the onset and severity of multiple disease conditions (allergy, atherosclerosis, hypertension and diabetes) [1, 5].

Lipids were long considered as part of the exchangeable energy supply for infants and young children, thus the primary concern was the degree of absorption of dietary fat as an important contributor to the energy supply during early life [1, 8].

**Essential Fatty Acids**

The essentiality of fats for human nutrition was identified only about 50 years ago when young children given skimmed milk and hydrogenated coconut oil demonstrated typical skin lesions and failed to gain weight compared to those given small amounts of energy from corn oil (2–4% total energy). This provided a strong base to maintain that infant diets had sufficient LA, the n-6 essential FA. A few decades later, in the late 1960s, the advent of total parenteral nutrition providing protein and glucose as sole sources of nutrition presented an opportunity to confirm that human infants require n-6 FAs for adequate growth. It was not until the 1980s that there was proof that n-3 FAs are essential for humans, considering the altered visual function of a child receiving high n-6 parenteral lipids, which was reversed by provision of LNA, the n-3 precursor found in soy oil. This was followed by information from nonhuman primates fed diets high in LA and extremely low in LNA before and after birth, which revealed altered retinal function and visual maturational delays in early life in animals given the low LNA diets. Studies in preterm infants postnatally fed corn oil (high in LA, low in LNA), soy oil (balanced LA and LNA), soy + marine oil (providing preformed DHA) or human milk (providing adequate LA, LNA and also preformed DHA) revealed that those receiving no DHA had altered electrical responses to light and significant delays in visual acuity maturation, which were only partially improved by LNA. These studies served to establish the need for LNA and suggested that at least for preterm infants DHA was also needed. Further studies over the past decade have established a need for n-3 FAs in term infants, with some but not all studies demonstrating a benefit of receiving preformed DHA. Several stable isotope studies using labeled LA and LNA have demonstrated a limited and highly variable capacity to convert these precursors into the corresponding LCPUFAs, AA and DHA, supporting the view that the latter may be considered conditionally essential during early life [1, 2, 9, 13].

**Fats in the First Year of Life**

High fat diets (40–60% energy) characteristic of infant feeding contribute to the energy density of the diet required to support rapid weight gain, and especially to the fat accumulation observed over the first year of life. This has been traditionally considered a desirable trait considering the increased risk of infection and potential dietary inadequacy after 6 months of life. However, the need for this fat gain in terms of survival may need to be reexamined as we presently face an environment that promotes energy excess and thus increases the risk of obesity and chronic diseases later in life. The recent 2006 WHO growth standards based on predominant breastfeeding for the first 6 months of life suggest a leaner model of growth for the second semester of life (see Chapter 4.1). In addition, the recent FAO/WHO 2004 energy recommendations based on actual energy expenditure from doubly labeled water studies are substantially lower than the history based on reported intakes, suggesting that the energy requirement and possibly the fat content after 6 months of life may need to be reexamined (see Chapter 1.3.2) [7, 8, 10, 12].

**Essentiality of PUFAs and LCPUFAs**

The essentiality of fats for human nutrition was identified only about 50 years ago when young children given skimmed milk and hydrogenated vegetable oils (coconut, palm, corn, soy, sunflower, safflower) provide LA- or oleic acid-rich for-
mulations and some LNA from soy oil attempting to mimic human milk composition (table 1). Coconut oil fractions rich in medium-chain triglycerides are used in an effort to promote absorption, especially in the feeding of preterm infants and those with fat malabsorption syndromes since C8–10 FAs are absorbed directly from the intestinal mucosa passing to the portal vein and are not dependent on bile acid micelle formation for digestion, absorption and uptake as chylomicrons into the lymphatic ducts. Over recent years DHA or DHA+AA have been added to artificial formulas. However, it is nearly impossible to fully replicate the unique fat composition and structure of human milk lipids. Human milk lipase activity further contributes to the improved fat digestibility of human milk. After 6 months, with the introduction of solid complementary foods, egg yolk, liver and fish can provide preformed DHA and AA (table 2) [3, 6, 14].

**Lipids in Human Milk**

Breast milk provides a ready source of both precursors and long-chain n-6 and n-3 derivatives, and is considered sufficient in these nutrients provided the mothers consume a nonrestrictive diet. The actual amount of essential FAs and LCPUFAs present in human milk varies depending on the maternal

<table>
<thead>
<tr>
<th>Source of oil</th>
<th>Fat g</th>
<th>Saturates</th>
<th>Monounsaturates</th>
<th>Polyunsaturates</th>
<th>(n-6) PUFA</th>
<th>(n-3) PUFA</th>
<th>Cholesterol, mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canola</td>
<td>100.0</td>
<td>7</td>
<td>59</td>
<td>30</td>
<td>20</td>
<td>9.3</td>
<td>0</td>
</tr>
<tr>
<td>Corn</td>
<td>100.0</td>
<td>13</td>
<td>24</td>
<td>59</td>
<td>58</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sunflower</td>
<td>100.0</td>
<td>10</td>
<td>19</td>
<td>66</td>
<td>66</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Rapeseed</td>
<td>100.0</td>
<td>7</td>
<td>56</td>
<td>33</td>
<td>22</td>
<td>11.1</td>
<td>0</td>
</tr>
<tr>
<td>Soya</td>
<td>100.0</td>
<td>15</td>
<td>43</td>
<td>38</td>
<td>35</td>
<td>2.6</td>
<td>0</td>
</tr>
<tr>
<td>Olive</td>
<td>100.0</td>
<td>14</td>
<td>47</td>
<td>8</td>
<td>8</td>
<td>0.6</td>
<td>0</td>
</tr>
<tr>
<td>Vegetable solid fat</td>
<td>100.0</td>
<td>25</td>
<td>45</td>
<td>26</td>
<td>3</td>
<td>1.6</td>
<td>0</td>
</tr>
<tr>
<td>Animal fat lard</td>
<td>100.0</td>
<td>39</td>
<td>45</td>
<td>11</td>
<td>10</td>
<td>1</td>
<td>95</td>
</tr>
<tr>
<td>Milk fat</td>
<td>81</td>
<td>50</td>
<td>23</td>
<td>3</td>
<td>21</td>
<td>1.2</td>
<td>219</td>
</tr>
</tbody>
</table>

**Table 1. Composition of commonly used vegetable oils**

<table>
<thead>
<tr>
<th>Source of oil</th>
<th>Fat g</th>
<th>Saturates</th>
<th>Monounsaturates</th>
<th>Polyunsaturates</th>
<th>(n-6) PUFA</th>
<th>(n-3) PUFA</th>
<th>Cholesterol, mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canola</td>
<td>100.0</td>
<td>7</td>
<td>59</td>
<td>30</td>
<td>20</td>
<td>9.3</td>
<td>0</td>
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<td>13</td>
<td>24</td>
<td>59</td>
<td>58</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sunflower</td>
<td>100.0</td>
<td>10</td>
<td>19</td>
<td>66</td>
<td>66</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Rapeseed</td>
<td>100.0</td>
<td>7</td>
<td>56</td>
<td>33</td>
<td>22</td>
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<td>0</td>
</tr>
<tr>
<td>Soya</td>
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<td>35</td>
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</tr>
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<td>Milk fat</td>
<td>81</td>
<td>50</td>
<td>23</td>
<td>3</td>
<td>21</td>
<td>1.2</td>
<td>219</td>
</tr>
</tbody>
</table>

**Table 2. Recommended fish as a source of EPA and DHA [4, 14]**

<table>
<thead>
<tr>
<th>Higher levels of EPA and DHA (&gt;1,000 mg/100 g fish)</th>
<th>Herring</th>
<th>Mackerel</th>
<th>Salmon</th>
<th>Tuna, bluefin</th>
<th>Greenland halibut</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medium level (500–1,000 mg/100 g fish)</td>
<td>Flounder</td>
<td>Halibut</td>
<td>Tuna, canned white</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low level (&lt;300 mg/100 g fish)</td>
<td>Tuna, skipjack</td>
<td>Tuna, canned light</td>
<td>Cod</td>
<td>Catfish</td>
<td>Haddock</td>
</tr>
</tbody>
</table>

**Table 3. Contribution of various food to trans fats consumed (percent of total) [14]**

<table>
<thead>
<tr>
<th>Food group</th>
<th>% Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cakes, cookies, crackers, pies, bread, doughnuts, fried fast chicken, etc.</td>
<td>40</td>
</tr>
<tr>
<td>Animal products</td>
<td>21</td>
</tr>
<tr>
<td>Stick margarine</td>
<td>17</td>
</tr>
<tr>
<td>Fried potatoes</td>
<td>8</td>
</tr>
<tr>
<td>Potato chips, corn chips, popcorn</td>
<td>5</td>
</tr>
<tr>
<td>Household shortening</td>
<td>4</td>
</tr>
<tr>
<td>Breakfast cereals, candy</td>
<td>5</td>
</tr>
<tr>
<td>Soy oil</td>
<td>2</td>
</tr>
<tr>
<td>USDA analysis reported 0 g trans fats in salad dressing.</td>
<td></td>
</tr>
</tbody>
</table>
diet. Human milk provides close to 50% of the energy as lipids. Oleic acid is the predominant FA, while palmitic acid is provided in the sn-2 position of triglyceride, enhancing its absorption. Preformed cholesterol in breast milk (100–150 mg/dl) provides most of what is needed for tissue synthesis, thus downregulating endogenous cholesterol synthesis in the initial months of life [7, 8].

Trans Fatty Acids

Trans FAs are the product of hydrogenation of vegetable oils (soy) with the object of making these less susceptible to peroxidation (rancidity), thus the processed foods prepared with trans FAs have a longer shelf life, which is in the interest of producers and retailers. However, the effect of these fats on lipoprotein metabolism is indeed more harmful than that of saturated fats (C14, C16), since they not only increase low-density lipoprotein (LDL) cholesterol, the cholesterol-rich atherogenic lipoprotein, but also lower high-density lipoprotein (HDL) cholesterol, the protective lipoprotein responsible for reverse cholesterol transport. The net effect is that these fats contribute substantially in raising the risk of cardiovascular disease (table 3) [11, 12, 15].

Fats in the 2nd Year of Life and Beyond

After 2 years of life, the recommendations for fat need to consider the level of habitual physical activity since the need for energy-dense food sources such as fat should be adjusted to the energy required to promote healthy weight and active living; the energy needs for growth after 2 years represent 2–3% of the daily needs. Sedentary children will meet their energy needs easily with fat energy of around 30% of the total, while active children may benefit from higher fat energy. Table 4 gives full details. Fat reduction has been advocated by some as a way to prevent diet-related chronic dis-

<table>
<thead>
<tr>
<th>Table 4. Fat supply for children older than 2 years for the prevention of nutrition-related chronic diseases (based on last seven references)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dietary component</strong></td>
</tr>
<tr>
<td>Total dietary fat intake</td>
</tr>
<tr>
<td>Saturated fatty acids</td>
</tr>
<tr>
<td>Polyunsaturated fatty acids (PUFAs)</td>
</tr>
<tr>
<td>n-6 PUFAs</td>
</tr>
<tr>
<td>n-3 PUFAs</td>
</tr>
<tr>
<td>n-6:n-3 ratio</td>
</tr>
<tr>
<td>Monounsaturated fatty acids</td>
</tr>
<tr>
<td>Cholesterol</td>
</tr>
<tr>
<td>Antioxidant vitamins</td>
</tr>
<tr>
<td>Potentially toxic factors ¹</td>
</tr>
<tr>
<td>Trans fatty acids</td>
</tr>
<tr>
<td>Erucic acid</td>
</tr>
<tr>
<td>Lauric and myristic acids</td>
</tr>
<tr>
<td>Cyclopropenoids</td>
</tr>
<tr>
<td>Hydroperoxides</td>
</tr>
</tbody>
</table>

¹ Limit processed foods and hard fats and hard margarine as a practical way to reduce the intake of saturated and trans fatty acids.
ease. There is clearly a need to promote energy balance and avoid energy excess that leads to unhealthy weight. This can be achieved by lowering fat or sugar in the diet; in terms of weight control there may be some benefit from reducing sugar rather than fat with regard to insulin responses and appetite control. In terms of cardiovascular disease prevention, the key aspect is the quality of the fat: decreasing saturated fat (especially C14 myristic and C16 palmitic acids) is crucial, in fact C18 stearic acid is neutral in terms of cholesterol, since most of it is converted to oleic acid by the liver. Thus, a mild elevation in LDL cholesterol is offset by a rise in HDL. The key issue in the prevention of obesity is keeping energy intake and expenditure in balance at a healthy weight. Reducing fat intake is one way of achieving this, but it may not be the most sustainable way [10, 12, 15].

Conclusions

- According to the breast milk model, the intake of lipids for the first 6 months of life should provide 40–60% of total energy, an n-6:n-3 ratio of 5–10:1, <1% industrially produced trans FAs, and be free from erucic acid
- After age 2 years, dietary fat should provide 30–35% energy: in the form of n-6 PUFAs 4–10% energy, n-3 1–2% energy, saturated fat <10% energy, trans fats <2% energy
- n-6 FAs should be limited to <10%, and total PUFAs <15% of total energy, n-9 oleic acid can bridge the difference
- The quality of the fat, more than the quantity, is important for lifelong health

References

1 General Aspects of Childhood Nutrition

1.3 Nutritional Needs

1.3.6 Fluid and Electrolytes

George J. Fuchs

Introduction

Maintenance of body water and electrolytes is the result of tightly regulated balances of intakes and outputs mediated by elaborate physiologic mechanisms. Sodium (Na⁺) retention causes volume expansion and depletion causes volume contraction. A net negative sodium balance results in a clinical state of extracellular fluid (ECF) volume contraction, the most common cause worldwide being infectious diarrheal disease resulting in dehydration.

Unlike sodium, whose distribution in the body is uneven because of active transport of the ion, water movement is passively determined in response to osmotic gradients. Body water, being freely diffusible, is therefore in equilibrium in relation to the distribution of its nondiffusible solutes.

Maintenance of body water involves the control of both intake/absorption governed by the gastrointestinal tract and excretion, but principally by excretion controlled by the kidney. Under normal conditions, losses via the gastrointestinal tract are small but can greatly increase in pathologic states such as diarrheal disease.

Diarrheal illness accounts for approximately 2.5 million deaths per year, with most deaths occurring in developing countries and many of these from dehydration [1]. The severity of dehydration is graded by clinical signs and symptoms that reflect fluid loss and that determine the treatment regimen to correspond to the degree of severity. Regardless of the etiology, more than 90% of dehydration can be safely and effectively managed with oral rehydration therapy using a prescribed fluid and electrolyte oral rehydration solution (ORS). Because malnutrition results in an increased frequency, severity, and duration of diarrhea, fluid and electrolyte replacement and nutritional therapy are the critical elements for recovery [2].
Regulation of Sodium Balance

Sodium absorption occurs in the gastrointestinal tract and excretion primarily by the kidney with small amounts excreted in sweat and feces. In pathologic conditions, especially diarrheal disease, normal gastrointestinal mechanisms of homeostasis become disturbed and can result in large, sometimes life-threatening fluid and electrolyte losses. The systems regulating renal sodium chloride (NaCl) and water excretion operate by a negative feedback loop consisting of an afferent (sensory) component, an efferent (messenger) component, and an effector organ [3]. The renal response is aimed at reconstituting ECF volume by decreasing the glomerular filtration rate and thus the filtered load of Na+ and, even more critically, by promoting tubular reabsorption of Na+ utilizing the various mechanisms of Na+ transport including exchangers, channels, and cotransporters. Receptors located in the renal juxtaglomerular apparatus detect reduced ECF volume and Na+ concentration, and stimulate renal Na+ retention via the renin-angiotensin cascade.

Regulation of Body Water

Plasma osmolality is the primary driver for thirst and, therefore, water intake, although under conditions of reduced ECF volume, such as severe dehydration, low blood volume assumes a greater role and will override tonicity [4]. Arginine vasopressin secreted from pituitary neuronal cells in response to signals from osmoreceptors binds to epithelial cell basolateral receptors of the otherwise water-impermeable nephron collecting tubule, stimulating insertion of water channels (aquaporines) into the apical cell surface and results in extraordinary movement of water from lumen to cell interior.

Gastrointestinal Regulation of Fluids and Electrolytes

In general, permeability of the tight junction between epithelial cells decreases distally so that the jejunum is the most and the distal colon and rectum the least permeable to the passive movement of electrolytes and water [5]. Ions traverse the epithelium by passing through the transcellular or paracellular routes throughout the length of the bowel by passive or active transport mechanisms. Passive movement of fluids follows, with paracellular transport, the main mechanism of flow in the small bowel, and transcellular flow predominating where the epithelia are tightly aligned and less permeable as in the distal colon. Cotransportation of Na+ with certain nutrients including glucose and amino acids at the apical surface of the upper villus in the small intestine is responsible for most Na+ and water absorption following a meal or ingestion of oral rehydration solution (fig. 1). The carrier specific for Na-glucose cotransport, SGLT-1, is preserved in most diarrheal diseases and thereby forms the basis for oral rehydration therapy [6]. In the fasted state or between meals, most NaCl is transported from the lumen via exchange (Na+/H+ and Cl-/HCO3-).

While sodium transport drives fluid absorption, Cl- excretion is the driving force for fluid secretion. Cl is taken up along the basolateral membrane of the epithelial cell by the electroneutral Na+/K+/2Cl- cotransporter and accumulates within the cell above its electrochemical equilibrium (fig. 2). Once within the cell, Cl exits into the intestinal lumen via Cl channels that open in response to regulatory agonists that invoke second messenger systems.

Intracellular Regulators of Ion Flux

A variety of hormones, neurotransmitters, and secretagogues bind to receptors along the epithelial cell membrane to initiate the intracellular
cascade involving the second messenger molecules of cyclic nucleotides (including cyclic adenosine monophosphate and cyclic guanosine monophosphate) and ionized cytosolic calcium (Ca$^{2+}$). These in turn activate protein kinases that exert direct control of ion channels to increase efflux of Cl through Cl channels down their electrochemical gradients and inhibition of electroneutral NaCl-coupled influx.

**Intercellular Regulators of Ion Flux**

Under normal conditions, intestinal transport of water and electrolytes is a finely tuned transcellular and paracellular phenomenon regulated by the complex interaction between the endocrine, paracrine, immune, and enteric nervous systems. In reality, these systems do not function as isolated units and their borders are indistinct and overlap [4]. Examples include serotonin and vasoactive intestinal peptide that function as either hormones or neurotransmitters or both depending on the precise physiologic situation. Certain bacterial enterotoxins such as cholera and cytotoxins simultaneously stimulate paracrine, neural, and immune responses, all of which may alter ion and water flux [7].

**Other Regulatory Factors**

Other factors influence fluid and electrolyte transport indirectly and include acid-base homeostasis, gut motility, luminal flow rates, intestinal permeability, blood oncotic pressure and plasma volume, venous and arterial pressure, and physical and psychological stress.
Effects of Environment and Physical Activity

Heat stress and physical activity may cause both fluid and electrolyte imbalances. In hot climates, a considerable volume of water may be lost through perspiration for evaporative cooling and is further increased with increased humidity and during periods of physical exertion (fig. 3) [8]. Compared to adults, children have a greater surface area to body mass ratio but lower sweating capacity and that has more important implications for heat tolerance than fluid and electrolyte disturbances. Breastfed infants, including low birth weight infants, in hot climates can be adequately maintained on breast milk exclusively and do not require supplemental water [9].

Table 1. Treatment of acute watery diarrhea, modified from King et al. [10]

<table>
<thead>
<tr>
<th>Degree of dehydration</th>
<th>Signs</th>
<th>Rehydration therapy (within 4 h)</th>
<th>Replacement of losses</th>
<th>Nutrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal (&lt;3%)</td>
<td>Well, alert</td>
<td>Not applicable</td>
<td>For each diarrheal stool or vomiting episode give: 60–120 ml ORS if &lt;10 kg b.w., 120–240 ml ORS if &gt;10 kg b.w.</td>
<td>Continue breastfeeding or resume age-appropriate diet after initial rehydration</td>
</tr>
<tr>
<td>Mild to Moderate (3–9%)</td>
<td>Sunken eyes, sunken fontanelle, loss of skin turgor, dry buccal mucous membranes</td>
<td>ORS 50–100 ml/kg over 3–4 h</td>
<td>Same as above</td>
<td>Same as above</td>
</tr>
<tr>
<td>Severe (≥10%)</td>
<td>Signs of moderate dehydration with one of the following: rapid thready pulse, cyanosis, cold extremities, deep breathing, lethargy, unconscious</td>
<td>Intravenous fluids 30 ml/h until pulse, perfusion, and mental status improve; then ORS 100 ml/kg over 4 h</td>
<td>Same as above</td>
<td>If unable to drink, give by nasogastric tube</td>
</tr>
</tbody>
</table>

Principles of Rehydration and Fluid Maintenance

The degree of dehydration as graded by clinical characteristics determines the fluid and electrolyte regimen to be used, regardless of the specific etiology. Except for severe dehydration or if the child is not able to tolerate enteral fluids, oral ORS (Na+) should be used for rehydration and accomplished rapidly over 3–4 h (table 1) [10]. WHO and UNICEF recommend a 245-mmol/l ORS of NaCl 2.6 g (75 mmol/l), glucose 13.5 g (75 mmol/l), KCl 1.5 g (20 mmol/l), and citrate 2.9 g (10 mmol/l). Breastfeeding should continue during and immediately following rehydration; in non-breastfed infants, an unrestricted age-appropriate diet should be provided immediately following initial rehydration. If formula is being used, it should not be diluted and does not need to be a specialized formula since lactose-containing formulas are usually well tolerated. Ongoing stool losses should be replaced with ORS.

Severely dehydrated children usually require initial rehydration with intravenous fluids, after which hydration can usually be maintained orally with ORS (table 1). Ringer’s lactate (Na+ 130 mmol/l, K+ 4 mmol/l, Cl− 109 mmol/l and lactate 28 mmol/l) with or without 5% dextrose is the preferred intravenous solution while normal saline (0.9% NaCl; Na+ 154 mmol/l) is an acceptable
alternative. In extreme situations or if the child is unable to keep up with ongoing stool losses, intravenous fluids are needed beyond the initial rehydration period (table 2) [2].

In developing countries where diarrheal disease is most prevalent and associated with the greatest mortality and morbidity, many affected children have concomitant malnutrition. Malnutrition results in an increased incidence, severity, and duration of diarrhea and is an underlying cause of much of the diarrheal disease-related mortality. Optimal prevention and management of diarrheal disease, therefore, requires attention to nutritional therapy including continued breastfeeding in breastfed infants and early refeeding during a diarrheal disease episode. Zinc supplementation promotes recovery from acute and persistent diarrhea; as well as decreasing post-diarrheal disease morbidity, it is now universally recommended as adjunctive treatment of children with diarrhea older than 6 months of age. Severely malnourished children with diarrhea have unique, stereotypical clinical abnormalities and require a specific, protocolized regimen to ensure safe, efficacious fluid and electrolyte reconstitution. A potential role for zinc in the treatment of acute diarrhea in developed countries has not been defined.

### Table 2. Guidelines for intravenous fluids for severe dehydration

<table>
<thead>
<tr>
<th>Age</th>
<th>First give</th>
<th>Then give</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants (&lt;12 months)</td>
<td>First give</td>
<td>Then give</td>
</tr>
<tr>
<td>Older children and adults</td>
<td>1 h</td>
<td>5 h</td>
</tr>
<tr>
<td></td>
<td>30 min</td>
<td>2.5 h</td>
</tr>
</tbody>
</table>

Modified from WHO [2]. Preferably start intravenous Ringer’s lactate (with or without 5% dextrose; normal saline is acceptable) immediately; give an oral rehydration solution until the intravenous line is started if the child can drink.

- Repeat once if radial pulse remains weak or not detectable.
- If the child is able to drink and keep up with stool losses, introduce ORS as described in table 1.

### References

Key Words

Vitamins · Minerals · Fortification · Supplements · Toxicity

Key Messages

- Micronutrients (vitamins and trace elements) are essential for growth and health
- They are obtained naturally from foods as well as through fortification and enrichment and by consuming supplements
- There are important nutrient–nutrient interactions among micronutrients
- Excessive intake of certain vitamins and trace elements can have adverse effects on child health

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Introduction

The same set of organic compounds and inorganic elements that are essential for adults are similarly indispensable for children of all ages, from premature infants to individuals in late adolescence. These include a total of 13 vitamins, 4 of which are classified as fat-soluble and 9 of which are classified as water-soluble. There are also some 9 inorganic trace elements which are classified as essential to human nutrition or beneficial to human health. Age- and gender-specific recommended dietary intakes of the micronutrients have been established. These apply exclusively to healthy infants, toddlers, children and adolescents. The net supply of nutrients available to a child, however, is determined by a series of factors described in Table 1.

Sources of Vitamins and Trace Elements

The three principal sources of micronutrients for a child are described in Table 2. All nutrients will be obtained from one or another of these formats.

Vitamins and Trace Elements Intrinsic to Foods

It takes a wide variety of different foods to obtain the entire range of necessary micronutrients in adequate amounts [1]. Micronutrients tend to be less varied and less dense in edible plants than in animals [2]. In addition, cooking, processing and storage destroy or elute nutrients before consumption. Moreover, it is important to understand the recent consensus that the vitamin A value of the provitamin A carotenoids found in green, orange and yellow fruits and vegetables is only one half of what had traditionally been considered [3]. It would take twice as many servings of carrots or broccoli to provide a given contribution to daily vitamin A needs than would have been estimated 8 years ago.
To the extent that plants are rich sources of vitamins E, C, K and folate, children should be encouraged to consume whole grains and green, yellow and orange vegetables to take advantage of these sources. Picky eaters are at a disadvantage in covering their required nutrient intakes from the basic diet [4].

The richest sources of certain nutrients may be cellular animal tissue items, such as red meat, liver and other visceral organ meats. These animal tissue sources, however, may be problematic in two ways: (1) these food items are generally among the least accessible and affordable in the child populations at greatest risk of deficiency, and (2) excessive dependence on animal sources for nutrition collides with guidelines to moderate consumption of cholesterol, saturated fats and red meat in order to lower the risk of chronic non-communicable diseases [5]. Viscera may be excessively rich in vitamin A. Moreover, some marine fish may have heavy metal contaminants, while herbicides and pesticides can contaminate inland river and lake fish. On the other hand, other vitamins/micronutrients are found in the diet, namely in grains, fruits and vegetables.

Biofortification is a new approach using conventional and biotechnology-genetic techniques to increase the density of nutrients in plants [6], including inducing the uptake of nutrients into grains and tubers that are not usually found in abundance, e.g. iron in rice, β-carotene (provitamin A) in maize and cassava.

Vitamins and Trace Elements Added to Foods
Extrinsic addition of micronutrients usually occurs in processing, or occasionally in the home prior to consumption. There are three important domains for addition of vitamins and minerals to foods: enrichment (adding back the levels of nutrients lost in processing); public health-directed fortification (adding a nutrient to a widely consumed item, such as iodine to salt, vitamin A to oil or sugar, folic acid to flour to counter a dietary deficit), and market-driven fortification (adding nutrients to commercial foods to enhance their market appeal) [7]. In the latter regard, certain breakfast cereals, when consumed with milk, provide the entire adult daily micronutrient requirement with a single serving. Such a serving would exceed the requirements for most juveniles, except for adolescents.

<table>
<thead>
<tr>
<th>Table 1. Factors conditioning the absorption and utilization of dietary micronutrients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antinutritional constituents</strong></td>
</tr>
<tr>
<td>Substances in the diet can reduce the absorption or utilization of essential nutrients. For example, phytic acid blocks the absorption of iron and zinc. Lead contamination interferes with the utilization of iron for red cell formation.</td>
</tr>
<tr>
<td><strong>Gastrointestinal health</strong></td>
</tr>
<tr>
<td>The secretory and absorptive integrity of the alimentary tract can be compromised by frequent diarrhea, <em>Helicobacter pylori</em>, and parasitoses.</td>
</tr>
<tr>
<td><strong>Efficiency of metabolic retention</strong></td>
</tr>
<tr>
<td>Once absorbed, a series of adverse factors related to intestinal and renal function, the intactness of the integumentary system and systemic immune responses, among others, can lead to excess wastage of nutrients.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2. Sources of micronutrients for human consumption</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intrinsic micronutrients</strong></td>
</tr>
<tr>
<td>Nutrients contained within the tissue matrix and fluid of edible items from the animal and plant kingdoms.</td>
</tr>
<tr>
<td><strong>Extrinsic (added) micronutrients</strong></td>
</tr>
<tr>
<td>Nutrients are added to foods as enrichment, in mass fortification by public health mandate, and/or with discretionary fortification, as in commercial foods or with nutrient mixes added to complementary foods in the home.</td>
</tr>
<tr>
<td><strong>Supplemental micronutrients</strong></td>
</tr>
<tr>
<td>Nutrients taken in pharmaceutical preparations (chewable candies, tablets, elixirs) in individual or combined formats.</td>
</tr>
</tbody>
</table>
Processed complementary foods, for consumption while an infant is in transition from exclusive breastfeeding (or infant formula feeding) to full weaning, should be fortified with micronutrients. Because of the much higher iron requirements from 6- to 12-month olds as compared to the 2nd year of life, the recommendable iron levels are quite distinct, whereas the micronutrient density of the other micronutrients can be relatively constant [8]. A recent innovation for discretionary home fortification of complementary foods is the use of iron and multinutrient ‘sprinkles’ to infant’s and toddler’s foods.

**Vitamin and Trace Element Supplementation**
This has two formats. There is public health-directed supplementation, as for vitamin A in countries with endemic hypovitaminosis, in which supplements (e.g. capsules) are distributed periodically to vulnerable age groups. The other format is self-prescribed multivitamin supplementation, in which families provide vitamins, trace elements or both (usually both in a multivitamin-mineral combination) to children. Pediatric vitamin-mineral supplements in attractive, candy-like presentations provide the entire pediatric recommended intakes and are commonly consumed and marketed throughout the world. If a child is healthy enough to absorb and retain the nutrients, deficiency states would be prevented by such practices.

An important aspect for the pediatrician is supplementation for specific therapeutic or prophylactic aims in at-risk groups. Iron and calcium given to preterm infants is one example. In adolescent practice where precocious pregnancy is a risk, attention to supplements of folic acid (to prevent neural tube defects), iron (to build stores), and iodine (to prevent cretinism, if in a goiter zone) would be important preventive considerations.

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**Table 3. Selected nutrient–nutrient interactions of importance in pediatric nutrition**

<table>
<thead>
<tr>
<th>Vitamin–vitamin interactions</th>
<th>Vitamin–Element interactions</th>
<th>Element–Element Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin E–vitamin A</td>
<td>Vitamin D–calcium</td>
<td>Iron–zinc</td>
</tr>
<tr>
<td>There is a mutual antagonism between these two vitamins</td>
<td>Work synergistically to assure the appropriate level of mineral accretion in bone</td>
<td>Iron and zinc exert a mutual competitive interaction for sites of intestinal absorption</td>
</tr>
<tr>
<td>Vitamin A–vitamin D</td>
<td>Vitamin C–iron</td>
<td>Calcium–iron</td>
</tr>
<tr>
<td>Excessive intake of preformed vitamin A can antagonize the action of vitamin D</td>
<td>Enhances the absorption of iron from plant sources in the diet</td>
<td>Calcium interferes with the absorption of both inorganic and heme iron from the diet</td>
</tr>
<tr>
<td>Folate–vitamin B&lt;sub&gt;12&lt;/sub&gt;</td>
<td>Vitamin E–selenium</td>
<td>Calcium–phosphorus</td>
</tr>
<tr>
<td>Excess intake of folate masks the hematological manifestations of vitamin B&lt;sub&gt;12&lt;/sub&gt; deficiency</td>
<td>Work synergistically to cover antioxidant protection of membrane and cytosolic zones of cells</td>
<td>Both inadequate or excessive intake of phosphorus will disturb the homeostatic regulation of calcium in the circulation</td>
</tr>
</tbody>
</table>

| Vitamin A–iodine | Vitamin A–iron | Iodine–selenium |
| Vitamin A deficiency concomitant with severe iodine deficiency increases the size of goiters, but prevents hypothyroidism | Vitamin A adequacy is required for full hematopoietic efficiency of iron incorporation into red cells | Selenium deficiency in combination with deficiency of iodine may be required for the hypothyroid (myxedematous) goiter phenotype |
| Vitamin A–iodine | Riboflavin–iron | Calcium–iron |
| Vitamin A–iron | Riboflavin adequacy is required for full hematopoietic efficiency of iron incorporation into red cells | Calcium interferes with the absorption of both inorganic and heme iron from the diet |

| Riboflavin–iron | Calcium–phosphorus | Iodine–selenium |
| Riboflavin adequacy is required for full hematopoietic efficiency of iron incorporation into red cells | Both inadequate or excessive intake of phosphorus will disturb the homeostatic regulation of calcium in the circulation | Selenium deficiency in combination with deficiency of iodine may be required for the hypothyroid (myxedematous) goiter phenotype |
Public health-directed supplementation for children is a logistic challenge. Vitamin A capsule distribution has been the basis of child-survival programs in low-income societies. Daily iron-folic acid supplementation has been recommended for 6- to 24-month-old children in areas of anemia endemicity [9], but the presence of malaria may be a strong contraindication [10]. Zinc is the newest nutrient to be added to population-wide pediatric distribution in developing countries with widespread stunting and child mortality [11].

Specific supplements with doses of vitamins and minerals above the recommended daily allowances, with the express purpose of improving health or preventing diseases, have limited scientific basis. Self-prescribing of mega-dose regimens to children should generally be discouraged, as this practice runs the risk of: (1) overloading the child with excessive amounts of the nutrient, and (2) relying on an inadequate and unproven intervention when evidence-based alternative treatment may be readily available.

Additional Theoretical and Practical Caveats and Precautions regarding Vitamin and Trace Element Nutrition

Certain ethnic, climatic, environmental or endemic disease conditions may modify the needs, generally in a manner to increase the amounts needed to obtain adequate nutrient concentrations in body reserves or sites of their metabolic or structure roles. It should also be recognized that the highest daily intake recommendations for some micronutrients of any period during the lifespan occur in the adolescent years.

The overall balance among micronutrients, both in the diet and in the body, has implications because of a series of recognized nutrient–nutrient interactions between vitamins, between trace elements and across the classes [12]. Selected examples are illustrated in table 3. Many of these

Table 4. A listing of some pertinent paradoxical associations and precautions related to dietary exposure to micronutrients

| The upper tolerable levels for zinc in toddlers and preschool children may be too low, as they are lower than the average amounts of zinc consumed by apparently healthy children in the United States |
| The traditional ideal is that all members of a family unit share the majority of meals as a family. However, the upper tolerable level of preformed vitamin A for children under 6 years is lower than the recommended daily intake of total vitamin A for pregnant or lactating women in the same household |
| The currently recommended intake levels for vitamin D, especially for adolescents and for individuals from darkly pigmented ethnic groups living in temperate latitudes such as Europe, North America, and southern Australia, may not be sufficient to maintain protective circulating levels of the vitamin. Pediatric dermatologists and nutritionists are in confrontation about sun exposure. The dermatology community advocates maximal sunscreen protection to avoid skin damage and malignancy risk, whereas maximizing vitamin D formation in skin at temperate latitudes requires relaxation of total solar avoidance |
| An upward spiral of market-driven fortification, with multiple manufacturers adding micronutrients to make their products more attractive and ‘nutritious’, runs the risk of providing children who consume these products with several times the daily recommended amounts of some vitamins |
| Folic acid fortification is mandated in many countries for the prevention of neural tube defects in the pregnancies of susceptible women. These higher folic acid intakes have additional benefits for adults for prevention of stroke and vascular disease. However, for adults with established dysplastic changes in the large bowel mucosa, higher folic acid exposure accelerates the progression to colorectal cancer. The implications of these – beneficial and harmful – effects for a pediatric population are currently unknown |
| Epidemiological evidence is accumulating that consumption of preformed vitamin A from animal sources and fortificants weakens bone mineralization. The extent and importance of such a process in childhood merits research attention |
have important implications for the formulation of diets and multinutrient formulations.

Both the Food and Nutrition Board of the United States and the European Food Safety Authority of the European Union have established upper tolerable intake levels for certain micronutrients, whose intake beyond a certain daily amount could be unsafe for the consumer. The interplay between essential risk of dietary deficiency and interventions to enhance micronutrient status leads to a series of paradoxical situations and evokes the need for certain precautions. A selection of these are outlined in table 4.

Future research is likely to reveal enzyme polymorphisms that commonly differentiate a greater or lesser susceptibility to defective utilization of dietary nutrients [13], as has currently been discovered with folic acid.

**Conclusions**

- Vitamin and trace elements get into the child from natural foods and beverages, fortified products and multimicronutrient supplements; each of these sources can be applied to correct dietary inadequacy
- The weaning period is a major challenge to providing adequate trace elements to the infant and toddler
- In the community setting, gastrointestinal pathogens and antinutritional substances in the diet can adversely affect micronutrient adequacy
- The convergences of sources from self-supplementation and expanding market-driven food fortification pose a short-term risk for vitamin and trace element overnutrition for some segments of the pediatric population

**References**

Introduction

The business of ‘growing up’ – physical growth, biological maturation and behavioral development – is complex and places many demands upon children and adolescents. Physical activity (PA) and physical fitness (PF), among other factors, are important in these processes.

PA is a behavior involving movement of the body through space. It is viewed most often in terms of energy expenditure and stresses and strains associated with weight bearing and ground reaction forces. PA has a performance component in specific movement skills and physical fitness. Settings and types of PA (sport, play, education, work, ‘exercise’, etc.) are strongly influenced by culture [1].

PF is a state or a condition which permits the individual to carry out daily activities, including PA, without undue fatigue and with sufficient reserve to enjoy active leisure pursuits. PF includes muscular strength and endurance, flexibility, cardiovascular and motor components. Morphological and metabolic indicators have been added to the more traditional concept of PF. Components of PF are related to PA at generally moderate levels [1, 2].

Low levels of PA and PF are independent risk factors for chronic disease and premature mortality among adults. Increased prevalence of obesity and risk factors and emergence of symptoms of metabolic and cardiovascular diseases during childhood and adolescence highlight the importance of PA and PF in preventive contexts [3]. On the other hand, persistence of chronic undernutrition in many parts of the world compromises the PA and PF of youth [1].

Measurement

Methods for estimating the habitual level of PA and energy expenditure (EE) are summarized in table 1. None of the methods covers all aspects of PA and EE; a combination of methods is needed to obtain a comprehensive estimate of the habitual level of PA and EE of an individual. Choice of
methods depends on the specific objectives of a study/survey, age of subjects, equipment and personnel. Surveys of PA and PF in various countries are summarized elsewhere [2].

**Variation with Age and Sex**

Estimated 24-hour EE (kcal/kg) based on doubly labeled water declines with age, beginning in early childhood (fig. 1). The decline is especially apparent during the second decade. Estimated EE is, on average, greater in males than in females and the difference between the sexes increases with age. EE in PA is the most variable component of EE. The ratio of total EE (TEE) to resting EE (REE) provides an estimate of the contribution of activity-related EE to TEE over 24 h. It is expressed as the physical activity level (PAL), which increases with age during childhood and adolescence in youth from industrialized countries, but more so in youth from rural areas and

---

**Table 1. Commonly used methods for the assessment of pattern and/or level of PA and EE**

<table>
<thead>
<tr>
<th>Method</th>
<th>Function assessed</th>
<th>Advantages</th>
<th>Drawbacks</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Questionnaire</td>
<td>PA</td>
<td>Simple, low cost; suitable for large-scale studies</td>
<td>Relies on memory; hard to quantify; low validity</td>
<td>The shorter the recall period the higher the validity</td>
</tr>
<tr>
<td>Interview</td>
<td>PA</td>
<td>More valid than a questionnaire</td>
<td>Relies on memory</td>
<td>Interviewer can corroborate information</td>
</tr>
<tr>
<td>Diary</td>
<td>PA</td>
<td>Short recall time</td>
<td>Interactive</td>
<td>Depends on child’s interpretation</td>
</tr>
<tr>
<td>Direct observation</td>
<td>PA, (EE?)</td>
<td>No need for recall; context documented</td>
<td>Expensive; depends on observer’s skill</td>
<td>‘Gold standard’ for specific behavioral aspects of activity</td>
</tr>
<tr>
<td>Time-lapse video or photography</td>
<td>PA, (EE?)</td>
<td>Objective, hard record available</td>
<td>Child is limited to predetermined area</td>
<td>Less expensive than direct observation</td>
</tr>
<tr>
<td>Movement counters</td>
<td>PA, (EE?)</td>
<td>Objective, little interaction; low cost</td>
<td>Do not detect specific movements</td>
<td></td>
</tr>
<tr>
<td>Accelerometry</td>
<td>PA, EE(?)</td>
<td>Same as counters, plus acceleration</td>
<td>Does not detect specific activities</td>
<td>Some validity vs. measurements of EE</td>
</tr>
<tr>
<td>HR monitoring</td>
<td>EE</td>
<td>Little interaction; inexpensive</td>
<td>HR affected not only by metabolism</td>
<td>Needs individual ‘calibration’ vs. VO₂</td>
</tr>
<tr>
<td>VO₂ metabolic cart</td>
<td>EE</td>
<td>Measures metabolism</td>
<td>Limited activities; need for mouthpiece or facemask</td>
<td>Useful for ergometry and VO₂–HR ‘calibration’</td>
</tr>
<tr>
<td>VO₂ portable equipment</td>
<td>EE</td>
<td>Measures metabolism away from the laboratory</td>
<td>Highly interactive; expensive</td>
<td>Limited pediatric use in prolonged observations</td>
</tr>
<tr>
<td>VO₂ canopy</td>
<td>EE</td>
<td>Measures metabolism</td>
<td>RMR only</td>
<td>Used in conjunction with HR monitoring</td>
</tr>
<tr>
<td>Respiration chamber</td>
<td>EE</td>
<td>Precise measurement of EE</td>
<td>Very limited quarters; expensive</td>
<td>Validating other tests; ideal for BMR</td>
</tr>
<tr>
<td>Doubly labeled water</td>
<td>EE</td>
<td>Best measure of EE; not interactive</td>
<td>Very high cost; requires at least 1 week</td>
<td>‘Gold standard’ for average EE, but not for profile of EE</td>
</tr>
</tbody>
</table>

PA = Physical activity; EE = energy expenditure; HR = heart rate; RMR = resting metabolic rate; BMR = basal metabolic rate. A question mark denotes uncertain validity. Reproduced with permission from Malina et al. [1].
cities of developing countries [1, 4]. Active children have a PAL of about 1.7–2.0.

The level of PA, on average, changes little or increases slightly with age during childhood and declines during adolescence. Though not all studies and PA contexts show a decline during adolescence [1, 2]. The physical environment and a variety of biological, social and psychological factors influence patterns and levels of PA.

PA is a characteristic that is at best moderately stable across childhood into adolescence [5]. The seeming instability reflects individual differences, age variation and limitations of assessment methods. Activities of young children tend to be largely non-organized, spontaneous, and comprised of intermittent brief bouts, while those of older children and adolescents tend to be more organized, regular and prolonged. The PA needs of children and adolescents vary with age (fig. 2).

Benefits of Physical Activity

Regular PA does not alter linear growth and biological maturation as ordinarily observed, but is important in the regulation of body weight and for the integrity of skeletal muscle and bone tissues [1]. Health benefits of PA in school-age youth are summarized in table 2.

How Much Activity?

The majority of intervention and experimental studies with school-age youth use programs of moderate-to-vigorous PA 30–45 min, 3–5 days/week [3]. A greater amount of PA is probably necessary to achieve beneficial effects of PA under free living conditions in which activities are often intermittent and unsupervised. Accordingly, school-age youth need 60 min or more of moderate-to-vigorous PA on a daily basis [3]. Children <5 years probably need a similar amount of daily PA, but the types and duration of specific activities are likely to vary. Nevertheless, activities for children and adolescents of all ages should be developmentally appropriate and enjoyable and should include variety.
Energy Expenditure, Physical Activity and Nutrition

Energy and protein requirements to support normal growth are highest in early infancy and subsequently decline. After about 2 years of age, only a small percentage of energy and protein intake supports growth, i.e., increase in size; the major portion supports tissue maintenance or replacement. Energy required for PA is the most variable component of overall EE [1].

Undernutrition

Chronic undernutrition during infancy and early childhood results in compromised growth, delayed development of proficiency in movement skills and reduced PA. School-age children of marginal to poor nutritional status show decreased total daily EE and PA. This is related in part to smaller body size. Reduced PA may limit movement skills in play and games, and in turn contribute to performance-fitness deficiencies [1]. Quasi-experimental observations suggest that mild-to-moderately undernourished boys differ from nutritionally normal boys in the capacity to increase EE in PA [6, 7]. They simply cannot keep up with better nourished boys during sport activities. Intestinal parasite load associated with chronic undernutrition may influence PA and PF. Treatment of school-age undernourished children for hookworm, whipworm and roundworm is associated with increasing spontaneous PA, improving cardiovascular fitness and improving growth and appetite [8, 9]. A related factor is illness; during periods of illness, children tend to be less active.

Obesity

Energy costs of PA differ between the obese and non-obese. Absolute EE is greater in obese children and adolescents, but after adjusting for dif-
ferences in body size or composition, EE is similar in the obese and non-obese [10]. Data based on questionnaires, heart rate or time and motion analyses suggest that obese children and adolescents are less active than their lean peers [11]. The PF of obese children and adolescents is compromised on tasks that require movement or projection of the body through space, e.g., runs and jumps. Mechanically, excess fat represents an inert load (dead weight) which must be moved. Obese youth are also characterized by reduced cardiovascular fitness. On the other hand, obese youth are absolutely stronger and more powerful in tasks that do not require movement or projection of the body [1].

**Conclusions**

- Regular PA is important for biological growth and maturation and behavioral development
- Regular PA has significant health promotion and disease prevention functions
- Children should participate in 60 min or more of daily, moderate-to-vigorous, developmentally appropriate, enjoyable PA
- The amount of PA needed to prevent unhealthy weight gain is not known
- Proficiency in movement skills, PA and PF are reduced under conditions of persistent undernutrition
- Chronically low levels of PA are often implicated in childhood obesity, but data for low levels of habitual EE/PA as a primary causative factor in obesity are relatively scant

**References**

Key Words
Metabolic programming of long-term health · Developmental origins of adult health · Breastfeeding and obesity · Perinatal nutrition · Disease risk prevention

Key Messages
- Nutritional and metabolic factors during sensitive, limited periods of early human development have a long-term programming effect on health, well-being and performance in later age, extending into adulthood and old age
- Evidence for early programming effects arises from in vitro experiments, animal models, retro- and prospective epidemiological studies, and first controlled intervention trials
- Obstetric and pediatric medicine are expected to achieve a much greater future role for prevention of long-term disease risks in the population
- The important effects on health of early nutrition programming justify major investments into research and improvement of practice

Introduction

Epidemiological studies, numerous animal models and clinical intervention trials provide ample evidence that nutritional and metabolic factors during sensitive, limited periods of early human development have a long-term programming effect on health, well-being and performance in later age, extending into adulthood and old age [1]. Biological programming has been defined as: ‘either the induction, deletion, or impaired development of a permanent somatic structure or the “setting” of a physiological system by an early stimulus or insult operating at a “sensitive” period, resulting in long-term consequences for function’ [2]. While the term programming was introduced into the scientific literature by Dörner [3] already in 1974, the concept has received broad attention primarily due to epidemiological studies published by Barker et al. [4] documenting inverse relationships between bodyweight at birth and at age 1 year, respectively, and the risks of hypertension, diabetes and coronary heart disease (fig. 1) in adulthood. These observations raised the hypothesis that maternal and fetal malnutrition during pregnancy induce both fetal growth restriction and increased later disease risk, whereas recent data suggest that accelerated weight gain after birth, which is associated with a low birthweight, might be a causal factor. The exploration of underlying mechanisms and the resulting effects of metabolic programming offers tremendous opportunities for early prevention of major health risks already during pregnancy and infancy, and they could provide both obstetric and pediatric medicine with a markedly increased role in promoting long-term health of the population.

The concept of early metabolic programming of long-term health is supported by physiological, epidemiological and clinical research [1, 5–7]. Experimental in vitro studies and in vivo animal studies elucidate the primary molecular path-
ways by which altered maternal nutrition either during pregnancy or lactation results in offspring being at an increased risk of later disease. Specific mechanisms by which later disease is programmed are defined, and the precise nutritional conditions that contribute to these processes are established. Evidence is accumulating that epigenetic programming of the genome altered by early nutritional interventions plays a major role. Also explored are critical windows during early development when nutrition programs one or more chronic degenerative diseases, such as obesity, cardiovascular disease, metabolic syndrome, diabetes, renal disease, allergy, autoimmune disease, and cancer. It is important to elucidate whether these outcomes are genotype-dependent, and to which extent they might be reversible and could be overcome by later nutritional or pharmacological interventions.

As an important example of nutritional programming in humans, the relationship between infant feeding and later obesity will be discussed here. Since many studies reported somewhat different growth patterns of populations of breast-fed and formula-fed infants, we assessed the potential long-term impact of breastfeeding on later body weight in a large cross-sectional survey of more than 9,000 children participating in the obligatory school health examination in Bavaria, Germany [8]. An assessment of early feeding, diet, and lifestyle factors revealed a clearly higher prevalence of obesity in children who had never been breastfed (4.5%) than in breastfed children (2.8%), with an inverse dose-response effect between the duration of breastfeeding and the prevalence of later obesity. The protective effect of breastfeeding was not attributable to differences in social class or lifestyle. After adjusting for potential confounding factors, breastfeeding remained a significant protective factor against the development of obesity (OR 0.75, 95% CI 0.57–0.98) and overweight (OR 0.79, 95% CI 0.68–0.93), with a dose-response relation between breastfeeding duration and later risk of overweight and obesity, respectively (fig. 2). A protective effect of breastfeeding was also found in a number of studies in other populations, whereas others found no benefit. Systematic reviews and meta-
analyses of cohort, case-control or cross-sectional studies concluded that breastfeeding provides a small but consistent protective effect [9–11]. However, these conclusions are only based on observational data because healthy infants cannot be assigned to breastfeeding on a randomized basis, and hence residual confounding cannot be excluded with certainty. The only published cluster randomized trial on breastfeeding promotion found no effects on later obesity, but basically all infants participating in this trial in Belarus had been breastfed, and the intervention only influenced the duration of breastfeeding. Thus, this study does not allow conclusions on the effects of early breastfeeding versus formula feeding [12].

Various hypotheses have been raised on potential causes for a protective effect of breastfeeding. The establishment of a biological plausibility and the elucidation of mechanisms which mediate the protective effect of breastfeeding would lend support to a causal effect of breastfeeding. We proposed that the protective effect of breastfeeding is at least in part due to lower growth rates in the first year, as compared to formula-fed infants, and is mediated by a lower protein content of human milk relative to formula [1].

Populations of breastfed infants show higher weight and length gains during the first year of life than formula-fed infants, whereas more rapid weight gain in infancy and the second year of life predisposes to childhood overweight and obesity [13–16]. These growth differences of breast- and formula-fed populations are most likely due to differences in metabolizable substrate intakes. Infants at the ages between 3 and 12 months have a 10–18% higher energy intake per kilogram bodyweight if fed formula as compared to breastfed infants. The difference in protein intake per kilogram bodyweight is even larger: it is 55–80% higher in formula-fed than in breastfed infants [1]. In epidemiological studies, high protein intakes in early childhood, but not the intakes of energy, fat or carbohydrate, were significantly related to an early adiposity rebound and to a high childhood BMI, corrected for parental BMI [1]. Thus, a high protein intake with infant formula in excess of metabolic requirements might predispose to an increased obesity risk in later life, a concept referred to as the ‘early protein hypothesis’. This question is being studied in a large randomized clinical trial with allocation of healthy term infants to formulae with higher and lower protein contents (the European Childhood Obesity Project, www.metabolic-programming.org). First results indicate that lowering of protein supply, reaching values which are close to intakes provided by breast milk, normalizes growth up to the age of 2 years, compared with the growth of breastfed populations. Further follow-up of the participating children should reveal whether this diet-induced normalization of early growth patterns will exert long-term health effects.

This is but one example of the numerous opportunities that should arise from a better un-
Standing of early metabolic programming and its underlying mechanisms. Further elucidation of the impact of early nutrition on long-term health is expected to contribute greatly to providing improved policies of nutrition both for women during pregnancy and lactation and their infants, and to enhancing standards of practice.

- Breastfeeding, compared to formula-feeding, is associated with a small but consistent risk reduction for overweight and obesity at later ages, which is of considerable public health relevance on a population basis.
- High weight gain in infancy and the second year of life predicts an increased risk of later overweight and obesity. Thus, it is prudent to avoid feeding practices that lead to excessive weight gain in early life.

Conclusions

- Optimal nutrition during pregnancy, lactation, and infancy is important not only for immediate outcomes such as fetal and infant weight gain and body composition, but also has long-term effects on child health, wellbeing and performance extending into adulthood and old age.

Acknowledgments

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References

Introduction

While nutritional safety is the outcome tested in appropriate clinical studies by nutrition science [1], chemical and microbial safety of food is not tested in humans but is the object of regulations, standards and codes of practice developed on a global basis, e.g. by the Codex Alimentarius established in 1961 by the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO), which is to be implemented by national legislation. Numerous scientific bodies consisting of independent experts advise on limits for residues, contaminants, naturally occurring toxins, food additives and infectious agents based on toxicological and microbial risk assessment to minimize the risk of food-borne diseases (details: International Portal on Food Safety, Animal and Plant Health, www.ipfsaph.org).

Food-borne diseases are caused by agents that enter the body through the ingestion of food and are a growing public health problem. Food- and water-borne diarrheal diseases kill approximately 1.8 million people annually, most of whom are children. In industrialized countries the percentage of people suffering from food-borne diseases each year has been reported to be up to 30%. They are caused by naturally occurring toxins such as mycotoxins, persistent organic pollutants such as dioxins and polychlorinated biphenyls (PCBs), heavy metals such as lead, cadmium and mercury, and by microorganisms such as salmonella, campylobacter, etc.

However, the production of safe foods, by ensuring plant and animal health, by applying Hazard Analysis and Critical Control Point (HACCP) principles and observing hygiene [2], must be complemented by appropriate and hygienic handling of food by consumers.
Residues

Residues in foods derive from deliberately applied substances, food additives, pesticides and veterinary drugs. For these substances maximal residue levels (MRLs) based on good practice (i.e. application at levels to achieve the desired effect but not higher) are defined. MRLs must be compatible with the acceptable daily intake (ADI) levels, which are the amounts of a chemical that can be ingested daily over a lifetime without producing appreciable health risks. They do not apply to infants below 3 months of age. Because infants and young children have food patterns with less variety than adults and consume more food per unit of body weight, lower MRLs are required for some pesticides in foods for infants and young children [3], meaning, for example in the European Community, the use of certain pesticides on crops intended for infants and young children is forbidden [4]. On an international level, residue levels are to be 'reduced to the maximum extent possible' for example in infant formula and cereal-based foods for infants and young children [5].

Contaminants

Contaminants from the environment in food are unintended and often unavoidable, e.g. dioxins, PCBs and heavy metals, or are introduced during processing. Naturally occurring contaminants are fungal mycotoxins, particularly in cereals, nuts and fruit juices. They are quite stable to normal cooking temperatures and toxic to the liver and/or the kidney, and some are carcinogenic in rodents. Maximum levels for different mycotoxins in various categories of food and animal feed have been set worldwide in the majority of countries [6]. Because it is impossible to completely eliminate mycotoxins in food and feed, until 1997 the aim was to have the mycotoxin levels as low as reasonably achievable. Both the Joint Expert Committee on Food Additives and Contaminants and the European Food Safety Authority have defined provisional tolerable weekly intake levels (table 1).

Nitrate, which is accumulated by some plants and can occur in water wells, is considered a contaminant, and maximum levels have been set for ready-to-eat vegetable meals for infants. Nitrate, itself not very toxic, is partially converted into nitrite, which can form carcinogenic nitrosamines with secondary amines from food, which in turn can induce methemoglobinemia in young infants at intakes of $\geq 7$ mg nitrate/kg per day, particularly in infants with still high levels of fetal hemoglobin and/or concomitant gastrointestinal or urinary tract infection. Home-prepared meals containing vegetables potentially high in nitrate (radish, beetroot, fennel, lettuce, kohlrabi, spinach) should therefore not be stored and rewarmed.

Heavy metals, particularly methylmercury in seafood products, cadmium taken up from the soil by plants, and lead mostly deriving from industrial waste in plants and via feed in animal food, are of particular concern for children because of their long half-life and because of neurobehavioral, neurotoxic and nephrotoxic adverse effects, respectively.

Organohalogen compounds, e.g. dioxins and PCBs, accumulate and persist for many years in body fat. They have adverse effects on development, reproduction, the immune and endocrine systems. Both for heavy metals and organohalogen compounds, maximum levels in food are recommended by the Codex Alimentarius, e.g. for lead [7] and contaminants in general [8].

Food Toxicology

The risk assessment of compounds used deliberately in the production of foods differs from that of contaminants, but the process is similar. In the first case ADIs are based on identified ‘no ob-
served adverse effect levels’ (NOAELs) from the most sensitive study in the most sensitive species, and by dividing the NOAELs by a safety factor (most often of 100) to account for interspecies and intraspecies variability in sensitivity. Safety factors can be modified according to the quantity and quality of available data and by taking the severity or irreversibility of an effect into account. The result of the same procedure applied to contaminants is a tolerable daily intake (TDI) or, in the case of contaminants with long half-lives, a tolerable weekly intake, sometimes a provisionally tolerable weekly intake. Dividing the NOAELs by the actual exposure of consumers permits an estimation of the margin of safety.

Compounds with genotoxic and/or carcinogenic activity have presumably no threshold for effects. Instead the margin of exposure can be estimated, that is, the ratio between a defined point on the dose-response curve in the animal carcinogenicity study and the human intake. A margin of exposure of 10,000 or higher is considered to be of low health concern [9].

Short-term intakes of a residue/contaminant in excess of ADI/TDI do not necessarily mean that adverse health effects will follow. However, children may be particularly susceptible, and the expected lifespan and, therefore, the available time for the manifestation of adverse effects in a young person are longer. Table 1 lists toxicological data on some important contaminants.

### Infectious Food-Borne Diseases

Microbial contamination of food can occur throughout the chain of food production, processing and storage. Microbial diseases which can be transferred from animals to man are zoonoses, the most important agents being salmonella, mycobacteria, brucella, campylobacter, listeria, toxoplasma, yersinia and parasites like trichinella and echinococcus.

Food-borne viral illnesses, e.g. noroviruses and hepatitis A, are on the increase. They relate predominantly to fresh products rather than to industrially produced foods, and/or are linked to

<table>
<thead>
<tr>
<th>Substance</th>
<th>Most recent assessment</th>
<th>Species</th>
<th>Relevant endpoint</th>
<th>LOAEL per kg body weight per day</th>
<th>PTWI per kg body weight per week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylmercury</td>
<td>JECFA, 2003 NRC, 2000</td>
<td>human</td>
<td>neurobehavioral development</td>
<td>1.6 µg</td>
<td>0.7 µg</td>
</tr>
<tr>
<td>Lead</td>
<td>JECFA, 2000</td>
<td>human</td>
<td>neurotoxicity</td>
<td>25 µg</td>
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<tr>
<td>Cadmium</td>
<td>JECFA, 2003</td>
<td>pig</td>
<td>renal toxicity</td>
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<tr>
<td>Dioxins and dioxin-like PCB</td>
<td>SCF, 2000/2001</td>
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<td>development, reproduction</td>
<td>14 pg WHO-TEQ</td>
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<tr>
<td>Ochratoxin A</td>
<td>JECFA, 2001; EFSA, 2006</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>8 µg</td>
<td>120 ng</td>
</tr>
</tbody>
</table>

LOAEL = Lowest observed adverse effect level; PTWI = provisional tolerable weekly intake; PCB = polychlorinated biphenyl; JECFA = Joint Expert Committee on Food Additives and Contaminants (FAO); NCR = National Research Council (USA); SCF = Scientific Committee on Food of the European Commission; EFSA = European Food Safety Authority; TEQ = Toxicity equivalent.
contamination of food by an infected food handler.

The impact of infectious diseases on mortality of children under five is more than two times greater in malnourished children. Apart from attempts to improve both the quality and quantity of food, continued frequent breastfeeding or, if possible, re-lactation are important measures [10] to minimize the risk from pathogens in foods or fluids and to profit from the protective factors provided by breast milk.

