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 pharyngo-esophageal 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
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

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**FIG. 1.** Maturation of the distal esophageal sphincter (D.O.S.) in preterm infants. (From Sarkar, ref. 14.)
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 approximately 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.
Lactase and thermoresistant maltase (glucoamylase) activities are very low until the sixth month of gestation, when they start increasing until they reach their adult values in the weeks preceding birth (43). Specific activity levels of acid aminopeptidase, dipeptidyl peptidase IV, and carboxypeptidase do not vary between the eighth and 22nd weeks of gestation, the former being one-third of, and the latter two similar to, the levels found in children (aged 7 months to 11 years) (45). Enterokinase, which has no digestive function per se, presents a unique pattern of development: Absent before 22 weeks, it rises between 24 and 26 weeks and reaches term values at 32 weeks of gestation. Furthermore, enterokinase-specific activity continues to rise after birth, being 2.5 times more active in infants less than 1 year, and 2.5 times more active in children aged 1 to 4 years, than in term neonates (44).

Finally, the molecular forms of many of these enzymes are different in the fetus than the adult. A greater anodal mobility for the fetal enzyme than for the adult enzyme has been recently described for intestinal (but not liver, bone, or kidney) alkaline phosphatase (46), neutral aminopeptidase, dipeptidyl peptidase IV, and sucrase (47). These differences may represent expressions of different genes or differences in post-translational processing. Moreover, the sucrase–isomaltase complex, which is found both in newborn and adult intestine as two polypeptides having the specificities and molecular weights of sucrase (140,000) and isomaltase (150,000), is found in fetuses of less than 28 weeks gestation as a simple large polypeptide chain of 260,000 daltons (Fig. 2), which is probably split into its subunits by the pancreatic proteases, especially elastase (48).

**Transport Processes**

Using everted gut sacs, it has been possible to show that glucose and alanine transport against a concentration gradient appears in the jejunum at 11 to 12 weeks, and then increases markedly, being five-fold higher by 16 weeks; it is at a similar

![FIG. 2. Brush border sucrase isomaltase of human small intestine, separated on polyacrylamide gel and detected by immunoblotting with a monospecific anti-sucrase antibody: (a,e) adult jejunum; (b) 15 weeks; (c) 30 weeks; (d) 39 weeks; (psi) prosucrase-isomaltase; (i) isomaltase subunit; (s) sucrase subunit. Before 30 weeks sucrase isomaltase was present only as the macromolecular precursor (psi). Fetal forms of the enzyme (psi and the subunits s and i) migrated slightly ahead of adult forms. (From Triadou et al., ref. 49).](image)
level in the ileum at 21 weeks of gestation (50,51). The fact that similar results have been found by recording increasing potential differences evoked by one or the other substrate demonstrates that, at least for glucose and neutral amino acids, Na\(^+\) coupled solute transport develops in parallel with the brush border (51,52) (Fig. 3). The increase in transport capacity corresponds to an increase of the number of transport sites, the affinity of the carrier for its substrate being constant during the period (10–24th weeks) of gestation considered (52). At 21 weeks “maximum” potential differences are three-fifths (59), and at birth two-thirds (53) of published adult values. However \textit{in vivo} perfusion studies have shown that glucose transport rate continues to increase in the first year(s) after birth, maximal glucose absorption rates in the proximal intestine of the infant being one-fourth to one-fifth of adult rates (54).

No data are available concerning the development of fructose, dibasic and dicarboxylic amino acids, and oligopeptide absorption in the human fetus. It has been recently shown by \textit{in vitro} accumulation of \(^3\)H-taurocholate in everted gut rings that active transport of bile salts does not occur in the fetus or in the term neonate, whereas it is fully developed by 8 months after birth, no data being available in between (55). This immaturity is confirmed by the fact that the fractional turnover rate of cholate is significantly higher in infants less than 10 months of age than in older children (56).

\textit{Cytoplasmic Enzymes and Intracellular Metabolism}

Activities of the two main cytosolic peptidases—glycyl-L-leucine peptidase, and imidopeptidase—are present in fetuses at 11 to 14 weeks of gestation, and do not increase further with gestational age (57). Lysosomal activities (\(\alpha\)-glucosidase, \(\beta\)-\(\delta\)-fucosidase, \(N\)-acetyl-\(\beta\)-glucosaminidase, \(\beta\)-glucuronidase, arylsulfatase, acid phosphatase) are also present at 10 weeks of gestation, when lysosomes are not yet organized (58,59), and remain stable throughout gestation at a level comparable to that in infants.

Nothing is known about human development of the intracellular events leading to triglyceride resynthesis by the enterocyte. However, in rats and guinea pigs,
fatty acid binding protein and the enzymes of the monoglyceride pathway are mature early in gestation at adult levels of activity (60, 61). The early appearance of chylomicrons in blood after a fat meal in infants is a reason to think that the situation may be similar in humans.

Development of the Pancreas

Ontogenesis

During the fourth to fifth week of gestation, the pancreas consists of two buds, which originate from the entoderm on the opposite sides of the duodenum. They fuse at about the seventh week, the body and tail of the pancreas arising from the dorsal bud, the head and uncinate process arising from the ventral bud (36). Subsequently, the ducts originally serving each bud join to form the duct of Wirsung. At 7 weeks of gestation the fetal pancreas consists of tubules and aggregates of undifferentiated epithelial cells. By 12 to 14 weeks a network of interconnected ductules is formed, and endocrine and exocrine tissue is differentiating. The first acinar cells appear at the 12th week and mature rapidly over the next 2 months. At 12 to 15 weeks small zymogen granules are seen in the acinar cells. They become progressively less numerous in weeks 16 to 20, when classical mature zymogen granules are becoming increasingly prominent. However, discharge of granules into the acinar lumen is never observed at this stage (62). Endocrine cells (α, β, δ) are first isolated, then aggregate in small groups and form discrete islets during the fifth month of gestation (62).

Pancreatic Enzymes

Lipase and trypsin levels, detectable in tissue homogenates of pancreas at 3 months of gestation, remain extremely low until the end of the second trimester. During the same period chymotrypsin is not measurable. During the last trimester of gestation, enzyme activities in tissue homogenates rise markedly until term. Proteolytic activity is first detectable in the fetal intestinal lumen at 26 weeks of gestation, when enterokinase is first detectable. Amylase is usually undetectable during gestation (63, 64) (Fig. 4).

At birth and during the following 4 weeks, α-amylase activity remains barely measurable in the duodenal juice, whereas trypsin, chymotrypsin, carboxypeptidase B, and lipase activities are fairly well developed, being one-tenth (in U/kg body weight) in term babies (and somewhat less in preterm babies) of the levels in children aged 9 months to 13 years (65). In the subsequent month(s), these activities rapidly attain adult levels and remain constant, except for α-amylase, which increases until 3 to 5 years of age (31). However, when the maximal concentration (U/ml duodenal fluid) obtained after stimulation is considered, the level increases until 2 to 3 years of age. The maximal increase is for α-amylase, the least for trypsin (66).
It seems, then, that in the case of the exocrine pancreas, as in the case of the intestinal mucosa, the increasing digestive and absorptive capacities noted in the first years of life are mainly due to growth of the organ (increased maximal pancreatic secretion, increased absorptive and digestive surface) and not to an augmented concentration of active molecules (enzymes or "carriers") per unit weight.

Regulation

The fact that the concentration of pancreatic enzymes in duodenal fluid is low, whereas zymogen content of acinar cells seems nearly normal near term, suggests a failure of enzyme release. Indeed, premature newborns appear to respond in the same manner and degree to cholecystokinin (CCK) as to secretin, whereas after 1 week of life the response to each hormone begins to be specific (67). Full-term newborns are not responsive to CCK, and even at 1 month of age this hormone increases the output of chymotrypsin only. At the same age a minimal (but statistically significant) response to secretin can be demonstrated, the protein content per milliliter of duodenal juice decreasing slightly (68). The reason for this lack of response of the human pancreas to secretagogues remains unknown, but may be related to the development of cellular receptors for these hormones.
Bile Salt Secretion

Bile acid synthesis and conjugation occurs in human fetal liver cultures as early as the 15th week of gestation (55). A detailed analysis of the bile acid content of human meconium by gas chromatography–mass spectroscopy has shown that the main bile acids (cholic, chenodeoxycholic, deoxycholic, and lithocholic acids) as well as several “atypical” bile acids (hydroxylated at positions 1 and 6; 3β-hydroxy-Δ5 compounds; bile acids of the 5 series) are present; this suggests that fetal bile acid synthesis differs markedly from that of the adult (69). This fetal pattern of synthesis seems to cease near term, since “atypical” bile acids are not found in serum of premature and term newborns (70). In the fetus, taurine conjugation is the preferred process, as witnessed by the fact that tauroconjugates represent 56%, glycoconjugates 5%, and sulfated compounds 36% of bile acids in meconium (69). However, taurine conjugation is substrate-limited, so that the glycine-taurine conjugate ratios described in newborn babies depend on the taurine content of the milk they receive, being below 1 when they are breast-fed (71).

