



Pharmacists' guide to infant formulas for term infants

Jennifer D. Smith, Valerie Clinard, and Connie Lee Barnes

Abstract

Objective: To provide pharmacists with the basic knowledge to counsel caregivers in appropriate infant formula selection and use.

Summary: Although the majority of infants are initially breast-fed, a transition to infant formula by the age of 6 months, either as a supplement or a replacement for human milk, is common in the United States. Manufacturers have capitalized on this growing demand for infant formulas to more closely mimic human milk by creating a variety of formulations. The mainstay of the formula market is iron-fortified cow's milk, which may have a distinct variation in carbohydrate, protein, and fat sources, depending on the manufacturer. Formulations are also available to match specific needs of the infant or family, including added rice for reflux, partially or extensively hydrolyzed for allergen sensitivity, or soy based for a vegan diet preference.

Conclusion: With an extensive array of infant formulas available, pharmacists and caregivers can be overwhelmed when selecting an appropriate product. However, with careful questioning and a basic knowledge of the available formulas, an initial selection can be provided to caregivers. In addition to assisting in infant formula selection, pharmacists should provide information on proper preparation, handling, and storage of the product.

Keywords: Infant formulas, nutrition, pharmaceutical products.

J Am Pharm Assoc. 2011;51:e28–e37.

doi: 10.1331/JAPhA.2011.09125

Received August 24, 2009, and in revised form February 3, 2011. Accepted for publication February 10, 2011.

Jennifer D. Smith, PharmD, CPP, BC-ADM, CDE, is Associate Professor of Pharmacy Practice; **Valerie Clinard, PharmD**, is Assistant Professor of Pharmacy Practice; and **Connie Lee Barnes, PharmD**, is Associate Professor of Pharmacy Practice, College of Pharmacy and Health Sciences, Campbell University, Buies Creek, NC.

Correspondence: Jennifer D. Smith, PharmD, CPP, BC-ADM, CDE, College of Pharmacy and Health Sciences, Campbell University, PO Box 1090, Buies Creek, NC 27506. Fax: 252-243-9888. E-mail: jsmith@cchnc.org

Published concurrently in *Pharmacy Today* and the *Journal of the American Pharmacists Association*.

Accreditation information

Provider: American Pharmacists Association

Target audience: Pharmacists

Release date: April 15, 2011

Expiration date: April 15, 2014

ACPE number: 202-000-11-112-H04-P

CPE credit hours: 1.0 hour (0.1 CEUs)

ACPE activity type: Knowledge based

Learning level: 1

Fee: There is no fee associated with this activity for members of the American Pharmacists Association. There is a \$15 fee for nonmembers.



The American Pharmacists Association is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education (CPE). The ACPE Universal Activity Number assigned to this activity by the accredited provider is 202-000-11-112-H04-P.

Disclosure: The authors and APHA's editorial staff declare no conflicts of interest or financial interests in any product or service mentioned in this article, including grants, employment, gifts, stock holdings, or honoraria. For complete staff disclosures, please see the Education and Accreditation Information section at www.pharmacist.com/education.

Learning objectives

At the conclusion of this activity, the pharmacist will be able to:

- Discuss the differences between four to five commercial infant formulas currently available.
- Identify at least one infant formula that could be recommended for each of the following conditions: cow's milk allergy, protein hypersensitivity, and gastroesophageal reflux.
- Describe at least three counseling points to caregivers on appropriate infant formula preparation and storage.

Assess your knowledge

Take a moment to assess your current knowledge by reviewing the case study and answering the following question. The answer to the case study question appears later in the article.

P.R.'s 2-month-old infant has serious, continued eczema but no other dermatologic disorders, vomiting, or diarrhea. P.R. noticed the exacerbation of eczema after switching from human milk to Similac last month. P.R. questions whether another type of formula is available. Which of the following would be an appropriate recommendation?

- Extensively hydrolyzed protein formula
- Partially hydrolyzed protein formula
- Thickened formula
- Amino acid–based formula
- Lactose-free formula

If you have been a caregiver for a newborn or infant who needs an alternative to human milk, you may have experienced the potentially overwhelming process of selecting an appropriate formula. Questions caregivers may have include the following: (1) Is the generic as good as the brand name? (2) Do I need to provide a special formula or is basic formula sufficient? (3) Is ready-to-use better than powder formula? Although caregivers have ready access to pharmacists, many pharmacists are unaware of how to assist caregivers with this type of product selection.

Nearly 75% of U.S. infants are initially breast-fed; however, most are provided commercial infant formula as either a supplement to human milk or as the only source of nutrition by age 6 months.^{1,2} Commercial infant formulas are used for various reasons and produced to closely mimic the nutrients found in human milk.^{3,4} The Food and Drug Administration (FDA) regulates infant formulas and provides specific nutrient requirements for these products, which are made from modified cow's milk or soy products and differ in the oil used, protein profile, and amount of fat.³⁻⁷ During the manufacturing process, the nutrients are altered so the formula more closely resembles human milk.⁵ However, no formula can duplicate all constituents of human milk, such as growth factors, antibodies, and enzymes. Although human milk is considered the ideal source of nutrition for developing infants, commercially prepared infant formula is a nutritionally suitable alternative.

Objective

This article seeks to provide pharmacists with knowledge to counsel caregivers in appropriate infant formula selection and use.

