Feeding the Premature Infant in the 20th Century

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ABSTRACT This article reviews the historical development of feeding the premature infant in the 20th century. It describes the early work determining the energy requirements of the preterm infant, the evolution of the use of human milk and its fortification for these infants, the development of special formulas for very-low-birth-weight infants and the various techniques/methods utilized including total parenteral nutrition. J. Nutr. 131: 426S–430S, 2001.

KEY WORDS: • premature infants • history • feeding

“In feeding the premature infant, only one food is to be considered, i.e., breast milk. Any attempt to feed these infants artificially is practically certain to meet with failure. This is so true that only success with food other than breast milk may be regarded as the result of good luck rather than good judgement” (Grulee 1912).

At the beginning of the 20th century, the care of the premature infant was in its infancy. Breast milk was the feeding of choice and the common practice was to begin the feeding of premature infants very soon after birth. This was largely a result of the work and teachings of Stephane Tarnier (1828–1897) and his even better known student Pierre Budin (1846–1907) at L’Hopital Maternite in Paris. Although obstetricians by training, they were the first clinicians to champion the care of the premature infant, or “weakling,” as they were known at the time. Key points of their care, which have come down to us through the published lectures of Budin were as follows: warming, protection from infection and nutrition (Budin 1907). In addition to advocating the use of breast milk, it was Tarnier who popularized the technique of gavage feeding in premature infants who were too weak to receive breast milk from a syringe, spoon or the breast (Berthod 1887).

Surprisingly enough, the basic energy requirements for infants were determined more or less during the late 19th century because it was relatively easy to place infants in the “closed systems” (bell jars) used to measure oxygen consumption and carbon dioxide production during this period (Nichols 1993). After Heubner determined the energy content of human milk in 1897, the energy quotient for premature infants was reported by a number of investigators between the years 1907 and 1920. The range was 95–160 kcal/(kg⋅d) (Nichols 1993). It was the practice to provide these infants with high energy intakes of 150–200 kcal/(kg⋅d) because it was the common belief that a high energy intake was not only required but that more rapid weight gain was beneficial. Gordon and Levine restudied the energy issue in the 1930s using a combination of closed (2 infants) and open circuit (9 infants) calorimetry. These premature infants ranged in birth weight from 1130 to 2220 g and were studied between 10 and 44 d after birth. The daily energy requirement was determined to be 120 kcal/(kg⋅d) [68 kcal/(kg⋅d) for catabolism, 18 kcal/(kg⋅d) lost in feces and 34 kcal/(kg⋅d) stored as energy]. Average weight gain was 16 g/(kg⋅d) (Gordon et al. 1940).

These energy requirements for growing premature infants have withstood the test of time.

It was in 1913 that Julius H. Hess (1876–1955) began the first continuously operated center for premature infants in the United States at Michael Reese Hospital in Chicago. Dr Hess, who had spent several years in Europe visiting centers caring for premature infants, also published the first book ever written dealing with the subject of the premature infant, [Hess (1922)]. Hess also advocated that human milk was the choice of feeding for the premature infant and that artificial milk preparations were a poor substitute, which resulted in an increased mortality rate. He advocated beginning feedings of breast milk in the second 12 h of life with the milk supplied by a wet nurse. During the first 3 wk of life, breast milk intake was progressively increased from 140 to 200 mL/(kg⋅d). His textbook had elaborate guidelines for “Hygiene of the Wet Nurse” and breast feeding the premature infant. He also favored gavage feeding with gravimetric flow for infants unable to nurse at the breast (Fig. 1). Even for breast-fed infants, he advocated water or a 1% lactose solution up to one sixth of the infant’s body weight, to be administered daily to “compensate for the loss of body fluids through the kidneys, bowels, lungs and skin.” If “artificial feeding” had to be used of necessity, he recommended a buttermilk and skim milk mixture with the addition of sugar (low fat, high carbohydrate) or boiled milk with the addition of water and sugar. Artificially fed infants...
were to be fed orange juice by wk 3 (2–4 mL/d) to counteract the effects of boiling. Small amounts of cod-liver oil were introduced at 4 wk and increased to 2 mL/d by 8 wk. He also recommended daily supplements of iron by wk 4. Solid foods were not instituted until mo 5, beginning with well-cooked cereal (Hess 1922).

