DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12th Edition

Chapter e21: Pediatrics: Oral Nutrition and Rehydration of Infants and Children

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CHAPTER SUMMARY FROM THE PHARMACOTHERAPY HANDBOOK

For the Chapter in the Schwinghammer Handbook, please go to Appendix 1, Pediatric Pharmacotherapy, Nutrition, and Neonatal Critical Care.

KEY CONCEPTS

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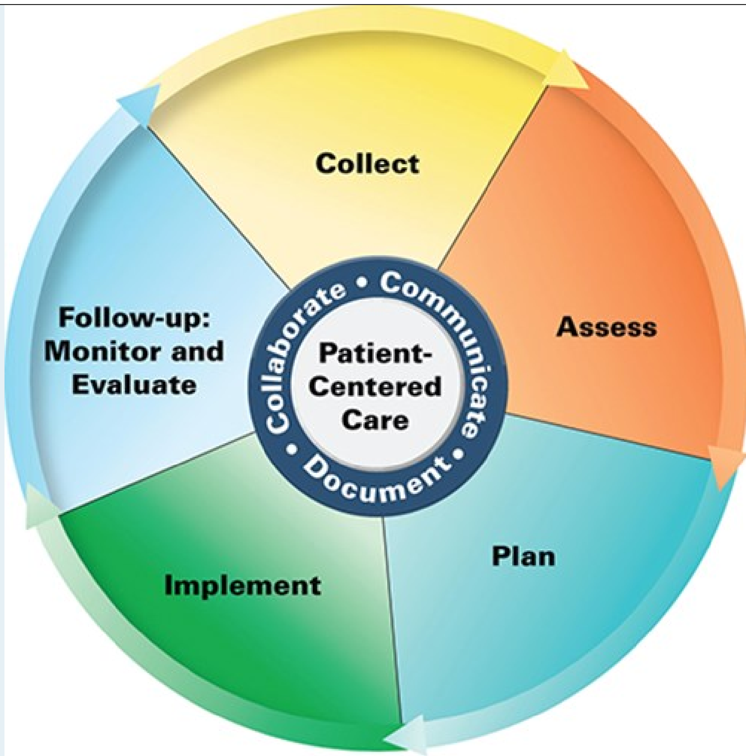
1. Human milk is the preferred source of nutrition for almost all neonates and infants, including those born prematurely.
2. A commercial infant formula is a nutritionally complete substitute if human milk is not available.
3. Cow milk-based formulas are consumed by most US non-breastfeeding infants, although there is increasing usage of other types of infant formulas.
4. When sufficient maternal or donor milk is not available, specific formulas designed for preterm low birth weight infants can be used to meet nutritional needs.
5. Some infants will require specialized formulas with altered macronutrients due to cow milk or soy protein sensitivities or conditions that lead to impaired nutrient digestion, absorption, or utilization.
6. Two nutrients, iron and vitamin D, are of particular importance in infant nutrition.
7. Human milk contains a variety of non-nutritive compounds with specific bioactive characteristics; formula manufacturers continue to modify their products to include these compounds.
8. Enteral formulas are available for children who need supplemental nutrition beyond a regular diet in most of the infant formula categories discussed and are used for similar indications.
9. Expressed human milk and infant formulas must be handled and stored properly.
10. Oral rehydration therapy (ORT) is a mainstay of treatment for mild-to-moderate dehydration; severe dehydration requires intravenous (IV) rehydration.

PATIENT CARE PROCESS

Patient Care Process* for Oral Nutrition and Rehydration of Infants and Children



Collect

- Patient characteristics (eg, age, diagnosis)
- Patient history (eg, medical, surgical, dietary)
  - Feeding history: human milk or formula (type, volume, caloric density)
- Objective data
  - Body weight
  - Length/stature, body mass index, head circumference
  - Labs, if appropriate, to assess alterations in organ function (eg, serum electrolytes, glucose, blood urea nitrogen, serum creatinine, albumin, liver function tests)
  - Intake and output (stools, vomiting, urine output)

Assess

- Nutrition status (see Chapter 164, "Assessment of Nutrition Status and Nutrition Requirements")
- Evaluate data for factors that would dictate formula selection
- Determine degree of dehydration and appropriateness of ORT

Plan*

- Choose an appropriate oral/enteral formula based on characteristics of the infant, child, or adolescent (see Chapter 166, "Enteral Nutrition")
- Recommend an alternative formula, when needed

- Develop a plan to meet an infant's iron and vitamin D needs based on current guidelines
- Make a referral to another provider (eg, physician, dietitian, lactation specialist), when appropriate
- Develop a plan for ORT for a patient with mild-to-moderate dehydration

Implement*

- Provide appropriate oral/enteral support using estimated goals (see Chapter 164, "Assessment of Nutrition Status and Nutrition Requirements")
- Provide an iron or vitamin D supplement to prevent deficiency
- Provide ORT per established guidelines
- Provide patient/caregiver education regarding the nutrition care or ORT plan

Follow-up: Monitor and Evaluate

- Appropriate growth (weight, length, head circumference)
- Gastrointestinal symptoms, tolerance to formula
- Laboratory parameters, as indicated
- Improvement in signs and symptoms of dehydration

* *Collaborate with patient, caregivers, and other healthcare professionals*

BEYOND THE BOOK

BEYOND THE BOOK

These activities are useful to enhance student understanding of the ASSESS and PLAN steps in the patient care process.

Part #1: For each case, use the manufacturer's websites provided to locate an appropriate infant formula.

Manufacturer	Website
Abbott Nutritionals	abbottnutrition.com
Gerber	medical.gerber.com
Mead Johnson Nutritionals	meadjohnson.com
Nestlé	nestlemedicalhub.com
Nutricia	nutricia-na.com

Case 1: Healthy, term baby whose mother desires to use a standard term infant formula rather than breastfeed.

List one potential option from each of these manufacturers: Abbott, Gerber, Mead Johnson

Case 2: Preterm baby born at 28 weeks gestation, being discharged home today from the NICU. Provider wishes to send the baby home on a preterm transition formula.

List one potential option from each of these manufacturers: Abbott, Mead Johnson

Case 3: A 3-month-old infant with signs and symptoms of cow milk protein allergy is being seen in clinic today. The baby's provider is looking for a hypoallergenic (free amino acid) infant formula.

List one potential option from each of these manufacturers: Abbott, Nestlé, Nutricia

Answers (examples, others may also be appropriate):

Case 1: Abbott: Similac Pro-Advance®; Mead Johnson: Enfamil® NeuroPro™ Infant®; Gerber: Gerber® Good Start® GentlePro

Case 2: Abbott: Similac® Neosure®; Mead Johnson: Enfamil® Enfacare®

Case 3: Abbott: Elecare®; Nestlé: Alfamino® Infant; Nutricia: Neocate® Synveo® Infant

Part #2: Review the patient case descriptions below and match the patient with the most appropriate formula. Each formula choice can be used only once.

Patient Case	Formula
1. Healthy term infant	A. Elecare®
2. Term baby with galactosemia	B. Human milk with HMF (human milk fortifier)
3. A 6-week-old infant with mild gastroesophageal reflux, starting non-pharmacologic therapy	C. Neocate®
4. Premature baby born at 26 weeks gestational age, now 9 weeks old, weight 2,050 g, being discharged to home	D. Ketocal® 3:1
5. A 4-week-old born with jejunal atresia, diagnosed with short bowel syndrome, beginning low volume feeds	E. Monogen®
6. A 3-year-old with gastrostomy tube needing nutrition supplementation due to growth faltering	F. Similac® Sensitive
7. Premature baby; gestational age 26 weeks, now 2 weeks old, weight 1,190 g	G. Similac® Neosure®
8. An 8-week-old baby who underwent repair of a congenital heart defect and has a chylothorax	H. Similac® Pro-Advance®
9. A 10-month-old baby with intractable seizures starting ketogenic diet	I. Gerber® Good Start® Soy
10. A 4-week-old baby with bloody stools, diagnosed with proctocolitis due to severe cow milk protein allergy	J. Nutren Junior®

Answers:

1. H; 2. I; 3. F; 4. G; 5. A; 6. J; 7. B; 8. E; 9. D; 10. C

INTRODUCTION

Nutrition in the first 1,000 days of life can play a pivotal role in infants, especially those born prematurely. Appropriate early nutrition is essential for growth and development to prevent adverse health outcomes later in life and improve cognition in adulthood. Obesity, hypertension, and diabetes mellitus may be programmed by nutrition status during this period.[1] Infancy is a period of rapid growth which is followed by continued but slower growth and development throughout childhood. Healthy term infants will double their birth weight in approximately 4 months and triple it by 12 months. Adequate nutrient intake, absorption, and utilization are vital to ensuring that growth and development progress normally. All practitioners providing health care for infants and children should be knowledgeable about appropriate pediatric nutrition to be able to quickly identify opportunities for intervention. Dietary reference intakes (DRIs)[2] established by the Food and Nutrition Board of the National Academies of Science, Engineering, and Medicine, for energy, protein, fat, trace elements, vitamins, electrolyte, and mineral requirements are discussed in Chapter 164. There are many choices for both standard and specialized formulas for infants and children. This chapter will review human milk and the various available formulas and their appropriate usage. Adolescents requiring nutrition supplementation beyond a regular diet will typically use feeding formulations appropriate for adults (see Chapter 166). Oral rehydration therapy will also be discussed in this chapter.

INFANT NUTRITION

A term newborn's stomach has a capacity of 20-90 mL. Gastric capacity increases to 90 to 180 mL by 1 month of age. Too rapidly advancing oral or enteral nutrition intake can lead to emesis, gastroesophageal reflux (GER), and other gastrointestinal (GI) symptoms. Frequent feedings (every 2-3 hours) are needed early in life due to the stomach's limited capacity and an infant's high metabolic demand (see Table e21-1). Human milk empties from the stomach at a faster rate than formula; thus, breastfed infants fed ad libitum (ad lib) may demand feeding more often than their formula-fed peers. Nutritive sucking ability develops at approximately 34 weeks gestational age; before that time, tube feedings are required. The inability to coordinate sucking, swallowing, and breathing when the respiratory rate is elevated above 60 breaths per minute also may necessitate tube feeding.

TABLE e21-1

Frequency and Volume of Feedings in Infants

Age	Daily Feedings	Volume per Feeding mL (ounces)
Birth-1 week	6-10	30- 90 (1-3)
1 week-1 month	7- 8	60-120 (2-4)
1-3 months	5-7	120-180 (3-6)
3-6 months	4-5	180-210 (6-7)
6-9 months	3-4	210-240 (7-8)
9-12 months	3	210- 240 (7-8)

Human Milk

1 Human milk is the preferred source of nutrition for almost all neonates and infants, including those born prematurely. However, human milk does not fully meet the nutritional needs of all premature infants, and fortification is often required. The American Academy of Pediatrics (AAP)[3], the World Health Organization (WHO)[4], and the Academy of Breastfeeding Medicine (ABM)[5] recommend exclusive breastfeeding (or use of human milk if tube- or

bottle-fed) for 6 months, and the use of iron-fortified formula when human milk is not available. After 6 months, complementary foods can be introduced; however, continued breastfeeding or provision of expressed human milk or iron-fortified formula is recommended until the infant is 12[3] to 24[4,5] months of age or for as long as desired.

Of infants born in 2017, 84.1% started breastfeeding at birth with 58.3% breastfeeding at 6 months, a rate only slightly higher than the 2015 rate. Despite the AAP/WHO/ABM recommendations for exclusive breastfeeding until 6 months, only 47% of infants were exclusively breastfed at 3 months, and this percentage dropped to 26% by 6 months. By 12 months of age, only 35% were still breastfeeding to some degree. While the 6-month breastfeeding rate was higher, the 12-month rate was slightly lower than for infants born in 2015.[6] The high breastfeeding initiation rate reflects an increasing desire by US mothers to breastfeed their infants, and the stronger emphasis placed on breastfeeding by US hospitals through the WHO Baby-Friendly Hospital Initiative (BFHI) which began in 1991. The BFHI assists hospitals in giving mothers the information, confidence, and skills to successfully initiate and continue breastfeeding and gives special recognition to hospitals that have implemented the program. More than 20,000 maternity facilities in 150 countries (600 facilities in the United States) have earned the Baby-Friendly Hospital designation.[7]

The health benefits of breastfeeding for both the baby and the mother are numerous (see Table e21-2). Human milk is well tolerated, promotes the development of immune function, and is associated with less diarrhea and other common pediatric infections. Protective antibodies, including SARS-CoV-2 antibodies, are transmitted to infants in human milk.[8] Human milk feeding has been associated with life-long benefits such as higher intelligent quotients (IQ) scores[9] and decreased risk of obesity[10,11] and type 1 and 2 diabetes mellitus.[12] It is less clear whether the use of human milk protects against atopic dermatitis and other allergies.[13] In addition to health and nutrition benefits, breastfeeding is less expensive, more convenient, and promotes mother-child bonding.

TABLE e21-2

Benefits of Human Milk/Breastfeeding

Benefits to Infant	Benefits to Mother	Benefits to Society
Complete nutrition[a]	Improved mother-child bonding	Improved mother-child bonding
Demonstrated growth and development benefits	Decreased postpartum bleeding	Decreased cost of supplemental formula through WIC program
Improved mother-child bonding	Decreased time to uterus involution	Decreased lost time from work due to infant illnesses
Decreased rates of upper respiratory tract infections (RSV, otitis media), GI disease (diarrhea, NEC, IBD), asthma, atopic dermatitis, obesity, type 1 and type 2 DM, hypertension, childhood leukemia, SUID	Decreased rates of postpartum depression, type 2 DM, hypertension, cardiovascular disease, rheumatoid arthritis, breast and ovarian cancer	Decreased overall healthcare costs, decreased disease burden
Higher IQ scores	Faster return to pre-pregnancy weight	
	Decreased cost	

[a]Vitamin D is required for all; iron is required in some.