### Infant Formula

Feeding breast milk substitutes requires the availability of clean and safe water and cooking facilities [11].

A typical example of the importance of HACCP principles in the production of foods, and sanitary measures to be applied by the consumer, is the case of *Enterobacter sakazakii* in powdered infant formula. This microorganism has caused outbreaks of sepsis, meningitis or necrotizing enterocolitis, especially in premature infants and those less than 2 months old. Although the overall incidence seems to be low, mortality rates between 20 and 50% have been reported. Powdered infant formula is not sterile, and even when manufactured under strict hygiene, the occurrence of low counts (1–3/g) of coliform bacteria cannot be prevented. *E. sakazakii* does not grow in the dry powder but starts to replicate after preparation with water and at temperatures $15\,^\circ C$. It can be destroyed by temperatures $60\,^\circ C$.

Measures to reduce the risk of infection include preparation in a sterile environment with boiled water ($170\,^\circ C$), feeding immediately after appropriate cooling, limiting of feeding duration and infusion via feeding tubes at room temperature to less than 4 h, and discarding uneaten residues [12].

### Conclusions

- Practical recommendations for the safe handling of food at home and elsewhere are given in table 2
- Toxicological safety of food is primarily the responsibility of the manufacturer
- Microbial safety of food is both the responsibility of the manufacturer and the person preparing and serving it

### Table 2. Recommendations for safe handling, preparation and storage of foods

- Wash hands before preparing and feeding
- Wash hands after going to toilet
- Use safe water or treat it to make it safe
- Wash and clean surfaces and equipment used for food preparation
- Use clean utensils to prepare and serve food
- Wash fruits and vegetables, especially if eaten raw
- Separate raw and cooked food and use separate utensils for preparing them
- Cook fresh, unpasteurized milk
- Cook food thoroughly, particularly meat, poultry, eggs and seafood (internal temperature at least $70\,^\circ C$)
- Serve foods immediately after preparation
- Keep cooked food hot ($>60\,^\circ C$) prior to serving
- Do not leave cooked food for more than 2 h at room temperature
- Discard uneaten prepared food or refrigerate (preferably $<5\,^\circ C$)
- Refrigerate all cooked and perishable food immediately (preferably $<5\,^\circ C$)
- Store raw and cooked food in separate containers
- Store food preferably dry
- Do not store food too long (even in refrigerator)
- Do not use beyond expiry date
- Do not thaw frozen food at room temperature
- Heat stored prepared food thoroughly ($>70\,^\circ C$)
References


1.7 Gastrointestinal Development, Nutrient Digestion and Absorption

Michael J. Lentze

**Key Words**
- Nutrient digestion
- Absorption
- Fetal intestinal development
- Motility

**Key Messages**
- The fetal human gut is prepared for the digestion and absorption of nutrients already at the 24th week of gestation
- Macronutrients, given even to premature babies, can be digested and absorbed
- The rate-limiting factor during fetal life, particularly for premature infants, is the development of motility

**Introduction**

The development of the gastrointestinal (GI) tract during intrauterine life for a human fetus is the prerequisite for survival in external life. The digestive and absorptive capacity of the intestinal organs as well as the contact of foreign pathogens with an active immune system guarantee the normal growth and wellbeing of an infant in early life. As the number of premature babies below 1,000 g is increasing, knowledge of the digestive and absorptive functions of the GI tract becomes of vital interest for neonatologists feeding these very low birthweight (VLBW) infants.

The GI tract has digestive, absorptive, secretory and barrier functions. In addition, it is part of the endocrine organ and the immunological system. The interaction between various organs and the complex structure and function of the GI tract develops during fetal life in order to provide the newborn baby with a functional GI system to survive in the external world. This includes the digestion and absorption of nutrients, transport through the gut as well as a barrier function to a large number of microbiota and the symbiotic life with them. Antigens need to be identified and taken care of without involving the whole body in an illness.

The human gut is formed from the endodermal layer of the embryo by incorporation of the dorsal part of the yolk sac during the infolding of the embryonic disc. At the 4th week of gestation the first tube has a length of 4 mm from the mouth to cloaca. During pregnancy it elongates about 1,000-fold until full-term. The stomach at term has a volume of about 30 ml, the small intestine a length of 250–300 cm, the large intestine a length of 30–40 cm. Between the 9th week of gestation and birth the small intestine undergoes extraordinary changes from a primitive stratified epithelium of undifferentiated epithelial cells into a fully differentiated organ with villi and crypts [1]. The formation of Peyer’s patches starts at 16–18 weeks of gestation when the first lymphocytes are seen in the lamina propria [2].
Parallel to the morphological changes during fetal development the digestive and absorptive functions of the GI tract begin to appear at the 10th week of gestation and fully express their activities between the 26th week of gestation and term or within the first month of life.

The brush border enzymes, lactase, maltase-glucoamylase and sucrase-isomaltase, are first determined at the 10th week of gestation (fig. 1). Sucrase-isomaltase reaches its full activity already by the 25th week of gestation, whereas lactase activity is fully developed by the 32nd week of gestation [3, 4]. As lactose is the predominant sugar in breast milk, the possibility exists that premature babies born before the 32nd week of gestation might lack full lactase activity when fed breast milk or a lactose-containing premature formula. However, the overall lactase activity along the small intestine even in VLBW infants is sufficient for hydrolyzing lactose into glucose and galactose.

The transport system responsible for the uptake of glucose and galactose, the sodium-dependent glucose transporter-1 (SGLT-1) is fully active already by the 25th week of gestation as is glucose transporter-5 (GLUT-5) [5]. For the digestion of proteins, the pancreatic enzymes, trypsin, chymotrypsin and carboxypeptidase, are first detected in the 24th week of gestation (fig. 2). Full activity is reached by the 26th week of gestation. Trypsinogen is activated by enterokinase in the 24th week of gestation. The brush border peptidases, the amino acid transporters as well as peptide transporters start their transport activi-
ties by the 10th week of gestation and reach full activity by the 25th week of gestation [6]. The digestion of proteins and the absorption of amino acids and dipeptides are effective already for VLBW infants. Fat digestion depends on various lipases and the formation of micelles. The activities of the responsible lipases, gastric and pancreatic lipases, are first measurable by the 24th week of gestation. Full enzyme activity develops steadily towards term and after birth. In the breastfed infant, breast milk lipase (bile salt-stimulated lipase) enhances fat digestion during the first weeks of life [7]. The digestion of starch is the last to develop during pregnancy and after birth. Pancreatic amylase is first detected in the 22nd week of gestation, but reaches its full activity as late as the 6th month after birth. Premature or term infants cannot easily digest large amounts of starch. Small amounts of starch can be given to premature and term infants without difficulty because amylose and amylopectin are also hydrolyzed by the action of sucrase-isomaltase and maltase-glucoamylase [8].

Although the digestive and absorptive capacity of the GI tract is well prepared for external life after birth even for premature babies, immature motility is the limiting system particularly for premature infants to cope with external feeding. Here, the response of the intestine to a bolus feed depends on the maturity of the gut. In small infants before 31 weeks of post-conceptional age, who are usually receiving low volumes of continuous enteral feed, ordinary postprandial activity does not occur [9]. Between 31 and 35 weeks post-conceptional age, postprandial activity is induced in infants by giving them larger volumes of feed. However, the activity remains in a fasting pattern with a superimposed more random postprandial activity. Finally, in infants over 35 weeks post-conceptional age, who receive large volumes of bolus feed, there is a disruption of the cyclical fasting activity and replacement with continuous

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**Fig. 2.** Development of pancreatic enzymes, gastric lipase and enterokinase during fetal life.
activity. Whether this motility pattern can be advanced by pharmacological measures, such as the administration of cortisol, remains to be seen [10, 11].

Conclusions

The feeding of premature infants below 35 weeks of gestation requires knowledge of the physiological functions at this time. Whereas digestive and absorptive functions are mostly developed from the 24th week post-conceptional age, GI motility is still not very active. Premature formulas or fortified breast milk can be applied to VLBW infants or extremely VLBW infants in small quantities. From the 31st week onwards the quantity of enteral feeds becomes less of a problem. As far as macronutrients are concerned, protein is well digested and absorbed. Lactose is also well digested and absorbed, but starch can only be digested in small quantities. The digestion of fat increases quickly from the 26th week of gestation and can be enhanced by the administration of breast milk which provides bile salt-stimulated lipase.

References

1 General Aspects of Childhood Nutrition

1.8 Gut Microbiota in Infants
Seppo Salminen · Mimi Tang

Key Words
Microbiota · Probiotics · Prebiotics · Health

Key Messages
• A healthy microbiota preserves and promotes host wellbeing and absence of disease, especially in the gastrointestinal tract
• Initial colonization with ‘pioneer bacteria’ is enhanced by both bacteria and galacto-oligosaccharides in breast milk and the microbiota of the mother. These pioneer bacteria direct the later microbiota succession which forms the platform for a healthy gut microbiota throughout one’s lifetime.
• The microbiota resembles that of adults by 1–2 years of age.
• Bifidobacterial numbers in children often remain higher than in adults.
• A disturbed microbiota succession during early infancy has been linked to an increased risk of developing infectious, inflammatory and allergic diseases later in life.
• Intestinal microbial colonization and its modulation through dietary means are important considerations during the first years of life.

Initial Establishment of Microbiota

Source of Original Microbiota
The microbiota of a newborn is acquired from the mother at birth and develops rapidly thereafter. It is initially strongly dependent on the mother’s microbiota, mode of delivery and birth environment [1, 2]. The microbiota of the mother is determined by genetic and environmental factors. Stress and dietary habits during later pregnancy have a significant impact on the microbiota at delivery, thus influencing the quality and quantity of first colonizers of the newborn. Subsequently, feeding practices (formula or breastfed) and the infant’s home environment influence the succession microbiota at the genus and species level, as well as species composition and numbers of bacteria.

Succession of Microbial Communities
The establishment of microbiota in the newborn occurs in a stepwise fashion. Studies in mice have shown that the first bacteria to colonize the newborn intestine (‘pioneer bacteria’) can modulate gene expression in host intestinal epithelial cells. This results in an altered intestinal microenvironment which influences the nature of subsequent intestinal colonization.

In the newborn, initial colonization with facultative anaerobes, enterobacteria, coliforms, lactobacilli and streptococci is rapidly followed by colonization with anaerobic genera such as Bifidobacterium, Bacteroides, Clostridium, and lactic acid bacteria. Molecular analyses demonstrate significant differences in the microbiota of formula-fed and breastfed infants with respect to bifidobacterial numbers and species composition. In breastfed infants, bifidobacteria constitute
from 60 to 90% of the total fecal microbiota, while lactobacilli comprise less than 1% [3]. The most common bifidobacterial species in breastfed infants are *B. breve, B. infantis* and *B. longue* [4]. In formula-fed infants the microbiota is more complex and influenced by the formula composition. The lactic acid bacteria composition in breastfed and formula-fed infants is similar, with *Lactobacillus acidophilus* group microorganisms such as *L. acidophilus, L. gasseri* and *L. johnsonii* being most common. Microbiota differences between breastfed and formula-fed infants have lessened with improved infant formulas.

### Gut Microbiota in the First 6 Months of Life

Breastfeeding for 4–6 months may assist in the development of healthy gut microbiota by providing bifidobacteria and lactic acid bacteria which reinforce colonization, and by supplying galacto-oligosaccharides that promote a healthy microbiota composition. Breastfeeding also facilitates the exchange of microbes between mother and infant via skin contact and exposure to microbiota in the immediate environment. Every individual has a unique characteristic microbiota during later phases of breastfeeding that comprises a dynamic mixture of microbes typical to each individual. Weaning, introduction of solid foods, and antimicrobial drug treatment will break the constant supply of oligosaccharides and microbes from the mother, thus affecting intestinal microbiota development.

Molecular analysis of bacterial communities in healthy babies during the first 10 months of life demonstrated progression from a simple profile in the first days of life to a more complex diverse profile with members of the genera *Bifidobacterium, Ruminococcus, Enterococcus, Clostridium,* and *Enterobacter* identified by 6 months of age [3]. *Bifidobacterium* and *Ruminococcus* species dominated the intestinal microbiota with high level stable expression over time. A pilot study in 6-month-old infants reported higher bifidobacterial levels and lower clostridial numbers in breastfed infants than infants receiving either formula or formula with prebiotics. Ongoing improvements in formulae have lessened these differences [5].

The healthy intestinal microbiota in infancy is characterized by a large gram-positive bacterial population and significant numbers of bifidobacteria, mainly *B. longum, B. breve* and *B. infantis*. Lactic acid bacteria may play a role in providing the right intestinal environment for bifidobacteria to dominate. A healthy microbiota during infancy is particularly important as this establishes the basis for healthy gut microbiota later in life.

### Gut Microbiota in Infants from 6 Months Onwards

After the first 6 months of life, the microbiota becomes more diverse [6]. Several studies have examined the progression of microbiota from 6–24 months of life (summarized in fig. 1). Weaning is associated with increased *Escherichia coli*, enterococci, bacteriodes and anaerobic gram-positive cocci and decreased enterobacteria. Differences between breastfed and formula-fed infants disappear.

By 1–2 years of age the microbiota resembles that of adults, although levels of bifidobacteria and enterobacteria in children (16 months to 7 years) remain higher than in adults.

### The Importance of a Healthy Microbiota: Biological Effects

The intestinal microbiota is crucial for normal development of the gut-associated lymphoid tissue (GALT), and has important effects on intestinal mucosal barrier function and other aspects of intestinal function.
**Immune Development**

Microbial colonization of the newborn intestine is required for normal immune development, which in turn is important for regulation of gut inflammatory responses and oral tolerance induction. The mucosal immune system of the gastrointestinal tract is constantly challenged by diverse antigens including microbial and food antigens. Such priming of the gut-associated lymphoid tissue is important for two opposing functions: mounting a response to pathogens and maintaining hyporesponsiveness to innocuous antigens. Mice raised in a germ-free environment fail to develop oral tolerance and have a persistent Th2-dependent antibody response [7]. This immune deviation can be corrected by reconstitution of intestinal microbiota, but only if this occurs during the neonatal period [7].

An important question is how the microbiota is altered by the significant changes in diet during the first years of life and how this impacts upon intestinal immune development. The host-microbe cross-talk during and after breastfeeding is critical in this regard. The strains of healthy gut microbiota are likely to stimulate local and systemic immune responses via pattern recognition molecules such as toll-like receptors providing the host with an anti-inflammatory stimulus and directing the host-microbe interaction towards immune tolerance. In particular, the bifidobacteria-dominated environment in childhood may provide a more anti-inflammatory stimulus than bacteria from adults which have been shown to be more proinflammatory. A complex microbial community is required to achieve a healthy microbiota that exhibits powerful anti-pathogenic and anti-inflammatory capabilities.

**Intestinal Function**

An absent or inadequate intestinal microbiota has been shown to cause defects in intestinal barrier function. The microbiota may also influence other intestinal functions. Before weaning, formula-fed infants have a greater ability to ferment complex carbohydrates than breastfed infants, probably due to the presence of a more complex microbiota. Following weaning these differences disappear. Breastfed infants have delayed establishment of mucin-degrading microbiota, but this increases in both groups between 6 and 9 months. Conversion of cholesterol to coprostanol commences after 6 months of age, and levels of ammonia, phenol, β-glucosidase and β-glucuronidase activity increase after weaning.
β-Glucuronidase activity is often higher in formula-fed infants; however, this difference resolves after weaning.

**Maintenance and Modulation of the Individually Optimized Healthy Microbiota**

The healthy gut microbiota created during early life must be maintained throughout life. Deviations in microbiota associated with disease can be redirected to the healthy balance by dietary means, for instance by using probiotics or prebiotics. Probiotics are defined as viable microbes which through oral administration produce health benefits to the host. Probiotics are members of the healthy gut microbiota that mimic the healthy microbiota of both a breastfed infant and the healthy infant, and are generally regarded as safe [8, 9]. Prebiotics are oligosaccharides that promote expansion of specific microbes with potential to maintain health. A prerequisite for the efficacy of prebiotics is that such strains are already present in the gut. Carefully designed combinations of probiotics and prebiotics may offer an optimal means for creating and maintaining a healthy microbiota, as this would mimic the mother–infant relationship of offering both microbes and oligosaccharides to the newborn infant.

It is important to recognize that individual probiotic bacterial strains can have distinct and specific effects [9]. Therefore, the effects of one probiotic strain cannot be generalized to another, and the individual properties of a probiotic strain must be evaluated prior to clinical application. For example, in a double-blind placebo-controlled trial, *Lactobacillus rhamnosus* GG (LGG) but not a mixture of 4 probiotic strains (LGG, *L. rhamnosus* LC705, *B. breve* Bbi99, *Propionibacterium* JS) was effective for the treatment of eczema [10]. LGG has also been shown to enhance IgA responses against rotavirus, which is not found with different strains of the same species [11]. Furthermore, in addition to species/strain specific effects of probiotics, the timing of probiotic administration may also be important. For example, in separate studies, LGG (alone or in combination with other probiotics and a prebiotic) and *L. reuteri* administered prenatally to mothers in the last 2–4 weeks of pregnancy and to the infant in the first 6 months of life have been reported to reduce the risk of developing eczema in childhood up to age 7 years [12–15]. In contrast, a bacterium that had not been characterised in preclinical studies, *L. acidophilus* LAVRI-A1, administered only to infants from 4 weeks to 6 months of life did not have any effect on eczema risk, suggesting that prenatal administration may be requisite for efficacy in the prevention of allergic disease [16]. These results highlight the different effects of specific probiotics, which are further supported by genomic studies.

Interestingly, a recent study of LGG administered prenatally to mothers from 36 weeks gestation and to infants for the first 6 months of life conducted in Germany failed to demonstrate a protective effect against the development of allergic disease [17]. This may reflect reduced power of the study (study population 94 as compared to 159 in the original Kalliomaki et al. study [12]), or geographic/population specific differences.

Similarly, prebiotic oligosaccharides have different microbiota-modifying properties. Although, most prebiotic components have been shown to enhance the bifidobacterial microbiota, detailed investigation of specific effects is required. A wide variety of galacto-oligosaccharides are found in breast milk, and have documented bifidogenic and health-promoting effects in the infant gut. However, some fructo-oligosaccharides have been reported to enhance levels of unknown microbes in the human gut, thus potentially facilitating untoward effects in infants. Therefore, when evaluating a probiotic or prebiotic for clinical use, the safety and clinical benefit of that specific product must be documented to verify efficacy before it can be recommended for clinical application.
Conclusions

- The healthy human microbiota is metabolically active and provides an important defense mechanism for the host. Deviations in its composition are related to multiple disease states.
- Evidence supports a crucial role for the infant microbiota and the first colonization steps in later health. Bifidobacteria play a key role in this process.
- The mother–infant contact has an important impact on initial microbiota development, providing the critical first inoculum at birth, promoting the bifidogenic environment through prebiotic galacto-oligosaccharides and microbes in breast milk and introducing environmental bacteria through contact with the infant.
- Both the succession of microbial communities during the first years of life and the sequelae of these events need to be clarified in more detail.
- The potential application of specific probiotics and/or prebiotics to influence microbiota development for the treatment and prevention of disease also warrants further evaluation.

References

Introduction

Breastfeeding provides optimal nutrition for the infant and also has many non-nutritional benefits for the child and mother. Therefore, it has been recommended by WHO and many countries that one should aim for exclusive breastfeeding of infants for about 6 months and for continued breastfeeding up to the age of 12 months or beyond. In populations with high rates of infectious diseases breastfeeding during the 2nd year of life or longer has been shown to reduce morbidity and mortality. There is a considerable interest in the public health aspects of breastfeeding and an increasing number of scientific studies exploring the mechanisms behind the numerous benefits of breastfeeding [1].

Nutrients and Other Substances in Human Milk

Human milk has about the same energy content as cow’s milk (about 670 kcal/l), while many important nutrients, such as protein, sodium, potassium, magnesium and zinc, are present at much lower contents, typically one third to half of the content found in cow’s milk (table 1). This is a reflection of the much slower growth velocity in humans, and thereby the lower need of nutrients important for growth. Human milk also contains many other substances apart from nutrients. These include hormones, growth factors, and immune-related compounds, such as antibodies (sIgA), leukocytes (B and T lymphocytes, neutrophils and macrophages), oligosaccharides, nucleotides and cytokines. It is likely that many of these non-nutritional substances are involved in many of the short- and long-term effects breastfeeding has on the infant.

Positive Effects on the Infant and Mother

Breastfeeding has significant positive effects on health and development during infancy, later during childhood and most likely also some effects during adulthood [2–4]. However, as most studies are observational, confounding is difficult to rule out, e.g. mothers who choose to breastfeed in industrialized countries are typi-
cally better educated and their children also have a lower risk of developing some diseases.

The most evident effect of breastfeeding is protection against infectious diseases, especially against diarrhea and respiratory tract infections. In developing countries mortality during the first years of life is considerably higher among those not being breastfed [5]. But also in industrialized countries the risk of infectious diseases, especially diarrhea, is significantly less among those being breastfed. These differences could be explained by passive protection of mucous membranes provided by the antibodies and other immune components in human milk, but there is also evidence that the child’s own immune system is influenced by breastfeeding. This could be the reason that some immune-related diseases, e.g. asthma, type-1 diabetes, inflammatory bowel diseases and some childhood cancers, are less common among breastfed children compared with children who had been predominantly formula-fed as infants. A consistent finding in many studies from both industrial and developing countries is a small but significant advantage of breastfeeding on later cognitive function. This effect is likely to be related to an optimal ratio between n-3 and n-6 fatty acids and the content of the long-chain polyunsaturated fatty acid docosahexaenoic acid in human milk. Breastfeeding has also an effect on growth. Breastfed infants gain weight faster during the first months of life and are leaner and slightly shorter than formula-fed infants at the age of 12 months [6]. This was the main reason why the WHO developed a new global growth standard based on breastfed infants (see Chapters 1.1 and 4.2). It has been suggested that the different growth patterns could be a reason why breastfed infants seem to have a lower risk of some non-communicable diseases, including obesity, later in life (see Chapter 1.5).

Breastfeeding is also relevant for maternal physiology and health. From a global perspective the most important effect is the inhibitory effect on ovulation, lactational amenorrhea, which in populations with low use of contraceptives enhances child spacing, and thereby has a positive effect on infant and young child health. Moreover, breastfeeding induces utilization of maternal body fat stores and can thus help to decrease excessive body fat depots, and it reduces the maternal risk for later development of type-2 diabetes, breast and ovarian cancer.

### Potential Untoward Effects of Breastfeeding

#### Transmission of HIV

Breastfeeding can cause mother-to-child transmission of HIV. However, in countries with a high prevalence of infectious diseases, especially diarrhea, early cessation of breastfeeding may re-
sult in a higher mortality than the mortality caused by transmission of HIV through breast milk. It is therefore recommended by the UN agencies that breastfeeding should only be avoided if replacement feeding is acceptable, feasible, affordable, sustainable and safe [7]. If that is not the case, it is recommended that the mother breastfeeds exclusively for the first 6 months, as this practice has been found to be associated with a three- to fourfold decreased risk of transmission compared to non-exclusive breastfeeding. After 6 months breastfeeding should stop as soon as it is possible to provide an adequate and safe diet without breast milk.

Hypernatremic Dehydration
If there are problems during the first 1–2 weeks after delivery in initiating milk production and no other fluids are given, there is a risk that the infant develops hypernatremic dehydration, which in severe cases can cause convulsions, brain damage and death. This can be prevented by supervision and support during the initiation of breastfeeding, monitoring weight loss and urine production, and provision of other fluids if there are signs of dehydration.

Environmental Contaminants
The content of environmental contaminants is higher in breast milk than in cow’s milk or infant formula, because of the accumulation particularly of lipid-soluble contaminants in maternal tissues. Several studies have shown an association between high levels of contaminants in the mother’s blood and negative effects on health and development of the infant. However, it is difficult to

<table>
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<td>Side effects possible</td>
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<td>Monitor baby for drowsiness</td>
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<td>Use alternative drug if possible</td>
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<td>Monitor baby for jaundice</td>
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<td>Use alternative drug ( may inhibit lactation )</td>
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<tr>
<td></td>
<td>Safe in usual dosage</td>
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<tr>
<td></td>
<td>Monitor baby</td>
</tr>
</tbody>
</table>

Table 2. Breastfeeding and mother’s medication

Breastfeeding contraindicated | Anticancer drugs ( antimetabolites ); Radioactive substances ( stop breastfeeding temporarily )
---|---
Continue breastfeeding | Side effects possible
---|---
Monitor baby for drowsiness | Use alternative drug if possible
---|---
Monitor baby for jaundice | Sulfonamides, dapsone
---|---
Use alternative drug ( may inhibit lactation ) | Estrogens, including estrogen-containing contraceptives, thiazide diuretics, ergometrine
---|---
Safe in usual dosage | Most commonly used drugs:
---|---
Monitor baby | Analgesics and antipyretics: short courses of paracetamol, acetylsalicylic acid, ibuprofen; occasional doses of morphine and pethidine
---|---
Antibiotics: ampicillin, amoxicillin, cloxacillin and other penicillins
---|---
Erythromycin
---|---
Antituberculosis drugs, antieprosy drugs ( see dapsone above )
---|---
Antimalarials ( except mefloquine, fansidar )
---|---
Antihelmintics, antifungals
---|---
Bronchodilators ( e.g. salbutamol ), corticosteroids, antihistamines, antacids, drugs for diabetes, most antihypertensives, digoxin
---|---
Nutritional supplements of iodine, iron vitamins
---|---

Breastfeeding

Environmental Contaminants
The content of environmental contaminants is higher in breast milk than in cow’s milk or infant formula, because of the accumulation particularly of lipid-soluble contaminants in maternal tissues. Several studies have shown an association between high levels of contaminants in the mother’s blood and negative effects on health and development of the infant. However, it is difficult to
disentangle the intrauterine exposure from the exposure through breast milk. There is general agreement that the positive effects of breastfeeding outweigh the potential negative effects, but also that it is important to reduce the level of contaminants in the environment and the mother’s diet.

**Maternal Medication**

Most drugs given to a breastfeeding mother are excreted in her milk. If possible, maternal medication should therefore be avoided. However, only a few drugs are contraindicated, i.e. anticancer drugs and radioactive substances. Other drugs might be given while monitoring the infant or alternative drugs may be considered. For an overview see table 2 [8].

**Support of Breastfeeding**

Many factors influence the initiation and duration of breastfeeding: cultural attitudes, the mother’s perception, and the attitudes of friends and family. The health profession plays an important role in educating and supporting the mother in breastfeeding. Traditional hospital routines with separation of the mother and infant, scheduled feeding intervals, and provisions of other drinks have a negative impact on the prevalence of breastfeeding. This is the reason why UNICEF and WHO launched the Baby Friendly Hospital Initiative 1992. By training hospital staff in the ten steps to successful breastfeeding (table 3) it has been possible to increase breastfeeding rates in many settings. Health professionals should also be trained to solve common problems during the first days after delivery, such as positioning of the infant, sore nipples, and sucking difficulties. To stop the negative influences from the marketing of infant formula, the World Health Assembly has adopted an international code on the marketing of breast milk substitutes.

**Breastfeeding of the Hospitalized Infant**

Breastfeeding is especially important in preterm infants, because human milk appears to have a protective effect on the immature gut. Preterm infants have a higher protein need, which should be covered by adding an appropriate human milk fortifier. If the mother cannot supply milk for her infant, provision of donor milk should be considered. This could be provided from individual donors or from a human milk bank. If donor milk is used, there are a number of procedures on testing, storage and pasteurization that have to be followed [9]. Human milk also has advantages for many term infants with medical problems. Mothers should be supported to express milk for their infants if they can suck. This milk can be fed by tube, bottle or cup.

<table>
<thead>
<tr>
<th>Table 3. The Baby-Friendly Hospital Initiative: ten steps to successful breastfeeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Have a written breastfeeding policy that is routinely communicated to all healthcare staff</td>
</tr>
<tr>
<td>- Train all healthcare staff in skills necessary to implement this policy</td>
</tr>
<tr>
<td>- Inform all pregnant women about the benefits and management of breastfeeding</td>
</tr>
<tr>
<td>- Help mothers initiate breastfeeding within 1.5 h of birth</td>
</tr>
<tr>
<td>- Show mothers how to breastfeed and maintain lactation, even if they should be separated from their infants</td>
</tr>
<tr>
<td>- Give newborn infants no food or drink other than breast milk, unless medically indicated</td>
</tr>
<tr>
<td>- Practice rooming in – that is, allow mothers and infants to remain together 24 h/day</td>
</tr>
<tr>
<td>- Encourage breastfeeding on demand</td>
</tr>
<tr>
<td>- Give no artificial teats or pacifiers (also called dummies or soothers) to breastfeeding infants</td>
</tr>
<tr>
<td>- Foster the establishment of breastfeeding support groups and refer mothers to them on discharge from the hospital or clinic</td>
</tr>
</tbody>
</table>
Conclusions

- Populations of breastfed infants have less infections and most likely less immune-related diseases, such as asthma, diabetes, and inflammatory bowel diseases, a small advantage in cognitive development and some protection against non-communicable diseases, e.g. obesity
- For the mother breastfeeding results in lactational amenorrhea and child spacing, which is important in populations with low use of contraceptives
- HIV-positive mothers should refrain from breastfeeding if replacement feeding is acceptable, feasible, affordable, sustainable and safe
- Feeding of human milk to preterm infants protects the immature gut and decreases the risk of necrotizing enterocolitis
- If the mother cannot provide breast milk for her preterm infant, provision of donor milk should be considered

References

Introduction

Breastfeeding is the ideal form of infant feeding which should be actively supported, promoted and protected [1, 2]. Infants who cannot be breastfed (or should not receive breast milk, or for whom breast milk is not available) should receive an infant formula intended to serve as a breast milk substitute, specially manufactured to satisfy, by itself, the particular nutritional requirements of infants during the first months of life up to the introduction of appropriate complementary feeding, and thereby to promote normal growth and development.

Infant formula is a product based on the milk of cows or other animals and/or other edible constituents of animals, including fish, or of plant origin, which have been proved to be suitable for infant feeding.

Gross compositional similarity with the human milk of healthy women is not an adequate indicator of the safety and suitability of infant formula [3]. The adequacy of infant formula composition should be determined by a comparison of its effects on physiological (e.g. growth patterns), biochemical (e.g. plasma markers) and functional (e.g. immune responses) outcomes in infants fed formulae with those of healthy, exclusively breastfed infants.

Infant formulae should only contain components in certain amounts that serve a nutritional purpose or other benefit. Since dietary composition in infants has a major impact on short- and long-term child health and development, the scientific evidence to support modifications of infant formulae beyond the established standards should be evaluated by independent scientific bodies prior to the acceptance of introduction of such products to the market.
Recommendations for Infant Formula Composition

The Codex Alimentarius (Latin for ‘food code’) is a collection of internationally recognized standards, guidelines, codes of practice and other recommendations related to foods, food production and food safety [4]. These texts are developed by the Codex Alimentarius Commission that was established in 1963 by the Food and Agriculture Organization of the United Nations (FAO), and the World Health Organization (WHO). The aims of the Commission are to protect the health of consumers, to ensure fair practices in the international food trade and to promote coordination of all food standards work undertaken by international governmental and non-governmental organizations. The Codex Standard 72 defining the compositional, quality and safety requirements for infant formula intended to meet the nutritional needs of healthy infants from birth to 1 year of age was adopted by the Codex Alimentarius Commission in 1981 [5]. The Codex Standard 72 was updated in 2007 [6]. Infant formula prepared ready for consumption must contain per 100 kcal the nutrients listed in table 1, with minimum and maximum levels where applicable.

The Concept of Follow-On Formula

The European Union Commission Directive 91/321/EEC of 14 May 1991 [7] defined follow-on formulae designed for infants after the introduction of foods other than milk. ‘Follow-on formulae’ are foodstuffs intended for particular nutritional use by infants when appropriate complementary feeding is introduced and constituting the principal liquid element in a progressively diversified diet. They should not be used as breast milk substitutes during the first 6 months of life. In the updated Directive 2006/141/EC of 22 December 2006 [8], their composition is very close to that of ‘infant formulae’ defined as foodstuffs intended for use by infants during the first months of life and satisfying by themselves the nutritional requirements of such infants until the introduction of appropriate complementary feeding (table 2).

Preparation, Storage and Handling of Infant Formula

Powdered formula is not a sterile product and may contain pathogenic bacteria such as *Enterobacter sakazakii* that can cause devastating sepsis, particularly in the first 2 months of life. In the home setting, powdered formula should be freshly prepared for each feed. Written guidelines for the preparation and handling of formula should be established for hospitals and daycare centers, and their implementation should be monitored [9]. If formula needs to be prepared in advance, it should be prepared on a daily basis and should be kept at 4°C or below for not more than 30 h. The use of sterile liquid formula is encouraged for healthy newborn infants in maternity wards.

Addition of Ingredients to Infant Formula

Thickening Agents

It is clear from clinical experience that the addition of thickening agents as starch or carob bean gum to infant formula (antireflux or antiregurgitation formula) can reduce moderate regurgitation and decrease nutrient losses in case of failure to thrive. However, since very few nutritional studies have been performed in infants, antiregurgitation formulae should not be used indiscriminately in healthy, thriving infants who spit up [10].

Long-Chain Polyunsaturated Fatty Acids

While there are indications that a supply of docosahexaenoic acid and arachidonic acid in infancy
Table 1. Essential composition of infant formula in liquid or powdered form [6]

<table>
<thead>
<tr>
<th>Component</th>
<th>Unit</th>
<th>Minimum</th>
<th>Maximum</th>
<th>GUL¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy</td>
<td>kcal/100 ml</td>
<td>60</td>
<td>70</td>
<td>–</td>
</tr>
<tr>
<td>Proteins²</td>
<td>1.8</td>
<td>3.0</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Lipids³</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total fat</td>
<td>g/100 kcal</td>
<td>4.4</td>
<td>6.0</td>
<td>–</td>
</tr>
<tr>
<td>Linoleic acid</td>
<td>mg/100 kcal</td>
<td>300</td>
<td>–</td>
<td>1,400</td>
</tr>
<tr>
<td>α-Linolenic acid</td>
<td>mg/100 kcal</td>
<td>50</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Ratio linoleic/α-linolenic acid</td>
<td>5:1</td>
<td>15:1</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Lauric + myristic acids</td>
<td>% total fatty acids</td>
<td>–</td>
<td>20</td>
<td>–</td>
</tr>
<tr>
<td>Trans fatty acids</td>
<td>% total fatty acids</td>
<td>–</td>
<td>3</td>
<td>–</td>
</tr>
<tr>
<td>Erucic acid</td>
<td>% total fatty acids</td>
<td>–</td>
<td>1</td>
<td>–</td>
</tr>
<tr>
<td>Total phospholipids</td>
<td>mg/100 kcal</td>
<td>–</td>
<td>300</td>
<td>–</td>
</tr>
<tr>
<td>Carbohydrates⁴</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
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<td>g/100 kcal</td>
<td>9.0</td>
<td>14.0</td>
<td>–</td>
</tr>
<tr>
<td>Vitamins</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin A⁵</td>
<td>μg RE/100 kcal</td>
<td>60</td>
<td>180</td>
<td>–</td>
</tr>
<tr>
<td>Vitamin D⁶</td>
<td>μg/100 kcal</td>
<td>1</td>
<td>2.5</td>
<td>–</td>
</tr>
<tr>
<td>Vitamin E⁷</td>
<td>mg α-TE/100 kcal</td>
<td>0.5</td>
<td>–</td>
<td>5</td>
</tr>
<tr>
<td>Vitamin K</td>
<td>μg/100 kcal</td>
<td>4</td>
<td>–</td>
<td>27</td>
</tr>
<tr>
<td>Thiamin</td>
<td>μg/100 kcal</td>
<td>60</td>
<td>–</td>
<td>300</td>
</tr>
<tr>
<td>Riboflavin</td>
<td>μg/100 kcal</td>
<td>80</td>
<td>–</td>
<td>500</td>
</tr>
<tr>
<td>Niacin⁸</td>
<td>μg/100 kcal</td>
<td>300</td>
<td>–</td>
<td>1,500</td>
</tr>
<tr>
<td>Vitamin B₆</td>
<td>μg/100 kcal</td>
<td>35</td>
<td>–</td>
<td>175</td>
</tr>
<tr>
<td>Vitamin B₁₂</td>
<td>μg/100 kcal</td>
<td>0.1</td>
<td>–</td>
<td>1.5</td>
</tr>
<tr>
<td>Pantothenic acid</td>
<td>μg/100 kcal</td>
<td>400</td>
<td>–</td>
<td>2,000</td>
</tr>
<tr>
<td>Folic acid</td>
<td>μg/100 kcal</td>
<td>10</td>
<td>–</td>
<td>50</td>
</tr>
<tr>
<td>Vitamin C⁹</td>
<td>mg/100 kcal</td>
<td>10</td>
<td>–</td>
<td>70</td>
</tr>
<tr>
<td>Biotin</td>
<td>μg/100 kcal</td>
<td>1.5</td>
<td>–</td>
<td>10</td>
</tr>
<tr>
<td>Minerals and trace elements</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iron</td>
<td>mg/100 kcal</td>
<td>0.45</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Calcium</td>
<td>mg/100 kcal</td>
<td>50</td>
<td>–</td>
<td>140</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>mg/100 kcal</td>
<td>25</td>
<td>–</td>
<td>100²</td>
</tr>
<tr>
<td>Ratio calcium/phosphorus</td>
<td>mg/mg</td>
<td>1:1</td>
<td>2:1</td>
<td>–</td>
</tr>
<tr>
<td>Magnesium</td>
<td>mg/100 kcal</td>
<td>5</td>
<td>–</td>
<td>15</td>
</tr>
<tr>
<td>Sodium</td>
<td>mg/100 kcal</td>
<td>20</td>
<td>60</td>
<td>–</td>
</tr>
<tr>
<td>Chloride</td>
<td>mg/100 kcal</td>
<td>50</td>
<td>160</td>
<td>–</td>
</tr>
<tr>
<td>Potassium</td>
<td>mg/100 kcal</td>
<td>60</td>
<td>180</td>
<td>–</td>
</tr>
<tr>
<td>Manganese</td>
<td>μg/100 kcal</td>
<td>1</td>
<td>–</td>
<td>100</td>
</tr>
<tr>
<td>Iodine</td>
<td>μg/100 kcal</td>
<td>10</td>
<td>–</td>
<td>60</td>
</tr>
<tr>
<td>Selenium</td>
<td>μg/100 kcal</td>
<td>1</td>
<td>–</td>
<td>9</td>
</tr>
<tr>
<td>Copper¹²</td>
<td>μg/100 kcal</td>
<td>35</td>
<td>–</td>
<td>120</td>
</tr>
<tr>
<td>Zinc</td>
<td>mg/100 kcal</td>
<td>0.5</td>
<td>–</td>
<td>1.5</td>
</tr>
<tr>
<td>Fluoride¹³</td>
<td>μg/100 kcal</td>
<td>–</td>
<td>100</td>
<td>–</td>
</tr>
<tr>
<td>Other substances</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Choline</td>
<td>mg/100 kcal</td>
<td>7</td>
<td>–</td>
<td>50</td>
</tr>
<tr>
<td>Myoinositol</td>
<td>mg/100 kcal</td>
<td>4</td>
<td>–</td>
<td>40</td>
</tr>
<tr>
<td>L-Carnitine</td>
<td>mg/100 kcal</td>
<td>1.2</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Optional ingredients¹⁴,¹⁵</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Taurine</td>
<td>mg/100 kcal</td>
<td>–</td>
<td>12</td>
<td>–</td>
</tr>
<tr>
<td>Total nucleotides¹⁶</td>
<td>mg/100 kcal</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Docosahexaenoic acid¹⁷</td>
<td>% total fatty acids</td>
<td>–</td>
<td>–</td>
<td>0.5</td>
</tr>
</tbody>
</table>
Guidance upper levels (GULs) are for nutrients without sufficient information for a science-based risk assessment. These values are values derived on the basis of meeting nutritional requirements of infants and an established history of apparent safe use. Nutrient contents in infant formulae should usually not exceed the GULs unless higher nutrient levels cannot be avoided due to high or variable contents in constituents of infant formulae or due to technological reasons.

The minimum value applies to cow’s milk protein. For infant formula based on non-cow’s milk protein other minimum values may need to be applied. For infant formula based on soy protein isolate, a minimum value of 2.25 g/100 kcal applies. Infant formula based on non-hydrolyzed milk protein containing less than 2 g protein/100 kcal and infant formula based on hydrolyzed protein containing less than 2.25 g protein/100 kcal should be clinically evaluated.

Commercially hydrogenated oils and fats must not be used in infant formula.

Lactose and glucose polymers should be the preferred carbohydrates in formula based on cow’s milk protein and hydrolysed protein. Only precooked and/or gelatinized starches, gluten-free by nature, may be added to infant formula up to 30% of total carbohydrates and up to 2 g/100 ml. Sucrose, unless needed, and the addition of fructose as an ingredient should be avoided in infant formula, because of life-threatening symptoms in young infants with unrecognized hereditary fructose intolerance.

Expressed as retinol equivalents (RE). $1 \mu g$ RE = 3.33 IU. Vitamin A = $1 \mu g$ all-trans retinol. Retinol contents must be provided by preformed retinol, while any carotenoid content should not be included in the calculation and declaration of vitamin A activity.

Calciferol: $1 \mu g$ calciferol = 40 IU vitamin D.

$1 \text{mg} \alpha$-TE ($\alpha$-tocopherol equivalent) = $1 \text{mg} \delta\alpha$-tocopherol. Vitamin E content must be at least 0.5 mg $\alpha$-TE/g polyunsaturated fatty acid (PUFA), using the following factors of equivalence to adapt the minimal vitamin E content to the number of fatty acid double bonds in the formula: 0.5 mg $\alpha$-TE/g linoleic acid (18:2n-6); 0.75 mg $\alpha$-TE/g $\alpha$-linolenic acid (18:3n-3); 1.0 mg $\alpha$-TE/g arachidonic acid (20:4n-6); 1.25 mg $\alpha$-TE/g eicosapentaenoic acid (20:5n-3); 1.5 mg $\alpha$-TE/g docosahexaenoic acid (22:6n-3).

Niacin refers to preformed niacin.

Expressed as ascorbic acid. This GUL has been set to account for possible high losses over shelf-life in liquid formulae; for powdered products lower upper levels should be aimed for.

Levels may need to be determined by national authorities.

This GUL should accommodate higher needs with soy formula.

Adjustment may be needed in these levels for infant formula made in regions with a high copper content in the water supply.

Fluoride should not be added to infant formula. In any case its level should not exceed 100 $\mu g$/100 kcal.

The following substances may be added in conformity with national legislation.

Only L(+)-lactic acid producing cultures may be used.

Levels may need to be determined by national authorities.

If docosahexaenoic acid (22:6n-3) is added to infant formula, the arachidonic acid (20:4n-6) content should reach at least the same concentration as docosahexaenoic acid. The content of eicosapentaenoic acid (20:5n-3), which can occur in sources of long-chain PUFA, should not exceed the content of docosahexaenoic acid. National authorities may deviate from the above conditions, as appropriate for the nutritional needs.
Table 2. Essential composition of follow-on formulae (FOF) when reconstituted as instructed by the manufacturer [8]

<table>
<thead>
<tr>
<th>Component</th>
<th>Unit</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Energy</strong></td>
<td>kcal/100 ml</td>
<td>60</td>
<td>70</td>
</tr>
<tr>
<td><strong>Proteins</strong></td>
<td>g/100 kcal</td>
<td>1.8</td>
<td>3.5</td>
</tr>
<tr>
<td>FOF manufactured from cow’s milk proteins</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>or from soy protein isolates, alone or in a mixture</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>with cow’s milk proteins</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Lipids</strong></td>
<td>g/100 kcal</td>
<td>2.25</td>
<td>3.5</td>
</tr>
<tr>
<td><strong>Total fat</strong></td>
<td>g/100 kcal</td>
<td>4.0</td>
<td>6.0</td>
</tr>
<tr>
<td>Linoleic acid</td>
<td>mg/100 kcal</td>
<td>300</td>
<td>1,200</td>
</tr>
<tr>
<td>α-Linolenic acid</td>
<td>mg/100 kcal</td>
<td>50</td>
<td>–</td>
</tr>
<tr>
<td>Ratio linoleic/α-linolenic acid</td>
<td>% fat</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>Lauric and/or myristic acid</td>
<td>% fat</td>
<td>–</td>
<td>20</td>
</tr>
<tr>
<td>Trans fatty acids</td>
<td>% fat</td>
<td>–</td>
<td>3</td>
</tr>
<tr>
<td>Erucic acid</td>
<td>% fat</td>
<td>–</td>
<td>1</td>
</tr>
<tr>
<td>Phospholipids</td>
<td>g/l</td>
<td>–</td>
<td>2</td>
</tr>
<tr>
<td><strong>Carbohydrates</strong></td>
<td>g/100 kcal</td>
<td>9.0</td>
<td>14.0</td>
</tr>
<tr>
<td>Total carbohydrates</td>
<td>% carbohydrates</td>
<td>–</td>
<td>20</td>
</tr>
<tr>
<td>Lactose</td>
<td>g/100 kcal</td>
<td>4.5</td>
<td>–</td>
</tr>
<tr>
<td>Sucrose and/or fructose and/or honey</td>
<td>% carbohydrates</td>
<td>–</td>
<td>20</td>
</tr>
<tr>
<td>Glucose</td>
<td>g/100 kcal</td>
<td>–</td>
<td>2</td>
</tr>
<tr>
<td>Fructo-oligosaccharides and galacto-oligosaccharides6</td>
<td>g/l</td>
<td>–</td>
<td>8</td>
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<tr>
<td><strong>Vitamins</strong></td>
<td>µg – RE/100 kcalβ</td>
<td>60</td>
<td>180</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>µg/100 kcal</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Vitamin Dβ</td>
<td>µg/100 kcal</td>
<td>4</td>
<td>25</td>
</tr>
<tr>
<td>Vitamin Eβ</td>
<td>mg α-TE/100 kcalα</td>
<td>0.5β</td>
<td>5</td>
</tr>
<tr>
<td>Vitamin K</td>
<td>µg/100 kcal</td>
<td>60</td>
<td>300</td>
</tr>
<tr>
<td>Thiamin</td>
<td>µg/100 kcal</td>
<td>80</td>
<td>400</td>
</tr>
<tr>
<td>Riboflavin</td>
<td>µg/100 kcal</td>
<td>300</td>
<td>1,500</td>
</tr>
<tr>
<td>Niacin</td>
<td>µg/100 kcal</td>
<td>35</td>
<td>175</td>
</tr>
<tr>
<td>Vitamin B6</td>
<td>µg/100 kcal</td>
<td>0.1</td>
<td>0.5</td>
</tr>
<tr>
<td>Vitamin B12</td>
<td>µg/100 kcal</td>
<td>0.1</td>
<td>0.5</td>
</tr>
<tr>
<td>Pantothenic acid</td>
<td>µg/100 kcal</td>
<td>400</td>
<td>2,000</td>
</tr>
<tr>
<td>Folic acid</td>
<td>µg/100 kcal</td>
<td>10</td>
<td>50</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>mg/100 kcal</td>
<td>10</td>
<td>30</td>
</tr>
<tr>
<td>Biotin</td>
<td>µg/100 kcal</td>
<td>1.5</td>
<td>7.5</td>
</tr>
</tbody>
</table>

**Minerals and trace elements**

<table>
<thead>
<tr>
<th>Component</th>
<th>Unit</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron</td>
<td>mg/100 kcal</td>
<td>0.6</td>
<td>2</td>
</tr>
<tr>
<td>Calcium</td>
<td>mg/100 kcal</td>
<td>50</td>
<td>140</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>mg/100 kcal</td>
<td>25</td>
<td>90</td>
</tr>
<tr>
<td>Ratio calcium/phosphorus</td>
<td>mg/mg</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Magnesium</td>
<td>mg/100 kcal</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>Sodium</td>
<td>mg/100 kcal</td>
<td>20</td>
<td>60</td>
</tr>
<tr>
<td>Chloride</td>
<td>mg/100 kcal</td>
<td>50</td>
<td>160</td>
</tr>
</tbody>
</table>
may have some beneficial effects, there is no unanimous agreement that an exogenous supply is needed, at least not after the first few months of life [11]. However, there is no evidence to suggest that concentrations within the range found in human milk are harmful. The addition of docosahexaenoic acid and arachidonic acids is therefore allowed in infant formula (table 1).

Ingredients Modulating the Intestinal Microflora (see Chapter 1.7)
Prebiotics (mainly fructo-oligosaccharides and galacto-oligosaccharides) are undigestible food components stimulating the growth and/or activity of one or a limited number of bacteria in the colon and thereby improving host health [12], whereas probiotics (mainly *Bifidobacterium bif-

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**Table 2 (continued)**

<table>
<thead>
<tr>
<th>Component</th>
<th>Unit</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potassium</td>
<td>mg/100 kcal</td>
<td>60</td>
<td>160</td>
</tr>
<tr>
<td>Manganese</td>
<td>µg/100 kcal</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>Iodine</td>
<td>µg/100 kcal</td>
<td>10</td>
<td>50</td>
</tr>
<tr>
<td>Selenium</td>
<td>µg/100 kcal</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Copper</td>
<td>µg/100 kcal</td>
<td>35</td>
<td>100</td>
</tr>
<tr>
<td>Zinc</td>
<td>mg/100 kcal</td>
<td>0.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Fluoride</td>
<td>µg/100 kcal</td>
<td>–</td>
<td>100</td>
</tr>
<tr>
<td><strong>FOF manufactured from soy protein isolates, alone or in a mixture with cow’s milk proteins</strong> [12]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iron</td>
<td>mg/100 kcal</td>
<td>0.9</td>
<td>2.5</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>mg/100 kcal</td>
<td>30</td>
<td>100</td>
</tr>
<tr>
<td><strong>Optional ingredients</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Taurine</td>
<td>mg/100 kcal</td>
<td>–</td>
<td>12</td>
</tr>
<tr>
<td>Total nucleotides</td>
<td>mg/100 kcal</td>
<td>–</td>
<td>5</td>
</tr>
<tr>
<td>Cytidine 5′-monophosphate</td>
<td>–</td>
<td>2.5</td>
<td></td>
</tr>
<tr>
<td>Uridine 5′-monophosphate</td>
<td>–</td>
<td>1.75</td>
<td></td>
</tr>
<tr>
<td>Adenosine 5′-monophosphate</td>
<td>–</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Guanosine 5′-monophosphate</td>
<td>–</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Inosine 5′-monophosphate</td>
<td>–</td>
<td>1.0</td>
<td></td>
</tr>
</tbody>
</table>

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1 The use of sesame seed oil and cotton seed oil must be prohibited.
2 The eicosapentaenoic acid (20:5n-3) content must not exceed the docosahexaenoic acid (22:6n-3) content. The docosahexaenoic acid content must not exceed that of n-6 LCP.
3 This provision does not apply to follow-on formulae in which soy protein isolates represent more than 50% of the total protein content.
4 Honey must be treated to destroy spores of *Clostridium botulinum*.
5 Glucose may only be added to follow-on formulae manufactured from protein hydrolysates.
6 Fructo-oligosaccharides (FOS) and galacto-oligosaccharides (GOS) may be added to follow-on formulae in a combination of 90% GOS and 10% FOS.  
7 RE = All trans retinol equivalent.
8 In the form of cholecalciferol, of which 10 µg = 400 IU of vitamin D.
9 α-TE = D-α-Tocopherol equivalent.
10 0.5 mg α-TE/g polyunsaturated fatty acids expressed as linoleic acid as corrected for the double bonds but in no case less than 0.5 mg/100 available kcal: 0.5 mg α-TE/1 g linoleic acid (18:2n-6); 0.75 mg α-TE/1 g α-linolenic acid (18:3n-3); 1.0 mg α-TE/1 g arachidonic acid (20:4n-6); 1.25 mg α-TE/1 g eicosapentaenoic acid (20:5n-3); 1.5 mg α-TE/1 g docosahexaenoic acid (22:6n-3).
11 Preformed niacin.
12 All requirements defined for FOF manufactured from cow’s milk proteins or protein hydrolysates must apply.
dum and Lactobacillus rhamnosus GG) are live microbial food ingredients that are beneficial to health [12]. Although they may have health benefits, no general recommendation on the supplementation of prebiotics, probiotics, and synbiotics, i.e. a mixture of prebiotics and probiotics, can be made in infancy [12–14].

### Indications for Soy Protein Formula

Soy is a source of protein that is inferior to cow’s milk protein, with a lower digestibility and bioavailability. For soy protein infant formulae, only soy protein isolates can be used. Soy protein formulae should only be used in specified circumstances because they may have nutritional disadvantages and contain high concentrations of phytate, aluminum and phytoestrogens (isoflavones), the long-term effects of which are unknown [15]. Soy protein formulae should not be used in preterm infants. Indications include severe persistent lactose intolerance, galactosemia, and vegan concepts. Soy protein formulae play no role in the prevention of allergic diseases and should not be used in infants with food allergy during the first 6 months of life. They have no indication in the prevention or management of infantile colic, regurgitation or prolonged crying.

### Conclusions

Infant formulae:
- are breast milk substitutes satisfying the nutritional requirements of infants from birth to 1 year of age. Their composition should follow the Codex Alimentarius Standard revised in 2007 [6]
- are products based on milk of cows or other animals and/or other edible constituents of animals, including fish, or of plant origin
- are not sterile products when powdered. Guidelines for their preparation and handling are necessary in institutional settings

No general recommendations on the addition of prebiotics, probiotics, and thickening agents to infant formula for healthy, thriving term infants can be made. Soy protein formulae are not the first choice of feeding for healthy infants.

### References


Introduction

The first 2 years of life are critical for the promotion of healthy growth and development of children. It is of utmost importance that the foods children receive are nutritionally adequate and safe. Exclusive breastfeeding for the first 6 months is recommended by the WHO for all populations. For those who cannot breastfeed, infant formula and other breast-milk substitutes, manufactured in accordance with codex standards, provide an alternate source of nutrition. Bottle-fed infants living in poor environments in developing countries are at a high risk of malnutrition and even death. It is estimated that 1.5 million babies die each year because they are not adequately breastfed [1]. When a mother uses an alternative to breast milk to feed her baby, it is important that she makes an informed decision. Although it is over 25 years since the introduction of the international code for the marketing of breast-milk substitutes [2], which aims to encourage breastfeeding and to restrict the promotion of infant formula, it is still not universally applied. There is a need for more effective implementation of the code.

The International Code

The International Code of Marketing of Breast-Milk Substitutes was adopted by the World Health Assembly (WHA) in 1981 to promote breastfeeding and to ensure that marketing of breast-milk substitutes and feeding bottles is appropriate [2]. The member States of WHA are to implement the code in national measures as a minimum requirement to promote healthy practices with respect to infant and young child feeding. Manufacturers and distributors are called on to abide by the international code independent of other measures. Non-governmental organizations, professional groups, institutions and individuals are called on to report violations.
Extracts from the International Code

Article 2 (products covered by the code): The code applies to the marketing, and practices related thereto, of the following products: breast-milk substitutes, including infant formula; other milk products; foods and beverages, including bottle-fed complementary foods, when marketed or otherwise represented to be suitable for use as a partial or total replacement of breast milk, feeding bottles, and teats.

Article 5.2 (provision of samples): Manufacturers and distributors should not provide, directly or indirectly, pregnant women, mothers, or members of their families with samples of products within the scope of this code.

Article 7.2 (provision of information for health workers): Information provided by manufacturers and distributors to health professionals regarding products in the scope of this code should be restricted to scientific and factual matters, and such information should not imply or create a belief that bottle feeding is equivalent or superior to breastfeeding.

Article 7.3 (provision of inducements to health workers): No financial or material inducements to promote products within the scope of this code should be offered by manufacturers or distributors to health workers or members of their families.

Article 7.4 (provision of samples to health workers): Samples of infant formula or other products within the scope of this code should not be provided for health workers except when necessary for the purpose of professional evaluation or research at the institutional level.

Violations of the International Code

Violations of the code are common throughout the world. For example, a survey carried out in 4 countries, Bangladesh, Poland, South Africa and Thailand, revealed the distribution of free samples of infant formula, other breast milk substitutes and feeding bottles, in contravention of articles 5.2 and 7.4 of the international code [3]. Most of the samples were reported to have come from a health facility; this suggests that samples given to facilities were passed on to mothers, whether or not that was the intention of the company donating the samples.

Breastfeeding campaigners have persistently highlighted breaches by companies in adhering to the WHO code. A recent briefing by Save the Children and an investigation by the Guardian include a catalog of evidence. For example, the briefing includes a report from Botswana where 30% of mothers reported to have been advised by a healthcare professional to use a specific brand of infant formula [4]. The Guardian investigation in Dhaka found that the walls of a doctor’s waiting room were covered with posters showing healthy babies and the brands of infant formula [5]. Practices recently reported from the Philippines include targeting mothers with ‘mothering classes’ and offering financial incentives for healthcare staff [6]. Community health workers received gifts such as T-shirts or jackets, and mothers were given free samples of infant formula. Studies show that distribution of free samples has a detrimental effect on breastfeeding [7, 8].

Monitoring the Code

Information provided by monitoring helps international organizations like the WHO and UNICEF, and national governments in the implementation of the code and to stop specific violations in a country. The reports on violations demonstrate the need for transparent, independent and effective controls on the marketing of baby food and bottles. Governments should ensure a consistent strategy of monitoring involving investigation, observation and recording of information. The basics of monitoring include familiarization with the main points of the international
code and the national measures; obtaining information on the breast-milk substitutes locally used; recording details about the company and brand names, hospitals/clinics where infant formula is used; descriptions of posters, displays, etc., and the reporting of violations to the appropriate body.

**Campaign for Ethical Marketing**

It is now recognized that voluntary initiatives alone are inadequate for implementation of the code for the marketing of breast-milk substitutes. Health professionals and breastfeeding organizations call for enforcement of stricter rules.

Under the international code, information provided by the manufacturers should not imply or create a belief that bottle feeding is equivalent or superior to breastfeeding. But many leading brands of infant formula carry misleading nutrition claims. Recently, legislation of the European Community has provided a limited list of acceptable claims, as well as a process by which any additional claims must be fully evaluated before they can be used [9], and these regulations are to be implemented in the national legislation of all member states. Baby milk manufacturers are ordered to drop all nutrition claims of baby foods, which suggest that they would be a superior alternative to breast milk. The aim is to ensure that mothers are not unduly influenced when deciding on their feeding practices.

**Education Campaign**

Health professionals and breastfeeding advocates consider that the lack of awareness about the importance of breastfeeding is an important contributory factor for the introduction of bottle feeding. Breastfeeding is the best source of nutrition for healthy babies, it promotes the development of the emotional bonding between the mother and child, bestows upon the newborn infant protection against infection, and contributes to protecting the mothers from closely spaced pregnancy. Mothers should be informed about the benefits of breastfeeding and the disadvantages associated with bottle feeding. Hospitals and maternity units can set important examples for new mothers. Despite the UNICEF’s Baby-Friendly Hospital Initiative launched in 1991 to support breastfeeding [10], mothers still receive contradictory advice. Those delivered normally can initiate breastfeeding within half an hour of birth, but they are often advised to give water or a breast-milk substitute which might have a negative impact [11]. The training of healthcare staff must be strengthened. Governments, organizations of pediatricians, obstetricians and other healthcare professionals, as well as other non-governmental organizations play important roles in implementing adequate standards and practices for the promotion, protection and support of breastfeeding, and for the restriction of undue marketing activities for breast-milk substitutes.

**Conclusions**

- Breast milk is the best source of nutrition for infants. For those who cannot breastfeed, infant formula provides an alternate source of nutrition
- When a mother uses an alternative to breast milk to feed her baby, it is important that she makes an informed decision and is not pressured by commercial promotions to use a substitute
- The International Code of Marketing of Breast-Milk Substitutes was introduced to promote breastfeeding and to regulate the marketing of breast-milk substitutes, and it needs to be strictly applied and enforced.
References

6 Help the Philippines Stand Up to Company Bullying: www.babymilkaction.org/CEM/cemnov06.html#1.
### Key Words

Complementary feeding · Infant · Breastfeeding

### Key Messages

- Complementary foods are defined by the WHO as any food or liquid other than breast milk. However, since many infants receive human milk substitutes from the first weeks of life, other authorities have suggested that the term, complementary food, should be applied to foods and liquids *other than* breast milk or infant formulas.

- Complementary foods are required for nutritional and developmental reasons. They should not be introduced before 17 weeks, but all infants should start complementary foods by 26 weeks.