Despite an early synthesis and the fact that bile acids are found in the gallbladder from the 22nd week of gestation (72,73), there is a period of relative secretory failure in premature and term newborns during the first 2 to 3 weeks of life, manifested by the fact that intraluminal bile salt concentration is then often well below the critical micellar concentration (2–4 mmol/liter) (73–75). This failure may be due in part to a “physiological” state of cholestasis existing at birth, as evidenced by the fourfold to sevenfold rise in serum bile acid concentration occurring in the days following birth (70). It is certainly related to the fact that bile acid synthesis and bile acid pool are limited, at the end of gestation, to values that in term newborns are half and in premature babies one-sixth of adult values (75,76).

Development of Bacterial Flora

Although not intrinsic to the child, the bacterial populations in the gastrointestinal tract are implicated in the child’s nutritional status, and are essential to complete the digestion of many nutrients, particularly dietary fibers, which are often introduced in the diet around 6 months of age (see below). The development of the intestinal flora depends more on the type of diet than on the age of the child.

Development of Bacterial Flora in Breast-fed Infants

During breast feeding

Sterile at birth, the intestinal lumen is colonized in the few hours following birth (Fig. 5). At 12 hr of life dominant bacterial species in the meconium are facultative anaerobes such as Enterobacteriaceae (mainly Escherichia coli) and streptococci, found in 80 to 90% of the cases in rapidly growing numbers until the 24th hour
(10^5–10^{10} bacteria/g of wet feces). During the same period of time, \textit{Bifidobacterium} and \textit{Clostridium} are found in less than 50\% and \textit{Bacteroides} in less than 30\% of the neonates. In the following days, and probably because of the favorable reduced environment created by the facultative anaerobes (78), bifidobacteria develop steadily and become the dominant bacterial species (10^{10}–10^{11} bacteria/g of wet feces) in nearly 100\% of the infants. Simultaneously or a few days later, facultative anaerobes are found less often (40–60\% of the cases) at lower counts (10^6–10^{10} bacteria/g of wet feces). After a peak on the second to fourth days of life, clostridia are seldom found in the stools (less than 20\% of the cases) although at still high counts (10^9–10^{10}/g of wet feces). Bacteroides are found in less than 30\% of the cases, at counts
between $10^8$ and $10^{10}$/g of wet feces. This population of flora, dominated by the classical "bleue," Gram-positive bifidobacteria (formerly classified as *Lactobacillus bifidus*), which comprises nearly 100% of all colonic bacteria, is stable for weeks or even months, as long as breast milk is the only food given to the child. It displays a powerful barrier effect against pathogenic species (77,79–81).

During this period of time, lactose is the only dietary carbohydrate reaching the colon and available to the colonic flora as an energy source. Pathways of carbohydrate fermentation by *Bifidobacterium* have been recently shown to lead to the production of acetic and lactic acid in comparable amounts (82–84), which, because of the low buffering capacity of human milk, create the low pH (< 5.5) typical of breast-fed infant stools (78). This acidity, favorable for the growth of *Bifidobacterium*, may be the main factor of the reduced growth of other possibly pathogenic bacterial species (*Enterobacteriaceae, Clostridium, Bacteroides*) (78).

*At and after weaning*

As soon as cow's milk or beikost is introduced in the diet, usually during the third to fifth months of life, the fecal flora starts changing rapidly (77,79), although *Bifidobacterium* remains one of the dominant bacterial species. Facultative anaerobes (*Enterobacteriaceae* and streptococci) are found more frequently (in more than 80% of the cases) at somewhat higher counts ($10^9$–$10^{10}$/g of wet feces for *Enterobacteriacea*, $10^7$–$10^9$/g of wet feces for streptococci). Among *Enterobacteriacea*, species other than *E. coli* (e.g., *Klebsiella* and *Enterobacter*) appear in significant numbers (79). Strict anerobes develop more slowly. Although found in 70 to 80% of stool specimens, *Clostridium* counts are usually low ($10^4$–$10^6$/g of wet feces). In contrast, *Bacteroides*, found also in more than 80% of the cases, become one of the dominant bacterial species ($10^{10}$–$10^{11}$/g of wet feces). Finally, around one year, the fecal flora of the child is similar to the adult fecal flora, where anaerobes outnumber aerobes by a factor of $10^1$ to $10^3$ (81).

*Introduction of mixed feeding*

As mixed feeding starts, the high buffering capacity of the meals renders the colonic contents less acidic, and this allows the growth of the characteristic "putrefactive" bacteria. Furthermore, other fermentable carbohydrates, such as dietary fiber, reach the colon. It is now known that the main bacterial species able to ferment plant polysaccharides, apart from *Bifidobacterium*, are *Bacteroides* and *Eubacterium* (85), which are detected at the end of the first year of life in the feces (77). Products of carbohydrate fermentation by these bacteria are diverse and include a variety of volatile fatty acids (mainly acetic, propionic, and butyric acids) and CO$_2$ and H$_2$ (78). When lactic acid is present, it is in low concentration, which may be explained by its being fermented by *Propionibacterium* (86). Stool pH is neutral, varying between 6.5 and 8.
Colonization of the gastrointestinal tract does not differ in formula-fed and breast-fed babies during the first 48 hr, with facultative anaerobes being the dominant bacterial species (Fig. 5). However, during the next days, and whatever the formula (dried cow's milk, adapted formula), bifidobacteria are found in the stools of nearly all infants in high counts \((10^{10} - 10^{11})\) as in breast-fed babies, but facultative anaerobes do not decrease in either frequency or number \((10^6 - 10^8)\), and gram-negative anaerobic bacteria become progressively part of the dominant species \((79,80)\). Clostridia are usually found in 50 to 80% of neonates as soon as the sixth day but are not dominant \((10^5 \text{ to } 10^7)\) \((87)\). Bacteroides, also present in 60 \((88)\) to 80% of neonates aged 6 to 10 days \((87)\), are immediately found in high numbers \((10^8 - 10^{10})\) and remain among the dominant bacterial species. The bacterial flora is more diverse than in breast-fed infants; it is also less stable \((89)\). Introduction of mixed food, including dietary fiber, does not modify the flora as in breast-fed babies, Bacteroides continuing only to increase in number over a period of a few months until their number and prevalence match those of Bifidobacterium. At the end of the first year of life the bacterial flora of children who were never breast-fed is very similar to the flora of those who have been breast-fed \((77)\). Finally the infant seems to exemplify the rare situation when apparently minor changes in diet may grossly alter the bacterial colonic flora; for example one cow's milk feeding per day is enough to shift the flora of an exclusively breast-fed infant to the flora pattern of a formula-fed infant \((90)\).

As a consequence of the absence of great variation of the colonic flora of bottle-fed infants during their first year of life, the products of carbohydrate fermentation found in the stools do not vary either: As early as the first week of life, the main fermentation products are volatile fatty acids (mainly acetic, propionic, and butyric acids) and \(H_2\) and \(CO_2\). Stool pH is neutral \((78)\).

In summary, it appears that the introduction of mixed feeding or weaning causes a major disturbance in the colonic bacterial ecology in breast-fed infants, whereas such an impact is not seen in formula-fed infants. It may be that the period of introduction of solid food is one when the breast-fed infant is at greater risk than the formula-fed one of developing GI infections \((90)\).
Digestive and Absorptive Capacities

Carbohydrate Digestion and Absorption

Lactose

Contributing about 40% of the energy load of human milk, lactose is one of the main nutrients that the intestine of the newborn has to digest and absorb immediately after birth. Since lactase activity is the limiting factor for the absorption of lactose, and since it reaches its maximum value near term (see above), the question has often been raised of the tolerance of neonates to the lactose load and of its metabolic utilization.