DM, diabetes mellitus; GI, gastrointestinal; IBD, inflammatory bowel disease; IQ, intelligence quotient; NEC, necrotizing enterocolitis; RSV, respiratory syncytial virus; SUID, sudden unexpected infant death; WIC, Supplemental Nutrition Program for Women, Infants, and Children.

There are few disadvantages or contraindications to human milk feeding. Breastfed infants may develop unconjugated hyperbilirubinemia (*breast milk jaundice* or *suboptimal intake jaundice of the newborn*), but this rarely necessitates breastfeeding discontinuation.[14] Occasionally, a mother may have to alter dietary intake to alleviate symptoms (gas, GER) in the infant. Breastfeeding or the use of mother's milk is contraindicated in mothers receiving chemotherapy and certain other medications such as amphetamines, ergotamine, and statins; mothers who are taking phencyclidine, cocaine, or cannabis; mothers with active brucellosis; and, in infants with galactosemia who require a lactose-free diet. While caution should be used, mothers enrolled in methadone clinics or who consume less than 0.5 g/kg alcohol right after nursing can breastfeed.[15] One comprehensive resource for information related to the use of drugs in lactation and breastfeeding is LactMed (https://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm).

Human immunodeficiency virus (HIV) can be passed from mother to child via breastfeeding. In the United States, both the CDC[16] and the AAP[17] discourage mothers living with HIV from breastfeeding or using their milk for their infants, regardless of antiretroviral therapy or maternal viral load. Conversely, WHO supports breastfeeding by HIV-infected mothers in many developing countries due to health issues related to the availability of clean water and affordable infant formula.[18] These contrasting recommendations may result in confusion for mothers living with HIV in the United States who wish to breastfeed and their healthcare providers.[19] Mothers living with HIV who elect to breastfeed must be counselled on the importance of adherence to their HIV treatment regimen and potential HIV prophylaxis for their infant. Mothers with untreated tuberculosis should pump until treated for at least 2 weeks and no longer infectious. Mothers with an active herpes simplex virus (HSV) infection on the breast, varicella infection presenting within 5 days before birth or 2 days after, or H1N1 influenza or SARS-CoV-2 must be isolated from their infants, but the infant can receive their mother's expressed milk.[8,15]

Donor Human Milk

For mothers unable to breastfeed or to supply sufficient milk for their infants, donor human milk is an acceptable alternative, especially for extremely premature infants. Donor human milk is available through donor human milk banks and used in many neonatal intensive care units (ICU). The Human Milk Banking Association of North American (HMBANA; www.hmbana.org) sets policies for donor human milk (not the US Food and Drug Administration [FDA]) and accredits 31 donor milk banks in the United States (28) and Canada (3) with others in development. Each milk bank also sets its own standards that may be more stringent than the HMBANA standards.[20]

Donor human milk is pooled from multiple, unpaid, extensively screened (health screening, blood serology testing) donors, which limits the risk of transmission of viral and bacterial infections. Holder pasteurization is used to eliminate viral and bacterial pathogens from the donated human milk and also decreases the overall number of neutrophils, stem cells, and IgA (50% loss) in the milk. However, it still supplies more of these beneficial components than if the infant were to receive formula. Donor human milk may contain cow milk or soy protein if the donor's diet contained dairy or soy, thus allergy symptoms can occur. Insurance coverage for donor human milk varies from state to state; however, the coverage rate for extremely premature and other high-risk infants is good. Access to donor milk for all who could benefit from its use is limited by supply, cost, and distribution issues.[21]

Macronutrients in Human Milk

Human milk is a complex mixture that is approximately 87% water, 3.8% fat, 1% protein, and 7% lactose. Fat and lactose provide 50% and 40% of the total energy, respectively.[22] Human milk contains enough water (87%) to meet an infant's fluid needs without additional fluid intake. The first fluid secreted by the breast after delivery is an intense yellow fluid (high in carotenoids) called *colostrum*. Although secreted in small amounts, it contains secretory immunoglobulin A (IgA), lactoferrin, leucocytes, and epidermal growth factor. By 2 to 4 weeks, human milk is considered *mature* and provides approximately 18 to 22 kcal/oz (2.5-3.1 kJ/mL) depending on the fat content.[23] Typically, an average of 20 kcal/oz (2.8 kJ/mL) is used for estimating an infant's caloric intake. The composition of human milk is dynamic—changing even from feeding to feeding. Lactose is the primary sugar in human milk. Human milk also contains prebiotic oligosaccharides (30 or more) with fructooligosaccharides (FOS) and galactooligosaccharides (GOS) being most abundant. These oligosaccharides mimic bacterial antigen receptors and prevent bacterial attachment to the intestinal wall.[22]

The principal proteins in human milk are casein (homologous to bovine beta-casein) and whey. Casein curdles in the stomach, but whey remains a liquid and is easier to digest. Whey proteins are broken down rapidly to free amino acids. The whey:casein ratio varies from 70:30 to 80:20 in early lactation and is 50:50 in late lactation.[22] The main whey proteins are alpha-lactalbumin, lactoferrin, and secretory IgA, but there are many others. These proteins also have non-nutritive functions, particularly in immune function.

Fat in human milk is ~95% triglycerides but varies with maternal diet. Palmitic acid (23%) and oleic acid (36%) are the predominant fatty acids. Fat generally provides ~50% of the energy provided. The two essential fatty acids, linoleic acid (18:2n-6; arachidonic acid [ARA] precursor) and alpha-linolenic acid (18:3n-3; eicosapentanoic acid [EPA]; docosahexaenoic acid [DHA] precursor), are essential for central nervous system development. Human milk also contains the long-chain polyunsaturated fatty acids (LCPUFA), DHA (22:6n-3) and ARA (20:4n-6), which are the most abundant LCPUFA in the brain. DHA and ARA constitute 12% to 15% of the fatty acids in the cerebral cortex and brain stem gray matter. Retinal tissue also has a high concentration of DHA in both rod and cone outer segments and is essential for usual function.[24] After birth, large amounts of these LCPUFA are required for the regulation of growth, inflammatory response, and immune function and the development of vision, cognitive (learning, memory, behavior), and motor system function.[22] LCPUFA intake appears to be particularly important for the developing premature brain because large amounts accumulate in the fetus via the placenta during the last trimester.[22] The concentrations of DHA and ARA in human milk vary but intake is about 60 mg/day. In human milk, the DHA concentration depends on maternal fish intake, but ARA is independent of dietary intake.[24]

Human Milk Fortifiers

Human milk at any stage of lactation cannot fully supply the nutrient needs of premature infants, especially those born earlier than 34 weeks gestation. Human milk fortifiers (HMF) were developed to allow fortification of an aliquot of human milk to increase nutrient delivery while continuing to provide human milk to premature infants. HMF is available in both liquid and powder preparations (Table e21-3). The liquid or powder is generally mixed with human milk in a ratio of 1 packet to 25 mL to yield a concentration of 24 kcal/oz (3.4 kJ/mL) or 1 packet to 50 mL for a 22 kcal/oz (3.1 kJ/mL) concentration. In addition to increasing energy delivery, these products also increase the delivery of protein, calcium, phosphorus, zinc, and other nutrients. Although some high-risk infants may still require HMF at discharge, most infants are not discharged on HMF due to cost and availability. HMF can be obtained for infants that meet qualifications through the US Special Supplemental Nutrition Program for Women, Infants, and Children (WIC). Human milk may also be fortified with a premature infant formula, a post-discharge premature infant formula, or a standard or specialty term infant formula depending on the infant's age, needs, and GI health. If a post-discharge premature infant formula is used for fortification, 1 teaspoonful powder is added to 90 mL of human milk to yield a concentration of 24 kcal/oz (3.4 kJ/mL). While quite common, this practice has been labeled *The Sprinkles Dilemma* because it results in uneven enrichment of nutrients and may not meet optimal nutrition intakes.[25] Table e21-4 provides examples of methods used to fortify human milk.

TABLE e21-3

Composition of Human Milk Fortifiers[a] (Selected Nutrients)

Nutrient	Similac® Human Milk Fortifier Powder[b,c]	Enfamil® Human Milk Fortifier[b]	Similac® Human Milk Fortifier Concentrated Liquid[b,c]	Enfamil® Human Milk Fortifier Acidified Liquid[b]	Similac® Human Milk Fortifier Hydrolyzed Protein Concentrated Liquid	Enfamil® Liquid Human Milk Fortifier High Protein[b]	Enfamil® Liquid Human Milk Fortifier Standard Protein
	per 0.9 g	per 0.71 g	per 5 mL	per 5 mL	per 5 mL	per 5 mL	per 5 mL
Calories, kcal (kJ)	3.5 (15)	3.5 (15)	7 (29)	7.5 (31)	7 (29)	7.5 (31)	7.5 (31)
Carbohydrate, g	0.45	< 0.1	0.81	< 0.3	0.75	0.11	0.28
Protein, g	0.25	0.275	0.35	0.55	0.5	0.56	0.42
Fat, g	0.09	0.25	0.27	0.575	0.21	0.58	0.58
Linoleic acid, mg	-	35	1	57.5	18	58	58
Sodium, mg	4	4	5	6.75	5	6.8	6.8
Potassium, mg	16	7.25	21	11.25	21	11.3	11.3
Calcium, mg	29	22.5	35	29	30	29	29
Phosphorus, mg	16	12.5	20	15.75	17	15.8	15.8
Magnesium, mg	1.7	0.25	2.2	0.46	2.1	0.46	0.46
Selenium, mcg	0.1	-	0.2	-	0.2	--	--
Iron, mg	0.08	0.36	0.11	0.44	0.11	0.44	0.44

Zinc, mg	0.25	0.18	0.3	0.24	0.31	0.24	0.24
Vitamin A, IU	155	237.5	197	290	197	290	290
Vitamin C, mg	6.3	3	7.7	3.8	7.7	3.8	3.8
Vitamin D, IU	30	37.5	35	47	35	47	47
Vitamin E, IU	0.8	1.15	1	1.4	1.0	1.4	1.4
Vitamin K, mcg	2.1	1.1	2.4	1.425	2.4	1.42	1.42

[a]Typical usage: mix 1 packet (powder) or 5 mL (liquid) in 25 mL.

[b]Also contains thiamin, riboflavin, pyridoxine, cyanocobalamin, niacin, folic acid, pantothenic acid, biotin, manganese, and copper.

[c]Also contains iodine, choline, inositol.

Data from Abbott Nutrition, www.abbottnutrition.com; Mead Johnson, www.meadjohnson.com

TABLE e21-4

Human Milk Fortification Options

	Protein (g/kg/day)	Calcium (mg/kg/day)	Phosphorus (mg/kg/day)
Recommended intake for premature infants	2.5-3.1	70-140	35-90
Nutrient intake at 120 kcal/kg/day (500 kJ/kg/day)			
HM alternating with PDF	2.5	85	50
HM alternating with HM + HMF powder[a]	~2.3	~129	~74
HM alternating with preterm 24 kcal/oz formula	2.7	136	76
HM + HMF powder[a]	~2.8	~205	~118

[a]Mixed to a 24 kcal/oz (3.4 kJ/mL) concentration.

HM: human milk; HMF: human milk fortifier; PDF: post-discharge formula 22 kcal/oz (3.1 kJ/mL)

Data from Abbotnutrition.com/tools-for-patient-care/nutrition-in-nicu

INFANT FORMULAS

2 A commercial infant formula is a nutritionally complete substitute when human milk is not available. Infant formula composition is mandated by an amendment to the Federal Food, Drug, and Cosmetic Act, the Infant Formula Act of 1980 (amended 1986). These standards and other information can

be found on the FDA website.[26] Regulations specify a minimum allowable amount of 29 ingredients and a maximum amount for nine ingredients, and manufacturers are required to test their products and report periodically to the FDA. Formulas exempted from these standards are labeled for use in infants with inborn errors of metabolism, low birth weight, or unusual medical or dietary problems, require a prescription for use, and cannot be sold retail.[26] Store-brand formulas are often more affordable, and caregivers can be assured that they will provide complete infant nutrition. Formulas that have been imported from outside the United States or purchased via the internet may not meet these FDA regulations and may cause harm.

The first commercial infant formula was introduced in the United States in 1919. In 2021, the $2.1 billion US infant formula market represented a decrease of 2.6% in annualized market size growth from 2016 to 2021.[27] The global infant formula market in 2018 was $24 billion with estimates of $45 billion by 2025.[28] Infant formulas are marketed in several forms: ready-to-feed, powder for reconstitution, and concentrated liquids that need to be diluted with water. The major infant formula manufacturers (Table e21-5) continuously modify their products to mimic human milk composition more closely and to improve nutrient delivery to infants with a variety of medical conditions. The manufacturer's website will likely have the most up-to-date information on a product. Formula choice depends on many factors including age, GI function, previous tolerance or intolerance to ingredients, nutritional requirements, and the presence of various diseases or conditions.

TABLE e21-5

Formula Manufacturers' Websites

Manufacturer	Website
Abbott Nutritionals	abbottnutrition.com
Ajinomoto Cambrooke Inc.	ajihealthandnutrition.com
functional formularies	functionalformularies.com
Gerber	medical.gerber.com
Kate Farms	KateFarms.com
Mead Johnson Nutritionals	meadjohnson.com
Nestlé	nestlemedicalhub.com
Nutricia	nutricia-na.com
Perrigo[a]	perrigopediatrics.com

[a]Manufacturer of all store brands such as Walmart, Target, Kroger, Amazon, Sam's Club, Costco, CVS/pharmacy, BJs, Walgreens.