Twenty years later in the second version of his textbook, Hess still advocated the use of breast milk for premature infants, but his guidelines now reflected the beginning of the dark period of the 20th century in the nutritional support of the premature infant (Hess and Lundeen 1941). This practice, to delay feedings for up to as long as 48 h in the smallest, sickest premature infants, originated in the United States. Budin’s earlier advice was ignored: “The path of pleasure for adults is drinking. May it not be the same for weaklings?” (Budin 1907). Hess wrote in his 1941 textbook: “It has been our experience that too early feeding may often be the cause of aspiration pneumonia and is, therefore, to be avoided. . . . Small premature babies (those weighing under 1200 g) were not fed for 24–48 h. . . . During this time the premature baby receives physiologic salt solution, subcutaneously in the thighs, one to three times daily.” He also recommended that infants <1000 g should not receive food by mouth for 24–48 h. This trend of delaying early feedings persisted as mainstream neonatal practice for 25 y. Not only was it thought that delayed feedings prevented aspiration pneumonia but also there was a growing belief that many premature infants were retaining an excessive amount of extracellular fluid so that early feeding was stressful to the infant’s kidneys (Hansen and Smith 1953). There were reports of severe weight loss (>20% of birth weight), hemocconcentration, hyperosmolality and hyperbilirubinemia in these infants during this period; because these were quickly reversed, however, when feedings were begun, clinicians obviously believed that premature infants could tolerate these initial periods of starvation without long-term adverse affects (Davies 1978, Hansen and Smith 1953). The 1958 version of Hess’s textbook had the following to say about initiating early feedings in the premature infant: “The average premature infant does better if it is not fed for at least 12 h after birth, and babies weighing <1200 g at birth are not fed for 36 to 72 h. All feedings are withheld for at least 48 h in any baby having marked generalized edema or respiratory embarrassment” (Lundeen and Kunstadter 1958). To be sure there were a few “voices in the wilderness during this period,” and in 1955 it was reported that there was a 28% lower mortality rate in premature infants who were fed between 12 and 24 h of life compared with a 41% rate when feedings were delayed until 36 h of life (Gleiss 1955).

Another major change in the 1940s resulted from the work of Gordon and co-workers (1947). These investigators reported that premature infants fed a diluted “half-skimmed cow’s milk formula” gained weight more rapidly than those fed breast milk. In this study, 122 premature infants (birth weight 1022–1996 g) were fed three different diets supplying 120 kcal/(kg·d). The three diets were human milk, evaporated cow’s milk formula and partially skimmed cow’s milk formula. The milk used in the two last-mentioned diets was diluted with water and Dextri-Maltose was added. For the 16 infants fed human milk, the average weight gain was 12.5 g/(kg·d), compared with 14.1 g/(kg·d) for the 39 infants fed evaporated milk and 15.7 g/(kg·d) for the 67 infants fed half-skimmed milk (Fig. 2). The differences between these three groups were significant. Differences were even more striking for the 49 infants with birth weights between 1000 and 1600 g. The
implications were that it was the increased protein in the cow’s milk–based feedings that promoted the increased weight gain in these infants, and this study led to the widespread use of such feedings in the premature infant. Furthermore, in 1943, Benjamin et al. (1943) compared premature infants fed human milk with infants fed a mixture of skimmed-milk and olive oil, and demonstrated that human milk, even in the presence of added vitamin D, was not the food of choice for the formation of the skeleton of premature infants unless supplemented with calcium and phosphorus. No wonder the 1958 revision of Hess’s textbook toned down the promotion of breast milk for premature infants and included an expanded section on “artificial feeding” (Lundeen and Kunstadt 1958).

It was not until the 1960s that the issues of fluid restriction and breast-milk feeding were revisited. First, after reports that delayed feedings resulted in long-term neurological developmental delays, and that early feedings prevented severe weight loss and reduced the incidence of hypoglycemia, hypermetraemia and hyperbilirubinemia, early feedings of premature infants was gradually reintroduced (Davies 1978). It was also pointed out that infants fed early did not have an increased incidence of aspiration pneumonia and that much of the edema reported in these infants previously could be attributed to tissue catabolism from starvation (Davies 1978).

Second, it was demonstrated that some of the weight gain attributed to artificial formulas for premature infants was secondary to the increased electrolyte intake and water retention with such formulas. Kagan et al. (1972) noted that both total body water and extracellular fluid volume of infants fed high protein, high solute load intakes were greater than those observed in patients receiving low solute formulas and human milk. The increase in dry weight (total weight gain minus increase in total body water) was similar with protein intakes ranging from 2 to 6 g/(kg·d). However, Babson and Bramhall (1969) reported no increase in dry weight gain when only minerals were added to a formula providing 1.5 g protein/100 mL. Their study also found that higher protein intakes from formula containing 3.5 g protein/100 mL did not lead to greater weight gains unless accompanied by higher solute intakes, although the increase in protein intake (regardless of solute load) did result in greater increase in length. They suggested that changes in length were a better indicator of nutritional adequacy of high protein/high solute load formulas.

