Feeding during Late Infancy and Early Childhood: Impact on Health
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For this 56th Nestlé Pediatric Nutrition Workshop, which took place in November 2004 in Noordwijk, The Netherlands, the topic ‘Feeding during Late Infancy and Early Childhood: Impact on Health’ was chosen. Moreover, it is the first time that a Nestlé Nutrition Workshop has been organized in the Netherlands, a market that has recently opened to the infant nutrition business.

In its resolution WHA54.2 (2001), the WHO recommends the promotion and support of exclusive breastfeeding for 6 months, and then the provision of safe and appropriate complementary foods whilst continuing breastfeeding until 2 years of age or beyond.

This resolution naturally challenges most of the prior feeding recommendations and probably also parental habits; moreover, all recently published studies demonstrate that most of the infants receive their first complementary solid food before 6 months of age. On the other hand, until recently it was strongly recommended not to introduce complementary food containing gluten before the age of 6 months; this has also been challenged by data showing that a too late introduction may be problematic in terms of gluten tolerance.

It must be acknowledged that this topic of feeding during late infancy has not been investigated as systematically as that concerning feeding during the 6 first months of life; therefore, a lot of work remains to be done.

Since 1984 (Nestlé Nutrition Workshop 10: Infant Nutrition), these aspects relating to the introduction of weaning foods (baby food, cereals, etc.) have not been reviewed systematically during a Nestlé Nutrition Workshop.

This 56th Nestlé Nutrition Workshop has been specifically developed to review the medical and scientific aspects of these topics and to sustain the Nestlé Development Nutrition Program (NDNP).

I would like to thank the two chairmen, Prof. Olle Hernell and Prof. Jacques Schmitz who are recognized experts in this field, for putting the program together and inviting the opinion leaders in these fields as speakers.
I would also like to thank Mrs. Marjan Skotnicki-Hoogland, Mrs. Mieke Beemsterboer and their team from Nestlé Nederland, who provided all logistic support, enabling the participants to enjoy the Dutch hospitality.

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Immune tolerance can be induced by respiratory or oral exposure to an antigen. Tolerance inducing strategies have been demonstrated in animal models of autoimmunity, allergy and transplantation. Mechanisms of tolerance involve clonal anergy, deletion and active suppression by regulatory T cells secreting immunosuppressive cytokines such as IL-10 and TGF-β or by cell-to-cell contact inhibition.

Immune regulation by the induction of oral tolerance to food antigens is thought to prevent food allergy [1]. The efficiency of oral tolerance induction depends on the age of the host, the nature of the antigen, the dose of this antigen administered and the microbial environment. Oral tolerance can be induced with intact antigens but also with peptides and enzymatic hydrolysates, which have the advantage of reduced allergenicity while keeping tolerance-inducing properties [2]. Animal models have shown that oral tolerance can be induced in utero, via nutrition of the pregnant mother [3] and also through breastfeeding. Whether this is true in humans remains to be demonstrated. The effect of the gastrointestinal microflora on induction and maintenance of oral tolerance to dietary antigens has been studied in a number of animal models [4, 5]. It is proposed that early colonization may affect the development of mucosal tolerance.

References

Prevention of Food Allergy during Late Infancy and Early Childhood

Jacques Schmitz

Epidemiological data show that the prevalence of allergic conditions continues to increase, at least in the developed world. It is difficult to imagine how genetic factors, the most important risk factors for the development of allergic diseases, could be responsible for such a trend. Among the environmental factors that could explain this rise in prevalence, two seem particularly worthwhile considering because they may lead to prevention: (a) the increased exposure to (new) environmental/oral sensitizing agents that may be fought by exclusion diets, and (b) the decreased bacterial load resulting from the increasing rate of cesarean delivery, the widespread use of sterile food, the frequent prescription of oral antibiotics during infancy, which may favor the Th2-allergic immunological reaction. This increased prevalence factor of allergic conditioning might be counteracted by the use of probiotics that would restore a normal Th1/Th2 equilibrium.

Prevention of Food Allergy by Exclusion Diets during the Weaning Period

The available studies, although rather old, suggest that delaying the introduction of solid food might reduce the risk of clinical food allergy and eczema. However, the magnitude of the effect is not well known (precise and important in one study, confounded with other measures in all other studies) and the duration of the period of avoidance is not known at all. Whereas there is a consensus to avoid solid foods before 3–4 months of age, at present there are no studies enabling a decision to be made on how long preventive measures need to be maintained.

Prevention of Atopic Disease through the Use of Probiotics

As the inverse association between infections early in life and allergic disease and the role of the commensal gastrointestinal
microflora in promoting a Th1-type immunity essential in controlling Th2 allergic inflammation are being better understood, it was logical to try to prevent the occurrence of atopic disease in children by giving them probiotics in their infancy.