- It is important to ensure that complementary foods provide adequate energy density (minimum 25% fat), and that the diet includes good sources of protein, iron and zinc. Strategies used to achieve this will vary in different environments.

### Introduction

Complementary foods are defined by the WHO as any food or liquid other than breast milk. This definition means that infant formulas and follow-on formulas (human milk substitutes, HMS) are regarded as complementary foods, which can be confusing, since many infants receive HMS from the first weeks of life. Other authorities (ESPGHAN [1]) have suggested that the term, complementary food, should be applied to foods and liquids *other than* breast milk or infant formulas.

Complementary foods are required during the second part of the first year of life for both nutritional and developmental reasons, and to enable the transition from milk feeding to family foods. From a nutritional point of view, the ability of breast milk to meet macro- and micronutrient requirements becomes limited, while from a developmental perspective, infants develop the ability to chew and start to show an interest in foods other than milk.

Current WHO recommendations on the age at which complementary foods should be introduced are based on consideration of the optimal duration of exclusive breastfeeding. However, since HMS are defined by WHO as a complementary food, it is difficult to translate this recommendation to formula-fed infants. Following a systematic review [2] and expert consultation in 2001 [3], WHO recommended that infants should be exclusively breastfed for 6 months, although this contrasts with current practice in many countries where complementary foods may be introduced starting from 3–4 months.

### Timing of Complementary Feeding

Complementary feeding recommendations and practices are generally not evidence-based and vary between countries. Gastrointestinal and renal functions are likely to be sufficiently mature...
by around 4 months of age to enable infants to process some complementary foods. With regard to neurodevelopment, there is a range at which infants attain the necessary motor skills to cope safely with complementary foods, but this is likely to fall within the 4–6 months period. There is general consensus that complementary foods should not be given before 17 weeks of age, as earlier introduction may be associated with an increase in fatness, respiratory symptoms and eczema later in childhood. The WHO recommends that infants should be exclusively breastfed for 6 months before the introduction of complementary foods [3]. This recommendation is based on the findings of a systematic review of the optimal duration of exclusive breastfeeding [2] comparing mother and infant outcomes with exclusive breastfeeding for 6 months versus 3–4 months in 20 eligible studies. From the perspective of infants in developed countries, one study from Belarus found that infants who were exclusively breastfed for 6 months experienced less morbidity from gastrointestinal infection than those exclusively breastfed for 3–4 months [2]. Although many countries have adopted the new WHO recommendation, sometimes with qualifications, other countries still recommend 4–6 months. A recent commentary by the ESPGHAN Committee on Nutrition considered all aspects of the timing and content of diet during the complementary feeding period and concluded that complementary foods should not be introduced before 17 weeks, but that all infants should start complementary foods by 26 weeks [1].

**Content of the Diet**

Most current guidelines for the gradual introduction of different foods during the complementary feeding period are based on cultural factors and food availability rather than scientific evidence. Whilst in developing countries, the focus is still on providing adequate nutrients to support growth and development, in more affluent environments, achieving a better balance of nutrients and avoiding excess may be more important.

Nutritional recommendations for the complementary feeding period are based on the concept that breast milk will not meet full requirements for energy, protein and micronutrients beyond about 6 months of age. Theoretically, the requirement for good quality early complementary foods – particularly those rich in iron and zinc – may be more important for breastfed infants, since an infant fed entirely on HMS will have higher micronutrient intakes from milk at this stage. In practice, however, it is generally considered undesirable and impractical to have different recommendations for breastfed and formula-fed infants.

**Energy**

Energy requirements remain high during the first year of life. The fat content of the diet is an important determinant of its energy density and should not be less than 25% of energy intake. A higher proportion might be required if the appetite is poor, the infant has recurrent infections or is fed infrequently. Reduced fat cow’s milk should not be introduced too early as it will reduce the energy density of the diet. In deciding when to introduce lower fat cow’s milk, consideration should be given to the rest of the infant’s diet, and to his or her growth. In countries with high rates of child obesity, it may be advantageous to accustom children to low fat products from a fairly early age.

**Iron and Zinc**

More than 90% of iron requirements during the complementary feeding period in a breastfed infant must be provided by complementary foods.
Potential strategies for achieving this include the use of fortified weaning foods, iron-fortified infant formulas and follow-on formulas, foods naturally rich in bioavailable iron such as meat, or the use of supplements. The most suitable strategy will vary in different circumstances. The same strategies may broadly be used to provide an adequate supply of zinc – a particularly important issue in developing countries where deficiencies are common. Cow’s milk is a very poor source of iron, and it is generally recommended that it should not be used as the main drink before 12 months of age.

Salt and Sugar

High intakes of salt in infancy may be associated with later higher blood pressure [4]. Furthermore, infants may become accustomed to a salty taste which could affect subsequent food preferences and intake. Hence it is generally agreed that salt should not be added to food during the complementary feeding period. Similarly, sugar is associated with the development of dental caries. Its use should be restricted, and it is important to ensure good dental hygiene practices as early as possible.

Gluten

For populations affected by celiac disease, the risk may be reduced if small amounts of gluten are gradually introduced while the infant is still being breastfed. The risk of celiac disease is higher if gluten is given before 3 months, and delaying exposure until 7 months or later may also increase the risk [5]. In genetically predisposed infants, both early (<3 months) and possibly late (≥7 months) introduction of gluten may be associated with a higher risk of developing type-1 diabetes.

Vegetarian Diets

If infants receive a vegetarian diet it is important that the diet includes a sufficient amount of milk (about 500 ml/day) and dairy products. Vegan diets should be discouraged in infancy because of the risk of B12 deficiency which can affect neurodevelopment.

Allergy

Certain foods, including egg, fish, nuts and seafood, are potentially allergenic. However, the evidence that delaying the introduction of such foods reduces the risk of developing food allergy is not currently convincing, even for infants with a family history of atopy [6]. Furthermore, the exclusion of fish – the richest natural source of n-3 fatty acids – and eggs from the diet could itself have undesirable nutritional consequences.

Taste and Food Acceptance

An important but poorly researched area is the potential effect of early diet on food acceptance and subsequent food preferences [7]. There may be ‘windows’ during infancy during which certain tastes are more readily accepted. Children are predisposed to like high energy foods, to prefer sweet and salty tastes and to reject new foods. However, these predispositions may be modified by early dietary experience. Hence, parents play an important role in establishing good dietary habits.

Conclusions

• Complementary foods should not be introduced before 17 weeks, but all infants should start complementary foods by 26 weeks.
• It is important to ensure that complementary foods provide adequate energy density (minimum 25% fat), and that the diet includes good sources of protein, iron and zinc. Strategies used to achieve this will vary in different environments.

• In populations at risk of celiac disease, gluten should be gradually introduced while the infant is still being breastfed.

• The complementary feeding period should be regarded as an important time for establishing good eating habits and food preferences. Sugar and salt should not be added to complementary foods.

References


2 Nutrition of Healthy Infants, Children and Adolescents

2.5 Allergy Prevention through Early Nutrition

Sibylle Koletzko

Key Words
Tolerance induction · Sensitization · Allergen avoidance · Breastfeeding · Atopic dermatitis

Key Messages
- Allergen contact during the first months of life modulates induction of tolerance and sensitization to food antigens
- Nutritional intervention can reduce the risk of allergic manifestations, particularly of atopic dermatitis and cow’s milk protein allergy during the first year of life in children with a positive family history for allergy
- Most data for allergy prevention through nutrition are generated from epidemiological, observational and intervention studies. While the first two types can describe associations and generate hypotheses, only results from intervention studies can prove a causal relationship
- The impact of breastfeeding on the risk of allergy is difficult to establish because randomized controlled intervention trials have not been performed for ethical reasons. Conclusions from observational cohort studies may not be valid due to selection bias and reverse causality
- Every hypoallergenic formula product should be evaluated because the degree of hydrolyzation or source of protein alone do not predict effects

Introduction

Contact with food allergens in early infancy modulates the development of tolerance to food allergens, and also the development of sensitization and allergic manifestations. Nutritional intervention aiming at a reduction in allergy risk should be started early in infancy [1]. Data on alimentary allergy prevention were obtained in observational cohort studies, which describe associations and can generate hypotheses, and in controlled intervention studies which can prove causal relationships. The available data do not support the conclusion that maternal elimination diets during pregnancy and lactation provide a benefit for allergy risk reduction in the infant. Data on breastfeeding effects on allergy are controversial. In infants with a positive family history of allergy and who are not exclusively breastfed, the use of certain infant formulae based on hydrolyzed proteins reduces the risk of allergic manifestations. Delayed introduction of complementary feeding has no proven benefit.

Maternal Allergy Avoidance during Pregnancy and Lactation

Maternal dietary allergen exclusion during pregnancy has been proposed as a potential strategy to reduce allergy risk in the offspring, but the available data do not support any beneficial effects [2]. Human milk contains food antigens arising from cow’s milk, egg, wheat and other foods a few hours after maternal consumption of the respective foods. The concentration of cow’s milk protein in breast milk is only 100,000 times lower than in cow’s milk itself, and does not correlate with the amount of antigen ingested by the
mother. Whether these low antigen amounts in breast milk induce sensitization or tolerance is not clear. In a randomized controlled trial, no beneficial effects of avoiding egg and milk consumption by lactating women was found on the development of children’s allergic disease until 5 years of age [3]. Maternal exclusion diets bear the risk of inadequate supply of certain nutrients. In the absence of beneficial evidence, maternal exclusion diets during pregnancy and lactation for allergy prevention are not recommended.

**Breastfeeding**

Breastfeeding is preferred for infants after birth because of nutritional, immunological and psychological benefits. The potential allergy-preventive effect of exclusive or partial breastfeeding has not been properly assessed because randomization of breastfeeding is not possible for ethical considerations [4]. Mothers who exclusively breastfeed differ markedly from those who feed formula with regard to education, socioeconomic factors, smoking, keeping pets at home, introduction of other foods, and many other factors which may influence the incidence of allergy. Inverse causality may play a role in non-randomized studies, i.e. mothers of infants with the highest degree of heredity or signs of atopy within the first months of life may tend to prolong exclusive and total breastfeeding [5]. Recent meta-analyses are not conclusive as to whether exclusive breastfeeding during the first months of life or long duration of any breastfeeding are beneficial for reducing allergy risk [6]. However, breastfeeding is strongly recommended for all healthy infants regardless of atopic risk.

**Feeding Hydrolyzed Infant Formulae**

Several intervention trials evaluated infant formulae based on partially or extensively hydrolyzed proteins compared to cow’s milk formula, often with non-randomized breastfed reference groups [7–10]. All published randomized trials were performed in infants with an increased atopic risk based on one parent or sibling affected by allergy, or both parents affected, or elevated cord blood IgE, or other criteria. Therefore, the results cannot be generalized to infants with non-atopic parents. Some of the studies included additional co-interventions, like maternal dietary or environmental restrictions, or delayed introduction of complementary feeding.

The analysis of results in a recent Cochrane review led to the conclusion that there is limited evidence for risk reduction of infant and childhood allergy and infant cow’s milk allergy with a hydrolyzed formula, compared to a cow’s milk formula [11]. In this analysis, many studies even of high quality were excluded because of a dropout rate of >20%. However, it is highly questionable whether this exclusion criterion should be applied for infant feeding trials starting at birth, where it is highly likely that feeding intentions expressed at the time of birth change over time [12]. For this and other reasons the Cochrane review has been heavily criticized, and the conclusions were challenged by an international panel of allergy experts [13].

The German Infant Nutritional Intervention (GINI) study is by far the largest double-blind, randomized controlled intervention trial in this area, and the only trial sponsored by a governmental grant rather than industry funds [7, 9]. The trial evaluated the allergy-preventive effects of feeding during the first 4 months of life, in addition to breastfeeding, three hydrolyzed formulae compared to a cow’s milk formula in high-risk infants. Among different atopic manifestations (atopic dermatitis, asthma, gastrointestinal manifestations, allergic rhinitis, urticaria), only the risk of atopic dermatitis was reduced by hydrolyzed formula. Compared to cow’s milk formula, an extensively hydrolyzed casein formula significantly reduced atopic dermatitis (per protocol and intention to treat analyses), and a partially
hydrolyzed whey formula significantly reduced atopic dermatitis (in the per protocol analysis only). In contrast, the extensively hydrolyzed casein formula (eHF-C) and partially hydrolyzed whey formula (pHF-W) appeared in the first year of life and persisted until 6 years, while the significant reduction in the extensively hydrolyzed whey formula (eHF-W) occurred in the 6th year only [8]. CMF = Cow’s milk formula.

Protein Sources Other than Cow’s Milk in Infant Feeding

The use of unmodified mammalian milk protein, including unmodified sheep, buffalo, mare’s or goat’s milk, or unmodified soy or rice milk, is not recommended for infants because their composition is inadequate to serve as the sole food source for infants [14]. Moreover, these milks are not recommended for infants with suspected or proven cow’s milk protein allergy because of the risk of possible allergic cross-reactivity. A recent Cochrane review concluded that infant formulae based on soy protein does not reduce allergy risk, including food allergy [15].

Complementary Foods

Most available data originate from large cohort studies. Very early solid food introduction within the first 3–4 months of life, with a high variety of different foods, seems to increase the risk of eczema, and possibly also of food allergy [5, 16, 17]. Delaying the introduction of solid foods beyond the 6th month of life has no protective effect and may even increase the risk for allergy [18]. This effect was also found for allergenic foods such as hen’s egg, cow’s milk, fish, and wheat [19, 20]. Thus it is recommended that complementary foods should not be introduced before the 17th week of life, but no later than the 26th week of life, regardless of the familial risk of allergy [21, 22].

Conclusions

- Maternal exclusion diet during pregnancy and lactation has no allergy-preventive effect and is not recommended
- Exclusive breastfeeding for the first 4–6 months of life and continuous breastfeeding during gradual solid food introduction are recommended for all infants
- In industrialized countries, solid food introduction should be started not before the 17th and not later than the 26th week of life, regardless of the hereditary risk for allergy
- If infant formula is used during the first 6 months of life in infants with a family history of allergy, a protein hydrolysate formula with documented reduced allergenicity should be given
- Formulations based on other milk proteins (sheep, buffalo, mare’s or goat’s milk), as well as soy or rice protein have no allergy-preventive effects and are not recommended
2.6 Toddlers, Pre-School and School Children

Hildegard Przyrembel

**Key Words**
- Food-based dietary guidelines
- Dietary habits
- Food preference
- Food choice
- Feeding skills
- Meals

**Key Messages**
- Toddlers and children should participate in family meals.
- Toddlers do not need specially prepared commercial foods for particular nutritional uses. The use of such meals is determined by convenience.
- Food-based dietary guidelines for children should name basic food groups, give approximate amounts to be consumed and provide exemplary recipes according to local habits.
- Nutrient supplements and fortified foods should be used only when indicated.
- Beverages of no or low energy content should accompany meals.

**Introduction**

The age range of 1 to approximately 12 years includes very different phases of development. With increasing motor skills, toddlers, some of whom are still partly breastfed, continue to feed themselves with an increasing variety of foods as part of the family diet. Food preferences developed in the first year of life tend to persist but are modified under the influence of parents, siblings and play mates. Pre-school and school children increase both the frequency and variety of social contacts outside the home and thereby food and meal choices.

A healthy diet for children should be devised on the basis of both scientific and practical considerations. Scientific criteria are the adequacy of the intake in comparison to recommendations for energy and nutrient intake to support normal development and growth, taking into account the preventive effects of an adequate diet on chronic diseases of adulthood. Practical criteria are regional or national dietary habits, availability and cost of foods, and taste preferences of children.

Food-based dietary guidelines for children have been devised. As an example the so-called optimised mixed diet (OptimIX) developed in Germany is described. Such guidelines can be easily adapted to different typical eating habits, meal schedules and differences in locally available basic foods. They are based on commonly available foods to be prepared at home, but leave room for the integration of ready-to-eat products and foods preferred by many children, like ‘fast foods’ and sweets.

**Principles of Children’s Diets and Eating**

Food-based dietary guidelines, based on the energy and nutrient needs of children and their preferences and on health aspects, provide advice on food selection, meal composition and meal
patterns, including recipes. The main food groups included are of high nutrient density: cereals and other starchy foods (bread, pasta, potatoes, etc.); vegetables, legumes and fruits; milk and dairy products; meat, poultry, eggs and (oily) fish; and fats and oils.

A list of reference amounts of the main food groups which provide >80% of the appropriate energy intake and 100% of all nutrients is part of OptimiX [3] (table 1). In addition, less than 20% of the energy intake is provided by ‘tolerated’ food groups, often of low nutrient but high energy density. These foods are not prohibited, but permitted to meet, e.g., the sweet preferences of some children and to permit flexibility in the composition of meals. The amounts of foods are guidance values, with the possibility to choose within a food group, e.g. instead of milk and milk products cheese can be consumed based on equivalency in the calcium content (100 ml milk corresponds to about 15 g of hard and 30 g of soft cheese). The amounts in table 1 need not be consumed every day, the aim should be the average amount per week. Variability in daily intake is normal and should be tolerated; the variability of daily energy intakes of children can be 50% around the average. Moreover, small and inactive children will eat smaller amounts than active and big children, and boys will consume more than girls of the same age. Children should be allowed from the start to determine the amounts they wish to eat and not be forced to empty their plates. This will permit them to eat to satiety and help to avoid overnutrition and overweight.

<table>
<thead>
<tr>
<th>Table 1. Adequate food consumption amounts according to age</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommended foods</strong> (≥80% of energy intake)</td>
</tr>
<tr>
<td><strong>Age, years</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>1</strong></td>
</tr>
<tr>
<td>------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Generous amounts</strong></td>
</tr>
<tr>
<td>Beverages, ml/day</td>
</tr>
<tr>
<td>600</td>
</tr>
<tr>
<td>Bread, cereal (flakes), g/day</td>
</tr>
<tr>
<td>80</td>
</tr>
<tr>
<td>Potatoes, pasta, rice, cereals, g/day</td>
</tr>
<tr>
<td>80</td>
</tr>
<tr>
<td>Vegetables, g/day</td>
</tr>
<tr>
<td>100</td>
</tr>
<tr>
<td>Fruit, g/day</td>
</tr>
<tr>
<td>100</td>
</tr>
<tr>
<td><strong>Moderate amounts</strong></td>
</tr>
<tr>
<td>Milk, milk products, ml or g/day</td>
</tr>
<tr>
<td>300</td>
</tr>
<tr>
<td>Meat, meat products, g/day</td>
</tr>
<tr>
<td>30</td>
</tr>
<tr>
<td>Eggs, number/week</td>
</tr>
<tr>
<td>1–2</td>
</tr>
<tr>
<td>Fish, g/week</td>
</tr>
<tr>
<td>50</td>
</tr>
<tr>
<td><strong>Small amounts</strong></td>
</tr>
<tr>
<td>Margarine, oil, butter, g/day</td>
</tr>
<tr>
<td>15</td>
</tr>
<tr>
<td><strong>Tolerated foods</strong> (≤20% of energy intake)</td>
</tr>
<tr>
<td>Age group</td>
</tr>
<tr>
<td>toddlers, schoolchildren</td>
</tr>
<tr>
<td>Cake, sweets, g/day</td>
</tr>
<tr>
<td>&lt;50</td>
</tr>
<tr>
<td>Jam, sugar, g/day</td>
</tr>
<tr>
<td>&lt;10</td>
</tr>
</tbody>
</table>

Modified from Kersting et al. [3].
OptimiX provides about 54% of the energy intake from mostly complex carbohydrates, 32% of energy from fat of mostly plant origin and 14% of energy from protein, half of animal and half of plant origin. The most suitable fat intake of toddlers is not known; it should not be less than 25% of energy [2, 4, 5]. Protein sources will reflect country- and culture-specific dietary habits, and plant protein can provide the majority of protein intake. In that case a variety of plant foods should be consumed, which compensate for each other’s deficiencies in certain indispensable amino acids. A vegan diet with no animal-derived food is not suitable for toddlers.

Meals and Meal Patterns

Whenever possible, meals should be consumed in the company of others and at regular times, while snacking should be avoided. The distribution of the basic and tolerated foods over different meals can vary, but all meals together add up to provide an adequate intake of all nutrients and energy. Toddlers will need more frequent meals than older children. The type of meals, both hot and cold, and the time of day at which they are consumed will vary between countries and families. Both cold and hot meals should be accompanied by a beverage. Cold meals will mostly consist of bread and cereals, dairy products and raw fruit and vegetables and thus provide the majority of the daily carbohydrate, fiber and calcium intake besides significant percentages of vitamin C and folate intake. Hot meals are based on potatoes, rice or pasta, vegetables and salads, while meat or fish serve as a supplement and need not be eaten every day of the week. Hot meals thus contribute significantly to the intake of numerous vitamins and minerals, like vitamin B6 and B12, magnesium, phosphorus and iodine.

Choice of Foods

Foods particularly manufactured and specially fortified with nutrients are not a necessary part of a healthy toddler’s diet, although a wide variety of such foods is available and is convenient to use. In circumstances where nutrient-dense foods are scarce, fortification or supplementation can, however, become necessary, particularly with regard to iron, iodine, zinc and calcium.

Self-prepared food for toddlers should not be salted. Varieties of processed foods with a low-salt content should be chosen.

*Bread and cereals,* but also rice and pasta should preferably be wholegrain products which contain B vitamins, magnesium, iron, fiber, protein and unsaturated fatty acids. A mixture of wholegrain and more refined products may be better accepted by young children.

*Vegetables and fruits,* if not served raw, should be boiled as briefly and in as little water as possible to reduce inevitable losses of vitamins, minerals and secondary plant substances, like carotenoids, phytosterins, polyphenols. While the primary choice of both fruit, legumes and vegetables should be those which are in season, it may be necessary to be more flexible in the case of strong dislikes. Fruit juices can substitute for fruit in exceptional cases.

*Milk and dairy products* are indispensable in all children’s diets as sources of calcium and other minerals as well as vitamins. From the age of 2 years full-fat milk products can be replaced by reduced-fat products.

*Meat and meat products* are important because of the well-available iron and zinc, particularly for toddlers and young children. Moreover, they provide high-quality protein and important B vitamins. Products low in fat should be preferred. Heme iron also increases the absorption of iron from plant food.

*Fish* is an important source of iodine and long-chain n-3 fatty acids and should be eaten at least once a week. Many children only accept
braised and fried fish, which might be high in fat.

To increase the quality of the fat consumed, at least half of the total fat intake, both ‘hidden’ and visible, should come from plant oils, preferably those with a high content of mono- and polyunsaturated fatty acids and which contain some α-linolenic acid (rape seed, soy, flaxseed) and sufficient vitamin E. These oils are practically free of trans fatty acids. An overall low fat use will further reduce the total intake of saturated and trans fatty acids.

Beverages should preferably be offered to toddlers from a cup and should be free of or low in energy (water or unsweetened herbal or fruit teas). Milk is not to be regarded as a beverage but as a food. Fruit juices can contain valuable vitamins and minerals, but, if undiluted, are high in sugars (>10% of weight). Fruit-based and cola beverages also often contain generous amounts of sugar and are unsuitable for relief of thirst. Sugar-sweetened beverages tend to be overconsumed, which can result in a positive energy balance and finally overweight [6–8].

Conclusions

- Dietary recommendations for toddlers (1–3 years) gradually approach those for children, adolescents and adults; the percentage of energy derived from fat should decrease from 40% to around 30%
- Children should be permitted (within reasonable limits) to determine the amount of food they consume from a range of basic food groups
- Preferences for taste should be respected to a certain degree

References

Introduction

Adolescence is the period from puberty to the stage of complete body maturation. Puberty can be defined as a maturational process of the hypothalamus-pituitary-gonadal axis resulting in growth and development of the genital organs and, concomitantly, in physical and psychological changes towards adulthood leading to the capacity to reproduce [1]. In adolescents, energy and nutrients are required not only for the maintenance of normal function and body stores, but also for growth and development. Growth velocity differs with age, with the highest growth rates occurring during the first 2 years of life and during puberty. Adolescence is a nutritionally vulnerable developmental stage because growth rate accelerates, and amplified caloric and global nutrition needs due to pubertal growth stimulate appetite.

All adolescents should have access to a safe and adequate food supply that promotes optimal physical, cognitive, social and emotional growth and development. As some chronic diseases of adulthood begin during childhood and adolescence, an optimal nutrition approach should be considered for recommendations focusing on adolescents, and this is a way to try to respond to the obesity epidemic that has recently emerged [2, 3].

Eating Patterns

As children grow up, diversification in sources of food and influences on eating behavior occur. Social constraints on families may necessitate the presence of multiple caregivers, eating out, and frequent fast food consumption. Many adolescents, because of parental work schedules, are alone at home and prepare their own snacks and meals. By early adolescence, peer pressure begins
to substitute for parental authority. Very often, meals and snacks are routinely obtained outside home, without any supervision. Adolescents often have discretionary funds to use for self-selected foods. Current eating patterns do not resemble the typical pattern of providing at least breakfast, dinner and a single snack at home, with lunch at school [4]. Sweetened beverage intakes contribute significantly to total caloric intake, and snacks often contribute to excess consumption of discretionary calories and displace foods containing essential nutrients [5]. Parallel to the psychosocial transition from dependence on parental authority to independent thought processes, food choices and purchases are increasingly made by the adolescent. Peer pressure for conformity, in part driven by media promotion of fast food directly to teens, contributes to overeating. Parental role modeling is important in establishing adolescents’ food choices; depending on their own food choices, parents can be either positive or negative role models [6].

Currently, many adolescents have a high intake of sweetened beverages, French fries, pizza, and hamburgers, with a concomitant low intake of fruits, vegetables, dairy products, whole grains, lean meats and fish. The described eating pattern results in consumption of excess fat, saturated fat, trans fat, and added sugars along with insufficient consumption of micronutrients such as calcium, iron, zinc, and potassium, as well as vitamins A, D, C and folic acid [5].

Growth as a Basis for Nutritional Requirements

There is a lack of specific scientific evidence on which to base the nutrient needs of adolescents. The recommended daily allowances (RDAs) for energy are based on median energy intakes of adolescents followed in longitudinal growth studies. RDAs for protein in this group are calculated from growth rates and body composition data, assuming protein use for growth is comparable with maintenance data for adults. Because of wide variability in growth rates, physical activity and metabolic rate, it is difficult to estimate specific nutrient requirements for adolescents. For practical reasons, dietary reference intakes (DRIs) for adolescents are categorized by chronological age rather than maturational development. Thus, health professionals should use them with caution, particularly in individual assessments. An adolescent’s nutritional status should be assessed on an individual basis, using information from clinical, biochemical, anthropometric, dietary and psychosocial assessments. There is no clear consensus on dietary recommendations for adolescents [7], but some accepted general ideas are described below.

Energy

The DRI values for energy at various chronological ages and for both sexes are shown in Chapter 4.2. The DRI for energy do not include a safety factor for increased energy needs (illness, trauma, stress) and are considered to be only average needs. Needs for adolescents will vary with physical activity and stage of maturation.

Protein

During adolescence, protein needs are related more closely to the growth pattern than to chronological age. Average intakes of protein in adolescents are generally well above the DRI. However, protein metabolism is particularly sensitive to energy restriction in adolescents during pubertal growth and maturation. Current dietary patterns of adolescent girls that result in restricted energy intakes represent potential health problems when protein sources are used to meet energy needs. The DRI for protein by chronological age are shown in Chapter 4.2.
Minerals

All mineral needs increase during adolescence. Adolescents at the peak of their growth velocity will require large quantities of nutrients. For some minerals, like calcium, iron and zinc, low intakes are often the result of the current food choices of adolescents. DRI for minerals are shown in Chapter 4.2.

Calcium

Given the accelerated muscular, skeletal and endocrine development, calcium needs are greater during puberty and adolescence than in childhood or the adult years. In fact, 45% of the skeletal mass is added during adolescence. The DRI for calcium is 1,300 mg/day in all adolescents. Adequate intake for calcium cannot be met with dairy-free diets while meeting other nutrient recommendations [8]. Calcium requirements are expressed as adequate intakes (AIs). The AIs address the needs of all individuals in a group, but lack of data or uncertainty in the data prevent being able to specify with confidence the percentage of people covered by this intake.

Iron

During adolescence, iron requirements are increased. In boys, this increase reflects not only the expanding blood volume, but also a rise in hemoglobin concentration that occurs with sexual maturation. In girls, menstruation typically starts about 1 year after peak growth. In girls with marginal dietary iron intakes and increased menstrual blood losses, iron-deficiency anemia may result. Conversely, iron-deficiency anemia may be a limiting factor for growth during adolescence.

Zinc

Zinc is known to be essential for growth and sexual maturation, and retention of zinc increases during puberty. Limited intake of zinc-containing foods may affect physical growth as well as the development of secondary sex characteristics [9].

Vitamins

The need for vitamins is also increased during adolescence. Because of increased energy demands, thiamin, riboflavin and niacin are required in increased quantity for the release of energy from carbohydrates. With great tissue synthesis, there is an increased demand for vitamins B₆ and B₁₂. There are also increased requirements for vitamin D (for rapid skeletal growth) and vitamins A, C and E are needed for new cell growth. The DRIs for vitamins are shown in Chapter 4.2.

Conclusions

- Diet should primarily rely on fruits and vegetables, whole grains, dairy products, beans, fish and lean meat
- Low intakes of saturated and trans fat, cholesterol and added sugar and salt should be promoted
- Foods that are rich in essential nutrients (e.g. calcium, iron) and that provide high amounts of dietary fiber and n-3 fatty acids should be emphasized
- Energy intake and physical activity should be appropriate for the maintenance of a normal weight for height
- Calorie-dense foods and beverages with minimal nutritional content must return to their role as occasional discretionary items in an otherwise balanced diet
References

Introduction

Adolescence is characterized by the World Health Organization as the period from 10 to 20 years of age. During this period the adolescent will acquire individual characteristics of differentiation, and experience growth, and physical and sexual development. During adolescence growth is accelerated and this has an important effect on nutritional needs and recommendations. At this age, many nutritional problems arise and become prevalent: inadequate growth patterns, anemia, excess weight and some situations that could indirectly affect nutritional balance, such as sports, stress, menarche, etc.

Adolescents are prone to very different eating patterns based on these modifications [1]. The various influences that could lead to inadequate food behaviors are peers, school, media, family and environment. Body changes and final formation of our personality are the main frames for food intake at this age. Economic stance may influence the development of food habits and generate nutritional problems [2].

Healthy feeding is part of the global challenge of a healthy lifestyle, especially in low income groups. Increasing physical activity and reducing sedentary life styles is of key importance in the prevention of chronic diseases and morbidity. Here we present some advice for healthy living:

Good nutrition is part of a good life.
Diseases of deprivation, mainly protein-energy malnutrition, are still a major public health problem in many parts of the world, despite the technological development reached by mankind in the last centuries. Although present all over the world, these diseases are particularly prevalent in developing countries and especially in the less favored layers of the population: they are frequently associated with other forms of nutritional deficiencies, such as anemia and hypovitaminosis [3]. When fighting malnutrition, foods specifically designed with trace element supplementation may enhance nutritional recovery at lower costs to the society. Anemia, vitamin A and zinc deficiencies could be resolved by food supplementation in adolescents with no regular access to adequate food staples.

Income commands the possibility of acquiring and using the goods and services that are essential to maintain a good health status, including food, housing, clothing and sanitation. In less developed countries, typical problems of poverty, such as malnutrition, anemia and food deprivation, occur together with problems that are characteristic of a modern life, such as the increasing prevalence of cardiovascular diseases, stress, obesity, among others [4].

At the same time, all over the world there is a major increase in eating disorders in children and adolescents. From the social point of view, the beauty standards adopted mainly by women (and encouraged by men) may enhance the development of eating disorders, since fashion clearly determines rules of thinness that are incompatible with adequate nutrition. The development of eating disorders in the population has been intensified by standards in which ‘thin’ means elegance and sensuality. The media are a catalyzing agent of this trend, considerably influencing the population and mainly female adolescents.

Among all nutritional disorders, obesity presents the highest increase in prevalence, not only in affluent but also in developing countries. Many inadequate lifestyle factors favor obesity: sedentary behavior, inadequate family habits, unsatisfactory food, excessive dietary fat and sugar intake, rapid eating, unbalanced snacks, and the frequent consumption of sweets and candies. Obesity in childhood and adolescence induces metabolic changes such as dyslipidemia, insulin resistance and hypertension already at an early age. Childhood obesity also bears a high risk of persistence into adult life, with an associated increased risk of atherosclerotic disease, hypertension, metabolic disorders, and early mortality. Considering that 70% of the obese adolescents become obese adults, and that child obesity is associated with a high morbidity and mortality later in life, the current increase in the prevalence of child obesity is most disturbing. In many populations the frequency of obesity is markedly higher in less educated and poorer families. Also in the Brazilian population, an inverse relationship between the prevalence of obesity and socio-economic status is observed, similar to findings in developed countries [4]. Thus, the obesity epidemic may widen even further the existing inequalities in health and quality of life between the rich and poor parts of the population.

Food in this transitional period of adolescence has many meanings. Even though adolescents need an adequate and balanced diet with an increasing need for iron, vitamins and mineral salts for normal growth and development, they look for a quick, modern meals that can identify them with the group, such as the typical fast food or junk food [5]. The frequent consumption of those quick meals, snacks, and soft beverages can imbalance the daily diet. A large amount of fats and an excess of sugars contribute to the increase in obesity observed in adolescents in many countries, including Brazil.

After puberty, specific nutritional needs persist. Adolescents need a higher ratio of many essential nutrients to total energy intake than adults to satisfy growth needs and the formation of lean tissues [3]. When growth ceases and maximum height is reached, the larger bone mineralization
and body maintenance still carry a higher need for many nutrients than in childhood. The physiological changes associated with reproduction capabilities may also change the needs for some nutrients, such as iron for girls after menarche and during pregnancy.

Some health problems of adolescents are closely related to nutrition. Many of the underlying factors in the development of a non-healthy adolescent arise from social factors including, among others, poverty and unemployment, sexual or ethnic prejudice, and the repercussions of social changes within families and society. Social inequalities may overwhelmingly interfere with the nutrition of the individual. However, during childhood and adolescence, the family aspect is critical for correction and prevention of risk factors and nutritional disorders.

Many factors determine food habits and may influence adolescents, such as family, peers, teachers, media and advertisements. It is very important for health professionals to understand these influences and to modify deleterious information.

A nutritionally adequate diet is important and should provide the energy and nutrients to sustain the adolescent growth spurt, the changes in body composition that take place during this period, and appropriate physical activity [6].

It is recommended that fats be consumed in moderation, mainly saturated fats from foods of animal origin. Recommendations for a high dietary fiber content and a lower fat intake generally do not have untoward effects on the energy and nutrient supply. Whenever necessary, health professionals should advise adolescents to limit the intakes of fat and enhance the dietary fiber intake, and promote physical activity and healthy life habits for the wellbeing of the population [7].

The marked increase in bone mass during adolescence requires a sufficient calcium supply. Approximately half of the adult bone structure is deposited during adolescence. Dietary calcium is important for adolescents to complete their linear growth peak, even if the deposition of that mineral continues for one more decade. Milk and milk products (preferably with a reduced milk fat content) are an excellent source of bioavailable calcium [8].

Food should be tasty and appealing because eating is one of the great pleasures in life. Health-care professionals can show adolescents that they do not need to stop eating the food they like, and that, sometimes, with small changes in their meals, they can reconcile the pleasure of eating with group acceptance, having a healthy meal that will provide them with the so desired appearance and performance. Fruit, legumes, vegetables, and grains (rice, corn, oat, and rye) should be the basis of a healthy meal. Meals with rice and beans, vegetables, legumes, fruit, and a moderate amount of lean meat and dairy products, are healthy and balanced. Special attention should also be given to the amount eaten [9].

One should also prevent, alert or detect as early as possible any possible risk behaviors in the diet that may lead to food disorders, such as anorexia, bulimia and eating compulsively.

Conclusions

- Promote regular physical activity: sports and active leisure
- Support regular meal times
- Discourage meals in front of the TV
- Drink plenty of liquids (preferably water!), but avoid soft drinks/sugared beverages
- Avoid frequent eating of sweets and fatty foods (e.g. fried foods and snacks); give preference to cooked or baked foods over fried foods
- Promote the regular and daily eating of fruits and vegetables (e.g. include vegetables in preparation of sandwiches)
References

Introduction

Food choices are strongly influenced by the culture of one’s community and country, or what is known as ‘food culture’. Food culture is created by a long tradition involving local food products, environment, climate, lifestyle, religion and related events. An established food culture influences dietary habits and behaviors, as well as consumption of food materials, throughout the region and country. It has been thought that food cultures could be preserved firmly; however, an observable change in dietary habits and patterns has occurred in many parts of the world in the last few decades, showing us that food culture is quite fragile. This has brought serious health problems to all generations, including children and adolescents.

Past

Japanese women and men both enjoy the highest levels of longevity and healthy life expectancy in the world [1]. One of the main reasons for this fact is the traditional Japanese food culture, which consists of a high consumption of fish, complex carbohydrates including dietary fiber, and a variety of protein sources including soybean [2].

Transition to the Current Clash of Cultures regarding Traditional and Global Foods

Over the last few decades in Japan, economic development, accompanied by internationalization and the infiltration of foreign cultures, has led to the breakdown of traditional order as well as that of traditional food culture. The traditional Japanese dietary habits have been strongly influenced by global food cultures. As a result, fast foods such as hamburgers, fried chicken, fried potato chips, pizzas, etc., have been displacing quite a large proportion of people’s diet, resulting in rapid disappearance of the traditional dietary habits,
particularly among children and adolescents. In other words, the clash of cultures has created various problems globally.

Change in Dietary Habits and the Consequences for Health

In Japan, the lipid energy content in people’s diet has increased steeply in the last few decades. The lipid energy intake increased from 14.8% in 1965 to 26.5% in 2000, but carbohydrate (grain) energy intake decreased from 72.1 to 57.5% [3]. In 2004, the lipid intake exceeded 30% of total energy in young adults, 35% in children, and in adolescents it was about 25% [4]. A noteworthy finding regarding lipid sources is that in 1965 the leading sources were soybean and its related products and seafood, but in 2004 it was meat [3] (fig. 1). Thus, saturated fatty acids and n-6 long-chain polyunsaturated fatty acid (PUFA) intake has increased and, in contrast, unsaturated fatty acid and n-3 long-chain PUFA intake has decreased [3]. At the same time, the consumption of...
high energy-dense foods and sugared drinks has increased, while vegetable consumption has decreased [3].

**Meal Patterns and Possible Consequences**

Meal patterns tend to be changing from the former norm of three home-cooked meals a day, eaten at fixed times with the family, to a new pattern among Japanese schoolchildren of eating out, going without breakfast, and eating alone [4]. Concurrently, the prevalence of obesity and metabolic syndrome, such as type-2 diabetes, has increased [5]. Among Japanese schoolchildren, the rates of overweight and obesity were approximately 4 and 10% in 1968 and 2004, respectively [4] (fig. 2). Regarding incidence of type-2 diabetes, it was 1.7 cases per 100,000 elder schoolchildren prior to the 1980s, and by 2000, depending on geographic location, the range of new cases had risen to 5–8 children per 100,000 [6, 7] (fig. 3). This increasing trend is similar to that in other Asian countries, such as China [8], Thailand [9], and Singapore [10].

Although a traditional Asian-type diet should provide an advantage in preventing obesity and its harmful consequences, global food culture has obviously predominated over the traditional dietary habits, after a period of clashing with it.

**Intervention**

In regions and countries such as Asia and the Mediterranean, people should reevaluate the advantages of their traditional diets, particularly foodstuffs, over fast food, and these traditional diets can be modified to make them acceptable to young people. Perhaps, applying a similar idea to other parts of the world can be recommended. Providing health education for both parents and children regarding healthy eating behaviors should be given high priority. Care messages from practitioners can help make this change more effective.

**Conclusions**

Globally, the clash of cultures has created various nutritional and health problems. One of the concerns is the increased consumption of energy-dense foods with high contents of saturated fatty acids and n-6 PUFA, associated with a high prevalence of obesity, type-2 diabetes even in children and adolescents, and other health risks. Thus, better health education is needed for both parents and children with a particular emphasis on healthy eating behavior, healthy meals and physical activity. The avoidance of fast foods and replacing them with foods of high n-3 PUFA contents and green and yellow vegetables should be promoted.

**References**

**Introduction**

The nutritional status of women before and during pregnancy is an important resource for the fetal and infant supply of nutrients. It is replenished and modified by nutrition before and during pregnancy and lactation. Maternal nutrition not only influences the health and wellbeing of the mother but also has immediate and long-term effects on the development and health of the infant [1].

**Body Mass Index**

Body mass index (BMI) before pregnancy is a simple and useful indicator of nutritional status in clinical practice. Optimally, height without shoes and weight should be measured before pregnancy [2].

**Gestational Weight Gain**

Gestational weight gain reflects fetal growth. A low weight gain is a risk indicator for intrauterine growth restriction and perinatal mortality, whereas a higher gain is a risk indicator for maternal diabetes, macrosomia, delivery problems, birth trauma and asphyxia. Intrauterine growth restriction as well as macrosomia may program obesity and the metabolic syndrome in later life [1, 2]. Total weight gain ranges for pregnant women with the best pregnancy outcomes for both mother and infant are classified according to prepregnancy BMI (table 1; fig. 1) [2, 3]. In full-term twin pregnancies a total weight gain of 16–20.5 kg is associated with a favorable outcome.

**Weight Loss after Delivery**

Weight loss after delivery is higher in lactating compared to non-lactating mothers. One year after delivery, prepregnancy weight should again be reached. The mean weight gain of women is about 1 kg with each child.
Energy Requirements

Energy requirements during pregnancy are highly variable. Energy-sparing adaptations can protect the mother and fetus from nutritional strains [4]. The additional energy cost of pregnancy averages 77,000 kcal [5]. For healthy women in the USA with a favorable pregnancy outcome and a normal BMI, the approximate energy needs compared to prepregnancy were [5, 6]:

- <100 kcal/day in the first trimester
- 300 kcal/day in the second trimester
- 500 kcal/day in the third trimester
- 500–600 kcal/day during lactation [5]

Dietary restrictions during pregnancy and lactation should be avoided. Monitoring weight gain provides an indicator of adequacy of energy intake.

Protein Intakes

Protein intakes to meet the average requirement of 50% of women are estimated as:

- 0.88 g/kg/day in pregnancy
- 1.05 g/kg/day during lactation [7]

Recommended dietary allowances (meeting the requirements of 97–98% women) average:

- 1.1 g/kg/day in pregnancy
- 1.3 g/kg/day during lactation [7]

While a high protein supply in pregnancy may be harmful [8], a balanced energy/protein supplement (protein <25% of energy) influenced pregnancy outcome favorably [8].

Physical Aerobic Exercise

Physical aerobic exercise (swimming, cycling, floor exercise programs) at least two or three times per week improves or maintains the physical fitness of pregnant women [9]. A very high

Table 1. Recommended total weight gain ranges for pregnant women by prepregnancy body mass index (BMI) [2]

<table>
<thead>
<tr>
<th>Weight-for-height category</th>
<th>Recommended total gain, kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (BMI &lt;19.8)</td>
<td>12.5–18</td>
</tr>
<tr>
<td>Normal (BMI 19.8–26.0)</td>
<td>11.5–16</td>
</tr>
<tr>
<td>High (BMI 26.0–29.0)</td>
<td>7–11.5</td>
</tr>
</tbody>
</table>

The recommended target weight gain for obese women (BMI >29.0) is at least 6.8 kg.
physical activity level and a high workload may constrain fetal growth, and under unfavorable environmental conditions may lead to pregnancy loss. A lower risk of abnormal glucose tolerance was observed in normal pregnant women who exercised during pregnancy [10]. Breastfeeding success is not influenced by exercise or physical activity.

**Recommended Dietary Allowances**

Recommended dietary allowances, i.e. the intake levels sufficient to meet the requirements of nearly all healthy pregnant and lactating women, or adequate intakes are listed in Table 2 [7]. Even in affluent populations, habitual intakes of some critical nutrients may be marginal or deficient (‘hidden hunger’) [11].

**Folic Acid.** An adequate and early supply of the B vitamin folic acid during the first 8 weeks of pregnancy has a strong protective effect against neural tube defects (NTD; spina bifida, anencephaly) [12]. Folate fortification programs of grain products have been introduced in about 40 countries worldwide and have been shown to markedly reduce NTD incidence. Women of childbearing age who may become pregnant and women during at least the first 2 months of pregnancy should aim to reach an added intake of 400 μg/day of folic acid from supplements, fortified foods, or the combination of both. To prevent the recurrence of NTD in a subsequent pregnancy, the folic acid supply should be maintained at 400 μg/day, or if previously discontinued 4 mg/day should be taken [7].

**Vitamin A** is required for normal embryonic development. In populations with a high prevalence of vitamin A deficiency, supplements are desirable, while in developed countries routine supplementation is not recommended. High doses (>3,000 μg/day preformed vitamin A) in early pregnancy may be teratogenic and should be avoided. But in populations with vitamin A deficiency even a single high dose supplement (60,000 μg) can be safely given to breastfeeding women in the first 2 months after delivery. It has been estimated that about a quarter of the vitamin A requirement may be covered by β-carotene which is not teratogenic.

**Iodine** is needed for the synthesis of thyroid hormones. The most extreme manifestation of iodine deficiency in pregnancy is cretinism, but more subtle alterations in growth and developmental impairment are often overlooked. Salt iodization has been implemented in many countries to prevent iodine deficiency, but iodine monitoring continues to indicate suboptimal supplies. A supplement containing 100 μg/day iodine is recommended in Europe before and during pregnancy, and during lactation.

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Pregnancy</th>
<th>Lactation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A, μg/day</td>
<td>770 (10%)</td>
<td>1,300 (85%)</td>
</tr>
<tr>
<td>Vitamin C, mg/day</td>
<td>85 (13%)</td>
<td>120 (60%)</td>
</tr>
<tr>
<td>Vitamin D, μg/day</td>
<td>5 (0%)</td>
<td>5 (0%)</td>
</tr>
<tr>
<td>Vitamin K, μg/day</td>
<td>90 (0%)</td>
<td>90 (0%)</td>
</tr>
<tr>
<td>Folate, μg/day</td>
<td>600 (50%)</td>
<td>500 (25%)</td>
</tr>
<tr>
<td>Vitamin B₁₂, μg/day</td>
<td>2.6 (8%)</td>
<td>2.8 (17%)</td>
</tr>
<tr>
<td>Calcium, mg/day</td>
<td>1,000 (0%)</td>
<td>1,000 (0%)</td>
</tr>
<tr>
<td>Iodine, μg/day</td>
<td>220 (47%)</td>
<td>290 (93%)</td>
</tr>
<tr>
<td>Iron, mg/dl</td>
<td>27 (50%)</td>
<td>9 (–50%)¹</td>
</tr>
<tr>
<td>Magnesium, mg/day</td>
<td>350 (12%)</td>
<td>310 (0%)</td>
</tr>
<tr>
<td>Phosphorus, mg/day</td>
<td>700 (0%)</td>
<td>700 (0%)</td>
</tr>
<tr>
<td>Zinc, mg/day</td>
<td>11 (38%)</td>
<td>12 (33%)</td>
</tr>
<tr>
<td>Total water, liters/day</td>
<td>3.0 (11%)</td>
<td>3.8 (41%)</td>
</tr>
</tbody>
</table>

The additional intake (%) compared to non-pregnant and non-lactating women of the same age group is given in parentheses. Data from the Food and Nutrition Board, Institute of Medicine, National Academies, USA. ¹ Depends on blood loss at delivery.
Iron deficiency in pregnancy increases the risk of maternal morbidity and mortality, premature birth, low birthweight and stillbirth. Many women start pregnancy with low iron stores. Infants of iron-depleted mothers have lower iron reserves, may develop iron deficiency earlier, and may have delayed mental and psychomotor development. The increased iron requirement during pregnancy usually cannot be covered by diet alone. Low dose iron supplements (20–40 mg/day) should optimally start before pregnancy. Breast milk iron levels are low and not increased by iron supplements after delivery, which rather serve to replenish maternal stores.

Zinc deficiency is common in developing countries, especially with parasitic infections. Zinc deficiency may cause malformations, growth retardation, and increased infant mortality. Zinc supplements during pregnancy are vital in populations at risk.

Calcium. The calcium transfer from the mother to the fetus is facilitated by calcium-regulating hormones, while the calcium levels in maternal serum and bone are protected. Calcium loss from bone occurs in breastfeeding mothers, regardless of dietary intake, and is reversed after weaning. Dairy products are good calcium sources. Alternatively, calcium supplements may be taken during pregnancy and lactation.

Vitamin D is required for absorption and utilization of calcium. Low serum 25-OH vitamin D levels are common in temperate climates, especially in winter and spring, but occur also in geographic locations with more sunshine where conventions do not allow sun exposure. Low fetal vitamin D stores can have long-term consequences for bone mineral content. In countries without vitamin D fortification of dairy products, pregnant women should receive vitamin D supplements at least during the winter, e.g. 5 μg/day [13].

Vitamin B12. A low vitamin B12 status is prevalent not only in strict vegetarians, but also in lacto-ovo-vegetarians, and even in those with habitually low meat consumption. A low supply increases the risk of abortions, preeclampsia and preterm delivery.

Vitamin B6 and Riboflavin. The vitamin B6 and riboflavin status of pregnant and lactating mothers is also critically reduced in many poor areas of the world.

Fat-Soluble Vitamins and Docosahexaenoic Acid. The concentrations of B vitamins, fat-soluble vitamins (A, D, E, K), and the long-chain polyunsaturated fatty acid docosahexaenoic acid in breast milk are dependent on maternal stores [11]. Women should have a regular dietary supply of these nutrients already in pregnancy, which continues in lactation (e.g. at least 200 mg/day of docosahexaenoic acid) [14].

Screening of all pregnant women for the risk of micronutrient deficiencies and provision of individually tailored advice is time-consuming and costly, indicators of micronutrient status in pregnancy are not easy to interpret, and some interventions may come too late to affect outcome, e.g. folic acid supplementation should start before conception for optimal prevention of neural tube defects.

Information and Education at the population level may achieve some effects and should be implemented starting from school age, but food fortification programs are more effective in achieving enhanced nutrient supplies on a population level. Most women who plan to become pregnant or are pregnant will benefit from supplements containing multiple micronutrients at adequate dosages.

Conclusions

- Weight gain should be monitored longitudinally on a graph according to prepregnancy BMI, and energy intake should be adapted to achieve adequate pregnancy weight gain [15].
- Women should eat a healthy mixed diet (food pyramid, food circle). Weight-losing diets should not be applied during pregnancy.
• Pregnant women should drink plenty of water.
• Aerobic, but not exhausting exercise is recommended during pregnancy and lactation.
• Pregnant women should be supplemented with folic acid, iodine, iron, and potentially also with other critical micronutrients, depending on individual or regional risk, in adequate dosages.
• Pregnant and lactating women should have a regular dietary supply of docosahexaenoic acid (on average at least 200 mg/day), which can be achieved by 1–2 meals of ocean fish per week, including fatty fish, or by use of enriched foods/supplements.
• Pregnant and lactating women should not consume alcohol and illicit drugs, should not smoke, and limit caffeine intake.
• Pregnant women should not consume raw or undercooked eggs and unpasteurized milk products. Meat and poultry should be thoroughly cooked, and fruits and vegetables should be washed before consumption.

References
Introduction

When the word vegetarian (from ‘vegetus’, meaning ‘lively’ or ‘vigorous’) was minted, halfway the 19th century, it included a diet with eggs and milk [1].

Vegetarianism is strongly linked to sociocultural traditions and religious, philosophical beliefs. In Buddhism and Hinduism it is practiced by some and for Seventh-Day Adventists it is part of daily routine. Followers of macrobiotics, transcendental meditation and anthroposophy all adhere to some form of a vegetarian diet. Environmental awareness about the negative ecological impact of meat and poultry production may lead to total abstinence from these products, while others only want to consume meat from ‘free range’ animals [1, 2]. Fear to contract bovine spongiform encephalopathy motivates avoidance of bovine meat products [3]. Approximately 2.5% of adults in the United States and 4% of adults in Canada follow vegetarian diets [4]. The wide spectrum of vegetarian diets ranges from avoidance of red meat only (‘semi-vegetarianism’) to that of all animal foods (‘vegans’). Halfway through the spectrum are ‘lacto-vegetarians’ and ‘lacto-ovo-vegetarians’, who also consume diary products or dairy products and eggs, respectively.

Clearly, the health consequences of vegetarian diets vary, depending on the dietary pattern followed. Children are at greater risk of nutritional deficiencies if very restricted vegetarian diets are followed. When joined with other dietary restrictions such as avoidance of vitamin and mineral supplements, objecting to food fortification or only consumption of ‘organic’ foods, growth and health risks are likely to increase. The long-term health benefits of vegetarian diets include reduced prevalences of hypertension, type-2 diabetes, and reduced mortality from ischemic heart disease [4, 5].
Vegetarian diets for children need to support normal growth, development and health, and to cover dietary reference intakes. Overall, nutritional needs can be covered, but within a narrower margin than with a non-vegetarian (omnivorous) diet [2, 3]. Dieticians and food scientists consider vegetarian diets a viable alternative to an omnivorous diet if well devised [4, 5]. Vegetarian diets can even offer a number of nutritional benefits, including lower levels of saturated fat, cholesterol, and animal protein as well as higher levels of carbohydrates, fiber, magnesium, potassium, folate, and antioxidants such as vitamins C and E and phytochemicals [4]. Infants and children on very restricted vegetarian diets, like macrobiotic diets, are at increased risk of nutrient deficiency and insufficient growth [4, 6, 7]. Exclusive breastfeeding by vegetarian mothers consuming well-balanced diets is sufficient for normal growth and development during the first 6 months of life. Problems arise when the vegetarian diet of the mother during pregnancy and lactation and that for the child during the weaning period and thereafter is very restricted [3, 4]. If no food of animal origin is consumed at all, as is the case for all vegans, the risk of specific nutrient deficiencies increases markedly.

Risk of Nutrient Deficiency

This applies to all nutrients that are: (1) exclusively found in foods of animal origin; (2) only in relative small quantities present in the vegan diet, and (3) poorly absorbed in the gut because of high oxalate or phytate content of the vegetarian diet. Health risks further increase if the practice of avoiding all animal products is coupled with an unwillingness to seek professional dietary advice and to accept supplementation or food fortification.

Vitamin B_{12} supplementation is already needed for all infants of marginally vitamin B_{12}-deficient vegan mothers because of the low vitamin B_{12} content of the breast milk. These infants start life with low stores of vitamin B_{12} and are at risk of developing vitamin B_{12} deficiency already early in childhood, which may result in permanent neurological damage before megaloblastic anemia develops [8]. Vitamin B_{12} supplementation or food fortification is indicated for all infants, children, adolescents and adults on a vegan or macrobiotic diet [4, 6, 7].

Vitamin D supplementation for fully breastfed infants of vegetarian mothers is only needed in case of limited exposure to sunlight, similar to infants of non-vegetarian mothers. Lacto- and lacto-ovo-vegetarian children consume sufficient vitamin D-fortified cow's milk [3]. Vitamin D supplementation is needed for all vegan children with inadequate exposure to sunlight.

Calcium intake of lacto- and lacto-ovo-vegetarian children is usually adequate [9]. This is generally not the case in children on vegan or macrobiotic diets. For those, very high intakes of calcium, rich green leafy vegetables and nuts will be needed. More effective is the use of calcium-fortified foods like soy products [3, 4]. Since intestinal calcium absorption is dependent on vitamin D, an adequate vitamin D intake may partly offset a low calcium content of the diet [3].

Iron deficiency is by far the most common micronutrient deficiency in children, more so in vegetarian and especially in vegan children, since the latter do not consume any heme iron from meat, poultry or fish [2, 3]. Iron availability from plant sources is much lower because of the presence of fiber, phytates, tannins and other phenols [2, 10, 11]. Iron absorption is enhanced by the presence of organic acids like ascorbic and citric acid. The risk of iron deficiency can be lessened by using plant food with a high iron content or iron-fortified food products, e.g. breakfast cereal [1–4].

Zinc deficiency is one of the least known dangers of vegetarian diets [2]. Food from animal sources contains zinc but does not contain zinc absorption-inhibiting factors such as phytate and...
oxalate compounds that are found in plant food [10, 11]. Like iron, zinc is amply present and bioavailable in red meat. Human milk contains zinc in bioavailable form, but children older than 7 months need some form of zinc supplement or fortified food [3]. Macrobiotics and vegans have a higher risk of zinc deficiency [2].

Conclusions

• A prerequisite for optimal growth, development and health is a vegetarian diet that has a sound dietetic basis and covers dietary reference intakes

• Vitamin B<sub>12</sub> supplementation or food fortification is indicated for all infants, children, adolescents and adults on a vegan or macrobiotic diet

• Vitamin D supplementation is needed for all vegan or macrobiotic children with inadequate exposure to sunlight

• Iron deficiency is more likely to occur in macrobiotic and vegan children

• Zinc deficiency is one of the least known dangers of vegetarian diets

References

3 Nutritional Challenges in Special Conditions and Diseases

3.1 Primary and Secondary Undernutrition

Kraisid Tontisirin · Lalita Bhattacharjee

Key Words
- Undernutrition · Infection · Feeding, infant and young child · Community · Integrated approach

Key Messages
- Undernutrition poses serious threats to children’s health
- Undernutrition exists in both poor and affluent societies
- Maternal, infant and young child feeding are important components of the essential care package
- Family and community orientation services should be provided at health centers
- Facilitating the delivery of health services at subnational levels and empowering the family and community are sustainable approaches to prevent and control undernutrition

Introduction

Nutrition plays a vital role in maintaining good health, and undernutrition generates vulnerability to a wide range of diseases and general ill health [1, 2]. Undernutrition diminishes the ability of all systems of the body to perform properly, with particular grave consequences in young children. Alongside the devastating effects on health and wellbeing due to undernutrition in developing countries, the rapid changes in diet and lifestyle – ‘nutrition transition’ – have resulted in escalating numbers of overweight and obese individuals with increased risks of chronic non-communicable diseases such as hypertension, heart disease and diabetes. The double burden of malnutrition, as it is called, is found to coexist within communities and even within households [3, 4]. For the purpose of this chapter, undernutrition refers to any physical condition implying ill health or the inability to maintain adequate growth, appropriate body weight and body composition, or to sustain acceptable levels of economically necessary and socially desirable physical activities brought about by an inadequacy in food, both in quantity and in quality. This chapter provides an understanding of primary and secondary undernutrition in that it must be viewed not only as a major factor in the causation of disease but also in exacerbating the disease situation which poses threats to children’s health. It suggests a strategic community-based approach towards addressing primary and secondary undernutrition, and provides practical examples of food-based nutrition actions for implementation in the developing world.
Definitions and Need to Assess the Extent of the Problem

Primary undernutrition is the outcome of insufficient food caused primarily by an inadequate intake of dietary or food energy whether or not any specific nutrient deficiency is present. Undernutrition is also defined as a dietary energy intake below the minimum requirement level to maintain the balance between energy intake and energy expenditure. Primary undernutrition, also referred to as protein-energy malnutrition (PEM), increases vulnerability to infectious diseases since energy, protein, and certain vitamins and minerals play crucial roles in immune function. In environmental contexts in which infectious diseases (especially diarrheal disease and respiratory tract infections) are common, the combination of PEM and infection can provoke a rapid deterioration of health that can even lead to death. Secondary undernutrition is due to secondary causes that limit an adequate supply of nutrients to the body. These include disorders that affect gastrointestinal function, wasting disorders and conditions that increase metabolic demands such as infections, hyperthyroidism, other endocrine disorders, burns, trauma, surgery, and other critical illnesses and conditions. The causes of primary and secondary undernutrition are multidimensional and synergistic, with inadequate food availability being the primary, and inadequate utilization of the food consumed the secondary factor [5]. Examples from Bangladesh and China show that even in food-secure or high-income households, some members may be undernourished while others may be overweight, suggesting that both situations may be seen within the same household [6]. Outside the critical period of childbirth, while undernutrition is a major cause of child death, a large proportion of child deaths are also related to infectious diseases. The WHO estimates that children under 5 years account for 90% of these deaths. A large proportion (60%) of these deaths are related to communicable and vaccine-preventable diseases. Although the reported coverage rates for most vaccines included in the WHO’s expanded program on immunization range from 67 to 99% in southeast Asian countries, in reality vaccination coverage rates are much lower [7].

