Much data demonstrate a striking relation between good nutrition and improved health status for children. Nevertheless, the encouragement of optimal infant nutrition continues to be a major priority for the practicing pediatrician. In the early years of pediatrics, the primary goal of nutritional support was to reduce neonatal mortality. Today, while reduction in morbidity and mortality continues to be a significant pediatric goal, the long-term objective of infant nutrition is to establish a base for optimal health into adulthood. With numerous uniquely designed formulas available to pediatricians, the array of possibilities regarding provision of neonatal nutrition is both large and confusing.

ENTERAL NUTRITION: FORMULA
What is really new and helpful in the way of formulas?

New and more nutritionally complete formulas for term newborns have been developed in recent years to supplement or substitute for human milk when the latter is not available. Further, special formulas have been designed specifically to meet the needs of hospitalized premature infants and to facilitate a closer simulation of intrauterine growth. More recently, formulas have been introduced to meet the unique nutritional needs of prematurely delivered infants after their discharge from the hospital. The needs of these older premature infants are perhaps best characterized as between those of the hospitalized premature and the healthy term infant. They often are starting their postdischarge existence with reduced nutrient reserves, but they are rapidly growing and must accrete nutrients at a more rapid rate than the normal term infant. Thus, their nutrient needs are better supported by a more nutrient-dense formula than the

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standard formula designed for full-term-newborns. In clinical trials, this formulation has been shown to result in improved linear growth and weight gain.  

How long do growing preemies need premature formula?  

The answer to this question is subjective and therefore controversial. The formula makers' literature indicates that premature formulas are intended for feeding rapidly growing, healthy, low birthweight infants below 2000 g. It has become customary in many nurseries, however, to continue small infants on premature formula until they are significantly larger than 2000 g. This is based on the increased need for certain nutrients (protein, calcium, phosphorus, sodium, etc) by rapidly growing "preemies" even into the postdischarge period. With the introduction of new formulas for postdischarge low birthweight infants, perhaps the use of premature formula beyond 2000 g will become less common in the future.  

How do I decide which formula is best for a baby?  

There are a variety of standard infant formulas available. All are acceptable for the healthy term infant who is not breast-feeding or the supplemented breast-fed infant. Although there are differences among these formulas, "the functional significance of the compositional differences among formulas is not fully understood."  

For most infants, a standard milk-based formula will be well tolerated. These resemble human milk and promote appropriate growth and biochemical tolerance. Both human milk-based and standard cow milk-based formulas contain lactose as the carbohydrate source. The predominate protein in human milk is whey and either whey or casein in standard formulas. Studies with term infants have not demonstrated an advantage of one type of protein over the other. Further, physical growth did not vary in clinical studies comparing the two types of protein, and neither offers a known biochemical advantage. In fact, the amino acid compositions of human and cow milk whey are different, which may be one reason no advantage is observed with whey versus casein predominate formulas for the term infant. Gastric emptying time has not differed between infants fed casein versus whey predominate milks in larger preterm infants. Vegetable oils are used for fat in standard formula; one also contains oleo from beef fat. These blends provide a mixture of mono and poly unsaturated and saturated fatty acids, and meet essential fatty acid requirements. However, for the premature infant, the incorporation of arachidonic and docosahexaenoic acid into formula is under investigation: these are present in human milk and may play a role in normal brain development.  

Human milk, the 'gold standard' by which formulas are measured, is an incredibly complicated substance, containing proteins not yet characterized.  

Are there any reasons to place a normal newborn on soy formula initially?  

In general, healthy term infants fed soy formulas have demonstrated good physical growth and biochemical tolerance. However, there is controversy regarding bone mineralization with soy formula. For the infant of a vegetarian family, soy formula is an acceptable choice.  

Infants born to families with a history of galactosemia should be placed on a lactose-free (soy) formula until the presence of galactose-1-phosphate uridyl transferase has been confirmed. Also, infants who have a family history of cow milk protein intolerance should be placed on soy or protein hydrolysate formula initially.  