Organ maturation and infant growth

Organ maturation is essential for proper digestion and nutrient absorption during infancy.⁸ The fetal gastrointestinal tract has the most growth during the third trimester of pregnancy. Therefore, infants delivered before 34 weeks' gestation may have different feeding requirements compared with term infants. Initially, the stomach of the term newborn (birth weight >5 lb, 8 oz) can only hold 20–90 mL; however, by the end of

the first month of life, the stomach is able to hold 90–150 mL.⁸ Therefore, newborns need to be fed every 2–3 hours, but this feeding interval is extended with increasing age. The feeding interval also may be extended in infants who are formula fed because formula is not emptied from the stomach as rapidly as human milk. Full-term infants are capable of carbohydrate digestion and have sufficient lactase activity. Therefore, most infants can tolerate lactose-containing formulas because lactase activity does not begin to decline until after 3 years of age in susceptible individuals. Protein digestion is variable during the first few months of life but will be comparable to that of an adult by 14 weeks of age.⁸

Weight, length/height, and head circumference are monitored for infants until 3 years of age using percentile-for-age growth charts (available at www.cdc.gov).⁸ These growth charts are intended for use in term infants, but can be used for premature infants after 40 weeks' gestation. The age of the preterm infant must be corrected. With proper nutrition, most term infants will double and triple weight by 4–6 and 12 months, respectively, and length will be doubled by the end of the first year.^{8,9}

Want to know more?

The focus of this article is on selecting a formula for healthy full-term infants. A more thorough review of infant nutritional standards can be found in APhA's *Handbook of Nonprescription Drugs*.

Nutrition standards for infants

The Food and Nutrition Board of the National Research Council is responsible for establishing dietary reference intakes and recommended dietary allowances for infants and children; however, FDA is responsible for the regulation of the amounts of nutrients added to formulas produced in the United States.⁸ For proper development, infant formulas should contain water, carbohydrates, protein, and fat in the recommended amounts. These requirements may differ slightly for premature infants initially, as well as for infants with certain medical conditions.

Full-term infants require carbohydrate intake of 60 g/day from age 0 to 6 months and 95 g/day from age 7 to 12 months.⁸ The primary source of carbohydrate in infant formulas is lactose.⁴ However, alternatives to lactose as a carbohydrate source include corn maltodextrin, corn syrup solids, and sucrose.

Protein requirements for infants and children younger than 4 years of age vary from 9.1 to 13.5 g/day.⁸ Research on the content of mature human milk reveals taurine, glutamic acid, and glutamine in abundance; thus, ensuring that formula-fed infants are receiving these amino acids is important.¹⁰ Similar quantities of glutamic acid and glutamine are found in human and cow's milk. However, taurine, which appears to provide a neuroprotective role in infants and children, is found in minimal quantities in cow's milk. Therefore, supplementing this essential amino acid during the manufacturing process of infant formulas is necessary.

Infants and children younger than 2 years require fat for proper growth and development. Originally, formulas were supplemented with linoleic (n-6) and linolenic (n-3) acid for fatty acid content, but more recently, the formulas have been supplemented with docosahexaenoic acid (DHA) and arachidonic acid (ARA).⁸ DHA and ARA are long-chain polyunsaturated fatty acids that are found in human milk.^{3,5} DHA and ARA are also found in higher amounts in the bloodstream of infants who are exclusively breast-fed compared with infants who are provided nutrition through a formula not containing DHA and ARA.³ Some DHA and ARA studies have demonstrated short-term positive effects on neurological development and visual function, but no long-term benefit data exist.⁵ Based on short-term data, manufacturers of infant formulas began to add DHA and ARA to products beginning in 2002. FDA has requested that manufacturers closely monitor these formulas through postmarketing surveillance because of the lack of long-term studies of these ingredients.

Available commercial infant formulas

Commercially prepared infant formula is available in three forms: ready to use, concentrated liquid, and powder. Ready-to-use infant formula is the most convenient type of infant formula because it does not require mixing with water.^{11,12} However, ready-to-use formula also is the most expensive. Both concentrated liquid and powdered formulas must be reconstituted with water before feeding. Thus, the safety of these formulas may be compromised if the water is of poor quality.¹ Powdered infant formula is the least expensive of the three formula types.^{1,5,13} Unlike ready-to-use and concentrated liquid formulas, powdered infant formula products are not considered sterile. They are not subjected to the same extremely high temperatures as liquid formulas during the manufacturing process and therefore may contain bacteria.^{1,5,13} Powdered infant formula has been associated with life-threatening infections attributed to the bacteria *Enterobacter sakazakii*.^{5,13,14} Thus, using powdered formulas for premature babies or those who are immunocompromised is not recommended. In addition to the form of infant formula used, caregivers must select either cow's milk- or soy-based formula and may require assistance in selecting a specialty formula if the infant is unable to tolerate the initial selection (Table 1).^{4-8,15-21}

Cow's milk-based formulas

The majority of available infant formulas are made with cow's milk that has been industrially modified to make the formula more comparable with human milk.^{5,12} Variations in different formulations of cow's milk formulas include the amount of protein, source of fat, and source of carbohydrate.⁴ In its natural state, cow's milk contains the proteins whey and casein in a ratio of 18:82. Formulas will vary in the amount of whey provided. For instance, some products will maintain the 18:82 ratio, whereas another formula may provide additional whey to more closely mimic the whey-to-casein ratio seen in human milk (range 48:52 to 60:40). Fat is provided through vegetable oils or a mixture of vegetable oils and animal fats. The primary

carbohydrate source in most commercially prepared infant formulas is lactose. However, maltodextrins and corn syrup solids may be alternatives used to provide a lactose-free formula or a formula that may be less irritating to the intestinal tract.

Many available cow's milk formulas and all soy-based formulas are available as iron-fortified products.⁷ Low-iron formulas are designated by a concentration less than 6.7 mg/L, and iron-fortified products contain an iron concentration of 6.7 mg/L or more.⁴ Before the 1960s, a high prevalence of iron deficiency in infants was noted; therefore, supplemental iron was added to infant formulas. The American Academy of Pediatrics (AAP) recommends iron-fortified formula for all infants and does not advise using low-iron formulas. Although low-iron formulas are available, they are for use in preterm infants under medical supervision.

