# Food allergy and breast-feeding

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**ABSTRACT**

*Breast-feeding is currently recommended as the optimal source of nutrition for infants; however, it is known that some individuals can excrete enough food antigens in breast milk to result in allergic reactions in infants, especially those already highly sensitized. These reactions can include non–immunoglobulin E (IgE) mediated reactions, such as atopic dermatitis or gastrointestinal symptoms, and IgE-mediated reactions, such as anaphylaxis, although rare. Food reactions in infants who are breast-fed is a unique challenge because identifying the culprit foods may be more difficult and special consideration must be taken in ensuring proper nutrition during periods of food avoidance for both the infant and mother. This article reviews what is currently known about food allergy in infants who are breast-fed as well as offers insights into a proposed evaluation.*

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The period of breast-feeding may play a role in food allergy, both in the sensitization phase or in the presentation of food allergy in already sensitized infants. Breast-feeding could impact sensitization to foods by either enhancing or preventing food sensitization, depending on the presence and levels of food antigens in human milk, the context of other immunologically active components, and the length of breast-feeding. The presence of several immunologically active components, including immunoglobulin A (IgA), immune complexes, cytokines, and oligosaccharides in human milk have been associated with the protection against food allergy during breast-feeding (for details see a recent review article[1]). Although the epidemiologic studies that assessed the effect of breast-feeding on the development of atopic disease concurred that breast-feeding provides benefit for atopic eczema and wheezing, the evidence is insufficient on prevention of food allergy,[2] which is reflected in the most recent American Academy of Pediatrics (AAP) guidelines.[3] This is due to small number of studies, varying definitions of breast-feeding and atopic diseases, reverse causality, the role of gene-environment interactions, and the lack of randomized controlled trials due to their unethical nature. Because the composition of human milk varies among mothers, so may the antiallergic protection it provides.

Breast-feeding may also contribute to the presentation of food allergy in infants by delaying symptom onset of food allergy until foods are directly introduced to the infant if the mother does not secrete significant amounts of food antigen into her breast milk or the levels are so low that the symptoms are not outwardly obvious (*e.g.*, atopic dermatitis or nonimmediate gastrointestinal symptoms). Although reported, it is rare for immediate symptoms to be seen in infants due to food allergens passed through mother's milk. The presence of food antigens in human milk has been shown to result in symptoms in some infants already highly sensitized during breast-feeding,[4] although their role in initial sensitization to foods is debated, and, to our knowledge, no randomized controlled trials exist on the topic.

## PRESENCE OF FOOD ANTIGENS IN HUMAN MILK

Dietary antigens that have been detected in mothers' milk include hen's egg ovalbumin,[5] cow's milk (CM) $\beta$-lactoglobulin,[4] wheat gliadin,[6] and peanut and Ara h2 and Ara h 6.[7] There is a large variation of the presence and levels of food allergens in human milk, and up to two-thirds of women do not secrete detectable levels of food allergens into their milk even after consumption of these foods.[1] After specific food consumption, 15–47% of the mothers had no detectable $\beta$-lactoglobulin,[4] 27% of mothers had no detectable ovalbumin,[5] and 65% had no detectable Ara h 2 in their milk.[7] As a reference, the level of $\beta$-lactoglobulin reported in human milk reaches those levels of milk protein peptides reported for hydrolyzed hypoallergenic infant formulas. $\beta$-Lactoglobulin is used as a marker for CM antigen excretion because there is no endogenous $\beta$-lactoglobulin