What is the earliest age that gastrointestinal symptoms of true formula intolerance appear?  

While formula intolerance could be related to the carbohydrate, protein, or fat content of milk, by far the most common intolerance is to carbohydrate and more specifically to lactose. Moreover, the etiology of lactase deficiency leading to lactose intolerance may be either congenital or acquired (secondary). Although more than one type of congenital/hereditary lactose intolerance exists, the clinical symptoms are similar. Vomiting, diarrhea, and weight loss or failure to gain weight generally occurs, usually early in life. In fact, vomiting may follow the first milk feed, but certainly is seen no later than the second or third day of life.  

However, acquired or secondary enzyme deficiency is much more common and is associated with intestinal injury. Gastroenteritis is associated with injury to the intestinal epithelium (brush border), which secondarily reduces lactase availability, resulting in lactose malabsorption and diarrhea. This enzyme deficiency is self-limiting and corrects with minimal intervention.  

What are indications for switching formulas?  

The biochemical variations in the composition of standard cow milk-based formulas are so minimal that changing from one to another is unlikely to have a measurable effect on growth, feeding acceptance, or tolerance. However, since many feeding problems are transient, the physician may suggest changing formula for the "temporizing" effect. While emotionally satisfying for some parents, this approach often has been mis-
New and more nutritionally complete formulas for term newborns have been developed in recent years to supplement or even substitute for human milk when the latter is not available.

interpreted as indicating improved feeding tolerance by the neonate secondary to the formula switch. This scenario is not uncommon among infants (or parents) experiencing colic or other feeding concerns. A change from cow milk-based formula to a soy-based formula offers a more significant alteration, but again, data supporting a cause-and-effect relation between the switching of formulas and any change in the baby’s feeding behavior in the absence of allergy are limited.

What clinical measures should be monitored for good infant nutrition?

Patterns and rates of weight gain provide an easy and acceptable means of assessing the adequacy of nutrition. The goal is 20 to 30 g per day during early infancy, which parallels the National Center for Health Statistics charts for term infants and the charts by Casey et al for premature infants. These charts also provide reference values for head circumference and length.

Does a baby on regular formula need to take vitamins?

The answer is no. Infant formulas with iron contain all essential nutrients that the healthy infant requires for the first 6 months of life. Only those on whole cow milk are at a limited intake (volume), and perhaps those with a decreased energy requirement may need vitamin supplementation. For example, vitamins A, D, E, and C are not indexed to energy metabolism and may need to be added to the infant’s diet.

How soon should iron and vitamin therapy be initiated in growing premature babies?

When premature infants consume human milk, a human milk fortifier should be added to the milk. Fortifiers theoretically provide sufficient carbohydrate, protein, minerals, and vitamins to bring total nutrients up to the guidelines recommended for preterm infants. Iron is not in human milk fortifiers and will need to be added as iron drops at 2 to 3 mg/kg/day. Iron supplementation should be added between 2 weeks and 2 months of age. The premature infant receiving formula with iron designed for the preterm infant does not require extra supplementation. Premature formulas have enough vitamins to meet the infant’s increased needs due to decreased body stores, rapid growth, and limited (volume) intake. Vitamins in premature formulas are greater than 200% of levels in standard infant formulas. The new formula designed for the premature infant after discharge contains 50% more vitamins.

All iron-fortified formulas will provide 2 mg/kg/day of iron when fed at 120 kcal/kg/day, which makes iron supplementation unnecessary. Early use of iron-fortified premature formulas have demonstrated better ferritin levels and a decreased incidence of iron deficiency anemia.

Does iron supplementation cause constipation?

The vast majority of infants will not develop gastrointestinal symptoms from iron-fortified formulas or iron drops. Clinical studies comparing low-iron with iron-fortified formulas demonstrated no differences in fussiness, cramping, regurgitation, colic, flatus, stool number, or stool consistency. A variation in stool color was noted.

Is there any reason not to use iron-supplemented formula?

