WEANING:

WHY, WHAT, & WHEN?

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Weaning

WHY, WHAT, AND WHEN?

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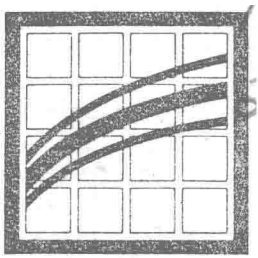

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Preface

The objectives of this volume of the *Nestlé Nutrition Workshop Series* are multiple. First, the most recent developments in immunology and gastrointestinal and renal physiology are presented with regard to the age at which the various functions and organs of newborns reach sufficient maturity to allow the introduction of semisolid foods without producing mechanical, metabolic, or immunological adverse effects. Because the acceptability of a diversified diet is merely one aspect of the problem, nutritional needs, particularly energy requirements, during the first year of life are discussed from a theoretical point of view.

Second, current practices of introducing foods other than milk into infant diets in both industrialized and developing countries are compared and the underlying reasons for the existing differences, as well as problems emerging from these practices, evaluated. The possible consequences of the introduction of supplements to breast-feeding are examined, not only because of their influence on nutrient bioavailability or the risk of bacterial and parasitic contamination, but also because of the effect they may have on the continuation of breast-feeding. In addition, the long-term consequences of the early introduction of a diversified diet, namely, the development of obesity, hypertension, and ischemic heart disease in later life, are reviewed.

For many reasons, therefore, it is inadequate to restrict the term *weaning* to mean "stopping breast-feeding"; rather, it should include all the phenomena involved with the introduction of nonmilk foods, regardless of whether given

1. to a child who has never been breast-fed;
2. to a child for whom the gradual substitution of semisolid foods (weaning foods or supplements) for mother's milk will sooner or later signify the end of breast-feeding and the introduction of a classical diversified diet;
3. or, as is the case in developing countries and for underprivileged groups in industrialized countries, to babies who continue to be breast-fed but whose inadequate growth clearly shows that their nutritional needs are not met, especially with regard to iron, and who require extra food.

We therefore consider it highly desirable that agreement be reached on an unambiguous and internationally recognized terminology to qualify the two processes that sometimes occur simultaneously or, in other cases, sequentially: The interruption of breast-feeding can precede the diversification of the diet or, on the contrary, be the end result.

The volume will be of interest to pediatricians, physicians, nutritionists, and scientists.

ANGEL BALLABRIGA
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Foreword

The term *weaning* may mean different things to different people. For some, weaning occurs whenever an infant receives significant amounts of foods other than breast milk: The transition from breast-feeding to bottle feeding for them would be "weaning."

We do not subscribe to this definition: For example, a low-birth-weight infant not breast-fed but sucessfully fed with a special infant formula is not "weaned." The definition of weaning that we have adopted is the following: in infant feeding, the transition from breast milk or infant formula to significant amounts of other foods.

Many pediatricians consider weaning to be a "second birth" to a more adult-like life and that the first months of life, during which the infant is usually breast-fed, are, nutritionally speaking, a prolongation of intrauterine life.

For mainly social and economic reasons, weaning takes place earlier in modern societies than in developing countries; however, the tendency to wean infants earlier and earlier, as seen in the late 1960s, is now wisely reverting to a more physiological approach.

Apparently a simple process, weaning is actually, in many respects, a complex operation nutritionally, immunologically, and physiologically, and it is for this reason that the tenth Nestlé Nutrition Workshop was devoted to this important subject.

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Development of Structure and Function of the Gastrointestinal Tract: Relevance for Weaning

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In different countries and societies there is a variety of successful weaning practices. This empirical observation leads immediately to the conclusion that there is a range of practices—qualitative, quantitative, and temporal—within which infants can thrive. In the elusive search for the "optimal" feeding regime, the changing nutritional requirements of the growing and developing infant must be matched to the maturation of functions and capacities of the gastrointestinal (GI) tract; however, it must also be remembered that within limits, some functional adaptation can occur.

This chapter considers the question "Weaning: what and when?," and proposes some tentative answers from the viewpoint of a pediatric gastroenterologist, as follows.