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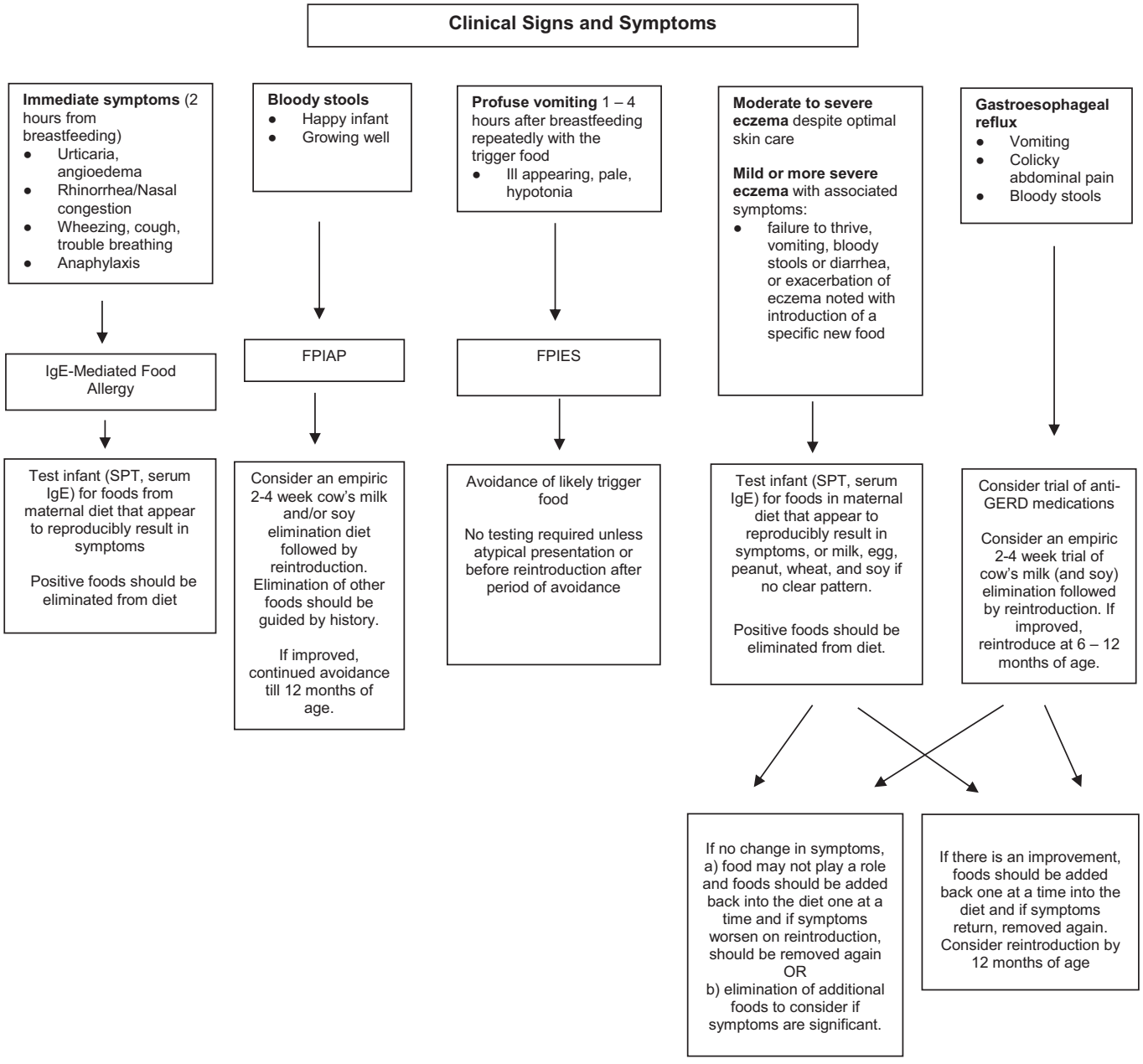


***Figure 1.*** *Suggested algorithm in the management of infants who are breast-fed and with concern of food allergies. Elimination of specific food in the diet refers to the maternal diet. If the infant is already fed the same foods, then a trial of elimination is recommended in the infant and mother unless symptoms were not present during exclusive breast-feeding and only occurred after the trigger food was introduced to the infant, in which case the mother's diet does not need to be restricted. Bloody stools refer to frank blood; point of care guaiac testing is not routinely recommended. FPIAP = Food protein–induced allergic proctocolitis; FPIES = food protein-induced enterocolitis syndrome; SPT = skin-prick testing. Adapted from Ref. 11.*

in human milk. Casein can be found in human milk, and it is highly homologous to bovine casein; therefore, it was not used as a marker for antigen excretion. There is variation in the timing of the appearance of antigens (1–2 hours for CM, 1–8 hours for peanut, and up to 8 hours for egg), the peak concentration (up to 10 ng/mL for $\beta$-lactoglobulin, 50–400 ng/mL for Ara h 2 and Ara h 6, and 4–8 ng/mL or even higher for hen's egg ovalbumin), and the disappearance of antigens differs between foods and individuals (1 to 12 hours). We demonstrated the role for dietary antigens in human milk in inducing symptoms in already sensitized infants during a physician-supervised oral food challenge.[4] The majority of those with a positive CM challenge result through human milk reacted within 2–9 hours from the last dose; simultaneously, increased levels of $\beta$-lactoglobulin in human milk were demonstrated.