Increments in blood glucose after an oral load of lactose (1.75 g/kg) are lower than after an equivalent load of glucose during the first 3 days of life, in term and premature infants (91–93); after the third day of life in preterms, glucose increments after lactose, although still lower, are not significantly different than increments after a glucose load (94,92). However, 5 of 17 premature babies had diarrhea after being fed with a milk supplemented with 6.1 g of lactose per 100 ml (total amount: 10.6 g/100 ml), compared to 1 of 12 babies receiving an added sucrose diet. The lactose-fed group had a greater degree of metabolic acidosis during the first year of life (94). This acidosis may have been related to colonic absorption of organic acids produced in large quantities by the bacterial flora.

The fact that significant (> 0.5%) quantities of reducing substances can be detected in the stools of both breast-fed infants and infants being fed modified cow’s milk formulas (6–7% lactose), and the identification of lactose, glucose, and galactose in these stools suggest that substantial quantities of lactose pass the ileocecal valve. Furthermore, it has been recently shown by sequential studies of breath hydrogen excretion in response to lactose feeding, that 66% or more of ingested lactose enters the colon and is fermented in premature infants, whether breast-fed or not. These infants received 8 (at 1 week) to 14 g/kg/day of lactose (at 6 weeks of life) (95). It was estimated that, above 4.5 g/kg/day, lactose was not absorbed but was fermented in the colon (95). Such a functional lactase insufficiency persists until the second postnatal month in normal infants and decreases thereafter (96,97) (Fig. 6). This “physiological” lactose malabsorption is clearly independent from the maximum enzymatic activity of the gut, which was estimated to be able to hydrolyze approximately 60 g/day of lactose (43); it may be related to feeding pattern, role of gastric emptying (see above), mobility, or streaming of intestinal contents (96). It underlines also the great efficiency of colonic salvage of malabsorbed carbohydrate, overall \(^{13}\)C-L-lactose absorption being nearly complete in term infants (98).

Starch, glucose polymers, and dietary fibers

In contrast to lactose, starch, even given in sizable amounts, is well tolerated by newborns, even though \(\alpha\)-amylase activity is extremely low at this age. Careful
balance studies have shown that 1-month-old normal infants are able to absorb perfectly 10 g/day of cooked wheat, corn, tapioca, or potato starch, and up to 40 g/day of cooked rice starch. At 30 months of age, 20 to 25 g/day of the same cooked starches are absorbed without fermentation. Finally, children of 1 to 2 years of age absorb 99% of 170 g/m²/day of cooked wheat or potato starch, the same amounts of noncooked potato starch being less well (93%) absorbed (99,100) (Table 1). Even low-birth-weight infants absorb 88% (81–97%) of 3.5 g of corn starch/kg/day without diarrhea (101). Although these high coefficients of absorption might be explained by the great efficiency of very low concentrations of α-amylase in

\[
\text{TABLE 1. Absorption of various starches in 1-month-old infants}^a
\]

<table>
<thead>
<tr>
<th>Subjects (n)</th>
<th>Starch in diet</th>
<th>Stool findings (g/day)</th>
<th>AC° (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Wheat 11</td>
<td>0.05</td>
<td>&gt;99.4</td>
</tr>
<tr>
<td></td>
<td>Corn 12</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tapioca 10</td>
<td>0.33</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rice 10</td>
<td>0.06</td>
<td>98.7</td>
</tr>
<tr>
<td></td>
<td>Potato 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rice 25</td>
<td>0.33</td>
<td>98.7</td>
</tr>
</tbody>
</table>

*aFrom De Vizia et al., ref. 100.  
°(AC) absorption coefficient.
the duodenal fluid, and by the fact that intestinal glucoamylase, fully developed at birth, could provide alternative pathways for starch digestion (100), it has been elegantly demonstrated that colonic bacterial fermentation has an important part in the net absorption of starch. By tracing the appearance in breath of $^{13}$C-enriched CO$_2$ derived from corn starch, and assessing fermentation of nonabsorbed carbohydrate by the colonic flora by measurement of breath H$_2$, it has been possible to show that (a) the extent to which the cereal is oxidized is equal to that of glucose and glucose polymers and (b) the more complex the carbohydrate, the more important the colonic fermentation (102) (Table 2).

The bacterial flora have an even more important role in the functional tolerance of dietary fibers. Some (mainly hemicellulose and pectic substances) are partially or nearly completely degraded to volatile fatty acids, CO$_2$ and H$_2$ by the colonic bacteria. However, some of the anaerobic species mostly implicated in their metabolism ($Bacteroides$, $Eubacterium$) reach significant levels only in the second semester of life. Although, to our knowledge, no data exist regarding the development of the digestibility of fibers in human infants, it would seem wise, in breast-fed babies, to introduce dietary fiber well after weaning, and, in bottle-fed babies, to introduce it progressively in the second semester, after other beikosts.

**Protein Digestion and Absorption**

The functional capacity of the newborn gastrointestinal tract to digest and absorb protein is difficult to evaluate. Classical balance studies are inadequate, since dietary proteins, in contrast to carbohydrates and lipids, are diluted in the intestinal lumen by endogenous proteins. Because of this limitation, no straightforward conclusion can be reached regarding the efficiency of gastrointestinal protein absorption with the latter technique. Nonetheless, the fact that the coefficient of $N$ "absorption" does not vary significantly with age, being around 85% even in prematures (103,104), and that after 1 year of age $N$ excretion in feces is nearly constant (105,106), allows the speculation that, although pancreatic trypsin secretion is not fully developed until 2 to 3 years of age, it is almost sufficient from birth.

| TABLE 2. Peak $H_2$ excretion in 16 infants after oral loads of glucose, glucose polymers, and corn starch* |
|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | Glucose         | Glucose polymers| Corn starch     | Lactulose       |
| Peak $H_2$ (ppm, m ± SD) | 19 ± 16         | 29 ± 18$^b$     | 40 ± 41$^a$     | 188 ± 211$^c$  |
| Infants > 20 ppm | 6               | 10              | 11              | 16              |

*From Shulman et al., ref. 102.
$^b p < 0.05$/glucose.
$^a p < 0.001$/other substrates.
More accurate knowledge of the magnitude of protein digestion and absorption in children is derived from the few studies concerned with the composition of the intestinal contents. During the 3 hr following a test meal containing 3.1 g/100 ml of cow’s milk protein, the percentage absorption of radioiodinated human serum albumin (RHSA) in the duodenum is similar in premature and full-term babies, being between 5 and 15%; the conclusion of this study was that premature newborns need not be fed with a protein hydrolysate (107). In infants 3 to 5 months old receiving a test meal containing 5 g/100 ml of cow’s milk protein, absorption of RHSA varied between 5 and 25% in the duodenum and between 25 and 40% in the jejunum (108). More decisive data were obtained by sampling ileocecal contents of normal infants up to 5 months of age receiving 150 ml/kg/day of milk; the protein load corresponding to breast milk was shown to be completely absorbed at all ages, and the ability to absorb casein increasing from the load of a cow’s milk formula containing 1.3% protein at 10 days of age, to 2.5% protein (but not 2.7%) at 5 months of age (10 g) (Fig. 7). This amounts to around 6 g/day of casein at 10 days and 20 g, or 3 to 4 g casein per feeding, at 5 months. A higher proteolytic capacity (1 g casein/kg/hour) has been extrapolated from the in vitro activity of 1 ml of duodenal juice to hydrolyze casein to peptides, by multiplying this activity by an estimated volume of secretion per hour (110). The proteolytic activity per milliliter is not very different from the values in adults and the functional capacity in children reflects the lower volume of their pancreatic secretion. However, in the same assay system the hydrolytic capacity for α-lactalbumin or β-lactoglobulin is more than 100 times lower than for casein (111).

Finally, it appears from these figures that during the first weeks of life for both premature and term babies, the upper limit to protein ingestion is not set by the functional capacity of the gastrointestinal tract but by the immaturity of renal excretion of N; in older infants there is a risk that if gut absorptive capacity is exceeded, mild digestive symptoms, manifesting as loose, foul-smelling, ‘‘putrefactive’’ stools, appear. In summary, these findings leave considerable freedom in the ways to introduce proteins at the time of weaning.