WIC Program

Parents who cannot afford to purchase enough formula may either inappropriately dilute the formula or limit the infant's intake to make the formula last longer. These practices can lead to electrolyte abnormalities (hyponatremia) and growth faltering. The federally funded WIC program began in 1974 serving about 88,000 infants with a budget of $10.4M. The WIC program is now the single largest purchaser of infant formula in the United States and serves more than 50% of all infants. In 2020, the WIC program served ~6.2 million participants (1.7M infants, 3.5M children, and 1.6M pregnant/lactating women) with a total budget of $4.9 billion.[29] State agencies are required by law to have competitively bid WIC formula rebate contracts with manufacturers. States agree to provide one brand of formula in return for substantial discounts (rebates); thus, the WIC provided brand varies from state to state. In 2017, these rebate-generated savings ($1.74 billion) allowed WIC agencies to serve an additional 1.55 million participants each month (21.25% of the estimated average monthly caseload).[30] Many infants and children eligible for WIC cannot participate due to insufficient WIC resources. Other factors, such as parental/caregiver education, may also limit participation in the WIC program.

Macronutrients in Infant Formulas

Infant formulas generally provide 20 to 24 kcal/oz (2.8-3.4 kJ/mL)(term) or 20 to 30 kcal/oz (2.8-4.2 kJ/mL)(preterm) and differ primarily in their macronutrient (carbohydrate, protein, fat) composition. These composition differences are the primary basis for selecting a product for a given infant. Table e21-6 provides a classification for available infant formulas with examples of each type.

TABLE e21-6

Formulas for Term or Near-Term Infants[a] (Examples, Not a Complete List)

Formula Type	Indications	Products	Comments
Cow milk-based	Normal functioning GI tract; no food allergies	Enfamil® Enspire™, Enfamil® NeuroPro™ Infant, Enfamil® PREMIUM™ A2, Enfamil® Reguline®, Enfamil® Infant, Enfamil® 24, Similac® Advance®, Similac® Advance® 20, Similac Pro-Advance® 20, Similac® for Supplementation (non-GMO),[b] Pure Bliss™ by Similac® (non-GMO),[b] Gerber® Good Start® A2, Nestle NAN 1 Pro, *Store Brand* Infant, *Store Brand* Advantage®, Kirkland Signature™ Procare®	Most commonly used; DHA and ARA added
Cow milk-based, organic	Normal functioning GI tract; no food allergies; caregiver prefers organic	Earth's Best Organic, Similac® Organic, Similac® Organic with A2 Milk, Baby's Only LactoRelief, Baby's Only Organic DHA&ARA, Plum Organics Organic, Gerber® Natura Stage 1 Organic	
Cow milk-based, kosher	Kosher diet preferred	Similac® Advance® Lamehadrin Infant Formula	BADATZ-certified
Partially hydrolyzed cow milk-based	Normal functioning GI tract; colic	Gerber® Good Start® GentlePro, Gerber® Good Start® SoothePro, Similac Pro-Total Comfort® 20, Similac Total Comfort® 20, Enfamil NeuroPro™ Gentlease®, Enfamil Gentlease®, Enfamil Enspire™ Gentlease®, *Store Brand* Tender®, *Store Brand* Gentle®, *Store Brand* Complete® Comfort	Whey protein; possibly easier to digest
Lactose-free	Normal functioning GI tract; symptoms of lactose sensitivity; galactosemia	Similac Pro-Sensitive® 20, Similac Sensitive® 20, Similac Pro-Total Comfort® 20, Similac Total Comfort® 20, *Store Brand* Sensitivity®	~0.1 g lactose per 100 kcal
Lactose-reduced	Normal functioning GI tract; symptoms of lactose intolerance	Enfamil NeuroPro™ Gentlease®, Enfamil Gentlease®, Enfamil Enspire™ Gentlease®, Enfamil NeuroPro™ Sensitive, *Store Brand* Complete® Comfort, Similac® For Spit-up, Similac® For Spit-up (non-GMO)[b]	
Cow-milk based, added rice starch	Gastroesophageal reflux; feeding intolerance	Enfamil A.R.™, Similac® For Spit-up, Similac® For Spit-up (non-GMO),[b] *Store Brand* Added Rice Starch	Requires gastric acid to thicken in the

			stomach
Soy protein-based	Lactose intolerance; galactosemia; vegetarian	Enfamil® ProSobee®, Gerber® Good Start® Soy, Similac® Soy Isomil® 20, *Store Brand* Soy	
Extensively hydrolyzed protein (semi-elemental; hypoallergenic)	Lactose intolerance; cow milk or soy protein allergy; malabsorption; short bowel syndrome	Nutramigen® (Liquids), Gerber® Good Start® Extensive HA®, Similac® Alimentum®, Pregestimil®, Nutramigen® with Enflora™ LGG®, *Store Brand* Hypoallergenic	Lactose-free; some fat as MCT
Amino acid-based (elemental; hypoallergenic)	Cow milk or soy protein allergy; severe food allergies; short bowel syndrome; malabsorption	Alfamino® Infant, Elecare® Infant, Neocate®, Neocate® Infant, PurAmino™	Lactose-free; some fat as MCT

ARA, arachidonic acid; DHA, docosahexaenoic acid; GI, gastrointestinal; GMO, genetically modified; MCT, medium chain triglycerides.

[a]May contain prebiotics, probiotics, or other non-nutrient additives.

[b]Made from fresh milk from grass-fed cows.

Data from Abbott Nutrition, Abbott Laboratories, Columbus, OH; Mead Johnson Nutrition, Glenview, IL; Nestlé SA, Vevey, Switzerland; Nutricia Advanced Medical Nutrition, Schiphol, the Netherlands; Perrigo, Allegan, MI.

Carbohydrates

There are several classes of dietary carbohydrates, including starch (glucose polymers) and disaccharides (sucrose, lactose), but only monosaccharides (glucose, fructose, galactose) can be absorbed. Digestion to monosaccharides depends on the intestinal brush border enzymes: sucrase, isomaltase, glucoamylase, and lactase. These enzymes are produced in response to a meal that contains carbohydrates, then degraded, so they must be resynthesized by the enterocytes before the next meal. All enzymes except lactase are synthesized in excess of the amount needed. Monosaccharides are transported across the enterocyte membrane. Glucose and galactose uptake is sodium-dependent, and fructose is absorbed via facilitated diffusion. Enzyme production and transport protein synthesis can be affected by genetic mutations resulting in carbohydrate maldigestion and malabsorption (eg, galactosemia, glycogen storage diseases).[31]

Carbohydrate sources in infant formulas vary and include lactose; corn syrup solids (glucose); maltodextrin; sucrose; and corn, tapioca, and potato starch. Cow milk-based formulas contain primarily lactose; corn syrup solids (glucose) may be added if the lactose has been removed or reduced. Formulas intended for infants with carbohydrate malabsorption or maldigestion contain maltodextrin; corn syrup solids (glucose); or modified corn, tapioca, or potato starch. Added sugars in infant formulas compared to human milk have been implicated in rapid weight gain and too rapid upward weight-for-age percentile crossing.[32]

Protein

Protein must be digested into small peptides or amino acids to be absorbed. Protein absorption begins with acid and pepsin in the stomach, then endo- and exopeptidases from the pancreas hydrolyze the protein in the duodenum and jejunum. There are many amino acid transporters in the enterocytes, and mutations can occur that alter their function. Peptides are absorbed through a sodium-dependent process by peptide transporter 1, which is also involved in drug absorption. There is significant transporter redundancy; some transporters have narrow substrate specificity for amino acids, while others have broader or overlapping substrate specificity for di- and tripeptides. A defect in one transporter usually does not result in the inability to absorb a specific amino acid or peptide.[33]

Protein sources in infant formulas include cow milk protein (casein and whey), soy protein, and casein and whey hydrolyzed to peptides and amino acids. Specialty infant formulas may contain hydrolyzed proteins that vary in the degree of hydrolysis from partial hydrolysis (peptide-based) to extensive hydrolysis (amino acid-based). Cow milk contains more than 30 proteins, but it is predominantly casein (82% casein), including α-casein, ß-casein, and κ-casein. Whey proteins include bovine immunoglobulin, lactoferrin, serum albumin, α-lactalbumin, and ß-lactoglobulin. Some cow milk-based formulas are altered to contain predominantly whey protein or are supplemented with whey to improve protein digestion. ß-lactoglobulin, α-lactalbumin, and casein are responsible for most cow milk allergies.[34]

Fat

Fat is an important calorie source for infants. Skimmed, nonfat cow milk is used to manufacture many infant formulas; thus, the fatty acids found in infant formulas are provided by the addition of coconut, corn, soy, sunflower, or safflower oil. Palm olein oil is no longer added as it decreases calcium absorption. The LCPUFA, ARA, and DHA, found in human milk are added to most infant formulas to mimic human milk. Infant formulas not supplemented with DHA and ARA provide minimal amounts. Addition of ARA and DHA (synthesized in a bioreactor) is supported by most nutrition experts, but addition to infant formulas is not mandated by regulatory authorities.[26] Most major baby formula companies have DHA- and ARA-supplemented versions of all their formulas. Although theoretically important, no cognitive benefit, as measured by academic performance, has been demonstrated with the addition of DHA and ARA.[35]

Medium chain triglycerides (MCT) are absorbed by simple diffusion which bypasses the need for lipase, bile (micelle formation), and transport via the lymphatic system. Additionally, unlike fatty acids, MCT transport into the mitochondria is carnitine independent. Infant formulas contain 0% to 87% of the fat as MCT depending on the intended patient population. An increased MCT supply is particularly important in patients with disturbances of fat digestion and absorption such as those with inadequate bile secretion, celiac disease, short bowel syndrome, inflammatory bowel disease, disturbed lymph flow, cystic fibrosis, some metabolic diseases, as well as in prematurely born neonates who have some degree of fat malabsorption. Because MCT are not a source of essential fatty acids, infants receiving a formula with high MCT content are at risk of developing essential fatty acid deficiency (EFAD).[36]

Formulas for Normal Healthy Infants

Term (or Near-Term) Infant Formulas

Many formulas are available for term infants (Table e21-6), and new or modified formulas are marketed each year as manufacturers continually strive to make their formulas as close to human milk as possible. The initial formula choice for a healthy term or near-term infant is generally made by the hospital, parent/caregiver, or WIC. The choice is based primarily on cost but may be based on other considerations. Caregivers often change their infant's formula without consulting a healthcare provider when there are concerns such as straining with stooling, constipation, excessive gas, frequent spitting up or vomiting, or colic. Parents should be educated that bloody stools and persistent or bilious vomiting may be signs of serious conditions, and medical attention should be sought rather than just changing the formula. Cow milk protein allergy occurs in 2% to 7.5% of infants and can present as wheezing, skin rash, diarrhea, or bloody stools; symptoms which require medical attention.[37]

Standard Cow Milk-Based Formulas

3 Cow milk-based formulas are consumed by most US non-breastfeeding infants; although there is increasing usage of other types of infant formulas. Neither whole, reduced fat, or skim cow or goat milk is suitable for infant nutrition without modification. Standard, cow milk-based formulas contain primarily lactose; modified cow milk protein (80% casein, 20% whey); vegetable oils (no MCT); DHA and ARA; and vitamins, minerals, and other nutrients to meet the needs of most infants. Lactose is added to improve the carbohydrate-to-protein ratio, and the butter fat in cow milk is replaced with vegetable oils to improve absorption. If ready-to-feed or mixed to the standard concentration, they generally provide 20 kcal/oz (2.8 kJ/mL). Prebiotics, probiotics, lutein, and other substances may be added separately or in proprietary blends to better mimic human milk depending on the product. There are many formulas with modifications for altered needs in this category (Table e21-6).

Partially Hydrolyzed Whey, Cow Milk-Based Formulas

Some formulas are cow milk-based but contain 100% enzymatically hydrolyzed whey protein, which more closely mimics human milk (~82% whey) (Table e21-6). Hydrolysis makes the protein less antigenic than non-hydrolyzed cow milk; however, they are not recommended for infants with cow milk protein allergy. These products are marketed as being more like human milk and easier to digest. They are nutritionally interchangeable with other standard, term infant formulas. They may be useful in infants with excessive gas or colic on another term infant formula. They have a more pleasant smell and appearance than other cow milk-based formulas.

Lactose-Free or Lactose-Reduced Cow Milk-Based Formulas

Lactose has prebiotic effects, softens stools, and enhances water, sodium, and calcium absorption, but it is not essential. While primary (congenital) lactase deficiency is rare, lactose concentrations begin to decrease after 3 years of age, and some children will show signs of lactose intolerance as young as 3 to 5 years of age. By adulthood, a large percentage of adults have lactose intolerance. Secondary disaccharidase deficiency, including lactase, can occur after a severe diarrheal illness, moderate-to-severe enterocolitis as seen in patients with *Clostridioides difficile* or Hirschsprung's disease, and other viral or bacterial GI infections or inflammation. Lactase is generally the first enzyme affected and the last to recover. Because bacteria in the colon ferment sugars to carbon dioxide and short chain fatty acids, lactose intolerance can lead to watery, explosive, painful (acidic) stools; vomiting; abdominal distention; and crampy abdominal pain.[15]

The term, *lactose-free*, applies to many formulas intended for use in infants and children because many extensively hydrolyzed and all soy formulas are lactose-free (Table e21-6). Cow milk-based formulas can be made lactose-free or lactose-reduced (20%-30% of standard cow milk-based formulas) by enzymatic hydrolysis. These formulas have corn syrup solids and/or sucrose rather than lactose and are intended for use in infants with intolerance to cow milk-based formulas when the symptoms are concerning for lactose intolerance.