While most infants do well on a cow's milk formula, approximately 2–4% of infants and young children will develop a cow's milk allergy (CMA).²² Onset of CMA occurs during the first few months of life and should not be confused with lactose intolerance attributable to primary lactase deficiency, which develops later in life.^{23,24} Symptoms of CMA may present as immediate (within minutes to 1 hour after ingestion) or late (up to 7–10 days after ingestion) onset.^{22,23} Rapid-onset symptoms include irritability, vomiting, wheezing, hives, rash, and bloody diarrhea.²³ Late-onset reactions are more common and include symptoms of loose stools, vomiting, irritability, and skin rashes. Most children with CMA will be able to tolerate milk by 3 years of age.²⁵ However, until then, formula-fed infants and toddlers may need a hypoallergenic formula, such as an extensively hydrolyzed protein (EHP) formula.

Lactose-free formulas

Lactose-free formulas are readily available, and their use does not demonstrate statistical differences in infant growth and development compared with using cow's milk formula.²⁴ In infants with acute gastroenteritis, secondary lactose intolerance may develop.⁴ For this, some pediatricians recommend using lactose-free formulas temporarily (up to 1 month) during the postdiarrheal refeeding period when symptoms of lactose intolerance are present. However, even with acute gastroenteritis, lactose digestion and absorption should be adequately maintained, thereby obviating the need for lactose-free formulas. Currently, AAP does not recommend lactose-free formulas to be used in infants with acute gastroenteritis, unless the infant has malnutrition or severe dehydration.²⁶

Soy formulas

Soy-based formulas do not contain cow's milk proteins or lactose; instead, they contain soy as the protein source.⁶ During the manufacturing process, vegetable oils (soy, palm, sunflower, olein, safflower, and coconut) are used as fat sources. Corn maltodextrin, corn syrup solids, and sucrose provide the carbohydrate content in these formulas. DHA and ARA are typically added to these formulations, and all available products contain iron.

Soy formulas have been available for almost 100 years, but more contraindications than indications exist.⁶ Soy-based for-

Table 1. Commercially available infant formulas^{4-7,15-21}

Formulation	Available products
Cow's milk–based formulas	Enfamil Lipil, Enfamil Premium Lipil, Enfamil Gentlease Lipil (replaces some of lactose with corn syrup), Similac Advance, Similac Advance Organic
Soy-based formulas	Enfamil Prosobee, Similac Soy Isomil, Similac Expert Care for Diarrhea, Good Start Soy PLUS
Partially hydrolyzed protein formulas	Enfamil Gentlease Lipil, Enfagrow Gentlease, Good Start Gentle PLUS, Good Start Soy PLUS
Extensively hydrolyzed protein formulas	Enfamil Nutramigen Lipil, Enfamil Nutramigen with Enflora LGG, Enfamil Pregestimil, Similac Expert Care Alimentum
Amino acid–based formulas	Neocate, Neocate Nutra, Neocate One+, Neocate Junior, Neocate Junior with Prebiotics, EleCare, Nutramigen AA Lipil
Formulas used for GERD	Enfamil AR (also marketed as RestFull), Similac Sensitive for Spit-Up
Lactose-free formulas	Enfamil Nutramigen Lipil, Enfamil Nutramigen with Enflora LGG, Similac Soy Isomil, Similac Sensitive for Spit-Up, Similac Sensitive (since the Early Shield was added, this product contains a very small amount of lactose), Good Start Soy PLUS
Formulas with probiotics	Enfamil Premium Lipil, Enfamil Nutramigen with Enflora LGG, Good Start Protect PLUS, Good Start 2 Protect PLUS
Formulas with prebiotics	Neocate Junior with Prebiotics, Enfamil Premium Infant with Natural Defense Dual Prebiotics, Similac Advance, Similac Sensitive, Similac Soy Isomil
Metabolic formulas/nutrient-altered formulas	Portagen, BCAD 1, BCAD 2, Phenyl-Free 1, Phenyl-Free 2, Phenyl-Free 2 HP, HCY 1, HCY 2, GA, LMD, OA 1, OA 2, PFD 1, PFD 2, WND 1, WND 2, 3232 A, RCF, Tyros 1, Tyros 2, Calcilo XD, Cyclinex-1, Cyclinex-2, Glutarex-1, Hominex-1, Phenex-1, Phenex-2, Pro-Phree, Propimex-1, Propimex-2, Pro Vi Min, Tyrex-1, Tyrex-2, MSUD Analog, XLeu Analog, XLys, XTrp Analog, XMet Analog, XMTVI Analog, XPhe, XTyr Analog, XMet, XCys Analog, Similac PM 60/40, Enfaport Lipil, Pregestimil Lipil
Next-stage/follow-up/or toddler formulas	Enfagrow Premium, Enfagrow Soy, Enfagrow Gentlease, Similac Go & Grow, Similac Go & Grow Soy, Good Start 2 Gentle PLUS, Good Start 2 Soy PLUS, Good Start 2 Protect PLUS, Nestle Follow-Up Good Start 2, Neocate One+, Neocate Junior, Neocate Junior with Prebiotics

Abbreviation used: GERD, gastroesophageal reflux disease.

mulas are indicated in infants with galactosemia and hereditary lactase deficiency and when a vegetarian diet is preferred.^{6,27} Some studies have evaluated the use of these formulas for preventing colic and/or managing infants with colic. However, AAP has issued a statement that using soy-based formulas for this purpose has no proven value. Some providers also recommend a trial use of soy-based formulas in infants with a documented CMA, given the great expense of EHP and amino acid–based formulas. However, AAP advises against this practice because of a 10–14% cross-sensitivity with soy-based formulas in patients with CMA^{6,28,29} and a 25–60% reaction in infants with enterocolitis.²⁸ In addition, speculation exists that soy isoflavones may reduce fertility in boys and induce early puberty in girls; however, the evidence is not conclusive.⁶

In infants treated for congenital hypothyroidism, soy-based formula should be used with caution because absorption of the thyroid hormone replacement may be altered when given concomitantly with soy.⁶ This effect on absorption may be seen by a prolonged increase in thyroid-stimulating hormone, which may necessitate a dose increase of thyroid hormone replacement. Thus, infants with congenital hypothyroidism who are fed soy-based formulas should be monitored closely.