Maternal Undernutrition

Maternal undernutrition, both acute and chronic, in the pre-pregnant and pregnant state is closely implicated in the etiology of PEM. Maternal undernutrition, which is often manifested as chronic energy deficiency, threatens health and survival because it increases mother’s susceptibility to life-threatening diseases and increases their risk of dying during child birth. Maternal mortality rates in developing countries such as south Asia are among the highest in the world [8]. Most mothers with chronic energy deficiency are likely to give birth to low birthweight babies (<2.5 kg).

Infant and Young Child Feeding

The importance of breast milk as the best and only food for infants up to about 6 months of age is universally recognized. At the policy level, the promotion and protection of and support for universal breastfeeding is reinforced by the Code of Marketing of Breast-Milk Substitutes. From 6 months, adequate complementary feeding should be given, while breastfeeding is continued to maintain normal growth rates [9]. The composition of the complementary food mix is therefore critical as it must be adequate in energy, protein and micronutrients and be given frequently enough to meet the nutrient needs of the infant. Several countries have undertaken the development of complementary feeding guidelines. Table 1 illustrates complementary feeding guidelines which could be integrated as part of an over-
all strategy to increase household food security and nutrition [10]. The rationale for the selection of complementary foods is based on the knowledge of what is culturally acceptable, foods that are locally available, and foods that can be made more readily available through promoting food production at the community level.

**Family and Community Orientation**

Family and community orientation services should be provided at health centers. Health professionals, particularly at sub-national levels (district) should plan and work in collaboration with the community to implement these services. As part of the planning process, the health services delivery personnel (at district/sub-national level) can act as facilitators in coordination with the community leaders (village level). The health professionals and the community leaders will need to set realistic goals collectively and develop workable plans for the prevention and control of undernutrition (PEM). A comprehensive health services package integrating many elements of health, nutrition, food production (in the case of subsistence farmer households and others), education and community development should be made available through the center to enable mothers and communities to support their children’s optimal nutrition [11]. Training of the community leaders and volunteers and support of district level leadership would need to be an ongoing part of the process [12].

The fact that undernutrition is understood to have many causes should not inhibit practical and appropriate actions. Rather, this understanding should promote a better awareness of sectoral opportunities that need to be availed of to overcome undernutrition. Health professionals at all levels should use information derived from their understanding more effectively in a timely manner. It should be used at the level where information is generated, particularly when the people who collect the data are best able to use it. This will link progressively decentralized decision-making by health professionals and communities. Health professionals would need to facilitate

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**Table 1. Suggested complementary feeding guidelines (adapted from Thailand complementary feeding guidelines)**

<table>
<thead>
<tr>
<th>Age</th>
<th>Feeding Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–6 months</td>
<td>Exclusive breastfeeding</td>
</tr>
<tr>
<td>6 months</td>
<td>Begin with rice gruel, ripe banana; add egg yolk, chicken liver or legumes, fish and dark green leafy vegetables or pumpkin or carrots</td>
</tr>
<tr>
<td>7 months</td>
<td>Add ground meat including chicken, whole egg, well-cooked soft fish (as appropriate), and other fruits like ripe papaya and mango, progressing slowly until the child takes one complete meal</td>
</tr>
<tr>
<td>8–9 months</td>
<td>Give 2 complete meals</td>
</tr>
<tr>
<td>10–12 months</td>
<td>Give 3 complete meals</td>
</tr>
</tbody>
</table>

**Table 2. Systematic approach to integrate primary healthcare in the prevention and control of undernutrition**

<table>
<thead>
<tr>
<th>First contact</th>
</tr>
</thead>
<tbody>
<tr>
<td>History and physical examination</td>
</tr>
<tr>
<td>Growth assessment</td>
</tr>
<tr>
<td>Assessment of the undernutrition problem</td>
</tr>
<tr>
<td>Initiation of health and nutrition education</td>
</tr>
<tr>
<td>Treatment/care plan</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Subsequent contact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth monitoring and promotion activities</td>
</tr>
<tr>
<td>Breastfeeding</td>
</tr>
<tr>
<td>Complementary feeding</td>
</tr>
<tr>
<td>Health and nutrition education</td>
</tr>
<tr>
<td>Immunization</td>
</tr>
<tr>
<td>Treatment of infection</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Family and community orientation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health professionals need to integrate health, nutrition and education modules and resources to prevent and control undernutrition</td>
</tr>
</tbody>
</table>
and provide the delivery of necessary and immediate medical services to the child and family and also specifically serve to involve the individual and family through a process of empowerment in undernutrition prevention and control strategies [13, 14]. This is but a systematic approach to integrate primary healthcare principles in the prevention and control of undernutrition (table 2).

**Conclusions**

- Prevention and control of undernutrition must entail a comprehensive approach and need to be undertaken by health and related professionals at individual and community levels

- Programs should be designed to strengthen the interface between service delivery and the community by creating a demand for the services

- Community leaders, through the community infrastructure, will need to organize mechanisms to identify and select community volunteers or ‘mobilizers’ who can actually provide the health services package at the community or household level

- A community-based approach can lead to improved outreach and coverage of services and will lead to an improvement in child health and nutrition on a sustainable basis

**References**

Micronutrients (vitamins and minerals) are essential for human health, growth, and development. Humans evolved as hunter-gatherers, expending large amounts of energy to obtain sustenance from wild plants and hunted game. The evolutionary complementary feeding of infants involved pre-masticated meat. As such, humans evolved consuming large amounts of a micronutrient-rich food. The advent of the agricultural era placed reliance on nutrients primarily on a narrow selection of grains and tubers, exposing humankind to the risk of vitamin and mineral deficiencies. Table 1 illustrates the various mechanisms that can contribute to nutrient deficiencies [1].

The Clinical Contexts of Micronutrient Deficiencies

The various contexts within which micronutrient deficiencies can occur are outlined in Table 2 [2]. Among the vitamins, deficiencies of vitamins A, D, C, B₆, B₁₂, thiamin, riboflavin, niacin, and folic acid can be encountered in free-living children in a public health context as a result of social or environmental adversity or abuse. Similarly, nutritional deficiencies of phosphorus, magnesium, iron, zinc, iodine, fluorine and selenium can occur in sectors of a free-living public. In a public health sense, deficiencies of micronutrients have recently been termed ‘hidden hunger’ because the nutrients responsible for the deficiency cannot be seen in the foods, and one might be consuming sufficient total energy and macronutrients, and still suffer a vitamin or mineral deficit [3].

Clinical deficiencies of vitamins E and K, pantothenic acid and biotin among vitamins, and
calcium, copper, selenium, molybdenum, chromium and manganese among minerals, have been documented only with severe disorders in pathophysiology or due to iatrogenic factors, or in some cases, with controlled experimental depletion in adult volunteers. The deficiencies of this group of nutrients do not represent a public health concern.

Specific Nutrient Deficiencies of Public Health Importance, Afflicting Those Consuming Poor Diets and under Environmental Stress

A selected cluster of six micronutrients merit in-depth mention and consideration as their prevention, mitigation, and therapy can represent a public health challenge.

Iron Deficiency and Iron Deficiency Anemia
Iron is the most important and challenging of the public health micronutrient deficiencies. It is estimated that from 2 to 5 billion of the world’s 6 billion inhabitants are iron-deficient, and from one third to one sixth of these have microcytic, hypochromic anemia attributable to iron deficiency. Iron deficiency has a series of functional consequences as outlined in table 3. These are common to the condition, whether or not it is associated with anemia. Hence, iron deficiency disorders can take a devastating toll on the fitness of both individuals and the communities of which they are a part [4].

Among the risk factors for iron deficiency are: reliance on iron-poor foods such as milk and dairy products (including human milk), rice, fruits, and fleshy vegetables; reliance on foods of low iron bioavailability, and blood-feeding parasites [5]. Iron deficiency is common in infants, in the second semester of infancy as well as in adolescence, due to rapid growth in boys and to the onset of menarche in girls.

The mechanisms of host defense against infection exclude iron from cells and sequester the
Iron Deficiency and Other Nutrient Deficiencies

Iron Deficiency
Iron deficiency is a common problem, affecting over 2 billion people worldwide. It is caused by a lack of dietary iron or poor absorption of iron, often leading to anemia. Iron is essential for the production of hemoglobin, which carries oxygen throughout the body. Iron deficiency can affect children, causing developmental delays and decreased learning capacity. In adults, it can lead to fatigue, weakness, and compromised immune function.

Micronutrient Deficiencies
Micronutrients are essential for normal growth, development, and maintenance of health. Deficiencies in these nutrients can lead to serious health consequences. Some common micronutrient deficiencies include:

1. **Iron Deficiency**
   - Iron is a crucial component of hemoglobin, which transports oxygen in the blood.
   - Deficiency can cause anemia, fatigue, and compromised immune function.

2. **Iodine Deficiency**
   - Iodine deficiency is common in areas with soil that is low in iodine.
   - It can lead to goiter, thyroid disorder, and decreased intelligence in children.

3. **Zinc Deficiency**
   - Zinc is involved in many processes, including growth and immune function.
   - Deficiency can lead to impaired immune function and growth retardation.

4. **Vitamin A Deficiency**
   - Vitamin A is essential for vision, immune function, and skin health.
   - Deficiency causes night blindness and xerophthalmia (dry eyes).

5. **Vitamin B12 Deficiency**
   - Vitamin B12 is crucial for cell growth and DNA synthesis.
   - Deficiency can lead to pernicious anemia and neurological damage.

6. **Riboflavin Deficiency**
   - Riboflavin is involved in energy metabolism and growth.
   - Deficiency causes fatigue, irritability, and growth retardation.

7. **Other Micronutrient Deficiencies**
   - Other deficiencies include vitamin D, vitamin C, and selenium, each critical for different body functions.

Addressing Micronutrient Deficiencies
Addressing micronutrient deficiencies requires a multifaceted approach, including dietary interventions, fortification of food products, and public health strategies. Increased awareness and education about the importance of micronutrients can also play a significant role in preventing deficiencies. Preventive interventions are crucial to ensure optimal health outcomes, especially in vulnerable populations such as children and pregnant women.
Reduced childhood micronutrient deficiencies have been recorded in children raised in cults with unorthodox vegetarian dietary practices.

**Chronic Clinical Disorders and Micronutrient Deficiencies**

Table 4 summarizes selected clinical disorders contributing to micronutrient deficiency. A series of nutrients that are wasted in the urine, including vitamin A and trace elements, will be lost in excess with systemic inflammatory responses, as seen in AIDS, tuberculosis, malaria and systemic parasitoses. Urinary nutrient wasting also occurs in certain renal diseases in which the glomeruli become porous, tubular reabsorption is impaired, or both.

The essential purpose of the alimentary tract is to obtain nutrients; therefore any digestive or absorptive disorders will compromise nutrient uptake [12]. Virtually all vitamins and minerals can be adversely affected by small bowel diseases. Blood loss leading to iron deficiency is common in inflammatory bowel disorders. Neuromuscular disorders interfere with proper chewing and swallowing, often limiting the quantity and variety of dietary intake.

Diabetes mellitus is associated with deficiency of a number of minerals. Magnesium, calcium and phosphorus can be wasted in chronic renal disease, as well as all water-soluble vitamins; fat-soluble vitamin levels in the circulation are frequently elevated. Chronic hemo- and peritoneal dialysis generally progressively deplete vitamins.

Acrodermatitis enteropathica and Menkes disease represent examples of congenital illnesses that affect the cellular transporters for zinc and copper, respectively. This results in total body depletion of zinc and the manifestations of severe zinc deficiency. The defect of copper transport in Menkes disease is not only in the gut but throughout the body, generating profound signs of copper depletion through impaired utilization of the metal.

**Iatrogenic Causes of Micronutrient Deficiencies**

Prescriptions and practices of clinical practitioners can contribute iatrogenic causes of micronutrient deficiencies. Improper formulation of infant formula, enteral feedings and parenteral infusions has produced deficiencies of vitamin E, zinc, copper, selenium, molybdenum and chromium, as well as chloride [13, 14]. A variant of this mechanism is the addition of a medication to a formula that destroys or inactivates a nutrient. Prolonged use of antibiotics, purging the intestinal flora, has contributed to vitamin K and biotin deficiency. Other medications interfere with the absorption or utilization of one or another micronutrient. Sulfasalazine, for example, interferes

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**Table 4.** Selection of chronic diseases of childhood frequently associated with micronutrient deficiency states

<table>
<thead>
<tr>
<th>Systemic diseases</th>
<th>Severe chronic diseases (tuberculosis, HIV/AIDS, malaria)</th>
<th>Rheumatoid arthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal diseases</td>
<td>Inflammatory bowel disease (Crohn’s disease, ulcerative colitis)</td>
<td>Small bowel disease (short bowel syndrome, celiac disease)</td>
</tr>
<tr>
<td>Neurological diseases</td>
<td>Neuromuscular disorders (cerebral palsy, muscular dystrophy)</td>
<td></td>
</tr>
<tr>
<td>Endocrinological disease</td>
<td>Diabetes mellitus</td>
<td></td>
</tr>
<tr>
<td>Renal disease</td>
<td>Chronic renal disease (glomerulonephritis, extracorporeal dialysis)</td>
<td></td>
</tr>
<tr>
<td>Congenital disorders</td>
<td>Acrodermatitis enteropathica</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Menkes disease</td>
<td></td>
</tr>
</tbody>
</table>

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with folate absorption and metabolism. Antacids and acid-blocking drugs create pH and secretory conditions in the stomach and upper intestine. The roster of drug–nutrient interactions compromising micronutrient malnutrition is exhaustive, and cannot be covered in full here.

Conclusions

- Children commonly develop overt deficiencies of only certain vitamins (A, D, C, B<sub>6</sub>, B<sub>12</sub>, thiamin, riboflavin, niacin, folic acid) and minerals (phosphorus, magnesium, iron, zinc, iodine, fluorine and selenium)
- The practitioner must know the signs and symptoms and appropriate interpretation of hematological, biochemical and functional indices of vitamin and mineral deficiencies
- The appropriate prescription of the deficient nutrient, combined with attention to the underlying cause(s) of deficiency, should restore an adequate state of micronutrient nutrition

References

1 Herbert V: The five possible causes of all nutrient deficiencies, as illustrated by deficiencies of vitamin B<sub>12</sub> and folate. Am J Clin Nutr 1973;26:77–88.
**Introduction**

Enteral nutrition (EN) is defined as oral feeding using special formulae, or tube feeding directly into stomach, duodenum or jejunum. In general, it should be introduced in a child who has a sufficient level of gastrointestinal function preserved, but is unable to meet energy and nutrient requirements by a normal oral diet. When compared to parenteral feeding, EN has numerous advantages such as preservation of gastrointestinal function, lower costs, better manageability and increased safety. EN should be considered when one or more of the factors presented in table 1 are identified [1]. Various clinical indications are listed in table 2.

There are only a few absolute contraindications for EN such as necrotizing enterocolitis, intestinal perforation, gastrointestinal obstruction, and severe/septic intra-abdominal infection.

When the clinical condition of the patient is stable, home EN should be considered [2]. Although a dedicated team approach is required whenever EN is provided [3], it is particularly important to teach parents and children the techniques required for EN before being discharged, such as nasogastric (NG) tube placement and maintenance, sterile feed preparation and administration, enteral pump management, and prevention, recognition and management of the most common complications.

Transition to normal oral feeds needs to be gradual, and EN can be stopped when oral intake satisfies caloric and nutrient requirements, while growth continues to be age appropriate.

**Enteral Formula Properties and Selection Criteria**

Enteral formulas differ in the source and content of nutrients, caloric density, osmolality, and cost [4]. At standard dilution, the energy content of infant formula is 0.67 kcal/ml and that of standard pediatric enteral feed is 1 kcal/ml. More concentrated enteral formulas are also available (1.3–2.0 kcal/ml) for patients with increased energy requirements or limited fluid intake. With regard to carbohydrates, maltodextrin and hy-
Dextrylized cornstarch or corn syrup are commonly used, while proteins mostly originate from cow’s milk (casein or whey) or soybeans. Lipids are administered predominantly as long-chain fatty acid based triglycerides (LCTs), or mixed with medium-chain fatty acid triglycerides (MCTs). When compared with LCTs, MCTs are rapidly hydrolyzed and absorbed directly into the portal circulation, even at low concentrations of pancreatic enzymes and bile acids. However, the energy content is lower, osmolality is higher, and they contain no essential fatty acids (EFAs). MCT-based enteral formulas include up to 50% of EFA-rich LCTs. A standard pediatric formula contains 40–55% of energy from carbohydrates, 10–15% from proteins, and 30–40% from lipids, and the majority of them are free of gluten and lactose. Polymeric formulas provide intact proteins. If proteins are hydrolyzed to an extent that can be tolerated by at least 90% of patients with verified allergy to the nitrogen source, the formula is called semi-elemental or oligomeric [5]. Monomeric/elemental formulas are nutritionally complete solutions containing amino acids, oligosaccharides, and fats as a mixture of LCTs and MCTs. A comparison of different types of formulas is presented in table 3.

In enteral formula selection, the following factors should be considered: (a) nutrients and energy requirements adjusted to the age and clinical condition of the patient; (b) history of food intolerances or allergy; (c) level of intestinal function; (d) site and route of formula delivery; (e) formula characteristics such as osmolality,
viscosity and nutrient density; (f) taste preference, and (g) cost. There are many specialized and disease-specific formulas, but for the great majority of pediatric patients, standard polymeric formula is sufficient and well tolerated, with the best cost-benefit ratio.

**Administration of EN**

**Sites of Delivery**

EN can be administered either into the stomach or into the proximal small intestine depending on: (a) gut status; (b) expected duration of EN, and (c) anticipated risk for aspiration. Among the two sites, intragastric feeding is associated with a more flexible feeding schedule, larger volume and higher osmotic tolerance, lower frequency of diarrhea and of dumping syndrome due to: (a) stimulation of normal digestive and hormonal responses; (b) antimicrobial properties; (c) tubes are more easily placed, and (d) the stomach serves as a reservoir gradually releasing nutrients. However, if there is acute pancreatitis or a high risk for aspiration, intrajejunal feeding is the preferred method. Transpyloric (intrajejunal) feeding should never be provided as an intermittent (bolus) feeding but always as a continuous feeding.

**Routes of Delivery**

If the expected duration of EN is short (<6–8 weeks), it is preferentially delivered by NG or nasoenteric tube, but if the expected duration is longer, a feeding gastrojejunoscopy is recommended, which is placed by endoscopy as the quickest and cheapest procedure with a low rate of complications [6, 7]. Among the different tubes, those made of polyvinyl chloride (PVC) are the least desirable because of the possible release of potentially toxic phthalate esters into the lipid-containing feeds, and if left in place for >4 days they may become rigid and cause lesions of the upper gastrointestinal tract [8]. Silicon and polyurethane tubes are more convenient, and can be safely kept in place for several weeks. Considering the required length of the NG tube, it should equal the distance between nose and the umbilicus. Placement into the stomach is confirmed by epigastric auscultation during injection of air, accompanied by measuring the pH of the aspirate which should be below 4. However, radiologic confirmation must be obtained when: (a) the pH of aspirate is >5; (b) an aspirate cannot be obtained, and (c) the patient’s condition changes during NG tube insertion with prolonged coughing, restlessness and discomfort or hoarseness [9].

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**Table 3. Comparison of different enteral formulas**

<table>
<thead>
<tr>
<th></th>
<th>Polymeric formulas</th>
<th>Oligomeric formulas</th>
<th>Monomeric formulas</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Protein content, g/l</strong></td>
<td>30–80</td>
<td>20–50</td>
<td>19.5–25</td>
</tr>
<tr>
<td><strong>Nitrogen source</strong></td>
<td>Polypeptides</td>
<td>Small peptides</td>
<td>Amino acids</td>
</tr>
<tr>
<td><strong>Carbohydrate content, g/l</strong></td>
<td>90–200</td>
<td>100–200</td>
<td>81–146</td>
</tr>
<tr>
<td><strong>Fat content, g/l</strong></td>
<td>20–90</td>
<td>5–20</td>
<td>35</td>
</tr>
<tr>
<td><strong>Caloric density, kcal/ml</strong></td>
<td>1–2</td>
<td>1–1.7</td>
<td>0.67–1</td>
</tr>
<tr>
<td><strong>Osmolarity, mosm/l</strong></td>
<td>300</td>
<td>300–500</td>
<td>300–600</td>
</tr>
<tr>
<td><strong>Advantages</strong></td>
<td>Palatable, cheap</td>
<td>Hypoallergenic, easily absorbed</td>
<td>Non-allergenic, immunomodulatory</td>
</tr>
<tr>
<td><strong>Disadvantages</strong></td>
<td>Requires intact gut, allergenic</td>
<td>Bitter taste, expensive</td>
<td>Hyperosmolar, expensive</td>
</tr>
</tbody>
</table>

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Modes to Deliver EN

EN delivery modes are intermittent, continuous and combined. Intermittent (bolus) delivery is physiologically more adequate, but in patients with a very impaired gut, continuous feeding is beneficial due to the lower thermogenic effect and improved substrate utility. An appropriate and constant flow can be ensured by using a peristaltic enteral pump. When the child can eat, both methods of feed delivery can be combined, with tube feeding overnight for 10–12 h and oral intake during the day. This combination preserves sensory and motor oral functions.

Initiation of EN

Initiation of EN should be gradual, depending on: (a) age; (b) clinical condition and gut status; (c) formula choice (polymeric versus elemental), and (d) route of delivery (stomach versus jejunum). A slow stepwise increase in volume and concentration is particularly important for patients with grossly impaired intestinal function.

Monitoring and Complications

Patients receiving EN should be monitored regularly for growth, fluid, energy and nutrient intake, therapeutic efficacy, and blood and biochemical changes.

Possible complications and preventive measures are listed in Table 4. Their occurrence can be minimized by: (a) avoidance of drip feeding and blenderized feeds; (b) using silicon and polyurethane NG tubes; (c) gradual initiation and stepwise increase in volume and concentration; (d) regular monitoring of residual gastric volumes; (e) strict adherence to management protocols, and (f) close supervision by a dedicated multidisciplinary team [3, 10].

Despite the broad range of potential complications, EN is a well-established, safe and effective method of improving a patient’s clinical condition, nutritional status and growth, particularly if procedural protocols are followed, and regular quality control is applied [11].

<table>
<thead>
<tr>
<th>Complications</th>
<th>Prevention and treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td>Formula selection</td>
</tr>
<tr>
<td>Diarrhea, nausea, vomiting, bloating, abdominal distension</td>
<td>Polymeric vs. pre-digested</td>
</tr>
<tr>
<td>Technical</td>
<td>Disease specific</td>
</tr>
<tr>
<td>Occlusion, migration</td>
<td>Feeding techniques</td>
</tr>
<tr>
<td>Metabolic</td>
<td>Bolus vs. continuous</td>
</tr>
<tr>
<td>Fluid, glucose and electrolyte imbalance</td>
<td>Gradual initiation of EN</td>
</tr>
<tr>
<td>Infective</td>
<td>EN administration</td>
</tr>
<tr>
<td>Gastroenteritis, septicemia</td>
<td>Delivery site (stomach vs. jejunum)</td>
</tr>
<tr>
<td>Psychological</td>
<td>Delivery route (tube vs. stoma)</td>
</tr>
<tr>
<td>Oral aversion, altered body self-image</td>
<td>Monitoring</td>
</tr>
<tr>
<td>Formula selection</td>
<td>Growth (weight, height/length, skinfolds)</td>
</tr>
<tr>
<td>Polymeric vs. pre-digested</td>
<td>Hematology, biochemistry</td>
</tr>
<tr>
<td>Disease specific</td>
<td>Multidisciplinary team approach</td>
</tr>
<tr>
<td>Feeding techniques</td>
<td>Protocol application and quality control</td>
</tr>
<tr>
<td>Bolus vs. continuous</td>
<td>Others</td>
</tr>
<tr>
<td>Gradual initiation of EN</td>
<td>Tube selection (PVC vs. silicon), maintenance</td>
</tr>
</tbody>
</table>

Table 4. Enteral feeding complications and preventive and therapeutic measures [12]
Conclusions

- Enteral nutrition is a safe and effective method of nutritional therapy
- Enteral nutrition should be used when oral feeds cannot sustain normal growth in a child with a reasonably preserved gastrointestinal function
- Selection of enteral formula depends on the age and clinical condition, but for the majority of patients a standard polymeric formula is the appropriate choice, with the best cost-benefit ratio
- Technical, metabolic, gastrointestinal, infectious and psychological complications may occur; close monitoring by a multidisciplinary team, application of procedural protocols, and regular quality control are therefore required

References

Introduction

Parenteral nutrition is generally indicated when adequate nutrition cannot be provided orally or enterally, to prevent or correct malnutrition, and to sustain appropriate growth. It should be avoided whenever possible through adequate care, specialized enteral nutrition and artificial feeding devices as appropriate, because parenteral nutrition is more costly and carries greater risks than oral or enteral nutrition. Parenteral feeding is not indicated in patients with adequate small intestine function in whom oral tube or gastrostomy feeding can be used. Exactly when parenteral nutrition should be initiated depends both on individual circumstances and the patient’s age and size. In small preterm infants, starvation for just 1 day may be detrimental, and parenteral feeding must be instituted shortly after birth if it is obvious that enteral nutrition will not be tolerated soon. In older children and adolescents, longer periods of inadequate nutrition (up to 7 days) may be tolerated, depending on the disease, age and nutritional status of the patient, and type of intervention (surgery or medical). Whenever possible, parenteral nutrition should be combined with some (at least minimal) enteral nutrition. Establishing a multidisciplinary pediatric nutrition support team for supervision of parenteral nutrition can improve the quality of care and save costs, hence it is highly recommended [1]. Ordering and monitoring parenteral nutrition should follow agreed algorithms to improve quality of care. Patients should be evaluated 2–3 times/week, e.g. clinical examination, weight, anthropometry, laboratory values, dietary intake as appropriate. The recommendations provided here are based on the evidence-based Guidelines for Pediatric Parenteral Nutrition [2]. Recommendations on parenteral substrate supply to stable patients are summarized in table 1.
Fluid needs vary markedly and must be adapted to the individual patient’s condition. For example, some renal or cardiac disorders require lower water intakes, whereas higher intakes are needed with enhanced fluid losses (fever, hyper-ventilation, diarrhea or enhanced losses from wounds or fistulae). Monitoring fluid status is necessary, as well as clinical status, body weight, and possibly water intake and excretion, blood electrolytes, acid base status, hematocrit, urine-

### Table 1. Recommended usual dosages for parenteral substrate supply to stable patients by age

<table>
<thead>
<tr>
<th>Age group</th>
<th>Water ml/kg</th>
<th>Energy kcal/kg</th>
<th>Amino acids g/kg</th>
<th>Glucose g/kg</th>
<th>Lipids, g triglycerides/kg</th>
<th>Sodium mmol/kg</th>
<th>Potassium mmol/kg</th>
<th>Calcium mmol/kg</th>
<th>Phosphorus mmol/kg</th>
<th>Magnesium mmol/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm</td>
<td>140–160</td>
<td>110–120</td>
<td>1.5–4</td>
<td>18</td>
<td>up to 3–4</td>
<td>2–5</td>
<td>2–5</td>
<td>2–5</td>
<td>0–6 months</td>
<td>0.5</td>
</tr>
<tr>
<td>Neonate (1st month)</td>
<td>140–160</td>
<td>90–100</td>
<td>1.5–3</td>
<td>18</td>
<td>up to 3–4</td>
<td>2–3</td>
<td>1–3</td>
<td>2–3</td>
<td>7–12 months</td>
<td>0.2</td>
</tr>
<tr>
<td>0–1 years</td>
<td>120–150</td>
<td>90–100</td>
<td>1–2.5</td>
<td>16–18</td>
<td>up to 3–4</td>
<td>2–3</td>
<td>1–3</td>
<td>2–3</td>
<td>0–6 months</td>
<td>0.2</td>
</tr>
<tr>
<td>1–2 years</td>
<td>80–120</td>
<td>75–90</td>
<td>1–2</td>
<td>1–3</td>
<td>up to 2–3</td>
<td>1–3</td>
<td>1–3</td>
<td>1–3</td>
<td>7–12 months</td>
<td>0.2</td>
</tr>
<tr>
<td>3–6 years</td>
<td>80–100</td>
<td>75–90</td>
<td>1–2</td>
<td>1–3</td>
<td>up to 2–3</td>
<td>1–3</td>
<td>1–3</td>
<td>1–3</td>
<td>0–6 months</td>
<td>0.2</td>
</tr>
<tr>
<td>7–12 years</td>
<td>60–80</td>
<td>60–75</td>
<td>1–2</td>
<td>1–3</td>
<td>up to 2–3</td>
<td>1–3</td>
<td>1–3</td>
<td>1–3</td>
<td>0–6 months</td>
<td>0.2</td>
</tr>
<tr>
<td>13–18 years</td>
<td>50–70</td>
<td>30–60</td>
<td>1–2</td>
<td>1–3</td>
<td>up to 2–3</td>
<td>1–3</td>
<td>1–3</td>
<td>1–3</td>
<td>0–6 months</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Depending on the condition and individual needs of the patient, different dosages may be required. Adapted from Koletzko et al. [2]. Reproduced with kind permission from Wolters Kluwer. K⁺ supplementation should usually start after onset of diuresis. Chloride supply usually equals the sum of sodium and potassium supply.

### Table 2. Recommended standard parenteral fluid supply (ml)

<table>
<thead>
<tr>
<th>Time after birth, days</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Term neonate</td>
<td>60–120</td>
<td>80–120</td>
<td>100–130</td>
<td>120–150</td>
<td>140–160</td>
<td>140–180</td>
</tr>
<tr>
<td>Preterm neonate</td>
<td>60–80</td>
<td>80–100</td>
<td>100–120</td>
<td>120–150</td>
<td>140–160</td>
<td>140–180</td>
</tr>
<tr>
<td>&gt;1,500 g</td>
<td>60–80</td>
<td>80–100</td>
<td>100–120</td>
<td>120–150</td>
<td>140–160</td>
<td>140–180</td>
</tr>
<tr>
<td>&lt;1,500 g</td>
<td>80–90</td>
<td>100–110</td>
<td>120–130</td>
<td>130–150</td>
<td>140–160</td>
<td>160–180</td>
</tr>
</tbody>
</table>

In neonates, parenteral fluid supply should be gradually increased over the first days of life. Adapted from Koletzko et al. [2]. Reproduced with kind permission from Wolters Kluwer.

### Table 3. Suggested increase in intravenous glucose supply (g/kg/day) over the first 4 days of parenteral nutrition

<table>
<thead>
<tr>
<th>Child’s weight, kg</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3</td>
<td>10</td>
<td>14</td>
<td>16</td>
<td>18</td>
</tr>
<tr>
<td>3–10</td>
<td>8</td>
<td>12</td>
<td>14</td>
<td>16–18</td>
</tr>
<tr>
<td>10–15</td>
<td>6</td>
<td>8</td>
<td>10</td>
<td>12–14</td>
</tr>
<tr>
<td>15–20</td>
<td>4</td>
<td>6</td>
<td>8</td>
<td>10–12</td>
</tr>
<tr>
<td>20–30</td>
<td>4</td>
<td>6</td>
<td>8</td>
<td>&lt;12</td>
</tr>
<tr>
<td>&gt;30</td>
<td>3</td>
<td>5</td>
<td>8</td>
<td>&lt;10</td>
</tr>
</tbody>
</table>

Adapted from Koletzko et al. [2]. Reproduced with kind permission from Wolters Kluwer.

### Water

Fluid needs vary markedly and must be adapted to the individual patient’s condition. For example, some renal or cardiac disorders require lower water intakes, whereas higher intakes are needed with enhanced fluid losses (fever, hyper-ventilation, diarrhea or enhanced losses from wounds or fistulae). Monitoring fluid status is necessary, as well as clinical status, body weight, and possibly water intake and excretion, blood electrolytes, acid base status, hematocrit, urine-
specific gravity and urine electrolytes. Postnatal fluid supply should be gradually increased (table 2).

**Energy**

Energy needs vary with physical activity, growth and the possible need to correct malnutrition. Energy supply can be adjusted based on formulae for energy expenditure (see Chapter 1.3.2) and during weight changes. Low energy supplies induce failure to thrive, but excessive energy intake (‘hyperalimentation’) must be avoided because it may induce metabolic imbalances, liver damage and, in malnutrition, re-feeding syndrome [3].

**Amino Acids**

Parenteral amino acid requirements are lower than enteral needs because parenteral nutrition bypasses intestinal amino acid uptake and utilization. Amino acid utilization requires an energy supply of ≈30–40 kcal per g of amino acids. In neonates requiring parenteral feeding, amino acid supply should start on the first postnatal day. Infants and young children should receive pediatric amino acid solutions with adequate amounts of cysteine, taurine and tyrosine (conditionally essential; see Chapter 1.3.3).

**Glucose**

Glucose is the only carbohydrate recommended for parenteral nutrition and should provide 60–75% of non-protein calorie intake. During the first days on parenteral feed, the glucose supply should be gradually increased (table 3). In pre-term infants glucose intake should begin with 4–8 mg/kg per min (5.8–11.5 g/kg per day) and increase gradually. In critically ill children glucose intake should be ≤5 mg/kg per min (7.2 g/kg per day). Glucose infusion for term neonates and children ≤2 years should not exceed 13 mg/kg per min (18 g/kg per day). Glucose intake should be adapted to the administration of drugs that impair glucose metabolism (e.g. steroids, somatostatin analogues, tacrolimus). Very high glucose intakes and marked hyperglycemia should be avoided because they may induce increased lipogenesis and tissue fat deposition, liver steatosis, enhanced CO2 production, impaired protein metabolism, and possibly increased infection-related morbidity and mortality [2]. In critically ill and unstable patients, glucose dosage should be lower and increased only according to the patient’s condition and blood glucose levels.

**Lipids**

Lipid emulsions supply essential fatty acids and energy at iso-osmolarity. Lipids should generally provide 25–40% of non-protein parenteral nutrition calories. Parenteral lipid intake is usually limited to 0.13–0.17 g/kg per h (3–4 g/kg per day) in infants and 0.08–0.13 g/kg per h (2–3 g/kg per day) in children. A stepwise increase in lipid infusion rates by 0.5–1 g/kg per day has not been shown to improve tolerance but allows monitoring for hypertriglyceridemia. Regular plasma triglyceride measurements are recommended during parenteral feeding, particularly in critically ill or infected patients. Dosage reduction should be considered at triglyceride concentrations during infusion >250 mg/dl in infants or >400 mg/dl in children, but a minimum linoleic acid intake to prevent essential fatty acid deficiency should always be given (preterm infants ≥0.25 g linoleic acid/kg per day, term infants/children ≥0.1 g/kg per day). In neonates requiring parenteral nutrition, lipids can start on day 1 of life and should start no later than day 3. In young infants, lipids should be administered continuously over about 24 h.

During phototherapy validated light-protected tubing for lipid emulsions is recommended to
decrease hydroperoxide formation. Lipid emulsions have no demonstrable effect on hyperbilirubinemia. There is no firm evidence on adverse effects in severe acute respiratory failure, but avoiding high lipid dosages in these patients appears prudent. In severe, progressive parenteral nutrition-associated cholestasis, a decrease or transient interruption of intravenous lipids should be considered [2].

Commercial lipid emulsions based on soybean oil, or mixtures of olive and soybean oil, or of medium-chain triglycerides and soybean oil are considered safe for pediatric parenteral feeding [2].

Other Aspects

Vitamins and minerals should be supplied with all parenteral nutrition provided over several days. Cyclical parenteral feeding (over 8–14 h/day) should be considered from the age of 3–6 months onwards [2, 4].

Individualized prescriptions of pediatric parenteral nutrition are widely used, but standard solutions are suitable for many pediatric patients with adequate monitoring and the possible addition of electrolytes/nutrients. Standard solutions can improve the quality and safety of parenteral feeding and reduce costs.

The risks of parenteral nutrition are best reduced by limiting the amount and duration [2, 5]. Persistent attempts should be made to increase the amount of enteral feedings as tolerated. Rather than enteral starvation, minimal enteral feeds should be given whenever possible, and an experienced pediatrician and an experienced dietician should be involved.

Conclusions

Parenteral Nutrition

- is an essential and often life-saving treatment for infants and children who cannot be adequately fed orally or enterally
- should only be used when all alternative options have been explored, including adequate care, specialized enteral nutrition and artificial feeding devices
- can induce severe adverse effects. The risk is reduced by a meticulous approach, establishment of a multidisciplinary nutrition support team, avoidance of unbalanced or excessive substrate supplies, strict hygiene measures to reduce catheter infections, concomitant minimal enteral feeding and forceful enhancement of enteral feeding where possible to limit the amount and duration of parenteral feeding

References

Introduction

The prevalence of obesity has been increasing during the last two decades in almost all countries (high and low income). Early treatment is required due to the adverse consequences of obesity, such as impaired glucose tolerance and diabetes, cardiovascular disease and hypertension, orthopedic disease and cancer.

Obesity develops during periods of positive energy balance resulting from an inadequately low regular physical activity and an inadequately high calorie intake. The fat and water contents of foods are the main determinants of the energy density of the diet. A lower consumption of energy-dense foods (i.e. high fat, high sugar and high starch) and energy-dense drinks (i.e. sugared drinks) contributes to a reduction in total energy intake. Conversely, a higher intake of energy-diluted food (e.g. vegetables and fruit), high in non-starch polysaccharides (e.g. wholegrain cereals) contributes to a reduction in total energy intake and can also improve micronutrient supplies.

The eating and physical activity behaviors of an individual child are strongly influenced by environmental and social factors. Therefore, the recommendations given here will only have limited success in an environment in which adequate physical activity is not supported and the consumption of high energy food is stimulated.

Treatment of obesity in children can be performed with behavioral-based training programs aiming at increasing physical activity and moderating energy intake. Such a program should last at least 6, better 12 months since changes in eating and physical activity behavior take time and need to be stabilized. A variety of professionals can accomplish many aspects of a training program: nurses, nurse practitioners, nutritionists, physicians, psychologists, and social workers.
The inclusion of parents and other persons of the closer social environment is important for the long-term results of such a program. Programs can be performed in groups with 10 or 12 members. However, additional individualized counseling is often required.

At the beginning of a training program, a dietary protocol can be helpful in describing the individual’s dietary intake, including the situations in which meals are consumed. Furthermore, a dietary protocol written during the training program may help to document the achieved goals and changes in dietary behavior. Modification of dietary intake and behavior should be performed in small steps which are achievable by the child and his/her parents. Regular contact of the parent and child with the trainer is essential to review and reinforce the previous goals of a healthy diet and activity as well as implementation of skills. It is important to include behavior therapy in the treatment of childhood obesity. The addition of behavioral techniques of contingency contracting, self-monitoring of caloric intake and weight, praise and stimulus control to nutrition education significantly improves the treatment results [1].

Obesity is a chronic disease requiring life-long attention to healthy eating and an active lifestyle. After an initial weight management program both the child and parents must continue to work actively to maintain behaviors.

Training programs for a parent or an adolescent who is not ready to change should be avoided since they may not only be futile but also harmful, because an unsuccessful program may diminish the child’s self-esteem and impair future efforts to improve weight.

The dietary goals for parents and their families are well-balanced, healthy meals and a healthy approach to eating. These changes should be considered permanent rather than a temporary eating plan for rapid weight loss. In the following paragraphs special dietary aspects and recommendations [2–4] are summarized.

**Fat Intake**

Excessive consumption of fat is believed to be a causative factor for weight gain. Furthermore, the adverse effects of saturated fat on the risk of cardiovascular disease are well documented. Diets with limited fat content (no more than 30%) are helpful for weight management.

**Intake of Carbohydrates**

A decrease in dietary fat will be accompanied by a compensatory increase in carbohydrate consumption. This may occur especially in the form of refined foods (e.g. breads, ready-to-eat cereals, soft drinks, cakes, and others). Such eating behavior might even increase body weight. By contrast, the majority of studies show that a high intake of non-starch polysaccharides (dietary fiber) promotes weight loss. A weight-stimulating effect of an increased consumption of sugar-sweetened soft drinks is well documented [5]. Furthermore, a decrease in the consumption of sugar-sweetened soft drinks leads to relative weight loss.

**Energy Density**

The consumption of a diet with high energy density may promote body weight gain [2]. Therefore, energy density is a critical factor determining energy intake.

**Portion Size**

Older children (after infancy) are less responsive to internal hunger and satiety cues and more reactive to environmental stimuli. Therefore, portion size is a critical factor determining energy intake.
The rising consumption of fast food in developed and developing nations might have particular relevance to the childhood obesity epidemic. This association might be due to the fact that fast food typically has a high glycemic index and a high energy density and is served in large portion sizes. Additionally, these foods tend to be low in fiber, micronutrients and antioxidants [2].

Parent–child interaction and the home environment can affect behaviors related to body weight development. Social support from parents and others correlate strongly with the participation in physical activity and healthy dietary behaviors. Access and exposure to a range of fruits and vegetables at home is important for the development of preferences for these foods.

### Fast Food

The rising consumption of fast food in developed and developing nations might have particular relevance to the childhood obesity epidemic. This association might be due to the fact that fast food typically has a high glycemic index and a high energy density and is served in large portion sizes. Additionally, these foods tend to be low in fiber, micronutrients and antioxidants [2].

### Family Factors

Parent–child interaction and the home environment can affect behaviors related to body weight development. Social support from parents and others correlate strongly with the participation in physical activity and healthy dietary behaviors. Access and exposure to a range of fruits and vegetables at home is important for the development of preferences for these foods.
School Environment

School environment is important and influences nutrition knowledge, eating patterns and physical activity behavior as well as sedentary behaviors. School-based programs for weight control can be effective [6].

Recommendations for nutrition in infants, children, adolescents, and families are given in table 1. Moreover, daily physical activity should be emphasized, aiming at a moderate physical activity of at least 1 h/day. Sedentary behaviors should be limited, with no more than about 1 h/day of video screen/television time. The placement of television sets in children’s rooms/bedrooms should be discouraged.

Conclusions

- Treatment of obesity in children can be performed on the basis of a behavioral-based training program aiming at increasing physical activity and improving energy intake in order to achieve long-term weight maintenance and allowing adequate nutrition for growth and development
- The inclusion of parents is important for the long-term results
- Successful dietary measures are: reducing the intake of energy-dense food and food with added sugars, as well as increasing the intake of food with high fiber content
- Eating and physical activity behavior of an individual child is strongly influenced by environmental and social factors. Therefore, treatment will have only limited success in an environment where adequate physical activity is inhibited and the consumption of high energy food is stimulated

References

Despite major advances, diarrheal disorders still kill 1.8 million children worldwide, mostly in developing countries. We have the know how and the interventions that can make a difference provided they are made available to all children in need.

Introduction

Despite considerable advances in the understanding and management of diarrheal disorders in childhood, they are still globally responsible for a major number of childhood deaths, estimated at 1.8 million deaths [1, 2]. While the global mortality for diarrhea has been reduced, the incidence remains unchanged at about 3.2 episodes per child year [3]. Young children, especially if malnourished and immunocompromised, are at greatest risk for more severe disease and complications.

Most diarrheal disorders form a continuum, with the majority of cases resolving within the first week of the illness and more severe acute episodes leading to child deaths [4]. A smaller proportion of diarrheal illnesses fail to resolve and persist for longer than 2 weeks [5]. These episodes of persistent diarrhea (PD) have been defined as episodes that began acutely but lasted for at least 14 days [6] and have been shown to identify children with a substantially increased diarrheal burden and between 36 and 54% of all diarrhea-related deaths [7].

Globally, infections represent the most important cause of acute diarrhea in children. Although poverty, poor water and sanitation represent fundamental risks, immediate risk factors for diarrhea include low birthweight, failure to breastfeed, inappropriate complementary foods and associated micronutrient deficiencies (especially vitamin A and zinc) [8]. The major pathogens causing acute diarrhea are detailed in table 1 and the common clinical syndromes associated with pathogens causing diarrhea are listed in table 2.

It is also important to highlight that in addition to the large proportion of acute diarrhea episodes that relate to rotavirus diarrhea, it is estimated that almost a quarter of all diarrhea deaths may be associated with dysentery, and a large proportion caused by Shigella organisms [9, 10]. Additional factors underlying the increased propensity to infection and poor intestinal repair
may include key micronutrient deficiencies that may influence this process. These may include both zinc and multiple micronutrient deficiencies [11]. These findings clearly have enormous implications for the preventive and therapeutic approaches to diarrhea.

**Prevention of Diarrhea**

Of various interventions that can prevent diarrhea among children in the developing world, provision of safe water and hygiene interventions are critical. It has been estimated that combined hand washing promotion, provision of safe water and sanitation interventions can lead to an at least 33% reduction in diarrhea (RR = 0.67; 95% CI 0.59, 0.76) [8, 11].

Other preventive interventions include exclusive breastfeeding and safe complementary feeding strategies to prevent diarrhea. Early and unhygienic introduction of milk other than breast milk and recurrent acute diarrheal episodes that are poorly managed are important predisposing factors to the development of PD, and it is important that these are prevented. Thus, in populations at risk, the promotion of early and exclusive breastfeeding for at least 6 months, avoidance of formula feeding, timely and adequate weaning with hygienic nutritious foods will help to prevent episodes of diarrhea. A combination of allocation of appropriate resources for public health and basic needs, staff training and community mobilization is necessary to reduce the global burden of diarrhea.

In recent years the development and availability of effective rotavirus vaccines offer a unique opportunity for reducing the burden and severity of diarrhea [12] with a protective efficacy approaching 80% for severe acute dehydrating diarrhea requiring hospitalization.

**Management of Acute and Persistent Diarrhea**

Oral rehydration therapy is the mainstay in the treatment of diarrheal episodes, and in recent years low osmolality oral rehydration solution has been recommended for rehydration [13]. In

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**Table 1. Infectious agents causing diarrhea in children**

<table>
<thead>
<tr>
<th>Bacteria producing inflammatory diarrhea</th>
<th>Bacteria producing non-inflammatory diarrhea</th>
<th>Viruses</th>
<th>Parasites</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Clostridium perfringens</em></td>
<td>Enteropathogenic <em>Escherichia coli</em></td>
<td>Astrovirus</td>
<td><em>Balantidium coli</em></td>
</tr>
<tr>
<td><em>Clostridium difficile</em></td>
<td><em>Vibrio cholerae</em> 01 and 0139</td>
<td>Enteric adenovirus</td>
<td><em>Cryptosporidium parvum</em></td>
</tr>
<tr>
<td>Enteroinvasive <em>E. coli</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Yersinia enterocolitica</em></td>
<td></td>
<td></td>
<td><em>Encephalitozoon intestinalis</em></td>
</tr>
<tr>
<td><em>Plesiomonas shigelloides</em></td>
<td>Enterotoxigenic <em>E. coli</em></td>
<td>Calicivirus</td>
<td><em>Entamoeba histolytica</em></td>
</tr>
<tr>
<td><em>Campylobacter jejuni</em></td>
<td></td>
<td>Rotavirus</td>
<td><em>Enterocytozoon bieneusi</em></td>
</tr>
<tr>
<td><em>Vibrio parahaemolyticus</em></td>
<td><em>Staphylococcus aureus</em></td>
<td>Cytomegalovirus</td>
<td><em>Giardia lamblia</em></td>
</tr>
<tr>
<td><em>Aeromonas</em></td>
<td><em>V. parahaemolyticus</em></td>
<td></td>
<td><em>Isospora belli</em></td>
</tr>
<tr>
<td><em>Shigella</em></td>
<td>Enterotoxigenic <em>E. coli</em></td>
<td></td>
<td><em>Strongyloides stercoralis</em></td>
</tr>
<tr>
<td><em>E. coli</em> 0157:H7</td>
<td></td>
<td>Herpes simplex virus</td>
<td><em>Trichuris trichiura</em></td>
</tr>
<tr>
<td><em>Salmonella</em></td>
<td></td>
<td>Norwalk agent-like virus</td>
<td></td>
</tr>
</tbody>
</table>
addition, the use of zinc supplements (10–20 mg/day for 10–14 days) is recommended as the mainstay in the treatment of acute diarrheal episodes [14]. In addition to these measures, continued appropriate enteral feeding of these children during diarrheal episodes accelerates clinical recovery from diarrhea. A proportion of cases who fail to respond adequately and continue to purge must be triaged for immediate assessment and appropriate therapy. It must be underscored that the most important factor for the prevention of prolonged episodes of diarrhea is the appropriate recognition and management of acute diarrheal episodes.

The management of PD in malnourished children is based on the principles of management of diarrhea and malnutrition. While a subgroup may be severely malnourished requiring rapid nutritional rehabilitation, often in hospital, in other cases ambulatory management may be possible. Given the long time it may take to recovery, prolonged hospitalization may be quite problematic in developing countries and, whenever possible, ambulatory or home-based therapy using culturally acceptable diets must be stressed [15].

The following represent the basic principles in the prevention and management of PD and a sug-
The suggested therapeutic approach is summarized in Figure 1.

**Initial Resuscitation and Stabilization**
Most children with PD and associated malnutrition are not severely dehydrated and oral rehydration with low osmolality oral rehydration solution may be adequate. However, acute exacerbations and associated vomiting may require brief periods of intravenous rehydration with Ringer’s lactate. Acute electrolyte imbalance, such as hypokalemia, and severe acidosis require correction. More importantly, associated systemic infections have been recognized in severely malnourished children with PD and must be screened for at admission and rapidly treated. In severely ill malnourished children requiring hospitalization, broad-spectrum antibiotics at initial admission and stabilization may be empirically started while awaiting cultures, but prolonged courses of antibiotics exceeding 7 days must be avoided.

**Enteral Feeding and Diet Selection**
Given that PD only rarely occurs in breastfed infants, any amount of breastfeeding must be continued, even in HIV-affected populations [16]. Despite mucosal abnormalities and diminution in digestive and absorptive mechanisms, most children with PD have adequate absorption...
capacity and tolerate enteral feeding. In general, therefore, withdrawal of milk and replacement with specialized (and expensive) lactose-free formulations is unnecessary. Most children with PD are not lactose-intolerant, but some reduction in lactose load to under 5 g/kg/day may be prudent [15]. Alternative strategies for reducing the lactose load in malnourished children with PD include addition of milk to cereals as well as replacement of milk with fermented milk products such as yogurt.

In rare instances when dietary intolerance precludes the administration of cow’s milk-based formulations or milk, it may be necessary to administer specialized milk-free diets such as a comminuted or blenderized chicken-based diet or an elemental formulation. The usual energy density of any diet used for the therapy of PD should be around 1 kcal/g, aiming to provide an energy intake of minimum 100 kcal/kg/day, and a protein intake of between 2 and 3 g/kg/day. The commonly used rice-lentil formulations in South Asia such as khitchri provide this energy density in combination with an optimal protein intake and amino acid ratio [17].

**Micronutrient Supplementation**
Most malnourished children with PD have associated deficiencies of micronutrients including zinc, iron and vitamin A. This may be a consequence of poor intake and continued enteral losses, and while the evidence supporting zinc administration in children with PD is persuasive, it is likely that these children have multiple micronutrient deficiencies. This may be of particular relevance in HIV endemic subjects. It is therefore important to ensure that all children with PD and malnutrition receive an initial dose of 100,000 units vitamin A and a daily intake of at least 3–5 mg/kg/day of elemental zinc. It is now recommended that all children with diarrhea receive a daily dose of 20 mg zinc for 10–14 days.

**Follow-Up and Continued Nutritional Rehabilitation in Community Settings**
Given the high rates of relapse in most children with PD and the association with severe acute malnutrition, it is important to address the underlying risk factors and institute preventive measures. These include appropriate feeding (breastfeeding, complementary feeding) and close attention to environmental hygiene and sanitation. This poses a considerable challenge in communities deprived of basic necessities such as clean water and sewage disposal in which recurrence of diarrhea is a distinct possibility.

In addition to the preventive aspects, the challenge in most settings is to develop and sustain a form of dietary therapy using inexpensive, home-available and culturally acceptable ingredients which can be used to manage children with PD. Given that the majority of cases of PD occur in the community and that parents are frequently hesitant to seek institutional help, there is a need to develop and implement inexpensive and practical home-based therapeutic measures. Available evidence indicates that it may be entirely feasible to do so in community settings using either home-available foods or inexpensive locally prepared ready-to-use therapeutic formulations [18].

Providing essential preventive and therapeutic interventions to reduce childhood diarrhea in health systems is necessary in order to achieve the millennium development goals of reducing child mortality by two thirds by the year 2015. Early and unhygienic introduction of milk other than breast milk and recurrent acute diarrheal episodes that are poorly managed are important predisposing factors in the development of prolonged diarrhea and must be prevented. These risk factors are generally prevalent in poor communities, and both poverty alleviation and social sector support mechanisms are fundamentally important. A combination of allocation of appropriate resources for public health and basic needs, staff training and community mobilization is
necessary to reduce the global burden of diarrhea. In many parts of the developing world it is important that these strategies are coupled with efforts to address the underlying social determinants of disease, poverty alleviation and an equity focus on addressing maternal and child health. In poor communities and health systems with limited resources, the following preventive strategies need to be introduced at scale:

1. Promotion of early initiation and exclusive breastfeeding for at least 6 months.
2. Promotion of safe water, hygiene and hand washing at the household level.
3. Adequate sanitation and waste disposal strategies [19].
4. Timely and adequate weaning with hygienic nutritious foods.
5. Prompt care seeking for diarrheal episodes and standard case management with low osmolality oral rehydration solution, zinc and adequate dietary therapy.
6. Vaccination strategies with measles and rotavirus vaccine.

Conclusions

- Despite vast advances in our understanding of the etiology and pathogenesis of diarrhea, acute and persistent diarrhea is still responsible for about 1.8 million child deaths annually.
- The preventive strategies for acute and persistent diarrhea are well recognized and include, for populations at risk, exclusive breastfeeding for the first 6 months, followed by appropriate complementary feeding strategies.
- Recent advances in the management of diarrhea, including the use of reduced osmolality oral rehydration solution and zinc supplements and appropriate use of antibiotics for bacterial diarrhea when needed, may significantly improve diarrhea outcomes and must be made available universally.
- Rotavirus vaccination strategies offer a unique opportunity to considerably reduce severe acute diarrhea-related morbidity and mortality.

References


3.7 HIV and AIDS

Haroon Saloojee · Peter Cooper

Key Words
HIV · AIDS · Nutrition · Feeding · Breastfeeding · Replacement feeding · Complementary feeding · Malnutrition · Micronutrients

Key Messages
- HIV infection has greater nutritional consequences for children compared to adults, simply because children have the additional nutritional demands of growth and development
- Balancing the risks of HIV transmission through breastfeeding with the risks of not breastfeeding in settings where access to safe replacement foods, healthcare and support are limited is one of the most difficult issues facing HIV-affected families
- When replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breastfeeding by HIV-infected mothers is recommended. Otherwise, exclusive breastfeeding is recommended during the first 6 months of life
- Micronutrient deficiencies are common in HIV-infected children, accelerating progression of HIV disease, which in turn leads to worsened nutritional status
- Antiretroviral (HAART) therapy is associated with improvements in weight, weight-for-height, mid-arm circumference and lean body mass in HIV-infected children

Introduction

Infants born to HIV-positive women have lower birthweights related to a lower gestational age, high viral loads and the effect of HIV on the mother herself [1].

Transmission through breastfeeding may account for up to half of the HIV infections in infants and young children (over 300,000 infections annually). The rate of HIV infection in breastfed infants is cumulative and roughly constant throughout the breastfeeding period. The overall risk of breastfeeding transmission is estimated as 8.9 transmissions/100 child years of breastfeeding (or about 0.74% per month of breastfeeding) [2].

The risk of transmission of HIV through breastfeeding varies in relation to maternal clinical and immunological status, plasma and breast milk viral load and possibly breast health (subclinical or clinical mastitis, cracked nipples, etc.) [3].

Feeding recommendations for infants of HIV-infected mothers in resource-poor settings remain controversial. The most appropriate infant feeding option continues to depend on the mother’s individual circumstances, including her health status and the local situation.

HIV infection in children can lead to poor weight gain, failure to thrive, slowed linear
growth (stunting) and wasting through decreased nutrient intake, gastrointestinal malabsorption, increased utilization, tissue catabolism and psychosocial factors (such as an unstable home environment). Higher viral load has been associated with a greater risk of growth failure.

Micronutrient deficiencies (such as vitamin A, selenium and zinc) are common and may accelerate progression of HIV disease, which in turn leads to worsened nutritional status.

Children with HIV and AIDS require high-energy, nutrient-dense diets and may require up to 200% of the recommended daily allowance. There are insufficient data to support a routine increase in protein intake. Fat requirements are unchanged.

**Feeding the HIV-Exposed Infant**

The current WHO recommendations on infant feeding by HIV-infected mothers state: ‘When replacement feeding is acceptable, feasible, affordable, sustainable and safe (“AFASS”), avoidance of all breastfeeding by HIV-infected mothers is recommended’ [4]. Otherwise, exclusive breastfeeding is recommended during the first 6 months of life. To minimize HIV transmission risk, breastfeeding should be discontinued as soon as feasible, taking into account local circumstances, the individual woman’s situation and the risks of replacement feeding (including infections other than HIV and malnutrition). Table 1 provides guidance on how this decision may be made.

Exclusive breastfeeding means giving a child no other food or drink, including water, in addition to breastfeeding with the exception of medicines, vitamin drops or syrups and mineral supplements. Replacement feeding means giving an infant who is not receiving any breast milk a nutritionally adequate diet until the age at which the child can be fully fed on family foods. WHO/UNAIDS/UNICEF recommend several variations of exclusive breastfeeding and replacement milk for infants of HIV-infected mothers (table 2).

**Breastfeeding**

Strategies which should be employed to minimize the risk of transmission during breastfeeding are outlined in table 3.

**Replacement Feeding**

Replacement feeding requires substituting breast milk with replacement milk (i.e. infant formula) before 6 months and with solid foods after 6 months. Safely prepared exclusive commercial infant formula will meet all the nutrient needs of the HIV-exposed infant if fed in amounts calculated to meet the infant’s energy requirements. Mothers who have recently been infected, have progressed to AIDS, or whose CD4 counts are below 200/μl, should be encouraged to consider replacement feeding (to reduce the high transmission risk).

**Transition to Replacement Feeds for Infants Who Have Been Exclusively Breastfed**

Early cessation of breastfeeding means completely stopping breastfeeding before age 2 years and, ideally, among HIV-positive mothers as soon as replacement feeding is ‘AFASS’. Complementary feeding is necessary for all infants by 6 months of age. Guidelines on how to manage the transition from exclusive breastfeeding to replacement feeding are offered in table 4. At 6 months, if replacement feeding is still not ‘AFASS’, continuation of breastfeeding with additional complementary foods is recommended. Well-chosen complementary foods, such as fresh orange juice, potatoes, dark green vegetables and meats, should supplement the nutrients that replacement milk does not adequately provide.

**Other Measures**

Adequately heat-treated, expressed milk of HIV-positive mothers does not transmit HIV and re-
### Table 1. Considerations for deciding on the most feasible infant feeding option for HIV-positive mothers

<table>
<thead>
<tr>
<th>Most feasible option</th>
<th>Breastfeeding/wet-nursing</th>
<th>unclear</th>
<th>replacement feeding or expressed, heat-treated breast milk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drinking-water supply</td>
<td>River, stream, pond, or well</td>
<td>Public standpipe</td>
<td>Piped water at home or ability to purchase clean water</td>
</tr>
<tr>
<td>Latrine</td>
<td>None or pit latrine</td>
<td>VIP latrine</td>
<td>Waterborne latrine</td>
</tr>
<tr>
<td>Income</td>
<td>Less than USD 15 available for formula each month</td>
<td>USD 15 available for formula most months</td>
<td>USD 15 available for formula every month (unless using expressed breast milk)</td>
</tr>
<tr>
<td>Food storage</td>
<td>No refrigerator or regular electricity supply available</td>
<td>Access to refrigerator with regular electricity supply, but not at home</td>
<td>Refrigerator at home with regular electricity supply</td>
</tr>
<tr>
<td>Preparation and fuel</td>
<td>Inability to boil water and utensils for every feed</td>
<td>Ability to boil water for every feed but with effort</td>
<td>Ability to boil water for every feed</td>
</tr>
<tr>
<td>Ability to prepare night feeds</td>
<td>Preparation of replacement feeds at night possible but with effort</td>
<td>Preparation of replacement feeds at night possible</td>
<td></td>
</tr>
<tr>
<td>Family and community support</td>
<td>Breastfeeding expected, and family unaware of HIV status</td>
<td>Replacement feeding acceptable, but family unaware of HIV status; or breastfeeding expected, but family aware of HIV status and willing to help with feeding</td>
<td>Family aware of HIV status and willing to help with feeding</td>
</tr>
</tbody>
</table>

From WHO, UNICEF, UNAIDS, UNFPA [5].