Iron-supplemented formula is inappropriate for children with hemosiderosis. This is an exceedingly uncommon disorder. Because iron needs consistently exceed intake secondary to rapid growth, there is virtually no reason not to use iron-supplemented formulas.

When can I use whole cow milk instead of breast milk or formula?

The nutritional composition of human milk is the “gold standard” for infant feeding. Accordingly, standard proprietary formula composition has been designed to be “similar” to that of human milk. However, the variation in protein and mineral composition, between human milk and whole cow milk is striking. These variations are of concern to the infant. First, whole cow milk protein occasionally generates allergy. Second, the large protein and mineral content of whole cow milk results in a significantly greater renal solute load compared with human milk. This increases the risk of dehydration.

Third, several reports have described gastrointestinal blood loss (and secondary iron deficiency) among infants and young children fed whole cow milk. For these reasons, the American Academy of Pediatrics Committee on Nutrition and others recommend the introduction of whole cow milk be delayed until 12 months of age.

What should the mother who is allergic to milk feed her baby?

This question is worriesome particularly for women who have had a previous child with milk allergy (colitis, bloody stools, or even frank shock) and who have had allergic phenomena of their own.
This mother could facilitate the safety of her infant by breast-feeding. However, if formula feeding is elected, cow milk protein substitutes are in order. A family history of milk allergy, particularly if manifested by anaphylactic reactions of any sort, should lead one to avoid milk proteins.

Cow milk protein allergy is thought to occur in infants who are not recognized clinically. Moreover, cow milk protein substitutes are readily available for allergic infants. Preparations of hydrolyzed casein are well tolerated. Soy bean preparations can substitute for cow milk protein but a significant percentage of patients will be sensitive to both soy and cow milk proteins, and these children should receive a hydrolyzed protein (casein) formula.

How much ‘spitting up’ is normal?

“Spitting up” is a manifestation of gastro-esophageal reflux. However, the lower esophageal sphincter is incompetent in most newborns, resulting in regurgitation of feedings for several days after delivery. Moreover, if the “spit up” has relatively small volume, no bile staining, and has curds, this is probably within normal limits. When the “spit up” is bile stained or large in volume (more than half of the feeding), this spitting up probably is not normal. Assessment of growth (weight gain) can help determine nutritional adequacy for these infants.

Because spitting up babies often are switched to a lactose-free soy formula, can this cause galactosemia to be missed?

Galactosemia was first described almost 100 years ago. Its incidence is approximately 1:50,000 live-born deliveries. Most galactosemic infants are normal at birth and develop signs and symptoms of dysfunction only after galactose feeding, usually in formula or human milk. Those infants who are totally or near totally unable to convert galactose-1-phosphate to glucose-1-phosphate secondary to enzyme deficiency will have significant spitting up and diarrhea. They also may have hepatosplenomegaly and cataracts. These are unlikely to be “missed” clinically unless they present with overwhelming infection. The relatively less symptomatic galactosemic infants may be missed if they are switched to galactose-free formula. These infants still would be diagnosed via the newborn screening procedure if red cell enzyme levels are measured rather than serum galactose concentrations. To make the diagnosis, one must obtain an enzyme analysis for galactose-1-phosphate-uridyil transferase, usually in the red blood cell membrane. In those states where galactosemia is not one of the inborn errors of metabolism routinely screened or where the screening process involves measuring serum galactose concentrations rather than enzyme levels, a higher index of suspicion must be maintained by the physician to avoid this oversight.

While formula intolerance could be related to the carbohydrate, protein, or fat content of milk, by far the most common intolerance is to carbohydrate and more specifically to lactose.

What are objective clinical criteria for deciding when orogastric tube feedings are indicated in premature infants?

Sucking and swallowing are intricately tied together. If these two processes are not coordinated appropriately, a baby could suck formula into his or her oropharynx, and instead of directing the formula into the esophagus, the formula could be aspirated. The esophageal response to swallowing is relatively uncoordinated in the first days of life for a full-term infant, and this is more dramatic and lasts longer for the premature infant. Effective suck and swallow coordination occurs around 32 to 34 weeks gestation. After this, sucking precedes swallowing and swallowing inhibits respiration. The inhibition of respiration during swallowing safeguards against aspiration. Prior to approximately 32 weeks gestation, most babies display uncoordinated suck and swallow reflexes. During this period, orogastric tube feedings are particularly beneficial in preventing aspiration of formula and therefore are preferable to oral feedings.