**FIG. 7.** Increasing functional capacity of infant small intestine to digest and absorb casein during the first 5 months of life, as estimated by presence (incomplete digestion and absorption) or absence (complete digestion and absorption) of residual casein in samples of ileocecal juice obtained by trans-intestinal intubation. Newborns received six feeds of milk reconstituted with increasing amounts of proteins (vertical axis). From Hirata et al., ref. 109.
Lipid Digestion and Absorption

Fecal fat is of dietary origin, with the exception of 1 g/day of obligatory fat excretion in feces (112). Balance studies are therefore adequate to assess the functional capacity of the gastrointestinal tract to absorb fat. With this technique, it has been repeatedly shown that there exists a "physiological" malabsorption of fat in premature and full-term newborn infants, even when they are fed with human milk (113). This malabsorption is mild even in prematures (absorption coefficient around 90%) when fed fresh human milk. After 2 months of age, fat absorption is normal (> 95%). When stored human milk is given, fat absorption may be as low as 75% in both prematures and full-term newborns, and becomes normal only after 3 months of age. Cow's milk fat is far less well absorbed, since 40 to 50% of ingested fat may be excreted in the stools of prematures and 15 to 35% during the first month of life in full-term babies. During the third month of life fat absorption remains below 90% (114).

Several factors have been implicated in this malabsorption, but the relative importance of each is not clearly established. It probably depends on the type and amount of ingested fat. In the case of human milk, the fact that fat absorption of pasteurized milk is 70% of that of fresh milk in preterm infants (115) has been interpreted as reflecting the physiological importance of a lipase present only in human and primate milk. In fact, this lipase, a glycoprotein of 90,000 daltons, stable at gastric pH, hydrolyzes long-chain triglycerides without positional specificity and is dependent on activation by bile salts (bile-salt-stimulated lipase) at the low concentrations found in the newborn duodenal fluid (116). Furthermore, it has been convincingly shown that human milk fat absorption is independent from (whereas butterfat absorption increases in parallel with) duodenal bile salt concentration in premature infants (74). Insufficient lipolytic activity (low lingual and pancreatic lipase), not insufficient bile salt secretion, appears to be the limiting factor of human milk fat absorption, whereas the opposite is true for butterfat absorption. Whatever milk is fed, this "physiological" steatorrhea should be avoided, because it may represent a loss of up to 20% of ingested energy in the newborn. This has been the reasoning that has led to the introduction of MCT in low-birthweight-infant formulas and vegetable oils in full-term formulas.

After 3 months of age, malabsorption (fat absorption ≤ 70%) is only observed when fat intake is high (5–7 g/kg/day) and is composed essentially of butterfat (114). However, at this age infants thrive normally and have normal stools, making high-fat diets not only deleterious but costly. In fact, low-fat regimens (2–3 g/kg/day) have been described as causing chronic nonspecific diarrhea (117) and long-chain triglycerides have been advocated to promote gut adaptation after extensive intestinal resection (118).

In summary, a gradual increase of ingested fat at weaning should have no adverse effects, nor should changing their origin have such effects.
Sucking, Chewing, and Swallowing

The entry of food into the mouth of an infant is a necessary prelude to swallowing. Under normal conditions this involves sucking liquid (milk) from a nipple or teat, and later acceptance from a spoon of food, which is fragmented and mixed with saliva by chewing. Both sucking and chewing are complex activities that have both innate and learned components.

In the context of the present paper, the development of the ability to chew is more important than consideration of sucking. However, it may be hypothesized that there are lessons from studies of sucking that can help our understanding of the development of chewing.

Sucking

The establishment of nutritive sucking must be preceded by a series of sequential coordinated actions (120). First, in the case of animals, the mother’s body must be approached and touched (this phase is in the control of the human mother when she picks up her baby); second, neonates of all species must approach, latch onto, and in some cases manipulate, the nipple. Only then can efficient, nutritive sucking be initiated.

There is evidence that such complex behavior depends upon several factors:

a. Maturation and integration of appropriate neural pathways (121). At a clinical level this is reflected in the three developmental stages of sucking (10,122). Very preterm infants make only mouthing movements with no effective suck. This phase is followed by the immature suck–swallow pattern, in which short bursts of 4 to 7 sucks occur at a rate of 1 to 1.5/sec but are not accompanied by coordinated swallowing. The mature pattern, seen in full-term infants within a few days of birth, comprises prolonged bursts of at least 30 sucks at a rate of 2/sec, with coordinated swallowing occurring 1 to 4 times during each burst (Fig. 8).

b. A learning process, which may have reflex, habituation, respondent conditioning, and instrumental conditioning paradigms (123). The last may be the most important.

The critical feedback that the infant gets from sucking is probably the overall stimulation of its mouth. Wolff (124) has shown that it is probably the flow of milk into the pharynx that switches sucking from the non-nutritive to nutritive mode. The structure and resiliency of the nipple, taste (see below), and smell (125) may be important additional conditioning stimuli. The role of hunger as a stimulus to nutritive sucking has not been adequately studied, but common sense suggests that it has a role. There is evidence that gastric filling has an inhibitory effect on sucking (121).

Under appropriate experimental conditions it can be shown that nutritive sucking can persist at least into late childhood (121).
Chewing

The essential "skill" that must be acquired by an infant to allow the progressive introduction of solid foods is chewing followed by coordinated swallowing. Although there are few direct data, we hypothesize that similar factors operate in the development of chew-swallow as in suck-swallow, namely (a) sequential neuronal development, (b) learned behavior, and (c) oral stimulation acting as a conditioning paradigm (Table 3).

Evidence for a developmental component in chewing comes from the observation that a neonate exhibits an extrusion reflex when a spoon is introduced into the anterior part of the mouth. The lips are pursed and the tongue pushes vigorously against the spoon. By 4 to 6 months, when a spoon containing pureed food is placed in the mouth, the tongue is depressed and food is accepted into the posterior part of the mouth and is swallowed. By 7 to 9 months rhythmic biting movements occur even if no teeth have erupted. Thereafter, biting strength and masticatory efficiency increase progressively throughout childhood (8).

The evidence that the ability to chew is also part of a learning process comes largely from observations of infants who, for medical or surgical reasons, cannot have solid foods introduced at the age of a few months. Examples include infants who have needed multiple surgery for congenital esophageal abnormalities (and who have been fed by gastrostomy) and infants with intractable diarrhea who have required prolonged parenteral nutrition. When solids are eventually tried at the age of 1 year or more, there is considerable difficulty in accepting them: The infant refuses them, refuses to chew, or vomits. Illingworth and Lister (126) have suggested that there may be a "critical period of development" during which infants can and must learn to chew.

It seems likely that the stimulus to chew will be affected by the texture of the food, and by its taste, smell, and appearance. There is evidence that these latter factors can influence sucking (see below, discussion of appetite).

<table>
<thead>
<tr>
<th>Developmental component</th>
<th>Neonatal extrusion reflex</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Acceptance of purees at 4 to 6 months</td>
</tr>
<tr>
<td>Learned component</td>
<td>Rhythmic biting at 7 to 9 months</td>
</tr>
<tr>
<td></td>
<td>Surgery for esophageal abnormalities</td>
</tr>
<tr>
<td></td>
<td>Intractable diarrhea fed by total parenteral nutrition</td>
</tr>
<tr>
<td></td>
<td>Concept of &quot;critical period&quot;</td>
</tr>
<tr>
<td>Nature of feeding</td>
<td>Texture</td>
</tr>
<tr>
<td></td>
<td>Taste</td>
</tr>
<tr>
<td></td>
<td>Smell</td>
</tr>
<tr>
<td></td>
<td>Appearance</td>
</tr>
<tr>
<td></td>
<td>Hunger</td>
</tr>
</tbody>
</table>
FIG. 8. Suck is represented in the first lead in each trace, and swallowing in the second and third leads. (A) Immature suck–swallow pattern. Swallowing occurs between sucking bursts; peristalsis is propagative (preterm infant: birth weight 1,740 g, gestation 33 weeks, age 3 weeks). (B) Mature suck–swallow pattern. Long sucking bursts with multiple swallows during sucking (preterm infant, now weighing 2,100 g at 6 weeks). (From Gryboski, ref. 122).
It is not necessary to have teeth in order to masticate certain solids, but obviously the serial acquisition of teeth from the age of about 7 months allows a progressive increase in the efficiency of cutting, grinding, and crushing of foods.

