Specialized Infant Formulas

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As reported in a previous *In Brief* on standard infant formulas, there are many choices for both standard (cow milk protein formulas) and specialized infant formula products available on the market. It is, therefore, incumbent on the pediatrician to have a good working knowledge of the indications for and benefits of the use of specialized formulas. This *In Brief* addresses the topic of specialized infant formulas.

The first soy formula was marketed in the 1920s, and soy formula currently makes up most of the nonstandard infant formulas sold, which includes approximately 20% of the US formula market. Soy formulas contain soy as the protein, and the primary carbohydrate sources are glucose polymers, corn syrup, maltodextrin, and sucrose. Hence, all soy formulas are lactose free. Although the American Academy of Pediatrics generally supports the use of standard cow milk protein infant formulas as the formula of choice for those who choose not to breastfeed, there are a few circumstances in which soy formulas should be selected. Children with galactosemia and hereditary lactase deficiency need to eliminate lactose intake from their diet, and families seeking a vegan alternative want to avoid the cow milk protein. It is rare for infants to have significant lactose intolerance before 2 years of age, hence there is little evidence that soy formulas or lactose-reduced or lactose-free formulas reduce the symptoms of colic or stooling difficulties despite the perceptions of parents. Soy formula is not recommended for use in preterm infants with a birthweight less than 1,800 g because premature infants who have been fed this have had lower serum phosphorous levels, higher alkaline phosphatase levels, and an increased degree of osteopenia. Also, for infants suspected of having a cow milk protein allergy (CMPA), soy formula should not be used because 5% to 14% of those who have cow milk allergy also have soy protein allergy. Concerns have been raised about the potential effects of phytoestrogens and isoflavones, which are present in higher levels in soy formula. However, retrospective follow-up studies of adults who were fed exclusively with soy formula during infancy show no reproductive or estrogen-related consequences.

During the past decade, a variety of more specialized infant formulas have reached the market. These formulas claim to treat or prevent conditions such as fussiness, gastroesophageal reflux disease (GERD), and atopy, among others. These formulas include those that may contain partially hydrolyzed proteins, carbohydrate blends that are lactose free or lactose reduced, thickeners, prebiotics/probiotics, or a combination thereof. The evidence is inconclusive as to whether these formulas make a difference for children with GERD or fussiness.

Formulas that contain partially hydrolyzed cow milk protein (PHFs) or extensively hydrolyzed cow milk protein (EHFs) are another group of specialty formulas. Hydrolyzed proteins consist of a combination of short-chain peptides and free amino acids. There is evidence that the use of EHFs or PHFs in high-risk infants (first-degree relatives who had allergy) reduces infant and childhood

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Questions and Answers for Consumers Concerning Infant Formula. US Food and Drug Administration. US FDA website. Available at: https://www.fda.gov:80/FDAgov/ForConsumers/ConsumerUpdates/ucm048694.htm

allergy and atopic dermatitis compared with standard cow milk–based formula. There is no evidence that the hydrolyzed formulas are superior to human milk in preventing these conditions. True CMPA has an incidence of 2% to 5% in infants. Infants with a confirmed diagnosis of CMPA should be fed human milk or, if formula fed, EHFs. A more severely affected group of infants, including those with non-IgE–mediated enterocolitis, failure to thrive, severe eczema, and/or symptoms during exclusive breastfeeding, may respond better to elemental/amino acid–based formulas than to hydrolyzed formulas that additionally contain short-chain peptides. Hence, if an infant does not respond appropriately to EHF, an elemental formula is next trialed. A small number of infants with colic do respond to hydrolyzed formulas, so a short trial of these formulas could be considered.

Formulas marketed to treat GERD include rice starches and/or other thickeners. The data are also mixed and inconclusive as to whether thickened milk is associated with reduced GERD symptoms such as crying and irritability. Prethickened formulas are not superior to the postmarket addition of cereals to standard infant formula or human milk. Owing to the recent concerns about arsenic in rice, and the prolonged exposure to rice cereals in infants that use thickened formulas, the American Academy of Pediatrics has made a recommendation to substitute oatmeal instead of rice cereal for postmarket thickening of formula or human milk. Commercial thickening agents should not be used owing to the association with necrotizing enterocolitis.

The addition of prebiotics and probiotics to some infant formulas is designed to more closely align the intestinal flora of formula-fed infants to that of breastfed infants. Specifically, most intestinal flora in breastfed infants consists of *Bifidobacterium* and *Lactobacillus*. Meta-analyses show that there is some evidence that the addition of prebiotics (nondigestible carbohydrates that promote the development of these bacteria in the colon) or probiotics (live organisms that colonize the colon) to infant formula may prevent the atopic conditions eczema and asthma. These bacteria seem to be an integral part of the development of the intestinal and systemic immune response. In addition, they are believed to be a component of the development of protection against pathogen colonization in the gut and aid nutrient absorption. There is also evidence that probiotics may prevent necrotizing enterocolitis in very low birthweight (1,000–1,500 g) infants.

In summary, there are myriad infant formula choices available to families. During the past 15 years there have been significant strides by infant formula manufacturers to more closely mimic the gold standard, human milk. There are data to support claims of health benefits from some of these changes, but not for all. The pediatrician plays an integral role in navigating these choices.

COMMENT: Only a small proportion of infants truly meet the criteria to require a specialized formula. Pediatricians need to be knowledgeable about these criteria and provide accurate advice. Although it used to be relatively easy to know the components of specialized formulas based on their names (ie, soy formulas had soy in their name and those with hydrolyzed proteins were confined to a few brands, the more widespread incorporation of hydrolyzed protein in brand names that were previously standard formulas has made this confusing. Specialized formulas for reflux, gassiness, or fussiness may have modifiers such as gentle, sensitive, for spit up, etc.

Special formulas for preterm infants have been developed and used for infants in the NICU, although breastfeeding is always encouraged. These preterm formulas have a higher caloric density of 24 kcal/oz and contain higher amounts of taurine, whey as the predominant protein, medium-chain triglycerides, calcium, phosphorous, and vitamins A and D. Preterm formulas are usually discontinued at hospital discharge when the infant weighs between 1,800 and 2,000 g and is approximately 34 weeks' gestation. These formulas are then replaced with preterm transitional formulas that have caloric densities of 22 kcal/oz and are continued until 6 to 9 months of age. Dr Milbrandt's *In Brief* can serve as a helpful guide to pediatricians to navigate formula choices.

– Janet R. Serwint, MD
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ANSWER KEY FOR MAY 2017 PEDIATRICS IN REVIEW

The Interplay between Pharmacokinetics and Pharmacodynamics: 1. E; 2. C; 3. E; 4. D; 5. B.
The Poisoned Pediatric Patient: 1. B; 2. B; 3. A; 4. E; 5. D.
Juvenile Idiopathic Arthritis – Changing Times, Changing Terms, Changing Treatments: 1. B; 2. D; 3. B; 4. E; 5. E.