Formulas with partially or extensively hydrolyzed protein

Infant formulas that are partially or extensively hydrolyzed reduce protein allergenicity in some infants because the protein

has been hydrolyzed.^{7,30} EHP formulas are referred to as hypoallergenic formulas, denoting that clinical trials have demonstrated that they can be tolerated by at least 90% of individuals allergic to cow's milk or soy-based formulas.^{25,30} However, the utility of EHP formula is minimized because of excessive cost (approximately three times that of standard formula) and its unpalatable taste.^{7,15} If atopic disease is associated with CMA, partially hydrolyzed protein (PHP) formulas should not be used because of the potential containment of cow's milk peptides. Approximately one-third to one-half of individuals with CMA may experience a reaction to PHP formulas. Thus, PHP formulas often are considered for prevention of allergies rather than treatment.

Both EHP and PHP formulas may be used in infants with a strong family history of atopic disease, as multiple studies have demonstrated that the use of these formulations may delay or prevent atopic dermatitis in infancy and early childhood.^{15,16,25} It appears that EHP formulas, specifically the extensively hydrolyzed casein-based formulas, may be more effective in atopic disease prevention than PHP formulas. However, it should be noted that neither EHP nor PHP formula has been directly compared with human milk for prevention of atopic diseases. Therefore, breast-feeding should never be avoided for this purpose.

Amino acid–based formulas

Amino acid–based formulas, also referred to as predigested formulas, are reserved for infants with protein hypersensitivity

or those who have failed therapy with EHP formulas.^{4,7} Similar to EHP formulas, their use is minimized by an exorbitant cost (compared with standard formula).⁴

Formulas for gastroesophageal reflux

Gastroesophageal reflux is a common complaint in infancy, reported at an incidence of 20–40%.³¹ Nonpharmacologic measures for treatment and prevention include elevating the head of the crib and providing small frequent meals and/or thickened feed. Pharmacologic agents are available, and surgery is an option for the most complicated cases. The available thickened formulas in the United States have added rice starch.^{7,32} This type of formula was developed to thicken once it reaches the stomach; thus, less regurgitation may be noted and standard bottle nipples may be used for feeding. Thickened feedings have demonstrated reduced regurgitation by approximately 0.6 episodes per day in studies, but the clinical significance of this

may be minimal.³¹ However, weight gain has been associated with thickened formulas and may be clinically important if the formula is used for a long duration. Concern exists regarding the use of thickening agents because decreased intestinal absorption of carbohydrates, fat, calcium, iron, zinc, and copper may occur. Unfortunately, a paucity of data exist to determine if the long-term use of thickening agents may result in harmful outcomes.

Other formulas

Formulas with prebiotics. Prebiotics are nondigestible dietary components that stimulate bifidobacteria and/or lactobacilli growth in the large intestines.^{9,33,34} This stimulation of beneficial intestinal flora eventually leads to a mild laxative effect and decreased pH of the stools.³⁴ It has been found that human milk contains oligosaccharide prebiotics and that infants who are fed formula supplemented with prebiotics have stools