Only formulas that are 100% lactose-free can be used in infants with galactosemia, an autosomal recessive inborn error of metabolism in which galactose cannot be properly metabolized due to a deficiency of galactose-1-phosphate uridyltransferase (GALT), leading to galactose accumulation in the blood.[31] These infants present within a few days of life with jaundice, poor feeding, and vomiting. Galactosemia is detected via a standard newborn screen, but the symptoms may develop before the results are available.

Pre-Thickened (Added Rice Starch) Formulas

Formulas with added rice starch (Table e21-6) were designed specifically for infants with GER which affects 20% to 40% of all infants to some degree. For years, infant formula has been thickened with cornstarch or rice cereal to attempt to keep it in the stomach after ingestion. Problems with adding rice cereal to a formula include inconvenience, difficulty in sucking the thickened formula from the bottle requiring making the bottle's nipple hole larger, increased coughing during feedings, excessive energy intake (each tablespoon rice cereal provides as many as 60 calories [250 J] from carbohydrate alone), delayed gastric emptying and concerns for arsenic exposure. Rice readily absorbs arsenic from the environment, about 10 times more of it than other grains. Arsenic has been found in all brands of infant rice cereal tested, and lower concentrations have been noted in all brands of non-rice and multigrain cereals.[15,38]

Formulas with added rich starch contain 30% rice starch. These formulas are much less viscous in the bottle than formula thickened with rice cereal (viscosity is about 30 times that of non-thickened formula). The formula thickens substantially (about 100-fold) when exposed to the acidic pH in the stomach. Thickening and efficacy depend on having an acidic gastric pH: viscosity increases greatly at a pH less than or equal to 5.5. The use of an acid suppressing agent may decrease the efficacy of these products; thus, they are intended for use prior to the pharmacologic GER therapy. Decreased regurgitation has been documented with these formulas; of note, only 4% were receiving concomitant acid suppression.[39] Pre-thickened formulas are probably no more effective for GER than standard term formulas thickened with corn starch or rice cereal, but they offer the important advantage of convenience and more balanced nutrition. Additionally, pre-thickened formulas flow freely through standard nipples decreasing the work required to suck the formula from the bottle. Thickened feeds (added rice formulas or adding rice cereal to a formula) are not recommended for premature infants born before 37 weeks gestation who have been discharged from the hospital in the past 30 days due to concern for necrotizing enterocolitis (NEC).[23,39]

Organic Formulas

The number of infant formulas labeled as *organic* continues to increase (Table e21-6), and their global market share continues to rise. The global organic infant formula market is expected to reach $7.7 billion (USD) by 2023.[40] The Organic Foods Production Act of 1990 mandates that the US Department of Agriculture (USDA) govern the standards for organic products. Any product labeled *certified organic* must contain at least 95% organically produced or processed agricultural products. These products are certified free of chemicals and may be preferred by caregivers. Cost and inclusion of genetically modified (GMO) ingredients may limit their use.

Follow-up Formulas

Nutrient needs change as infants age and formula is no longer the sole source of nutrition. Most cow milk- and soy-based infant formulas are available in formulations modified for use by older infants and toddlers (usually 9-24 months of age). These are referred to as *follow-up, follow-on,* or *toddler* formulas (Table e21-7). Toddler formulas generally provide similar calories but more calcium and phosphorus (190%-300%) and iron (11%-33%) than term formulas. Some formulas also have increased protein and certain vitamins. These products provide no advantages over continuing a standard formula until 12 months of age followed by transitioning to whole cow milk; thus, the choice to use one of these formulas is based solely on caregiver preference and cost.[41] Despite no clearly defined role for these *toddler* formulas, they continue to have good global sales due to extensive marketing.[42]

TABLE e21-7

Follow-on, Follow-up Formulas for Toddlers

Formula	Formula	Formula
Enfamil Brand Formulas (MJ)	*Similac Brand Formulas* (A)	*Gerber Brand Formulas*
Enfagrow® PREMIUM™ Toddler Vanilla Flavor Nutritional Drink	Go & Grow by Similac® Toddler Drink	Gerber® Good Start® GentlePro 2
Enfagrow PREMIUM™ Toddler Natural Milk Flavor Nutritional Drink	Go & Grow by Similac® Sensitive® Toddler Drink	Gerber® Good Start® Soy 2
Enfagrow Neuropro™ Toddler Vanilla Flavor Nutritional Drink	Go & Grow by Similac® Milk-based Toddler Drink	Gerber® Good Start® A2 Toddler
Enfagrow Neuropro™ Toddler Natural Milk Flavor Nutritional Drink	Pure Bliss™ Toddler Drink by Similac®	Gerber® Good Start®
Enfagrow® PREMIUM™ Toddler Transitions®	Similac® Organic Toddler Drink with A2 Milk	Nestlé NAN® PRO Toddler
Enfagrow® Toddler Transitions® Gentlease®	Similac® Lamehadrin Toddler Drink	

Data from Abbott Nutrition, Abbott Laboratories, Columbus, OH; Mead Johnson Nutrition, Glenview, IL; Nestlé SA, Vevey, Switzerland.

Specialty Infant Formulas

Formulas for Preterm Infants

4 When sufficient maternal or donor milk is not available, specific formulas designed for preterm low birth weight infants can be used to meet their unique nutritional needs. Formulas marketed for premature infants (Table e21-8) supply nutrients needed to promote growth and body composition changes that mimic that of a normal fetus through gestation. Lactase activity rises relatively late in fetal life; thus, premature infants have reduced lactose digestion compared to term infants. Formulas intended for premature infants have a higher caloric density, less lactose, more MCT (40%), and more protein with a higher percentage of whey (whey:casein 60:40), and more sodium, potassium, phosphorus, calcium, vitamins A and D, zinc, and folic acid than term formulas. The use of these formulas in premature infants improves growth (weight, length, and head circumference), bone mineralization (near intrauterine accretion rates), and biochemical indices of nutrition status compared to unfortified human milk or term infant formulas.[43]

TABLE e21-8

Formulas for Premature Infants

Formula	Energy kcal/dL (kcal/oz)	Protein g/dL	Fat g/dL	Vitamin D IU/mL	Calcium mg/dL	Phosphorus mg/dL	Iron mg/dL
Mature human milk	65-70 (19.5 - 21)	1.03	3.5	Variable (based on mother’s intake)	20 - 25	12 - 14	0.3 - 0.9
Premature Infant Formulas							
Similac® Special Care® 20	67.6 (20)	2.03	3.67	101.4	121.7	67.6	1.22
Similac® Special Care® 24	81.2 (24)	2.43	4.41	101.4	146.1	81.2	1.46
Similac® Special Care® 24 High Protein	81.2 (24)	2.68	4.41	121.7	146.1	81.2	1.46
Similac® Special Care® 30	101.4 (30)	3.04	6.71	182.6	152.2	101.4	1.83
Enfamil® Premature 20 Cal/fl oz	67.6 (20)	2.2	3.4	200	112	61	1.22
Enfamil® Premature 24 Cal/fl oz	81.2 (24)	2.7	4.1	240	134	73	1.46
Enfamil® Premature 24 Cal/fl oz HP	81.2 (24)	2.9	4.1	240	134	73	1.46
Enfamil® Premature 30 Cal/fl oz	101.4 (30)	3.3	5.1	300	167	91	1.83
Post-discharge Formulas							
Similac® Neosure®	74 (22)	2.1	4.1 (MCT 25%)	52	78	46	1.3
Enfamil® EnfaCare®/Enfamil NeuroPro™ EnfaCare®	74 (22)	2.1	4 (MCT 20%)	53	90	50	1.3
Protein Supplements							
Liquid Protein Fortifier per 6 mL (Abbott)	4	1					

MCT, medium chain triglycerides. For unit conversion purposes multiply values in kcal/oz by 0.1415 to give kJ/mL; values in mg/dL by 10 to give mg/L; and values in g/dL by 10 to give g/L.

Data from Abbott Nutrition, Abbott Laboratories, Columbus, OH; Mead Johnson Nutrition, Glenview, IL.

Formulas for preterm infants are generally available in ready-to-use bottles primarily for in-hospital use; however, these formulas may be used after discharge in selected high-risk infants. Most state WIC programs will supply these formulas for infants that meet specific criteria for their use. A preterm infant will receive one of these formulas until reaching a weight of at least 1,800 g to 2,000 g (~4-4.4 lb). Infants with bronchopulmonary dysplasia, cardiac anomalies, or other conditions that increase nutrition needs may benefit from continuing these formulas longer. Although the standard caloric density of these products is 24 kcal/oz (3.4 kJ/mL), they are available as 20 kcal/oz (2.8 kJ/mL), 24 kcal/oz (3.4 kJ/mL) with high protein, and 30 kcal/oz (4.2 kJ/mL). The higher concentration formulas can be fed directly or mixed with lower concentration formulas or human milk to increase caloric density and avoid the use of powdered supplements.

Post-Discharge Premature Infant Formulas

Few studies have evaluated the nutrition needs of premature babies after discharge. Many infants (as many as 79% in some series) leave the neonatal ICU having experienced poor growth with a weight-for-age less than the 10th percentile at 36 weeks postconceptional age.[44] It is generally assumed that with the need for continued catch-up growth in these infants, their nutrition requirements are higher than their term peers. Post-discharge preterm infant formulas were developed to span the gap between term and preterm formulas. The European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) advocates the use of these post-discharge formulas for preterm infants not receiving human milk who have not gained adequate weight at discharge until 40 to 52 weeks post-conceptional age, especially those who would not tolerate the larger volume of feedings needed with a 20 kcal/oz (2.8 kJ/mL) formula.[45] The standard caloric concentration of these formulas is 22 kcal/oz (3.1 kJ/mL), and they provide higher amounts of protein, calcium, phosphorus, and vitamins than term formulas (Table e21-8). Typically, if one of these formulas is used, additional vitamin and iron supplementation is not required. If a term infant formula or unfortified human milk is used for post-discharge feeding, additional vitamin and mineral supplementation may be required. Infants are generally transitioned to these formulas at a weight of 1,800 to 2,000 g or 34 weeks postconceptional age. A common practice is to continue a post-discharge formula until between 9 and 12 months corrected gestational age, but careful attention to growth velocity is important to avoid excessive *catch-up* weight gain.

Two meta-analyses that evaluated the use of post-discharge formulas compared to standard term formulas in preterm infants after discharge did not show a significant difference in growth outcomes, but the trials evaluated were heterogeneous.[46,47] The use of these formulas has been associated with lower fat mass, corrected for body size, at 6 months corrected age when compared to term formula or human milk.[48] This difference in central adiposity may have implications for obesity in later life. Growth during late infancy and childhood is a major determinant of later health.[49]

Soy Protein-Based Formulas

Soy-based formulas have been available in the United States since the 1920s. Despite their long-term availability, there are few true indications for soy-based infant formulas. However, approximately 12% to 20% of infants receiving formula are receiving a soy-based formula.[50] Additionally, the increased demand for more organic baby food products and plant-based diets is expected to stimulate a ~3% increase in global sales of soy-based formulas by 2028.[51] Soy formulas (Table e21-6) contain sucrose; corn syrup solids; corn maltodextrin; soy protein supplemented with methionine, carnitine, and taurine; and vegetable oils, including soy, sunflower, safflower, and coconut. DHA and ARA are routinely supplemented. They are free of cow milk protein, casein, whey, sucrose, and lactose. Soy formulas have a high concentration of phytates (antioxidant substances found in plants) and about 30% of phosphorus binds to these phytates; thus, soy formulas are supplemented with 20% more calcium and phosphorus than cow milk-based infant formulas.[52] Soy phytates and fiber oligosaccharides also bind iron and zinc; thus, soy formulas are supplemented with higher amounts of iron and zinc than cow milk-based formulas. With the current formulations, bone mineralization and serum calcium, phosphorus, and alkaline phosphatase concentrations in infants consuming them are equivalent to term infants fed cow milk-based formulas through 12 months of age.[52]

Soy-based formulas can be used in infants with lactose intolerance, galactosemia, and cow milk protein allergy, and if the caregiver prefers a vegan or vegetarian option. Because they are sucrose-free, they can be used in infants with sucrase-isomaltase deficiency, a rare genetic disorder. The use of soy formulas in patients with cow milk protein allergy is controversial. Sensitivity to soy protein develops in 7% to 35% of infants with enteropathy or enterocolitis associated with cow milk allergy, especially if younger than 6 months.[52] No benefit has been demonstrated with the use of soy protein-based formulas in atopic disease or infantile colic or fussiness, but there are few contraindications if caregivers choose to use them.

Soy formulas are contraindicated in premature infants weighing less than 1,800 g due to slower growth and decreased bone mineralization (osteopenia) even with the additional calcium and vitamin D added to these products. This effect on bone formation is partially due to the higher aluminum content of soy-based formulas. Aluminum can accumulate with kidney insufficiency and compete with calcium for absorption; thus soy-based formulas should be avoided in premature infants and infants with kidney dysfunction.[52] Infants with cystic fibrosis should not receive soy formulas because of worse nutrition outcomes observed with these formulas.