In an important randomized placebo-controlled trial concerning 159 infants and their mothers in families with a history of atopic disease, capsules containing either a placebo or $10^{10}$ CFU of lactobacillus GG were given 2–4 weeks before delivery to the mother and for 6 months to the infants. Children were examined at ages 3, 6, 12, 18 and 24 months. Atopic eczema was diagnosed in 35% of children aged 2 years. The frequency of atopic eczema in the probiotic group was half that of the placebo group: 15/64 (23%) vs. 31/68 (46%), RR 0.51, 95% CI 0.32–0.84. Two years later the effect was still observed: 14 of 53 children receiving lactobacillus had developed eczema compared to 25 of 54 receiving placebo (RR 0.57, 95% CI 0.33–0.97), suggesting that the preventive effect of lactobacillus GG on eczema extended beyond infancy. Although these studies need to be confirmed, they open a new avenue in the prevention of atopic manifestations.

It is important to note that recent progress in our understanding of mucosal immunity and the role of bacterial burden on the development of tolerance in infancy make it possible to envisage prevention strategies for food allergy other than exclusion diets, the efficiency of which is still being discussed as their magnitude and time frame are uncertain. Careful nutritional follow-up of these children is needed.
Celiac Disease: Effect of Weaning on Disease Risk

Olle Hernell, Göte Forsberg, Marie-Louise Hammarström, Sten Hammarström and Anneli Ivarsson

Next to atopic diseases, celiac disease (CD) is now recognized as the most common chronic disease in children. As for other chronic inflammatory conditions the etiology is multifactorial [1]. A recent Swedish incident case–referent study, conducted during a period when the incidence of CD in children below 2 years of age had increased dramatically over a few years [2], strongly suggested that the feeding pattern during the weaning period affects disease risk. Introducing gluten gradually while the infant is still being breastfed seems to have a protective effect, and every month of continued breastfeeding after the introduction reduces the risk further [3]. Repeated infections during the first 6 months of life also increase the risk of developing CD, particularly in combination with being fed large amounts of gluten when this is first introduced into the diet. It is, however, uncertain if the age at which gluten is introduced is an independent risk factor for CD development [3]. Hence, a preventive strategy seems to be to promote breastfeeding and recommend parents introduce gluten-containing food gradually before breastfeeding is discontinued.

In a recent study we noticed that rod-shaped bacteria frequently adhered to the intestinal mucosa in CD patients, but not in controls, and that the presence of bacteria was associated with a particular lectin-staining pattern of the mucosa, which could facilitate bacterial adhesion [4]. Whether these yet undefined bacteria can precipitate disease in genetically susceptible individuals is not yet known. There is a strong intraepithelial lymphocyte response in CD with increased expression of interferon-γ and interleukin-10, without a concomitant increase in the expression of tumor necrosis factor-α or transforming growth factor-β1, and with a marked shift in the interferon-γ and interleukin-10 production from the lamina propria to the epithelium. This may cause both recruitment of intraepithelial lymphocytes and
a leaky epithelium. Hence, the epithelial reaction may be critical for disease development in CD [5].

The mechanism behind the protective effect of breastfeeding remains to be understood, although it is known that breast milk is a rich source of down-regulatory transforming growth factor-β1 and has immune-modulating effects that last also beyond the breastfeeding period. Moreover, breastfeeding affects colonization of the gut.

References

Gut Microbiota in Infants between 6 and 24 Months of Age

Seppo Salminen and Miguel Gueimonde

The indigenous microbiota of the infant gastrointestinal tract is created through complicated contacts and interaction with the microbiota of the parents and the infant’s immediate environment. Nature-induced initial colonization is enhanced by galacto-oligosaccharides in breast milk and the microbiota of the mother. This process directs the later microbiotic succession and health of the infant throughout the rest of his/her life. Thus, the understanding and positive guidance of the process through dietary means are important targets when facilitating the mother–infant relationship through birth, breastfeeding, weaning and first years of life. This process forms the platform for creating healthy adult gut microbiota.

The establishment of the gut microbiota is usually characterized by the following steps: early colonization at birth with facultative anaerobes depending on the mode of delivery with rapid succession by anaerobic genera such as Bifidobacterium, Bacteroides, Clostridium and Eubacterium. New molecular methods indicate that lactic acid-producing bacteria may account for less than 1% of the total microbiota while bifidobacteria can range from 60 up to 90% of the total fecal microbiota in breastfed infants.

After the first 6 months of life, the microbiotic succession diverts towards a more diverse community. At weaning the differences observed between breastfed and formula-fed infants disappear due to the increase in the numbers of enterococci, Bacteroides, Clostridium and anaerobic cocci in the former group. Increases in E. coli, and enterococci have also been reported after weaning. The levels of Bacteroides and anaerobic gram-positive cocci also appear to increase gradually during and following weaning, whereas enterobacteria often decrease. Some of the changes are illustrated in figure 1.

Following weaning, healthy microbiota, identified as the normal microbiota of an individual that both preserves and promotes well-being
and absence of disease especially in the gastrointestinal tract, will gradually be created.

Creating healthy gut microbiota during early life must be followed by proper maintenance and enhancement of the individual balance. During times of disease or following detectable deviations in initial microbiotic development, later maintenance can be achieved by directing gut microbiota into a healthy balance by dietary means, for instance by using probiotics or prebiotics.