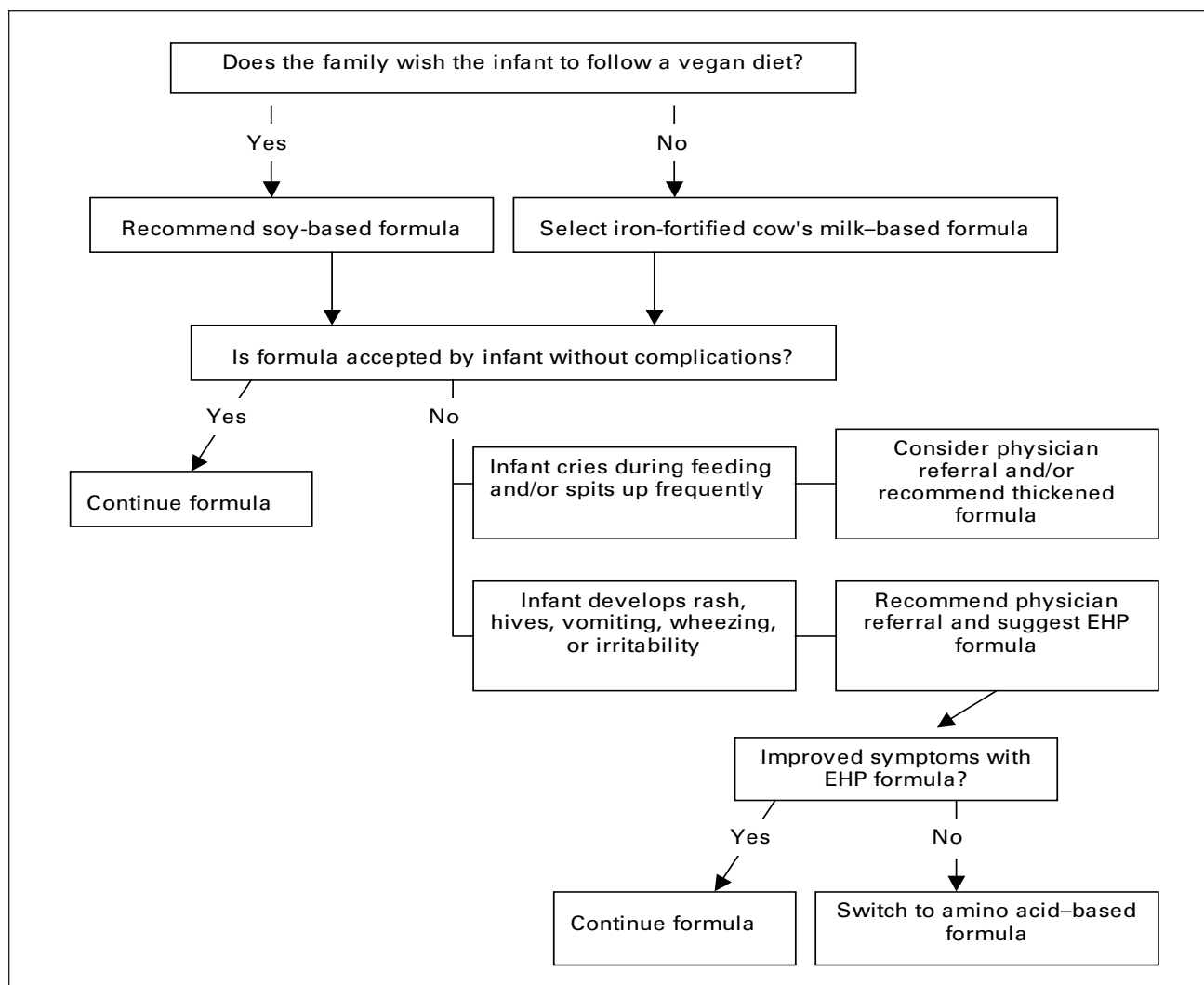


Figure 1. Selection of infant formula for a term infant^{4,3-7,12,25,30,31}

Abbreviation used: EHP, extensively hydrolyzed protein.

Table 2. Preparation of available infant formulas^{13,39}

Ready to use: No preparation necessary
Liquid concentrate: Dilute with equal parts clean water
Powdered formula: Typical use is one scoop per 2 oz clean water (check manufacturer directions). Water should be boiled first and allowed to cool before feeding to infant.
<i>Caution:</i> Counsel caregivers on the importance of reconstituting powders with the appropriate amount of water to avoid water toxicity, inadequate nutritional intake, or dehydration.

that more closely resemble the stools of breast-fed infants in frequency and pH.^{9,34} Prebiotics added to infant formulas are typically in the form of galactose oligosaccharide and fructose oligosaccharide, but further studies are needed to determine the utility of these agents in infant formulas.³⁴

Formulas with probiotics. Probiotics are living organisms (e.g., lactobacilli) that colonize in the gastrointestinal tract to promote health benefits.^{35,36} Probiotics differ from prebiotics in that an exogenous species of bacteria are introduced into the gut rather than stimulating an indigenous species.³⁷ Although this is a growing field of research, evidence for benefit of probiotics in infant formula is currently lacking.^{35,36}

Metabolic formulas. Metabolic formulas are designed for infants with rare metabolic disorders, including maple syrup urine disease, phenylketonuria, and tyrosinemia.³⁸ These formulas also contain a carbohydrate and fat source, but the protein is altered to account for the inborn error of metabolism.^{27,38} Metabolic formulas are intended to be used as supplemental nutrition and only under medical supervision.³⁸

Nutrient-altered formulas for specific disease. Some infants may require an adjustment in mineral intake, such as calcium, phosphorous, iron, and/or potassium.²⁷ Formulas for infants with renal impairment have alterations in the protein and electrolyte content, whereas formulas for infants with serum calcium disorders, neonatal hyperparathyroidism, or osteopetrosis contain lower levels of calcium and phosphorus, with some formulations available without vitamin D. Nutrient-altered formulas should be used only under medical supervision.

Follow-up formulas. These formulas contain a higher level of calcium needed for infants who are 6 months or older.⁷ However, no evidence supports that this type of formula is superior to other formulas in infants age 6–12 months.

Toddler formulas. Toddler formulas are manufactured for supplemental feeding for toddlers between 1 and 3 years of age.⁷ They contain increased protein and minerals and may be of benefit in toddlers who receive inadequate amounts of nutrition in solid feedings.⁴

Product selection guidelines

After the pharmacist understands the types of formulas available (e.g., cow's milk, soy), determining the initial formula for a healthy, full-term infant becomes quite simple. Figure 1 depicts a simplistic approach to product selection. As demonstrated in Figure 1, the pharmacist should recommend an iron-fortified

Table 3. Storage recommendations after reconstitution or opening of container³⁹

Refrigeration
Powder formula: Store no longer than 24 hours
Concentrated liquid: Store no longer than 48 hours
Ready-to-use formula: Store no longer than 48 hours
Room temperature
Powder, concentrate, or ready to use: Keep no longer than a total of 2 hours ^a
After feeding begins
All formulations should be discarded after 1 hour. Formula should not be refrigerated for later feedings.

^aIf bottle has been warmed, discard after 1 hour

cow's milk formula to all caregivers except those choosing a vegan diet for the infant. If the formula initiated is not tolerated, the pharmacist can assist based on symptoms (Figure 1)^{3–7,12,25,30,31} or dietary needs (Table 1),^{4–7,15–21} depending on the severity of the reaction to the intolerable formula. When cost is a consideration in selecting an infant formula, pharmacists can recommend the store brand formulations with confidence because FDA requires all formulas to contain the same nutrient density.¹²

Infant formula preparation

Safe preparation

Before preparing any infant formula, caregivers should take all precautions to minimize contamination by washing their hands. Surprisingly, this was an important step in formula preparation overlooked by many highly educated mothers in a study performed by Labiner-Wolfe et al.² from 2005 to 2007. In the study, 55% of mothers of infants aged 1.5 to 4.5 months neglected to wash their hands properly before preparing infant formula. Because proper hand washing is imperative in preventing the spread of infection to infants, this should be discussed with all caregivers, regardless of education level.