Soy-based infant formulas contain soy isoflavones and phytoestrogens which has raised concerns related to sexual development and reproductive health as well as immune and thyroid function later in life. These concerns are now considered unfounded. There are no differences in adult weight or height, age of puberty onset, fertility, or immune function noted in long-term assessments of those who receive soy-based formulas in childhood.[52,53]

Infants with congenital hypothyroidism receiving thyroid supplementation should not be given soy products with thyroid replacement therapy as the isoflavones interfere with thyroid hormone absorption. It is best to completely avoid soy-based infant formula in infants with hypothyroidism requiring thyroid hormone supplementation. However, if soy formula use is unavoidable, higher thyroid hormone dosages may be needed and careful monitoring of thyroid function (free thyroxine [free T_4], thyroid stimulating hormone [TSH]) is required.[53]

Extensively Hydrolyzed Protein Formulas

5 Some infants will require specialized formulas with altered macronutrients due to cow milk and soy protein sensitivities or conditions which lead to impaired nutrient digestion, absorption, or utilization (Table e21-9). The protein in these *extensively hydrolyzed* formulas has undergone heat-treated enzymatic hydrolysis resulting in small peptides (di-, tri-, and short chain) and free amino acids. These products are often differentiated based on the percentage of MCT in the product (0%-60%); those with more MCT may be used in patients with generalized malabsorption syndromes. These formulas are typically less palatable and more expensive than other infant formulas.

TABLE e21-9

Specialty Formulas for Term or Near-Term Infants[a]

Formula	Macronutrient Source			Other	Indications
	Carbohydrate	Protein	Fat		
Extensively Hydrolyzed Formulas (semi-elemental, hypoallergenic)					
Similac® Alimentum®	Maltodextrin, sucrose, tapioca starch	Casein hydrolysates, cystine, tyrosine, tryptophan	MCT 33%; safflower and soy oil	Reduced lactose; corn-free	Malabsorption, intractable diarrhea, short bowel syndrome, cystic fibrosis, biliary atresia, cow milk protein allergy
Nutramigen® (Liquids)	Corn syrup solids, modified corn starch	Casein hydrolysates	Corn oil 100%		
Nutramigen® Enflora™ LGG®			MCT 10%	*Lactobacillus rhamnosus GG*	
Pregestimil®	Corn syrup solids, modified tapioca starch	Casein hydrolysates	MCT 55%, corn oil		
Gerber® Extensive HA®	Maltodextrin, potato starch	Whey protein	MCT 49%; soy, safflower, palmitic, and vegetable oil	*Bifidobacterium lactis*	
Free Amino Acid Formulas (elemental, hypoallergenic)					
Elecare®	Corn syrup solids	Free amino acids	MCT 33%		Malabsorption, intractable diarrhea, short bowel syndrome, cystic fibrosis, biliary atresia, severe food allergies, cow milk protein allergy, eosinophilic esophagitis
Neocate® Syneo® Infant	Corn syrup solids	Free amino acids	MCT 8%; sunflower and canola oil	*Bifidobacterium breve*, FOS, inulin	
Neocate® Infant DHA/ARA					
Alfamino® Infant	Corn syrup solids, modified tapioca starch	Free amino acids	MCT 43%		
PurAmino™	Corn syrup solids	Free amino acids	MCT 33%; sunflower and soy oil		

ARA, arachidonic acid; DHA, docosahexaenoic acid; FOS, fructooligosaccharides; MCT, medium chain triglycerides.

[a]Not intended to be a complete listing; check manufacturers' websites for additional products and to verify content.

Data from Abbott Nutrition, Abbott Laboratories, Columbus, OH; Mead Johnson Nutrition, Glenview, IL; Nestlé SA, Vevey, Switzerland; Nutricia Advanced Medical Nutrition, Schiphol, the Netherlands.

Common indications for these products include cow milk protein allergy, cystic fibrosis, biliary atresia, short bowel syndrome, and generalized malabsorption. About 10% of patients with cow milk or soy protein will react to extensively hydrolyzed protein formulas. These patients will require a 100% amino acid-based product. These formulas are generally less palatable; thus acceptance varies. They are also much more expensive than other formulas. These formulas are not recommended for colic or GER due primarily to cost and palatability, but for an infant with severe symptoms, a short trial (1-2 weeks) is appropriate. The calcium and phosphorus content of these formulas is not adequate for premature infants; thus, supplementation or fortification may be required if a premature infant requires one.

Free Amino Acid Formulas

Amino acid-based formulas are the most hypoallergenic because protein is broken down to amino acids (no peptides). They may be referred to as *elemental* which refers only to the protein component. They are indicated in children with cow milk, soy protein, or multiple food protein allergies, especially those with proctocolitis or eosinophilic esophagitis (EOE), a chronic immune-mediated inflammatory condition.

Proctocolitis manifests as rectal bleeding with onset between 2 and 8 weeks of age in breast- or formula-fed infants who are otherwise healthy (no vomiting, diarrhea, feeding difficulties, or growth issues). Mothers of infants with proctocolitis who wish to continue breastfeeding must remove all cow milk and soy from their diets. After eliminating cow milk and soy from the diet, improvement can be seen in just a few days and usually within 2 weeks. In patients with EOE, three dietary regimens are effective for normalization of the esophageal biopsy in most patients: strict use of an amino acid–based formula; dietary restriction based on multimodality allergy testing; and dietary restriction based on elimination of likely food antigens (milk, wheat, soy, eggs, nuts, fish/seafood).[54,55]

High MCT-Containing Formulas

In several infant formulas, a high percentage of the fat is provided as MCT; these formulas also contain higher concentrations of fat-soluble vitamins. The protein component is not hydrolyzed, however, making them unsuitable for patients with generalized malabsorption (short bowel syndrome). Formulas with high MCT concentrations (see Table e21-10) are used in patients with abnormal lymphatic drainage such as chylous ascites, chylothorax,[56] and lymphangiectasia. Because MCT do not form micelles, they are readily absorbed throughout the intestine directly into the bloodstream, bypassing the lymphatic system. Thus, a diet very high in MCT (and very low in LCPUFAs) may dramatically decrease lymphatic flow; thereby decreasing chylous drainage. These formulas are also used in patients with pancreatic insufficiency (cystic fibrosis), bile acid deficiencies (biliary atresia, cholestatic jaundice, intestinal resection), and long chain fatty acid oxidation defects (long chain acyl CoA dehydrogenase deficiency [LCAD], carnitine palmitoyl transferase deficiency [CPTD], and primary and secondary lipoprotein lipase deficiency [hyperlipoproteinemia type 1]). Due to their low LCPUFA content, these formulas provide insufficient essential fatty acids; thus, long-term use confers a substantial risk of EFAD. Formulas high in MCT have a higher osmolality which may cause loose stools or diarrhea.[36]

TABLE e21-10

High MCT-Containing Formulas

Formula	Carbohydrates	Protein	Fat
Enfaport[TM] (liquid, 30 kcal/oz [4.2 kJ/mL])	Corn syrup solids, lactose-free, not galactose-free	Whey 60% Casein 40% (non-hydrolyzed)	MCT 83% DHA, ARA
Monogen® (powder)	Maltodextrin	Cow milk Whey predominant (non-hydrolyzed)	MCT 84% DHA, ARA
Portagen®[a] (powder)	Corn syrup solids, sucrose	Cow milk (non-hydrolyzed)	MCT 87%

ARA, arachidonic acid; DHA, docosahexaenoic acid; MCT, medium chain triglycerides

[a] Not recommended for infant nutrition.

Data from Mead Johnson Nutrition, Glenview, IL; Nutricia Advanced Medical Nutrition, Schiphol, the Netherlands.

Enfaport® is available only as a 30 kcal/oz (4.2 kJ/mL) liquid formulation. If used in an infant younger than 1 year of age, dilution is required, and proper caregiver and staff education must be ensured. Portagen® is not recommended as an infant formula, especially for infants who may be immunocompromised, due to the risk of contamination associated with the inability to fully sterilize powders brought to light with the death of a neonate caused by *Enterobacter* (now *Chronobacter) sakasakii* contamination of formula powder and the recent infant formula shortage precipitated by bacterial contamination of powdered formulas in a manufacturing plant. Monogen® is also only available as a powder.

Low Mineral/Metabolic Formulas

A number of formulas are manufactured specifically for infants with inborn errors of metabolism or other metabolic diseases. Examples of these formulas and their indications are provided in Table e21-11. One formula in this category is Similac PM® 60/40, a low mineral (calcium, phosphorus, iron, potassium) formula for use in infants with kidney dysfunction or hypercalcemia. This formula is a whey protein concentrate with sodium caseinate, lactose, high oleic safflower, soy, and coconut oils. It is vitamin D-free for use in patients with Williams syndrome, neonatal hyperparathyroidism, and osteopetrosis, conditions associated with hypercalcemia. Calcilo-XD® is also a low calcium formula for use in patients with hypercalcemia. The calcium-to-phosphorus ratio (2:1) and low sodium concentration make the formula less suitable for low birth weight infants, and supplementation may be required if used in this population.

TABLE e21-11

Formulas for Inherited Metabolic Disorders[a]

Product	Indication	Characteristic
3232 A (MJ)	Carbohydrate intolerance; disaccharidase deficiency	Sugar must be added
Calcilo XD® (A)	Hypercalcemia, Williams syndrome, osteopetrosis, primary neonatal	Low calcium, vitamin D-free

	hyperparathyroidism	
Cyclinex®-1/Cyclinex®-2 (A) WND® 1/WND® 2 (MJ)	Urea cycle disorders, gyrate atrophy, Hyperornithinemia-hyperammonemia-homocitrullinuria (HHH) syndrome	Non-essential amino acid-free
Glutarex®-1/Glutarex®-2 (A) GA (MJ)	Glutaric aciduria type 1	Lysine- and tryptophan-free
Hominex®-1/Hominex®-2 (A) HCY 1/HCY 2 (MJ)	Homocystinuria, hypermethioninemia	Methionine-free
I-Valex®-1/I-Valex®-2 (A) LMD (MJ)	Leucine metabolism disorders	Leucine-free
Ketonex®-1/Ketonex®-2 (A) BCAD 1/BCAD 2 (MJ)	Maple syrup urine disease (MSUD), beta-ketothiolase deficiency	Isoleucine-, leucine-, and valine-free
PFD Toddler/PFD 2 (MJ) Pro-Phree® (A)	Amino acid metabolic disorders	Protein-free
Phenex®-1/Phenex®-2 (A) Phenyl-Free® 1 / Phenyl-Free® 2 / Phenyl-Free® 2 HP (MJ)	Phenylketonuria (PKU)	Phenylalanine-free
Propimex®-1/Propimex®-2 (A) OA 1/OA 2 (MJ)	Propionic or methylmalonic acidemia	Methionine- and valine-free; low isoleucine and threonine
Provimin® (A)	Abetalipoproteinemia, many others	Protein, vitamins, minerals, iron only
RCF® (A)	Carbohydrate intolerance	Sugar must be added
Similac® PM 60/40 (A)	Kidney disease, hypercalcemia	Low in calcium, phosphorus, iron, potassium
Tyrex®-1/Tyrex®-2 (A) Tyros 1/Tyros 2 (MJ)	Tyrosinemia type I, II, or III	Phenylalanine- and tyrosine-free

[a] Not intended to be a complete listing; check manufacturers' web sites for additional products and to verify content.

Data from Abbott Nutrition, Abbott Laboratories, Columbus, OH; Mead Johnson Nutrition, Glenview, IL.

Several products are carbohydrate-free (Table e21-11). These formulas are used in infants who are unable to tolerate the carbohydrates in human milk or infant formulas due to congenital disorders of carbohydrate metabolism and absorption (eg, disaccharidase deficiency). These products contain extensively hydrolyzed cow milk and soy protein, vegetable oils (82% MCT), tapioca starch, but no carbohydrates. Simple sugars (glucose polymers, fructose) are added gradually to improve tolerance. Generally, the sugar is added to make the caloric density the same as standard infant formula (20 kcal/oz [2.8 kJ/mL]). These products may not supply adequate essential fatty acids.

Formulas for the Ketogenic Diet

The ketogenic diet is an effective non-pharmacological treatment for drug-resistant childhood seizures.[57] A ketogenic diet mimics the body's response to starvation, when the body shifts to a ketotic state, shifting metabolism from carbohydrate to fat utilization for fuel. The ketogenic diet is a high fat (71%-90% of energy) and low carbohydrate (5%-19% of energy) that contains adequate protein to support growth. Each component of the diet is calculated in a specific proportion by a trained registered dietitian. While a small amount of human milk or standard infant formula may be allowed, most infants will receive a formula specifically designed for the ketogenic diet such as KetoCal™ 4:1 and KetoCal™ 3:1 (Nutricia, Gaithersburg, MD) and KeoVie™ 4:1 and KetoVie Peptide™ 4:1 (Cambrooke Therapeutics). The ratio in the name refers to the ratio of fat (g) to carbohydrates plus protein (g). For example, in KetoCal™ 3:1, for every 3 g fat, there is 1 g of carbohydrates plus protein. Classically, children younger than 2 years of age receive a 3:1 formula and children 2 to 12 years of age receive a 4:1 formula; however, this may vary. Patients on ketogenic diets must receive frequent monitoring of growth, electrolytes, liver function, serum lipids, carnitine, vitamins, and trace minerals. Most patients will also require a carbohydrate- and lactose-free (to avoid disruption of the ketotic state) supplement to provide additional selenium, vitamin D, B vitamins, magnesium, and iron. If supplements or medications are required that cannot be given in a sugar-free form, the dietitian can calculate the nutrition prescription with these carbohydrates included.