**Suggested Reading**

Carbohydrate Intolerances

C.M. Frank Kneepkens and J. Hans Hoekstra

Carbohydrates are responsible for 25–50% of the daily energy intake. Glycolytic enzymes hydrolyze the carbohydrates to form monosaccharides. Glucose and galactose are actively transported; fructose absorption takes place through facilitated diffusion. Unabsorbed carbohydrates (mainly resistant starch and dietary fiber) enter the colon, serving as a fuel for the gut microflora. In carbohydrate malabsorption, the supply of soluble carbohydrates may surpass the fermentative capacity of the colonic flora. Unabsorbed carbohydrate is degraded by bacterial glycosidases, resulting in the production of gases and short-chain fatty acids (SCFAs). Normally, about 90% of all SCFAs are absorbed; they promote the absorption of water and electrolytes, and provide the body with about 70% of the original carbohydrate energy. This is called colonic salvage.

In carbohydrate malabsorption, the unabsorbed carbohydrates may surpass the fermenting capacity of the microflora, thwarting the colonic salvage mechanism. Regular consumption of lactose may, however, cause an increased fecal mass rather than clinical symptoms. Colonic salvage may be less efficient in young infants and in toddler diarrhea, and is impaired in antibiotic-associated diarrhea. The looseness of the feces in diarrhea is a function of fecal solid composition. Fat increases looseness of the stools, while fiber improves consistency. Rapid small intestinal transit results in less efficient absorption. Conversely, carbohydrate malabsorption decreases transit time by increasing the osmolarity of the gut contents.

‘Carbohydrate malabsorption’ and ‘carbohydrate intolerance’ should not be used interchangeably. Malabsorption indicates incomplete absorption, and intolerance points at the clinical symptoms that may result. When the supply of unabsorbed carbohydrates exceeds the fermentative capacity of the microflora, fermentation is incomplete, and not SCFAs, but lactate and monosaccharides will prevail in the colon. This is a staged process and the end result depends not only on colonic salvage, bacterial adaptation and the type of solids present,
but also on the type, the properties, the load and the rate of delivery of the carbohydrates involved. While fibers mainly increase fecal mass, oligosaccharides tend to increase gas production and water retention, and lactate and other breakdown products may irritate the bowel wall. This results in true carbohydrate intolerance, with symptoms of abdominal pain, distended abdomen, borborygmi and flatulence or osmotic diarrhea.

The malabsorption of mono-, di-, and oligosaccharides can be due to primary defects or be secondary to damage to the bowel wall (enteropathy). In addition, the absorptive capacity of the small intestine is limited for some carbohydrates, e.g. fructose which is thought to play a role in toddler diarrhea, while other carbohydrates are not absorbed at all. Secondary carbohydrate malabsorption is seldom a clinical problem, but rather requires treatment of the underlying condition. The main primary defects of carbohydrate absorption are glucose-galactose malabsorption, disaccharide intolerance I (sucrase-isomaltase deficiency), and congenital lactase deficiency. They all result in profuse watery diarrhea after consumption of the sugars involved. Not a defect, but rather the normal situation, is adult-type hypolactasia, the condition in which lactase activity declines after weaning. The clinical consequences thereof vary considerably in between malabsorbers and also between adults and children. Small amounts of lactose invariably are tolerated by all adult malabsorbers, and children seem to be more tolerant than adults. Although lactase activity may start declining significantly in 3- to 4-year-olds, adverse effects will not be seen before several years later.

In conclusion, carbohydrate malabsorption does not necessarily imply intolerance. Colonic salvage enables the body to retain most of the energy and prevents diarrhea. Only a few conditions, generally presenting early in life, require targeted dietary measures. Secondary lactose malabsorption is mostly transitory and seldom necessitates dietary lactose reduction. Adult-type hypolactasia is not a problem until school age and can often be managed by simple measures.
Chronic Nonspecific Diarrhea of Childhood

R.E. Kleinman

Approximately 50 years of observation and investigation have led to the definition of chronic nonspecific diarrhea of childhood, or toddler’s diarrhea, as a functional bowel disorder with no consequences for growth, development or long-term health. This occurred in 1999 when a working team published a set of definitions for childhood functional gastrointestinal disorders following on the Rome criteria published for adults [1]. Functional diarrhea, which the team recognized was also known as toddler’s diarrhea, chronic nonspecific diarrhea and irritable colon of childhood, was defined by daily painless passage of 3 or more large unformed stools for more than 4 weeks, with an onset of between 6 and 36 months of age, and passage of stools during waking hours in children who were thriving on an adequate calorie intake.