ENTERAL NUTRITION: HUMAN MILK

Is there evidence that breast milk is superior to formula?

The nutrient and anti-infective properties of human milk have been studied intensely and reported by physicians and nutrition scientists. The American Academy of Pediatrics Committee on Nutrition recommends that infants be breast-fed whenever possible. Human milk is an incredibly complicated substance, containing proteins not yet characterized. Several are growth modulators of potential importance to the developing neonate. Perhaps because of what is unknown, as much as what is known, human milk continues to be considered the ideal infant feeding.

What are contraindications to breast-feeding, especially acute, short-term maternal illness?

There are a limited number of maternal drugs and infections that contraindicate breast-feeding. Breast milk from some women with hepatitis B infection contains the hepatitis B virus and therefore could be transferred to a recipient breast-fed infant. Clinical studies of the risk of infection to the breast-feeding
Infants who have a family history of cow milk protein intolerance should be placed on soy or protein hydrolysate formula initially.

infant, however, have not been consistent. Infants delivered to hepatitis B-positive women may be safely breast-fed according to the American Academy of Pediatrics Committee on Infectious Disease after receiving hepatitis B immune globulin and human hepatitis B vaccine.40

Cytomegalovirus (CMV) also has been identified in the milk of CMV-infected women,41 leading some to conclude that maternal CMV infection contraindicates breast-feeding. However, because the milk also contains CMV protective antibodies, the breast-feeding infant has little risk of infection, and nursing is considered safe.38

Cases of group B streptococcal disease have been reported in infants breast-fed by milk containing this organism.42 Therefore, group B streptococcal mastitis may be a contraindication to breast-feeding.

The transmission of human immunodeficiency virus (HIV)-1 via breast-feeding has been reported.43 Therefore, maternal HIV-1 infection contraindicates breast-feeding.

Breast cancer in newly diagnosed women may be considered a reason not to encourage breast-feeding. This is not because of the risk of cancer transmission, but to allow maternal treatment. Immune chemotherapy does contraindicate breast-feeding.44

Finally, acute short-term maternal illnesses (ie, temperature elevation) may be considered contraindications to breast-feeding. With maternal fever, the risk to the infant most often is unknown. Nevertheless, the routine hospital approach is conservative, ie, until a source for the fever is determined (or the fever disappears), withholding breast-feeding is recommended fearing transmission of infection to the infant. Little objective data support this. Often, if the mother has an infection, her milk will contain antibodies to the source, will provide protection to the infant.45

Does a baby need vitamin and mineral supplements while breast-feeding?

It has been recommended that vitamin D, iron, and fluoride be supplemented to the breast-fed infant.43 Infant vitamin D status is dependent on exposure to sunlight and the vitamin D content of the mother's milk. Similarly, the mother's diet and her sunlight exposure determine her milk vitamin D concentration. During winter months in northern climates, vitamin D is not synthesized in the skin46 secondary to the reduced ultraviolet content of winter sunlight at northern latitudes. Both the mother and infant should have an adequate dietary source of vitamin D in these areas during portions of the year.