As noted previously, both liquid concentrate and powdered formulas require dilution with an appropriate amount of clean water (Table 2).^{1,13,39} If too much water is added, the infant may not receive adequate caloric and nutrient intake. Conversely, if an insufficient amount of water is added, the infant may suffer from dehydration, diarrhea, vomiting, and/or excessive intake of calories. Proper reconstitution of the powdered formula should be a diligent counseling point stressed by pharmacists, especially in times of economic difficulty. Rather than saving money by overdiluting the formula, caregivers may inadvertently induce water toxicity and malnutrition in the infant.^{1,40} Because powdered formulations are not sterile, the World Health Organization recommends mixing them with water that has been heated to no less than 158°F (70°C), in order to reduce the risk of infection with *E. sakazakii*, then cooling before feeding.^{3,41} However, according to FDA, it is safe to use ordinary tap water that has been boiled for 1 minute and then cooled.³ It is important to reinforce the need to cool the water quickly to body temperature (98°F) before feeding to prevent burns. In reality, nursery water and bottled water are commonly used for reconstitution without

heating of the water. Some concern exists that the use of bottled water to reconstitute powdered formula may contribute to excessive fluoride levels, thereby increasing the risk of fluorosis.⁴² Caregivers should follow the recommendations of FDA but may consider using nursery water or bottled water for reconstitution when traveling or in compromised situations.

Safe storage

Because of the potential for substantial microbial growth in reconstituted infant formula, changes have been made to storage recommendations.^{13,39} Previously, storing formula prepared from powder in a refrigerator for no more than 48 hours was considered a safe recommendation. However, this recommendation has now been changed to no more than 24 hours' refrigeration for reconstituted powder formulas. Storage recommendations for infant formulas are noted in Table 3.³⁹ Insulated bags and ice packs may be used for infant formula storage when traveling.⁴¹

Conclusion

Selecting the appropriate formula for an infant can be as challenging for health professionals as it is for caregivers. However, pharmacists can help in the selection with proper questioning (Figure 1). Term infants should be initiated on a cow's milk-based formula unless the family prefers a vegan diet for the infant. An alternate formula should be recommended only if the infant develops complications after the initiation of cow's milk- or soy-based formula. Rice-thickened formulas may be recommended for infants experiencing frequent spit up and fussiness, whereas EHP formulas may be recommended for infants with a suspected allergy to cow's milk-based formulas. No titration period is necessary when switching formulas. Caregivers should be encouraged to report adverse events associated with the use of infant formulas to health professionals. Health professionals then should report this information to FDA's MedWatch program (800-332-1088 or www.fda.gov/medwatch).¹³

All caregivers should be counseled on proper preparation and storage of infant formula, regardless of education level. This counseling should include proper hand washing, use of water for mixing (if necessary), whether refrigeration is necessary, and the length of time that mixed or open formula is considered usable. Insulated bags and ice packs also should be recommended for outings and traveling with prepared formula.

Although pharmacists may not typically receive an abundance of questions regarding infant formula initiation, they can be a valuable resource to caregivers who are confused and intimidated by the vast selection of available infant formulas. By understanding the difference in formula types (ready to use, liquid concentrate, and powder) and constituents (variations in fat, proteins, and carbohydrates), pharmacists can provide appropriate recommendations for infant formulas. Further, pharmacists can ensure that caregivers are receiving appropriate consultation on proper preparation, handling, and storage of infant formulas, in an effort to prevent the spread of infection.

Assess your knowledge case study response

Answer: a. Rationale: An extensively hydrolyzed protein (EHP) formula would be an appropriate selection for an infant with an eczema flare. A partially hydrolyzed protein formula would be sufficient and should be selected if an EHP formula is not tolerated. Amino acid-based formulas should be a last-line option because of increased expense and decreased palatability.

References

- Centers for Disease Control and Prevention. Breastfeeding report card: United States: 2008: outcome indicators. Accessed at www.cdc.gov/breastfeeding/pdf/2008BreastfeedingReportCard.pdf, March 9, 2011.
- Labiner-Wolfe J, Fein SB, Shealy KR. Infant formula-handling education and safety. *Pediatrics*. 2008;122(suppl 2):S85-90.
- Food and Drug Administration. FDA 101: infant formula. Accessed at www.fda.gov/ForConsumers/ConsumerUpdates/ucm048694.htm, March 9, 2011.
- Kleinman RE (Ed.). *Pediatric nutrition handbook*. 6th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009:61.
- World Health Organization. *Infant and young child feeding: model chapters for textbooks for medical students and allied health professionals*. Geneva: World Health Organization; 2009.
- Bhatia J, Greer F, American Academy of Pediatrics Committee on Nutrition. Use of soy protein-based formulas in infant feeding. *Pediatrics*. 2008;121:1062-8.
- Tsang G. Infant formula 101. Accessed at www.healthcastle.com, March 23, 2009.
- Chessman KH. Infant nutrition and special nutritional needs of children. In: Berardi RR, Ferreri SP, Hume AL, et al., Eds. *Handbook of nonprescription drugs*. 16th ed. Washington, DC: American Pharmacists Association; 2009:467-96.
- Meyer R. Infant feeding in the first year. 1. Feeding practices in the first six months of life. *J Fam Health Care*. 2009;19:13-7.
- Agostoni C, Carratu B, Boniglia C, et al. Free amino acid content in standard infant formulas: comparison with human milk. *J Am Coll Nutr*. 2000;19:434-8.
- FamilyDoctor.org. Infant formula. Accessed at <http://familydoctor.org/online/famdocen/home/children/parents/infants/178.html>, March 9, 2011.
- Mayo Clinic. Infant formula: which formula is right for your baby? Accessed at www.mayoclinic.com/health/infant-formula/PR00058, March 23, 2009.
- Food and Drug Administration. Health professionals letter on *Enterobacter sakazakii* infections associated with use of powdered (dry) infant formulas in neonatal intensive care units. Accessed at www.fda.gov/Food/FoodSafety/Product-SpecificInformation/InfantFormula/AlertsSafetyInformation/ucm111299.htm, March 9, 2011.
- Centers for Disease Control and Prevention. *Enterobacter sakazakii* infections associated with use of powdered infant formulas—Tennessee, 2001. *JAMA*. 2002;287:2204-5.
- Thygarajan A, Burks AW. American Academy of Pediatrics recommendations on the effects of early nutritional interventions on the development of atopic disease. *Curr Opin Pediatr*. 2008;20:698-702.