Chronic nonspecific diarrhea is clearly a common condition, seen frequently by primary care physicians and pediatric gastroenterologists. Dietary fat intake has been shown to play a role in a significant number of children with chronic nonspecific diarrhea. In 1979 Cohen et al. [2] reported 5 patients with the onset of chronic nonspecific diarrhea that coincided with efforts to restrict fat in the children’s diets in an attempt to protect against the occurrence of coronary vascular disease in later life. When the fat in the diet was increased to between 35 and 50% of total calories, the diarrhea symptoms resolved in all 5 of these children. A number of authors have suggested that the excessive consumption of beverages such as fruit juice that contain high concentrations of various sugars contributes to or causes chronic nonspecific diarrhea. The principle carbohydrates of fruit juices include sucrose, fructose, glucose and sorbitol. National surveys in the United States have shown that almost 90% of infants consume juice and 10% of children 2–3 years old drink more than 12,355 ml/day [3]. When apple juice was eliminated from the diets of many of those with chronic nonspecific diarrhea, normalization of the frequency and consistency of the stools occurred.
Greene and Ghishan [4] documented that almost one fifth of the 85 patients they reported on with chronic nonspecific diarrhea consumed more than 2.5 times their daily fluid requirement in addition to their usual diet. Most of the fluids consumed by their patients with chronic nonspecific diarrhea were hypertonic because of the high concentrations of carbohydrate, although 3 of these patients were consuming large volumes of water alone. Thus it is clear that fluid intake in excess of the capacity of the intestinal tract to absorb it, and in many cases combined with a high osmotic load, is an important factor in the development of chronic nonspecific diarrhea in many children.

Laboratory investigations, including the use of breath hydrogen tests, are of no use or benefit when the criteria for chronic nonspecific diarrhea in childhood are met. The most useful approach to this disorder is to provide reassurance to the parents, to normalize the child’s diet within current guidelines for carbohydrate, protein, fat and fluid intake, and to observe the child. The symptoms of chronic nonspecific diarrhea may decrease significantly simply by asking parents to create a diet diary and record stool frequency and consistency for a 1-week period before any specific dietary interventions are initiated. This disorder inevitably resolves by the time the child starts school. There is an overlap between this disorder and irritable colon of childhood, and some of those children with a diagnosis of chronic nonspecific diarrhea who have intermittent periods of diarrhea after starting school may in fact have irritable bowel syndrome.

References

Fetal development of the structure and function of the gastrointestinal tract is a complex process. The muscular layers derive from the mesenchymal tissue in the gut by the 4th to the 6th weeks of gestation in a rostral caudal fashion. The circular muscle layer appears first, followed by the longitudinal muscle coat, and last by the muscularis mucosa at 22–23 weeks of gestation [1].

Groups of muscle cells located in the circular layer differentiated to form the interstitial cells of Cajal that act as pacemakers by driving the slow wave frequency and coordinate neural input to gut smooth muscle. Intrauterine maturation of the interstitial cells of Cajal correlates with the initiation of electrical rhythmicity. A delayed maturation of the interstitial cells of Cajal could be involved in the pathophysiology of gastrointestinal dysmotility seen in some neonates and children [2].

Extrinsic neural input to the gastrointestinal tract comes from the central nervous system, the sympathetic and the parasympathetic systems. The enteric nervous system, or gut brain, provides most of the intrinsic neural regulation.

Neural crest cells migrate to the intestine via the vagal and sacral portion of the spinal cord. The undifferentiated cells are first detected in the stomach and duodenum at 7 weeks and then in the rectum at 12 weeks. Development of the enteric nervous system continues after birth and through at least the first 12–18 months of life.

By 23 weeks of gestation the complete nitrergic pattern, as observed in the postnatal gut, has matured. Defects of nitrergic innervation have recently been found in congenital gut anomalies such as pyloric stenosis and Hirschsprung’s disease. Gastric emptying of swallowed amniotic fluid in the intestine may be demonstrated in the human fetus at 30 weeks of gestation.

Small intestinal motor activity in neonates is mainly characterized by a motor pattern that is not typically seen in adults: the non-propagating cluster of contraction. The migrating motor complex appears between 32 and 35 weeks of gestation [1]. Only 25% of preterm
infants display a mature type of feeding pattern, while about 75% display a prompt cessation of motor contraction after feeding.

Several studies have shown that gut function and subsequent milk tolerance is improved by trophic feeding. This practice accelerates the whole gut transit by enhancing the migrating motor complex. It is responsible for surges in the plasma concentration of several enteric hormones and peptides which alter gut motility and may cause stimulation of the enteric nervous system [3]. Enteral nutrition also represents a trigger for the ontogeny of colonic motility.

Meconium can be found in the fetal rectum after 21 weeks of gestation. In a large study observing bowel habits in 844 preterm infants, a direct relation between the volume of milk ingested and stool frequency throughout the first 8 weeks after birth was reported [4]. Infants receiving human milk had consistently higher defecation rates, and passed softer stools than those receiving formula milk, regardless of gestational age and feed volume. The finding of a modal frequency of 1 stool/day in the unfed neonate suggests that there is an intrinsic pattern of large bowel motor activity present as early as 25 weeks of gestation.

High-amplitude (>60 mm Hg) propagating contractions decrease in frequency from several per hour after a meal in awake toddlers to just a few per day in adults. The colon in toddlers seems to have fewer tonic and phasic non-high-amplitude propagating contractions compared to the colon of older subjects.

The ongoing developmental maturation of bowel function results in intestinal hypomotility with the consequent postponement of meconium passage. Extreme prematurity and delayed enteral feeding are significantly associated with delayed passage of the first stool in more than one study [5].