### Table 2. WHO/UNAIDS/UNICEF [6] feeding options for infants of HIV-infected mothers

<table>
<thead>
<tr>
<th>Breast milk</th>
<th>Replacement milks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exclusive breastfeeding by the mother for 6 months and continuing until age 2 years, or as long as mother chooses exclusive breastfeeding by the mother with early cessation, with rapid weaning to replacement milk as early as feasible Breast milk expression with heat treatment; expressed milk fed via cup Wet-nursing by an HIV-uninfected mother</td>
<td>Commercial infant formula, prepared according to manufacturer's directions Fresh full cream milk; with added water, sugar, and micronutrients; boiled before use Evaporated full cream milk or powdered full cream milk; with added water, sugar, and micronutrients</td>
</tr>
</tbody>
</table>

All feeding options recommend introduction of complementary foods at 6 months of age.
Table 3. Strategies to minimize the risk of HIV transmission during breastfeeding

<table>
<thead>
<tr>
<th>Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Practice exclusive breastfeeding – ideally for 6 months</td>
</tr>
<tr>
<td>Stop breastfeeding as soon as replacement feeding is acceptable, feasible, affordable, sustainable and safe – preferably no later than 6 months</td>
</tr>
<tr>
<td>Good lactation management (early initiation, attachment, positioning, frequent feeds, learning to express) can prevent breastfeeding problems such as cracked nipples, engorgement and mastitis</td>
</tr>
<tr>
<td>When cracked or bleeding nipples, mastitis or abscesses do develop, continue feeding from the unaffected side, and regularly express milk from the affected side and discard it</td>
</tr>
<tr>
<td>Condoms must be used during sexual intercourse throughout the lactation period</td>
</tr>
<tr>
<td>Oral thrush or mouth ulcers in the infant should be promptly treated</td>
</tr>
<tr>
<td>Expressed breast milk can be heat treated; for instance, during periods of increased risk of transmission secondary to cracked nipples, or during transition from exclusive breast to replacement feeding</td>
</tr>
</tbody>
</table>

Table 4. Advice for mothers on how to manage the transition from exclusive breastfeeding to replacement feeding

<table>
<thead>
<tr>
<th>Advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allow the infant to adjust to the new feeding pattern over a period of 2 days to 2 weeks</td>
</tr>
<tr>
<td>Accustom the infant to cup feeding by introducing expressed breast milk by cup. One strategy to help the baby adapt to cup feeding is to offer expressed breast milk by cup between regular breastfeeds</td>
</tr>
<tr>
<td>Eliminate one breastfeed at a time once the infant accepts cup feeding and replace with expressed breast milk given by cup</td>
</tr>
<tr>
<td>Express breast milk and discard it if the breasts become engorged during this process. Cold compresses may reduce inflammation due to engorgement</td>
</tr>
<tr>
<td>Avoid reinitiating breastfeeding after completing the transition to replacement feeding. Resist the desire to breastfeed at night or when the child wants comforting</td>
</tr>
<tr>
<td>If it is necessary to offer breast milk after replacement feeds have commenced ensure that the milk is heat-treated and given by cup</td>
</tr>
</tbody>
</table>

Feeding the HIV-Infected Child

At their first contact with a healthcare professional, all children with HIV should have their anthropometric status (e.g. weight, height, head circumference and arm circumference) measured, and should be screened for nutritional problems. In addition, a 24-hour recall or diet record should be obtained and compared with estimated needs to assess adequacy of intake. Follow-up assessment should be conducted every 1–6 months, depending on the child’s age, identified concerns, and nutritional status.

Nutritional therapy is best given orally. Since it is difficult to calculate the precise caloric needs of an HIV-infected child, the energy intakes for HIV-infected children experiencing weight loss need to be increased by 50–100% over established requirements for otherwise healthy uninfected

...
children [8]. The formula volume should be increased as much as can be tolerated. If the child is eating solids, adding a high-fat supplement such as oil or margarine may be helpful. Commercial nutritional supplements are an acceptable alternative.

Enteral supplementation should be considered if the child cannot eat or absorb adequate calories orally to sustain growth. Nasogastric tube feedings should be tried first, to demonstrate the child’s ability to gain weight with supplemental enteral feedings. Additional nighttime feedings are most practical, since they allow the child to eat normally during the day. Complications include sinusitis and worsening esophageal candidiasis. Caregivers may be unable or unwilling to maintain nasogastric feeding. If nasogastric tube feedings improve growth, placement of a more permanent device, such as a gastrostomy tube, should be considered. Parenteral nutrition should be reserved for HIV-infected children who continue to lose weight on an aggressive enteral program, or for children who have persistent diarrhea with weight loss or severe recurrent or chronic pancreatic or biliary tract disease. However, central venous catheters pose their own additional risk for sepsis.

Highly Active Antiretroviral Therapy

The initiation of highly active antiretroviral therapy (HAART) is associated with improvements in many growth parameters for HIV-infected children. Immediate gains first manifest in weight and arm muscle circumference. Lean body mass improves as well, while a height response occurs more slowly. Body mass index does not increase in all children, but improvements are greatest in children with the lowest baseline body mass index and who have more advanced HIV disease. Children are not spared the metabolic effects of HAART, and they too have a significant (up to 33%) risk of lipodystrophy. No therapeutic strategies to diminish the clinical and biochemical features of the fat redistribution syndrome have been described in children.

Conclusions

• Infant feeding should be considered part of a continuum of care and support services for HIV-infected women and children
• Decisions about the optimal feeding mode for HIV-exposed infants are difficult and depend on parents’ individual choice. However, health workers can assist this decision-making by discussing safety considerations with parents
• A focus on the growth and nutrition of the HIV-infected child at each visit is warranted. An adequate diet, prevention of opportunistic infections and HAART all contribute to ensuring satisfactory growth
• There is limited evidence for routine micronutrient supplementation, other than vitamin A

Micronutrients

Micronutrient deficiencies are common in HIV-infected adults and children and may accelerate progression of HIV disease, which in turn leads to worsened nutritional status [8]. Nutritional interventions might restore intestinal absorption and increase CD4 cell numbers. Adequate micronutrient intake is best achieved through an adequate diet. Few randomized trials have examined the efficacy of direct micronutrient supplementation of children born to HIV-infected mothers. In keeping with WHO recommendations, children younger than 5 years born to HIV-infected mothers living in resource-limited settings should receive periodic (every 4–6 months) vitamin A supplements in the same dose as other children. There are no evidence-based guidelines on the appropriate prescription of micronutrient supplements for HIV-infected children.
References


### 3 Nutritional Challenges in Special Conditions and Diseases

#### 3.8 Cholestatic Liver Diseases

**Edmond Rings**

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**Key Words**

Cholestatic liver disease • Fat malabsorption • Vitamins, fat-soluble

**Key Messages**

- Cholestatic liver disease (CLD) in children negatively affects nutritional status, growth and development
- Poor dietary intake is an important factor in the pathophysiological basis of malnutrition in children with CLD
- For children with CLD, the dietary energy intake is usually increased to levels of 120–150% of the daily reference intake
- Continuous nasogastric drip-feeding may be needed in infants to guarantee optimal uptake of nutrients
- A marked reduction of bile acids in the intestinal lumen, as observed in cholestasis, reduces absorption of fat-soluble vitamins A, D, E and K, and supplements may be needed

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### Introduction

Cholestatic liver disease (CLD) in children negatively affects nutritional status, growth and development, leading to an increased risk of morbidity and mortality [1]. Nutritional strategies to optimize feeding of children with CLD are available. Patients with CLD, however, form a heterogeneous group and the clinical manifestations of their disease vary. This makes a tailor-made dietary approach for these children crucial.

Poor dietary intake is an important factor in the pathophysiological basis of malnutrition in children with CLD. Often energy expenditure is increased in these children. Their nutritional status may be further compromised by decreased absorption of macronutrients, in particular of fat. The obstruction or absence of bile ducts often observed in CLD leads to accumulation of bile acids in hepatocytes, which results in liver damage. As a result, the enterohepatic circulation of bile acids is interrupted. The resulting reduction or absence of bile acids in the intestinal lumen leads to impaired micellization and therefore to strongly reduced absorption of fats and fat-soluble nutrients [2]. At an early age, fat absorption is critical, since fat accounts for the most important dietary energy source (up to 50% of total ingested energy in milk-fed infants). Furthermore, essential fatty acids (EFAs) and long-chain polyunsaturated fatty acids (LCPUFAs) are indispensable for proper development and function of different organs. Micronutrient absorption might also be affected in CLD, including absorption of fat-soluble vitamins, A, D, E and K.

### Dietary Intake

The dietary prevention or treatment of failure to thrive during CLD involves some general principles applicable to virtually all patients, and some individual tailor-made approaches. Poor dietary intake is an important factor in the pathophysiological basis of malnutrition in children with CLD...
CLD. Reduced gastric volume as a result of organomegaly and ascites, vomiting, and hypoglycemia leads to limited absorption of the required dietary nutrients when administered in regular (bolus) feedings. Fatigue, anorexia, nausea, diarrhea, altered or reduced ability to taste, and early satiety may all contribute to decreased ingestion of food. Additionally, many diet modifications, for example sodium, fluid or protein restrictions, make food even more difficult to eat. These dietary restrictions are imposed on patients with relatively high risks on fluid overload and encephalopathy which, when left untreated, can lead to serious and often irreversible defects [3]. Under these circumstances, continuous nasogastric drip-feeding may be needed to guarantee maximal uptake of nutrients. Apart from reduced intraluminal bile acid concentrations, other consequences of CLD, such as gastrointestinal bleeding, impaired digestive enzyme production and secretion, mucosal congestion, villous atrophy, bacterial overgrowth or pancreatic insufficiency can lead to maldigestion and malabsorption of nutrients. In addition, even certain medications can aggravate malabsorption. For example, cholestyramine binds to bile acids in the intestinal lumen and thereby further reduces absorption of fat-soluble nutrients. Also, the reduced availability of specific nutrients involved in digestion and/or absorption of other nutrients, specifically vitamins and minerals, affects intestinal absorption [3].

**Macronutrients**

In CLD, the nutritional status may be further compromised by decreased absorption of macronutrients, including fat, carbohydrates and proteins [4]. For children with CLD, the dietary energy intake is usually increased to levels of 120–150% of the dietary reference intake of energy for age and gender. The adaptation of the diet involves the increment of the concentration and amount ingested. At an early age, fat accounts for the most important dietary energy source (up to 50% of total ingested energy in infants fed human milk or infant formula). EFAs and LCPUFAs are indispensable for proper development and function of different organs, for example the central nervous system. In CLD, up to 60% of the fat components, particularly long-chain triglycerides, are substituted by medium-chain triglycerides (MCTs), whose absorption can occur relatively independent of the presence of bile components in the intestinal lumen. Breastfed children receive additional formula and MCT-rich oil, while for older children feeding with formula is often prolonged and energy-rich liquids are provided. Adequate intake of EFAs and LCPUFAs is not frequently monitored in CLD patients, but strived for by providing these fatty acids in ample amounts in the diet. Nevertheless, we reported that about 70% of children with CLD requiring liver transplantation have biochemical indications of EFA and LCPUFA deficiency [5].

In children with CLD, carbohydrate homeostasis can be affected by hepatic failure itself, for example by decreased capacity of gluconeogenesis. Frequently, also peripheral utilization of glucose is reduced, which may decrease the risks of hypoglycemia. In CLD, hepatic degradation of insulin may also be decreased, which may be one of the causes for the twofold higher insulin response in CLD compared to control patients. Elevated plasma levels of insulin in combination with glucose tolerance imply insulin resistance, which could be further aggravated by increased circulating free fatty acids as seen in CLD [3]. The carbohydrate content can be increased by supplementation of formula with maltodextrin.

Addition of proteins and especially specific amino acids such as branched chain amino acids could improve the nutritional status of children with CLD [6]. However, care must be taken because an excess of protein can negatively influence encephalopathy.
Micronutrients

The absence of bile acids in the intestinal lumen as observed in cholestasis reduces absorption of fat-soluble vitamins A, D, E and K. Adequate absorption of fat-soluble vitamins during CLD can usually be obtained by profoundly increasing the daily-administered dosages, well above regular recommendations for the age groups (table 1) [7]. Serum levels of fat-soluble vitamins are regularly monitored in order to adapt dosages. Calcium uptake is at risk as a result of the formation of non-soluble calcium-fatty acid soaps during fat malabsorption. Hypovitaminosis D may increase renal loss of phosphate, and hypovitaminosis A may induce zinc deficiency. Zinc deficiency has a negative impact on cognitive function, appetite and taste, immune function, wound healing and protein metabolism. In addition, zinc deficiency has frequently been associated with essential fatty acid deficiency [8]. Finally, uptake of selenium can be disturbed due to essential fatty acid deficiency, and iron depletion is seen as a result of gastrointestinal bleeding, insufficient uptake, transport and handling of iron. In addition, liver dysfunction strongly reduces storage capacity of vitamins such as folate, riboflavin, nicotinamide, pantothenic acid, pyridoxine, vitamin B₁₂, thiamine and vitamin A. Hepatocellular injury in CLD also results in defects in vitamin activation, conversion, release and transport [3]. Addition of zinc to the diet could counteract a part of the poor dietary intake.

Conclusions

• Nutritional strategies are available to optimize feeding of children with cholestatic liver disease (CLD)
• In CLD, the nutritional status may be compromised by decreased absorption of macronutrients, including fat, carbohydrates and proteins
• Adequate absorption of fat-soluble vitamins during CLD can usually be obtained by profoundly increasing the daily-administered dosages

References

3 Malabsorptive Disorders and Short Bowel Syndrome
Olivier Goulet

Key Words
Short bowel syndrome • Intestinal adaptation • Protracted diarrhea of infancy • Parenteral nutrition • Oral feeding • Enteral feeding • Breast milk • Long-chain fat-containing formulas • Medium-chain triglycerides • Hydrolyzed protein formulas • Amino acid formulas • Small intestinal bacterial overgrowth • Feeding aversion

Key Messages
• Protracted diarrhea of infancy or short bowel syndrome require parenteral nutrition together with oral feeding or enteral feeding. The use of the gastrointestinal tract as early and as much as possible, according to clinical tolerance, should be promoted and feeding aversion prevented
• Adaptation – the physical and physiological processes by which the intestine compensates for loss of intestinal length or function – is optimized with the provision of oral feeding or enteral feeding
• Direct contact with nutrients, pancreaticobiliary secretions, and neurohormonal factors explain how the use of the gastrointestinal tract promotes adaptation. It may also contribute to prevent cholestasis and liver disease
• Intestinal microflora has both positive (short-chain fatty acid production) and deleterious effects (intraluminal bacterial overgrowth) and may be modulated in short bowel syndrome patients
• Composition of dietary intake regarding breast milk, amino acid- and long-chain fat-containing formulas remain controversial. Very few randomized trials have been performed. The routes (oral, gastric, trans-pyloric) and the modes (bolus, continuous, both) of feeding are also debated

Introduction
The so-called ‘protracted diarrhea of infancy’ (PDI), which has become a rare condition in developed countries, is caused by severe malabsorption secondary to an acquired intestinal mucosa injury due to infection, inflammation or allergic reaction. ‘Intractable diarrhea of infancy’ refers to congenital enteropathies involving the development or renewal of intestinal mucosa that lead to very long lasting or often irreversible intestinal failure [1]. Short bowel syndrome (SBS) is a state of malabsorption following extensive small intestinal resection. The functional consequences as well as the prognosis of SBS depend on the age-adjusted small bowel length, site of resection and occurrence of cholestasis [2]. The cause of resection and age of the patient also influence the functional capacity of the remnant gut and its potential for adaptation [2, 3]. By maintaining an optimal nutritional status during the long period required for adaptation of the remnant small intestine, parenteral nutrition (PN) is the cornerstone of management, but as much oral or enteral feeding as possible should be provided to the patient via the intestine in order to improve the physiological processes of short bowel adaptation. Moreover, in infants or children oral feeding skills have to be acquired or maintained. Different concepts exist with respect to what the composition of feeding (elemental, semi-elemental or polymeric) and the mode of delivery (oral feeding or gastric tube feeding) should be. Cur-
rent studies do not provide evidence-based data for establishing recommendations for SBS patients. Patients suffering disease involving the intestinal mucosa or gut motility also require protracted periods of PN.

**Rationale for Enteral Feeding**

The use of the gastrointestinal tract is vital for preserving or restoring normal intestinal structure and function [3]. Functional intestinal adaptation refers to the gross anatomic and histologic changes that occur after extensive intestinal resection. Following bowel enlargement and villi lengthening, the intestinal absorptive surface area increases, and absorptive function gradually improves. Changes in intestinal motility, commensal microbiota, and barrier function are associated with the anatomic and histologic changes. The use of the intestinal tract plays a critical role in the process of intestinal adaptation, based on the effects of direct nutrient contact with the mucosa, pancreatic and hepatobiliary secretions, and the release of circulating hormones. In patients with PDI or SBS, only a few clinical trials have been performed, but they support that enteral feeding maintains and/or promotes intestinal function [4–6]. The choice of the diet as well as the mode of delivery remains debated (tables 1, 2).

**Which Diet Is to Be Used**

*Breast milk* contains lactose and is considered to be not well tolerated in patients with reduced intestinal surface area. Breast milk contains many factors that may promote intestinal adaptation and was shown to improve immune function, as well as the genesis of a fecal microflora rich in lactobacilli and bifidobacteria. In infants with SBS, the percentage of days that infants received breast milk was correlated with fewer days of PN use [7]. Breast milk should be used as often as possible in patients with neonatal SBS by breastfeeding or tube feeding.

The choice of enteral formula is controversial. A limited mucosal absorptive surface area can lead to lactose, long-chain fatty acid and protein malabsorption. In PDI, electrolyte and metabolic balance can be difficult to achieve. In SBS patients, complex nutrients may promote mucosal cell proliferation via direct contact with disaccharides [8]. Additionally, colonic exposure to luminal nutrients promotes release of trophic factors that enhance small bowel mucosa trophicity.

*Oligo- and polysaccharides* are poorly tolerated by patients, being broken down by osmotically active organic acids that can present a major osmotic load to the distal small intestine and colon. In patients with intractable diarrhea of infancy, carbohydrate content should not exceed 40% of calories and be lactose-free.

*Fiber supplementation,* by promoting the production of short-chain fatty acids, such as butyrate, have trophic effects on the small intestine.

*Long-chain triglycerides* are poorly absorbed in patients with reduced absorptive surface. In case of small intestine bacterial overgrowth, bacteria metabolize and inactivate bile acids, preventing the solubilization necessary for long-chain triglyceride digestion.

*Medium-chain triglycerides* (MCTs) are rapidly hydrolyzed by pancreatic lipase and are less dependent on an extensive absorptive surface for adequate absorption. They are water-soluble and can be absorbed intact, directly into the portal circulation [9]. Excessive intake of MCTs can cause diarrhea and ketosis, while MCTs do not provide essential fatty acids. Current clinical practice is based on formulas containing no more than 60% MCTs as fat.

Whether the molecular form of the nitrogen intake might influence PN duration and/or the occurrence of non-IgE-mediated sensitization and allergic enteritis remains debated. The link be-
Table 1. Which type of diet should be used

**Breast milk**
- Contains lactose, growth factors, nucleotides, long-chain fatty acids, glutamine, and other amino acids that promote intestinal adaptation
- Promotes microbiota rich in lactobacilli and bifidobacteria
- In infants with SBS, it reduces the duration of parenteral nutrition
- Should be used as much as possible in neonatal SBS by breastfeeding or tube feeding

**Enteral formulas**
**Carbohydrates**
- Breast milk
  - Currently no benefit demonstrated
- Glutamine (Gln)
  - Not yet established whether this type of formula can influence the outcome of SBS
- Elemental amino acid-based formula
  - Largely used and recommended in SBS patients
  - No demonstrated advantages in comparison with intact protein infant formula

**Lipids**
- Hydrolyzed protein formulas
  - Used for many years
  - Have changed the incidence and outcome of protracted diarrhea of infancy
  - Lactose-free and contain MCTs
  - Not yet established whether this type of formula can influence the outcome of SBS
- Medium-chain triglycerides (MCTs)
  - Rapidly hydrolyzed by pancreatic lipase
  - Do not provide essential fatty acids
  - Less dependent on an extensive absorptive surface for adequate absorption
  - Water-soluble and absorbed intact, directly into the portal circulation
  - As part of lipid supply appropriate for most infants with SBS
  - Excessive intake can cause diarrhea
  - Recommended use of formulas containing no more than 60% MCTs as fat
- Long-chain triglycerides
  - Poorly digested in case of small intestine bacterial overgrowth because of bile acid changes
  - Poorly absorbed in patients with severe malabsorption
  - Have trophic effects on small intestinal mucosa
  - Supplementation with n-3- or n-6-polyunsaturated fatty acids may enhance mucosal growth
  - Rapidly hydrolyzed by pancreatic lipase
  - Do not provide essential fatty acids
  - Less dependent on an extensive absorptive surface for adequate absorption
  - Water-soluble and absorbed intact, directly into the portal circulation
  - As part of lipid supply appropriate for most infants with SBS
  - Excessive intake can cause diarrhea
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**Nitrogen**
- Hydrolyzed protein formulas
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- Lactase-free and contain MCTs
- Largely used and recommended in SBS patients
- Elemental amino acid-based formula
  - Not yet established whether this type of formula can influence the outcome of SBS
- Glutamine (Gln)
  - Currently no benefit demonstrated

Table 2. Management and outcome of neonatal short bowel syndrome (SBS) according to anatomical characteristics

SBS is a very variable condition which can be as mild as that following terminal ileal resection to a very debilitating condition which follows total jejun-ileal and colonic resection. Management and outcome vary according to the cause, the extent and site of resection, and the degree of adaptation of the remaining bowel. Patients with dilated, poorly motile segments of small bowel (gastrochisis, atresia, necrotizing enterocolitis) could benefit from an approach aiming to reduce bowel dilatation and small intestinal bacterial overgrowth (SIBO), since they may rapidly develop severe liver disease. Adapted parenteral nutrition (PN), delivered as soon as tolerance permits by cyclical infusion, is mandatory. Early oral feeding (OF) should be promoted while the benefits of continuous enteral feeding (CEF) should be balanced in combination with PN; the risk of ‘intestinal overload’ with subsequent SIBO and tube feeding induce food aversion and eating disorders.

- **SBS with small bowel length (SBL) of <40 cm with loss of the ileocecal valve (ICV) and associated partial or large colectomy:** Patients need very long-term home PN, often indefinite. The indication to reduce PN is weight gain beyond the desired limit and the fact that a reduced rate of infusion does not cause electrolyte imbalance and dehydration. Patients with total colectomy or permanent proximal jejunalostomy will remain indefinitely dependent on PN.

- **SBS with SBL of <40 cm or only duodenum with totally or largely intact colon:** Patients need long-term home PN. However, many infants and children may have a degree of adaptation and require less PN and benefit from orally and/or enterally administered nutrients. Some of them may be progressively weaned from PN. Infants with duodeno-right colon anastomosis have no chance of being weaned from PN and should not receive CEF instead of oral feeding to protect the liver and promote optimal psychological behavior. These patients are at the highest risk of developing D-lactic acidosis.

- **SBS with SBL of 40–100 cm with loss of the ICV and associated partial or large colectomy:** Patients require mid-term home PN and can immediately be fed orally. Adapted CEF combined with oral feeding may help to reduce the PN duration. Bile salt-induced diarrhea may impede rapid PN weaning.

- **SBS with SBL of 40–100 cm with terminal ileum and the entire colon:** Patients require very short-term PN and can immediately be fed orally. Adapted CEF in combination with oral feeding may help to significantly reduce PN duration.

- **SBS with terminal ileum resection:** Patients have a bile salt-induced diarrhea, and benefit from the administration of 1-2 g of cholestyramine 3 times a day to bind bile salts left unabsorbed by the resected ileum. Vitamin B12 plasma levels should be measured and if low, supplemental B12 should be provided by intramuscular injection at a dose of 100-150 µg orally or 1,000 µg every 6 months.
between small intestine bacterial overgrowth, abnormal mucosal permeability and associated protein sensitization is possible, but the relevance of elemental diets has also not been clinically established (table 3). Only very few clinical trials involving elemental formulas are currently available to establish recommendations. Patients with dilated, poorly motile segments of small bowel should benefit first from an approach aiming to reduce bowel dilatation and small intestine bacterial overgrowth, since these patients may develop severe liver disease [10].

Hydrolyzed protein formulas (HPFs) have been used for many years and have changed the incidence and outcome of PDI during the last decades. HPFs have been evaluated by comparison with intact protein infant formula in a crossover study of 60 days duration in 10 infants with SBS [11]. No effect of formula type was observed on growth, nitrogen absorption, or mucosal permeability. In general, HPFs are lactose-free and contain MCTs [11, 12].

Elemental amino acid-based formulas (EA-ABFs) have been introduced more recently for infants suffering from severe allergic diseases. It is not yet established if this type of formula can influence the outcome of SBS. The beneficial effects of EAABFs were reported in an open trial involving only 4 SBS patients with persistent feeding intolerance [7]. A retrospective study found a shorter duration of PN dependency with the use of EAABFs [13]. Current data are not yet sufficient to recommend such expansive formulas for infants and children with SBS.

**Glutamine** (Gln), a nonessential amino acid, plays an important role in energy metabolism of the intestinal mucosa and other rapid turnover tissues. A randomized controlled pilot study of Gln-supplemented enteral feeding in infants with intestinal failure failed to show any advantages [14]. Gln cannot be recommended unless larger multicenter trials in infants with intestinal failure can provide evidence.

### Table 3. Small intestine bacterial overgrowth (SIBO)

- Several factors intrinsic to short bowel syndrome (SBS) predispose to SIBO and explain its high prevalence in this patient population
- Poorly motile segments of the short bowel in close proximity to the colon are common in patients with SBS and dysmotility, and the stagnation and contamination that results promote abnormal growth of bacteria in the small intestine
- SIBO may significantly compromise the digestive and absorptive functions and may delay or prevent weaning from parenteral nutrition
- Traditional clinical tests for overgrowth may be unreliable
- Management may include surgery if advocated. Antibiotic therapy should vary according to the risk of selecting highly resistant bacterial strains
- Intestinal microbiota play an important role in intestinal adaptation and should be preserved as much as possible
- The use of probiotics offers potential based on experimental evidence, but there is a lack of sufficient data from human studies
- α-Lactic acidosis is secondary to bacterial hypermetabolism, especially in the colon, as a consequence of intestinal malabsorption

**Definition**

Colony-forming units (CFUs) per milliliter of bacteria in the proximal small bowel
- Overgrowth of >10³ CFUs/ml
- Overgrowth of >10⁵ CFUs/ml provided that the species of bacteria isolated from the jejunal aspirate are those that normally colonize the large bowel or provided that those same species are absent from the saliva and gastric juice
- Breath hydrogen testing

**Caused by small intestine stasis from:**
- Intestinal obstruction (e.g. stenosis, narrowed anastomosis)
- Blind loop from termino-lateral anastomosis
- Dilated and poorly motile segments of small bowel in close proximity to the colon
- Contamination from inappropriate enteral feeding

**Consequences**
- Small intestine mucosal injury with villous atrophy and subsequent malabsorption
- Increased small intestine mucosal permeability
- IgE-mediated sensitization and allergic enteritis
- Gram-negative sepsis from bacterial translocation
- Cholestasis and end-stage liver disease (cirrhosis)

**Management**
- Reversal or removal of any predisposing condition(s)
- Redo-anastomosis
- Enteroplasty
  - Small intestinal tapering and lengthening (Bianchi procedure)
  - Serial transverse enteroplasty (STEP procedure)
  - Appropriate nutritional support/replacement
- Suppression or eradication of the contaminating bacterial flora
  - Intermittent bowel decontamination with antibiotics
  - Use of probiotics
  (Lactobacillus GG, Saccharomyces boulardii, etc.)
Water electrolyte losses from persistent diarrhea or end-jejunostomies should be replaced parenterally, based on the electrolyte concentration of the lost fluids. Monitoring the urine sodium concentration provides guidance for correcting or preventing Na depletion (<10 mEq/l), even if serum sodium is near normal. Magnesium and trace element losses can occur with high stoma output. Zinc supplements are often used empirically, given that serum values do not reliably reflect body stores. Ileal resection or diversion lead to fat-soluble vitamin and vitamin B₁₂ deficiency requiring monitoring and (parenteral) supplementation.

### Advancement of Feeding

Whatever the route of feeding (table 4), enteral feeding advancement can occur as long as fluid and electrolyte balance is maintained and nutritional goals achieved (table 5). Enteral feeding

<table>
<thead>
<tr>
<th>Devices</th>
<th>Indications</th>
<th>Contraindications</th>
<th>Advantages</th>
<th>Disadvantages or risks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oral feeding</strong></td>
<td>None</td>
<td>To be used systematically</td>
<td>Artificial ventilation Oro-facial malformation</td>
<td>Discontinuous physiologic mode of feeding Self-regulation of intake EGF release by salivary glands Promote bowel adaptation Psychological behavior</td>
</tr>
<tr>
<td><strong>Gastric feeding</strong></td>
<td>Nasogastric</td>
<td>Nutritional support &lt;3 months</td>
<td>Severe GE reflux, Slow gastric emptying</td>
<td>Easy to place even at home</td>
</tr>
<tr>
<td></td>
<td>Percutaneous endoscopic gastrostomy</td>
<td>Nutritional support &gt;3 months</td>
<td>Repeated abdominal surgery Abnormal gastric anatomy</td>
<td>Fewer occlusions with larger bore, one-step low-profile devices available</td>
</tr>
<tr>
<td></td>
<td>Surgical gastrostomy</td>
<td>Nutritional support &gt;3 months</td>
<td>Poor candidate for surgery</td>
<td>Immediate placement of low-profile device, direct visualization of stomach</td>
</tr>
<tr>
<td><strong>Duodenal or jejunal feeding</strong></td>
<td>Nasojugal</td>
<td>Short term for patients with severe GERD, gastric dysmotility</td>
<td>Recent proximal surgical anastomosis</td>
<td>Radiologic or bedside placement techniques, noninvasive</td>
</tr>
<tr>
<td></td>
<td>Gastrojejunal</td>
<td>Longer-term EF for patients with severe GERD, gastric dysmotility or need for gastric decompression</td>
<td>Recent proximal surgical anastomosis</td>
<td>Endoscopic or radiologic placement, through existing gastrostomy tube</td>
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<td></td>
<td>Jejunal</td>
<td>Long-term EF for patients with severe GERD, upper intestinal dysmotility</td>
<td>Dyssmotility</td>
<td>Direct surgical access to small intestine</td>
</tr>
</tbody>
</table>

EGF = Epidermal growth factor; GE = gastroesophageal; GERD = gastroesophageal reflux disease; EF = enteral feeding.
may eventually be transitioned to oral/bolus feedings, or oral/bolus and nocturnal feedings to allow more freedom from the feeding pump. The transition from intestinal failure to adequate intestinal function can take weeks, months, and sometimes years. The infant with SBS improves bowel function over time due to the opportunity for further intestinal growth. Provision of oral feeding plays a major role in the management of any child with intestinal failure, even for those in whom complete weaning from PN seems unlikely.

**Conclusions**

- Intestinal adaptation following resection is a physiological process best enhanced by the early use of the gastrointestinal tract, especially by oral feeding
- Continuous enteral feeding has advantages for digestion/absorption of nutrients but should be used carefully to avoid ‘intestinal overload’ of poorly motile segments of the short bowel and development of eating disorders
- Breastfeeding may be used, and may be complemented with hydrolyzed protein formulas containing up to 60% medium-chain triglycerides. Current data are not sufficient for recommending elemental amino acid-based formula for infants and children with short bowel syndrome
- Small intestinal bacterial overgrowth may significantly compromise digestive and absorptive functions and may delay or prevent weaning from total parenteral nutrition

**Table 5. Modes and management of feeding**

<table>
<thead>
<tr>
<th>Mode</th>
<th>Description</th>
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<tbody>
<tr>
<td>Oral feeding (OF)</td>
<td>Is the most physiological and the most stimulating for intestinal adaptation</td>
</tr>
<tr>
<td>Continuous enteral feeding (CEF)</td>
<td>Is beneficial in patients with SBS or IDI, by improving saturation of carrier transport proteins, thus taking full advantage of the available absorptive surface area as compared to intermittent feeding</td>
</tr>
<tr>
<td>Oro-pharyngeal shunting</td>
<td>Suppresses the direct stimulation of salivary glands resulting in lower release of EGF that is an important intestinal mucosa trophic factor</td>
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<tr>
<td>Continuous infusion</td>
<td>Leads to the loss of self-regulation of intake with vomiting or intestinal stasis with increased risk of SIBO with subsequent sepsis, liver injury, etc.</td>
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</tbody>
</table>

**Progression and monitoring of feeding program**

- Intestinal transit must be well established by colo-anal transit or ostomy
- Absence of contraindications
  - Patient’s general condition (sepsis, bleeding, respiratory distress syndrome, etc.)
  - Bloody stools
  - High ostomy or stool output, >3 ml/kg per h ostomy output
  - Bilious and/or persistent vomiting
  - Electrolyte instability
- Quantifying feeding tolerance
  - Stool or ostomy output
  - Reducing substances in stools or ostomy output
  - Recurrent vomiting and abdominal distension
- Ultimate goals
  - Provide 150–200 ml/kg per day, 100–140 kcal/kg per day
  - If ostomy/stool output precludes advancement at 20 cal/oz for 7 days
  - Increasing caloric density of the formula can be performed
  - Isocaloric reductions in PN support simultaneously with feeding advancement

**Warning**

- EF can induce severe adverse effects related to intestinal overload and/or bacterial contamination with subsequent SIBO
- A meticulous approach, avoidance of excessive enteral formula supply, strict hygiene measures
- Concomitant oral feeding prevents psychological disorders and eating aversion

**SBS** = Small bowel syndrome; **IDI** = intractable diarrhea of infancy; **EGF** = epidermal growth factor; **SIBO** = small intestine bacterial overgrowth; **EF** = enteral feeding; **PN** = parenteral nutrition.
References

Introduction

Celiac disease (CD) is an autoimmune disorder occurring in genetically susceptible individuals, and triggered by the ingestion of a well-identified autoantigen (gluten). It affects primarily the small intestine, where it progressively leads to flattening of the small intestinal mucosa. Three cereals contain gluten and are toxic for celiac patients: wheat, rye, and barley. Screening studies have shown that CD has a very high prevalence, occurring in about 1% of the general population throughout Europe and North America [1]. In Latin America, North Africa, the Near and Middle East and Northwest India, CD’s prevalence, when assessed, has been reported at similarly high values. In the Saharawi population, CD has been found in as many as 5% of the general population [2]. It must be emphasized that not all those affected by CD (children and adults alike) are symptomatic, and that even symptomatic patients may present diverse problems, not everyone showing the classic presentation with gastrointestinal complaints. However, diagnosing CD in all affected individuals is imperative, as the condition can be fully reverted to normal with a timely institution of a gluten-free diet (GFD), thus preventing the many complications that have been described in untreated patients and that eventually may lead to a shorter life expectancy.

Pathophysiology

A clear genetic predisposition exists, as CD only occurs in individuals who are either positive for the haplotype HLA-DQ2 or DQ8. An autoimmune component is present, as demonstrated by specific serology for antibodies to the enzyme tissue transglutaminase (TGA).

Both the adaptive and the innate immune systems are involved in the cascade of events leading to intestinal damage. The adaptive immune response to gluten has been well elucidated with the identification of specific peptide sequences able
to bind specifically to HLA-DQ2 or DQ8 molecules and to then stimulate gluten-specific CD4 T cells.

As for the innate immunity, the intraepithelial CD8+ T-lymphocytes play an important role in the destruction of epithelial cells.

CD is a chronic inflammatory disorder leading, if untreated, to the destruction of the small intestinal villi, with consequent malabsorption of nutrients and minerals. The lesions occur in the proximal small intestine with typical histological changes of villous atrophy, crypt hyperplasia and increased intraepithelial lymphocytosis. Such damage follows a progressive course, and specific histological stages have been described that can be classified [3] as follows:

- Type 0 or pre-infiltrative stage (normal)
- Type 1 or infiltrative lesion (increased intraepithelial lymphocytes)
- Type 2 or hyperplastic lesion (type 1 + hyperplastic crypts)
- Type 3 or destructive lesion (type 2 + villous atrophy of progressively more severe degrees, denominated 3a, 3b and 3c)

### Clinical Presentation

Four possible presentations of CD are recognized [4] (table 1):

**Typical:** Characterized mostly by gastrointestinal signs and symptoms.

**Atypical or extra-intestinal:** Gastrointestinal signs/symptoms are minimal or absent. Various extra-intestinal manifestations are present.

**Silent:** The small intestinal mucosa is damaged and CD autoimmunity can be detected by serology, but there are no symptoms.

**Latent:** Asymptomatic, and with normal mucosa morphology. These individuals have genetic compatibility with CD and may also show positive autoimmune serology. Full-blown CD may ensue at a later time.

<table>
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<tr>
<th>Table 1. Presentations of celiac disease</th>
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<tr>
<td><strong>Latent</strong></td>
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‘Typical’ Celiac Disease: Gastrointestinal Manifestations

The so-called ‘typical’ form of CD presents characteristically between 6 and 24 months of age. Symptoms begin at various times after the introduction of weaning foods containing gluten. Infants and young children typically present with chronic diarrhea, anorexia, vomiting, abdominal distension, abdominal pain and poor weight gain or weight loss. Malnutrition can be severe if the diagnosis is delayed. Behavioral changes are common and include irritability and a sad mood. Older children with CD present with gastrointestinal manifestations, but symptoms typically are less evident and include nausea, bloating, abdominal pain, constipation and intermittent diarrhea. The variability in the age at onset of symptoms is possibly dependent on the amount of gluten in the diet and other environmental factors such as duration of breastfeeding.
‘Atypical’ Celiac Disease: Extra-Intestinal Manifestations

More and more patients are being diagnosed without typical gastrointestinal manifestations, and at an older age. It is currently estimated that about half of the patients with newly diagnosed CD in fact do not present with gastrointestinal symptoms. In infants and toddlers, gastrointestinal symptoms and failure to thrive clearly predominate, while during childhood minor gastrointestinal symptoms, inadequate rate of weight and height gain, and delayed puberty tend to be more common.

Table 2 reports the main extra-intestinal manifestations of celiac disease, briefly summarized below.

- **Dermatitis herpetiformis**: A blistering skin rash involving elbows, knees, and buttocks associated with dermal granular immunoglobulin A (IgA) deposits. Rash as well as mucosal morphology improves on a GFD
- **Dental enamel hypoplasia**: Only involves the permanent dentition and may be the only presenting manifestation of CD
- **Iron-deficiency anemia**: Possibly the most common manifestation of CD in adults
- **Short stature and delayed puberty**: As many as 10% of children with ‘idiopathic’ short stature may have CD in the absence of any sign of nutritional deficiencies. Adolescent girls may have delayed menarche
- **Chronic hepatitis, hypertransaminasemia**: As many as 9% of patients with elevated transaminase levels of unclear etiology may have silent celiac disease. Liver enzymes normalize on GFD
- **Arthritis, arthralgias**: Arthritis can be a common extra-intestinal manifestation of adults with CD including those on GFD. Up to 3% of children with juvenile chronic arthritis may have CD [5]
- **Osteopenia/Osteoporosis**: Approximately 50% of children and 75% of adults at the time of diagnosis of CD have a low bone mineral density of various severity. Bone mineral density improves on GFD, and in children may return to normal in as little as 1 year after starting the diet
- **Neurological problems**: CD may cause occipital calcifications and intractable epilepsy. The association with cerebellar ataxia is well described in adults, and other lesions involving the white matter have also been described

### Associated Diseases

CD is associated with a number of other disorders: several autoimmune conditions and a few genetic syndromes, the most common of which are listed in table 3.

- **Type-1 (insulin-dependent) diabetes (IDDM)**: Approximately 8% of patients with IDDM have increased levels of TGA and show typical features of CD on duodenal biopsy. The appearance of CD serology may occur at any time after the diagnosis of IDDM, thus highlighting the need for repeated testing. Most commonly, patients with IDDM and CD have no or only mild gastrointestinal symptoms. As some of these symptoms are also seen in patients with diabetes (e.g. bloating or diarrhea), diagnosis of CD may be missed, unless a screening is performed. Although there is no
convincing evidence that the GFD has any obvious effect on diabetes, it is thought that these patients will have to follow the diet, in order to prevent all long-term complications of CD. Thus, the case for screening type-1 diabetics for CD seems well founded [6].

• **Down syndrome:** The prevalence of CD in Down syndrome has been found to be between 8 and 12%. The majority of Down patients with CD have some gastrointestinal symptoms, such as abdominal bloating, intermittent diarrhea, anorexia, failure to thrive; however, about one third of them do not present any gastrointestinal symptoms.

### Diagnosis

The evidence-based guidelines introduced in 2005 by the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) [7] describe in great detail a correct diagnostic approach. They substantially follow the same lines of previous guidelines proposed by the European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) in 1990 [8]. The algorithm presented in figure 1 describes the suggested diagnostic approach to a child with predominantly gastrointestinal symptoms. It should be noted that CD can effectively be screened by the serum level of the autoantibody against tissue TGA, which has proven to be a highly sensitive test [9]. Anti-endomysial antibodies, thought to actually measure the same antibody as TGA, appear to be somewhat less sensitive, but more specific, with a specificity approaching 100%.

### Treatment

Total lifelong avoidance of gluten ingestion is the cornerstone treatment for CD. Wheat, rye and barley are the grains containing toxic peptides. When children with symptomatic CD adhere to a GFD, they can be expected to resolve their gastrointestinal symptoms typically within a few weeks, showing additional normalization of nutritional measures, improved growth in height and weight (with resultant normal stature), and normalization of hematological and biochemical parameters. Furthermore, treatment with a GFD reverses the decrease in bone mineralization and the risk for fractures, and – if instituted early enough in the course of the disease – has been proven effective in avoiding the increased mortality rates that are otherwise associated with CD [10, 11].

### Prevention

There is new evidence showing that CD onset can be prevented, or at least markedly delayed, when gluten is introduced in small amounts in geneti-
Celiac disease is an autoimmune inflammatory disorder of the small intestine triggered by gluten, and is a very common chronic disease.

- It occurs more commonly in relatives of celiac patients and in some at-risk groups
- It causes gastrointestinal symptoms, predominantly chronic diarrhea with wasting, but also many extra-intestinal manifestations that can be present alone
- Once suspected, the patient should be screened with transglutaminase + total serum IgA, and if positive referred to a pediatric gastroenterologist for a confirmatory biopsy before the gluten-free diet is begun
- A gluten-free diet typically reverses all signs and symptoms within a short time
- Monitoring of the patient to verify ongoing dietary compliance is fundamental in order to ensure that all possible complications, including malignancies, are avoided

### Conclusions

- Celiac disease is an autoimmune inflammatory disorder of the small intestine triggered by gluten, and is a very common chronic disease

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**Fig. 1.** Diagnostic approach to children presenting with gastrointestinal (GI) symptoms consistent with celiac disease (CD). tTG = Tissue transglutaminase; GE = gastroenterologist; EMA = anti-endomysial antibody; GFD = gluten-free diet. From Guandalini [4].

<table>
<thead>
<tr>
<th>Chronic diarrhea and failure to thrive</th>
<th>Chronic or recurrent GI symptoms such as:</th>
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<tr>
<td>Obtain tTG and total serum IgA</td>
<td>• Abdominal pain</td>
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<td>• Abdominal distention</td>
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<td>• Anorexia</td>
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<td>• Vomiting</td>
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<td>• Constipation</td>
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<tr>
<th>IgA &lt; 5 mg/dl?</th>
<th>Obtain tTG-IgG</th>
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<td>tTG or tTG-IgG if IgA-deficient abnormally high?</td>
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<tr>
<td>No</td>
<td>Celiac disease excluded</td>
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<td>Consult pediatric GE</td>
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<td>Endoscopic biopsy + EMA</td>
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<th>Pathology not CD</th>
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<tr>
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<td>EMA abnormal</td>
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<tr>
<td>CD excluded</td>
<td>Review pathology</td>
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<td>? Repeat biopsy</td>
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<td>? GFD</td>
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<th>Pathology of CD</th>
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<tr>
<td>EMA normal</td>
<td>EMA abnormal</td>
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<tr>
<td>CD diagnosed</td>
<td>GFD for 6–12 months</td>
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<td></td>
<td>Rechallenge and rebiopsy</td>
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</table>

| tTG or tTG-IgG if IgA-deficient abnormally high? |
| No                                      | Celiac disease excluded                  |
| Yes                                     | Consult pediatric GE                     |
|                                         | Endoscopic biopsy + EMA                  |

**Fig. 1.** Diagnostic approach to children presenting with gastrointestinal (GI) symptoms consistent with celiac disease (CD). tTG = Tissue transglutaminase; GE = gastroenterologist; EMA = anti-endomysial antibody; GFD = gluten-free diet. From Guandalini [4].
References

**Key Words**

Food allergy · Lactose intolerance · Enteropathy, food protein-induced · Enterocolitis syndrome, food protein-induced · Proctocolitis, food protein-induced · Elimination diet · Hypoallergenic formula · Amino acid-based formula · Hydrolyzed formula · Soy formula

**Key Messages**

- **Food allergy** is mediated by an immune reaction against food proteins, whereas **food intolerances** can be caused by any food constituent and do not involve immunological mechanisms.
- The treatment of food allergies involves strict avoidance of the offending food antigen, either by use of a hypoallergenic infant formula or a specific elimination diet. By contrast, in patients with food intolerances small quantities of the offending food ingredient are generally tolerated (dose-response relationship).
- Infants and young children with gastrointestinal food allergies, if presenting with persistent vomiting or diarrhea, are at high risk of failure to thrive, particularly if there are associated feeding difficulties.
- Correct identification of food allergies and intolerances in infancy and childhood is important in order to prevent growth impairment and nutritional deficiency states.
- Close monitoring of dietary intake and growth parameters, regular re-assessment of persistent allergies and dietary introduction of tolerated food proteins are essential steps in the nutritional management of children with food allergies.

**Introduction**

Food allergy represents the failure to achieve or maintain immune tolerance to one or several food proteins [1]. There has been a recent dramatic increase in the incidence of food allergies in many developed countries (6% children, 2% adults) [2]. Although this increase has been attributed to low rates of early childhood infection or exposure to endotoxin (hygiene hypothesis), the exact reasons remain unclear.

Cow’s milk, egg, peanut, tree nuts, fish, soy and wheat cause about 95% of food allergies [2, 3]. These allergies may present clinically with a range of systemic reactions (urticaria, angioedema, anaphylaxis), or involve the skin, gut and respiratory tract [2, 3]. Multiple food allergies are common, particularly in early childhood.

Food intolerance is characterized by an adverse reaction to any (non-protein) food constituent, without interacting with the immune system [1]. Examples are malabsorption of fat or carbohydrates which can present with abdominal bloating, pain or diarrhea [4]. Food intolerances may indicate the presence of underlying gastrointestinal conditions (e.g. celiac disease, intestinal lymphangiectasia) or metabolic disorders (e.g. hereditary fructose intolerance).

The treatment of food allergies is based on the elimination of specific food proteins until tolerance has developed [3–5]. The treatment of food intolerance follows the same principles but may vary according to the underlying condition.
Gastrointestinal food allergies presenting with persistent vomiting, diarrhea or decreased protein/energy intake may cause failure to thrive [4, 5]. The correct and early diagnosis of food allergies is therefore important in order to prevent nutritional deficiency states and growth impairment [5].

Pathophysiology

Two main types of food allergy can be distinguished based on the timing of the clinical reaction in relation to the food ingestion (fig. 1) [1–3]. Immediate-onset reactions occur within minutes after ingestion of a food. In these patients the allergy is mediated by food-specific immunoglobulin E (IgE) antibodies [2]. Delayed-onset reactions occur within several hours to days after ingestion and may involve the gut, skin or respiratory tract. These reactions are cell-mediated (lymphocytes, eosinophils) and typically lack evidence of systemic IgE sensitization (skin prick tests and food-specific serum IgE antibodies negative) [2, 3, 6].

An increasing number of food allergens have been characterized, e.g. β-lactoglobulin in milk, ovomucin in hen’s egg or ara c1 in peanut [2]. On each of these proteins, epitope regions have been mapped that interact with either IgE antibody or T-cell receptor. Conformational epitopes (with a 3-dimensional structure) may be inactivated by...
heating or acidification. For example, egg allergic patients may tolerate baked egg while uncooked egg causes adverse reactions.

### Clinical Manifestations of Food Allergy

Food allergy may present with a diverse range of clinical manifestations [3] (table 1). Immediate reactions typically consist of urticaria, angioedema, oral tingling or itching, vomiting or diarrhea. Anaphylaxis is the term used to describe severe immediate-type reactions with either respiratory compromise (wheeze, stridor, cough) and/or hypotonia or collapse [7]. Anaphylaxis may occur in response to small doses of allergen and can be fatal, particularly in adolescents and young adults with concomitant unstable asthma [7].

Delayed reactions consist mainly of gastrointestinal or cutaneous reactions [3, 4, 8]. The role of food allergy in respiratory disorders, such as asthma, is much less well defined. Atopic dermatitis with onset within the first months of life is closely related to food allergy [3]. The gastrointestinal reactions can be divided into food protein-induced enteropathy, enterocolitis syndrome (FPIES) and proctocolitis (table 1) [4, 8]. Enteropathy and proctocolitis may occur in exclusively breastfed infants [9], whereas FPIES seems to require direct ingestion of the allergen by the infant [10]. Recently, eosinophilic esophagitis has

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**Table 1. Gastrointestinal food allergy**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Clinical features</th>
<th>Investigations</th>
<th>Complications</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>Food protein-induced enteropathy</td>
<td>Affects formula-fed infants (cow’s milk or soy) Persistent diarrhea Occasional vomiting Failure to thrive</td>
<td>SPT/RAST-negative Intestinal biopsy: villous atrophy and crypt hyperplasia Duodenal disaccharidases reduced (lactase deficiency)</td>
<td>Secondary lactose intolerance Protein-losing enteropathy Hypoproteinemia and edema Iron deficiency anemia</td>
<td>Strict cow’s milk- and soy-free diet Extensively hydrolyzed formula usually sufficient; if not tolerated, change to amino acid-based formula</td>
</tr>
<tr>
<td>Food protein-induced enterocolitis syndrome (FPIES)</td>
<td>Profuse vomiting 2–3 h after intake of foods Does not occur in breastfed infants Common allergens are cow’s milk, soy, grains (wheat, rice) and chicken Chronic forms may present with persistent diarrhea, vomiting and failure to thrive Low-grade rectal bleeding</td>
<td>SPT/RAST-negative Atopy patch test may be positive</td>
<td>Acute dehydration and hypovolemic crisis in about 20% of first presentations (may be mistaken for sepsis or gastroenteritis)</td>
<td>Strict avoidance of offending food item Requires hypoallergenic formula if previous reaction to cow’s milk or soy</td>
</tr>
<tr>
<td>Food protein-induced proctocolitis</td>
<td>May occur in breast- or formula-fed infants within the first weeks of life Low-grade rectal blood loss, often mixed in with mucus Infants otherwise well and thriving</td>
<td>SPT/RAST-negative Rectal mucosa shows increased lymphocytes and eosinophils, with focal epithelial ulceration</td>
<td>Iron deficiency anemia uncommon</td>
<td>In formula-fed infants, extensively hydrolyzed formula; if not tolerated, change to amino acid-based formula Breastfed infants often respond to maternal elimination diet</td>
</tr>
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</table>
been recognized as a condition associated with food allergy that often responds to dietary elimination [11].

**Lactose Intolerance**

Lactose is a disaccharide that is digested into glucose and galactose by the small intestinal brush border enzyme, lactase. Failure to absorb lactose will result in bacterial fermentation of the sugar, presenting as flatulence, diarrhea, acidic stools and perianal skin excoriation. Lactose malabsorption should not be confused with cow’s milk allergy (table 2) [3, 4]. Dietary lactose restriction is usually sufficient to control gastrointestinal symptoms. Secondary forms of lactose intolerance may be transient and resolve after the underlying gastrointestinal condition has remitted, e.g. viral gastroenteritis or celiac disease.

**Investigation**

The investigation of food allergy relies on three pillars: measurement of food-specific serum IgE antibodies (by radioallergosorbent assay or CAP-FEIA) [2], skin prick testing [6] and food challenge.
Recently, atopy patch testing has been suggested as a new test for delayed food allergy, but its exact role has remained an area of ongoing research [12]. Patients with proven food allergy need to be reassessed on a regular basis in order to detect the development of tolerance to the offending food. This will often involve open food challenges in order to demonstrate tolerance or ongoing allergies. Due to the risk of anaphylaxis these challenges should be supervised by a trained allergist with access to resuscitation equipment [7].

**Dietary Management of Food Allergy**

In children with specific IgE-mediated food allergy, e.g. to cow’s milk, egg or peanut, all foods containing the offending antigen need to be avoided. As allergens are commonly disguised in manufactured food products, this involves careful reading of ingredient labels [5]. In infants, allergies to multiple foods are common. For example, in infants with cow’s milk allergy, concomitant allergy to egg, soy or wheat may be present [3].

Several hypoallergenic formulas are available for the treatment of infants with cow’s milk and soy allergy (table 4). These hypoallergenic formulas are tolerated by at least 90% of infants with cow’s milk allergy [13]. Cross-reactivity between cow’s milk and soy is relatively common in infants. Soy formula is therefore no longer considered a first-line cow’s milk substitute, particularly in infants under 6 months [14]. In breastfed infants, a maternal elimination diet may be effective as intact food antigens in breast milk can elicit allergic manifestations in the infant [9]. However, the clinical benefit of maternal elimination diets is an area of ongoing research. An adequate maternal intake of protein and micronutrients (recommended maternal calcium intake 1.2 g/day provided as separate portions distributed throughout the day) needs to be maintained.

There are two main types of hydrolyzed cow’s milk formula, partially hydrolyzed and exten-
sively hydrolyzed formula [13, 15]. Partially hydrolyzed formula may play a role in allergy prevention but it is not suitable for infants with established clinical signs of cow’s milk allergy [16]. These infants require an extensively hydrolyzed formula or, if not tolerated, an amino acid-based formula [15]. In infants older than 6 months soy may also be a suitable alternative [14]. Calcium supplementation should be considered in children on dairy-free diets. A dietician is usually required to monitor broad-based elimination diets for nutritional adequacy [5].

**Conclusions**

- Hypoallergenic formulas (extensively hydrolyzed formula or amino acid-based formula) are used in the treatment of cow’s milk allergy in formula-fed infants. Soy formula may be suitable in older infants, but cross-reactivity between cow’s milk and soy protein is relatively common.
- In breastfed infants with food allergic manifestations (e.g. early-onset atopic dermatitis, food protein-induced proctocolitis), a maternal elimination diet may control symptoms in the infant. Prolonged maternal elimination diets should be supervised by a dietitian.
- Lactose intolerance is the most common food intolerance and is treated with a low-lactose diet. Causes of secondary lactose intolerance, such as celiac disease, should be considered in the differential diagnosis.

| Table 4. Formulas used in the treatment of infants with food allergies or intolerances |
|-----------------------------------------------|-----------------------------------------------|
| Type of formula | Features and indications |
| Partially hydrolyzed cow’s milk-based formula | Contains relatively large cow’s milk protein fragments/peptides Not suitable for treatment of cow’s milk allergy May play a role in allergy prevention in early infancy |
| Extensively hydrolyzed cow’s milk-based formula (whey-predominant or casein-predominant) | First treatment choice for formula-fed infants with cow’s milk allergy Contains small cow’s milk protein peptides Residual allergenicity due to trace amount contamination with relatively intact cow’s milk proteins Infants with previous cow’s milk anaphylaxis require introduction of extensively hydrolyzed formula under medical observation Not tolerated by approximately 10–20% of infants with cow’s milk allergy |
| Amino acid-based formula | Protein-free formula (contains mixture of free amino acids) Nutritionally complete formula Treatment of choice if infant is intolerant to extensively hydrolyzed formula (including infants with multiple food allergy of infancy) |
| Soy formula | No longer considered appropriate as cow’s milk protein substitute in infants under 6 months of age May play a role in treatment of cow’s milk allergy in older infants |
| Lactose-free cow’s milk-based formula | Contains intact cow’s milk protein (same as in standard cow’s milk-based formula) Useful in infants with transient lactose intolerance (e.g. after acute gastroenteritis) Not suitable for infants with secondary lactose malabsorption due to cow’s milk protein-induced enteropathy |
References


Introduction

Gastroesophageal reflux (GER) refers to the passage of gastric contents into the esophagus or oropharynx. GER can be a daily, normal physiological occurrence. Gastroesophageal reflux disease (GERD), however, refers to the troublesome symptoms and complications that may develop secondary to persistent GER [1]. GERD complications include esophagitis, growth disturbance, feeding aversion, and respiratory disease.

Although the physiology of GER is different in children and adults, the primary pathophysiological mechanisms resulting in GERD are similar in all age groups, even as early as 38 weeks gestation. These mechanisms include transient relaxation of the lower esophageal sphincter (LES), inhibition of esophageal body peristalsis, and an inappropriate decrease in LES resting tone in the absence of swallowing [2–4].

Though virtually all infants regurgitate, about 3% of normally developing infants have clinically significant GERD. In most infants, GER symptoms, especially regurgitation, peak by 2–4 months and resolve by 1 year of age [5]. Contrary to previous beliefs, GERD may not be outgrown. Recent studies indicate that persistent GERD in children up to age 2 years may recur in the preadolescent or older child [6]. Additionally, once GERD is clinically or endoscopically evident in a child or adolescent, it can be a chronic life-long condition in a substantial percentage of these patients.

Although no population-based epidemiological studies have been performed, for reasons that remain unexplained GERD is being increasingly recognized in children particularly in countries where GERD was relatively uncommon [7]. There is also a rising prevalence of severe GERD-related
outcomes such as erosive esophagitis and Barrett's esophagus. Thus, earlier detection and treatment of GERD in children may lead to better outcomes later in life. This review will describe the symptoms, diagnosis, and management of this chronic disease in children.

**Symptoms**

Normal physiological GER is substantially more common in the first year of a child’s life compared to adults. Gastric contents may frequently reflux into the esophagus (30 ± 20 times daily) [8]. Normal regurgitation appears to peak at 2–4 months of age and soon after 1 year of age resolves (fig. 1).

Beyond this age, persistent regurgitation is replaced by other GERD-related symptoms, including abdominal pain, morning nausea or discomfort [9]. Heartburn, a cardinal symptom of GERD in adults, generally does not manifest until adolescence. Table 1 lists manifestations that should raise concern for GERD. Infants can present with frequent regurgitation, vomiting, poor weight gain, feeding refusal, and irritability.

However, irritability is not very specific and often is a poor indicator of pathologic acid reflux. In addition, the combination of arching of the back, torsion of the neck, and lifting of the chin suggests Sandifer syndrome. This GERD-associated condition, often confused with torticollis, has its peak occurrence at 18–36 months of age. Conversely, the presence of rectal bleeding, eczema, and a family history of atopic disease may suggest cow’s milk protein allergy rather than GERD.

GERD-specific symptoms in childhood vary by age and change in character as the child gets older, if GERD persists over time. Extra-esophageal manifestations of GERD may be more common than previously believed and can be the only symptoms of GERD. Of the extra-esophageal GERD-associated conditions, head and neck manifestations include dental erosions, pharyngitis, and vocal cord disorders such as laryngitis. Respiratory manifestations include nocturnal cough or wheezing, reactive airway disease, asthma and recurrent pneumonias. Although it is postulated that apnea is a sequelae of GERD, studies showing benefit of acid suppression in infants with apnea are lacking.
Diagnosis

A thorough history and physical examination can be the key to diagnosis of GERD, with specific attention to the child’s age, as well as the character and frequency of GERD-related symptoms. The original North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition clinical practice guidelines for GERD in children recommended that a trial of acid suppression should be considered based on history and physical examination (fig. 2). The proton pump inhibitor (PPI) test has been effective in adults, with resolution of symptoms being the diagnostic test for GERD.

In the U.S., a random sample of the American Academy of Pediatrics was recently surveyed on their knowledge, attitudes and practice styles with respect to pediatric GERD, and responded that, if testing for GERD in children, the upper gastrointestinal series (UGI) would be their first test of choice [10]. However, the UGI is a reasonable approach to assess for anatomic abnormalities (e.g., hiatal hernia, vascular rings, intestinal malrotation) amenable to surgical correction. Unfortunately, the UGI is at best 50% sensitive and specific for diagnosing GERD [11].