16. Greer FR, Sicherer SH, Burks AW, et al. Effects of early nutritional interventions on the development of atopic disease in infants and children: the role of maternal dietary restriction, breastfeeding, timing of introduction of complementary foods, and hydrolyzed formulas. *Pediatrics*. 2008;121:183–91.
17. Abbott Laboratories. Similac. Accessed at <http://similac.com/baby-formula>, June 25, 2010.
18. Nestle. Gerber Good Start. Accessed at www.gerber.com/All-Stages/products/formula.aspx, March 9, 2011.
19. Mead Johnson & Company. Enfamil Healthcare Professional Resource Center. Accessed at www.mjn.com/app/iwp/hcp2/content2.do?dm=mj&id=/HCP_Home2/ProductInformation/hcpProducts/hcpInfants&iwpst=MJN&ls=0&csred=1&r=3473697522, January 28, 2011.
20. Abbott Laboratories. Abbott Nutrition for Healthcare Professionals. Accessed at <http://abbottnutrition.com/Infant-And-New-Mother/Infant-And-Baby-Formula.aspx>, January 28, 2011.
21. Nutricia Advanced Medical Nutrition. Metabolics at a glance. Accessed at www.shsna.com/pages/metabolics_glance.htm, January 28, 2011.
22. Hill DJ, Murch SH, Rafferty K, et al. The efficacy of amino acid-based formulas in relieving the symptoms of cow's milk allergy: a systematic review. *Clin Exp Allergy*. 2007;37:808–22.
23. Nemours Foundation. KidsHealth: milk allergy in infants. Accessed at http://kidshealth.org/pagmanager.jsp?dn=KidsHealth&lic=1&ps=107&cat_id=132&article, March 9, 2011.
24. Heyman MB. Lactose intolerance in infants, children, and adolescents. *Pediatrics*. 2006;118:1279–86.
25. Høst A, Halken S. Hypoallergenic formulas: when, to whom and how long: after more than 15 years we know the right indication. *Allergy*. 2004;59(suppl 78):45–52.
26. King CK, Glass R, Bresee JS, et al. Managing acute gastroenteritis among children (oral rehydration, maintenance, and nutritional therapy). *MMWR Recomm Rep*. 2003;52(RR-16):1–16.
27. Joeckel RJ, Phillips SK. Overview of infant and pediatric formulas. *Nutr Clin Pract*. 2009;24:356–62.
28. American Academy of Pediatrics, Committee on Nutrition. Hypoallergenic infant formulas. *Pediatrics*. 2000;106:346–9.
29. Cox H, Husby S. Debate: current challenges in the management of food allergies. *J Pediatr Gastroenterol Nutr*. 2008;47(suppl 2):S53.
30. Bahna SL. Hypoallergenic formulas: optimal choices for treatment versus prevention. *Ann Allergy Asthma Immunol*. 2008;101:453–9.
31. Horvath A, Dziechciarz P, Szajewska H. The effect of thickened-feed interventions on gastroesophageal reflux in infants: systematic review and meta-analysis of randomized, controlled trials. *Pediatrics*. 2008;122:e1268–77.
32. Mead Johnson & Company. Enfamil: infant formula. Accessed at www.enfamil.com/infant-formula-and-nutrition.htm, March 9, 2011.
33. Osborn DA, Sinn JK. Prebiotics in infants for prevention of allergic disease and food hypersensitivity. *Cochrane Database Syst Rev*. 2007;4:CD006474.
34. Rao S, Srinivasjois R, Patole S. Prebiotic supplementation in full-term neonates. *Arch Pediatr Adolesc Med*. 2009;163:755–64.
35. Osborn DA, Sinn JK. Probiotics in infants for prevention of allergic disease and food hypersensitivity. *Cochrane Database Syst Rev*. 2007;4:CD006475.
36. Braegger C, Chmielewska A, Decsi T, et al. Supplementation of infant formula with probiotics and/or prebiotics: a systematic review and comment by the ESPGHAN Committee on Nutrition. *J Pediatr Gastroenterol Nutr*. 2011;52:238–50.
37. Parracho H, McCartney AL, Gibson GR. Probiotics and prebiotics in infant nutrition. *Proc Nutr Soc*. 2007;66:405–11.
38. Food and Drug Administration. Current marketing and use of powdered infant formula in the United States. Accessed at www.fda.gov/ohrms/dockets/ac/03/briefing/3939b1_tab4c_cover-sheet.pdf, January 22, 2011.
39. Enfamil. Preparing your baby's bottle. Accessed at www.enfamil.com/app/iwp/enf10/content.do?dm=enf&id=/Consumer_Home3/NewBorns/NewBorns_Articles/preparingbottle&iwpst=B2C&ls=0&csred=1&r=3477143060, March 9, 2011.
40. American Academy of Pediatrics. Water intoxication in the news: a reminder to use formula according to directions. Accessed at www.aap.org/advocacy/releases/dec08infantformula.htm, January 22, 2011.
41. Herbold NH, Scott E. A pilot study describing infant formula preparation and feeding practices. *Int J Environ Health Res*. 2008;18:451–9.
42. Buzalaf MA, Damante CA, Trevizani LM, Granjeiro JM. Risk of fluorosis associated with infant formulas prepared with bottled water. *J Dent Child*. 2004;71:110–3.

CPE exam

Instructions: The assessment test for this activity must be taken online; please see “CPE information” below for further instructions. There is only one correct answer to each question. This CPE activity will be available online at www.pharmacist.com no later than April 30, 2011.