References

Motility and Allergy

L. Bueno

Food allergy is associated with digestive symptoms suggesting alterations in gastrointestinal motility. Animal models have enabled the evaluation of motor alterations linked to antigen challenge in sensitized animals. Successful induction of sensitization to dietary proteins in animals has been shown to require strict attention to the type and dose of antigen, the strain and age of animals, the requirement for adjuvant and the route of immunization. In both rats and guinea pigs, the major antigens investigated to date have been the cow’s milk antigens and egg albumin. Immunization is generally performed by the parenteral administration of antigen to maximize the consistency of the response, but oral sensitization to β-lactoglobulin by a liquid meal is successfully used in guinea pigs to induce motility alterations associated with oral challenge [1]. Oral challenge affects gastrointestinal and colonic motility. Both gastric and intestinal slow waves are altered corresponding to a reduction in frequency, these effects being locally mediated as demonstrated by challenging isolated segments [2]. In fasted rats, the intestinal motor activity is characterized by migrating motor complexes that are suppressed for several hours after a meal. In Hooded Lister rats sensitized to egg albumin, oral antigen challenge disrupts the migrating motor complex pattern replaced by a ‘fed’-type pattern for 2–3h (fig. 1). Colonic motility and transit are also affected by oral antigenic challenge in egg albumin-sensitized rats, these effects correspond to colonic inhibition associated with diarrhea [3, 4]. Local mast cell degranulation appears to play an important role in the genesis of immediate and sustained motor alterations at both intestinal and colonic levels. Serotonin and, to a lesser extent, histamine released locally trigger the immediate response. In contrast, the long sustained motor response to challenge involves the brain-gut axis and particularly the afferent vagal fibers, the brain release of IL-1β and the local release of substance P. Most of these motor alterations are strongly reduced or suppressed after previous treatment with mast cell stabilizers.
Fig. 1. Mediators and afferent nerves involved in jejunal motility disorders associated with egg albumin-sensitized Hooded Lister rats. From Castex et al. [5].

**References**

The Role of Dietary Fiber in Childhood and Its Applications in Pediatric Gastroenterology

Freddy T.M. Kokke, Jan A.J.M. Taminiau and Marc A. Benninga

The Dietary Fiber Definition Committee of the American Association of Cereal Chemists defines dietary fiber as ‘the edible parts of plants or analogous carbohydrates that are resistant to digestion and absorption in the human small intestine with complete or partial fermentation in the large intestine. Dietary fiber includes polysaccharides, oligosaccharides, lignin, and associated plant substances. Dietary fibers promote beneficial physiological effects including laxation, and/or blood cholesterol attenuation and/or blood glucose attenuation.’

According to the American definition, food components having the above properties can also be taken as dietary fibers such as resistant starch and non-digestible oligosaccharides. Resistant starch is the sum of starch and starch-degradation products not absorbed in the stomach and small intestine. Three types can be separated: RS1, physical non-approachable starch (lentils, beans); RS2, ungelatinized starch (bananas and potatoes), and RS3, retrograded starch (mainly amylose). Legumes appear to be the single most important source of resistant starch, with as much as 35% of legume starch escaping digestion.

Non-digestible oligosaccharides are naturally present in food, mostly in fruits, vegetables or grains. They consist mainly of fructo-oligosaccharides (FOS). In nature these are mainly found in inulin. If the fructose molecule is exchanged by a galactose molecule then galacto-oligosaccharides (GOS) occur. The latter are found in soybeans. Today both FOS and GOS are also recognized as prebiotics. Prebiotics beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon. Recent data indicate that a prebiotic mixture of FOS and GOS is able to stimulate the development of a microbial flora similar to that of
breast-fed infants. These prebiotics might play a role as modulators of
the postnatal development of the immune system. Furthermore the
GOS/FOS mixture significantly increased the number of bifidobacteria
and reduced the number of pathogens in term as well as in preterm
infants when compared with a group of infants fed a formula without
supplement. Also stool consistency and fecal pH were positively
affected. It must be stated that the effect of prebiotics is only tempo-
rary and strictly related to intake. More research is needed to delineate
optimal fiber intake for infants and children under 2 years of age, the
quantity and the types of fibers that would be most appropriate, and
whether prebiotic supplementation leads to measurable long- and
short-term benefits for infants.

The effect of dietary fiber on the gastrointestinal tract is
explained by its osmotic properties, its stimulating effect on intestinal
motility and the water-retaining capacity in the intestine. The minimal
intake for children and adolescents 3–20 years of age is the age of the
child plus 5 g of dietary fiber/day (age + 5). The current concern about
recommending a high-fiber diet is that it has the potential to reduce
the energy density, reduce the calorie intake, and thereby cause poor
growth, especially in very young infants. Secondary to these factors is
the concern that such diets reduce the bioavailability of iron, calcium,
magnesium and zinc. However, most investigators nowadays state
that when the dietary fiber intake is according to the recommenda-
tions given above and the dietary fiber is consumed within a proper
balanced diet, mineral deficiencies will be of no real concern.