Although rare, symptoms of food allergy may not resolve even after strict elimination of major allergenic foods in lactating mother's diet and discontinuation of breast-feeding and initiation of hypoallergenic formula may be required. This may be due to (1) inadequate extent of or adherence to maternal food elimination diet, (2) symptoms not being related to food allergy, or (3) infant reacting to endogenous human milk proteins. This could be due to cross-reactivity between bovine and human milk proteins, many of which have a high level of similarity and resulting extremely high identity between specific IgE–binding epitopes[8] or due to genuine sensitization to endogenous human milk proteins. When using immunoblot inhibition and skin-prick tests (SPT), IgE reactive to human milk antigens was detected in the subjects allergic to CM.[9] Utilizing a rat basophilic leukemia mediator release assay (RBL-2H3 cells) and activation assays (basophil activation test), the presence of cross-linking IgE antibodies to human milk $\alpha$-lactalbumin has been demonstrated in individuals with milk allergy,[10] including infants who were showing symptoms, despite a maternal strict and extensive food elimination diet.[8]

## PRESENTATION, EVALUATION, AND MANAGEMENT OF FOOD ALLERGY IN AN INFANT WHO WAS BREAST-FED

Overall, the evaluation of food allergies in infants who are breast-fed involves a thorough history taking. For certain conditions, a diagnostic elimination diet should be attempted but with the understanding that foods should be introduced back into the diet if no improvement and/or to confirm benefit so as to limit unnecessary avoidance. A detailed summary of the literature on the presentation of food allergic symptoms in an infant who was breast-fed was recently published by us.[11] An algorithm is shown in Fig. 1 as a guide for the management of these conditions.[11]

### IgE-Mediated Food Allergy

IgE-mediated food allergy is uncommon in an infant who is exclusively breast-fed, although there have been a few case reports.[12,13] In patients with symptoms suggestive of an IgE-mediated food allergy within 2 hours of breast-feeding, a detailed history, including symptoms and maternal diet, are vital in the proper diagnosis. A symptom and food diary is highly recommended in these cases because it can help to elicit possible triggers. Based on the history, SPT and/or serum specific IgE testing should be done to the suspected foods. Foods with positive testing should be avoided in both the maternal diet and the infant diet. Oral food challenge is the criterion standard for a diagnosis of IgE-mediated food allergy and should be considered in certain situations, depending on a clinical history, testing, and suspicion. An epinephrine autoinjector should be prescribed for these patients as well.

### Atopic Dermatitis

Atopic dermatitis is common among infants and will likely be frequently seen by pediatricians and allergists. For detailed information on atopic dermatitis and the role in food sensitization, please refer to the article on atopic dermatitis in this issue.[14] Not all infants with atopic dermatitis require a food allergy evaluation, but it should be considered for those patients with moderate-to-severe disease that remains poorly controlled, despite an adequate skin care regimen.[15,16] We propose that milder eczema should be evaluated if there is worsening of symptoms related to the introduction of a new food or if there are significant comorbidities, *e.g.*, failure to thrive. A food and symptom diary can be beneficial in the evaluation. SPT (always performed on eczema-free skin), and, possibly, serum specific IgE testing, depending on clinical context, should be obtained for suspected foods from the history as well as other commonly implicated food allergens as appropriate (possibly CM, egg, peanut, soy, and/or wheat).[15,16]

Foods that show sensitivity should be removed from the maternal diet. If there is an improvement, a stepwise reintroduction should be attempted to confirm the suspicion for food allergy because spontaneous resolution of atopic dermatitis can occur. The reintroduction of implicated foods into the maternal diet helps in confirming the suspicion and prevents unnecessary dietary restrictions. This may be done at home, irrespective of infant's specific IgE levels, unless the history suggests an anaphylactic reaction through the mother's milk. If the skin remains well controlled after introduction, then the food can be continued in the diet. If the skin worsens again on introduction, it increases the suspicion of food allergy and these foods should be avoided.

If there is no change or improvement in symptoms, these foods should be resumed one at a time into the maternal diet. If the eczema significantly worsens with food introduction, the foods should then again be removed from the diet. Alternatively, if symptoms are severe, then the possibility that additional foods play a role should be considered. This would include other foods regularly consumed in large quantities in the maternal diet, which is commonly seen during restriction of other highly allergenic foods. If the eczema is severe and the suspicion of a food allergy is high, then an empiric elimination diet can be considered, even with negative testing results. The same approach as mentioned above should be taken to limit the unnecessary avoidance of foods.

Once the infant is ready for introduction of solid foods, careful consideration must be taken in the

setting of positive testing. An epinephrine autoinjector should be prescribed to an infant with positive testing results who is currently avoiding the implicated foods. Timely introduction (oral challenge) should be offered for those with a small skin test.[17] If initially deferred due to large skin test or positive food challenge result, then the timing of reintroduction is based on trending SPT size and serum specific IgE levels, and these levels should be monitored periodically to capture periods of possible tolerance, so that foods are not avoided unnecessarily. Based on the testing, oral food challenge in the office may be considered before home introduction of the food is attempted.

### Gastrointestinal Manifestations

Gross blood in the stool can have a variety of causes, many of which are nonallergic. These include, although are not limited to, anal fissures, intussusception, Meckel diverticulum, infectious colitis, malignancy, inflammatory bowel disease, and coagulopathy.[18] These should be ruled out, based on history, physical examination, suspicion, and evaluation when warranted.