Finally, in the 1970s, Raia and colleagues (1976) pointed out that protein quality, not quantity, played an important role in the feeding of the premature infant. In these studies, infants were randomly assigned to pooled (banked) human milk (protein content 1.0 g/dL) or one of four isoscaloric cow’s milk–based formulas differing in protein quantity (1.5 vs. 3.0 g/dL) and quality (ratio of whey proteins to casein of 60:40 or 18:82). Although the weight gain was highest in the infants receiving the high protein formula [protein intake of 4.5 g/(kg·d)], some of these infants developed azotaemia, hyperammonemia and metabolic acidosis. The intrauterine rate of weight gain was not achieved in any group. This study suggested that human milk was as adequate for low-birth-weight (LBW)3 infants as currently available formulas. Another study from the early 1980s clearly established that LBW infants fed their own mother’s milk had an improved growth rate compared with premature infants fed pooled, mature, donor milk (Gross 1983). This was largely thought to be due the higher protein content of preterm breast milk compared with milk from term mothers during the first few weeks of lactation. Although this work led to a resurgence in the use of mother’s own milk for preterm infants, even in Gross’s study, the infants did not achieve the intrauterine rate of growth.

Since the 1940s, it had been known that human milk was deficient in protein, calcium, phosphorus, sodium, iron, vitamins and trace minerals and would not satisfy the intrauterine requirements of the growing premature infant. The 1941 edition of Hess’s textbook recommended supplemental vitamins for both breast-fed and formula-fed premature infants. Heird and Anderson (1977) pointed out these deficiencies in their review on this topic, but also noted that at this time, infants fed human milk grew as well as those receiving formula, and that it remained to be demonstrated that the ideal rate of weight gain for premature infants ex utero was the in utero rate of weight gain. Despite this, in 1977, in its first statement on the nutritional needs of LBW infants, the American Academy of Pediatrics (AAP) concluded that “the optimal diet for the LBW infant may be defined as one that supports a rate of growth approximating that of the third trimester of intrauterine life, without imposing stress on the developing metabolic or excretory systems” (AAP 1977).

The 1980s saw the commercial development of special formulas3 for very-low-birth-weight (VLBW) infants (birth weight ≤1000 g). Compared with standard formulas, these contained more protein (2.2 g/dL), Na (1.5 mEq/dL), Ca (150 mg/dL), P (80 mg/dL) and vitamins per 100 mL, which more adequately met the needs of the premature infant who required smaller total volumes of feedings with higher concentrations of nutrients compared with larger premature infants. These formulas allowed for the delivery of ~3 g/(kg·d) protein and 6.5 g/(kg·d) fat with an intake of 150 mL/(kg·d). They also contained 50% of the fat as medium-chain triglycerides. Clinical studies with these formulas designed for the needs of the VLBW infant clearly showed the advantages of improved growth compared with human milk without the metabolic abnormalities reported with previous formulations (Cooper et al. 1984, Greer and McCormick 1988, Gross 1983, Schanler and Oh 1985, Tyson et al. 1983). In the 1980s and 1990s, with the development of commercially available human milk fortifiers for preterm infants, such fortification of human milk become the standard of care for the LBW infant. Even so, comparative studies continued to show that infants fed these special formulas for VLBW infants grew faster than those fed fortified human milk (Atkinson et al. 1981, Schanler and Garza 1987, Schanler et al. 1999). These human milk fortifiers contain protein, vitamins and minerals that in theory will meet the intrauterine needs for growth in these infants when added to human milk.

In the last 25 y, two other clinical issues had a great effect on the feeding of VLBW infants. The first of these is a disease of the intestinal tract, necrotizing enterocolitis. Although the term was first used in the early 1950s by Quaiser (1952), it really became a clinical problem with the remarkable overall improvements in neonatal intensive care of the 1960s and 1970s. No other single disease has a greater effect on the enteral nutrition of premature infants because it is the fear of this disease by care givers that typically governs when feedings

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3 Abbreviations used: AAP, American Academy of Pediatrics; LBW, low birth weight; TPN, total parenteral nutrition; VLBW, very-low-birth-weight.
are started, how rapidly they are advanced, what kind of feeding is used and when they are interrupted. In the 1990s it was argued that feedings of human milk, even with fortification, may decrease the incidence of this disease in LBW infants (Schanler et al. 1999).