In cases where the diagnosis of GERD may not be obvious based on symptoms, esophageal pH monitoring can accurately measure the frequency and duration of acid exposure. In order to ‘prove’ and document GERD, a symptom diary is essential. In addition, the pH metry study may also be useful in the child who has an incomplete symptom response and/or intermittent symptom breakthrough despite therapy. However, studies demonstrated variability of pH monitoring in over 34% of subjects, and pH-monitoring systems cannot measure non-acid reflux. Thus, multi-channel intraluminal impedance monitoring, particularly when combined with pH metry, may be the most accurate way of evaluating acid and non-acid reflux. For patients above 6 years of age, wireless pH metry systems provide continuous monitoring for 48–72 h, allowing participation in normal daily activities. Validation of both the wireless pH metry system and impedance is still lacking in pediatric age groups.

If GERD symptoms do not resolve or return after a 2- to 4-month trial of acid suppression, referral to the pediatric gastroenterologist for esophagogastroduodenoscopy (EGD) with biopsies is suggested. In addition, when hematemesis or occult bleeding occurs in the face of GERD symptoms, EGD may be indicated to assess the presence and severity of GERD. EGD can also detect erosive (macroscopic) or histologic (microscopic) esophagitis, strictures, Barrett’s esophagus, and eosinophilic esophagitis, a potential GERD masquerader [12, 13]. Other diagnostic modalities in-
include esophageal manometry (used to document transient LES relaxations and esophageal body peristalsis abnormalities), nuclear scintigraphy, and esophageal ultrasound, but there are few studies justifying their use routinely in children.

**Treatment**

The primary goals of treatment are to resolve symptoms, improve overall quality of life, and resolve and prevent complications of GERD. In ‘uncomplicated’ GERD, conservative measures such as thickening the formula, giving smaller feeds more frequently, and upright positioning for at least 30 min after feeds may be sufficient to decrease regurgitation. In addition, thickening can increase the caloric density of the formula, which may benefit infants who have weight gain issues as a result of GERD (1 tablespoon of rice cereal per 2 ounces of formula increases the caloric density to 27 kcal per ounce). Prone positioning may decrease regurgitation but is not recommended due to the increased risk for sudden infant death syndrome. However, these approaches may be ineffective in resolving the acid-related consequences of reflux. If milk protein intolerance or allergy is suspected, a 2- to 4-week trial of protein (partial whey or casein) hydrolysate formula should be considered (fig. 3).

When pharmacotherapy is required, H₂-receptor antagonists may be effective for mild GERD in children. However, tachyphylaxis develops quickly with symptom recurrence within days to a few weeks of treatment. Thus PPIs are becoming the preferred treatment for GERD in infants and children. PPIs have been shown in pediatric studies to be safe and effective. Omeprazole at doses ranging from 0.5 to 4 mg/kg has been shown to decrease GERD symptoms in children after only 14 days [14]. Lansoprazole given at doses of 15 or 30 mg once or twice daily, based on weight, resulted in resolution of erosive esophagitis after 3 months of treatment in one study [15]. Recently, esomeprazole has been shown to improve GERD-related symptoms and resolve extra-esophageal manifestations after 8–12 weeks of therapy in children 12–17 years of age [16]. In

![Algorithm for the evaluation and management of suspected GERD in infants. H2RA = H₂ receptor antagonist; PPI = proton pump inhibitor; EGD = esophagogastroduodenoscopy; UGI series = upper gastrointestinal series.](image-url)
Regurgitation and Gastroesophageal Reflux

In general, studies have suggested beginning PPI treatment at a dose of 1 mg/kg per day divided into one or two doses. Prokinetics such as metoclopramide are effective in approximately 50% of children with GERD; however, they can be associated with neurological side effects. Thus, usage should be limited to children with regurgitation-predominant symptoms. Finally, anti-reflux surgery should be considered in children with complications of GERD such as aspiration (with or without oral-pharyngeal dysfunction), Barrett’s esophagus, and esophageal strictures. Predictors of fundoplication success are response to medical therapy and surgeon experience [11].

Conclusions


References

Feeding disorders are surprisingly common in children. It has been estimated that 25–35% of normal children have a mild feeding disorder, and up to 80% of children with developmental disabilities have difficulty in feeding. Further analysis of prevalence indicates that half of all toddlers are not consistently hungry at mealtime, and about one third show food selectivity [2]. Severe feeding problems are noted with greater frequency in children with physical disabilities (26–90%) and among those with medical illness and prematurity (10–49%) [3–5].

Children with feeding disorders are a heterogeneous group but can be broadly divided into three categories: children who are healthy and without significant comorbid conditions; those who have digestive disorders (gastroesophageal reflux being the most common), and those with special needs, especially chronic neurologic disorders. Feeding irregularities in healthy children are often temporary, and most resolve spontaneously. In others, however, the problem may be persistent and require intensive professional care.

Feeding disorders have multiple etiologies which include medical, behavioral, nutritional, psychological and environmental factors (table 1). However, rarely does a child with a feeding
disorder have a single etiology causing poor oral nutrition. Given that children’s feeding progresses in a biologic, maturational, learning and nurturing environment, feeding disorders are best diagnosed and treated by multi-faceted approaches that encompass evaluation of these processes. This is best accomplished with an interdisciplinary variety of pediatric specialists including physicians, nurse practitioners, nutritionists, occupational therapists, speech therapists, psychologists and social workers. This team must establish a diagnostic and therapeutic plan based on a careful prenatal, birth and neonatal, and current history. This includes the onset, course, frequency of feeding patterns and behaviors as well as assessing medical conditions that may be associated with the feeding difficulties. Medical issues are commonly associated with pediatric feeding disorders and may be etiologic factors or comorbid conditions.

<table>
<thead>
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<th>Conditions associated with pediatric feeding disorders</th>
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<tr>
<td><strong>Total food refusal</strong></td>
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<td><strong>Food refusal by volume</strong></td>
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<td><strong>Food refusal by texture</strong></td>
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<td><strong>Food refusal by type</strong></td>
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<td><strong>Bottle dependency</strong></td>
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<td><strong>Maladaptive behaviors</strong></td>
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<tr>
<td><strong>Disorders of the oral and pharyngeal phases of swallowing</strong></td>
</tr>
<tr>
<td><strong>Anatomic lesions</strong></td>
</tr>
<tr>
<td>Cleft lip and/or palate</td>
</tr>
<tr>
<td>Pierre-Robin sequence</td>
</tr>
<tr>
<td>Choanal atresia</td>
</tr>
<tr>
<td>Laryngeal clefts</td>
</tr>
<tr>
<td>Macroglossia</td>
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<tr>
<td>CHARGE association</td>
</tr>
<tr>
<td><strong>Acquired structural abnormalities</strong></td>
</tr>
<tr>
<td>Dental caries</td>
</tr>
<tr>
<td>Tonsillar hypertrophy</td>
</tr>
<tr>
<td>Viral/inflammatory stomatitis</td>
</tr>
<tr>
<td>Retropharyngeal mass</td>
</tr>
<tr>
<td>Candida stomatitis</td>
</tr>
<tr>
<td><strong>Cardiopulmonary effects</strong></td>
</tr>
<tr>
<td>Chronic lung disease</td>
</tr>
<tr>
<td>Complex congenital heart disease</td>
</tr>
<tr>
<td>Reactive airway disease</td>
</tr>
<tr>
<td>Tachypnea</td>
</tr>
<tr>
<td><strong>Neuromuscular disorders</strong></td>
</tr>
<tr>
<td>Familial dysautonomia</td>
</tr>
<tr>
<td>Cerebral palsy</td>
</tr>
<tr>
<td>Pseudo-bulbar palsy</td>
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<tr>
<td>Bulbar atresia or palsy</td>
</tr>
<tr>
<td>Cranial nerve anomalies</td>
</tr>
<tr>
<td>Muscular dystrophic disorders</td>
</tr>
<tr>
<td>Arnold-Chiari malformation</td>
</tr>
<tr>
<td>Myelomeningocele</td>
</tr>
<tr>
<td><strong>Intracranial mass lesions</strong></td>
</tr>
<tr>
<td><strong>Disorders of the esophageal phase of swallowing</strong></td>
</tr>
<tr>
<td>Cricopharyngeal achalasia</td>
</tr>
<tr>
<td>Tracheoesophageal fistula</td>
</tr>
<tr>
<td>Esophageal mass</td>
</tr>
<tr>
<td>Esophageal stricture</td>
</tr>
<tr>
<td>Esophageal web</td>
</tr>
<tr>
<td>Esophageal rings</td>
</tr>
<tr>
<td>Vascular rings/aberrant vessels</td>
</tr>
<tr>
<td>Foreign bodies</td>
</tr>
<tr>
<td><strong>Disorders of the lumen</strong></td>
</tr>
<tr>
<td>Peptic esophagitis</td>
</tr>
<tr>
<td>Candida esophagitis</td>
</tr>
<tr>
<td>Viral esophagitis</td>
</tr>
<tr>
<td>‘Pill’ esophagitis</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
</tr>
<tr>
<td>Behcet syndrome</td>
</tr>
<tr>
<td><strong>Motility disorders</strong></td>
</tr>
<tr>
<td>Achalasia</td>
</tr>
<tr>
<td>Diffuse esophageal spasm</td>
</tr>
<tr>
<td>Chronic pseudo-obstruction</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
</tr>
<tr>
<td>Polymyositis</td>
</tr>
<tr>
<td><strong>Genetic disorders</strong></td>
</tr>
<tr>
<td>Prader-Willi syndrome</td>
</tr>
<tr>
<td>Trisomy 21</td>
</tr>
<tr>
<td>Cornelia de Lange syndrome</td>
</tr>
<tr>
<td>Velo-cardio-facial syndrome</td>
</tr>
<tr>
<td>Rett syndrome</td>
</tr>
<tr>
<td><strong>Metabolic disorders</strong></td>
</tr>
<tr>
<td>Urea cycle abnormalities</td>
</tr>
<tr>
<td>Hereditary fructose intolerance</td>
</tr>
<tr>
<td>Hypothyroidism</td>
</tr>
<tr>
<td><strong>Miscellaneous</strong></td>
</tr>
<tr>
<td>Gastroesophageal reflux</td>
</tr>
<tr>
<td>Constipation</td>
</tr>
<tr>
<td>Gas-bloat syndrome</td>
</tr>
<tr>
<td>Dumping syndrome</td>
</tr>
<tr>
<td>Food allergies</td>
</tr>
<tr>
<td>Sensory loss (visual/auditory impairment)</td>
</tr>
</tbody>
</table>
Evaluations also include careful physical examinations and diagnostic studies (table 2) to help determine associated medical conditions and evaluate swallowing anatomy and safety (table 3).

Most children with feeding disorders will spontaneously improve with time. However, strategies are available to their caregivers to improve mealtime behaviors and minimize the food refusal or food selectivity behavior. These include establishing mealtime consistency, minimizing meal disruption, repeatedly presenting the food on a number of routines, and developing a positive reinforcement pattern for appropriate mealtime behavior.

Therapy directed at resolving complex feeding issues requires the professional team to identify the predisposing, precipitating and perpetuating factors involved in the feeding pattern of abnormal eating behaviors [6] (table 4). Once airway safety has been established, a variety of treatment approaches are available to increase oral intake, advance food texture and, if possible, progress to self-feeding. Medical therapies are directed toward alleviating organically based feeding difficulties and often may require medication, surgical intervention and employing alternate routes of nutrition such as enteral tube feeds to deliver sufficient calories.

Initial therapy is aimed at making changes to feeding routines, schedules, environment and skills of the child’s caregivers. This includes addressing issues such as sleep patterns, bowel habits and sibling interactions. Dieticians are an integral part of the treatment process as often rela-

---

**Table 2. Diagnostic evaluation of patients with feeding disorders**

<table>
<thead>
<tr>
<th>Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detailed history and physical examination</td>
</tr>
<tr>
<td>Upper gastrointestinal contrast radiography</td>
</tr>
<tr>
<td>Esophagogram</td>
</tr>
<tr>
<td>Small bowel follow through</td>
</tr>
<tr>
<td>Video-fluoroscopic swallow study</td>
</tr>
<tr>
<td>Gastric emptying study</td>
</tr>
<tr>
<td>pH monitoring</td>
</tr>
<tr>
<td>Esophagogastroduodenoscopy with biopsies</td>
</tr>
<tr>
<td>Antroduodenal manometry</td>
</tr>
<tr>
<td>Fiberoptic endoscopic evaluation of swallowing</td>
</tr>
<tr>
<td>Complete blood count</td>
</tr>
<tr>
<td>Comprehensive metabolic panel</td>
</tr>
<tr>
<td>Thyroid function</td>
</tr>
<tr>
<td>RAST analysis for food allergies</td>
</tr>
<tr>
<td>Skin test for food allergies</td>
</tr>
<tr>
<td>Plasma amino acids</td>
</tr>
<tr>
<td>Urine organic acids</td>
</tr>
<tr>
<td>Karyotype</td>
</tr>
</tbody>
</table>

**Table 3. Oral motor assessments and therapy**

<table>
<thead>
<tr>
<th>Assessment of swallowing function and safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical evaluation – assess head and neck position, tongue and jaw movement, dentition, airway sounds, speech assessment and seating position</td>
</tr>
<tr>
<td>Modified barium swallow assesses oral, pharyngeal and upper esophageal phases of swallowing</td>
</tr>
<tr>
<td>Texture assessment</td>
</tr>
<tr>
<td>Non-nutritive oral stimulation</td>
</tr>
<tr>
<td>Decreases oral hypersensitivity</td>
</tr>
<tr>
<td>Facilitates management of secretions</td>
</tr>
<tr>
<td>Establish or retrain swallowing mechanism</td>
</tr>
<tr>
<td>Develop oral motor movement for sound production</td>
</tr>
</tbody>
</table>

**Table 4. Development of feeding disorders**

<table>
<thead>
<tr>
<th>Predisposing factors</th>
<th>Precipitating factors</th>
<th>Perpetuating factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperament of child and caregivers</td>
<td>Acute illness</td>
<td>Continued pain or discomfort</td>
</tr>
<tr>
<td>Recurrent illness</td>
<td>Injury</td>
<td>Reinforcement from behaviors</td>
</tr>
<tr>
<td>Low resilience</td>
<td>Pain</td>
<td></td>
</tr>
<tr>
<td>Parental depression or poor coping ability</td>
<td>Child endangerment or neglect</td>
<td></td>
</tr>
</tbody>
</table>

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tively simple concepts of food preparation, food storage and nutritional value of foods are poorly understood. In some circumstances, enteral feeding management is an essential part of the treatment process and adjustments should be made prior to the development of a more intrusive treatment procedure.

Specialized feeding is not limited to routes of feeding. The diet itself is crucial to maintain the wellbeing of the child. This includes appropriate understanding of sound nutritional guidelines, and also includes the use of specialized formulas to deliver appropriate nutrients to the gastrointestinal tract due to impairment of the gastrointestinal tract or specific metabolic needs, e.g. ketogenic diet.

Applied behavior analysis is utilized to treat feeding problems including food refusal, food selectivity and disruptive mealtime behaviors. Applied behavior analysis can be used successfully to treat caregiver mismanagement of feeding issues. These principles include establishment of systematic feeding routine, altering the texture of food presented to the rewarding appropriate eating behavior and ignoring food refusal behavior. Negative or punishing behavior is discouraged. Parent training involves instruction, discussion, skill acquisition, role playing and practice techniques with trained clinicians.

The importance of understanding and treating oral-motor issues in children with feeding difficulties cannot be underestimated. Oral motor techniques to improve muscle tone and postural control provide important foundations to the eating process. The use of adaptive seating systems is a key component to feeding children with physical disabilities, providing head, neck and truncal support.

Conclusions

- Feeding disorders in young children are surprisingly common
- Feeding disorders are multifactorial and occur as a result of medical, sensory, social and environmental reasons
- Enteral feeding should be utilized for those who are unable to eat orally or who are very malnourished
- While on enteral feeds, children should continue to receive nutritive and non-nutritive oral motor therapy
- Caregiver training and education are essential for maintenance of feeding success
- Most children with feeding disorders can be effectively treated, but often require an experienced feeding team

References

Introduction

Provision of adequate nutrition for preterm infants presents unique challenges. Meeting the very high nutrient needs of these infants (table 1) is difficult and fraught with risks related to the physiological limitations of these infants [for an overview see 1, 2]. The most important of these limitations is immaturity of the intestinal tract. It necessitates the use of parenteral nutrition during the early days and weeks of life in infants with early preterm birth. Parenteral nutrition carries various risks, including the risk of infections and the risk of metabolic complications. Immaturity of the intestinal tract is also the reason why preterm infants are susceptible to necrotizing enterocolitis (NEC). Although enteral feedings per se do not cause NEC, feedings increase the risk of NEC and therefore are used very cautiously. The multiple risks associated with the provision of nutrients explain why the nutrient intakes received by preterm infants tend to fall short of requirements. The growth failure that results from inadequate nutrient intakes is predictive of impaired neurocognitive development later in life. Efforts to improve nutrient intakes are therefore important.

Nutritional support of preterm infants occurs in two distinct phases which each carry their own risks and challenges. During the early phase nutrients are predominantly provided via the parenteral route, while enteral (trophic) feedings assist the immature intestinal tract in its gradual maturation but provide few nutrients to the infant. During the late phase infants are on exclusive enteral feedings and are expected to grow normally. If provided the necessary nutrients, preterm infants may also show catch-up growth, i.e., are making up some of the ground typically lost during the early phase.
For normal or catch-up growth to happen, the infant must receive the requisite amounts of nutrients. Failure to receive adequate amounts of nutrients, principally protein, leads to growth failure. The amounts of protein and energy required for normal growth are summarized in table 1. The requirements for catch-up growth are higher (see below).

**Early Nutrition**

During the immediate postnatal period, the objective of nutritional support is twofold, to provide an uninterrupted flow of nutrients so that the anabolic state can continue with minimal interruption, and to support the immature gastrointestinal tract in its transition to a mature state. As this maturation progresses, a gradual shift occurs from exclusive parenteral nutrition to exclusive enteral nutrition. The early nutrition period ends when full enteral feedings are reached.

**Parenteral Nutrition**

In immature infants, parenteral nutrition should begin immediately (within 2 h of birth) and must provide, as a minimum, glucose, amino acids, electrolytes, calcium, phosphorus and magnesium. It is acceptable for the amount of amino acids to be less than 3.5 g/kg per day (table 1) for a short period. The initiation of lipid emulsion is less urgent and a delay for up to 48 h is probably acceptable. The initial rate need not be more than 0.5 g lipids/kg per day. The efficacy and safety of parenteral nutrition starting immediately after

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**Table 1. Requirements for protein and energy (based on factorial approach)**

<table>
<thead>
<tr>
<th>Body weight, g</th>
<th>500–700</th>
<th>700–900</th>
<th>900–1,200</th>
<th>1,200–1,500</th>
<th>1,500–1,800</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetal weight gain, g/day</td>
<td>13</td>
<td>16</td>
<td>20</td>
<td>24</td>
<td>26</td>
</tr>
<tr>
<td>Fetal weight gain, g/kg per day</td>
<td>21</td>
<td>20</td>
<td>19</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td><strong>Protein, g/kg</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inevitable loss</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Growth (accretion)</td>
<td>2.5</td>
<td>2.5</td>
<td>2.5</td>
<td>2.4</td>
<td>2.2</td>
</tr>
<tr>
<td><strong>Required intake</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parenteral</td>
<td>3.5</td>
<td>3.5</td>
<td>3.5</td>
<td>3.4</td>
<td>3.2</td>
</tr>
<tr>
<td>Enteral</td>
<td>4.0</td>
<td>4.0</td>
<td>4.0</td>
<td>3.9</td>
<td>3.6</td>
</tr>
<tr>
<td><strong>Energy, kcal/kg</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loss</td>
<td>60</td>
<td>60</td>
<td>65</td>
<td>70</td>
<td>70</td>
</tr>
<tr>
<td>Resting expenditure</td>
<td>45</td>
<td>45</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Miscellaneous expenditure</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Growth (accretion)</td>
<td>29</td>
<td>32</td>
<td>36</td>
<td>38</td>
<td>39</td>
</tr>
<tr>
<td><strong>Required intake</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parenteral</td>
<td>89</td>
<td>92</td>
<td>101</td>
<td>108</td>
<td>109</td>
</tr>
<tr>
<td>Enteral</td>
<td>105</td>
<td>108</td>
<td>119</td>
<td>127</td>
<td>128</td>
</tr>
<tr>
<td><strong>Protein/energy, g/100 kcal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parenteral</td>
<td>3.9</td>
<td>3.8</td>
<td>3.5</td>
<td>3.1</td>
<td>2.9</td>
</tr>
<tr>
<td>Enteral</td>
<td>3.8</td>
<td>3.7</td>
<td>3.4</td>
<td>3.1</td>
<td>2.8</td>
</tr>
</tbody>
</table>
birth have been demonstrated [3]. Full parenteral nutrition should be maintained until enteral feedings of 20 ml/kg per day are regularly tolerated. As feedings are increased, the amount of parenteral nutrition is tapered, with total (parenteral plus enteral) intake of nutrients always at full level.

Enteral Nutrition
The anatomically and functionally immature intestine can undergo maturation in a relatively short time, given the necessary stimulation is provided in the form of trophic feedings. Enteral (at least trophic) feedings should be started on the first day of life. Feeding volumes initially may be as low as 2 ml every 6 or 4 h. In very premature infants, stimulation of the gut is initially the sole objective of enteral feedings. Motility serves as a marker of gut maturation and is monitored clinically through the assessment of gastric residuals. As gastric emptying improves, it is assumed that the ability to digest and absorb nutrients also is improving. Gastric emptying thus serves as an important clinical guide in early enteral feeding. The risk of NEC is quite low with trophic feedings but increases subsequently as feeding volumes increase.

The preferred trophic feeding is maternal milk or, when not available, donor milk. Donor milk may also be used to supplement maternal colostrum, which is usually available only in small amounts during the first few days. Donor milk is pasteurized and free of viruses such as HIV and cytomegalovirus. Although pasteurization diminishes some of its protective factors, donor milk still is protective against NEC [4] and is preferable to formula. Preterm formula must be used when human milk is not available. Feeding volumes may be kept low for several days or may be increased as gastric residuals diminish. At each new level, the adequacy of gastric emptying (absence of gastric residuals) must be ascertained before the feeding volume is further increased. The presence of gastric residuals does not require cessation of feedings as long as there are no signs suggestive of NEC. The use of trophic feedings leads to earlier establishment of full feedings and to earlier hospital discharge without a significant increase in NEC [5]. Feeding volumes should be increased by 20 ml/kg each day or less. Although more rapid increases are safe, intestinal maturation requires time and more rapid increases are not recommended. When feeding volumes are 80–100 ml/kg per day, fortification of breast milk should be initiated. Parenteral nutrition should be discontinued when enteral feedings provide more than 90% of required nutrient intakes.

Late Nutrition
The late period begins when full feedings are established and parenteral nutrition is discontinued. Feedings are fortified human milk or, when not available, special formulas with a protein content of 3 g/100 kcal. Breast milk must be fortified to increase the protein and mineral content in order to meet the preterm infant’s high needs. Any of the commercially available fortifiers are suitable, although all provide less than an optimal amount of protein. The objective of nutrition is to allow growth to proceed parallel to intrauterine growth channels. Also, infants who have fallen behind during the early phase may be able to show catch-up growth. The protein and energy intakes listed in table 1 are needed to support growth at the intrauterine rate. If the infant is to catch up in growth, intakes must be further increased by 10–20%.

Providing the required protein intake is important but difficult. If the infant is fed formula, the protein/energy ratio (3.0 g/100 kcal) tends to be close to the required ratio, except for very small infants. If the infant is fed fortified human milk, the protein/energy ratio is almost always too low and hence the protein intake inadequate [6]. The reason is that fortifiers are de-
signed to raise the protein/energy ratio from 2.1 g/100 kcal (typical of human milk at 2 weeks after parturition) to about 3.0 g/100 kcal. As table 1 shows, such a protein/energy ratio is adequate for larger infants only. More importantly, the protein content of human milk after 2 weeks of lactation is less than 2.1 g/100 kcal and the protein/energy ratio of fortified milk is therefore much less than 3.0 g/100 kcal and inadequate for small infants (<1,500 g). For small infants, additional protein should be added. This can be done by adding more than the standard amount of fortifier (e.g., 50% more) or by adding extra protein. A method for BUN-guided fortification has been described by Arslanoglu et al. [7].

Conclusions

- Nutritional support must begin at birth and should be complete at all times
- The smaller the infant, the more important it is not to allow a nutrient deficit to accrue
- Parenteral nutrition initially is the sole provider of nutrition in very preterm babies
- In very preterm babies, enteral (trophic) feeds initially have the sole function of supporting the immature gastrointestinal tract in its transition to a mature state
- Once gastric residuals have subsided, feedings are advanced slowly until full feedings are reached
- Preferred feeding is breast milk, which must be fortified with protein and minerals to meet the high needs of preterm infants
- Routine fortification is inadequate for very small infants and additional protein should be provided

References

3 Nutritional Challenges in Special Conditions and Diseases

3.14.1 Feeding the Low Birthweight Infant in a Resource-Restricted Environment

Fredrick N. Were

Key Words
Nutrient needs, high • Enteral feeds • Crystalloids • Mothers’ milk • Feed volume • Micronutrients

Key Messages
- Enteral feeds must be started early and aggressively increased to nutritionally adequate volumes whenever the option of total parenteral nutrition is not available.
- The use of large total daily feed volumes in smaller more frequent aliquots is helpful when high-density nutrient milk preparations are not available to provide adequate nutrition at lower volumes.
- Whenever possible, breast milk fortification or supplemental preterm formula is preferred for the most vulnerable infants, such as very low birthweight infants and those with postnatal growth failure.
- Vitamins and iron should be supplemented especially in those on unfortified breast milk or standard formula.

Introduction

Preterm and low birthweight infants have higher nutritional needs than their more mature and larger counterparts. Quantitative analysis indicates that such infants need intakes of 3.6–4. g and as much as 120 kcal/kg/day to achieve adequate growth if fed enterally [1]. In countries with restricted health budgets, these requirements must always be derived from milk preparations, even in the smallest or sickest babies, if total parenteral nutrition is not available. The milk produced by mothers who deliver prematurely (PM) contains 1.9 (range 1.1–3.5) g protein and 75 kcal/100 ml during the first 14–28 days following delivery [2]; however, this drops to 0.9 g protein and <70 kcal thereafter [2]. Alternative feeds available in poor countries include cow’s or standard formula with grossly inadequate nutritional value (table 1). When available, breast milk fortification and preterm formula (PTF) are used to easily achieve the needs of small infants [3, 4]. The main challenge in resource-restricted environments is therefore to innovate strategies of maximizing nutrition from available/affordable milk products. The innovations must be undertaken while minimizing the risk of feed intolerance, necrotizing enterocolitis [5], and overload-related cardiac complications [6].

The suggested strategies include: maximal utilization of PM, pooling PM to be used by older infants, use of larger volumes (>240 ml/kg/day) after 14–28 days, selective breast milk fortification and deliberate supplementation of mother’s milk with PTF [7, 8].

This chapter reviews the use of crystalloids during the acute phase, the rapid transition from crystalloids to milk, the optimizing of full enteral feeding, and the addition of some essential micronutrients as innovations to use when under-funded.
Initial Crystalloids

Many small infants develop early complications making immediate enteral feeding hazardous. Even healthy babies may not tolerate enteral feeds immediately after birth. Intravenous crystalloids are often required to support circulation, blood sugar and electrolytes as summarized in Table 2 during this period. During this phase, infants can receive small feed volumes (trophic feeds) to stimulate their gut [9].

<table>
<thead>
<tr>
<th>Type of milk</th>
<th>Birthweight category</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;1.0 kg</td>
</tr>
<tr>
<td>BM, 1st 28 days</td>
<td>220</td>
</tr>
<tr>
<td>BM, &gt;28 days/standard formula</td>
<td>400</td>
</tr>
<tr>
<td>PTF</td>
<td>170–200</td>
</tr>
<tr>
<td>Fortified BM</td>
<td>200</td>
</tr>
<tr>
<td>1:1 PTF and BM &gt;28 days</td>
<td>280–300</td>
</tr>
<tr>
<td>1:1 BM and donor PM</td>
<td>300</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Food value of milk, per 100 ml</th>
<th>Protein, g</th>
<th>Energy, kcal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Term BM</td>
<td>0.9</td>
<td>60–75</td>
</tr>
<tr>
<td>Preterm BM</td>
<td>1.9</td>
<td>70–75</td>
</tr>
<tr>
<td>PTF</td>
<td>2.0–2.4</td>
<td>80–85</td>
</tr>
<tr>
<td>Fortified BM</td>
<td>2.0</td>
<td>74–93</td>
</tr>
<tr>
<td>1:1 PTF and BM</td>
<td>1.5–1.7</td>
<td>70–80</td>
</tr>
<tr>
<td>1:1 BM and donor PM</td>
<td>1.5</td>
<td>70–75</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Daily requirements of micronutrients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A</td>
</tr>
<tr>
<td>Vitamin C</td>
</tr>
<tr>
<td>Vitamin D</td>
</tr>
<tr>
<td>Vitamin E</td>
</tr>
<tr>
<td>Vitamin B1</td>
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<tr>
<td>Vitamin B2</td>
</tr>
<tr>
<td>Vitamin B6</td>
</tr>
<tr>
<td>Iron</td>
</tr>
<tr>
<td>Folate</td>
</tr>
</tbody>
</table>

BM = Breast milk; PM = breast milk from mothers who delivered prematurely; PTF = preterm formula.

Table 1. Required volumes of milk needed to provide 4 g/kg of protein and the nutritional value of available milk preparations

Enteral Feeds

Initiation

It is possible for even the smallest or the sickest infants to be safely fed enterally if the primary condition is stable. Healthy infants can feed on day 1 while sick ones start from days 2–4 (fig. 1). Though necrotizing enterocolitis has been associated with enteral feeding [10], there is no conclusive evidence that early feeding adds to the risk. Full feeds should therefore be achieved by day 5–10 in most infants.
**Table 2. Administration of crystalloids**

<table>
<thead>
<tr>
<th>Birthweight kg</th>
<th>Daily fluid intake, ml/kg</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>day 1</td>
<td>day 2</td>
</tr>
<tr>
<td>≤1.0</td>
<td>100</td>
<td>120</td>
</tr>
<tr>
<td>1.0–1.5</td>
<td>80</td>
<td>100</td>
</tr>
<tr>
<td>&gt;1.5</td>
<td>60</td>
<td>80</td>
</tr>
</tbody>
</table>

| Type of crystalloid | 10% dextrose | 10% dextrose with 2–3 mmol/kg/day of sodium and potassium, or mixture of Darrow’s, Hartman’s or Ringer’s at 4:1 ratio with 50% dextrose |

**Breast Milk**

The breast milk of mothers in advanced lactation has a nutritional value of 0.9 g protein and 60–70 kcal/100 ml (table 1). During the first 14–28 days, however, mothers who deliver prematurely produce milk (PM) with a protein content ranging from 1.1 to 3.5 (median of 1.9) g/100 ml [2]. During the first 14 days, infants can therefore grow on 220, 200 and 180 ml/kg/day if weighing <1.0, 1.0–1.5 and >1.5 kg, respectively. Thereafter, infants weighing <1.5 kg will require up to 400 ml/kg of their mothers’ milk for adequate nutrition.
Such large volumes are unlikely to be tolerated in practice and may even overload the infants with lipids and other nutrients. In the absence of fortification the highest tolerated volume should be tried even in the smallest infants. This may succeed with smaller aliquots given every 1 or 2 h for babies weighing <1.0 and 1.0–1.5 kg. Donor PM at a 1:1 ratio with own mother’s milk will also allow the use of lower volumes (280–300 ml/kg/day). The preferential use of donor PM keeps the volumes at pre-day-14 levels. The HIV status of donors must be known to exclude the risks of HIV transmission.

**Micronutrients**

The daily requirements of micronutrients including vitamins and iron (table 1) should be given to all very low birthweight infants as recommended [10] and indicated in figure 1.

**Breast Milk Fortification and Preterm Formula**

Where available, this option makes it possible to provide the requirements for most small babies with the traditional 180–200 ml/kg/day (table 1). If only limited financial reserves are available for selective fortification or PTF, then infants weighing <1.5 kg or those who either fail to grow well on the large volumes of mothers’ milk recommended above or develop volume-related intolerance can benefit from the technology.

As has been reported [7, 8], deliberate 1:1 mixing of PTF with breast milk reduces the volume required for better growth (table 1). The required volumes for different types of milk are summarized in table 1.

**Conclusions**

- In the absence of total parenteral nutrition, enteral feeds should be started on day 1 for all stable babies and not delayed beyond day 4 for even the sickest infants
- The best milk strategy available should always be preferred. Larger volumes of nutritionally poorer milk should be adopted as tolerated. Milk pooled from mothers who delivered prematurely offers an option to cut down on volumes
- With a smaller budget, breast milk fortification and/or preterm formula can be used for special groups such as very low birthweight infants and those with poor growth on maximal volumes of standard milk
- Vitamins and iron should be provided to all infants born weighing less than 1.5 kg

**References**

Diabetes mellitus type 1 is the most frequent endocrinological disturbance of childhood. It amounts to 5–10% of the total diabetic population. In more than 95% of affected children it is an autoimmunological disease. The aim of therapy is a near normal serum glucose concentration and the avoidance of hypoglycemia and ketoacidosis, in order to minimize the risk of diabetic angiopathy.

Disorders requiring anabolism and prevention of protein degradation represent a threat with respect to the accumulation of toxic metabolites. This review addresses phenylketonuria (accumulation of phenylalanine), maple syrup urine disease (accumulation of leucine) and urea cycle disorders (accumulation of ammonia, NH₃).

Disorders requiring glucose stabilization are those threatening hypoglycemia and can pathophysio logically be reduced to disturbances of glycogen degradation and gluconeogenesis. The latter can be described as having a defect of gluconeogenetic enzymes and with an insufficient energy supply for gluconeogenesis (fatty acid oxidation defect).

Disorders requiring the restriction of energy turnover (glucose to avoid lactic acidosis) are defects located in the mitochondria (mitochondriopathies) and mainly comprise pyruvate dehydrogenase (PDH) deficiency and disorders of the respiratory chain.

Diabetic Ketoacidosis

Rehydration
In most cases of diabetic ketoacidosis dehydration amounts to about 10%. To stabilize the circulatory volume, half of the calculated fluid requirement should be administered within the first 8 h and the second half in the following 16 h. However, as we are dealing with a hypertonic dehydration despite a low serum sodium concentration, serum osmolality should be lowered not faster than 4 mosm/l per hour. For rehydration
0.9% NaCl solution or Ringer-lactate solution is adequate. When the serum glucose concentration is lowered to \( \sim 250 \text{ mg/dl} \) (~14 mmol/l) the infusion should contain glucose (i.e. 0.9% NaCl:5% glucose = 1:1) to avoid the risk of dropping into hypoglycemia. In conscious patients, rehydration can be assisted by oral fluid intake.

**Insulin Supplementation**

Continuous intravenous infusion of about 0.05 IU regular (short-acting) insulin/kg per hour. The amount of insulin is adapted after hourly controls of the serum glucose concentration.

**Anti-Acidosis Treatment**

Because rehydration is the most effective form of anti-acidotic treatment, only in extremely severe cases (pH 7.0 or below; HCO\(_3\)-<5 mmol) should a slight buffering with NaHCO\(_3\) be considered. Aggressive buffering may result in paradoxic acidosis of the cerebrospinal fluid with ensuing loss of consciousness.

**Electrolyte Supplementation**

In diabetic ketoacidosis the following deficits can usually be assumed: sodium 5–6 mmol/kg, chloride 3–5 mmol/kg, and potassium 3–6 mmol/kg. The serum potassium concentration should be monitored closely because effective treatment of diabetic ketoacidosis tends to induce pronounced hypokalemia.

**Dietetics of Diabetes Mellitus Type 1**

**Dietetic Treatment of Diabetes Mellitus Type 1**

There is no need to use any of the commercially available special diabetic food products. Qualitatively valuable, mainly homemade foods may be used. Carbohydrates should be classified according to their glycemic index. A trend towards a mainly vegetarian diet should be encouraged, but in this case attention needs to be paid to iron, calcium, vitamin D and vitamin B\(_{12}\) intakes. Ideally 50% of the calories should be consumed as carbohydrates with a low glycemic index.

If a conventional insulin therapy (2–3 injections/day with a mixture of rapid and intermediate acting insulin) is performed, e.g. in the toddler age group, a strictly regulated and disciplined dietary intake should be followed. The dietary intake should be harmonized with physical activity and the amount of insulin injected. Normally the required amount of insulin is \( \sim 0.8–1.0 \text{ IU/kg per day} \). In teenagers an intensified insulin treatment (\( \geq 4 \text{ injections/day supplying basal insulin, meal insulin in doses proportional to nutritional load, and extra insulin when needed to correct high glucose levels} \)) allows a sufficiently liberal food intake, adapted to the needs of daily life.

**Disorders Requiring Anabolism and Avoidance of the Accumulation of Toxic Metabolites**

**Phenylketonuria**

Deficient activity of phenylalanine hydroxylase (>400 mutations known) leads to a markedly increased serum phenylalanine (Phe) concentration, while tyrosine is normal or decreased. The prevalence in central Europe is \( \sim 1:10,000 \), in Turkey and Ireland \( \sim 1:5,000 \). Early treatment, starting in the neonatal period, allows normal psychomotor development of the child.

The principle of dietary treatment is a restricted protein intake to the amount needed for protein synthesis, with concomitant supplementation of a Phe-free amino acid preparation to cover the total protein requirements, aiming at a plasma Phe concentration of 0.7–4 mg/dl (42–240 \( \mu \text{mol/l} \)) up to 10 years and 0.7–15 mg/dl (42–900 \( \mu \text{mol/l} \)) up to 16 years. Because of the rapid growth of infants and young toddlers, more Phe per kilogram bodyweight is tolerated in this age group than in older children. The need for additional tyrosine intake is covered by commercial Phe-free protein supplements.
The Phe requirement in the first year of life is about 30–50 mg/kg per day. Starting in the 3rd year of life this requirement is about 10–20 mg/kg per day (table 1) [1].

Affected infants may be partially breastfed: first a predetermined amount of the Phe-free preparation is given, followed by feeding at the mother’s breast. The amount of breast milk tolerated will usually be about half the amount taken by a healthy infant.

The diet should be continued for life; however, after puberty serum Phe concentrations up to 20 mg/dl (1,200 μmol/l) are tolerated.

### Maternal Phenylketonuria

Adult women with phenylketonuria wishing to become pregnant must lower their serum Phe concentration to <4 mg/dl (240 μmol/l) already before conception to prevent congenital heart defects, microcephaly and mental retardation in the child. With ongoing pregnancy Phe tolerance increases. Tyrosine must be supplemented.

### Maple Syrup Urine Disease

Maple syrup urine disease is caused by a deamination defect of the branched chain amino acids (leucine, isoleucine and valine). The iso-leucine metabolite 2-keto-3-methylvaleric acid causes the characteristic maple syrup smell. The forms of manifestation are: severe in the first days of life, mild intermittent form, and the thiamine responsive form. In mild forms, the first symptoms may manifest as late as in adulthood.

The treatment principles at manifestation are:

1. Stop protein administration to avoid accumulation of toxic ketoacids
2. Forced diuresis (furosemide 0.5–1 mg/kg every 6–12 h) up to hemofiltration for the elimination of ketoacids
3. Buffer therapy of acidosis
4. Intravenous glucose 10–20 g/kg per day; if needed + insulin (0.01–0.5 IU/kg per hour). Insulin additionally stimulates the uptake of branched chain amino acids into muscle cells
5. Thiamine (5–10 mg/day)
6. Energy supply (>100 kcal/kg per day), including calories from fat (e.g. 0.5–1 g/kg per day i.v.)

Long-term treatment principles are similar as in phenylketonuria: restriction of the protein intake to reduce the uptake of leucine, isoleucine and valine. Rapidly growing children have a higher tolerance of the branched chain amino acids (table 2) [2]. The total protein requirement is covered with commercially available amino acid mixtures free of branched chain amino acids.

Breast milk has very low leucine concentrations and should therefore be used preferentially. As in phenylketonuria the affected infant receives about half the amount of milk as a leucine-isoleucine-valine-free formula, and the other half as breast milk. Food products used after the breastfeeding period are selected according to nutritional tables.

Organic acidemias, such as propionic acideemia, methylmalonic acidemia, and isovaleric acidemia, present in a similar way and the treatment principles correspond to those mentioned above. With the accumulation of high amounts of activated organic acids (Acyl-CoAs) the carnitine

---

### Table 1. Recommended phenylalanine intake in patients with phenylketonuria

<table>
<thead>
<tr>
<th>Age, months</th>
<th>Phenylalanine, mg/kg per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>34 (27–41)</td>
</tr>
<tr>
<td>12</td>
<td>28 (21–35)</td>
</tr>
<tr>
<td>18</td>
<td>26 (20–32)</td>
</tr>
<tr>
<td>24</td>
<td>23 (18–28)</td>
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<tr>
<td>30</td>
<td>22 (17–27)</td>
</tr>
<tr>
<td>36</td>
<td>20 (15–25)</td>
</tr>
<tr>
<td>42</td>
<td>19 (14–24)</td>
</tr>
<tr>
<td>48</td>
<td>18 (13–23)</td>
</tr>
<tr>
<td>54</td>
<td>17 (12–23)</td>
</tr>
<tr>
<td>60</td>
<td>17 (12–23)</td>
</tr>
<tr>
<td>66</td>
<td>16 (12–20)</td>
</tr>
<tr>
<td>72</td>
<td>15 (10–20)</td>
</tr>
</tbody>
</table>
requirements are increased, and patients are supplemented with about 100 mg L-carnitine/kg per day.

Urea Cycle Defects

The enzymatic defects of the urea cycle are localized both in- and outside the mitochondria. Their characteristic symptom is protein intolerance with hyperammonemia, leading to severe encephalopathy. In severe forms the acid-base homeostasis is altered towards alkalosis. Ammonia detoxification via glutamate and glutamine formation leads to an energy deficit via the depletion of citric acid cycle metabolites. This is thought to be the cause of brain edema.

Treatment Principles at Manifestation
Plasma ammonia concentrations of >200 μmol/l (340 μg/dl) require emergency treatment:
(1) Stop protein intake
(2) Intravenous glucose and lipids in amounts to support anabolism
(3) Forced diuresis
(4) Hemodialysis at plasma ammonia concentrations of >400 μmol/l (680 μg/dl)
(5) Sodium phenylbutyrate 250 mg/kg in 10% glucose (NH₃ elimination as N in phenyl-acetylglutamine) or sodium benzoate 250 mg/kg in 10% glucose (NH₃ elimination as N in hippuric acid). During phenylbutyrate therapy the plasma concentrations of the branched chain amino acids must be watched
(6) Arginine hydrochloride 210 mg (1 mmol)/kg in 10% glucose

Principles of Long-Term Treatment
Protein restriction should be carried out in combination with points 5 and 6 above. Protein degradation should be minimized by provision of an adequate energy intake. For optimal growth the provision of a supplement with essential amino acids is needed to direct surplus N into protein synthesis (table 3) [3]. This mixture should be rich in branched chain amino acids and poor in tryptophan (high tryptophan concentrations lead to a lack of appetite). The administration of arginine is essential because it is not sufficiently formed during inadequate urea synthesis.

Disorders Requiring Glucose Stabilization

Medium-Chain Acyl-CoA Dehydrogenase Deficiency
Medium-chain acyl-CoA dehydrogenase deficiency is the most frequent fatty acid oxidation defect presenting clinically after a fasting period of some hours or during minor infections and

Table 2. Leucine, isoleucine and valine requirements of patients with maple syrup urine disease

<table>
<thead>
<tr>
<th>Age</th>
<th>Leucine mg/kg per day</th>
<th>Isoleucine mg/kg per day</th>
<th>Valine mg/kg per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–6 months</td>
<td>100–60</td>
<td>90–30</td>
<td>95–40</td>
</tr>
<tr>
<td>6–12 months</td>
<td>75–40</td>
<td>90–30</td>
<td>60–30</td>
</tr>
<tr>
<td>1–4 years</td>
<td>70–40</td>
<td>85–20</td>
<td>85–30</td>
</tr>
<tr>
<td>4–7 years</td>
<td>65–35</td>
<td>80–20</td>
<td>50–30</td>
</tr>
<tr>
<td>7–11 years</td>
<td>60–30</td>
<td>30–20</td>
<td>30–25</td>
</tr>
<tr>
<td>11–15 years</td>
<td>50–30</td>
<td>30–20</td>
<td>30–20</td>
</tr>
<tr>
<td>15–19 years</td>
<td>40–15</td>
<td>30–10</td>
<td>30–15</td>
</tr>
</tbody>
</table>

Table 3. Protein supply in patients with urea cycle defects

<table>
<thead>
<tr>
<th>Age group</th>
<th>Natural protein g/kg per day</th>
<th>Mixture of essential amino acids g/kg per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants</td>
<td>0.5–1.3</td>
<td>0.3–0.6</td>
</tr>
<tr>
<td>Toddlers</td>
<td>0.5–1.0</td>
<td>0.3–0.5</td>
</tr>
<tr>
<td>Schoolchildren</td>
<td>0.5–1.0</td>
<td>0.2–0.3</td>
</tr>
</tbody>
</table>

1 0.6 g essential amino acids correspond to 1 g protein equivalent.
physical stress with lethargy, vomiting, seizures (Reye-like symptoms).

Treatment principles: avoidance of fasting periods; provide an adequate glucose supply using complex carbohydrates, mainly during the night; uncooked cornstarch may be useful; 50–100 mg L-carnitine/kg per day.

Sugar Intolerances

Galactosemia (Galactose-1-Phosphotriuridyltransferase Deficiency)
As galactose is present in breast milk as well as in most infant formulas, the clinical symptoms (vomiting, jaundice, liver function problems leading to disturbed blood coagulation and bleeding disorders) appear with the onset of milk feeding which is usually immediately after birth.

Treatment principles: Avoidance of lactose and galactose intake. The long-term outcome is disappointing because endogenous galactose production during cell turnover (up to ~2 g/day) cannot be stopped.

Hereditary Fructose Intolerance
(Fructose-1-Phosphotrialdolase Deficiency)
The clinical symptoms appear with the first fructose exposure, which depends on the way of feeding and may be at any time during the first year of life (symptoms like in galactosemia).

Treatment principles: Elimination of fructose, sucrose and sorbitol from the diet. A high degree of suspicion with regard to industrial food products (which often contain fructose) has to be developed. Patients generally develop a strong aversion to sweet taste, therefore an unintentional fructose intake is rare.

Glycogen Storage Defect 1
(Glucose-6-Phosphatase Deficiency)
In glycogen storage defect 1 (GSD-1) the generation of free glucose is not feasible, and glucose formation from galactose, fructose or protein is not possible. Serum glucose concentrations are therefore dependent on the intake of free glucose. Fasting tolerance is only about 2 h before hypoglycemia occurs.

Treatment principles: Frequent carbohydrate-containing meals during the day, and continuous glucose intake during the sleeping hours in the night by a nasogastric glucose infusion (10 mg/kg per min) is recommended. Oligosaccharide-containing solutions can be used. Starting in the toddler age group uncooked cornstarch (~2.5 g/kg) can be used to reach a fasting tolerance of up to 7 h. The slow glucose release is only preserved when cornstarch is not heated or mixed with carbonate-containing drinks. A slow glucose release can also be obtained when, e.g., rice is only cooked for 4 min.

Defects of Gluconeogenesis
Deficiencies of pyruvate carboxylase, phosphoenolpyruvate carboxykinase, fructose-1,6-diphosphatase, glucose-6-phosphatase = GSD-1. As gluconeogenesis is active when the liver glycogen stores are depleted, the treatment principle is to supply glucose as early as possible so that gluconeogenesis is not needed. However GSD-1 has to be considered separately (see above).

Disorders Requiring Restriction of Energy Turnover

Pyruvate Dehydrogenase Defect, Citric Acid Cycle Defects, Electron Transport Chain Defects (Mitochondrial Defects)
NADH is produced especially during glucose degradation. Hydrogen processing in the mitochondria finally leads to ATP formation. A disturbance in the metabolic steps of hydrogen processing always leads to a backing up of NADH and thus to lactic acid formation.

Treatment principles: Reduction of glucose administration to reduce lactic acidosis. The nutritional basis of treatment is a ‘ketogenic diet’ with
emphasis on fat and protein intake. Vitamin B₁ (thiamine pyrophosphate) and lipoic acid are the coenzymes of PDH and should be supplemented in PDH deficiency. In cases of respiratory chain defects a cocktail of ‘artificial electron acceptors’ can be tried.

**Conclusions**

**Diabetes**
- No special dietetic food products are necessary
- 50% of the calories as low glycemic index carbohydrates

**Phenylketonuria**
- Infants can be partially breastfed
- The lifelong diet provides limited amounts of natural protein (determined by phenylalanine tolerance) plus a phenylalanine-free amino acid mixture to meet calculated protein requirements
- Female patients desiring pregnancy must limit serum phenylalanine to <4 mg/dl (242 µmol/l) to prevent fetal damage

**Maple Syrup Urine Disease**
- Branched chain amino acid-free amino acid mixture; add isoleucine and valine at abnormal leucine concentrations

**Organic Acidemias**
- Most require L-carnitine (100 mg/kg per day)

**Medium Chain Acyl-CoA Dehydrogenase Deficiency**
- Avoid fasting periods, especially during minor infections and physical stress

**Galactosemia**
- Avoid dietary lactose/galactose

**Hereditary Fructose Intolerance**
- Avoid dietary fructose, sucrose, sorbitol and honey

**Glycogen Storage Defect 1**
- Galactose, fructose and protein cannot be used as sources for glucose
- Frequent supply of glucose/glucose polymers

**References**


Hypercholesterolemia

Berthold Koletzko

Key Words

Hypercholesterolemia, familial · Low-density lipoprotein cholesterol · Dietary treatment · Fat, saturated · Plant sterols

Key Messages

- Children with severe hypercholesterolemia should be diagnosed and treated early to reduce the risk for premature cardiovascular morbidity and mortality.
- Dietary modification can be initiated from the age of 2–3 years onwards.
- Modifying dietary fat intake with limitation of saturated fats and their replacement by monounsaturated and polyunsaturated fats are the most important factors.
- Preferential consumption of complex and slowly digested carbohydrates over sugars moderately reduces plasma cholesterol levels but is often difficult to achieve in children.
- Soluble (but not insoluble) dietary fiber may contribute to cholesterol lowering and may be recommended to selected, highly motivated families.

Introduction

A large body of evidence from epidemiological and intervention studies in adults demonstrates that high plasma concentrations of cholesterol and particularly of low-density lipoprotein (LDL) cholesterol are risk factors for the early development of premature cardiovascular diseases such as coronary heart disease and stroke, and for the associated increased mortality [1, 2]. In children, high plasma cholesterol and LDL cholesterol lead to enhanced early development of vascular damage in autopsy studies, and clinical studies using ultrasound techniques show increased lipid deposition in the vascular intima and decreased vascular distensibility. For the general population, including children, healthy lifestyles and dietary habits that promote cardiovascular health are advocated [2, 3]. Children with markedly elevated cholesterol, for example due to primary genetic disorders such as familial hypercholesterolemia, should be diagnosed early and treated effectively. The basis of intervention in children with hypercholesterolemia is dietary modification, as described here. In selected children who do not achieve a satisfactory reduction in plasma cholesterol concentrations with diet alone, the use of lipid-lowering drugs in addition to diet should be considered.

Lipoproteins

Lipids are transported in the plasma by lipoproteins (table 1), which carry apoproteins that mediate their receptor binding and tissue uptake. Triglyceride-rich chylomicrons are formed in intestinal epithelial cells with absorbed dietary fats, are secreted into the lymph and consecutively transported into the blood stream. Chylomicron triglycerides are hydrolyzed by lipoprotein lipase.
linked to the capillary endothelium. Lipolysis products are taken up and utilized by tissues. Lipoprotein lipase also hydrolyzes triglycerides in very low-density lipoproteins (VLDLs) synthesized in the gut and liver. This lipolysis results in formation of intermediate-density lipoproteins and further of LDL in the circulation. LDLs are rich in cholesterol and apoprotein B100, bind to apoprotein receptors in hepatocytes and peripheral cells, and transport cholesterol to tissues. High plasma concentrations of LDLs lead to increased deposition of cholesterol in the vascular intima, atherosclerotic vascular damage and premature coronary artery disease. LDL cholesterol can be measured directly by using ultracentrifugation, but in clinical practice is usually determined after an overnight fast using the Friedewald formula: LDL cholesterol (mg/dl) = total cholesterol (mg/dl) – HDL cholesterol (mg/dl) – [triglycerides (mg/dl) × 0.2]. (To convert cholesterol in mg/dl into mmol/l multiply by 0.0259.) Increased plasma levels (>30 mg/dl) of lipoprotein (a), an LDL particle with added apoprotein (a), are an independent risk factor for coronary artery disease and juvenile thrombosis. The liver and gut secrete apoprotein A containing high-density lipoprotein (HDL) low in cholesterol (‘nascent HDL’), which takes up cholesterol from tissues and from VLDL and LDL and transports it back to the liver. In contrast to LDL, high plasma levels of HDL are protective against the development of atherosclerotic diseases. While reference values for cholesterol differ among various populations and geographic locations, levels considered desirable in children in the USA are shown in table 2.

<table>
<thead>
<tr>
<th>Table 1. Characteristics of plasma lipoproteins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chylomicrons</td>
</tr>
<tr>
<td>Major lipids</td>
</tr>
<tr>
<td>Major apoproteins</td>
</tr>
<tr>
<td>Formation</td>
</tr>
<tr>
<td>Major function</td>
</tr>
</tbody>
</table>

VLDL = Very low-density lipoprotein; LDL = low-density lipoprotein; HDL = high-density lipoprotein.

<table>
<thead>
<tr>
<th>Table 2. Cholesterol levels considered desirable, borderline and undesirable in children and adolescents (&lt;20 years) by the United States National Cholesterol Education Program [3]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desirable level, mg/dl</td>
</tr>
<tr>
<td>Total cholesterol</td>
</tr>
<tr>
<td>LDL cholesterol</td>
</tr>
<tr>
<td>HDL cholesterol</td>
</tr>
<tr>
<td>Triglycerides</td>
</tr>
</tbody>
</table>

LDL = Low-density lipoprotein; HDL = high-density lipoprotein. To convert values expressed in mg/dl into mmol/l multiply by 0.0259 (cholesterol) or 0.0113 (triglycerides).

Hypercholesterolemia

The heterozygous form of familial hypercholesterolemia is one of the most frequent inherited metabolic disorders, affecting about 1 in 500 newborns in Europe and North America. The under-
lying defect in LDL receptor function is dominantly inherited (i.e. affects ≈50% of children of an affected parent). From the onset of enteral feeding, levels are markedly increased for LDL cholesterol (usually >180 mg/dl), total cholesterol (>250 mg/dl) and apoprotein B (>150 mg/dl; Frederickson hyperlipidemia type IIa). In untreated patients, coronary heart disease may occur already at middle age. Diagnosis is based on repeated measurement of plasma lipoproteins in the fasted state and family history (dominant inheritance), and if desired by molecular genetics. The rare homozygous form of familial hypercholesterolemia is found in 1 in 1,000,000 individuals and leads to excessive levels of cholesterol (>600 mg/dl) from infancy due to practically complete deficiency of LDL receptor function. Affected children develop xanthomas already in the first decade of life and usually die before the age of 20 years unless effectively treated by extracorporeal LDL apheresis or liver transplantation. A phenotype similar to the heterozygous form of familial hypercholesterolemia is found in children with familial defective apoprotein B also leading to defective receptor binding or LDL. Its prevalence is almost as high as the LDL receptor defect. Secondary hyperlipidemias (table 3) are not rare in children and can often be influenced by treating the underlying disorder or by elimination of causative substances. Severe and lasting secondary hyperlipidemias may necessitate treatment similar to primary genetic hyperlipidemias.

**Dietary Treatment of Hypercholesterolemia**

Treatment should achieve a lasting lowering of cholesterol, thereby reducing the risk of premature cardiovascular morbidity and mortality, while supporting a good quality of life and enjoyment of eating, at normal HDL cholesterol (>45 mg/dl). Dietary modification should be considered at LDL cholesterol >130 mg/dl [4] (table 2). Prerequisites for an effective dietary change are good information and motivation of patient and family, which should be supported by repeated counseling and practical training.

Dietary modification can be initiated from the age of 2–3 years onwards [3]. Modifying dietary fat intake is the most important factor. Saturated fatty acids with 12–16 carbon atoms (primarily animal fats and some tropical oils) and trans-isomeric fatty acids (primarily from hydrogenated fats) increase LDL cholesterol (table 4) and should not exceed 8–12% of the dietary energy intake. Dietary fat should preferentially comprise monounsaturated fatty acids (>10% of energy; primarily rapeseed and olive oils), which reduce LDL and increase HDL cholesterol (table 4), and moderate amounts of polyunsaturated fatty acids (7–10% of energy; e.g. corn and sunflower seed oils). Limiting the total fat intake to 30–35% of energy intake contributes to the desired limitation of saturated and trans-fatty acid

**Table 3. Selected secondary hyperlipidemias in children and adolescents**

<table>
<thead>
<tr>
<th>Hypercholesterolemias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute intermittent porphyria</td>
</tr>
<tr>
<td>Anorexia nervosa</td>
</tr>
<tr>
<td>Cholestatic liver diseases</td>
</tr>
<tr>
<td>Cushing syndrome</td>
</tr>
<tr>
<td>Hypothyreosis</td>
</tr>
<tr>
<td>Nephrotic syndrome, renal failure, dialysis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hypertriglyceridemias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Glycogen storage disease type 1</td>
</tr>
<tr>
<td>Pancreatitis</td>
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<table>
<thead>
<tr>
<th>Combined hyperlipidemias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Glycogen storage disease type 1</td>
</tr>
<tr>
<td>Hepatitis</td>
</tr>
<tr>
<td>Nephrotic syndrome, renal failure, dialysis</td>
</tr>
<tr>
<td>Drugs: β-blockers, corticoids, estrogens, progesterone, thiazide diuretics</td>
</tr>
<tr>
<td>Pregnancy</td>
</tr>
<tr>
<td>Systemic lupus erythematoses</td>
</tr>
</tbody>
</table>
Dietary cholesterol intake should be <300 mg/day [1–3]. Preferential consumption of complex and slowly digested carbohydrates over sugars (mono- and disaccharides) moderately reduces plasma cholesterol levels. Soluble dietary fiber (e.g., parts of oat bran, psyllium) may also contribute to cholesterol lowering, but not insoluble fiber (e.g., wheat bran) [5]. However, diets with strictly limited sugar and high fiber content are difficult to maintain for many children and should only be recommended for selected, highly motivated families.

Patients and their family members require intensive dietary counseling by a physician and a dietician or nutritionist. Concomitant to dietary treatment, normal weight and regular physical activity are encouraged and smoking is strongly discouraged. Dietary records may indicate existing problems and help achieve improvements. The effect of treatment is assessed by repeated measurements of LDL cholesterol (every 3–6 months). Dietary fat modification may reduce LDL on average by 10–15% [6], with marked inter-individual variation partly predicted by the apoprotein E genotype: individuals with the apoprotein E4 phenotype (≈10–15% of the European population) with higher mean cholesterol and lower triglyceride levels show a stronger response of plasma cholesterol to dietary cholesterol intake. In contrast, individuals with apoprotein E3 (≈75–80% of the population) show a lesser response to dietary cholesterol restriction.

The regular consumption of plant sterols or plant stanols from enriched spreads or other enriched foods (also available as granulates) can markedly reduce plasma LDL cholesterol by an additional 10–15% [7] and is encouraged. If dietary modification alone does not achieve a satisfactory reduction in plasma LDL, additional drug treatment with statins, ezetimibe or anion exchange resins may be considered from the age of about 10 years onwards [8], but diet should be continued.