OTHER NUTRIENT CONSIDERATIONS

6 Two nutrients, iron and vitamin D, are of particular importance in infant nutrition.

Iron

Term babies are born with adequate iron stores; for premature infants, the younger the gestational age, the greater the total body iron deficit at birth. Iron deficiency is associated with anemia and poor neurodevelopmental outcomes. Most infant formulas are fortified with iron, and infants receiving one of these formulas usually do not require additional iron supplementation. Human milk, however, is low in iron and exclusively breastfed infants require iron supplementation.

Premature infants receiving human milk who are 1 month of age should receive iron at a dose of 2 mg elemental iron/kg daily through 12 months of age. Up to 3 mg elemental iron/kg daily may be needed in low and very low birthweight infants. Premature infants who are formula-fed may require supplementation depending on the formula.[15] Iron supplementation (1 mg/kg daily) is recommended beginning at 4 months of age for term infants receiving exclusive human milk feeding or less than 50% of their daily feedings as iron-fortified formula.[15,58] Introduction of iron-fortified solid foods at 6 months of age generally provides an adequate supply of iron, and the need for continued supplementation should be re-addressed at that time. Routine monitoring of iron studies (serum ferritin, transferrin saturation, serum iron) is not warranted unless anemia does not respond after 1 month of appropriate iron supplementation.[58]

Vitamin D

Vitamin D and calcium deficiencies are common worldwide causing nutritional rickets and osteopenia, which can dramatically impact growth, development, and overall health. Despite ready access to vitamin D supplements, cases of rickets are still documented in the United States, often in exclusively breastfed infants not receiving vitamin D supplementation. Current AAP and global recommendations recommend that all infants receive 400 international units (10 μg) daily starting a few days after birth regardless of their mode of feeding until they are consuming at least 32 oz (~950 mL) of vitamin D-fortified formula or cow milk[59,60] unless the mother ingests at least 6,400 international units (160 μg) daily.[61] After 12 months of age, the recommended intake in children and adolescents is 600 international units/day. Liquid vitamin D supplements are unpalatable, and caregivers often discontinue the supplement due to vomiting or refusal by the infant. Education regarding the importance of vitamin D for bone health and other outcomes is important.

Monitoring of vitamin D serum concentrations (25-OH-vitamin D) is not indicated in most infants and children. For those with risk factors for vitamin D deficiency (cystic fibrosis, short bowel syndrome, biliary disease, long-term parenteral nutrition), target ranges have been defined as: sufficient, > 20 ng/mL (50 nmol/L); insufficient, 12 to 20 ng/mL (30 to 50 nmol/L); and, deficient, < 12 ng/mL (30 nmol/L).[60] Vitamin D toxicity is uncommon but hypercalcemia and hypercalciuria can be seen with a serum 25-OH-vitamin D concentration greater than 100 ng/mL (250 nmol/L) and a decreased serum parathyroid hormone (PTH) concentration.[60]

Non-Nutrient Additives in Infant Formulas

7 Human milk contains a variety of non-nutritive compounds with specific bioactive characteristics; formula manufacturers continue to modify their products to include these compounds.[62] Non-nutritive additions to formulas, and even some nutritive ones, have been questioned due to the increase in manufacturing costs without definitive evidence to support their need.

Prebiotics and Probiotics

A healthy gut is of major importance in infancy as it contributes to growth and development of immunity. Microbial colonization of the GI tract starts before or right after birth. It is well-established that human milk- and formula-fed infants have different intestinal microbiomes.[62–64] To try to mimic the effect of human milk on the GI microbiome, both pre- and probiotics have been added to some infant formulas.

Prebiotics are indigestible, fermentable carbohydrates (oligosaccharides) that are not fully digested in the small intestine. Prebiotic oligosaccharides are the third most prevalent component of human milk.[65] They promote the growth and activity of beneficial gut flora, lactobacilli, and bifidobacterium and prevent proliferation of pathogenic bacteria. Examples of prebiotics include inulin, FOS, and GOS. Fermentation of these oligosaccharides produces short chain fatty acids that are used by the colonocytes for energy, thus protecting the mucosal barrier. Term infant formulas supplemented with prebiotics promote growth similar to infants fed human milk or non-supplemented formula.[63] Infants receiving prebiotic-containing formula have an increased frequency of softer stools than those fed non-supplemented formula, but stools are comparable to those of infants fed human milk.[65]

Probiotics are live, nonpathogenic microorganisms (bacteria, fungi) with beneficial effects on the host. They interfere with the adherence of pathogenic bacteria, increase the intestinal immunologic barrier, and modulate the inflammatory response. Probiotics modulate intestinal inflammation by inhibiting pathogen growth, improving mucosal health and integrity, and regulating intestinal immune response. Human milk is an important source of beneficial bacteria that colonize the infant gut. Human milk contains between 10^3 and 10^6 bacteria per milliliter depending on the analysis method used. Human milk contains a variety of probiotics; *Bifidobacterium spp.* predominate, but *Lactobacillus spp.,* are also found in high concentrations.[63] *Lactobacillus rhamnosus GG*, also found in the intestine of breastfed infants, has been found to decrease diarrhea in infants receiving antibiotics.

Some infant formulas are supplemented with probiotics, including *Bifidobacterium lactis* or *L. rugieri,* to more closely mimic human milk and to promote a healthy immune system. *B. lactis* has been associated with a decreased risk of NEC likely due to its protective effects on the gut barrier function. Advanced microencapsulation technology has allowed the bacteria added to infant formulas to be protected from destruction before reaching the site of action (colon).[66] While probiotics are found in human milk and considered safe, concerns remain regarding their use in infants who are immunocompromised, chronically debilitated, or seriously ill with indwelling medical devices.[67]

Lutein

Infancy and early childhood are critical times for eye and brain development. The retina and the brain share the same embryological origin from the neural tube formed around the fourth week of gestation.[68] Lutein is found in high concentrations in the macula of the eye and is the predominant carotenoid in the brain.[69] In the eye, lutein is an antioxidant and a high-energy blue light filter. Age-related differences in the transmission of optic radiation to the retina have been observed for blue light (400-500 nm), the most energetic wavelengths of visible light radiation. The retina of a young child is exposed to much more blue light than an older person.[68]

Lutein is a lipophilic xanthophyll dietary carotenoid found in many fruits, vegetables, and human milk. Animals do not synthesize carotenoids de novo; thus, infants must consume lutein through human milk or supplemented infant formulas. Lutein supplementation has the potential for long-term protection again blue light damage to the eyes and may be important for cognitive function across the lifespan.[68,69] Lutein supplementation may improve brain network connectivity, especially in the default and sensory-motor and default and dorsal attention and visual and somatosensory networks.

Lutein is a safe molecule with an extensive consumption from the diet. Lutein is GRAS (generally recognized as safe) in the United States for adding to foods, including infant formulas. The European Food Safety Agency (EFSA) has established the safety and bioavailability of lutein in infant formulas.

Lactoferrin

Lactoferrin is the major whey protein in all mammalian milk. There is a high (~70%-80%) structural and functional similarity between bovine lactoferrin (bLF) and human lactoferrin. Functions of lactoferrin include antibacterial/antiviral activity, antioxidant activity, immunomodulation, trophic effects on enterocytes and enteric Caco2 cells, and benefits on the GI microbiota.[70–72] Cow milk has low concentrations of bLF, so some manufacturers have supplemented cow milk-based formulas with bLF to more closely mimic human milk. Formulas supplemented with bLF, prebiotics, DHA, and ARA compared to non-supplemented term infant formula result in equivalent growth but softer stools, consistent with stools of breast-fed infants.[71] In some, discontinuation of the supplemented formula occurs secondary to fussiness and gas, which may also occur with formulas supplemented with prebiotics alone.[71] Infants receiving formula supplemented with bLF compared with non-supplemented formula have a decreased prevalence of acute GI symptoms (diarrhea, vomiting) and decreased days with acute respiratory symptoms (nasal congestion, cough).[72] The FDA considers bLF as GRAS.

Milk Fat Globule Membrane (MFGM)

The lipid droplets of milk fat globules (including those found in breast milk) are stabilized by a three-layered membrane, the milk fat globule membrane (MFGM), which maintains triglyceride dispersion in the aqueous phase of the milk. The MFGM is composed primarily of polar lipids (phospholipids, glycosphingolipids), proteins (mainly glycoproteins), and apolar lipids (cholesterol, cerebrosides).[73] MFGM is produced by the mammary gland epithelium, has antibacterial and antiviral activity, and improves GI maturation and central nervous system myelination.[73] An extensive review of the role of MFGM in infant health and development can be found elsewhere.[74]

MFGM is a component of bovine milk that has historically been discarded in infant formula preparation as most formulas contain vegetable oils with much different structures. Recent improvements in manufacturing technology have allowed concentration of bovine MFGM, making it feasible to add to infant formula. Infants receiving formula supplemented with MFGM (also supplemented with bLF) had an accelerated neurodevelopmental profile at day 365 and improved language subcategories at day 545. There were also fewer diarrhea and respiratory-associated adverse events through 545 days of age.[75]

PEDIATRIC FORMULAS (1-13 YEARS)

8 Enteral formulas are available for children who need supplemental nutrition beyond a regular diet in most of the infant formula categories discussed and are used for similar indications (Table e21-12). These products are available in caloric densities of 18.9 kcal/oz to 45 kcal/oz (0.63-1.5 kcal/mL or 2.7-6.4 kJ/mL, respectively) and have vitamin and mineral contents suitable to meet the needs of older children. Children older than 13 years of age will generally receive a product intended for use in adults (Chapter 166). The choice of formula depends on age, GI function, previous tolerance, allergies, nutrition requirements, and organ function.

TABLE e21-12

Formulas for Children 1-13 Years of Age[a]

Formula	Mfr	Macronutrient Source			Indications
		Carbohydrate	Protein	% Fat as MCT	

Standard Polymeric Formulas					
Pediasure® 1.0 Cal Pediasure® 1.0 Cal with Fiber Pediasure® 1.5 Cal Pediasure® 1.5 Cal with Fiber Pediasure® Grow & Gain Pediasure® Grow & Gain with Fiber Pediasure® Grow & Gain Organic Pediasure® Enteral Formula 1.0 Cal Pediasure® Enteral Formula 1.0 Cal with Fiber Pediasure Sidekicks® Pediasure® Pro Pediasure® Reduced Calorie	Abbott	Corn maltodextrin, sugar	Milk protein	-	Normal functioning GI tract
Nutren Junior® Nutren Junior Fiber®	Nestlé	Maltodextrin, sugar	Milk protein, whey (50%)	20%	
Boost® Kid Essentials™ Boost® Kid Essentials™ 1.0 Boost® Kid Essentials™ 1.5 Boost® Kid Essentials™ 1.5 with Fiber	Nestlé	Brown rice syrup, sugar	Milk protein	-	
Blenderized / Whole Food Formulas					

Compleat® Pediatric Compleat® Pediatric Reduced Calorie Compleat® Pediatric Organic Blends[b]	Nestlé	Brown rice syrup; fruits and vegetables; corn-free, low lactose	Milk protein; chicken powder; pea protein; soy-free	20%	Long-term tube feeding when whole food preferred; some can be used orally for patients with food allergies
Nourish[b,c]	functional formularies	Plant-based; dairy-, gluten-, and corn-free	Plant-based; dairy-, soy-, and nut-free	Plant-based	
Pediatric Standard 1.2[b,c]	Kate Farms	Brown rice syrup; dairy-, gluten-, and corn-free	Pea protein; dairy-, soy-, and nut-free	42%	
Pediasure Harvest™[b]	Abbott	Plant-based; dairy-, gluten-, and lactose-free	Plant-based; contains soy	Plant-based	
Extensively Hydrolyzed Formulas					
Pediasure® Peptide 1.0 Cal Pediasure® Peptide 1.5 Cal	Abbott	Corn maltodextrin	Whey hydrolysate	60%	Malabsorption, maldigestion, intractable diarrhea, short bowel syndrome, cystic fibrosis, biliary atresia
Peptamen Junior® Peptamen Junior® 1.5 Peptamen Junior® HP Peptamen Junior® Fiber Peptamen Junior® with Prebio™ Peptamen Junior® PHGG	Nestlé	Maltodextrin, cornstarch, sugar	Whey hydrolysate	60%	
Pediatric Peptide 1.0 Pediatric Peptide 1.5[b,c]	Kate Farms	Brown rice syrup; dairy-, gluten-, and corn-free	Hydrolyzed pea protein; dairy-, soy-, and nut-free	42%	

Compleat® Pediatric Peptide 1.5	Nestlé	Brown rice syrup; fruits and vegetables; corn-free, low lactose	Hydrolyzed pea protein	40%	
Nourish Peptide Formula	functional formularies				
Nutramigen® with Enflora™ LGG® Toddler	Mead Johnson	Corn syrup solids; lactose-, and sucrose-free	Casein hydrolysate	-	
Amino Acid Formulas					
Elecare® Jr	Abbott	Corn syrup solids	Amino acids	33%	Malabsorption, intractable diarrhea, short bowel syndrome, cystic fibrosis, biliary atresia, severe food allergies
Neocate® Junior	Nutricia	Corn syrup solids	Amino acids	8%	
Neocate® Splash	Nutricia	Maltodextrin, sugar	Amino acids	1.8%	
PurAmino™ Jr / PurAmino™ Jr Vanilla	Mead Johnson	Corn syrup solids, modified tapioca starch	Amino acids	33%	
Vivonex® Pediatric	Nestlé	Maltodextrin, modified cornstarch	Amino acids	70%	

[a] Not intended to be a complete listing; check manufacturers' web sites for more products and to verify content.