1. What weaning foods can be given?
   a. The composition should depend mainly on the presence of appropriate biochemical pathways for digestion, absorption, and utilization of each nutrient.
   b. The quantity of each nutrient should depend on the digestive and absorptive capacity of the GI tract for different substrates. In practice, it may also depend on appetite.
2. At what age can weaning foods be introduced?
   a. This will depend partly on the development of the "functional capacity" of the GI tract as outlined above.
   b. It will also depend on maturation of "mechanical" factors, especially chewing and swallowing.
3. At what age may certain foods be introduced? The answer lies in a complex amalgam of behavioral, psychosocial, and cultural factors.
4. By what age must weaning foods be introduced?
   a. The most important consideration is nutritional.

b. There are also behavioral or neurodevelopmental factors—a "critical period" for learning to accept solid food.

The main body of the paper will consider these questions in detail. An attempt will be made to develop an argument that links functional capacity to "learned" aspects of eating. First, a review of those aspects of the development of GI structure and function that are needed as background will be given.

ASPECTS OF THE DEVELOPMENT OF THE GASTROINTESTINAL TRACT

Mouth, Esophagus, and Stomach

Development of Taste Buds

Anatomical studies suggest that the gustatory system may be functional before birth (1). At the seventh week of fetal life collections of elongated cells appear on the dorsal surface of the fungiform papillae, which by week 12 have taken the form of primitive buds. By 15 weeks the taste bud resembles the adult bud and comprises cells whose long axis extends through the whole thickness of the epithelium. The apical ends of the buds communicate with the oral cavity through a cell-lined pore, and hairlike 3 μm processes extend from the apical end of the cell into the pore. Electron microscope studies confirm that these processes are composed of microvilli (2).

The nerve supply develops at the same time as the taste buds. By 11 weeks subepithelial nerves have penetrated the epithelium and associate closely with the developing buds. In subsequent weeks the nerve bundles increase in complexity, forming a network under the buds.

In summary, there is morphological evidence that the apparatus for tasting is developed by 16 weeks. Is it functional during fetal life? There are, of course, no data, but there is evidence that the ability to taste is active at birth (3) and continues to develop in postnatal life (4). This is discussed in detail later.

Fetal Swallowing

Swallowing behavior has been demonstrated in the human fetus at 12 weeks (5), and it has been calculated that the more mature fetus swallows 500 ml or more of amniotic fluid each day (6). De Snoo (7) showed that an injection of saccharin into the amnion caused the fetus to increase its normal swallowing rate.

Developmental Physiology of Swallowing

This has been well reviewed by Herbert (8). Swallowing is usually divided into three parts: oral, pharyngeal, and esophageal. In the oral phase, the food is separated by the lips and jaws anteriorly and by elevation of the soft palate posteriorly. The food is forcibly ejected into the oropharynx by a rocker-like movement of the tongue against the hard palate, assisted by an elevation of the floor of the mouth and depression of the soft palate. Only the oral phase is voluntary.

The pharyngeal phase starts when the bolus reaches the oropharynx. The pharyngeal constrictors contract, and the pharyngoesophageal sphincters relax. The bolus is diverted round the laryngeal opening by the glossoepiglottic fold and the epiglottis. When the pressure wave of the pharyngeal constrictors reaches the superior esophageal sphincter, the latter relaxes and food enters the esophagus. The pharyngeal phase is accompanied by associated safety mechanisms that prevent reentry into the oral cavity or entry into the larynx or trachea, and that are coordinated by a complex neural pathway in the medulla.

In the esophageal phase, the bolus is transported via a peristaltic wave to the stomach. Following reflex relaxation of the superior esophageal sphincter there is a short period of increased contraction to prevent regurgitation of the bolus into the pharynx. When the primary peristaltic wave reaches the lower esophagus there is reflex relaxation of the lower esophageal sphincter and the food bolus enters the stomach.

Gryboski et al. (9) have shown significantly lower mean resting pressures in the superior esophageal sphincter during the first days of life. They have also shown (10) that the esophageal response to deglutition is uncoordinated in the first 48 hr of life, with very rapid peristalsis, biphasic waves, and frequent simultaneous contractions.