### Conclusions

- At normal HDL cholesterol (>45 mg/dl), dietary modification should be considered in children with LDL cholesterol >130 mg/dl
- Dietary saturated and trans-fats should be limited to 8–12% of energy intake (E%), while

---

**Table 4. Effects of dietary fats on plasma LDL and HDL cholesterol**

<table>
<thead>
<tr>
<th>Dietary fats</th>
<th>Food sources</th>
<th>Cholesterol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saturated fatty acid (12–16 carbons)</td>
<td>Fatty milk products (butter, cream), fatty meats, coconut oil</td>
<td>↑↑↑↑↑ ↑</td>
</tr>
<tr>
<td>Trans-fatty acids</td>
<td>Hydrogenated fats (deep frying fats, hard margarine, baked goods); ruminant fats (milk, beef, lamb)</td>
<td>↑↑ ↓</td>
</tr>
<tr>
<td>Monounsaturated fatty acids (e.g. oleic acid)</td>
<td>Rapeseed and olive oil, avocado</td>
<td>↓↓ ↑</td>
</tr>
<tr>
<td>Polysaturated fatty acids (e.g. linoleic acid)</td>
<td>Most vegetable oils (e.g. corn oil, sunflower seed oil), soft margarine</td>
<td>↓↓ ↓ (at high intakes)</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>Eggs, offal</td>
<td>↑ =</td>
</tr>
</tbody>
</table>

LDL = Low-density lipoprotein; HDL = high-density lipoprotein.
References


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Enteral Nutrition in Inflammatory Bowel Disease

Anne M. Griffiths · Megan Carricato

3.17 Enteral Nutrition in Inflammatory Bowel Disease

Introduction

Enteral feeding of formulated food can be used to correct or prevent malnutrition in inflammatory bowel disease. Its additional benefit as primary therapy was fortuitously discovered when Crohn disease patients given exclusive enteral nutrition pre-operatively experienced improvement not only in their nutritional status as intended, but also in clinical and laboratory parameters of intestinal inflammation [1]. Since then enteral nutrition has been an alternative to corticosteroid treatment of active Crohn disease, which is employed more often in children than adults and is more widely accepted in Europe than in North America [2]. Efficacy is supported by data from randomized controlled trials versus corticosteroids, and from comparative trials of different formulae [3, 4]. The mechanism of action remains conjectural, but may involve alteration in the enteric microflora, known to be important in Crohn disease pathogenesis [5].

Treatment algorithms for Crohn disease are changing rapidly. Increased and earlier use of immunomodulatory drugs and the availability of biologic agents have reduced dependence on corticosteroids and have made mucosal healing a realistic goal. Nevertheless, for patients willing to accept dietary restrictions and to comply with the demands of its therapeutic regimens, exclusive enteral nutrition remains a safe alternative option. The focus of this chapter will be on the use of enteral nutrition as primary therapy of intestinal inflammation. It aims to instruct physicians in the selection of patients most likely to respond, and to provide a very practical guide to implementation.
Treatment of Active Crohn Disease

Most data concerning the efficacy of enteral nutrition in treating active Crohn disease relate to clinical endpoints (i.e. improvement in symptoms and laboratory markers of inflammation). Clinical response to enteral nutrition has been associated with endoscopic healing in uncontrolled studies [6].

Patient Selection

Roughly 50–60% of Crohn disease patients treated with enteral nutrition in clinical trials achieve clinical remission [3]. As with all therapies, response rates vary depending on the characteristics of the patient population. Patients with macroscopic inflammation located predominantly in the small intestine are most likely to be successfully treated with enteral nutrition. Patients with Crohn disease confined to the colon are generally considered to respond less reliably [7]. Recent onset disease may be more responsive than disease of longer duration [3]. Enteral nutrition has not been used to treat active ulcerative colitis.

Therapeutic Regimens

Exclusive versus Supplementary Enteral Nutrition

To be successful, enteral nutrition should be administered as the sole source nutrition. Allowance of regular food during treatment of active disease appears to compromise efficacy [8], and may also render the child satiated, and less able to tolerate the desired amounts of formulated food. Oral intake of water and/or clear (see-through) fluids are allowed.

Mode of Administration

Liquid diets may be sipped orally (see discussion of palatability below), or administered via a silastic nasogastric feeding tube (size 6 or 8 French). When a nasogastric feeding tube is used, most children learn to insert the tube themselves at night and to administer the required volume of formula overnight. The tube is removed each morning to facilitate normal daytime activities. When use over a period of months is contemplated, an indwelling gastrostomy tube may be inserted.

Target Volume and Calories

Enteral nutrition should be prescribed in the amount necessary to provide 100% of the patient’s estimated caloric and protein requirements. Patients with Crohn disease fail to down-regulate their resting energy expenditure in the presence of malnutrition, likely due to effects of proinflammatory cytokines [9]. Energy requirements may be calculated using normal predictive equations with the patient’s ideal bodyweight for height, or using the current weight with allowance for catch-up weight gain (approximately 20% extra calories) [10].

Table 1. Protocol for the gradual increase in feeds

<table>
<thead>
<tr>
<th>Initial hourly infusion rate</th>
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</thead>
<tbody>
<tr>
<td>20–40 ml/h orally</td>
</tr>
<tr>
<td>1–2 ml/kg per hour (using actual body weight)</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Increasing enteral feeds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase by 10 ml every 6–8 h (as tolerated) until 24-hour infusion goal rate is reached (should take 36–48 h to reach goal)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cycling enteral feeds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduce the number of hours of enteral feeding by 2–3 h each night as tolerated. Divide the total 24-hour goal volume by the desired number of hours for the enteral feed to determine the nasogastric feed rate</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Final goal of overnight feeds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feeds should run for 10–14 h overnight (dependent on lifestyle and tolerance) Maximum feed rate is approximately 6–8 ml/kg per hour</td>
</tr>
</tbody>
</table>
Infusion rates should be increased in a step-wise manner considering individual tolerance. A sample protocol for the gradual increase to full feeds is given in Table 1. Most young patients aim ultimately to complete the necessary infusion over a 10- to 14-hour period each night.

Choice of Formula

Polymeric, peptide-based and amino acid-based formulae have all been used to treat active Crohn disease [3]. There is general agreement that the protein content of liquid diets does not influence efficacy [3]. Dietary lipids, however, can modulate inflammation by a variety of mechanisms which influence the cellular production of cytokines and eicosanoids [11, 12]. Excess n-6 polyunsaturated fatty acids (PUFAs) would be expected to attenuate the effect of enteral nutrition in treating Crohn disease, whereas a relative increase in n-3 PUFAs might be beneficial.

Given the influence of fat content on efficacy, a conventional elemental liquid diet (because of the low fat content) is recommended to optimize the likelihood of response, if nasogastric tube feeding is to be employed. The treatment benefit of a low-fat, even n-3 PUFA-enriched elemental diet, compared to a conventional polymeric diet is admittedly small (<30% difference in response rates) [13]. Therefore, if a child or adolescent is determined to drink (rather than enterally administer) formula, a polymeric liquid diet would be more appropriate because of its greater palatability.

Duration of Exclusive Enteral Nutrition

The required duration of exclusive enteral nutrition has not been well defined. Improvements in clinical and laboratory parameters occur quickly, often by 2 weeks. Most gastroenterologists, however, suggest continuing therapy for a minimum of 4 weeks, longer if the child has not yet reached his/her ideal weight.

Reintroduction of Solid Food

Although some clinicians have investigated the merits of a specific exclusion diet following induction of clinical remission by exclusive enteral nutrition, most pediatric gastroenterologists simply reintroduce foods gradually. Particularly if the patient is known to have a relatively stenosed segment of intestine, it may be prudent to offer a low fiber diet initially, following completion of the enteral nutrition regimen. A sample regimen for food reintroduction is given in the table 2.

Maintenance of Clinical Remission

One of the limitations of liquid diet therapy has been the observed tendency for symptoms to recur promptly following its cessation. In most studies 60–70% of patients experience a relapse within 12 months of stopping enteral nutrition.

Two nutritional strategies can be considered to maintain remission: firstly, ‘cyclical exclusive enteral nutrition’, meaning nocturnal infusion of a liquid diet and avoidance of regular food in 1 of 4 months [14], or secondly, ‘supplementary enteral nutrition’, i.e. continuation of nocturnal nasogastric feeding 4–5 times weekly as supplement to an unrestricted ad libitum daytime diet [15].

Facilitation of Linear Growth

Impairment of linear growth commonly complicates pediatric Crohn disease. The major contributing (and inter-related) factors are the direct growth-inhibiting effects of proinflammatory cytokines produced by the inflamed intestine and chronic undernutrition [16]. Inappropriate use of chronic corticosteroid therapy will also impede linear growth. Treatments which are steroid-sparing and which induce and
sustain mucosal healing will be associated with reduced cytokine production and linear growth facilitation. Resumption of normal linear growth during enteral nutrition maintenance regimens is a marker of therapeutic success. Conversely, if a child merely gains weight but does not grow in height, it can be assumed that the inflamed intestine is not healing, and that other methods of treating the inflammation must be adopted.

**Conclusions**

- Exacerbations of Crohn disease, particularly involving the small intestine, may be treated with 4–6 weeks of exclusive enteral nutrition
- Because relapse is common following cessation of enteral nutrition, strategies to maintain remission must be planned
- Nutritional strategies include cyclical exclusive enteral nutrition (1 of 4 months) or nocturnal supplementary enteral nutrition (in addition to regular ad libitum daytime intake)
- Normal (and catch-up) linear growth are markers for the success of therapy

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**Table 2. Sample regimen for reintroduction of solid foods**

<table>
<thead>
<tr>
<th>Day of introduction</th>
<th>Description of foods</th>
<th>Examples of foods</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–4</td>
<td>Low fiber grains</td>
<td>White flour breads/bagels/buns/plain pasta/roti/flatbread/rice Plain crackers, pretzels, plain cookies (e.g. arrowroot, digestive) Hot cereals: cream of wheat Cold cereals (dry): low fiber, low fat (e.g. no granola) Plain muffins without nuts or dried fruit</td>
</tr>
<tr>
<td>5–9</td>
<td>Low fat/fiber meat and alternative sources</td>
<td>Plain and tender cuts of chicken/turkey/lamb/veal/beef/pork Low fat fish Smooth low fat peanut butter (limited amounts) Tofu Eggs (prepared with little to no fat) Note: avoid fried, cured, and processed meats; regular fat peanut butter, dried or canned peas, beans, lentils</td>
</tr>
<tr>
<td>10–14</td>
<td>Low fiber vegetables and fruit</td>
<td>Raw fruits without membrane and skin All canned/stewed fruits without skin and seeds Tender, cooked vegetables, no skins/seeds Note: vegetables and fruit should be prepared using low fat cooking methods Soups with allowed meat, vegetables, rice, noodles (avoid highly seasoned soups, cream soups)</td>
</tr>
<tr>
<td>15–17</td>
<td>Low fat dairy products</td>
<td>Low fat milks, yogurts, cheeses</td>
</tr>
<tr>
<td>18</td>
<td>Regular diet as tolerated</td>
<td>Increase fat and fiber gradually to assess tolerance</td>
</tr>
</tbody>
</table>
References


Introduction

Cystic fibrosis (CF) is the most common life-threatening autosomal recessive disease in Caucasians with an incidence of 1 in 2,500 live births. The disease is caused by mutations in the cftr gene on chromosome 7 which codes for a cAMP-regulated chloride channel [1]. Non-functioning CFTR protein affects epithelial ion and water transport in a variety of organs including the respiratory, gastrointestinal, hepatobiliary, reproductive and sweat glands. The lack of CFTR function in the pancreatic duct is responsible for obstruction and autodigestion of the pancreas in utero leading to exocrine pancreatic insufficiency (PI) in 85% of CF infants.

The early growth of infants with CF PI is dependent on the age at diagnosis. Clinical diagnosis may be difficult unless meconium ileus occurs, typically in only 15% of the cases. The remaining patients are diagnosed later, mainly presenting as failure to thrive with steatorrhea accompanied in some cases with respiratory symptoms. An increasing number of countries have initiated newborn screening for CF using a serum marker of PI, which has been shown to facilitate an earlier diagnosis with better growth and nutritional status [2]. Longer-term studies after neonatal screening are now revealing reduced pulmonary disease progression [3].

Numerous studies have shown that underweight and poor linear growth in children and malnutrition in adults are independent factors predicting mortality [4, 5]. Together with this, undernutrition has been shown to have an adverse effect on the outcome of lung transplantation [6]. These data reinforce the importance of prevention and early detection of growth failure leading to the aggressive management of nutritional deficits at all ages. This has led to the publication of nutritional guidelines in Europe and in North America [7, 8].
Infants

The evaluation of an infant with CF should be expedited. If PI is established by tests for steatorrhea and indirect pancreatic function tests, pancreatic enzyme replacement therapy should be initiated as soon as possible. Breastfeeding is encouraged. Enzymes are given with all foods and milk products including predigested formulas containing medium-chain triglyceride. Babies require powder which should be taken with fruit sauce and a pretreatment application of a thin layer of zinc-based baby ointment to the mouth and perianal area to avoid skin excoriation. The enzymes should be administered at the beginning of and during the meal. The initial dose of enzymes should be approximately 5,000 IU lipase/kg per day. The dose may be increased gradually according to symptoms and objective assessment of growth and fat absorption. In many instances, caloric density needs to be increased and this may be achieved by fortifying breast milk, adding fat or carbohydrate or concentrating the formula. Once solid food is introduced, enzymes should be titrated by fat intake. The maximum dose is 10,000 IU lipase/kg per day. Fat-soluble vitamin (ADEK) supplementation should be initiated according to the current recommendations [7, 8]. Hyponatremic alkalosis may occur in infants especially during the summer months; supplementation with sodium chloride is recommended.

Toddlers

As infants are introduced to table foods, it is important that the diet should be balanced, with moderately increased fat and protein content (table 1). Parents need to be in control, routinely adding calories to maintain growth. The child with CF should avoid low-fat food and grazing. The dietician should promote positive interactions around meals. Mealtime must not turn into a battleground which is the catalyst for poor feeding behavior.

School-Age Children

This is the age at which to encourage the child to obtain a basic knowledge of the physiological processes eventually leading to increasingly taking responsibility for practical enzyme and nutritional management.

Adolescence

This stage is associated with increased growth, puberty and increased physical activity. This adds up to markedly increased nutritional requirements which are often difficult to attain. Pulmonary infections are more common, as is the onset of CF-related diabetes and, in a small minority of cases, CF-related liver disease. Female patients are at a greater risk for nutritional failure at this time [9]. This may be partly due to dissatisfaction with weight and body shape in healthy adolescent females. Growth retardation and pubertal delay occur with increased social pressure and psychosocial stress. These factors must be considered when nutritional advice is provided to teenagers.

Follow-Up

A formal dietary assessment should be undertaken annually. This should incorporate a review of nutritional intake, enzyme dose and timing of administration, and vitamin supplements. An-
Thropometry should be performed regularly and body mass index percentile charts are now considered the most accurate interpretation of nutritional status. Bone health is an increasing concern in CF [10]. Bone mineral density and body composition should be assessed by dual-energy X-ray absorptiometry [11].

**When Things Go Wrong**

Figure 1 demonstrates the pathogenesis of malnutrition in CF [12]. As pulmonary disease worsens and resting energy expenditure increases, other factors predispose to an energy deficit. The frequency and severity of infections increase, inducing anorexia and/or vomiting and reduce intake. Weight loss results causing loss of muscle tissue, respiratory muscle wasting reduces effective coughing further contributing to the deterioration in lung function. Malnutrition is known to cause immune dysfunction. Taken together, a vicious cycle is established leading to further deterioration.

**Management of the Malnourished Child**

Once poor growth is identified, patients must be evaluated more frequently. The visits must include medical, nutritional and behavioral input. Figure 2 shows an algorithm for the workup.

**Nutritional Intervention**

If the reason for the poor weight gain is poor intake, the first strategy must be to gradually increase calories at mealtimes. This may be achieved in mild cases by a step-wise approach. Firstly, to-
together with the parents an ‘individualized plan of action’ surrounding the preferred foods of the child may be used. For example, if the child likes fish, the parents should be encouraged to prepare this in a high-calorie setting by frying the fish and adding mayonnaise. The parents should be encouraged to give ice-cream, cakes and other high-calorie foods with liberal administration of extra oil and glucose polymers. The next stage is the administration of high-energy supplements which have been shown to achieve significant increases of energy intake in some studies [13]. The long-term effect of supplements is controversial and they must not take the place of meals [14]. If this fails, enteral feeding should be commenced [15]. The choice of access should be made together with the family but generally nasogastric feeding is started before gastrostomy placement. Calorically dense formulas (1.5–2.0 kcal/ml) are well tolerated and initially nocturnal infusion is encouraged to promote normal eating behavior during the day. However, in some cases, 24-hour nasogastric feeding may be required. Our experience is that once families see success after 6–8 weeks of nasogastric feeding, gastrostomy placement is welcomed. Patients with excessive nausea, bloating or vomiting may benefit from prokinetic drugs or semi-elemental or elemental formula.

Fig. 2. Plan of action for poor weight gain in cystic fibrosis. GERD = Gastroesophageal reflux disease; CFRD = cystic fibrosis-related diabetes; DIOS = distal intestinal obstruction syndrome; IBD = inflammatory bowel disease.

Conclusions

- The overall goal is that every patient with cystic fibrosis should achieve normal growth
- This requires regular surveillance including age-specific individualized expert advice with nutritional care plans to suit each patient
- Nutritional intervention should be appropriately timed to influence the evolution of the disease
- Nutritional support is an integral part of the care of patients with cystic fibrosis
- At diagnosis all patients require pancreatic and nutritional assessment
- Patients must be carefully monitored and dietary counseling provided
- Nutritional evaluation and support are age-related
- Patients who fail to respond require enteral supplementation
- Nutritional status impacts on the progression of cystic fibrosis
References


Introduction

Adequate enteral nutrition is essential for infants and children with heart disease to sustain appropriate growth in weight and height over time. Acyanotic lesions typically impact weight more than height, whereas cyanotic lesions impact weight and height [1, 2]. Growth parameters for infants and children with congenital heart disease (CHD) are not well established in the literature. Inadequate caloric intake is felt to be a predominant cause of growth failure or failure to thrive in infants with CHD, particularly with hemodynamically significant CHD [1].

Clinically significant CHD and the impact on growth are often most challenging for the practitioner. These infants and children typically are those with cyanotic CHD, large left to right shunt, valve regurgitation, congestive heart failure (CHF), depressed function, or pulmonary hypertension [1]. Any hemodynamic impairment in the presence of CHF can negatively impact the infant or child with CHD [1, 3]. Clinically, CHF is often seen with poor feeding, tachypnea, hepatomegaly and tachycardia [4] (table 1).

Surgical or interventional procedures can include one or multiple procedures over infancy and childhood, placing increased nutritional needs on the infant or child. Failure to provide these nutritional needs can further impact postoperative morbidity and length of stay [5] in addition to long-term growth and development.

A common risk factor for impaired growth in patients with CHD is gastroesophageal reflux (GER), particularly with clinically significant CHD [7]. In addition, the presence of other risk factors for growth impairment include prematurity, genetic and extracardiac anomalies, and recurrent respiratory infections [6, 7]. When contributing risk factors are present, it is essential that these risk factors be addressed with the primary care physician and other specialists collaboratively, thus promoting a multidisciplinary approach to meet the growth and nutritional needs of infants and children with CHD (see fig. 1a and b).
Monitoring Growth and CHD

Surgical or Interventional Procedure
The timing and sequence of surgical and/or interventional catheterization procedures depend on the individual patient’s anatomy, hemodynamic data, and clinical status upon consultation with the pediatric cardiologist and cardiothoracic surgeon. The inability to maintain a steady incline in the plotted growth or a plateau in growth may be an indication that an intervention might be required to promote growth and development.

Medical Management
Medical management of growth disturbances focuses on symptomatic improvement of CHF symptoms and promotion of optimal growth. Under the direction of a pediatric cardiologist, multiple medications are common in the management of CHF and poor ventricular function [1]. Digoxin, diuretics (furosemide, aldactone, aldactazide and diuril), and afterload-reducing agents (captopril, enalapril, and lisinopril) are common medication choices available for use as clinically indicated in consultation with pediatric cardiology. Electrolytes may need to be monitored if increasing the renal solute load with higher concentrations of formula [8], adjusting or maintaining on diuretics, dehydration, viral illness, or intolerance of feeds is a concern. Oxygen therapy may be utilized in those patients with pulmonary hypertension and hypoxemia [1]. Availability of an infant scale sensitive to 10 g or greater is useful in tracking appropriate weight gain in infants with CHD. The literature shows that infants, especially with single ventricle physiology, tend to show a plateau of growth at about 4 months of age [9]. Earlier intervention ultimately provides the patient with less preoperative nutritional depletion and a more hemodynamically stable heart disease lesion at an earlier age.

Optimize Caloric Intake
If gastrointestinal function is adequate, enteral feeds should always be utilized, preferentially over parenteral nutrition. Enteral feeds are more physiologic, safer, more accessible, and cost-effective than parenteral nutrition. Rapid advancement to full enteral feeds as clinically tolerated is becoming more of a current trend in care [3, 5].

Increasing caloric density of feedings is a practical strategy to meet nutritional needs in patients with CHD. Term neonatal goal feedings should target 150 ml/kg per day and 120 kcal/kg per day for patients with significant CHD, such as shunt-dependent single ventricle anatomy. Given the higher caloric needs of these patients with hemodynamically significant CHD, breast milk is often not optimal for growth when utilized solely.

The caloric density of breast milk can be increased by adding powdered formula to reach about 80–90 kcal/100 ml. Non-breastfeeding infants may receive commercially available stan-

<table>
<thead>
<tr>
<th>Table 1. Cardiac lesions at risk for growth delay [1, 2, 6]</th>
</tr>
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<tbody>
<tr>
<td>Acyanotic CHD lesions: weight growth disturbance^a</td>
</tr>
<tr>
<td>– Aortic stenosis</td>
</tr>
<tr>
<td>– Pulmonary stenosis</td>
</tr>
<tr>
<td>– Coarctation of the aorta</td>
</tr>
<tr>
<td>– Ventricular septal defect^b</td>
</tr>
<tr>
<td>– Patent ductus arteriosus^b</td>
</tr>
<tr>
<td>– Atrial septal defect^b</td>
</tr>
<tr>
<td>– Atrial ventricular valve regurgitation^b</td>
</tr>
<tr>
<td>– Semilunar valve regurgitation – less common^b</td>
</tr>
<tr>
<td>Cyanotic CHD lesions: weight and height growth disturbance^c</td>
</tr>
<tr>
<td>– Double outlet right ventricle</td>
</tr>
<tr>
<td>– Transposition of the great arteries</td>
</tr>
<tr>
<td>– Tetralogy of Fallot with or without pulmonary atresia</td>
</tr>
<tr>
<td>– Tricuspid atresia</td>
</tr>
<tr>
<td>– Hypoplastic left heart syndrome</td>
</tr>
</tbody>
</table>

^a If significant shunting and/or presence of pulmonary hypertension is noted, then height disturbances may be observed.
^b Lesions prone to pulmonary over-circulation have a greater impact on growth.
^c Hypoxemia accompanied by CHF has a greater impact on growth. Hypoxemia length in years is thought to impact growth retardation.

E
dard formulas (60–70 kcal/100 ml). Standard caloric preparation of breastmilk or formula can be increased by adding more powder to water ratio or, additionally, with fortification options (MCT oil or protein supplements) to achieve ≈80–90 kcal/100 ml with reasonable patient tolerance. Feedings of ≈100 kcal/100 ml are also an option but carry a higher risk of intolerance in infancy. Increasing caloric density can decrease the feeding volumes if GER and volume sensitivity are an issue. Many recipe choices are available in practice, please check with your nutritionist or health care specialist for details on the most practical approach for your patient and family.

Monitoring growth and tolerance of feedings is an important assessment required at the initiation of feeds, advancement of feedings, and over time [10]. Infants and children have been reported to need up to 150 kcal/kg per day or more, particularly with significant CHF, stress, and surgery [6, 11]. Doctor et al. [12] identified growth following cardiac surgery for infants with CHD. Bottlefed infants gained a median of 20 g/day, combination breastfed and bottlefed infants gained a median of 5 g/day, and exclusively breastfed infants lost a median of 49 g/day [12].

Older infants and children can increase their calories by drinking whole milk and high calorie
enteral supplement feedings (see Chapter 3.3). Avoidance of non-caloric drinks should be stressed. Small meal portions and fluid volume can help improve caloric intake. Foods high in protein, carbohydrate, and fats should be encouraged [10].

**Appropriate Consults**
Consultations with a nutritionist, speech therapist, and gastroenterologist can be used when concerns arise regarding optimizing caloric intake, ability to feed orally, strategies to improve oral feeding and decrease fatigue, and tolerance of feedings and/or GER.

**Modes of Enteral Nutrition**
Ideal enteral nutrition is all oral (PO). A notable number of patients are unable to meet their nutritional needs. If oral feeding is insufficient, methods to deliver optimal nutrition in neonates and infants can be achieved by supplemental tube feedings. Steltzer et al. [10] in 2006 describe a feeding strategy for neonates postoperatively following cardiac surgical palliation or complete repair. Rapid advancement of full enteral feeds in neonates and infants is best achieved initially with a more flexible long-dwelling 6.5–8 French nasogastric (NG) feeding tube. These tubes can last for up to 30 days and are more secure than oral gastric tubes. Advancement in the volume and caloric density of feedings can be done with PO/NG feeding plans to promote optimal oral feeding skills. PO feeds no longer than 20–30 min are attempted first, followed by the remaining volume of the feed given via the NG tube by gravity and a pump, with a total PO and NG feeding time of 60 min to allow adequate gastric emptying before the next feed is started.

Once goal calories are reached for 2 or more days and the infant is taking greater than 50% of volume needed to meet goal calories, the NG tube can be removed for a 24-hour trial of all-PO feedings. For example, a 3.5 kg infant status post stage 1 Norwood surgical palliation with shunt depen-
bolus feedings during the day for 4–5 feeds, and a continuous gastric drip feed at night can be used [10]. Jejunal feeds must be given via continuous drip and typically over many hours up to 24 h a day. Schedules can be adjusted to allow for some pump time off, should PO be ordered in the feeding plan in consultation with specialists.

**Non-Cardiac Etiology**

The presence of other risk factors including genetic abnormalities, prematurity, extracardiac anomalies, GER, and recurrent respiratory infections (causing hypoxemia) can also impact growth [1, 7]. Management of GER with an acid-neutralizing agent such as ranitidine, lansoprazole, or omeprazole can be used to prevent erosive esophagitis. To prevent recurrent respiratory infections, palivizumab can be used in high-risk patients with CHD to prevent respiratory syncytial viral infections. Pneumococcal vaccine with continuous antibiotic prophylaxis can be used in patients with asplenia according to the routine immunization guidelines of the American Academy of Pediatrics [1].

**Conclusions**

- A multifaceted approach by healthcare providers is essential to optimize growth and minimize growth disturbances in patients with congenital heart disease (CHD)
- Meeting increased caloric needs is essential to the promotion of growth in infants and children with CHD and requires diligent care by practitioners
- Gastroesophageal reflux is common in infants, particularly with clinically significant CHD, and should be treated
- Prevention of infectious and viral illness is important to prevent dehydration, hypoxia, and further hemodynamic compromise
- Appropriate and early consults with pediatric cardiology, cardiothoracic surgery, nutrition, speech, and gastroenterology should be utilized to promote the growth and development of patients with CHD

**References**

Introduction

Acute Renal Failure
Acute renal failure (ARF) is a sudden, potentially reversible, inability of the kidneys to maintain normal body composition, usually accompanied by oliguria (urine output <0.5 ml/kg per hour or <1 ml/kg per hour in a neonate). This results in salt and water retention, catabolism and metabolic disturbances (low bicarbonate and calcium, high potassium, phosphate and urea).

Dietary intervention is an important part of the management of ARF because it can:
• Prevent catabolism (which contributes to hyperkalemia and hyperphosphatemia)
• Control the volume of fluid intake
• Control metabolic abnormalities (urea, calcium, phosphate, potassium)
• Aid recovery

Chronic Kidney Disease and Dialysis
Adequate nutritional intake can be difficult to achieve in children with chronic renal failure (CKD). This is reflected in poor growth, a progressive problem as renal function deteriorates, so that around 50% of children are below the normal range for height at the start of renal replacement therapy. Short stature is associated with increased morbidity and mortality.

The purpose of dietary intervention in the care of patients with CKD is to:
• Control the symptoms of uremia: inadequate energy from non-protein sources will result in the use of dietary protein for energy, and inadequate protein will result in catabolism of body tissues, both by increasing plasma urea (and potassium) levels
• Prevent complications: particularly renal bone disease due to inappropriate intakes of phosphate and calcium
• Promote optimum growth: by the provision of adequate energy, protein, vitamins and minerals
• Preserve residual renal function: by the provision of adequate, but not excessive, protein
striction so that feeds need to be concentrated and are often unpalatable. Many children, therefore, need enteral feeding. Parenteral nutrition should only be considered if enteral nutrition is not tolerated.

The feed in a child with conservatively managed ARF is particularly important because it can control metabolic and fluid abnormalities so that the need for dialysis can be prevented in the short term. However, if oliguria is prolonged it is rarely possible to provide adequate nutrition so that dialysis becomes necessary to ‘provide space’ for feeds, allowing the diet and fluid allowance to be liberalized.

Dietary specifications for ARF are shown in table 1, and the plan for management in figure 1 [1].

### Chronic Kidney Disease and Dialysis

Anorexia and vomiting (due to abnormal gastric motility and delayed emptying) are common in CKD; therefore, prevention of malnutrition or its treatment is a crucial part of management. Loss of height potential is greatest in infancy (the time when there is the greatest possibility for catch-up growth with nutritional intervention), but can occur at any age [2].

| Table 1. Specifications for the diet in acute renal failure (ARF) |
|----------------------|---------------------------------------------------------------|
| Volume               | Depends on daily fluid removal (urine ± dialysate losses)    |
| Energy               | High, to prevent catabolism                                   |
| Salt                 | Low, except in the unusual circumstance of polyuric ARF      |
| Protein              | Low, to prevent a high plasma urea, unless on prolonged peritoneal dialysis when a higher protein intake may be required |
| Phosphate            | Low, to prevent hyperphosphatemia                              |

**Energy**

Spontaneous oral intake may be inadequate. In the first instance, oral energy supplements may be enough, but if the growth rate begins to decelerate, enteral feeding by nasogastric tube or gastrostomy should be introduced (fig. 2). The aim is to achieve the estimated average requirement, using height age for infants and children <0.4th centile for height. This allows catch-up growth in children under 2 years and gives some benefit in older children. Energy intake may need to be increased to replace feed lost by vomiting. Vomiting may respond to oral prokinetic agents but, if severe, Nissen fundoplication may need to be considered. Children on peritoneal dialysis (PD) absorb glucose from the dialysate (8–12 kcal/kg body weight per day), which should be taken into account in children who gain weight excessively [3].

**Protein**

The aim for protein in CKD is the reference nutrient intake (RNI; again using height age for infants and children <0.4th centile for height), which most children achieve spontaneously. However, when the glomerular filtration rate falls below 25 ml/min per 1.73 m², reduction of protein intake may be necessary. The aim is to keep plasma urea levels <20 mmol/l in infants and children under 10 years, and <30 mmol/l in older children with a normal plasma albumin and normal growth. The first step is to ensure adequate energy intake. If urea levels remain raised despite this, protein intake should then be reduced in 0.2-g/kg steps towards the RNI. Weaning solids should be low in protein and phosphate, e.g. baby rice, pureed fruits and vegetables. As the infant takes more protein from solids, protein intake from milk should be adjusted. Cow’s milk and cow’s milk products may need to be restricted. About 70% of protein should be from high biological value sources, e.g. meat, fish, cheese, eggs or milk (NB: phosphate content may limit the use of cheese, eggs and milk). The re-
maining protein is given as lower biological value sources, e.g. bread, rice, potatoes, pasta and biscuits, allowed freely and only restricted if uremia is uncontrolled despite optimum energy intake. In contrast, children on dialysis need increased protein to compensate for dialysate losses, which are greatest with PD, particularly so in infants and after peritonitis (table 2). Energy-dense feeds providing as much as 2 cal/ml can be used in children on a fluid restriction [4].

**Potassium**
Plasma potassium levels >6.0 mmol/l are most often due to inadequate energy; energy intake should therefore be optimized. If hyperkalemia is >6.5 mmol/l or persistent, a low potassium, low phosphate formula can be mixed with the feed.

**Phosphate and Calcium**
Control of plasma phosphate and calcium is necessary to prevent renal bone disease. Dietary phosphate may need restriction when the glo-

---

**Fig. 1.** Nutritional management of acute renal failure. RNI = Reference nutrient intake.
merular filtration rate falls below the normal range, and almost always when <50 ml/min per 1.73 m² (table 3). Calcium absorption can be low due to inadequate hydroxylation of vitamin D by the kidneys, and can be increased by administration of vitamin D in its active form.

**Vitamins and Minerals**

The RNIs for all micronutrients also apply for children with CKD, except for vitamins A and D. Renal excretion of vitamin A metabolites is impaired in CKD and high plasma levels can be associated with hypercalcemia, anemia and hyperlipidemia. Vitamin D is usually prescribed in its activated form at a dose that requires regular adjustment to prevent renal osteodystrophy. If the diet is inadequate or severely restricted, a vitamin and mineral supplement may be needed. Children on PD require vitamin C, pyridoxine and folic acid to offset dialysate losses. Hyperhomocysteinemia occurs in CKD and is an independent risk factor for cardiovascular disease. Folic acid lowers plasma homocysteine levels, so folic acid supplementation is likely to be beneficial [5].

**Table 2.** Protein requirements in children on dialysis [6]

<table>
<thead>
<tr>
<th>Boys and girls</th>
<th>Recommended protein intake g/kg per day peritoneal dialysis</th>
<th>hemodialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm</td>
<td>3.0–4.0</td>
<td>3.0</td>
</tr>
<tr>
<td>0–6 months</td>
<td>2.1–3.0</td>
<td>2.1</td>
</tr>
<tr>
<td>6–12 months</td>
<td>2.0–3.0</td>
<td>1.5–2.0</td>
</tr>
<tr>
<td>1–2 years</td>
<td>2.0–3.0</td>
<td>1.5–1.8</td>
</tr>
<tr>
<td>2–puberty</td>
<td>2.5</td>
<td>1.0–1.5</td>
</tr>
<tr>
<td>Pubertal</td>
<td>2.0</td>
<td>1.0–1.5</td>
</tr>
<tr>
<td>Postpubertal</td>
<td>1.5</td>
<td>1.0–1.5</td>
</tr>
</tbody>
</table>

**Table 3.** Phosphate restriction in chronic kidney disease (CKD)

<table>
<thead>
<tr>
<th>Bodyweight, kg</th>
<th>Phosphate restriction, mg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10</td>
<td>&lt;400</td>
</tr>
<tr>
<td>10–20</td>
<td>&lt;600</td>
</tr>
<tr>
<td>20–40</td>
<td>&lt;800</td>
</tr>
<tr>
<td>&gt;40</td>
<td>&lt;1,000</td>
</tr>
</tbody>
</table>

**Fig. 2.** Management of feeds in chronic kidney disease (CKD).
Conclusions

Acute renal failure:
- Dietary intervention is necessary from the onset
- Strict control of fluid, energy, protein, potassium and phosphate intake can delay the need for dialysis but make it difficult to achieve adequate nutrition
- Diet can be liberalized by dialysis
- If peritoneal dialysis becomes prolonged, protein intake may need to be increased

Chronic kidney disease and dialysis:
- Individual dietary prescription is essential
- Enteral feeding is indicated in both infants and children when oral intake is inadequate to maintain growth
- The dietary prescription will vary depending on the severity of chronic kidney disease and type of dialysis
- Protein requirements are higher on peritoneal dialysis, particularly after peritonitis
- Vitamin preparations containing vitamin A should not be used

References

Anorexia nervosa (AN) and bulimia nervosa (BN) are eating disorders (EDs) which usually start in the mid-teens and affect around 10% of teenagers. However, a very early start during puberty is becoming more frequent, and occasionally some cases start later, in their 30s or 40s. In both syndromes the patients aim to lose weight and be thin, despite their extreme emaciation, due to a distorted body image and weight (features are shown in tables 1 and 2).

Common features found in these patients are also dissatisfaction and impassive attitudes together with their admiration of misunderstood fashion trends. This lifestyle philosophy could simply be unconscious alarm signs (table 3) expressed by patients towards their families and friends, although this theory is still controversial and under discussion. Table 4 shows other common characteristics upon physical examination.

Patients with EDs are malnourished, although their symptoms are somewhat different from those shown in typical protein-energy malnutrition (table 5). Thus, this particular situation of malnutrition has been defined as relative protein-energy malnutrition [1].

Moreover, alterations in the immune systems of these patients are seen, although surprisingly they have repeatedly been found to be free from immunologically related diseases, such as common viral infections or allergies [2–8]. In fact, data in the scientific literature are very controversial due to the heterogeneity of ED patients.
Table 1. The pathophysiological features of restrictive anorexia nervosa and the binge/purging subtype of anorexia nervosa currently used in the diagnosis

<table>
<thead>
<tr>
<th>Restrictive anorexia nervosa</th>
<th>Binge/purging subtype</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 A disturbed perception of body weight and self-image</td>
<td>1 All the characteristics cited above</td>
</tr>
<tr>
<td>2 Self-starvation with significant weight loss in short periods of time</td>
<td>2 Self-induced vomiting</td>
</tr>
<tr>
<td>3 Primary or secondary amenorrhea</td>
<td>3 Abuse of laxatives, diuretics and anorexigens</td>
</tr>
<tr>
<td>4 Physical hyperactivity and sleep disturbances</td>
<td></td>
</tr>
<tr>
<td>5 Bizarre behavior and attitudes about food</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. The pathophysiological features of the purging type and the non-purging type of bulimia nervosa currently used in the diagnosis

<table>
<thead>
<tr>
<th>Purging type of bulimia nervosa</th>
<th>Non-purging type of bulimia nervosa</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Binge eating, defined as the rapid, compulsive consumption of a large quantity of food in a very short period of time, usually less than 2 h</td>
<td>1 Alternative periods of restricting diets and binge-eating</td>
</tr>
<tr>
<td>2 Self-induced vomiting</td>
<td>2 Compulsive physical exercise</td>
</tr>
<tr>
<td>3 Abuse of laxatives, diuretics and anorexigens</td>
<td>3 Compensatory means (self-induced vomiting, abuse of laxatives, diuretics and anorexigens)</td>
</tr>
</tbody>
</table>

Table 3. The most frequent alarm signs expressed by eating disorder patients

<table>
<thead>
<tr>
<th>1 Moodiness</th>
<th>1 Fragile nails and hair</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 An intense desire to be alone, especially at meal times</td>
<td>2 Dehydrated and pale skin</td>
</tr>
<tr>
<td>3 A compulsive desire to do exercise at any time of the day</td>
<td>3 Orange-colored palms of hands</td>
</tr>
<tr>
<td>4 A significant weight loss or fluctuating weight changes</td>
<td>4 Amenorrhea in women</td>
</tr>
<tr>
<td>5 Multiple and unjustified visits to the toilet</td>
<td>5 Bradycardia and low pulse</td>
</tr>
<tr>
<td>6 Unjustified missing of meals at home</td>
<td>6 When vomiting is present: wounds in the corner of the mouth and Russell signs (wounds in knuckles and palms of hands)</td>
</tr>
</tbody>
</table>

Table 4. Physical examination characteristics

Table 5. Nutrient intake pattern of anorexia nervosa patients

<table>
<thead>
<tr>
<th>1 Primary nutrient inadequacy, avoiding carbohydrate and fat intake</th>
<th>1 Each patient can show variable degrees of malnutrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 Protein intake: apparently quite preserved</td>
<td>2 Adaptive mechanisms triggered by the restricted intakes</td>
</tr>
<tr>
<td>3 Micronutrient deficiencies are not as frequent as expected (due to the quality of the food choices of the patients), at least until the illness is far advanced</td>
<td>3 Neuroendocrine and psychopathological alterations together with energy restrictions affect the immune system in a complex way</td>
</tr>
</tbody>
</table>

Table 6. Heterogeneity of patients with eating disorders

These premises could explain the controversial findings in patients with eating disorders regarding immune function and their apparent resistance to infection.
Recognition of Different Types of Eating Disorders

Apart from typical EDs, such as AN and BN, other types must be taken into account: binge-eating disorders which represent stable syndromes, and EDs not otherwise specified (EDNOS).

EDNOS have been defined to be a separate cluster of EDs among borderline women, rather than a prodromal or residual form of a more clear-cut case of AN or BN. EDNOS represent the most common EDs diagnosed in specialized treatment settings.

Partial EDNOS syndromes have also been reported in the literature, and are most frequent both in adolescents and adults.

EDNOS-purging only has been found to be clinically significant, lying somewhere between women with lifetime BN purging subtype and healthy controls [9].

Other atypical ED syndromes to bear in mind are: psychogenic vomiting, functional dysphagia, craving, and alexithymic AN.

Alexithymia core features are: difficulties in identifying and describing feelings; difficulties in distinguishing feelings from the bodily sensations of emotional arousal; impaired symbolization as evidenced by a paucity of fantasies and other imaginative activity, and a tendency to focus on external events rather than inner experience.

The possible link between alexithymia and psychosomatic or psychopathological disorders is now well documented. Overweight and obesity are very frequent in those patients suffering from binge-eating. In particular, alexithymia has been suggested to be frequently observed in obese or bulimic patients.

Differential Diagnoses to Be Considered

A typical pattern has been defined in EDs, which is characterized by the following two main features: (1) obsession to be slim, in the case of AN this feeling is accompanied by significant weight loss and amenorrhea, and (2) severe body dissatisfaction.

Patients with BN are also characterized by disturbed eating attitudes showing a lack of eating control, very frequently developing binge-eating followed by purging behavior (vomiting and laxative abuse), which may be interchangeable. However, the use of multiple purging methods has been associated with greater severity over time [10].

In addition, patients with obsessive-compulsive disorder have been shown to score significantly higher than healthy control subjects on all eight subscales of the Eating Disorder Inventory: drive for thinness; bulimia; body dissatisfaction; ineffectiveness; perfectionism; interpersonal distrust; interceptive awareness, and maturity fears.

How to Manage Malnutrition in Eating Disorders

Food and nutritional recovery are key aspects in the treatment of ED. Therapists must be conscious of the great importance of the fact that patients have to be fed despite their difficulties in eating properly.

Patients with AN reluctantly accept external control from their therapists.

As patients with EDs suffer from mental disturbances, it is necessary to implement a life plan jointly developed by nutritionists, psychiatrists and/or psychologists. To this end, there must be specialized treatment units, in which nurses are especially well trained.

In order to be re-fed, a significant number of patients must be admitted to hospital for 30–40 days.
If a good nursing team is available, tube feeding use is exceptional and is only used when a natural re-feeding method does not work. Enteral feeding is not necessary, unless a false reduction of admission is found by the therapist. Parenteral nutrition is rarely necessary.

If re-feeding is carried out at home, patients and their parents must be trained.

The use of dining rooms in daycare centers is very helpful, and patients can follow an eating plan under the intensive care of nurses.

Food supplements can be used, especially during admission, in order to reinforce re-feeding and especially micronutrient and fiber intake. However, it is very important that patients become used to eating common foods at appropriate times during the day.

**Principles of Behavioral Therapy**

Behavioral therapy is the first part of the psychotherapy that will last for 4–5 years. This therapy includes several psychological techniques applied to patients in order to regain common and normal food habits which have been lost or perturbed due to the mental disorder.

These techniques involve strong pressure on the patients to help them eat properly, including body position, how to use cutlery, feeding rhythm, resting time after eating, and avoiding compensatory maneuvers. These techniques are authority-based and during the first steps are more focused on negative reinforcements than on positive reinforcements and awards.

Both during admission to the hospital or in daycare centers, behavioral therapies are realized by nurses, at home by parents or relatives, and in all cases, they must be supervised by a specialized psychiatrist or psychologist.

**Conclusions**

- Patients must be treated by multidisciplinary groups including psychiatrists, psychologists, nutritionists, dietitians, endocrinologists, and pediatricians
- Diagnosis and treatment must be adequate at very early stages of the illness to enhance the prognosis
- Patients must be treated by professionals when the first symptoms are seen
- Although in most cases clinical analyses seem to be correct, it is important to highlight that these patients show a trend towards leucopenia, together with relative lymphocytosis and depleted cell-mediated immune function
- Nevertheless, patients with eating disorders surprisingly show a low risk of suffering from infections and allergies, although when recovering from anorexia nervosa or bulimia nervosa the opposite is the case

**References**


Introduction

Leukemia accounts for 30–45% of childhood cancers, lymphomas for 9–15%, and solid tumors (e.g. medulloblastoma, Wilm’s, neuroblastoma, etc.) for around 40%. Malnutrition is common in children with malignant disease, with prevalence estimates ranging from 6 to 50% depending on the type, stage and location of the tumor. The highest risk posed to nutritional status comes from advanced stage solid tumors, acute myeloblastic leukemia, multiple relapse leukemia, head and neck cancer, medulloblastoma, and bone marrow or stem cell transplantation. Cachexia (weakness, anorexia, weight loss, altered substrate metabolism) is common and related to metabolic demands related to both tumor burden and the effects of treatment. Cytokines such as tumor necrosis factor, interleukin-1 and -6 and interferon-γ also play an important role. Rather than conserving energy and protein reserves in response to starvation, the child with malignant disease may increase energy expenditure, proteolysis and gluconeogenesis, more characteristic of acute metabolic stress.

General risk factors for malnutrition are shown in table 1. Learned food aversion associated with nausea-inducing treatment sometimes leads to anticipatory vomiting. Chemotherapy may adversely affect food intake and gastrointestinal function by causing oral or esophageal ulceration,
altered taste perception, anorexia, nausea, vomiting, and enteritis with malabsorption and diarrhea. Radiation therapy to the head and neck can cause mucositis, anorexia, nausea, vomiting, dysphagia, dry mouth and altered taste, while radiation to the abdomen may cause enteritis, sometimes followed by stricturing of the bowel.

Bone marrow transplantation (BMT) or stem cell transplantation are used in children with a range of malignant and non-malignant conditions. Chemotherapy and/or radiation therapy are used to reduce host cells to the point that donor stem cells will engraft (allogeneic BMT), or to reduce the tumor burden and rescue the patient with his/her own stem cells (autologous BMT). Priming chemotherapy causes severe nausea, vomiting and oral ulceration, and is often associated with diarrhea, protein losing enteropathy, and depletion of zinc and electrolytes [1, 2]. Most children undergoing BMT stop eating either as a result of these side effects, or because eating becomes an issue over which they have little or none. Impairment of gastrointestinal barrier function increases the risk of viral, bacterial and fungal infection. Episodes of sepsis are associated with protein catabolism and negative nitrogen balance. Enteral feeds should be prepared in a manner that renders them low in bacterial load (‘clean feeds’); parenteral nutrition (PN) may be necessary, but when tolerated enteral tube feeds (ETFs) are associated with better nutritional response and sense of wellbeing.

### Provision of Nutritional Support

The multidisciplinary hematology-oncology team should develop a nutritional care plan for each patient. The goals of nutritional support are to reduce morbidity and minimize or prevent complications such as infection and growth failure; improved nutritional intake can help promote a sense of wellbeing. There is no evidence that nutritional support promotes tumor growth. Baseline nutritional status should be established, including eating habits and any problems over food perceived by the family. Weight measurement is inaccurate as an indicator of nutritional status in children with a large tumor mass, and mid upper arm circumference and skinfold thickness measurements are more reliable methods of assessment and monitoring [3]. Neutropenic patients must avoid food that may carry a high microbial load, such as poorly cooked meats, soft cheeses, pate and shellfish; however, most infections are hospital-acquired and not food-borne, so over-restriction of food choices may be counterproductive. Mucositis (painful mouth ulcers ± superinfection), vomiting and anorexia often limit oral intake. Routine saline mouth washes are used, together with adequate pain relief (opiates if necessary). Frequent small meals of appetizing food are

---

**Table 1.** Risk factors for nutritional compromise

<table>
<thead>
<tr>
<th>Decreased food intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inadequate amount of food offered</td>
</tr>
<tr>
<td>Unappetizing food; lack of flexibility in meeting child’s preferences</td>
</tr>
<tr>
<td>Too much food</td>
</tr>
<tr>
<td>'Forced' feeding</td>
</tr>
<tr>
<td>Reduced appetite from illness</td>
</tr>
<tr>
<td>Symptoms associated with disease or treatments, e.g. nausea, vomiting, sore mouth, pain, diarrhea, breathlessness, etc.</td>
</tr>
<tr>
<td>Repeated fasting for treatments or procedures</td>
</tr>
<tr>
<td>Mucositis, swallowing or chewing difficulties</td>
</tr>
<tr>
<td>Difficulty self-feeding</td>
</tr>
<tr>
<td>Poor child/carer interaction at mealtimes</td>
</tr>
<tr>
<td>Impaired conscious level</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Increased nutritional requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Illness/metabolic stress</td>
</tr>
<tr>
<td>Wound or fistula losses</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Impaired ability to absorb or utilize nutrients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Due to disease or treatment, e.g. chemotherapy causing enteropathy or pancreatic exocrine impairment</td>
</tr>
<tr>
<td>Infection as a consequence of immunosuppression</td>
</tr>
</tbody>
</table>
more likely to be accepted, and advice with regard to the use of high calorie foods should be given routinely. There should be flexibility with regard to menu choice, mealtimes and parental involvement; children on the ward should be encouraged to eat together at mealtimes. Tastes may be bitter or metallic with some drugs (e.g. procarbazine, cyclophosphamide) or food may have no taste at all. Some children develop a liking for strong flavors (pickles, spices). Serving food with sauces and gravies will increase moisture and help swallowing if the mouth is dry. Food can be purchased from the shop/canteen or brought in from home if tempting meals cannot be provided in hospital. The use of a reward system (star chart) may motivate some younger children to eat, but rewards need to be appropriate to the child’s age and goals must be achievable and relevant.

### Enteral Tube Feeding and Parenteral Nutrition

ETF or PN are likely to be needed when

- The child is malnourished at diagnosis
- Loss >5% body weight during treatment
- Weight for height <90%
- Drop in weight across two centiles
- Food intake <80% estimated requirement
- Triceps skinfold thickness <5th centile
- Bone marrow transplant patient

Long-term use of ETF in infants often leads to later feeding difficulties and early advice should be sought from a speech and language therapist. Gastrostomy may be considered if tube feeding is required for more than 4 weeks, or if the nasogastric tube is not tolerated (e.g. severe mucositis; vomiting). Ideally, older children should be al-

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Cause</th>
<th>Possible solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>Unsuitable feed in a child with impaired gut function</td>
<td>Change to hydrolyzed formula or modular feed</td>
</tr>
<tr>
<td></td>
<td>Excessive infusion rate</td>
<td>Slow rate and increase as tolerated</td>
</tr>
<tr>
<td></td>
<td>Intolerance of bolus feeds</td>
<td>Frequent, smaller feeds, or change to continuous feeds</td>
</tr>
<tr>
<td></td>
<td>High feed osmolarity</td>
<td>Build up strength of feed slowly and give by continuous infusion</td>
</tr>
<tr>
<td></td>
<td>Microbial contamination of feed</td>
<td>Use sterile, commercially produced feeds when possible; prepare other feeds in clean environment</td>
</tr>
<tr>
<td></td>
<td>Drugs (e.g. antibiotics, laxatives)</td>
<td>Review drug prescription</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>Excessive infusion rate</td>
<td>Slowly build up feed infusion</td>
</tr>
<tr>
<td></td>
<td>Slow gastric emptying</td>
<td>Encourage lying on right side; prokinetics</td>
</tr>
<tr>
<td></td>
<td>Constipation</td>
<td>Maintain regular bowel habit with adequate fluid intake, fiber-containing feed and/or laxatives</td>
</tr>
<tr>
<td></td>
<td>Medicines given at the same time as feed</td>
<td>Allow time between giving medicines and giving feed, or stop continuous feed for a short time</td>
</tr>
<tr>
<td></td>
<td>Psychological factors</td>
<td>Review feeding behavior; consider referral to psychologist</td>
</tr>
<tr>
<td>Regurgitation/aspiration</td>
<td>Gastroesophageal reflux</td>
<td>Correct positioning; feed thickeners; drugs; continuous feeds; jejunal tube (consider fundoplication)</td>
</tr>
<tr>
<td></td>
<td>Dislodged tube</td>
<td>Secure tube adequately and regularly review position</td>
</tr>
<tr>
<td></td>
<td>Excessive infusion rate</td>
<td>Slow infusion rate</td>
</tr>
<tr>
<td></td>
<td>Intolerance of bolus feeds</td>
<td>Smaller, more frequent feeds, or continuous infusion</td>
</tr>
</tbody>
</table>

**Table 2. Enteral tube feeding: problems and potential solutions**
allowed to choose between a nasogastric tube or percutaneous endoscopic gastrostomy tube. Tube feeds are generally given overnight to allow normal activities and oral intake during the daytime. Tube feeding [4] may result in a number of complications including vomiting, regurgitation/aspiration and diarrhea (see table 2 for potential solutions). Whereas the enteral route should be used for nutritional support whenever possible, PN and ‘bowel rest’ are sometimes necessary when chemotherapy causes severe gastrointestinal side effects. Standard PN regimens may be used, although the possibility of refeeding syndrome should be considered in the malnourished patient [5], and regimens may require modification in the light of nutritional response. It is important to consider and regularly review the objectives of nutritional support in individual patients. Monitoring will include assessment of nutritional intake, anthropometry, biochemical and hematological parameters, general clinical state, gastrointestinal function, and feeding tube/central venous catheter integrity.

Late Nutritional Complications

A decrease in physical activity during illness leads to a reduction in energy expenditure. In children treated for acute lymphoblastic leukaemia, about 40% may later become obese [6]. Cranial irradiation is also a risk factor for developing obesity. In addition to an increase in fat mass, late nutritional complications from treatment of childhood malignancies include a reduction in growth rate and in lean body mass. Reduced bone mineral density can result from decreased activity, reduced calcium intake and the effects of corticosteroid treatment; under-mineralization may persist in a small proportion of patients.

Conclusions

* Always try to
  * Identify child’s favorite foods; these are best avoided whilst having chemotherapy as they may develop a permanent dislike to them
  * Offer small, frequent meals
  * Encourage dietary supplements
  * Provide skilled dietetic supervision
  * Manage side effects of chemotherapy effectively (nausea, vomiting)
  * Consider need for tube feeding early, especially in high nutritional risk patients
  * Remember that a child may eat better at home
  * Use parenteral nutrition when appropriate (i.e. when enteral feeds are precluded by gastrointestinal dysfunction)

References

### Key Words
Intensive care · Burn injury · Trauma · Critical illness

### Key Messages
- Malnutrition leads to increased morbidity and mortality in pediatric hospital patients, with particularly severe consequences in critically ill children
- Both under- and overfeeding have negative consequences
- Trauma and burn injury require additional attention with regard to nutritional requirements
- Guidelines in this area are not evidence-based because little research has been conducted

### Introduction

During critical illness and recovery thereafter, adequate nutritional support is an essential aspect of the clinical management of pediatric intensive care patients [1]. Adequate feeding is essential for complete recovery and normal functioning of the growing child. Thus clinicians in the pediatric intensive care unit (PICU) are challenged to provide adequate nutrition for optimal tissue synthesis and immune function while avoiding complications of under- or overfeeding.

The prevalence of malnutrition is high among children admitted to a PICU, including burn and trauma patients [2–4]. Protein-energy malnutrition in hospital patients is associated with increased mortality and morbidity, including a higher risk of infections due to poor immune defense, wound healing problems, reduced gut function, longer dependency on mechanical ventilation and longer hospital stay [2, 5].

Studies have shown that the nutritional status of children admitted to a PICU deteriorates during hospitalization [3], as children often do not receive adequate feeding.

Besides underfeeding, also overfeeding has negative consequences. It is of no benefit in maintaining a lean body mass, which results in the excessive synthesis of fat. This may induce hepatic steatosis and impaired liver function, and increase the risk of hyperglycemia. Hyperglycemia itself results in a higher mortality and morbidity in critically ill adults [6]. The synthesis of fat increases CO$_2$ production which may contribute to ventilatory compromise, with longer ventilator dependency [1].

Trauma and burn injury in children are associated with increased systemic energy expenditure (EE), severe muscle catabolism and wasting, and growth delay. Appropriate nutritional support as part of daily therapeutic interventions has been shown to improve mortality and morbidity [7].

### Nutritional Requirements

A major problem in clinical practice is to define the nutritional requirements for critically ill children, as demands range widely with altered metabolic states determined by the children’s age and
nutritional status. Moreover, metabolic responses may greatly vary as well, depending on the nature of the injury and the variability of the individual response to the same type of injury [8, 9].

The exaggerated catabolic response that is typically seen in children hospitalized for burn injuries, coupled with exudation of nutrients through the damaged skin, means that requirements for energy, protein and other nutrients are especially high in this category. The extent of hypermetabolism is related to the percentage of burned surface area. In trauma patients, especially with head injury, energy demands are increased.

Energy
In practice, the daily energy demands of critically ill children should be individually calculated based on one of the following methods:

(1) Measurement of EE by indirect calorimetry (total daily energy requirement) in sedated, ventilated children, and resting EE (REE) in non-ventilated children

(2) Estimation of REE by predictive equations based on weight, age and sex

(3) Estimation using dietary reference intakes (DRI) for healthy children matched for age and sex

The preferred method is measuring the EE, as several factors present in the critically ill child can influence basic metabolic rate (table 1). The measured EE is the minimum amount of energy needed. The Schofield formula is a useful alternative [10] for estimating REE and is shown in table 2. Additional factors should be taken into account to calculate total energy needs such as activity factor, illness factor, growth factor and absorption coefficient in case of enteral feeding. In general, infants require 10–20% more calories when fed enterally than when fed parenterally, whereas the differences are smaller in children (close to 10%) primarily because of more effective enteral absorption with older age.

In table 3 an overview is given of the nutritional requirements in critically ill children fed enterally.

Amino Acids
Both protein synthesis and protein breakdown are intensified in critical illness, but the latter predominates. Thus, critically ill children typically manifest a net negative protein balance, which may clinically be noted by weight loss, negative nitrogen balance and skeletal muscle wast-

---

**Table 1.** Factors influencing energy expenditure in critically ill children

<table>
<thead>
<tr>
<th>Increase in energy expenditure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
</tr>
<tr>
<td>Surgery</td>
</tr>
<tr>
<td>Activity</td>
</tr>
<tr>
<td>Fever</td>
</tr>
<tr>
<td>Weaning from mechanical ventilation</td>
</tr>
<tr>
<td>Drugs: pressor agents, catecholamines</td>
</tr>
<tr>
<td>Pain, anxiety</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Decrease in energy expenditure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanical ventilation</td>
</tr>
<tr>
<td>Temperature-controlled environment</td>
</tr>
<tr>
<td>Drugs: sedatives, analgesics, β-blockers</td>
</tr>
<tr>
<td>Progression of sepsis to septic shock</td>
</tr>
</tbody>
</table>

**Table 2.** Schofield formulas for estimation of resting energy expenditure (kcal/day) [10]

<table>
<thead>
<tr>
<th>Age years</th>
<th>Boys</th>
<th>Girls</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–3</td>
<td>60.9 x weight (kg) – 54</td>
<td>61.0 x weight (kg) – 51</td>
</tr>
<tr>
<td>3–10</td>
<td>22.7 x weight (kg) + 495</td>
<td>22.5 x weight (kg) + 499</td>
</tr>
<tr>
<td>10–18</td>
<td>17.5 x weight (kg) + 651</td>
<td>12.2 x weight (kg) + 746</td>
</tr>
</tbody>
</table>

In order to calculate total energy needs, the following additional factors must be taken into account.

Illness factor of critically ill children: 1.2–1.6 in PICU patients, 1.4 in burn patients, and 1.3–1.5 in trauma patients.

Activity factor of critically ill children: 1.0–1.1.

Growth factor of critically ill children: 1.0 in the acute phase; in reconvalescent phase: 1.3 when age <4 months, 1.1 when age 4–12 months, 1.0–1.04 for older children.
ing. Fortunately, supplementation of amino acids does improve protein balance by increasing protein synthesis [11, 12]. It is possible to change a catabolic state into anabolism, even at low energy intakes, when the child is provided with enough amino acids. Providing adequate dietary protein is, therefore, a very important nutritional intervention in critically ill children.

**Carbohydrates**
Glucose is the major energy source in critical illness, but excessive carbohydrate intake results in a high CO\textsubscript{2} production. A high carbohydrate intake is associated with lipogenesis and less fat oxidation [13]. Reduced morbidity and mortality have been observed with the use of insulin to maintain strict normoglycemia in critically ill adults [14]. No studies in children have been published as yet.

**Fats**
Lipid metabolism is generally accelerated by illness and physiologic stress, and lipids are a prime source of energy. A minimum linoleic acid intake of 0.1 g/kg per day should be administered to infants and older children in order to prevent essential fatty acid deficiency. The dosage of fat should not exceed the capacity for lipid clearance and should be adapted if marked hyperlipidemia occurs.