**Swallowing**

Although a swallowing reflex exists in the fetus, it appears that the complex development of pharyngoesophageal function is closely linked to the development of the appropriate skills of oral ingestion. For example, Gryboski et al. (10) showed that coordinated peristalsis developed at the same time as mature sucking. By analogy, the ability of the pharynx and esophagus to accept and propel solid residue depends on the texture and size of the bolus, which is obviously a function of efficient chewing.

Bosma (127) has argued elegantly that there is a caudocephalic sequence of development in certain functions of the primitive foregut that are superimposed on the more traditional description of cephalocaudal gradients. Pharyngeal function matures ahead of oral function, with the result that the pharynx should be “able” to accept what the mouth “gives” to it.

The answer to the question, What foods may be given during weaning? has many facets. It concerns the availability of certain foods and local customs. These important geographical and cultural factors are beyond the scope of this paper. The question also centers on the palatability of food, and the development and control of appetite.

**The Physiology of Appetite Development and Control**

From the outset there are semantic problems—for example, the difference between hunger and appetite. The authors found helpful the distinction drawn by Castonguay et al. (128): Hunger is concerned with the question “Is there anything to eat?” and appetite relates to the question “What do I want to eat?”

There is of course a great deal of overlap. Both hunger and appetite are influenced by central and peripheral somatic stimuli as well as by environmental factors and disease states. Recent research has concentrated on the central and peripheral neuroendocrine control of appetite, and on aspects of learned behavior.

**The Central and Peripheral (Neuroendocrine) Control of Appetite**

In a recent review, Morley and Levine (129) concluded that a multiplicity of central neurotransmitters is involved. Evolutionary processes have apparently produced a complex “fail-safe” control system, with several redundant or accessory features. The regulatory transmitters involved in appetite regulation may be arranged in a cascade system, analogous to that of clotting factors and complement fixation.
The similarities between the monoaminergic and peptidergic control of appetite and the central control of analgesia, temperature, and a range of GI secretory functions suggest that there may be a degree of overlap in the control of these closely related life-supporting systems.

In a summary of the peripheral control of appetite, Smith (130) concluded that neuroendocrine and sensory aspects of the GI tract are the major mechanisms that provide the information used by the central neural network to decide to terminate eating. Oral signals, perhaps including taste, a putative gastric satiety hormone (bombesin?), and postgastric hormones including CCK, somatostatin, and pancreatic glucagon, may all be involved.

The Overall Control of Macronutrient Intake

The mechanisms that ensure a macronutrient intake over prolonged periods that is sufficient for growth, development, and activity are obscure, and there are wide species variations in feeding patterns. The evidence that such mechanisms exist in human infants was given by the fascinating (and unrepeatable) study in 1928 of Davis (131) who allowed three normal, exclusively breast-fed infants of 7½ to 9 months to "self-select" from a tray of foods offered each day. Over 6 to 12 months of the experiment, during which the infants thrived, they were omnivorous. Eating was governed not only by their caloric needs but showed definite preferences, which changed from time to time in an unpredictable way (Fig. 9).

Appetite for Specific Substances

Apart from the effects of salt deficiency in rats, there is little good evidence that deficiencies lead to specific food preferences. Certain deficiency states—e.g., thiamin in rats—may, however, lead to an increased willingness to accept novel foods.

The Role of Learning in Appetite Behavior

It appears that innate appetites and satiety are few (132). These can be elicited by extreme conditions like gross salt deficiency or intestinal dumping or by stimuli poorly related to nutrient supply or need, like sweetness (133) and large distensions of the stomach.

The importance of learned behavior in relation to eating solids in early childhood is exemplified by the recent studies of Birch and Marlin (134). These workers observed the relationship, in 2-year-old children, between frequency of exposure to foods and preference for these foods. There was a highly significant correlation (p < 0.01) between exposure frequency and subsequent voluntary choosing, showing that preference is an increasing function of exposure frequency (Fig. 10). These data are consistent with the "mere exposure" hypothesis (135), as well as with the
FIG. 9. Source of calories during a 6-month period in 3 infants (aged 6–9 months at beginning of experiment) who were allowed to "self-select" their diet. (From Davis, ref. 131).
The other aspect of learned behavior that is crucial to an infant's acceptance of solid foods concerns chewing. The importance of a "critical period" for acquisition of this behavioral skill has already been discussed.

**Palatability and Taste**

Taste is restricted to sweet, salt, bitter, and acid. The hedonic factor concerning food, called palatability, involves the taste, smell, and texture of food and has been shown to be an important factor in determining consumption (136).

**Taste**

The human infant has a "sweet tooth." This has been shown by, among others, Crook and Lipsett (137), who found that feedings or increasing sugar concentrations alter sucking patterns, with longer bursts of activity, shorter pauses, and a slower pace of sucking within each burst (Table 4). There is also evidence that increasing sweetness increases total intake of food, a phenomenon that is stable at least during the first 6 months of life (138).

The neonate also responds to saltiness, which has been confirmed in several studies using facial expressions, tongue movements, and modification of sucking patterns (139–144). Preliminary data by Daniel and Lipsett (cited in reference 142) show that a salty feeding alters heart rate in a different pattern from that found...
TABLE 4. Response of heart rate and sucking in groups of full-term neonates fed 5% and 15% sucrose solutions for two periods of 3 min separated by a period of non-nutritive sucking*

<table>
<thead>
<tr>
<th>Experimental period</th>
<th>Group 5-15</th>
<th></th>
<th>Group 15-5</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5% NN</td>
<td>15%</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>155.40</td>
<td>177.60</td>
<td>170.70</td>
<td>165.50</td>
</tr>
<tr>
<td>IRT (sec)</td>
<td>0.77</td>
<td>0.82</td>
<td>0.81</td>
<td>0.75</td>
</tr>
<tr>
<td>BL</td>
<td>48.80</td>
<td>76.40</td>
<td>55.10</td>
<td>41.60</td>
</tr>
<tr>
<td>NB</td>
<td>6.10</td>
<td>3.70</td>
<td>4.60</td>
<td>5.90</td>
</tr>
<tr>
<td>IBI (sec)</td>
<td>10.20</td>
<td>10.50</td>
<td>11.40</td>
<td>13.60</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>136.30</td>
<td>146.50</td>
<td>141.70</td>
<td>135.90</td>
</tr>
</tbody>
</table>

*(R) total sucks; (IRT) mean interval between responses within a sucking burst; (BL) mean number of responses in a burst; (NB) number of sucking bursts; (IBI) mean interburst interval; (HR) mean heart rate during final quarter of sucking period. (From Crook et al., ref. 137).

during a sweet feeding. These workers propose tentatively that salt is hedonically negative for the newborn. On the other hand, infants will suckle avidly if given a relatively high concentration of salt, as occurred during an accidental mass poisoning in a nursery where salt was substituted for sugar in the feedings (143).

Attempts to study the development of preference for salty foods are conflicting. There is some evidence that children of 2 years of age prefer salted to unsalted foods and that this preference continues through childhood. There are no clear measures of the amount of salt preferred or whether the amount changes in this age. Although there is some suggestion of a change in hedonic response to salt from negative to positive during the first few years of life, this may be a function of the context in which the salt is presented or the preference measured (142).

Olfaction

By analyzing facial expressions, newborns have been shown to respond to smell as well as taste (133). There is evidence that they can discriminate between smells (125). With present knowledge, it is impossible to say whether this is a simple sensory-resolving power only, or whether there are hedonic components of liking and disliking. Studies in older infants suggest that olfactory preferences arise from associative learning (144).

Palatability

The palatability of food has been shown to be an important factor in the eating habits of obese children. Ballard et al. (145) studied children 9 to 11 years old in a school canteen and found that normal children left twice as much "palatable"
food on their plates as did obese children, while there was no difference in the amount of "unpalatable" food left uneaten.

Nutritional Factors

The predominant physiological reason for introducing solids is nutritional. Breast feeding or feeding with a "starting" formula is usually nutritionally adequate for the first 6 months of life. The median daily energy intake, between 6 and 12 months, of around 100 kcal/kg that was found in a prospective study of normal Australian infants by Boulton (146) could theoretically be met by breast milk, but such a regime would pose problems of volume for both producer and consumer.