Food protein–induced allergic proctocolitis (FPIAP) should be considered in healthy infants with blood-streaked stools, sometimes mixed with mucous. This is a clinical diagnosis based on the history, and testing is not warranted. Of note, microscopic blood does not usually warrant further evaluation and stool guaiac testing is not typically recommended in the evaluation of food allergy because there is a high rate of false positives.[19] Treatment of FPIAP involves maternal dietary elimination, usually of CM and soy because these are the most commonly implicated triggers, but other foods can be eliminated based on suspicion.[20] For severe cases, an amino acid–based formula can be considered initially to allow for gastrointestinal healing. Improvement may be seen in as early as 72–96 hours but may take up to several weeks. Hidden sources of antigen should be explored if symptoms continue, although it should be noted that soybean oil and lecithin are generally tolerated in individuals with soy allergy. FPIAP is usually self-limited, with more than half of infants developing tolerance by 1 year of age and almost all developing tolerance by 3 years of age.[21] Tam[22] provides further information in this issue on food-induced proctocolitis.

Gastroesophageal reflux and "frequent spit ups" are common among infants who are breast-fed. There currently is limited evidence to suggest an empiric elimination trial or allergy evaluation in patients with reflux symptoms alone; however, there is a subset of infants for whom CM allergy is indistinguishable from gastroesophageal reflux disease.[23] The possibility of CM allergy should also be considered in the presence of comorbid conditions, such as atopic dermatitis or poor growth. A trial of reflux medications can initially be considered. If symptoms persist with full medication compliance, then a diagnostic elimination of CM can be attempted, followed by reintroduction within 1–2 weeks to confirm the diagnosis.[24] CM introduction to evaluate for tolerance should be attempted between 6 and 12 months of age because most reflux is improved by this time.[25]

Food protein-induced enterocolitis syndrome (FPIES) should be considered if vomiting is severe, repetitive, delayed (1–4 hours after ingestion), and accompanied by an ill appearance. FPIES is uncommon among infants exclusively breast-fed, but case reports exist. FPIES can be seen more commonly with the introduction of CM or soy formula or solids (especially oat, rice but also other foods). This is a clinical diagnosis, and SPT and/or serum IgE testing is not necessary but can be considered if there is a concern of IgE-mediated symptoms and should be done before reintroduction.[26] Treatment remains avoidance of the trigger food, with periodic reassessment over time, because the majority of patients will develop tolerance. For more detailed information, Anvari and Davis[27] provide a review on FPIES in this issue.

Colicky abdominal pain is not uncommon among infants, but studies are mixed on the role of food antigens. It is reasonable to consider an empiric elimination diet of CM in infants with severe colic, especially if there is a comorbid atopic history or other gastrointestinal symptoms.[28] This should only be done for a short time, and CM should be resumed if there is no change in symptoms. There currently is no consistent evidence that CM elimination is warranted for isolated constipation.

## NUTRITIONAL IMPLICATIONS

Proper supplementation of maternal and infant diets is crucial during strict elimination diets, such as calcium and/or vitamin D supplementation for the mother and a tolerated hypoallergenic formula for the infant during CM elimination. Counseling by a registered dietician with expertise in food allergy is highly recommended to ensure the nutritional adequacy of the maternal and infant diet, especially when several foods are being avoided.

Sometimes symptoms of food allergy, especially eczema or nonspecific gastrointestinal symptoms, do not resolve after maternal avoidance diet. This may be due to nonadherence to a maternal food elimination diet, unidentified food triggers, symptoms that are not related to food allergy, or reactivity to endogenous human milk proteins, as discussed above. Although this is rare, the clinical experience is that these infants' symptoms only resolve after discontinuation of breast-feeding and initiation of hypoallergenic formula. More often, further manipulation of the maternal diet can result in sufficient symptom control to allow continuation of breast-feeding. Rarely, this may include elimination of several foods in

the maternal diet or consumption of a few foods, which should be done in close follow up with a nutritionist.

## CLINICAL PEARLS

- Maternal dietary antigens have been detected in human milk, albeit in low quantities and not in all mothers.
- The presence of food antigens in human milk has been shown to result in symptoms of food allergy during breast-feeding in some infants already highly sensitized, although the role of food antigens in initial sensitization to foods is debated, and no randomized controlled trials exist on the topic.
- Symptoms of food allergy during breast-feeding include, rarely, immediate symptoms, such as hives and anaphylaxis, or delayed onset of repetitive vomiting as in FPIES, and, more commonly, atopic dermatitis, gastroesophageal reflux disease, vomiting, diarrhea, and bloody stools.
- Proper supplementation of the maternal and infant diet is crucial during strict elimination diets to ensure the nutritional adequacy.

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