The lower esophageal sphincter is a functional structure found at the gastroesophageal junction and can readily be identified manometrically as a zone of high pressure at rest. However, the anatomical structures that constitute the sphincter are not known with certainty (11). In studies of the lower esophageal sphincter in infants, it has been shown that its functional length and the mean resting pressure rise progressively with age in the first 6 months of life (12). However, studies of continuous pH recordings in the lower esophagus (to test reflux of gastric contents) suggest that the sphincter is functionally effective at birth (13,14) (Fig. 1).

Gastric Function

Reservoir and motor functions

The stomach receives food, stores it, reduces solids to fine particles, and regulates delivery into the duodenum. The proximal area of the stomach has a reservoir function that allows the fundus to increase in volume without increasing intragastric

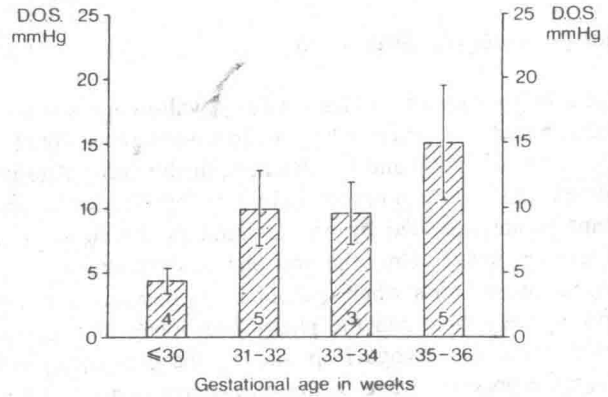

FIG 1. Maturation of the distal esophageal sphincter (D.O.S.) in preterm infants. (From Sarkar, ref. 14.)

pressure (15). The distal area of the stomach is involved in the emptying of solids, and also plays a part in emptying of liquids.

Gastric emptying depends on the size of the pyloric opening and on the difference between intragastric and intraduodenal pressures. Distension of the stomach will increase gastric emptying rate, while high osmolality, fat, and acid in the duodenum will slow the process (16). The consistency of the meal is also important in determining the rate of emptying, and fluids leave the stomach faster than solids (17). Inhibition of gastric emptying by the products of protein digestion are probably mediated by the same duodenal osmoreceptors that are stimulated by amino acids and carbohydrates.

Gastric motor activity after digestion differs according to whether liquid or liquid/solid meals are ingested. Liquid meals produce a period of inhibition of all phasic pressure changes in the fundus and antrum (18), whereas ingestion of solids produces vigorous contractions in the stomach at the rate of 3/min that begin in the upper body of the stomach and progress distally, with gradual acceleration (19). After the first postprandial hour (in adults), the frequency of contraction decreases gradually. Experimentally, the main stimulus in these contractions and the associated phasic pressure changes in the antrum has been the physical characteristics (solid masses of a certain size) of the meal. In practice this will be determined by the efficiency of chewing.

There are no data on the development of the differential motor response of the infant stomach to foods of differing consistency.

Gastric emptying has been studied extensively by Cavell (20). He has shown that human milk is emptied in a biphasic pattern, with an initial rapid phase followed by a slower phase, whereas formula is emptied in a linear fashion with significantly increased half-emptying time (21). The available evidence suggests that the osmoreceptors that control gastric emptying are active at birth (22). In the research

of Cavell (21) the milks that were compared had the same lactose content and osmolality. It was postulated that the differences in gastric emptying pattern were the result of the fat and/or protein content of the milks.

Gastric acid and pepsin secretion

A synthesis of the work of several authors allows the following conclusions about the development of gastric acid secretion in early life. Basal gastric acid secretion occurs within minutes of birth and gradually increases over several hours to reach levels near those of control populations of older children; the original studies demonstrating alkaline pH during the first few hours of life failed to take account of the effects of swallowed amniotic fluid (23,24).

From the age of a few hours until 10 days, acid secretion either increases (25) or stays constant (26). Between 10 and 30 days, all studies show that acid secretion decreases (27). Thereafter, there is a 10-fold increase by the age of 12 weeks (0.01–0.1 mEq/kg/hr) and another 2-fold increase by the age of 24 weeks (0.24 mEq/kg/hr), by which time secretory capacity approaches the lower limit for adults (28).