The second issue was the high fluid intakes that were recommended for VLBW infants in the 1970s, after the long period of time in which starvation and very low fluid volumes in the first days of life were the norm. This was the result of increasing concerns about the very high insensible water loss rates in VLBW infants. They were treated in overhead warmers to maintain body temperature, often with phototherapy, and in a relatively low humidity environment. There was also the need to increase energy intake during a time in which it was difficult to give concentrated solutions of glucose parenterally. Those providing care were also concerned about the immaturity of the renal glomerulus in which the glomerular filtration rate was lower in the preterm than the term infant, and the inability of the premature kidney to concentrate urine. Others were concerned about the need to increase the renal excretion of the solute load associated with increasing nutritional intakes. All of this led to a large overestimation of the water needs of the premature infant, and it was not uncommon for the total fluid volume to exceed 200 mL/(kg·d) in the smallest infants (Roy and Sinclair 1975). These high fluid intakes compromised administration of other nutrients and were ultimately associated with an increased incidence of patent ductus arteriosus, congestive heart failure and even necrotizing enterocolitis (Bell et al. 1980, Stevenson 1977). This led to a gradual reduction in the initial fluid rates for premature infants in the 1980s to reflect more accurately true fluid needs. Environmental changes were made as well, with improvements in islettes and humidification of ventilators, which lowered insensible water losses.

Any history of the feeding of the premature infant in the 20th century would be incomplete without mentioning the advances made in total parenteral nutrition (TPN), which became available with the use of catheters for central fluid administration only in the 1960s. The technical advancement of this practice continued into the 1990s, with perfection of the technique for placing very fine central catheters (28-gauge) percutaneously through peripheral veins. Dudrick et al. (1968) were the first to maintain an infant with small bowel atresia via a hypertonic mixture of protein hydrolysate and glucose through an indwelling intravenous catheter for 44 d. The availability of intravenous lipid emulsions for use in LBW infants in the late 1970s finally permitted adequate growth in VLBW infants. They were treated in overhead warmers to maintain body temperature, often with phototherapy, and in a relatively low humidity environment. There was also the need to increase energy intake during a time in which it was difficult to give concentrated solutions of glucose parenterally. Those providing care were also concerned about the immaturity of the renal glomerulus in which the glomerular filtration rate was lower in the preterm than the term infant, and the inability of the premature kidney to concentrate urine. Others were concerned about the need to increase the renal excretion of the solute load associated with increasing nutritional intakes. All of this led to a large overestimation of the water needs of the premature infant, and it was not uncommon for the total fluid volume to exceed 200 mL/(kg·d) in the smallest infants (Roy and Sinclair 1975). These high fluid intakes compromised administration of other nutrients and were ultimately associated with an increased incidence of patent ductus arteriosus, congestive heart failure and even necrotizing enterocolitis (Bell et al. 1980, Stevenson 1977). This led to a gradual reduction in the initial fluid rates for premature infants in the 1980s to reflect more accurately true fluid needs. Environmental changes were made as well, with improvements in islettes and humidification of ventilators, which lowered insensible water losses.

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### Table 1

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
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<tbody>
<tr>
<td>1890s</td>
<td>(Tarnier and Budin): Lectures on care of the “weaking”; early feedings of breast milk advocated; popularized gavage feeding technique (Berthod 1887, Budin 1907).</td>
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<td>1913</td>
<td>(Hess): Established unit for premature infants at Michael Reese Hospital, Chicago (Hess 1922).</td>
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<td>1940–1965</td>
<td>(Hess and others): Delayed fluids/feeding for premature infants up to 96 h of age (Hess and Lundeen 1941).</td>
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<td>1960s</td>
<td>(Gordon and Levine): Respiratory metabolism studies confirm energy requirement of 120 kcal/kg/d for growing premature infants (Gordon et al. 1940).</td>
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<td>1943</td>
<td>(Benjamin): Human milk even with added Vitamin D does not support skeletal growth for premature infants (Benjamin et al. 1943).</td>
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<td>1947</td>
<td>(Gordon and Levine): Premature infants grow faster when fed “half-skimmed cow’s milk formula” compared with human milk (Gordon et al. 1947).</td>
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<td>1960s</td>
<td>(Dudrick): First total parenteral nutrition (TPN) usage in premature infants (Dudrick et al. 1968).</td>
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<td>1980s</td>
<td>(Babson): Development of special formulas (increased protein, minerals, vitamins with medium-chain triglycerides) for very-low-birth-weight (VLBW) infants.</td>
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<td>1990s</td>
<td>(Benjamin): Food for the premature infant in the 20th century. By way of conclusion, this paper will summarize the current thinking about nutrition for the premature infant at the beginning of the 21st century: &quot;Optimal nutrition is critical in the management of small preterm infants. No standard has been set for the precise nutritional needs of infants born prematurely that is comparable to the breast milk standard for term infants. Present recommendations are designed to provide nutrients to approximate the rate of growth and composition of weight gain for a normal fetus of the same postconceptional age and to maintain normal concentrations of blood and tissue nutrients. Initially after birth, the management of acute neonatal illnesses and gradual advancement of feeding to minimize the risk of feeding-related complications, such as necrotizing enterocolitis, may conflict with the nutritional goal of obtaining rapid growth in preterm infants&quot; (AAP 1998).</td>
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### Literature Cited