**Trauma**
Trauma and specifically head injury should receive 140% of REE in non-paralyzed patients, and 100% in paralyzed patients. This recommendation is derived from adult guidelines since only limited studies in children are available.

**Burn Injury**
In pediatric burn patients several additional formulae for determining energy needs are in use (table 4), but have been shown to underestimate EE [15]. The measurement of EE is highly recommended in this population.

Protein requirements in burned children are much higher than in normal children. In addition to increased loss of protein across the burn wound, there is a great demand for protein for wound healing, host defense and gluconeogenesis as amino acids become a primary source of energy. Current recommendations for patients with burns to more than 10% of the body surface area are 20% total kcal provided from protein/amino acids, 40–50% from carbohydrates, and up to 30% from fats.

**Nutritional Support**

**Indication and Goal**
Nutritional support is important in the management of the critically ill patient when oral food intake is inadequate or not possible. It is employed to minimize the loss of lean body mass and support the synthesis of critical visceral proteins.
Timing of Nutritional Support
Nutritional support should be started within the first 24 h from admission to the ICU in children who are hemodynamically stable and have a functioning gastrointestinal tract.

Route of Nutritional Support
Enteral nutrition (EN) via tube feeding is the preferred method of feeding the critically ill patient. EN reverses the loss of gastrointestinal mucosal integrity, maintains intestinal blood flow, preserves IgA-dependent immunity, and contributes to the maintenance of the host immune response. Meta-analyses of clinical studies have reported that EN as opposed to parenteral nutrition is associated with a lower risk of infection and also cost savings [16].

Total or additional parenteral nutrition (PN) is recommended when contraindications for EN exist, or when patients cannot be fed sufficiently via the enteral route within the first few days of ICU stay (see figure 1 for these conditions).

Postpyloric as opposed to gastric tube placement is associated with reduced gastric residual volume and reflux, but adequately powered trials are not available to support prevention of aspiration pneumonia.

Type of Formula
There are no studies available that support the clinical advantage of oligomeric formulas in critically ill children instead of polymeric formulas (see Chapter 3.3). There is no evidence as yet on the use of immune-modulating formulas, e.g. formulas enriched with glutamine, arginine or nucleotides, in the critically ill child. This can be considered in burn injury and trauma patients.

Compliance
It is important to realize that large discrepancies may arise between prescribed and delivered or prescribed and required nutrients due to inadequate delivery or poor compliance [17]. The main reasons for inadequate delivery of nutrients can be divided into four groups which are shown in

---

Table 5. Main reasons for inadequate delivery of nutrients and recommendations for prevention

<table>
<thead>
<tr>
<th>Causes of noncompliance</th>
<th>Recommendation for prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid volume restriction e.g. cardiac patients</td>
<td>Condensation of formula</td>
</tr>
<tr>
<td>Gastrointestinal dysfunction¹</td>
<td>Transpyloric enteral feeding Prokinetics (Additional) parenteral feeding</td>
</tr>
<tr>
<td>Fasting in anticipation of diagnostic or surgical procedure</td>
<td>Increase in subsequent feeding rate to compensate for the missed volume (Additional) parenteral feeding</td>
</tr>
<tr>
<td>Airway tube management</td>
<td>Continuous transpyloric feeding [20] Increase in subsequent feeding rate to compensate for the missed volume (Additional) parenteral feeding</td>
</tr>
<tr>
<td>Material related²</td>
<td>Pro-active approach of medical personnel</td>
</tr>
</tbody>
</table>

¹ For example: vomiting, nausea, retentions, diarrhea, abdominal pain.
² For example: gastric tube occlusion or displacement, electric pump dysfunction, absence of venous access, administration of medication that interferes with enteral feeding, and the administration of medication over the same venous catheter.
Follow-Up of Nutritional Support

Once nutritional support is started, its adequacy may be assessed by parameters of nutritional status, such as anthropometric measurements and indirect calorimetry. The minimum standard for

Table 5. Recommendations for the prevention of noncompliance are given. Furthermore, it is necessary to compare delivered intake with prescribed intake on a daily basis.
nutritional assessment should include measurements of weight, mid upper arm circumference and possibly length and indirect calorimetry (EE and RQ).

An overall practical nutritional guideline is shown in figure 1.

Conclusions

Nutritional support in the critically ill child:
- Is an essential aspect of clinical management and should be integrated in daily care
- Should generally be administered within the first 24 h following admission
- Consists of enteral feeding, administered either by the gastric or transpyloric route, unless a contraindication for enteral feeding is present, or adequate amounts of enteral feeding are not reached within the first few days of intensive care unit stay
- Must consist of a condensed formula in patients with fluid restriction
- Must be followed up concerning the delivery of nutrients, achieved nutritional status, and changes in energy need during admission

References

4 Annex

4.1 The WHO Child Growth Standards

Mercedes de Onis

Key Words
Growth standards • Growth references • Nutritional status • Anthropometry • Nutritional assessment

Key Messages
• Growth assessment is a key screening tool to assess child health and nutritional wellbeing
• Anthropometry is the most universally applicable, noninvasive method to assess the growth status of children
• The interpretation of the growth trajectory is highly dependent on the growth charts used
• The WHO Child Growth Standards, based on the physiological growth of healthy breastfed infants, are the growth charts recommended by WHO for universal application
• Anthropometric measurements need to be accurate. Adequate equipment and the use of standardized techniques are essential for reducing measurement error and minimizing bias

The full set of tables and charts is presented on the WHO website (www.who.int/childgrowth/en), together with tools such as software and training materials that facilitate their clinical application. The disjunction observed at 24 months in the length/height-based charts represents the change from measuring recumbent length to standing height. Standards for other anthropometric variables (i.e. mid upper arm circumference, and triceps and subscapular skinfolds) are also available in the website.

Introduction

Assessing childhood growth remains a mainstay of pediatric care in all settings, from the most advanced healthcare centers to those faced with severe resource constraints. If adequate growth is achieved, the probability is high that children will be healthy and well-nourished. The documentation of abnormal growth, on the other hand, signals that something is not going well and flags the need for careful diagnostic follow-up and action. The value of growth assessment is thus its principal utility as a key screening tool to assess children’s general wellbeing, identify growth faltering and excessive growth, evaluate maternal lactation performance and infant feeding practices, and monitor children with medical conditions known to adversely affect growth, such as renal and cardiac conditions.

This Annex presents growth charts for
• weight-for-age
• length/height-for-age
• weight-for-length/height
• body mass index-for-age
• head circumference-for-age
in percentile values for boys and girls aged 0–60 months.
Growth assessment is best done by the appropriate use and interpretation of anthropometric indexes [1]. Anthropometry is the single most universally applicable, inexpensive, and noninvasive method available to assess the proportions, size, and composition of the human body. The successful assessment of growth using anthropometry is founded on (a) the selection of an appropriate anthropometric indicator, (b) the accuracy and reliability of the anthropometric measures taken, and (c) the proper interpretation of the values by selecting suitable growth charts and cutoffs to assess risk or classify children according to variable degrees of undernutrition and overweight/obesity.

The growth charts presented in this Annex are a subset of the WHO Child Growth Standards [2, 3], which are based on an international sample of healthy breastfed infants and young children [4].

The origin of the WHO Child Growth Standards dates back to the early 1990s when WHO initiated a comprehensive review of the uses and interpretation of anthropometric references. This analysis showed that the growth pattern of healthy breastfed infants deviated to a significant extent from the NCHS/WHO international reference [5]. The expert group concluded from these and other related findings that the NCHS/WHO reference did not adequately describe the physiological growth of children and that its use to monitor the health and nutrition of individual children or to derive estimates of child malnutrition in populations was flawed. In particular, the reference was inadequate for assessing the growth pattern of healthy breastfed infants because it was based on predominantly formula-fed infants, as are most national growth charts in use today. The group recommended the development of new standards, adopting a novel approach that would describe how children should grow when free of disease and when their care follows healthy practices such as breastfeeding and non-smoking [6]. This approach would permit the development of a standard as opposed to a reference merely describing how children grew in a particular place and time. Although standards and references both serve as a basis for comparison, each enables a different interpretation. Since a standard defines how children should grow, deviations from the pattern it describes are evidence of abnormal growth. A reference, on the other hand, does not provide as sound a basis for such value judgments, although in practice references often are mistakenly used as standards.

Following a Resolution from the World Health Assembly in May 1994 endorsing these recommendations, the WHO Multicentre Growth Reference Study (MGRS) [4] was launched in 1997 to collect primary growth data that would allow the construction of new growth charts consistent with ‘best’ health practices.

The goal of the MGRS was to describe the growth of healthy children. Implemented between 1997 and 2003, the MGRS is a population-based study conducted in six countries from diverse geographical regions: Brazil, Ghana, India, Norway, Oman, and the USA [4]. The study combined a longitudinal follow-up from birth to 24 months with a cross-sectional component of children aged 18–71 months. In the longitudinal component, mothers and newborns were enrolled at birth and visited at home a total of 21 times at weeks 1, 2, 4 and 6; monthly from 2–12 months; and bimonthly in the second year.

The study populations lived in socioeconomic conditions favorable to growth. The individual inclusion criteria were: no known health or environmental constraints to growth, mothers willing to follow MGRS feeding recommendations (i.e. exclusive or predominant breastfeeding for at least 4 months, introduction of complementary foods by 6 months of age, and continued breastfeeding to at least 12 months of age), no maternal smoking before and after delivery, single term birth, and absence of significant morbidity. Rigorously standardized methods of data collection and procedures for data
management across sites yielded high-quality data.

The length of children was strikingly similar among the six sites, with only about 3% of variability in length being due to inter-site differences compared to 70% for individuals within sites [7]. The striking similarity in growth during early childhood across human populations means either a recent common origin as some suggest [8] or a strong selective advantage associated with the current pattern of growth and development across human environments.

Of 1,743 mother–child dyads enrolled in the MGRS longitudinal sample, 882 complied with the study's infant-feeding and non-smoking criteria and completed the follow-up period of 24 months. The compliant sample was used to construct the WHO standards from birth to 2 years of age combined with 6,669 children from the cross-sectional sample from age 2 to 5 years [9]. Data from all sites were pooled to construct the standards [7]. The generation of the standards followed state-of-the-art statistical methodologies [2,3]. The concordance between the smoothed curves and empirical percentiles was excellent and free of bias at both the median and the edges, indicating that the resulting curves are a fair description of physiological growth of healthy children [2].

Concluding Remarks

The WHO Child Growth Standards were derived from children who were raised in environments that minimized constraints to growth such as poor diets and infection. In addition, their mothers followed healthy practices such as breastfeeding their children and not smoking during and after pregnancy. The standards depict normal human growth under optimal environmental conditions and can be used to assess children everywhere, regardless of ethnicity, socioeconomic status and type of feeding. They also demonstrate that healthy children from around the world who are raised in healthy environments and follow recommended feeding practices have strikingly similar patterns of growth [7]. The International Pediatric Association has officially endorsed the use of the WHO standards describing them as 'an effective tool for detecting both undernutrition and obesity, thus addressing the double burden of malnutrition affecting populations on a global basis' [10].

Note: WHO holds copyright of the WHO Child Growth Standards.

Conclusions

Early recognition of growth problems, such as growth faltering and excessive weight gain relative to linear growth, should become standard clinical practice by:

- The routine collection of accurate weight and height measurements to enable monitoring of childhood growth
- The interpretation of anthropometric indices, such as height-for-age and BMI-for-age, based on the WHO Child Growth Standards
- The early intervention after changes on growth patterns (e.g., upward or downward crossing of percentiles) have been observed to provide parents and caregivers appropriate guidance and support
References

Length/height-for-age GIRLS
Birth to 5 years (percentiles)
Weight-for-length BOYS
Birth to 2 years (percentiles)
Weight-for-length GIRLS
Birth to 2 years (percentiles)

WHO Child Growth Standards

World Health Organization
BMI-for-age BOYS
Birth to 5 years (percentiles)

WHO Child Growth Standards
BMI-for-age GIRLS

Birth to 5 years (percentiles)

WHO Child Growth Standards
Key Words
Growth assessment · Growth references · Anthropometry · Interpretation

Key Messages
- Growth charts are essential tools for the interpretation of growth measurements in children
- Growth references (examples: CDC, Euro-Growth) describe the growth of populations of children as they exist at a given time in a given location
- Growth standards (example: WHO Child Growth Standards) describe the growth of children who live in favorable circumstances, receive optimal nutrition and show desirable growth characteristics
- Anthropometric measurements need to use proper techniques. Measurements of recumbent length must be interpreted against charts of recumbent length, and measurements of standing height must be interpreted against charts of standing height

Introduction
Growth assessment is an integral part of childhood health monitoring. For interpretation, growth measurements must be compared to appropriate norms. Such norms have traditionally been provided by growth references which describe the growth of children living in a defined geographic area who are deemed healthy. The relative position of a child undergoing assessment in comparison with reference data determines whether the child’s growth is judged normal or abnormal. Widely used growth references are the CDC Growth Charts [1] and the Euro-Growth Charts [2]. Both were released in 2000. In spite of minor exceptions in the case of the CDC charts, these charts essentially describe the growth of all children living, respectively, in the United States and Europe. This sets them apart from the WHO Growth Standards [3, 4], which describe the growth of children worldwide who live in favorable circumstances, receive optimal nutrition and show desirable growth characteristics. The distinction between references and standards has implications for the use of growth charts. Whereas the use of references requires some element of judgment on the part of the user, the use of standards is inherently simpler as it requires little or no judgment on the part of the user.

The CDC Growth Charts: United States
The CDC charts [1] were created to replace the widely used NCHS/WHO charts because of inadequacies identified in the latter. The CDC charts are based on a large number of nationally representative data from various national surveys conducted between 1976 and 1994. The exception are data for the first year of life, which are few in
number and were obtained partly from infants representing lower socioeconomic strata. Also, data for subjects >6 years of age from the most recent national survey (1988–1994) were excluded because of the increased prevalence of high weight in that sample. The data were strictly cross-sectional. State-of-the-art smoothing procedures were used to generate centile curves. For birth to 3 years charts for weight for age and (recumbent) length for age are available. For ages 2–20 years charts for weight for age, height for age and body mass index are available.

The Euro-Growth Charts

The Euro-Growth charts [2] were the result of a multinational effort. Data for these charts were gathered from birth to 5 years of age in children who were born between 1990 and 1993 and lived close to 22 measurement sites in 11 European countries. Data were gathered longitudinally, with 1,746 children being followed to age 1 year, 1,071 to age 3 years and 571 to age 5 years. Data were analyzed cross-sectionally using state-of-the art smoothing techniques.

Euro-Growth provides a software (www.Euro-Growth.org), which calculates weight and length gains and raises a warning flag if gain of an infant is outside the ± 2SD range. Z scores can be calculated and growth references can be corrected for parental height, gestational age, and duration of exclusive breastfeeding.

Comment

In contradistinction to the recently published WHO Growth Standards [3, 4], the CDC charts and the Euro-Growth charts are growth references. They represent, with minor exceptions, the growth of healthy children living in the respective geographic areas. The distinction is important to the user of the charts. A growth reference simply describes what exists and therefore leaves it up to the user to judge whether a given child’s growth is normal, or healthy, or neither. A standard, on the other hand, already incorporates a large element of judgment and requires little if any judgment from the user. This would seem to be a distinct advantage when charts are used by untrained observers who lack the ability to render judgments.

General Comment on Growth Assessment

The importance of using proper measurement techniques cannot be overemphasized. In particular measurements of recumbent length are difficult to perform and require specific equipment, training and effort if reproducible measurements are to be obtained. Measurements of length must be interpreted using charts for length, and measurements of height must be interpreted using charts for height. The distinction is important largely in the overlap area between 1 and 3 years of age.

Single measurements of growth are subject to error due to multiple sources. Erroneous measurements can lead to grossly erroneous judgments regarding the growth of a child. The accuracy of growth assessments is greatly improved if two or more measurements are performed at different times. This not only minimizes the impact of the errors of single measurements, it also permits an assessment of time trends and thus strengthens the assessment of a child’s growth vis-à-vis the growth reference or standard.

Conclusions

• Growth monitoring, an essential part of childhood health maintenance, requires accurate anthropometric measurements and interpretation of growth measurements with the help of growth charts.
• If reference charts are used, such as the CDC Charts or the Euro-Growth Charts, a certain amount of judgment is required on the part of the user for proper interpretation of measurements

• The use of growth standards, such as the WHO Growth Standards, on the other hand, requires relatively little judgment on the part of the user

References


Fig. 1. CDC length-for-age and weight-for-age for boys birth to 3 years.
Fig. 2. CDC length-for-age and weight-for-age for girls birth to 3 years.
Fig. 3. CDC stature-for-age and weight-for-age for boys 2–20 years.
Fig. 4. CDC stature-for-age and weight-for-age for girls 2–20 years.
Fig. 5. CDC body mass index-for-age for boys 2–20 years.
Fig. 6. CDC body mass index-for-age for girls 2–20 years.
Fig. 7. **a** Euro-Growth length-for-age for boys birth to 2 years. **b** Euro-Growth height-for-age for boys 2–5 years.
Fig. 8. a Euro-Growth length-for-age for girls birth to 2 years. b Euro-Growth height-for-age for girls 2–5 years.
Fig. 9. a Euro-Growth body mass index for boys birth to 2 years. b Euro-Growth body mass index for boys 2–5 years.
Fig. 10. a Euro-Growth body mass index for girls birth to 2 years. b Euro-Growth body mass index for girls 2–5 years.
Fig. 11. Euro-Growth weight-for-age for boys birth to 5 years.

Fig. 12. Euro-Growth weight-for-age for girls birth to 5 years.
4 Annex

4.3 Reference Nutrient Intakes for Infants, Children and Adolescents

Berthold Koletzko · Maria Hermoso

Tables with reference nutrient intakes are presented as published by (in alphabetical order) Australia and New Zealand; Germany, Austria and Switzerland; the Nordic nutrition recommendations; United Kingdom; United States and Canada; World Health Organization (WHO) with the Food and Agriculture Organization (FAO) and the United Nations University (UNU).

Acknowledgement

The authors’ work in this area is carried out with partial financial support from the Commission of the European Communities, specific RTD Programme ‘Food Quality and Safety – Integrating and Strengthening the European Research Area’, within the 6th Framework Programme, research contract No. FP6-036196-2 (Aligning nutrient recommendations across Europe with special focus on vulnerable groups and consumer understanding – EURRECA). This chapter does not necessarily reflect the views of the Commission and in no way anticipates future policy in this area.

Table 1 and 2. Australia and New Zealand nutrient reference values for diary food energy (table 1) and nutrients (table 2) in healthy infants, children and adolescents (modified from nutrient reference values including recommended dietary intakes from Australia and New Zealand 2005)

Table 1. Energy (male/female)

<table>
<thead>
<tr>
<th>Age months</th>
<th>Energy kJ/day</th>
<th>Age years</th>
<th>Energy MJ/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2,000/1,800</td>
<td>3</td>
<td>3.4/3.2</td>
</tr>
<tr>
<td>2</td>
<td>2,400/2,100</td>
<td>4</td>
<td>3.6/3.4</td>
</tr>
<tr>
<td>3</td>
<td>2,400/2,200</td>
<td>5</td>
<td>3.8/3.6</td>
</tr>
<tr>
<td>4</td>
<td>2,400/2,200</td>
<td>6</td>
<td>4.1/3.8</td>
</tr>
<tr>
<td>5</td>
<td>2,500/2,300</td>
<td>7</td>
<td>4.3/4.0</td>
</tr>
<tr>
<td>6</td>
<td>2,700/2,500</td>
<td>8</td>
<td>4.5/4.2</td>
</tr>
<tr>
<td>7</td>
<td>2,800/2,500</td>
<td>9</td>
<td>4.8/4.5</td>
</tr>
<tr>
<td>8</td>
<td>3,000/2,700</td>
<td>10</td>
<td>5.1/4.7</td>
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<td>9</td>
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<td>5.4/4.9</td>
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<td>10</td>
<td>3,300/3,000</td>
<td>12</td>
<td>5.8/5.2</td>
</tr>
<tr>
<td>11</td>
<td>3,400/3,100</td>
<td>13</td>
<td>6.2/5.5</td>
</tr>
<tr>
<td>12</td>
<td>3,500/3,200</td>
<td>14</td>
<td>6.6/5.7</td>
</tr>
<tr>
<td>15</td>
<td>3,800/3,500</td>
<td>15</td>
<td>7.0/5.8</td>
</tr>
<tr>
<td>18</td>
<td>4,000/3,800</td>
<td>16</td>
<td>7.3/5.9</td>
</tr>
<tr>
<td>21</td>
<td>4,200/4,000</td>
<td>17</td>
<td>7.6/5.9</td>
</tr>
<tr>
<td>24</td>
<td>4,400/4,200</td>
<td>18</td>
<td>7.7/6.0</td>
</tr>
</tbody>
</table>
Table 2. Nutrient values (male/female)

<table>
<thead>
<tr>
<th>Age</th>
<th>Total fat g/day</th>
<th>n-6 poly-unsaturated fats, g/day</th>
<th>n-3 poly-unsaturated fats, g/day</th>
<th>Total LCn-3 (DHA+EPA+DPA), mg/day</th>
<th>Calcium mg</th>
<th>Magnesium mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–6 months</td>
<td>31</td>
<td>4.4</td>
<td>0.5</td>
<td>210</td>
<td>30</td>
<td>75</td>
</tr>
<tr>
<td>7–12 months</td>
<td>30</td>
<td>4.6</td>
<td>0.5</td>
<td>270</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>1–3 years</td>
<td>5</td>
<td>0.5</td>
<td>40</td>
<td>500</td>
<td>700</td>
<td>230</td>
</tr>
<tr>
<td>4–8 years</td>
<td>8</td>
<td>0.8</td>
<td>55</td>
<td>700</td>
<td>240</td>
<td></td>
</tr>
<tr>
<td>9–13 years</td>
<td>10/8</td>
<td>1.0/0.8</td>
<td>70</td>
<td>1,000 (9–11 years)</td>
<td>1,300 (12–13 years)</td>
<td></td>
</tr>
<tr>
<td>14–18 years</td>
<td>12/8</td>
<td>1.2/0.8</td>
<td>125/85</td>
<td>1,300 (9–11 years)</td>
<td>410/360</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age</th>
<th>Iron mg/day</th>
<th>Iodine μg/day</th>
<th>Zinc mg/day</th>
<th>Vit. A, mg retinol equivalent/day</th>
<th>Vit. D μg/day</th>
<th>Vit. K μg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–6 months</td>
<td>0.2</td>
<td>90</td>
<td>2.0</td>
<td>250 (retinyl esters)</td>
<td>5.0</td>
<td>2.0</td>
</tr>
<tr>
<td>7–12 months</td>
<td>11</td>
<td>110</td>
<td>3</td>
<td>430</td>
<td>5.0</td>
<td>2.5</td>
</tr>
<tr>
<td>1–3 years</td>
<td>9</td>
<td>90</td>
<td>3</td>
<td>300</td>
<td>5.0</td>
<td>25</td>
</tr>
<tr>
<td>4–8 years</td>
<td>10</td>
<td>90</td>
<td>4</td>
<td>400</td>
<td>5.0</td>
<td>35</td>
</tr>
<tr>
<td>9–13 years</td>
<td>8</td>
<td>120</td>
<td>6</td>
<td>600</td>
<td>5.0</td>
<td>45</td>
</tr>
<tr>
<td>14–18 years</td>
<td>11/15</td>
<td>150</td>
<td>13/7</td>
<td>900/700</td>
<td>5.0</td>
<td>55</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age</th>
<th>Thiamine mg/day</th>
<th>Riboflavin mg/day</th>
<th>Niacin mg niacin equivalent/day</th>
<th>Vit. B₆ mg/day</th>
<th>Folate μg dietary folate equivalents/day</th>
<th>Vit. B₁₂ μg/day</th>
<th>Vit. C mg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–6 months</td>
<td>0.2</td>
<td>0.3</td>
<td>2 (preformed niacin)</td>
<td>0.1</td>
<td>65 (folate)</td>
<td>0.4</td>
<td>25</td>
</tr>
<tr>
<td>7–12 months</td>
<td>0.3</td>
<td>0.4</td>
<td>4</td>
<td>0.3</td>
<td>80</td>
<td>0.5</td>
<td>30</td>
</tr>
<tr>
<td>1–3 years</td>
<td>0.5</td>
<td>0.5</td>
<td>6</td>
<td>0.5</td>
<td>150</td>
<td>0.9</td>
<td>35</td>
</tr>
<tr>
<td>4–8 years</td>
<td>0.6</td>
<td>0.6</td>
<td>8</td>
<td>0.6</td>
<td>200</td>
<td>1.2</td>
<td>35</td>
</tr>
<tr>
<td>9–13 years</td>
<td>0.9</td>
<td>0.9</td>
<td>12</td>
<td>1.0</td>
<td>300</td>
<td>1.8</td>
<td>40</td>
</tr>
<tr>
<td>14–18 years</td>
<td>1.2/1.1</td>
<td>1.3/1.1</td>
<td>16/14</td>
<td>1.3/1.2</td>
<td>400</td>
<td>2.4</td>
<td>40</td>
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</table>
Table 3. German, Austrian and Swiss reference values (male/female) for the average daily energy and nutrient intakes in populations of healthy children and adolescents (modified from reference intakes for Germany, Austria and Switzerland 2002)

<table>
<thead>
<tr>
<th>Age</th>
<th>Energy kcal/kg/day</th>
<th>Protein g/kg/day</th>
<th>Fat % of energy</th>
<th>Essential fatty acids % of energy</th>
<th>Calcium mg/day</th>
<th>Magnesium mg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–&lt;4 months</td>
<td>110</td>
<td>2.0–2.2</td>
<td>45–50</td>
<td>4.5</td>
<td>500</td>
<td>40</td>
</tr>
<tr>
<td>4–&lt;12 months</td>
<td>95</td>
<td>1.2–1.6</td>
<td>35–40</td>
<td>3.8</td>
<td>500</td>
<td>60</td>
</tr>
<tr>
<td>1–&lt;4 years</td>
<td>100</td>
<td>1.2</td>
<td>30–35</td>
<td>3.0</td>
<td>600</td>
<td>80</td>
</tr>
<tr>
<td>4–&lt;7 years</td>
<td>90</td>
<td>1.1</td>
<td>30–35</td>
<td>3.5</td>
<td>700</td>
<td>120</td>
</tr>
<tr>
<td>7–&lt;10 years</td>
<td>75</td>
<td>1.0</td>
<td>30–35</td>
<td>3.5</td>
<td>800</td>
<td>170</td>
</tr>
<tr>
<td>10–&lt;13 years</td>
<td>60/55</td>
<td>1.0</td>
<td>30–35</td>
<td>3.5</td>
<td>900</td>
<td>230/250</td>
</tr>
<tr>
<td>13–&lt;15 years</td>
<td>55/45</td>
<td>1.0</td>
<td>30–35</td>
<td>3.5</td>
<td>1,000</td>
<td>310</td>
</tr>
<tr>
<td>15–&lt;19 years</td>
<td>45/40</td>
<td>0.9/0.8</td>
<td>30–35</td>
<td>3.5</td>
<td>1,200</td>
<td>400/350</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age</th>
<th>Iron mg/day</th>
<th>Iodine µg/day</th>
<th>Zinc mg/day</th>
<th>Vit. A mg retinol equivalent/day</th>
<th>Vit. D µg/day</th>
<th>Vit. K µg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–&lt;4 months</td>
<td>6</td>
<td>50</td>
<td>5</td>
<td>0.5</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>4–&lt;12 months</td>
<td>8</td>
<td>80</td>
<td>5</td>
<td>0.6</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>1–&lt;4 years</td>
<td>8</td>
<td>100</td>
<td>7</td>
<td>0.6</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>4–&lt;7 years</td>
<td>8</td>
<td>120</td>
<td>10</td>
<td>0.7</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>7–&lt;10 years</td>
<td>10</td>
<td>140</td>
<td>11</td>
<td>0.8</td>
<td>5</td>
<td>30</td>
</tr>
<tr>
<td>10–&lt;13 years</td>
<td>12/15</td>
<td>180</td>
<td>12</td>
<td>0.9</td>
<td>5</td>
<td>40</td>
</tr>
<tr>
<td>13–&lt;15 years</td>
<td>12/15</td>
<td>200</td>
<td>15/12</td>
<td>1.1/1.0</td>
<td>5</td>
<td>50</td>
</tr>
<tr>
<td>15–&lt;19 years</td>
<td>12/15</td>
<td>200</td>
<td>15/12</td>
<td>1.1/0.9</td>
<td>5</td>
<td>70/60</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age</th>
<th>Thiamine mg/day</th>
<th>Riboflavin mg/day</th>
<th>Niacin mg niacin equivalent/day</th>
<th>Vit. B6 mg/day</th>
<th>Folate µg dietary folate equivalents/day</th>
<th>Vit. B12 µg/day</th>
<th>Vit. C mg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–&lt;4 months</td>
<td>0.3</td>
<td>0.3</td>
<td>5</td>
<td>0.3</td>
<td>80</td>
<td>0.5</td>
<td>40</td>
</tr>
<tr>
<td>4–&lt;12 months</td>
<td>0.4</td>
<td>0.5</td>
<td>6</td>
<td>0.6</td>
<td>80</td>
<td>0.8</td>
<td>50</td>
</tr>
<tr>
<td>1–&lt;4 years</td>
<td>0.7</td>
<td>0.8</td>
<td>9</td>
<td>0.9</td>
<td>120</td>
<td>1.0</td>
<td>55</td>
</tr>
<tr>
<td>4–&lt;7 years</td>
<td>1.0</td>
<td>1.1</td>
<td>12</td>
<td>1.2</td>
<td>160</td>
<td>1.5</td>
<td>60</td>
</tr>
<tr>
<td>7–&lt;10 years</td>
<td>1.1</td>
<td>1.2</td>
<td>13</td>
<td>1.4</td>
<td>200</td>
<td>1.8</td>
<td>65</td>
</tr>
<tr>
<td>10–&lt;13 years</td>
<td>1.2</td>
<td>1.4/1.3</td>
<td>15/14</td>
<td>1.6/1.5</td>
<td>240</td>
<td>2.0</td>
<td>70</td>
</tr>
<tr>
<td>13–&lt;15 years</td>
<td>1.4/1.2</td>
<td>1.5/1.4</td>
<td>17/15</td>
<td>1.8/1.6</td>
<td>300</td>
<td>3.0</td>
<td>75</td>
</tr>
<tr>
<td>15–&lt;19 years</td>
<td>1.6/1.3</td>
<td>1.8/1.7</td>
<td>20/16</td>
<td>2.1/1.8</td>
<td>300–400</td>
<td>3.0</td>
<td>75</td>
</tr>
</tbody>
</table>
### Table 4.
Nordic nutrition recommendation intake values (male/female) for daily energy intake and nutrients intake
for healthy infants, children and adolescents (adapted from the Nordic nutrition recommendations 2004: Norway, Sweden, Finland, Denmark, Iceland)

<table>
<thead>
<tr>
<th>Age</th>
<th>Energy MJ/day</th>
<th>Protein % of energy</th>
<th>Fat % of energy</th>
<th>Essential fatty acids, % of energy</th>
<th>Calcium mg/day</th>
<th>Magnesium mg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>6–11 months</td>
<td>3.2</td>
<td>7–15</td>
<td>30–45</td>
<td>4 1</td>
<td>540</td>
<td>80</td>
</tr>
<tr>
<td>12–23 months</td>
<td>4.1</td>
<td>10–15</td>
<td>3</td>
<td>0.5</td>
<td>600</td>
<td>85</td>
</tr>
<tr>
<td>2–5 years</td>
<td>5.3</td>
<td>30–35</td>
<td></td>
<td></td>
<td>600</td>
<td>120</td>
</tr>
<tr>
<td>6–9 years</td>
<td>7.7</td>
<td></td>
<td></td>
<td></td>
<td>700</td>
<td>200</td>
</tr>
<tr>
<td>10–13 years</td>
<td>9.8/8.6</td>
<td></td>
<td></td>
<td></td>
<td>900</td>
<td>280</td>
</tr>
<tr>
<td>14–17 years</td>
<td>12.3/9.6</td>
<td></td>
<td></td>
<td></td>
<td>900</td>
<td>350/280</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age</th>
<th>Iron mg/day</th>
<th>Iodine μg/day</th>
<th>Zinc mg/day</th>
<th>Vit. A, mg retinol equivalent/day</th>
<th>Vit. D μg/day</th>
<th>Vit. K μg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<tr>
<td>6–11 months</td>
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<td>50</td>
<td>5</td>
<td>300</td>
<td>10</td>
<td>–</td>
</tr>
<tr>
<td>12–23 months</td>
<td>8</td>
<td>70</td>
<td>5</td>
<td>300</td>
<td>10</td>
<td>–</td>
</tr>
<tr>
<td>2–5 years</td>
<td>8</td>
<td>90</td>
<td>6</td>
<td>350</td>
<td>7.5</td>
<td>–</td>
</tr>
<tr>
<td>6–9 years</td>
<td>9</td>
<td>120</td>
<td>7</td>
<td>400</td>
<td>7.5</td>
<td>–</td>
</tr>
<tr>
<td>10–13 years</td>
<td>11</td>
<td>150</td>
<td>11/8</td>
<td>600</td>
<td>7.5</td>
<td>–</td>
</tr>
<tr>
<td>14–17 years</td>
<td>11/15</td>
<td>150</td>
<td>12/11</td>
<td>900/700</td>
<td>7.5</td>
<td>–</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age</th>
<th>Thiamine mg/day</th>
<th>Riboflavin mg/day</th>
<th>Niacin mg niacin equivalent/day</th>
<th>Vit. B₆ mg/day</th>
<th>Folate μg dietary folate equivalents/day</th>
<th>Vit. B₁₂ μg/day</th>
<th>Vit. C mg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>6–11 months</td>
<td>0.4</td>
<td>0.5</td>
<td>5</td>
<td>0.4</td>
<td>50</td>
<td>0.5</td>
<td>20</td>
</tr>
<tr>
<td>12–23 months</td>
<td>0.5</td>
<td>0.6</td>
<td>7</td>
<td>0.5</td>
<td>60</td>
<td>0.6</td>
<td>25</td>
</tr>
<tr>
<td>2–5 years</td>
<td>0.6</td>
<td>0.7</td>
<td>9</td>
<td>0.7</td>
<td>80</td>
<td>0.8</td>
<td>30</td>
</tr>
<tr>
<td>6–9 years</td>
<td>0.9</td>
<td>1.1</td>
<td>12</td>
<td>1.0</td>
<td>130</td>
<td>1.3</td>
<td>40</td>
</tr>
<tr>
<td>10–13 years</td>
<td>1.2/1.0</td>
<td>1.4/1.2</td>
<td>16/14</td>
<td>1.3/1.1</td>
<td>200</td>
<td>2.0</td>
<td>50</td>
</tr>
<tr>
<td>14–17 years</td>
<td>1.5/1.2</td>
<td>1.7/1.3</td>
<td>20/15</td>
<td>1.6/1.3</td>
<td>300</td>
<td>2.0</td>
<td>75</td>
</tr>
<tr>
<td>Age</td>
<td>Energy kcal/kg/day</td>
<td>Protein g/kg/day</td>
<td>Fat, % of energy</td>
<td>Essential fatty acids % of energy</td>
<td>Calcium mg/day</td>
<td>Magnesium mg/day</td>
<td></td>
</tr>
<tr>
<td>-------------</td>
<td>--------------------</td>
<td>-----------------</td>
<td>-----------------</td>
<td>----------------------------------</td>
<td>----------------</td>
<td>-----------------</td>
<td></td>
</tr>
<tr>
<td>0–&lt;3 months</td>
<td>545/515</td>
<td>12.5</td>
<td>–</td>
<td>–</td>
<td>525</td>
<td>55</td>
<td></td>
</tr>
<tr>
<td>4–&lt;6 months</td>
<td>690/645</td>
<td>12.7</td>
<td>–</td>
<td>–</td>
<td>525</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>7–&lt;9 months</td>
<td>825/765</td>
<td>13.7</td>
<td>–</td>
<td>–</td>
<td>525</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>10–&lt;12 months</td>
<td>920/865</td>
<td>14.9</td>
<td>–</td>
<td>–</td>
<td>525</td>
<td>80</td>
<td></td>
</tr>
<tr>
<td>1–&lt;3 years</td>
<td>1,230/1,165</td>
<td>14.5</td>
<td>–</td>
<td>–</td>
<td>350</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>4–&lt;6 years</td>
<td>1,715/1,545</td>
<td>19.7</td>
<td>–</td>
<td>–</td>
<td>450</td>
<td>120</td>
<td></td>
</tr>
<tr>
<td>7–&lt;10 years</td>
<td>1,970/1,740</td>
<td>28.3</td>
<td>–</td>
<td>–</td>
<td>550</td>
<td>200</td>
<td></td>
</tr>
<tr>
<td>11–&lt;14 years</td>
<td>2,220/1,845</td>
<td>42.1/41.2</td>
<td>–</td>
<td>–</td>
<td>1,000/800</td>
<td>280</td>
<td></td>
</tr>
<tr>
<td>15–&lt;19 years</td>
<td>2,755/2,110</td>
<td>55.2/45.0</td>
<td>–</td>
<td>–</td>
<td>1,000/800</td>
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<table>
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<th>Iron mg/day</th>
<th>Iodine µg/day</th>
<th>Zinc mg/day</th>
<th>Vit. A, mg retinol equivalent/day</th>
<th>Vit. D µg/day</th>
<th>Vit. K µg/day</th>
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<tbody>
<tr>
<td>0–&lt;3 months</td>
<td>1.7</td>
<td>50</td>
<td>4.0</td>
<td>350</td>
<td>8.5</td>
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<td>4.0</td>
<td>350</td>
<td>8.5</td>
<td>–</td>
</tr>
<tr>
<td>7–&lt;9 months</td>
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<td>60</td>
<td>5.0</td>
<td>350</td>
<td>7</td>
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<td>10–&lt;12 months</td>
<td>7.8</td>
<td>60</td>
<td>5.0</td>
<td>350</td>
<td>7</td>
<td>–</td>
</tr>
<tr>
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</tr>
<tr>
<td>4–&lt;6 years</td>
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<td>100</td>
<td>6.5</td>
<td>400</td>
<td>–</td>
<td>–</td>
</tr>
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<td>110</td>
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<td>500</td>
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<td>–</td>
</tr>
<tr>
<td>11–&lt;14 years</td>
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<td>300/600</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>15–&lt;19 years</td>
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<td>140</td>
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<td>700/600</td>
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<table>
<thead>
<tr>
<th>Age</th>
<th>Thiamine mg/day</th>
<th>Riboflavin mg/day</th>
<th>Niacin mg niacin equivalent/day</th>
<th>Vit. B6 mg/day</th>
<th>Folate µg dietary folate equivalents/day</th>
<th>Vit. B12 µg/day</th>
<th>Vit. C mg/day</th>
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<td>0–&lt;3 months</td>
<td>0.2</td>
<td>0.4</td>
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<td>50</td>
<td>0.3</td>
<td>25</td>
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<td>4–&lt;6 months</td>
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<td>0.4</td>
<td>3</td>
<td>0.2</td>
<td>50</td>
<td>0.3</td>
<td>25</td>
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<tr>
<td>7–&lt;9 months</td>
<td>0.2</td>
<td>0.4</td>
<td>4</td>
<td>0.3</td>
<td>50</td>
<td>0.4</td>
<td>25</td>
</tr>
<tr>
<td>10–&lt;12 months</td>
<td>0.3</td>
<td>0.4</td>
<td>5</td>
<td>0.4</td>
<td>50</td>
<td>0.4</td>
<td>25</td>
</tr>
<tr>
<td>1–&lt;3 years</td>
<td>0.5</td>
<td>0.6</td>
<td>8</td>
<td>0.7</td>
<td>70</td>
<td>0.5</td>
<td>30</td>
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<tr>
<td>4–&lt;6 years</td>
<td>0.7</td>
<td>0.8</td>
<td>11</td>
<td>0.9</td>
<td>100</td>
<td>0.8</td>
<td>30</td>
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<tr>
<td>7–&lt;10 years</td>
<td>0.7</td>
<td>1.0</td>
<td>12</td>
<td>1.0</td>
<td>150</td>
<td>1.0</td>
<td>30</td>
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<tr>
<td>11–&lt;14 years</td>
<td>0.9/0.8</td>
<td>1.2/1.1</td>
<td>15/12</td>
<td>1.2/1.0</td>
<td>200</td>
<td>1.2</td>
<td>35</td>
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<tr>
<td>15–&lt;19 years</td>
<td>1.1/0.8</td>
<td>1.3/1.1</td>
<td>18/14</td>
<td>1.5/1.2</td>
<td>200</td>
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Table 6. Energy

<table>
<thead>
<tr>
<th>Age, months</th>
<th>Energy, kcal/day</th>
<th>Age, months</th>
<th>Energy, kcal/day</th>
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<tbody>
<tr>
<td>1</td>
<td>472/438</td>
<td>11</td>
<td>817/742</td>
</tr>
<tr>
<td>2</td>
<td>567/500</td>
<td>12</td>
<td>844/768</td>
</tr>
<tr>
<td>3</td>
<td>572/521</td>
<td>15</td>
<td>908/837</td>
</tr>
<tr>
<td>4</td>
<td>548/508</td>
<td>18</td>
<td>961/899</td>
</tr>
<tr>
<td>5</td>
<td>596/553</td>
<td>21</td>
<td>1,006/952</td>
</tr>
<tr>
<td>6</td>
<td>645/593</td>
<td>24</td>
<td>1,050/997</td>
</tr>
<tr>
<td>7</td>
<td>668/608</td>
<td>27</td>
<td>1,086/1,033</td>
</tr>
<tr>
<td>8</td>
<td>710/643</td>
<td>30</td>
<td>1,121/1,077</td>
</tr>
<tr>
<td>9</td>
<td>746/678</td>
<td>33</td>
<td>1,157/1,113</td>
</tr>
<tr>
<td>10</td>
<td>793/717</td>
<td>35</td>
<td>1,184/1,139</td>
</tr>
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<td>3–18 years</td>
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<td>3–18 years</td>
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</tr>
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Table 7. Nutrient values (male/female)

<table>
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<tr>
<th>Age</th>
<th>Protein g/day</th>
<th>Fat g/day</th>
<th>Polyunsaturated fatty acids g/day</th>
<th>Calcium mg/day</th>
<th>Magnesium mg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–&lt;6 months</td>
<td>9.1</td>
<td>31</td>
<td>4.4</td>
<td>210</td>
<td>30</td>
</tr>
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<td>7–&lt;12 months</td>
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<td>30</td>
<td>4.6</td>
<td>270</td>
<td>75</td>
</tr>
<tr>
<td>1–&lt;3 years</td>
<td>13</td>
<td>30–40</td>
<td>7</td>
<td>500</td>
<td>80</td>
</tr>
<tr>
<td>4–&lt;8 years</td>
<td>19</td>
<td>25–35</td>
<td>10</td>
<td>800</td>
<td>130</td>
</tr>
<tr>
<td>9–&lt;13 years</td>
<td>34</td>
<td>25–35</td>
<td>12/10</td>
<td>1,300</td>
<td>240</td>
</tr>
<tr>
<td>14–&lt;18 years</td>
<td>52/46</td>
<td>25–35</td>
<td>16/11</td>
<td>410/360</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age</th>
<th>Iron mg/day</th>
<th>Iodine μg/day</th>
<th>Zinc mg/day</th>
<th>Vit. A, mg retinol equivalent/day</th>
<th>Vit. D μg/day</th>
<th>Vit. K μg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–&lt;6 months</td>
<td>0.27</td>
<td>110</td>
<td>2</td>
<td>400</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>7–&lt;12 months</td>
<td>11</td>
<td>130</td>
<td>3</td>
<td>500</td>
<td>5</td>
<td>2.5</td>
</tr>
<tr>
<td>1–&lt;3 years</td>
<td>7</td>
<td>90</td>
<td>3</td>
<td>300</td>
<td>5</td>
<td>30</td>
</tr>
<tr>
<td>4–&lt;8 years</td>
<td>10</td>
<td>90</td>
<td>5</td>
<td>400</td>
<td>5</td>
<td>55</td>
</tr>
<tr>
<td>9–&lt;13 years</td>
<td>8</td>
<td>120</td>
<td>8</td>
<td>600</td>
<td>5</td>
<td>60</td>
</tr>
<tr>
<td>14–&lt;18 years</td>
<td>11/15</td>
<td>150</td>
<td>11/9</td>
<td>900/700</td>
<td>5</td>
<td>75</td>
</tr>
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<table>
<thead>
<tr>
<th>Age</th>
<th>Thiamine mg/day</th>
<th>Riboflavin mg/day</th>
<th>Niacin, mg niacin equivalent/day</th>
<th>Vit. B₆ mg/day</th>
<th>Folate, μg total folate/day</th>
<th>Vit. B₁₂ μg/day</th>
<th>Vit. C mg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–&lt;6 months</td>
<td>0.2</td>
<td>0.3</td>
<td>2</td>
<td>0.1</td>
<td>65</td>
<td>0.4</td>
<td>40</td>
</tr>
<tr>
<td>7–&lt;12 months</td>
<td>0.3</td>
<td>0.4</td>
<td>4</td>
<td>0.3</td>
<td>80</td>
<td>0.5</td>
<td>50</td>
</tr>
<tr>
<td>1–&lt;3 years</td>
<td>0.5</td>
<td>0.5</td>
<td>6</td>
<td>0.5</td>
<td>150</td>
<td>0.9</td>
<td>15</td>
</tr>
<tr>
<td>4–&lt;8 years</td>
<td>0.6</td>
<td>0.6</td>
<td>8</td>
<td>0.6</td>
<td>200</td>
<td>1.2</td>
<td>25</td>
</tr>
<tr>
<td>9–&lt;13 years</td>
<td>0.9</td>
<td>0.9</td>
<td>12</td>
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<td>300</td>
<td>1.8</td>
<td>45</td>
</tr>
<tr>
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<td>1.2/1.0</td>
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<td>16/14</td>
<td>1.3</td>
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### Table 9. Calcium and magnesium (male/female)

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<th>Calcium, mg/day</th>
<th>Magnesium, mg/day</th>
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</thead>
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<td>0–6 months</td>
<td>300 (human milk)</td>
<td>26 (human-milk-fed)</td>
</tr>
<tr>
<td></td>
<td>400 (cow’s milk)</td>
<td>36 (formula-fed)</td>
</tr>
<tr>
<td>7–12 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–3 years</td>
<td>500</td>
<td>60</td>
</tr>
<tr>
<td>4–6 years</td>
<td>600</td>
<td>76</td>
</tr>
<tr>
<td>7–9 years</td>
<td>700</td>
<td>100</td>
</tr>
<tr>
<td>10–18 years</td>
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</tr>
<tr>
<td></td>
<td>1,300</td>
<td>230/220</td>
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</table>

For table 10, see next page.

### References

Table 10. Trace elements and vitamins (male/female)

<table>
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<tr>
<th>Age</th>
<th>Iron, mg/day</th>
<th>Iodine g/day</th>
<th>Zinc, mg/day, depends on:</th>
<th>Thiamine mg/day</th>
<th>Riboflavin mg/day</th>
<th>Niacin, mg niacin equivalent/day</th>
<th>Vit. B$_6$ mg/day</th>
<th>Folate, µg folate equivalents/day</th>
<th>Vit. B$_{12}$ µg/day</th>
<th>Vit. C mg/day</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>15% bio-availability</td>
<td>12% bio-availability</td>
<td>10% bio-availability</td>
<td>5% bio-availability</td>
<td>high availability</td>
<td>moderate availability</td>
<td>low availability</td>
<td></td>
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</tr>
<tr>
<td>0–6 months</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>90</td>
<td>1.1</td>
<td>2.8</td>
<td>6.6</td>
<td>375</td>
<td>5</td>
</tr>
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<td>7–12 months</td>
<td>6.2</td>
<td>7.7</td>
<td>9.3</td>
<td>18.6</td>
<td>90</td>
<td>0.8 (HM-fed)</td>
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<td>8.4</td>
<td>400</td>
<td>5</td>
</tr>
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<td></td>
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<td></td>
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<td></td>
<td>2.25 (formula-fed)</td>
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<td>4.8</td>
<td>5.8</td>
<td>11.6</td>
<td>90</td>
<td>2.4</td>
<td>4.1</td>
<td>8.3</td>
<td>400</td>
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<td>17.8</td>
<td>120</td>
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<td>5.6</td>
<td>11.2</td>
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<td>(11–14 years)</td>
<td>(11–14 years)</td>
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<td>150</td>
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<td>(pre-menarche)</td>
<td>(pre-menarche)</td>
<td>(pre-menarche)</td>
<td>(15–17 years)</td>
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<td></td>
<td>21.8</td>
<td>27.7</td>
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<td>37.6</td>
<td>(6–12 years)</td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>Age</td>
<td>Thiamine mg/day</td>
<td>Riboflavin mg/day</td>
<td>Niacin, mg niacin equivalent/day</td>
<td>Vit. B$_6$ mg/day</td>
<td>Folate, µg folate equivalents/day</td>
<td>Vit. B$_{12}$ µg/day</td>
<td>Vit. C mg/day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–6 months</td>
<td>0.2</td>
<td>0.3</td>
<td>2</td>
<td>0.1</td>
<td>80</td>
<td>0.4</td>
<td>25</td>
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<tr>
<td>7–12 months</td>
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<td>0.4</td>
<td>4</td>
<td>0.3</td>
<td>80</td>
<td>0.7</td>
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<tr>
<td>1–3 years</td>
<td>0.5</td>
<td>0.5</td>
<td>6</td>
<td>0.5</td>
<td>150</td>
<td>0.9</td>
<td>30</td>
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<td></td>
</tr>
<tr>
<td>4–6 years</td>
<td>0.6</td>
<td>0.6</td>
<td>8</td>
<td>0.6</td>
<td>150</td>
<td>1.2</td>
<td>30</td>
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</tr>
<tr>
<td>7–9 years</td>
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<td>0.9</td>
<td>12</td>
<td>1.0</td>
<td>300</td>
<td>1.8</td>
<td>35</td>
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<td></td>
</tr>
<tr>
<td>10–18 years</td>
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<td>1.3/1.0</td>
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<td>1.3/1.2</td>
<td>330</td>
<td>2.4</td>
<td>40</td>
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</table>
4.4 Feeding My Baby – Advice for Families

Berthold Koletzko · Katharina Dokoupil

The advice given herein has been compiled for families in an affluent country setting in Europe. Modification may be necessary for other settings.

Whether breastfeeding or infant formula – feeding of the baby not only provides nutrition, it also comprises tender loving care, attention and closeness.

Breastfeeding

- Breastfeeding is the natural way of feeding for healthy infants
- Breast milk is easy to digest, always available, comes at the right feeding temperature, and carries little infectious risk
- Numerous anti-infective components in breast milk reduce the infant’s risk of infectious diseases, particularly with respect to diarrhea
- Breastfeeding encourages close body contact between mother and infant
- For most babies full or exclusive breastfeeding offers adequate nutrition during the first 4–6 months of life. But even a shorter period of full or exclusive breastfeeding with additional supplemental feeding is worthwhile – any breastfeeding is strongly encouraged
- The introduction of complementary feeds should not discourage continuation of breastfeeding, rather the infant should continue to be breastfed after the introduction of complementary feeds. Mother and child decide how long to continue breastfeeding

Practical Recommendations for Breastfeeding

The baby should be attached to the breast within the first hour after birth whenever possible. Particularly during the first days after birth the mother should ask for help, support, and practical advice how to position the baby. The child should be turned towards the mother with its whole body and take not only the nipple but a larger portion of the breast into its mouth. Breastfeeding can also be performed after a cesarean section.

To promote the formation of breast milk, the baby should suckle on both breasts during the first days. A larger amount of milk will be produced a few days after birth. Temporary supplementary feeding with water or other liquids should only be offered if it is deemed necessary by the pediatrician or the pediatric nurse.

The baby should be breastfed whenever it wishes to suckle, also at night. In the first weeks most infants take 8–12 meals in 24 h.

Breastfeeding promotes the gradual loss of the mother’s body weight and the extra body fat stores that were deposited during pregnancy. The amount of fat loss increases with the duration of full breastfeeding. Additional active weight reduction during breastfeeding with use of restrictive diets is not recommended because it may have undesirable effects on milk composition.

Breastfeeding women should consume a varied diet and plenty of liquids. A good supply of
iodine (iodized salt, supplements with 100–150 μg/day) and long-chain n-3 fatty acids (200 mg DHA/day, provided by 1–2 weekly meals of sea fish including fatty fish) is recommended. Breastfeeding women should refrain from smoking and consumption of significant amounts of alcoholic drinks. Only very few mothers of babies with proven food intolerances are advised to exclude allergenic foods from their own diets upon individual advice from their pediatrician or dietician, but the use of food exclusion for the prevention of allergies in infants is not recommended.

**Infant Formula**

If breastfeeding is discontinued before 1 year of age, an iron-fortified, commercial infant formula should be used. In the first months of life only infant formula should be used, which can be continued throughout the first year of life. Follow-up formulas are only appropriate after complementary feeds have been introduced into the infant’s diet.

In infants who are not fully breastfed and who have parents or siblings suffering from allergic diseases, the pediatrician should be consulted regarding the use of hydrolyzed infant formula during the first 6 months of life.

Manufacturers’ recommendations should be followed carefully with respect to the preparation of bottles. Both too low and too high concentrations of formula milks are detrimental. Milk bottles must always be freshly prepared and fed within approximately 2 h. Leftovers should be discarded to prevent the occurrence of bacterial infections. Frozen and then defrosted breast milk must be handled in the same way. It is important to keep bottles and nipples clean and dry. Powdered formulas have to be prepared with fresh and clean drinking water. The use of water filters is not recommended. If water contains high levels of nitrate (>50 mg/l; especially in domestic wells) or water pipes made of lead are used (in some old buildings) bottled water suitable for preparing infant formula should be used. The suitability of water from domestic wells should be assessed in each case.

**Fig. 1.** Feeding concept in the first year of life.
Infant formulas based on soy protein and other so-called 'special formulas' are only indicated in very few special situations and should only be used upon the recommendation of a pediatrician. Self-prepared bottle feeds from cow’s milk, the milk of other animals (goat, mare, sheep’s milk) and other sources (such as almond milk) pose serious risks and should not be used.

**Feeding Solid Foods (Complementary Foods, Beikost)**

From about the end of the first half of infancy, breast milk and infant formula on their own cannot adequately meet the nutrient requirement of a healthy baby. For their optimal development infants require additional nutrients, such as the trace elements iron and zinc. The introduction of solid foods over time should gradually get the child used to an increasing variety of foods and, around the age of about 1 year, to family foods. The first complementary foods should not be given later than the age of 26 weeks but not before the age of 17 weeks. As the first solid food, a mixture of pulpy vegetables, potatoes and meat can be recommended which provides iron and zinc with high bioavailability (fig. 1). In about monthly intervals, additional meals consisting of cereals with milk and a fruit-grain pap may be introduced (fig. 1). From the age of about 10 months bread (initially soft) may be offered. Gluten-containing cereals (wheat, rye, barley, for example in porridge, bread, biscuits and rusks) should initially be given only in small quantities, and preferably while the infant is still being breastfed, to reduce the risk of developing of intolerance (celiac disease). No benefits of a generally low-allergen diet in infancy have been documented, and hence the exclusion or delayed introduction of complementary food products considered allergenic is not recommended.

**Beverages**

When 3 meals per day of complementary feeding are given, children should be offered water. Prior to reaching 3 solid food meals per day, no liquid in additional to breast milk or infant formula is needed, except for situations with fever, vomiting or diarrhea. Regular cow’s milk should be offered as a drink only after the first year of life to avoid adverse effects, for example on iron absorption.
Infants and children with growth faltering often need an enhanced intake of energy and nutrients. Increasing the energy density, i.e. the amount of energy per food portion or per milliliter of a liquid food, can increase the total energy intake even when the total amount of food taken remains limited. Such an increase in energy density can be achieved by using one or several elements of a stepwise approach.

**Elements of a stepwise approach to increase energy and nutrient supply**

| (1) | Analysis of needs, diet and feeding situation |
| (2) | Individual, professional counseling on dietary choices and on feeding practice |
| (3) | Offer meals and snacks more frequently |
| (4) | Preferential choice of energy-dense foods, drinks and snacks |
| (5) | Enrichment of formula and home foods with glucose polymers and/or oils |
| (6) | Use of drinkable supplements (sip feeds) |
| (7) | Tube feeding (nocturnal/continuous) |
| (8) | Parenteral nutrition |

**Infants: Options for Increasing Energy Density of Expressed Human Milk or Infant Formula**

**Increased Concentration of Infant Formula**

The use of 15% powder instead of 13% increases energy density by 15%. The concentration should be increased stepwise according to individual tolerance. Concentrations of >17% (+30% energy density) should usually be avoided.

*Disadvantage:* Increased formula density increases renal solute load and may reduce tolerance.

**Addition of Glucose Polymers**

Glucose polymers (dextrin maltose or glucose polymer mixtures) can be added with stepwise increasing concentrations from 1 up to 4 g/100 ml, which adds ≈3.9–15.6 kcal/100 ml milk/formula. The concentration should be increased stepwise according to individual tolerance.

*Disadvantage:* The supply of essential nutrients per kilocalorie is reduced and may not always be sufficient, particularly for catch-up growth.

**Addition of Glucose Polymer – Fat Mixtures to Infant Formula**

Preparations of glucose polymers with either vegetable oil (e.g. soybean oil, rapeseed oil) or medium chain triglycerides (MCTs) from coconut oil can be added in stepwise increasing concentrations from 1 to 4 g/100 ml, which adds ≈5.1–10.5 kcal/100 ml milk/formula. The concentration should be increased stepwise according to individual tolerance.

Usually mixtures with vegetable oils providing long-chain fats should be used. Mixtures with MCTs are only indicated in cases of severe fat
mal-assimilation (e.g. marked cholestasis). MCTs may be quickly hydrolyzed when added to human milk which can limit tolerance.

Disadvantage: The supply of essential nutrients per kilocalorie is reduced.

Addition of Oils or of Fat Emulsions
Vegetable oils can be mixed with milk/formula and provided at ≈1 g/kg body weight per day; 9 kcal/g. Added oils tend to separate (oil droplets on the surface) and, depending on the mode of feed delivery, may only be delivered in part to the recipient infant.

An enteral vegetable oil (long-chain triglyceride) in water emulsion providing 4.5 kcal/ml is available which can be mixed with milk/formula.

Disadvantage: The supply of essential nutrients per kilocalorie is reduced.

Use of Enteral Infant Feed
High-energy infant feeds (≈1 kcal/ml) with balanced nutrient composition are a good alternative particularly for infants who need a high energy and nutrient density over prolonged time periods.

Children: Preferential Choice of Energy-Dense Foods, Drinks and Snacks

- Energy-dense foods, e.g. deep fried foods (French fries), fatty foods
- Energy-dense drinks, e.g. milk shakes, high-fat milk/chocolate drinks. For many children it is easier to drink extra calories than to take them with more solid foods
- Energy-dense snacks, e.g. ice-cream without or with extra whipped cream, chocolate, chocolate mousse or energy-dense puddings (with cream), potato chips (fried in oil), nuts, nuts with raisins

Children: Options for Increasing Energy Density of Foods

Addition of Fats and Oils to Foods
Use of extra butter, margarine, vegetable oils, cream, fatty cheese, e.g. extra fat, cream and cheese with vegetables, starchy foods, milk products. Increase concentration stepwise according to individual tolerance.

Disadvantage: The supply of essential nutrients per kilocalorie is reduced and may not always be sufficient, particularly for catch-up growth.

Addition of Glucose Polymers to Drinks and Semisolid Foods
Glucose polymers can be added in stepwise increasing concentrations up to 5–10 g/100 g (19.5–38 kcal/100 g) in pre-school children and up to 10–15 g/100 g (38–58.5 kcal/100 g) in school-age children to drinks (e.g. milk, tea, juice) and semisolid foods (e.g. soups, pureed vegetables). Increase concentration stepwise according to individual tolerance.

Disadvantage: The supply of essential nutrients per kilocalorie is reduced and may not always be sufficient, particularly for catch-up growth.

Use of Liquid Feeds with High Energy and Nutrient Density
High-energy liquid feeds (sip feeds, ≈1–1.5 kcal/ml) with balanced nutrient composition are a good alternative, particularly for children who need a high energy and nutrient density over prolonged time periods.
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