Peptic activity is found in the fetal stomach by 16 weeks, and increases markedly between 28 and 40 weeks (29,30). After birth maximum pepsin secretion parallels maximum acid secretion (25,34) and reaches adult levels by 18 months.

Intragastric pH exceeds the pH optimum for pepsin in the early weeks of life. In theory, the relative failure of gastric digestion of protein could result in increased numbers of macromolecules entering the upper intestine.

The normal newborn has hypergastrinemia (31), but the parietal cells are unresponsive to exogenous gastrin (32). The development of responsiveness to gastrin in young rats has been shown to coincide with the maturation of mucosal receptors for the hormone (33). Presumably such development takes place in young infants, but details are lacking.

Secretion of intrinsic factor

Again, there have been few studies. The development of intrinsic factor (IF) secretion is precocious compared to acid secretion. By birth levels in gastric juice after stimulation are 50% of adult values, and adult values are found by 3 months of age (25,34).

Lingual lipase

The age at which lingual serous glands—which are thought to secrete in humans, as in rats, a lipase of 44,000 to 48,000 daltons that is resistant to low pH, mostly active toward medium chain triglycerides (MCTs), and not dependent on bile salts—develop is not yet known. However, such lipolytic activity is found as early as 25 weeks gestation in gastric aspirates obtained at birth in premature newborns; this activity increases by 80% after 34 weeks gestation and reaches adult levels in full-

term newborn infants (35). It is suggested that this compensates for low pancreatic lipase and bile salt secretions during the neonatal period (see below).

Small and Large Intestine

Morphogenesis

The intestine elongates approximatley 1000-fold from the fifth to the 40th week of gestation (36). It has been found, at autopsies, to increase from 1.4 m at 19 weeks of gestation to 2.5 to 3.0 m at birth (37,38). Its length continues to increase during infancy and early childhood, and stabilizes around 4.5 m when body length is above 1 m (38).

The process of differentiation progresses aborally. Villi begin to form in the duodenum at 7 to 8 weeks, in the jejunum at 9 to 10 weeks, and in the ileum at 14 weeks. Crypts appear at 10 to 12 weeks of gestation (36). In the colon, true villi develop between 12 and 16 weeks of gestation. Still observable at 25 weeks, they disappear near term (39).

The small intestinal epithelium is multilayered until the eighth week. As villi develop the epithelium becomes columnar, and by 12 weeks a single layer of epithelial cells lines the jejunal villi. Simultaneously glycogen deposits decrease in size and number, and microvilli form. By 12 weeks they are regularly disposed in the jejunum and have reached the appropriate length of 1 μm, resembling a mature brush border. However, the terminal web is still irregular and the apical part of the cell contains an abundant tubular system and numerous "meconium corpuscles," which decrease between 18 and 22 weeks (40). Mature microvilli seen in the colon at 16 weeks, disappear by 28 to 30 weeks of gestation (39). Goblet cells appear in the proximal intestine at 9 to 10 weeks, while gastrin-, secretin-, and cholecystokinin-secreting cells appear at 12 weeks of gestation (41,42).

Brush Border Hydrolases

Appearance of the microvillus hydrolases is not strictly correlated with the development of the brush border structure. Alkaline phosphatase, for example, which lines the luminal side of the epithelial cells, is detected by histochemical techniques as early as the fourth or fifth week of gestation. Activities of the sucrase-isomaltase complex are detectable in the jejunum by the seventh week, and increase steadily from the 10th to the 15th week of gestation. At that stage they perform 50%—and, between the sixth and eighth months, 75%—of the activities at birth, after which they do not increase further (43,44). In the colon, sucrase activity (as neutral aminopeptidase) appears around 11 weeks, increases at 14 weeks, begins to decrease around 28 weeks, and disappears at term (39). However, sucrase-specific activity never exceeds one-tenth of adult jejunal activity. Trehalase, neutral aminopeptidase, and glutamyl transferase follow a similar pattern, the latter declining after birth