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Guest Editorial

Let them eat cake

The growing appreciation of food allergy as an important public health problem stimulates exploration of novel food allergy therapies.[1] Cow's milk allergy is the prime target of such therapies because cow's milk is one of the most common food allergens in infants and young children; severe cow's milk allergy has been reported as a cause of fatal anaphylaxis. Cow's milk and dairy based foods are an important source of nutrition in the pediatric diet. Cow's milk protein is also ubiquitous in commercial food products. Therefore, avoidance of cow's milk protein significantly affects quality of life by limiting selection of allowed foods as well as social aspects such as, eating out, attending parties, family gatherings, and other social events.[2,3] While most children outgrow cow's milk allergy, a recent study reported that in a subset of children with peak lifetime cow's milk-specific immunoglobulin E (IgE) antibody concentration exceeding 50 kIU/L, cow's milk allergy was likely to persist well into the teenage years.[4] In the absence of curative therapy, management focuses on dietary avoidance, nutritional counseling, and prompt treatment of acute allergic reactions.

We have previously reported that the majority of cow's milk and egg allergic children tolerate these ingredients in extensively heated (baked) forms.[5,6] Children who incorporated baked products with milk or egg into their diet had normal growth, normal intestinal permeability, and no adverse effects on chronic atopic conditions such as atopic dermatitis, allergic rhinitis, and asthma. Furthermore, introduction of baked milk or egg seems to accelerate development of tolerance to unheated milk and egg, positioning introduction of baked milk and egg as a form of oral immunomodulation. Children who incorporated baked milk into the diet were 16 times more likely to become tolerant to unheated milk compared with a comparison group of children who continued strict avoidance of milk ingredients.[7] Children who incorporated baked egg into the diet were 14.6 times more likely than children in the comparison group ($P < .0001$) to develop regular egg tolerance, and they developed tolerance earlier (median 50.0 vs 78.7 months; $P < .0001$).[8]

The retrospective study by Bartnikas et al[9] entitled "Predicting Food Challenge Outcomes for Baked Milk: Role of Specific IgE and Skin Prick Testing" published in the current issue of *the Annals*, explores tolerance to milk in extensively heated (baked) products. Among 35 milk-allergic children who underwent oral food challenges to muffins and cupcakes, 83% tolerated baked milk, confirming prior observations. However, 3 of those who passed supervised challenges and added baked milk to the diet reported subsequent reactions to baked milk products at home. Although no follow-up repeat oral food challenges were performed to confirm these reactions and the details of home introduction of baked milk products were not available, the report highlights the caveats and complexities of the baked milk diet.

Table 1
Dietary guidelines to include milk in baked food products

Allowed	Not allowed
• Store-bought baked goods (such as rolls, muffins, cupcake, cookies, crackers, and bread) with milk or milk protein ingredients listed as the 3rd ingredient or further down the list of ingredients.	• Store-bought baked goods (such as rolls, muffins, cupcake, cookies, crackers and bread) with milk or milk protein ingredients listed as the first or second ingredient.
• Home baked goods (such as rolls, muffins, cupcakes or cookies) that have 240 mL milk per batch of a recipe (yield 6 servings per batch) or approximately 40 mL baked milk per serving.	• Home baked goods with more than 40 mL baked milk per serving.
• Home baked items with center that is thoroughly cooked through (not moist or soft). Products should be baked in individual serving size: cupcake, not cake; brownie muffins, not brownies; rolls, not bread.	• Full-sized home baked products such as cakes, brownies, and breads (commercial breads are safe) that may not be fully cooked in the middle.
• Baked milk containing baked goods with milk-free chocolate chips.	• Baked milk containing baked goods with milk chocolate chips.
• Remember to check store-bought products and ingredients based on the patient's other food allergies in order to avoid a reaction to other allergens.*	• Continue to avoid milk products that are not fully baked such as milk-based frostings, icings, and milk-containing flavorings that are topically applied after the product is baked.*

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*Servings are specified in the nutritional information section of the food label or determined by the yield of the recipe.

Undercooked/insufficiently baked products that are soggy or wet in the middle such as large cakes, breads, or products containing additional ingredients that change the properties of the food matrix may result in increased availability of milk protein and cause allergic reaction in children who tolerate well-baked products (Table 1). Introduction of baked milk into the diet necessitates dietary counseling to avoid mistakes and improve adherence.

The authors also analyzed the immunologic parameters such as skin prick tests with whole cow's milk and casein commercial extracts and serum specific IgE antibodies directed against cow milk, casein, and beta-lactoglobulin in an attempt to establish >90% positive predictive values for tolerating baked milk challenge. Their findings are generally in agreement with previously reported data regarding diagnostic performance of skin test with whole cow's milk extract and casein IgE.[6,10,11] The novel aspect includes skin prick test with casein, which has not been explored previously. The utility of casein skin prick test needs to be further evaluated before recommending casein SPT for diagnosis of baked milk allergy in clinical practice.

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However, caution is strongly advised when applying the proposed cut-points derived retrospectively from a small cohort of subjects to a recommendation to introduce baked milk at home. Our experience with a large (225) number of milk-allergic children indicated that those who reacted to baked milk had more severe reactions than those who tolerated baked milk, but subsequently reacted to unheated milk. Furthermore, the analyses have not been adjusted for age and it is possible that the proposed diagnostic cut-off levels may not be applicable to younger children who are more likely to react to baked milk during the challenge. Thus, the safest approach to introducing baked milk remains under physician supervision during the food challenge.

Nevertheless, the current study adds to the body of evidence supporting the modification of the existing management paradigm of strict dietary milk avoidance in favor of the more individualized approach based on the tolerance to milk in baked products. Additional large clinical trials are necessary to validate this approach and to determine biomarkers of tolerance to milk in baked products.

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