Therefore in practical terms, the nutritional demands of the growing infant in the second 6 months of life require the addition of calorie-dense beikost. Although a feeding regime for weanlings can be designed simply on the basis of physiological needs, cultural, psychosocial, and historical factors should be considered also.

The recommendations of the Committee of Nutrition of the European Society for Paediatric Gastroenterology and Nutrition (ESPGAN) (147) are sound. They are as follows:

a. In giving advice about the introduction of beikost, note should be taken of the sociocultural milieu of the family, the attitudes of the parents, and the quality of the mother-child relationship.

b. In general, beikost should not be introduced earlier than 3 months nor later than 6 months. It should be started in small amounts, and both the variety and quantity should be increased slowly.

c. By the age of 6 months, not more than 50% of the energy content should derive from beikost. For the remainder of the first year, breast milk, formula, or equivalent dairy products should be given in a quantity of not less than 500 ml daily.

d. There is no need to specify the type of beikost (cereals, fruits, vegetables) to be introduced first. In this respect national habits and economic factors should be considered. It is not necessary to make detailed recommendations regarding the age when animal proteins other than milk should be started, but the introduction of certain foods known to be highly allergenic, such as eggs and fish, is probably best deferred until 5 to 6 months.

e. Gluten-containing foods should not be introduced before 4 months of age, and should perhaps be further postponed until the age of 6 months.

f. Foods with a potentially high nitrate content, such as spinach or beets, should be avoided during the early months.

g. In infants with a family history of atopy, potentially highly allergenic foods should be strictly avoided during the first year.

The committee listed the potential disadvantages of introducing beikost too soon as (a) interference with breast feeding, (b) excess renal solute load and hyperosmolality, and (c) induction of food allergy.
Behavioral Considerations

A second important reason for introducing solids at the appropriate time is behavioral. As discussed above, there may be a "critical period" of neuronal or brain development during which the normal infant learns to chew. If an infant misses this learning experience at the appropriate time (which probably extends from around 6 months till the end of the first year), severe feeding problems can ensue subsequently.

CONCLUSION

When we began to collaborate to write this review, we entertained the slight hope of being able to address the question What is the optimal weaning regime? Our conclusion must be that, on the basis of present knowledge, a range of feeding practices is permissible.

Human societies have developed a collective wisdom about the selection and preparation of foods, which is transmitted from generation to generation. Only a very limited number of potential food items are actually eaten by humans, and availability and custom seem equally important determinants. Weaning is no exception.

REFERENCES


**DISCUSSION**

*Dr. McNeish:* *Weaning* is used by different people in different ways; it is used, for instance, to indicate that foods other than milk are introduced, but also that breast milk is no longer given; in other words, it is the end of a stage. I think the word *weaning*, in an English sense, describes the period of life between which food is introduced and milk is withdrawn. So, I think in common English usage it can be used to describe the events within that period, and it is for us to define what we want to talk about within that period: Do we want to talk about the introduction of food? Do we want to talk about how long that period should be before milk is discontinued?
Dr. Shanti Ghosh: For many years I have crusaded against this word weaning, as far as Indian practices of feeding the babies are concerned, because it means different things to different people. Many people, including the medical profession, feel that it probably means the stopping of breast feeding—breast milk being gradually withdrawn, and the other foods started. Now we do not want breast milk to be withdrawn, we want the breast feeding to continue for as long as the mother is able to feed the baby and as long as her cultural, social, and personal habits allow. In certain areas we are asking the people who are poor to simply modify the family food for the baby, in which case weaning means introduction of family food. In the higher socioeconomic groups where mothers are able to prepare special foods, we could say weaning means introduction of semisolids. Weaning really has so many different meanings for so many people, and as I said, a lot of people think it means stopping breast feeding and just introducing solids.

Dr. Hahn: I don’t quite agree with this, because weaning is an exact word which gives a description of what is happening. It means stopping breast feeding. In my opinion, when you give any kind of artificial milk as a replacement of breast milk, any formula, you are in fact already weaning. There is a suckling period when the baby depends on breast milk or some other milk; then there is a weaning period which is quite clear: it means while the baby is being weaned, it is also receiving other food; and then there is the postweaning period. For research purposes it is really important to distinguish between these periods.

Dr. Shanti Ghosh: Weaning means we are deliberately stopping something and starting something else. Now our concept of feeding a child is not to stop breast milk but to add something to it. We are not stopping anything, we are going on feeding the child with what it was eating earlier—breast milk—but adding other things to it as the breast milk quantity decreases.

Dr. Hahn: That is the “weaning period.”

Dr. Davies: I would like to support what Dr. McNeish has mentioned. If we wish to be pedantic, the term weaning is derived from the ancient Anglo-Saxon wenian, which means “to become accustomed to something different.”

Dr. Ashfaq Ahmad: Weaning means to accustom to, it does not mean total cessation of breast milk. What we understand by weaning in the developing countries is that you carry on with breast milk feeding because that may be the only source of first-class protein. Therefore, the introduction of a weaning diet includes milk and doesn’t exclude breast feeding.

Dr. Jayesinghe: I think the problem could be obviated by dropping the word weaning and using the term weaning period.

Dr. Poskitt: I shall be discussing this further in my talk, but the Oxford English Dictionary definition of weaning has two meanings: One is “to accustom to food other than milk” and the other is “to disengage or cure from habit by enforced abstinence of counter-attractions,” and thus both sides of the argument are covered. I feel very strongly that the former definition should be used, namely; to accustom to food other than milk rather than to disengage from breast feedings or milk feeding of any kind.

Dr. Vis: For more than 10 years I have attended meetings on weaning. Each time the same discussion appears, and each time I request that a glossary be included in the first page of the proceedings, with the exact definition of each word—not only weaning and weaning food, but also supplement, complement, substitute to breast milk, and so on. For instance, I do not think that a weaning food need be food other than milk, since cow’s milk, for example, given as a puree, may be a weaning food. Therefore this definition is unclear. Another example: In developing countries and in very traditional populations, complements
or supplements are given not for a few weeks or a few months, but sometimes for 2 or more years because breast feeding is long-lasting. Is that a weaning period? I do not believe it; it is something else. So, we really need very clear definitions.

**Dr. Narasinga Rao:** I would like to agree with Dr. Ghosh. We should not waste time in semantics. "Introduction of solid foods" should be the proper definition of weaning and surely not "taking a child away from the breast."

**Dr. Ballabriga:** The definition of the word *weaning* may perhaps vary in different cultures. For instance, in Latin America, the *destete* used for *weaning* means that the *teta*, the breast, is withdrawn from the child. In these conditions, does "weaning" mean that the child no longer gets human milk, or a mixture of human milk, cow's milk, and solids at the same time?

**Dr. McNeish:** So far in the discussion, I think the important point which has emerged is that there are certain bad practices which should be changed. This is partly due to a misinterpretation by many people of the word *weaning*, which they are using to equate with bad practices, and therefore I totally agree with Dr. Ghosh. Our task is really to decide how to pass on the good messages about infant feeding, and if the message that we are trying to pass on is introduction of family foods, and if the word *weaning* is part of that message, then we shouldn't concentrate on semantics. We should drop that word rather quickly and concentrate on the positive side of how and when we introduce foods other than milk, and also recommend to physicians how long milk feeding can be continued.

**Dr. Ferguson:** Speaking as an immunologist, I feel that we should not neglect the consequences, over and beyond the nutritional one, when any foreign substance is introduced into the gastrointestinal tract. Microbiological and immunological changes occur, and these will be influenced by withdrawal of the protective properties, specific and nonspecific, of maternal milk.

**Dr. Rafique Ahmed:** According to this definition of *weaning*, i.e., stopping breast feeding and introducing artificial feeding, a child who has never been breast-fed for some reason can never be weaned. This cannot possibly be the right definition, it must be the "transition" from milk, whether natural or artificial, to solids.

**Dr. Guesry:** I have a question for Dr. Schmitz. You point out that bacteria from the colon play quite an important role in the early weeks after birth in the digestion of carbohydrates. At first I thought that they were working only as scavengers, but you mentioned that they are helping in absorption. Do we have any idea how efficient this process is?

**Dr. Schmitz:** With regard to lactose, you can estimate the efficiency of colonic salvage by calculating the difference between what you guess is left after absorption in the small intestine and what you assay in the stools. According to some authors, colonic salvage could account for at least 40% of lactose absorption. This figure may be between 10 and 20% for glucose polymers and starch, depending on the type of starch. At the present time, we are studying the absorbability of different kinds of starch with the breath hydrogen test, and are confirming data by De Vizia that, according to the kind of starches, the colonic salvage may be very different. It is certainly very important.