Fiber can likely play a valuable role both in the prevention and
treatment of several gastrointestinal disorders. However, there is an
obvious need for large clinical trials to test the efficacy and safety of
fiber as a therapeutic agent in the clinical treatment of children with
constipation, diarrhea, irritable bowel syndrome and acute appendicitis.
Early Influences on Taste Preferences

Peter Leathwood and Andrea Maier

A range of factors can influence developing taste and flavor preferences. Here we briefly outline some of them and evaluate their potential importance from an evolutionary psychobiology perspective.

Genetics

Genetic influences provide sensitivity to different tastes and aromas plus an innate preference for sweet and dislike for bitter. These hedonic responses are not fixed and can change with experience. Thus people learn to like bitter drinks such coffee or beer. Genetics are also responsible for inherited differences in taste and aroma sensitivity (particularly to bitter tastes), which in turn can influence food preferences and choices. To date, the effects observed are not large, although the observation that children who are insensitive to the bitterness of 6-n-propyl-thiouracil tend to like sweeter foods and are also more likely to have caries merits further examination.

Prenatal Effects

Aromas of some foods eaten by the pregnant woman find their way into her amniotic fluid, and can influence the infant’s responses shortly after birth [1]. Thus, if women consume an anise-flavored drink during the last weeks of pregnancy the infants respond positively to anise aroma when tested shortly after birth.

Early Postnatal Experiences

Similarly, flavors of some foods (e.g., garlic, vanilla) eaten by lactating mothers find their way into her milk. Thus mother’s milk provides a potentially rich and complex sensory experience for the infant, reflecting in part the mother’s eating habits and food culture.
At weaning, breast-fed infants tend to adapt more rapidly to new foods than bottle-fed infants, suggesting that their richer sensory experience may facilitate acceptance. In addition, flavors experienced during the first few months of life appear to influence later preferences. Thus adults who had been exposed to vanilla-flavored starter formula as infants showed a detectable preference for vanilla 20–30 years later [2].

There is an evident adaptive advantage for infants to develop a mild but not overwhelming preference for food flavors experienced in their mother's milk. These flavors reflect her food choices and the food choices of her culture. The simple fact that she survived long enough and was fit enough to reproduce and suckle her child, shows that her food choices must at least have been adequate, if not positively good. But, as the infant grows up, other influences on food preference and choice come into play, so these early effects cannot be expected to lead to exclusive preferences [3].

**Experiences at Weaning**

If weanling infants are given experience of a variety of foods, they tend to accept new foods more readily. In addition, if infants are offered a new (initially rejected) food on several occasions (e.g., 8–10 times), most show increases in acceptance and intake. However, caregivers usually give up after 2–3 refusals. This suggests that they should be encouraged to persist a little longer [4].

It seems that taste preferences for specific foods can develop early but do not always generalize from one food to another. Thus, at 6 and 24 months of age, infants who had previously been fed sugar water consumed more sugar water in a taste test than those who had not. Intake at 2 years correlated with intake at 6 months (but not at birth), suggesting that innate acceptance can be modified early in life and that early exposure to sugar water had long-lasting effects on acceptance of sucrose in water. There were, however, no differences in consumption frequency of other sweet foods or drinks. It seems that these experiences provide a sense of what should or should not be sweet rather than setting a general hedonic responsiveness to sweetness [5].

**Post-Weaning Preferences**

Several studies have shown that patterns of preference are remarkably stable from 2 to 8 years old. Children who liked the most foods at 2–3 years old liked the most at 8. They also liked the same foods at each time, so that consistency (percent agreement for specific
foods) was 84%. In addition, there was no significant increase in the number of foods liked. If anything, between 2 and 4 years old, children became more conservative with respect to the foods they would accept [6].

**Discussion and Conclusions**

It has been argued that, for early humans living out their lives in the same food environment, there would be a survival advantage for the child to be open to accept new foods during the first 2 years (i.e., early exposure to food flavors in mother’s milk plus a full seasonal cycle of exposure to adult foods) followed thereafter by a gradual decrease in willingness to experiment (where the costs of experimentation would be higher as the child becomes more mobile and is less protected by parents).

Taken together, the early influences on food preferences described in the earlier sections of this review fit this pattern. In the first few months of life, infants do accept unusual flavors more easily and tend to like them years later. Foods liked at 2–3 years old are appreciated throughout childhood, and few new foods are added to or subtracted from the set of liked foods. It seems, however, that once a particular food becomes accepted and familiar, the preference can be long-lasting. Thus preferred levels of sweetness in particular foods may be established in the first 2 years of life [7].

This reading of early influences leads to several practical conclusions (some of which certainly need to be studied further before being recommended).

(1) Mother’s milk reflects the flavors of foods she eats and these can influence her child’s food preferences later in life, suggesting that the lactating mother should regularly eat the range of healthy foods that she wants her child to accept later on.

(2) Infants more readily accept new foods and flavors during the period from weaning to 2 years of age, and few new foods are easily accepted in the remaining years of childhood, so it seems worth making sure that the child experiences a wide range of healthy foods during this period.