[b] Certified organic.

[c] Hypoallergenic.

GI, gastrointestinal; MCT, medium chain triglycerides; Mfg, manufacturer.

Data from Abbott Nutrition, Abbott Laboratories, Columbus, OH; Kate Farms, Santa Barbara, CA; Mead Johnson Nutrition, Glenview, IL; Nestlé SA, Vevey, Switzerland; Nutricia Advanced Medical Nutrition, Schiphol, the Netherlands; Nutritional Medicinals, LLC, Centerville, OH.

Blenderized Formulas

Blenderized formulas have become increasingly popular in pediatrics as society places a higher value on more natural foods. These products may be preferred by some families because they more closely mimic "real food" for their child (psychosocial). Others may receive them due to intolerance to other formulas or for other perceived health benefits.[76] A blenderized diet could be homemade from whole foods, a mixture of a commercial formula with pureed foods, or a commercially available ready-to-use formula (see Table e21-12). Blenderized products are generally higher in fiber and may be beneficial in patients on long-term nutrition support, especially those with neurological deficits, who have a high incidence of constipation. To comply with the AAP and WHO recommendations for adding complementary foods to infants' diets, blenderized diets are generally not used in infants younger than 6 months of age. Whole cow milk should be avoided until 12 months due to the risk of GI bleeding, anemia, electrolyte imbalances, metabolic acidosis, and folic acid and iron deficiency.[15] Many blenderized formulas are thicker than other formulas and, if given via a small-bore feeding tube or if given via a feeding pump, may require dilution with water. The risk of bacterial contamination is high with these products, limiting their hang time (when continuous rather than bolus tube feedings are used).[76] Generally, these formulas are more expensive than other products due to the manufacturing process. Documentation of intolerance to other products may be required to obtain insurance coverage, and collaboration with a case manager, social worker, or registered dietitian may help to ensure that the family receives assistance.

HUMAN MILK AND INFANT FORMULA SAFETY

Human Milk

9 Expressed human milk and infant formulas must be handled and stored properly. Human milk should be stored in 2- to 4-ounce (60 to 120 mL) aliquots. Human milk may be stored at room temperature (up to 77°F [25°C]) for 4 hours, or if cleanly expressed, a maximum of 8 hours. Once a bottle is started, it should be consumed within 2 hours, and if not, the remaining may be refrigerated and used at the next feeding. While human milk can be stored in the back of the refrigerator, if it is not going to be used within 24 hours, it should be frozen. Human milk can be frozen in the back of a freezer with a separate door (0°F [-18°C]) for 9 months and in a chest or deep freezer (-4°F [-20°C]) for 12 months. Once thawed (by placing in a warm water bath, never in the microwave), human milk should be used within 24 hours.[15]

There may be considerable loss of fat, fat-soluble vitamins, and phospholipids when human milk is administered via a feeding tube. When using frozen and thawed milk, there is more loss than when using fresh, never frozen, milk. Expressed milk stored for 3 days is associated with less loss than when milk is fresh. For infants receiving human milk through a feeding tube, intermittent administration (bolus or intermittent infusion) is preferred over continuous infusion, if possible. For human milk feedings, the hang-time should not exceed 4 hours.[77]

Infant Formula

Formulas are available as powders requiring reconstitution, ready-to-use liquids, and concentrated liquids requiring dilution with water. Powders are not sterilized; thus, neonates in ICUs and immunocompromised infants should receive an alternative whenever possible. When powdered formula is used, it is important that proper preparation technique is used and that the reconstituted formula is stored properly. Boiling water should not be used to reconstitute powders as it may disrupt nutrient delivery and may not kill all organisms. Small quantities should be mixed at one time. If formula is mixed from powder, it should be stored in the refrigerator and discarded after 24 hours. Once a can of powder has been opened, unused powder should be discarded after 30 days. Unused ready-to-use or concentrated liquids should be discarded if not used within 48 hours. If used for tube feedings, formula should be allowed to hang at room temperature for no more than 4 hours unless chilled. Feeding tube bags with pouches for ice packs are available.

For infants with volume intolerance (GER, heart disease, liver failure), poor growth, or altered nutrient needs, formulas may be concentrated to a higher than standard caloric density by adding less water to a powder or concentrate or adding a modular component to a ready-to-use or prepared liquid (Table e21-13). In general, concentrating to more than 27 kcal/oz (3.8 kJ/mL) by adding less water is not recommended. Consultation with a registered dietitian is recommended when an infant's formula requires significant manipulation from the standard concentration. Concerns with concentrating formula beyond the standard density include vomiting, constipation, high renal solute load due to excessive protein, and excessive weight gain. Improper mixing to a concentration below the standard may result in diarrhea, poor weight gain, hyponatremia, and other electrolyte imbalances. Regardless of the feeding regimen, parents/caregivers should be educated and given written instructions on the proper preparation of their infant's formula (if not breastfeeding) prior to discharge from the hospital or leaving an office visit. Knowledge should be re-assessed at each visit with a healthcare provider, especially for an infant with growth faltering or other nutrition-related issues.

TABLE e21-13

Modular Nutrient Additives

Nutrient Supplied	Products Available
Carbohydrate	Moducal®, Polycose®, SolCarb®, corn starch[a]
Protein	ProMod®, Casec®, Beneprotein®, ProStat®, Essential Amino Acid Mix, Complete Amino Acid Mix
Fat	MCT Oil®, Microlipid®
Carbohydrate and fat	Duocal®
Pectin and carbohydrate	Banana Flakes®
Carbohydrate, fat (MCT/LCT), protein	MCTprocal™
Fiber	Nutrisource® Fiber, Benefiber®

[a] Glycemic index < 50; useful in ketogenic diet.

ORAL REHYDRATION

In the United States., fluid and electrolyte disturbances from acute gastroenteritis result in many outpatient visits and hospitalizations but only a small number of deaths each year. Rotavirus was the leading cause of viral diarrhea and the main cause of severe disease and hospitalization until the introduction of the rotavirus vaccine. In countries with the rotavirus vaccine, norovirus is now the leading cause of moderate to severe diarrhea, traveler's diarrhea, and food poisoning outbreaks in children younger than 2 years of age.[78] In developing countries, acute diarrhea is common resulting in ~500,000 deaths in 2018, a number significantly less than the 4 to 6 million deaths reported in 1980, the year a pivotal article on the effectiveness of glucose and electrolyte solutions (oral rehydration solutions) was published.[79] Infants and young children become mildly to severely dehydrated more quickly due to higher fluid needs and higher frequency of poor oral intake with illness. Signs and symptoms of dehydration are listed in Table e21-14.

TABLE e21-14

Signs and Symptoms of Dehydration

Mild-to-Moderate Dehydration	Severe Dehydration
Restlessness	Lethargy
Irritability	Unconsciousness
Sunken eyes	Significant thirst, very dry mouth
Rapid pulse	Prolonged skin tenting
Increased thirst, dry mouth	Weak or absent pulse
Mild skin tenting	Low blood pressure
Decreased urine output	Minimal to no urine output
Dark urine	Poor capillary refill
Decreased tears	
Depressed fontanelle (young infants)	
Slow capillary refill	

10 Oral rehydration therapy (ORT) is a mainstay of treatment for mild-to-moderate dehydration; severe dehydration requires IV rehydration. The principles of ORT are simple: give fluid orally (or via nasogastric tube) that contains sodium and glucose, and the co-transport of glucose and sodium across the intestinal membrane will take water with it. Sodas and commercial juices cannot be used for ORT because they do not contain enough sodium or contain too much glucose or both. Additionally, the sugar in juice may result in more stool volume due to its osmotic effect. The original WHO recommended *standard osmolality* oral rehydration solution (ORS) contains a concentration of sodium of 90 mmol/L and glucose of 13.5 g/L resulting in an osmolality of 333 mOsm/L. In 2002, WHO amended its recommendation to use a ORS containing sodium 75 mEq/L (mmol/L) and glucose 13.5 g/L resulting in an osmolality of 245 mOsm/L (low osmolality ORS).[80] The reason for this change was that the higher osmolality solution increased stool output in a high percentage of patients due to its osmotic effects in the intestine. The lower osmolality solution is as effective as the higher one without dramatically increasing stool volume.[81] Polymer-based ORT solutions are marketed. These solutions contain *glucose polymers* in the form of whole rice, wheat, sorghum, and maize. Because amylase is generally not affected by diarrhea, amylase is available to slowly break down these starches into glucose, which then provides the carrier molecules for co-transport of sodium and water across the intestinal epithelium, resulting in rehydration of the extracellular fluid (see Chapter 68, "Disorders of Sodium and Water Homeostasis"). Comparison of glucose-based and polymer-based ORS has not demonstrated a significant difference in outcomes such as hyponatremia, vomiting, or the need for IV fluid.[82]

Despite CDC[83] recommendations for ORT for children with mild-to-moderate dehydration, use in the United States is limited. Advantages of ORT are that it reduces the need for outpatient and emergency department visits, requires less emergency department staff time, reduces the length of emergency department visits, avoids the placement of an IV catheter, avoids the use of IV fluids, and can be administered in the home. Contraindications to ORT include altered mental status due to aspiration risk, abdominal ileus, and underlying intestinal malabsorption syndromes (short bowel syndrome). Cost also is a consideration with ORT. Families may not be able to purchase the solution; thus, providing ORT in a clinic or emergency department setting may limit the overall cost to the patient. If a patient is unable to take the ORT solution by mouth, then a nasogastric tube may be placed, and the solution given via the tube. This method of administration has been effective and more cost-effective than IV therapy but may not be preferred by the patient or family.

Tables e21-15 and e21-16 provide volumes of intake and solutions used for ORT, respectively. The use of a commercially available product is preferred to the use of home recipes to limit errors, but commercial products are not readily available to all, and recipes are available online for homemade ORS. If the patient can sit up and drink, they can usually receive ORT. For mild dehydration, 50 mL/kg of ORT solution should be administered over the first 4 hours using a spoon, syringe, medicine cup, or other devices. A rule of thumb is 1 mL/kg (0.5 mL/lb) every 5 minutes. If the patient is thirsty and asks for more, it should be given. For moderate dehydration, 100 mL/kg (50 mL/lb) is recommended for the first 4 hours. While mild dehydration can be managed in the home, moderate dehydration should be managed in a physician's office or emergency department, and severe dehydration should be treated in a health care facility with IV fluids. After 4 hours, if the child has taken all the ORS, the patient may be sent home and maintenance fluids, calculated using the Holiday-Segar method (see Chapter 68), given until the illness resolves. Simplified, this is 1 oz (30 mL) per hour for infants, 2 oz (60 mL) per hour for toddlers, and 3 oz (90 mL) per hour for older children. It is also recommended that the child receive an additional 10 mL/kg (5 mL/lb) for every loose stool and 2 mL/kg (1 mL/lb) for every vomiting episode to prevent further dehydration. Due to the complexity of these guidelines, parents and caregivers will need to be educated regarding the specific volumes required in their child.

TABLE e21-15

WHO Guidelines for Oral Rehydration in Children

Recommended Volume of ORT to Correct Dehydration		
Weight (kg)[a]	**Age**[a]	**ORS, mL in first 4 hours**[b]
Less than 5	Younger than 4 months	200-400
5-7.9	4-11 months	200-400
8-9.9	12-23 months	600-800
10-15.9	2-4 years	800-1,200
16-29.9	5-14 years	1,200-2,200
30 or more	15 years or older	2,200-4,000
Recommended Volume after Stooling to Prevent Dehydration		
Age (y)	**Recommended Volume (mL)**	**Maximum Daily Volume (mL)**
< 2	50-100	500
2-9	100-200	1,000
≥ 10	At least 100-200, but as much as desired	2,000

[a] Use age only if weight is not available.

[b] Volume for first 4 hours can also be calculated by multiplying the weight (kg) by 75.

TABLE e21-16

Oral/Enteral Hydration Solutions (examples only)

Product	Sodium (mEq/L)	Potassium (mEq/L)	Chloride (mEq/L)	Base (mEq/L)	CHO (g/L)	Osm (mOsm/L)	Other
Recommended Concentration	**60-90**	**15-25**	**50-80**	**8-12**	**Equal to sodium; < 111 mmol/L**	**200-310**	
Rehydration Solutions—replace fluid deficits							
WHO (Unicef), original[a]	90	19.2	21	30	13.5	333	
WHO (Unicef), modified	75	20	65	10	13.5	245	
Bana – Adult	68.6	10.3			2		
Ceralyte 70 (packets)	70	20	60	30	40 (rice)	< 260	
Ceralyte 90 (packets)	90	20	80	30	40 (rice)	< 275	
Drip Drop Solution	60	20	8	80	16	< 200	
Pedialyte Advanced Care+[b]	60	20					Zinc
Maintenance solutions—prevent fluid deficits							
Pedialyte®, Pedialyte® Freezer Pops, Pedialyte Advanced Care[b]	45	20	35	30	25	388	Zinc
Ceralyte 50 (packets)	50	20	40	30	40 (rice)	< 260	
Enfamil® Enfalyte®	50	25	45	33 (citrate)	30	160	
Clear Liquids and Sports Drinks (for comparison only—not rehydration or maintenance solutions)							
Juice	2	30	-	0	69	730	
Soda	3	-	-	13	70	700	
Gatorade (G2)[c]	20	3.2	17	30	21	305	
Gatorade Prime[c]	40.5	7.6	17	30	195	305	

[a] Gold standard for rehydration solutions.

[b] Contains prebiotics.

[c] Other forms available; sugar-free Gatorade available; caution with sugar substitutes.