**Dr. Narasinga Rao:** You discussed the absorbability of carbohydrates and proteins from milk and cereal sources. In developing countries, we have been advocating mixtures of cereals and legumes for the preparation of weaning foods. What is your opinion on the absorbability of carbohydrates and proteins from legumes?

**Dr. Schmitz:** From the plant polysaccharides, thus also true for polysaccharides from legumes, lignin is practically undigested, and cellulose only partly—around 30%; but hemicelluloses are quite well digested—up to 50%—in the colon. So, depending on the type of
fiber you are giving, some of these plant polysaccharides may be digested by the baby. However, the bacterial flora of the colon may not be well adapted, at least during the first 6 months of life, to digesting these fibers.

*Dr. Rey:* Dr. Schmitz, are you sure that the fermentation of carbohydrates, for example, of lactose, takes place only in the colon and not in the ileum?

*Dr. Schmitz:* This depends on the presence of bacteria in the ileum; the ileum is not supposed to harbor bacteria which are able to ferment the carbohydrates. Hydrogen appears in breath at the time the carbohydrates reach the cecum. I think there is good evidence that fermentation of carbohydrates takes place only, or mostly, in the colon.

*Dr. Rey:* You did not say anything during your talk on the role of the pH in the production of H₂. I think it could be interesting to say a few words on this aspect of H₂ production, because you showed very well in your work on glucose–galactose malabsorption that when the pH is below 5 or 4.5, the flora is modified in a way that it cannot produce H₂. I wonder if we really can study lactose absorption in newborns with the breath hydrogen test. For example, you showed a slide from Douwes (*Arch Dis Child* 1980;55:512–5) suggesting that lactose absorption was complete after 2 months; but another explanation could be that the flora was modified in a way that it became unable to produce H₂ at 2 months of age. Furthermore, I am not sure that we may say that the flora of a breast-fed infant is unable to digest weaning foods. It is perhaps enough to change the food for a few days to modify the intestinal flora of the child.

*Dr. Schmitz:* Your comments on pH are very important, and you are right. Lifschitz was the first to study this problem; I cannot explain the contradiction he described, showing that breast-fed infants have a low pH in their stools and hydrogen in their breath. I think we should not compare this situation, where there is a kind of selection of bacteria which is certainly different in the case of glucose–galactose malabsorption which we have studied together. We have to admit that the stool pH may be low in babies who excrete hydrogen.

*Dr. Ferguson:* My question relates to the role of bacteria in carbohydrate digestion. Studies in adults have shown the importance of gastric acid and cleanliness of food, together with normal motility, in maintaining a low bacterial flora in the small intestine. Immunological factors seem much less relevant than these others. We have been shown the results of studies of gut flora of breast-fed British or American human infants. Are there any studies of the normal gut flora of breast-fed children in developing countries where the environment is less clean?

*Dr. Schmitz:* There are two studies on the gut flora of infants during their first year of life, one by Mata, which is 15 years old, and a recent one by Stark and Lee. They have described the same flora as in industrialized countries.

*Dr. Anantharaman:* Dr. Schmitz, could you comment on the efficiency of absorption of carbohydrates in instances where the intestinal microflora has been modified? For example, would plant carbohydrates be efficiently utilized where bacteroides are prevalent, or vice versa?

*Dr. Schmitz:* The germs supposed to be capable of digesting plant polysaccharides are *Bacteroides, Eubacteria,* and also some bifidobacteria. An important point, however, as was already mentioned by Dr. Rey, and one that has been demonstrated fairly well in the studies I alluded to, is that in a breast-fed baby one bottle of cow's milk (or formula) per day is enough to completely modify the bacterial flora. It is therefore possible that the introduction of vegetables could also modify the bacterial flora and improve the digestion of plant polysaccharides. However, we don't know very much about this kind of adaptation.
Dr. Davies: We seem to know very little about the role of the teeth in determining the time solid foods should be introduced. Does the appearance of teeth provide a marker of change in gastrointestinal function? In some traditional communities, teeth eruption actually determines when non-milk foods might be introduced.

Dr. McNeish: The definition of a good question is one that you cannot answer! I like your second hypothesis, because even though we know there is a variation of "normal" in the time appearance of the first dentition, on average, the first tooth appears at a time when, for nutritional reasons, we might be thinking that it was a good idea to be adding other foods. When we talk about the appearance of the teeth, this is really the eruption of the teeth; they are in fact well developed several months before but have not erupted through the gums. I do not know of any association between the appearance of the teeth in a mechanistic sense and gastrointestinal function. There is no question that children whose teeth eruption is delayed will still make chewing and biting movements with their gums even though they haven't got any teeth. I do not think it is the teeth that make you chew. However, the possible significance of teeth to a mother is another thing. I would like to hear other people comment on that.

Dr. Schmitz: Dr. McNeish, you mentioned a "critical learning period" during which the infant learns to take solid food and to chew, and you said that, for instance, children who had esophageal surgery and therefore missed this critical learning period can present with difficulties. Are there any studies on eating difficulties in later life of children who have been weaned too late and who therefore could have missed the learning period?

Dr. McNeish: Again, no, I do not know of any such studies on feeding difficulties in relation to early feeding experiences, because all the statements on this subject, as far as I can see, are hypotheses and questions rather than answers. If you accept the premise that learning is an experience and that with practice you can become, in a sense, even more efficient, then you can argue that by the time you have had two or three new experiences, your adaptive capacity to react to more new experiences is greater.

If you come back to taste and smell, it has been suggested that the breast-fed infant, by virtue of the variation in composition of mother's milk from time to time according to substances that she herself may ingest, is subjected to a rather richer range of experience in tasting than is a formula-fed infant. The hypothesis has therefore been put forward that breast-fed babies should be easier to wean onto a range of new food because in a sense they are already accustomed to new experiences. That is hypothesis. In lower animals, there is quite a degree of so-called neophobia; the animals will be very frightened of, or averse to new food. They will be very suspicious. As far as one can determine, and again I allude to the studies of Birch et al., they have found very little evidence of neophobia in human infants. There is a certain suspicion of new foods and of course they prefer well-known food, but they will try anything. We published a study on 17 children who failed to thrive without organic cause, in whom the etiology was thought by us to be a feeding disorder of severe degree and of psychological origin, with a very disturbed mother–child relationship; all 17 children had been bottle-fed as compared to control groups which I won't discuss in detail, in which the frequency of breast feeding approximated the frequency of breast feeding in our population at large. Of course, if you classify people by having been exclusively

bottle-fed, you classify many more things than just the feeding experience—social class in Britain, and economic circumstances, and so on. It is very difficult to draw a straight line between one and the other, but there is at least one study in which feeding difficulties later on were exclusively in the bottle-fed, with a behavioral connotation. So, I don’t think I have the answer to your question, but these are nice thoughts that a rich feeding experience makes an even richer experience even more comfortable and more possible.

Dr. Anantharaman: An age-old Indian practice is to put powdered sugar at the tip of the tongue of the newborn infant. It could be premised that this is to induce the sucking behavior. Are similar practices documented in other societies? In this context, Dr. McNeish, I would be interested in your comments on taste preferences in the newborn infant.

Dr. McNeish: I am not a comparative behavioral scientist, so I do not know what the feeding practices are throughout the world. I think most traditional practices must have some very good observation at their source; otherwise, they would not have been continued in culture just for traditional reasons. There is no question at all that sucrose in the mouth does increase the length of sucking. Also the pause between sucking episodes is shortened, and the pressure of the suck is strengthened. So you may very well be right that practice has a reason and can even be a stimulus to adequate sucking. Now, what do babies prefer? You can show differences, but when we use the word *prefer*, we mean hedonic choice, concerned with sensual pleasures. It is very difficult to say that when babies’ behaviors are different, they are being sensuous. I do not know if babies “prefer.” They certainly have behaviors which we would interpret as being preferring in the emotional sense, in that they feed more avidly and so on. Sweetness a little later on in life, in the so-called toddler age range, is definitely a very important determinant of food choice. Young children do like sweet foods, and since it is a learning experience, that builds on itself; once they have tasted sweet foods, they will want more.