(3) ‘Repeated exposure’ can increase acceptance of new foods. If the infant dislikes a new (healthy) food on the first 2–3 occasions it is offered, many mothers give up. It may be better to persist for up to 8–10 tries.

(4) Preferred levels of sweetness in particular foods seem to be influenced by early and current experiences, so perhaps it is better to begin with the levels of sugar one considers healthy.
As Benton [8] has pointed out, healthy eating programs often teach basic nutritional information. It may be better to teach parents more about child development in the hope that an understanding of innate tendencies, effects of early experiences and child psychology will be of more help.

References

Junk Food

Michael Gracey

Overweight and obesity are at epidemic rates in many industrialized countries and are increasing rapidly in societies in transition to Westernized lifestyles. This contributes to cardiovascular disease, hypertension, type-2 diabetes and other ‘lifestyle’ diseases [1, 2]. This is also occurring in previously traditional groups like Australian Aborigines, even in remote areas, where store foods now determine patterns of eating and drinking [3]. What is the role of junk foods in this ‘public health crisis’ [1].

‘Junk Food’ Consumption and Body Weight

‘Junk foods’ are those consumed immediately or soon after purchase. But some published lists include: sweetened drinks; confectionaries and sweets, including chocolates; biscuits (‘cookies’) and cakes; chips (‘crisps’); frozen dairy products, including ice creams and yogurts, and breakfast items. It is contentious whether these items are intrinsically ‘junk’ or if their pattern of habitual consumption is nutritionally significant. After all, what food could be more nutritious yet ‘fast’ than an apple?

About 30% of US children and adolescents consume commercial ‘fast foods’ on a given day; they consume more dietary energy, more energy-dense food, more total fat, more total carbohydrate, more added sugars and sweetened drinks, less milk and fewer fruits and non-starchy vegetables [4].

‘Junk’ Drinking Patterns

The contribution of sweetened drinks to overweight needs more attention. There has been a 500% increase in per capita soft drink consumption over the past 50 years in the USA where the prevalence of childhood overweight has doubled over the past 20 years. Excessive soft drink consumption is linked with: (a) overweight/obesity; (b) reduced milk consumption, calcium deficiency and osteoporosis, and (c) dental
caries and erosion of dental enamel. Soft drinks are a concentrated source of dietary sugar and excessive dietary energy intakes.

**A Possible ‘Doomsday Scenario’**

Type-2 diabetes and other 'lifestyle' diseases including overweight/obesity, cardiovascular disease, hypertension and chronic renal insufficiency are epidemic in many countries and cause millions of deaths annually. These disorders have their origins in infancy and early childhood. This is becoming a massive problem in developing societies and in previously traditional groups changing to Westernized living. These newer lifestyles are more sedentary and often have dietary energy intakes too high for their needs. Junk foods are major contributors to this. Zimmet [5] likens this to a potentially uncontrol-lable ‘Doomsday scenario’.

**Other Issues**

Television viewing encourages snacking, junk food consumption and displaces fruit and vegetable eating; other sedentary pastimes, like computer games, exacerbate this. Most junk foods are energy-dense which promotes weight gain. People tend to consume a similar *bulk* of food regardless of its energy density because of a poor ability to down-regulate intake according to energy content and their needs for energy balance [6]. This helps explain why junk foods *and* their pattern of habitual consumption cause overweight and obesity.

**References**

Individual differences in physiological and behavioral factors affecting body weight regulation may be determined not only by genes, but also by environmental influences during development. This article reviews briefly evidence from human epidemiologic and animal model studies that, during infancy and early childhood, nutrition serves as an important signal for ‘fine-tuning’ various metabolic systems, and thereby influences obesity susceptibility throughout life. The primary focus is an evaluation of the specific hypothesis that nutrition during infancy and early childhood modifies obesity susceptibility by perturbing epigenetic mechanisms. Based on data from animal model studies, environmental influences during prenatal and early postnatal development can both permanently alter body weight regulation and affect the establishment and maintenance of epigenetic gene regulatory mechanisms. Epigenetic dysregulation can cause obesity, and the epigenetic development of physiological systems relevant to energy homeostasis continues into the postnatal period. It is therefore likely that postnatal metabolic imprinting of epigenetic gene regulatory mechanisms plays a role in determining individual susceptibility to obesity. Improving our understanding of the biologic mechanisms whereby nutrition influences developmental epigenetics may eventually enable the formulation of early postnatal nutritional interventions aimed at decreasing individual obesity susceptibility.
Long-Term Effects of Weaning Habits: Type-1 Diabetes

Outi Vaarala

It has been shown in animal models that dietary factors at weaning modify the cytokine profile of islet-infiltrating islets and has an effect on the development of autoimmune diabetes [1]. Dietary factors associated with the risk of type-1 diabetes both in animal models and in epidemiological studies include the intake of vitamin D and exposure to cow's milk (CM) and wheat gluten. Vitamin D has immunoregulatory properties and it modifies the function of both the innate and adaptive (likely indirectly) immune systems [2]. Vitamin D supplementation in infants is highly recommended by studies showing that regular vitamin D supplementation is associated with reduced risk of type-1 diabetes [3].