1. S.P. presents with several manufacturer samples for infant formulas that she received during her pregnancy. She has breast-fed her infant for the past 3 months but would now like to initiate an infant formula as a human milk replacement. The infant was full term and has tolerated the human milk well. The family has no dietary restrictions. Which of the following types of infant formulas would be the most appropriate to suggest to S.P. for formula initiation?
 - a. Similac Soy Isomil
 - b. Enfamil Premium Lipil
 - c. Good Start Gentle PLUS
 - d. Similac Go & Grow
 - e. Neocate
2. A caregiver presents to the pharmacy counter holding Enfamil AR Lipil, which was recommended for her infant who spits up frequently. The caregiver notes that the container labeling states it is a thickened formula. Should she purchase bottle nipples with larger holes?
 - a. Yes; the formula will thicken upon standing in the bottle, necessitating larger nipple opening for optimal fluid flow.
 - b. Yes; the formula will be extremely thickened when first mixed, necessitating a larger nipple opening for optimal fluid flow.
 - c. No; the thickened formula will ensure the infant cannot take in too much fluid at one time, thus minimizing frequent spit up.
 - d. No; the thickened formula will flow as regular formula and will not become thickened until it reaches the stomach.
3. A mom presents to the pharmacy with her crying 4-month-old, 17-lb infant. She notes that she initiated Good Start Gentle Plus 3 days ago, and during the past few hours, the infant has developed hives and wheezing. She continues to cry, which seems to make the wheezing worse. No other changes have occurred in the diet or environment of the child. What is your recommendation on a dose of Benadryl for her infant and a different formula?
 - a. Give 0.5 tsp Children's Benadryl (diphenhydramine 12.5 mg/5 mL) for hives and recommend switching the formula to a thickened formula
 - b. Give 0.5 tsp Children's Benadryl (diphenhydramine 12.5 mg/5 mL) for hives and recommend an extensively hydrolyzed protein formula
 - c. Give 0.5 tsp Children's Benadryl (diphenhydramine 12.5 mg/5 mL) for hives and recommend an amino acid-based formula.
 - d. Give 0.5 tsp Children's Benadryl (diphenhydramine 12.5 mg/5 mL) for hives and continue current infant formula.
 - e. Give the caregiver an immediate referral to the emergency department.
4. Amino acid-based formulas are for infants with protein hypersensitivity because they are:
 - a. Lactose-free formulas.
 - b. Completely predigested formulas.
 - c. Extensively hydrolyzed formulas.
 - d. Necrotizing enterocolitis resistant.
 - e. Fortified with rice starch.
5. Which of the following formula preparation/storage counseling points regarding powdered formulas is correct?
 - a. To reconstitute, dilute with equal amounts of powder and clean water.
 - b. After reconstituting, store in the refrigerator for no longer than 48 hours.
 - c. After reconstituting, store at room temperature for no longer than 72 hours.
 - d. After feeding has begun, discard unused portion after 1 hour.
 - e. After feeding, refrigerate unused reconstituted portion for a later feeding.

6. Which of the following infant formulas would be most appropriate to recommend as an initial formula to a family that prefers a vegan diet for their 5-month-old infant?
 - a. Good Start Gentle PLUS
 - b. Enfamil Lipil
 - c. Similac Advance
 - d. Enfagrow
 - e. Similac Soy Isomil
7. J.P. visits the pharmacy with his 18-month-old child. The child tolerated Enfamil Lipil formula well but now refuses to switch to cow's milk. J.P. also is concerned because his child only wants juice, bananas, or cookies. He has been unsuccessful in transitioning the toddler to vegetables, meats, or a variety of fruits. Which of the following would be the most appropriate recommendation for J.P.'s child to improve nutrition?
 - a. Continue Enfamil Lipil formula
 - b. Begin Enfamil Nutramigen Lipil
 - c. Begin Enfamil AR
 - d. Begin Enfacare Lipil
 - e. Begin Enfagrow Premium
8. Which of the following is not a symptom of cow's milk allergy?
 - a. Hives
 - b. Tachycardia
 - c. Bloody diarrhea
 - d. Vomiting
 - e. Irritability
9. Which two ingredients are now routinely added to infant formulas for the potential positive effects on neurological development and visual function?
 - a. α -Linoleic acid and vitamin A
 - b. Vitamins B₆ and B₁₂
 - c. Docosahexaenoic acid and arachidonic acid
 - d. Calcium and vitamin D
 - e. Eicosapentaenoic acid and fish oil
10. Which of the following statements is true regarding infant formulas with probiotics?
 - a. Probiotics are dietary components that stimulate growth of good bacteria in the gut.
 - b. Probiotics are added to formula in the form of galactose oligosaccharides.
 - c. Infant formulas with probiotics are a preferred choice in infants with maple syrup urine disease.
 - d. Powdered formulas containing probiotics should be refrigerated before mixing.
 - e. Lactobacillus is an example of an organism found in infant formulas containing probiotics.

CPE information

To obtain 1.0 contact hour of CPE credit (0.1 CEUs) for this activity, complete and submit the CPE exam online at www.pharmacist.com/education. A Statement of Credit will be awarded for a passing grade of 70% or better. You will have two opportunities to successfully complete the CPE exam. Pharmacists and pharmacy technicians who successfully complete this activity before April 15, 2014, can receive credit.

Your Statement of Credit will be available online immediately upon successful completion of the CPE exam.

CPE instructions: Get your documentation of credit now! Completing a posttest at www.pharmacist.com/education is as easy as 1-2-3.

1. Go to Online CPE Quick List and click on the title of this activity.
2. Log in. APhA members enter your user name and password. Not an APhA member? Just click "Create one now" to open an account. No fee is required to register.
3. Successfully complete the CPE exam and evaluation form to gain immediate access to your documentation of credit.

Live step-by-step assistance is available Monday through Friday 8:30 am to 5:00 pm ET at APhA Member Services at 800-237-APhA (2742) or by e-mailing InfoCenter@pharmacist.com.