Dr. Merchant: I would like to say a few words regarding the neural development necessary for sucking, swallowing, and chewing. The reflex of sucking and swallowing is present even before birth. But as far as chewing is concerned, this develops any time after 4 to 6 weeks. If a stimulus is not applied when this neural development is taking place—if you allow a child to go on sucking a bottle or the breast for a period of 1 year without introduction of solids or semisolids—then there is a good chance that this child will become a very poor chewer and swallower of solid foods. I feel that the introduction of weaning food is absolutely essential and that the chewing reflex must be stimulated anytime between 4 and 9 months. There is no doubt that there is a relationship between prolonged sucking and poor eating, as well as between the early introduction of solid diets and good eating habits.

Dr. Anantharaman: In view of the fact that there is already a taste acuity present at birth, and a neuroendocrine involvement in taste development, would you be in favor of inducing a stimulus to modify, in one way or another, the development of taste preference in the child, and its later development?

Dr. McNeish: The short answer is: I think the apparatus is there if you chose to use it, but I don’t know that I’m convinced yet of the need to do so. However, we have to be careful in this approach. While you can show that taste can be used to modify feeding habits, the sucking reflex is so strong in very young infants that the taste in the mouth may play a minor role in modifying early eating habits. By the end of this conference I hope that we may decide whether we should try to influence babies’ behavior very early on as to what they like and don’t like. I don’t think I am prepared to answer that question, but in practice for very young infants, it may be difficult because the actual will to suck—the reflex—is so strong it overwhelms other things.
Dr. Rey: I was very interested by the concept of "critical period" which Dr. McNeish developed. We know from our experience of long-term parenteral or enteral nutrition how difficult it sometimes is to give even a bottle to an infant who was fed artificially for 9 months or 1 year. Do we have any idea of the chronology of this critical period? Could this concept provide some useful information on the ideal time for weaning? I would like to add just one comment: We know that, in the rat, for example, there is a "weaning crisis" during which the anatomy of the gut changes; some enzymes appear and some others disappear. Do we have any information about a similar crisis for the gastrointestinal tract development in humans?

Dr. McNeish: I will take your first question first: The concept of the critical period was first introduced by Illingworth and has also been described by Dr. Merchant. I think it is just the example of individual clinical experience which taught that the end of this period appears to be around about the age of 1 year or 15 months; if the introduction is delayed beyond that period, then many will experience difficulties. You ask, Is there an early period by which time you should begin to have that experience? To be honest, I have no answer to that. Before I turn to your second question, since you mentioned children on parenteral nutrition, I wish to introduce not only the difficulties that they have in chewing and swallowing because perhaps they have missed the critical period, but also the bizarre preferences of taste that they may develop. We studied a child who had an obscure enteropathy and who was exclusively parenterally fed between the ages of 3 months and 15 months, but then we were able to gradually wean this child on to an oral diet. For a time we used oral elemental formulae, in a sense highly unnatural foods. Then, as he recovered, we began to introduce normal food; he now hates ice cream, he has never eaten a sweet thing, he drives his mother mad. He loves such things as avocados and will eat as many as you will give him. He drinks protein hydrolysate in preference to anything else. If you offer him any of the conventional foods of childhood, he spits them out. So, he has learned to eat, by conventional terms, very abnormally, and his taste preference has been totally distorted by what we did to him at the age of 15 to 18 months. He is now 4 years old, very healthy, but existing on a diet which in terms of composition and flavor would be very unacceptable to anybody else. I return to your question about the "crisis." The rat has a crisis; I don't think the human infant has a crisis except that there appears to be very early switching-on of certain digestive enzymes promoted by the first few feeds. I do not know of any later crisis determined by age. Do you, Dr. Schmitz?

Dr. Schmitz: No, I don't.

Dr. Hahn: Dr. McNeish, you mentioned in your talk something about a nasty smell. I wonder how you define nasty because, from what we have heard, that word is absolutely subjective? The other question to anyone here, particularly from India, is when does an Indian child start to like curry?

Dr. McNeish: You are quite right that the word nasty is defined by the culture in which you live. Children will tolerate smells that adults find very nasty. Why they begin to think of smells as "nasty" is presumably either as associative learning or indeed it may be instruction, "keep away from that, it is nasty."

Dr. Shanti Ghosh: It is true that we do advise mothers, when we advise them to give semisolids, not to add too many spices. It is nonetheless amazing how soon a baby gets used to the family food. He takes part of the other people's plates. One very brief comment on the traditional practices of putting sugar in the baby's mouth: Many people put sugar, most people of course prefer honey. While this is a good traditional habit that will encourage sucking, on the other hand, we have the other absolutely contradictory habit of not giving
the baby colostrum. For two days most mothers will not give any colostrum, they just give water and various other things, even cow's milk, rather than giving the breast because it is supposed to be bad. This is one of our big problems in the health and nutritional education of the mothers.

**Dr. Guesry:** You know that the modern trend, I would even say the fashion, is to remove every sweet carbohydrate from the diet of the baby for two reasons: to avoid cariogenecity and to avoid induction of obesity later on. I know that Peter Hahn, Thomas Anderson, and many others will touch again upon this problem, but I would like to have Dr. McNeish's personal point of view on the addition of sucrose to milk.

**Dr. McNeish:** It is a personal point of view. The answer can be considered in two ways: It can be a nutritional one or a behavioral one. You can say that there is no nutritional reason to add sugar to milk; milk, properly reconstituted, contains the right energy density for a baby who is being fed appropriately. So, there is no nutritional reason to increase the calorie density. With regard to the advantages, because that I think is behind your question, could there be any advantage to later eating habits of getting the baby accustomed to sweet taste? Until I met the child I have just described with the bizarre eating habits, I would have said there was no evidence that there was a critical period for introducing sweets in order to make them acceptable later on, but I would now modify that in the light of this one very instructive case. There clearly is a critical period, and there is a period by which if you have not had a certain taste experience, you will later find it very difficult. But, whether or not there is an early period by which time this should be introduced, I cannot say. So, the short answer to the question on my views regarding adding sugar to milk—I don't know of any valid reason for doing so.

**Dr. Ashfaq Ahmad:** I feel that there cannot be a cutoff point at which we can introduce a weaning diet, because the babies do differ from each other; they are individuals with their development and their own likes and dislikes. We know from our experience that if weaning is delayed for a very long time, in later life we encounter feeding difficulties. My question to Dr. McNeish is: Has anybody studied groups of children to find out what points in common they have when they are ready for introduction to a weaning diet? If you have certain common points in a group of children, then these could help mothers or doctors, indicating that a particular child is now ready for the introduction of a weaning diet.

**Dr. McNeish:** I don't know if I fully understand the question. Are you asking: Are there indications which a mother should be able to recognize or a doctor should be able to recognize as indicating now is the time to start?

**Dr. Ashfaq Ahmad:** Yes. We know that certain babies will not accept a weaning diet if you start at 4 months but he will be ready around 6 or 9 months. Other babies will be ready much ahead of that time and you can introduce a successful weaning diet at the age of 4 months. But has anybody carried out studies on this subject with a group of babies? Do you have any sort of indication that the mother could recognize?

**Dr. McNeish:** Yes. I was privileged to hear data which will shortly be published by Mike Rowland et al. working in Gambia, in which they have addressed themselves to at least one aspect of just that question. They have been following cohorts of babies and they have been looking to see whether it is growth patterns or some other aspect of feeding behavior that is triggering the mother's indication that "now is the time for weaning." They showed that it is the smallest babies who tend to be weaned first, in other words, small size seems to be a trigger to the mother that she should be doing something more for her child.

**Dr. Davies:** I would like to make a small contribution to your last comment and refer you to a study which we undertook in Leicester (U.K.) about seven years ago in which we
directed ourselves to the questions of when and why European children were introduced to non-milk foods. The study was undertaken at a time when there was some anxiety about the problem of obesity in relation to early weaning. We studied 50 newborn infants born to primigravid mothers. Ninety percent of women, when asked why they introduced a non-milk food to their children replied: because they were hungry, being less satisfied after a feed and waking more frequently. The mothers responded instinctively using their own basic common sense and introduced them to a non-milk food. When we then looked at these infants according to whether they were bottle-fed or breast-fed, we found that the average time for introducing non-milk foods to those bottle-fed infants was 3 months and to breast-fed 5 months.