Weaning to hydrolyzed formula instead of CM formula decreases the incidence of autoimmune diabetes in animal models due to a shift to a Th2 cytokine profile in islet-infiltrating T cells [1]. In humans, the evidence from epidemiological case-control studies as well as from the first prospective follow-up studies of children at genetic risk of type-1 diabetes is contradictory [2]. The TRIGR study, which is a randomized intervention study, is being performed in Europe and North America. In the TRIGR study, children at genetic risk of type-1 diabetes are weaned to either casein hydrolysate or to CM formula during the first 6–8 months of life [4]. The preliminary results of the TRIGR pilot study indicate that weaning to hydrolyzed formula could decrease the appearance of β-cell autoimmunity.

Recent data on the introduction of dietary gluten at the weaning period suggest that both early and late exposure could imply an increased risk for β-cell autoimmunity in children at genetic risk [5, 6]. Accordingly, a safe window for gluten exposure could be between 3 and 6 months of age. The response to gluten may be aberrant in infants with a genetic risk of type-1 diabetes since the risk genotype is shared between type-1 diabetes and celiac disease.

The identification of dietary factors as risk factors of type-1 diabetes is challenged by the fact that almost all children are exposed to
putative dietary factors, and additional modifying factors are needed for the manifestation of clinical disease. Aberrancies of the gut immune system in children prone to type-1 diabetes may, at least, partly explain the harmful effects of dietary factors in these individuals, whereas the same dietary factors may be innocent in the majority of children. The available data indicate that the risk ratios related to the dietary factors are relatively low, which implies that the etiological fraction of an individual dietary factor is low. It should be emphasized, however, that the elimination of an identified risk factor, which explains for example 10% of the disease risk, results in prevention of type-1 diabetes in a remarkable number of children yearly.

References

We know a lot about the short-term effects of complementary feeding and how an optimal diet can prevent poor growth, malnutrition and nutrient deficiencies. However, we know very little about its long-term effects. Although there is general agreement about the scientific principles of what constitutes an optimal complementary diet, the recommendations differ considerably from country to country. Feeding practices and recommendations are often based more on tradition than on science.

In low income countries the feeding period, from 6 to 18 months, is critical for the promotion of optimal growth, development and health. Global statistics have helped to identify this period as the time when stunting and wasting develops because of very rapid growth. In industrialized countries it is also the period when failure to thrive is seen. One of the causes can be extreme diets given because of parental beliefs about healthy eating. One example is families adhering to a macrobiotic diet in Holland, which resulted in considerable growth retardation, delayed motor development, rickets, iron deficiency and B12 deficiency [1]. A macrobiotic diet is high in fiber, low in energy and contains no animal products.

Because of the health problems associated with inadequate complementary feeding, such as high mortality in late infancy and early childhood in low income countries, the WHO made complementary feeding a high priority and convened several expert consultations which resulted in the Global Strategy on Infant and Young Child Feeding [2]. In the proceedings of a WHO global consultation on complementary feeding in Geneva 2001, guiding principles for complementary feedings, developed in collaboration with the PAHO, were presented [3]. These focus on age for introduction of breastfeeding, continuation of breastfeeding, amount, energy density, nutrient content and consistency of complementary food, meal frequency, the use
of vitamin-mineral supplements and fortified products, safe preparation and storage and feeding during illness. Furthermore, the guidelines emphasize responsive feeding, giving a set of principles for psychosocial care during feeding.

A set of guidelines based on current knowledge and aimed at the WHO European region has been developed [4]. As this region includes both highly industrialized countries and low income countries, like those in Central Asia, these guidelines cover a broad range of socioeconomic conditions.

The many research issues and questions that need to be addressed to improve the understanding and practice of complementary feeding were discussed at a workshop arranged by the International Pediatric Association and the European Society of Pediatric Gastroenterology, Hepatology and Nutrition in 1999. The proceedings include a long list of research priorities [5].

The challenge in complementary feeding is to understand how it affects long-term health, development and growth. There is increasing evidence that postnatal nutrition and growth play an important role in the early origins of adult disease hypothesis [6] and that complementary feeding is likely to program effects. Breastfeeding has important long-term effects and it is plausible that other foods given during infancy and early childhood can also have long-term effects. There are several hypotheses on long-term effects. For example: a high protein intake has been suggested to increase the risk of overweight and obesity later during childhood; a high intake of saturated fat in early childhood might have an adverse effect on the risk of cardiovascular disease, and the fatty acid composition of the diet might influence the risk of atopy and asthma later on. However, the evidence for these hypotheses is as yet not strong. New data suggest that cow’s milk can stimulate linear growth in young children, even in those who are already receiving an adequate diet with a high protein content [7]. Thus, the traditional concept that growth is optimal if there are no deficiencies may be too simplistic. It is also likely that food preferences and appetite control are established during the early months and years, and this may have long-term effects. With the obesity epidemic and the increase in overweight in young children, the influence of the early diet on body composition, weight gain and later overweight and obesity is of special interest.

References


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