Rickets has been reported in some older breast-fed infants even in southern climates. These reports almost always describe infants who have had minimal exposure to the sun and whose mothers had inadequate dietary vitamin D and limited sunlight exposure.47 A vitamin D supplement of 200 to 400 IU per day for neonates is adequate to prevent rickets.48,49

Human milk has a low-iron content compared with formula, but most infants have enough iron stores at birth to avoid iron deficiency for 4 to 6 months with minimal iron supplementation.13 The controversy revolves around whether iron supplementation should be limited to infants with low iron stores or routinely provided to all breast-fed infants.50 Although human milk iron concentration is low, the iron is readily absorbed, reducing the likelihood of iron deficiency in the first 6 months of life. However, if additional foods (usually solids) are introduced into the diet prior to 6 months, iron drops or iron-fortified foods should be given since iron absorption from human milk will decrease with the introduction of supplemental foods.51

Fluoride supplementation was previously recommended to facilitate mineralization of teeth in the exclusively breast-fed infant.52 This recommendation was made because the fluoride content of human milk is low and cannot be easily elevated with maternal intake of fluoride. However, secondary to several reports of fluorosis, fluoride supplementation is no longer recommended for infants younger than 6 months.53

Vitamin D and iron supplements can be provided easily with a multiple vitamins with iron preparation. The additional vitamins in such a preparation are not actually needed, but are provided at a dose that will not cause harm.

What is the current thinking in terms of breast-feeding and necrotizing enterocolitis?

Necrotizing enterocolitis typically occurs in premature infants who have had some form of perinatal stress (hypoxia or ischemia) and enteral feeding. Therefore, feeding has been closely scrutinized.

Reports of mother's milk offering protection against the development of necrotizing enterocolitis was first presented at the Society for Pediatric Research in 1974 by Dr Jane Pitt. Discussion in subsequent years has focused on whether protection is actually provided by mother's milk and if so, by what mechanism(s).44 Certainly, human milk offers the infant protection against infectious morbidity,55 including several enteric pathogens.56 Some studies suggest human milk offers protection against necrotizing enterocolitis,57,58 so many neonatal intensive care units encourage this. The evolution in understanding if and how this occurs continues.
PARENTERAL NUTRITION
What are the guidelines for parenteral feeding in premature infants?

The nutritional support of low birthweight infants commonly involves parenteral nutrition for varying periods following birth. Further, the high frequency of respiratory disease and intestinal hypomotility in many infants limits the usefulness of enteral feeding in the first few days of life.

In planning parenteral fluid and electrolyte therapy for neonates, several physiologic events must be considered. An isotonic contraction of the extracellular fluid space appears to be a normal adaptive phenomenon in all newborns resulting in weight loss from birth in the first 3 to 4 days of life. This is regulated in part by the hormone atrial natriuretic peptide. This weight loss normally constitutes 4% to 8% in term and slightly more in premature neonates. It is frequently exacerbated by transepithelial water loss, an insensible loss of free water via skin and lungs, and must be compensated for by replacement fluid therapy. Sodium is spilled in the urine with the isotonic contraction of the extracellular fluid. Therefore, neonatal parenteral fluid and electrolyte support is designed to simultaneously allow the normal contraction of the extracellular fluid space and to prevent dehydration from transepithelial water loss.

Our guidelines for term or near-term premature infants include fluid (10% dextrose) with no electrolytes at approximately 80 mL/kg/day for the first 24 hours of life. Then sodium at 2 mEq/kg/day is added, with potassium also added (1 mEq/kg/day) at about 48 hours if the patient has good urine output and is normokalemic. If parenteral alimentation is required beyond 3 to 4 days, a more nutrient-complete fluid containing protein, fat, minerals, and vitamins in addition to glucose and electrolytes is needed. Conversely, for the infant who is expected to require parenteral nutrition for several days or weeks, protein may be added on day one of life.

How long can a term or near-term newborn remain nothing by mouth before some sort of parental nutrition is begun?

Since increased calorie needs are generated by the routine stress of birth, plus that of asphyxia, hypothermia, and respiratory distress, neonates usually should not be left nothing by mouth for periods in excess of 2 to 4 hours without an IV. Initially, no electrolytes need be added for these children, and within 24 to 48 hours with clinical improvement, enteral feeding may be initiated and parenteral nutrition reduced. This shift is done by maintaining a combined parenteral and enteral intake of approximately 150 mL/kg/day. If enteral feedings are begun within the first 24 to 48 hours and progress normally, adequate electrolyte, vitamin, mineral, protein, fat, and carbohydrate intake should occur.

REFERENCES