Data from Essential Medicines and Health Products Information Portal A World Health Organization resource. Available at:

apps.who.int/medicinedocs/en/d/Js4950e/2.4.html

Signs of adequate ORT (rehydration) include no skin tenting or thirst, a strong pulse, and adequate urination. Once the patient is rehydrated, a regular age-appropriate diet should be initiated. Breastfed infants may continue to feed during ORT, but if held, then breastfeeding should be resumed as soon as ORT is complete. Early resumption of a regular diet does not worsen symptoms of diarrhea and may decrease its duration. Occasionally, if diarrhea is prolonged, a lactose-free infant formula may be considered for a few days, especially if the infant's usual formula seems to worsen symptoms when feeding is reinstituted.

ABBREVIATIONS

ARA	arachidonic acid
bLF	bovine lactoferrin
DHA	docosahexaenoic acid
EFAD	essential fatty acid deficiency
EOE	eosinophilic esophagitis
FDA	Food and Drug Administration
FOS	fructooligosaccharides
GER	gastroesophageal reflux
GI	gastrointestinal
GOS	galactooligosaccharides
HIV	human immunodeficiency virus
HMF	human milk fortifier
ICU	intensive care unit
IV	intravenous
IgA	immunoglobulin A
LCPUFA	long-chain polyunsaturated fatty acids
MCT	medium chain triglycerides
MFGM	milk fat globule membrane
NEC	necrotizing enterocolitis
ORS	oral rehydration solution
ORT	oral rehydration therapy
WIC	US Special Supplemental Nutrition Program for Women, Infants, and Children

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SELF-ASSESSMENT QUESTIONS

1. A 7-day-old infant is in the clinic today for the first well-baby check. A review of the chart shows that the newborn screen was resulted as positive for galactosemia. The infant is currently being breastfed. Which of the following is the *best* approach for feeding this infant?

   A. Continue breastfeeding; educate mother to avoid cow milk

   B. Change to Enfamil® NeuroPro™ Infant

   C. Change to Similac® Pro-Total Comfort® 20

   D. Change to Enfamil® NeuroPro™ Gentlease®

2. A healthy, near-term neonate, born at 37 weeks estimated gestational age, will receive infant formula at discharge because his mother does not wish to breastfeed. Which of the following would be the *most appropriate* choice for this infant?

   A. Similac Pro-Advance® 20

   B. Enfamil® Enfacare®

C. Similac® Special Care® 24

D. Neocate® Synveo® Infant

3. A 3-month-old who was transitioned from breastfeeding to Gerber Good Start® Soothe is brought to clinic by the father who reports bloody stools for the past 2 days. The child otherwise looks healthy and has been gaining weight appropriately. The provider suspects cow milk protein allergy. Which of the following infant formulas would be the *most appropriate* option for this infant?

A. Similac® Neosure®

B. Similac® PM 60/40

C. Monogen®

D. Gerber® Good Start® Extensive HA®

4. A 2-month-old, term infant underwent cardiothoracic surgery to repair a congenital heart defect. One week after restarting feeds with human milk, a pleural effusion was seen on the morning chest X-ray. The infant was diagnosed with a chylothorax. Initially, parenteral nutrition was used for 4 weeks, but enteral feedings will be started today. Which of the following would be the *bes*t formula choice for this infant?

A. Nutramigen® Enflora™ LGG®

B. Neocate® Infant DHA/ARA

C. Enfaport™

D. Alfamino® Infant

5. A mother in the United States with which of the following would be discouraged from either breastfeeding or using expressed milk to feed her infant?

A. Active tuberculosis; receiving treatment for 5 days

B. HIV, receiving antiretroviral therapy and a low viral load

C. Varicella; onset of symptoms 3 days prior to delivery

D. H1N1 influenza, receiving no treatment

6. Which of the following is correct information about human milk storage that should be provided to a breastfeeding mother who is taking her newborn home from the hospital?

A. When expressed milk is offered to the infant in a bottle immediately after pumping, any remaining may be refrigerated and used for the next feeding, if within 4 hours.

B. Fresh human milk may remain at room temperature for up to 12 hours.

C. Expressed human milk may be refrigerated for up to 2 weeks.

D. Expressed human milk can be kept in a deep freezer for up to 24 months.

7. A 6-year-old child (weight, 20 kg) is brought to the emergency department with a 2-day history of diarrhea with vomiting. The child has not been drinking well over the past 12 hours, and the parents were concerned for dehydration. The emergency physician confirms mild dehydration and recommends a trial of oral rehydration therapy (ORT). Per WHO guidelines, which of the following is the *most appropriate* volume and administration recommendations for ORS during the first 4 hours?

A. 2,000 mL at a rate of 200 mL every 5 minutes

B. 2,000 mL at a rate of 20 mL every 2-5 minutes

C. 1,000 mL at a rate of at least 50 mL every 15 minutes

D. 1,000 mL at a rate of at least 20 mL every 5 minutes

8. A 3-week-old term infant is being seen in clinic today for the first well-baby visit. The infant is being exclusively breastfed. The parents state that the infant is receiving no medications or supplements. Which of the following is the *best* recommendation for this infant?

A. No additional medications or supplements are needed now; return to clinic in 1 month.

B. Start vitamin D (ergocalciferol) 400 international units and iron sulfate 2 mg/kg elemental iron daily.

C. Start vitamin D (ergocalciferol) 400 international units daily.

D. Start iron sulfate 2 mg/kg elemental iron daily.

9. Infants may need more concentrated formulas (higher than the standard 20 kcal/oz [2.8 kJ/mL]) for a variety of reasons. Infant formulas can be reconstituted with less water to increase the caloric concentration. When concentrating a powder or concentrate formula by adding less water, what is the generally accepted *maximum* concentration recommended?

A. 22 kcal/ounce (3.1 kJ/mL)

B. 24 kcal/ounce (3.4 kJ/mL)

C. 27 kcal/ounce (3.8 kJ/mL)

D. 30 kcal/ounce (4.2 kJ/mL)

10. Severe food allergies require the use of a specialized infant formula. Which of the following is a formula of choice for a 5-month-old infant with severe food allergies?

A. Similac® Alimentum®

B. Monogen®

C. Pregestimil®

D. PurAmino®

11. A 10-year-old boy (weight, 35 kg) is in the PICU after suffering a burn in a motor vehicle accident. He has a transpyloric feeding tube with the tip in the jejunum. He suffered no injuries to his gastrointestinal tract. The burn team requests a high protein formula to begin tube feedings. Which of the following would be the *best* formula for this child?

A. Peptamen Junior®

B. Nutren Junior®

C. Peptamen Junior® HP

D. Pediasure® 1.5 Cal

12. Which of the following modular additives provides a source of both carbohydrate and fat?

A. Duocal®

B. Microlipid®

C. MCT Oil®

D. Polycose®

13. Which of the following would be the *most appropriate* initial formula for a premature infant with severe short bowel syndrome for whom human milk is not available?

A. Enfamil® AR

B. Similac® Special Care® 24

C. Enfamil® Enfacare®

D. Elecare®

14. Which of the following benefits has been associated with exclusive breastfeeding in infants?

A. Increased risk of obesity in later life

B. Increased risk of childhood leukemia

C. Decreased intelligence quotient (IQ) at 12 months of age

D. Decreased risk of viral gastroenteritis in infancy

15. Which of the following is a potential effect of lutein justifying its addition to infant formulas?

A. Improved neurodevelopment leading to better memory

B. Better calcium and phosphorus bone deposition that improves bone mineralization

C. More rapid maturation of the immune system

D. Improved visual acuity and protection from blue light

SELF-ASSESSMENT QUESTION-ANSWERS

1. **C.** Infants with galactosemia should not ingest lactose or galactose. Similac Pro-Total Comfort® 20 is lactose- and galactose-free; therefore, safe for this infant's nutrition. Human milk is high in lactose and maternal dietary changes cannot eliminate lactose from the infant's diet, so breastfeeding is contraindicated in this infant. Enfamil® NeuroPro™ Infant is a cow milk-based product which contains lactose. Enfamil NeuroPro™ Gentlease® has less lactose than standard cow milk-based infant formulas but still contains lactose.

2. **A.** Similac Pro-Advance® 20 is an appropriate infant formula for a healthy, near-term infant who is not being breastfed. Enfamil® Enfacare® is a post-discharge formula for premature infants going home from the hospital and the nutrient composition is not appropriate for a term infant. Similac® Special Care® 24 is a premature infant formula for low-birth-weight premature infants and not indicated in a healthy 37- week gestation infant. Neocate® Synveo® Infant is an amino acid-based infant formula indicated for children with various conditions that require a hypoallergenic or predigested formula.

3. **D.** Gerber® Good Start® Extensive HA® is an extensively hydrolyzed protein infant formula which can be used for infants with cow milk protein

allergy. Similac® PM 60/40 is a cow milk-based formula with low calcium and other alterations in mineral content for patients with hypercalcemia. Similac® Neosure® is a transitional formula for premature infants after they reach ~1.8 kg to 2 kg. It contains cow milk protein and would be unsuitable for this infant. Monogen® is a high medium chain triglyceride (MCT)-containing formula, which is derived from cow milk, so not suitable for this infant.

4. **C.** Infants with chylothorax should be initiated on a high MCT formula like Enfaport™. Limiting the long chain fatty acids ingested will help to diminish flow through the lymphatic system allowing time for the leak to fully heal. Nutramigen® Enflora™ LGG® (10%), Neocate® Infant DHA/ARA (8%), and Alfamino® Infant (43%) all contain some MCT; however, it is not enough for an infant with a chylothorax.
5. **B.** In the United States, mothers with HIV infection, irrespective of treatment status, are encouraged to not give their infants their breast milk either directly through nursing or by expressing a feeding with a bottle. Mothers with active tuberculosis, varicella, and H1N1 influenza should be physically separated from their infants until a specific amount of time for each condition has passed, but they may express milk and have someone feed it to their infant using a bottle.
6. **A.** Fresh expressed milk can be offered to a infant in a bottle, then the remaining can be placed in the refrigerator and used for the next feeding (within 4 hours). Since newborns eat every 2 to 3 hours, this is the best answer. Fresh expressed human milk should remain at room temperature for a maximum of 8 hours (4 hours is best). Human milk should remain refrigerated for no more than 8 days and frozen in a deep freezer for no more than 12 months.
7. **D.** For mild dehydration, the WHO guidelines for ORT recommend 50 mL/kg (1,000 mL) over the first 4 hours, trying to get the child to take at least 1 mL/kg (20 mL) every 2-5 minutes with a syringe, teaspoon, or medicine cup. A higher volume (50 mL, 2.5 mL/kg) may not be tolerated in a child with emesis. For moderate dehydration, the desired volume is 100 mL/kg (2,000 mL) with the same caveat about administering small volumes at a time.
8. **C.** Human milk is low in vitamin D content. The American Academy of Pediatrics and the World Health Organization recommend that infants who are exclusively breastfed receive a vitamin D supplement at a daily dosage of 400 international units shortly after birth, so this infant should be started on a vitamin D supplement. A term infant is born with adequate iron stores so that iron supplementation is not required until 4 months of age.
9. **C.** When concentrating infant formula with less water, each of the nutrients is provided in a greater concentration than if providing the standard 20 kcal/ounce (2.8 kJ/mL) formula. Therefore, unless under the direction of a nutrition specialist, infant formula should not be concentrated to a concentration higher than 27 kcal/ounce (3.8 kJ/mL).
10. **D.** Infants with severe food allergies will require a hypoallergenic, free amino acid-based formula such as PurAmino®. Similac® Alimentum® is a partially hydrolyzed formula and may be used for cow milk protein allergy in some infants but is not a free amino acid-based product and cannot be used for an infant with severe food allergies. Monogen® contains a higher proportion of calories from medium chain triglycerides but has intact protein; thus, it is unsuitable for this infant. Pregestimil® is an extensively hydrolyzed infant formula but is not a free amino acid-based formula.
11. **C.** Peptamen Junior® HP has a higher percentage of the calories from protein and would be most appropriate for this patient. Peptamen Junior®, Nutren Junior®, and Pediasure® 1.5 Cal are all formulas that are appropriate for a 10-year-old child, but they are not high-protein formulas.
12. **A.** The modular additive, Duocal®, contains both fat and carbohydrate. Microlipid® and MCT Oil® are modulars that provide additional calories from fat. Polycose® is a source of glucose polymers.
13. **D.** An infant with severe short bowel syndrome will require a hydrolyzed protein formula to allow for improved absorption. Of the formulas listed, Elecare® is the only one that is hydrolyzed and would be appropriate for an infant with short bowel syndrome. Enfamil® AR is a polymeric formula with added rice for infants with gastroesophageal reflux. It is contraindicated in preterm infants. Similac® Special Care® 24 is a premature infant formula, but it is not suitable for an infant with malabsorption. Enfamil® Enfacare® is also a polymeric formula used for premature infants during the transition from the hospital to home; it is not suitable for an infant with short bowel syndrome.
14. **D.** Human milk contains immunoglobulins from the mother that are transmitted to the infant. Breastfed infants have a decreased incidence of viral

gastroenteritis compared to their formula-fed peers. Human milk has many beneficial effects for the infant including a decreased risk of obesity and childhood leukemia as well as higher IQ scores in later life.

15. **D.** Lutein has significant effects in the eye, particularly protection against damage from blue light exposure. Other additives such as docosahexaenoic acid (DHA) are more associated with improved neurodevelopment. Additives such as lactoferrin are associated with immune function. None of the current formula non-nutrient additives improves bone mineralization.