
Cow's milk allergy: is there a cure?

In the pediatric population, cow's milk is one of the most common food allergens. Present treatment options are wanting because they consist solely of strict avoidance with appropriate supportive care when inadvertent exposure occurs.¹ Thus, it is of no surprise that studies have demonstrated significant anxiety and reduction in quality of life with attempting to avoid such ubiquitous food allergens.² Although in the past it was believed that cow's milk allergy (CMA) usually disappeared by age 3 years (in 85% of sufferers), recent studies have highlighted a more delayed time to tolerance.³ Currently, there are no curative procedures in the case of food allergy; however, there has been recent interest in the use of oral-induced tolerance in food-allergic patients. Note, however, that immunotherapy to foods has a long history. As early as 1930, Freeman⁴ reported that with the use of subcutaneous immunotherapy, a state of tolerance was induced in a fish-allergic patient. A more recent publication⁵ demonstrated that subcutaneous immunotherapy to peanut, although effective, resulted in an unacceptable adverse effect profile. In an attempt to improve the therapeutic index, attention has been focused on oral immunotherapy (OIT). In the case of milk, several recent studies⁶⁻⁹ have demonstrated hope, with efficacy rates of 75% to 86%. Regimens have varied from rush protocols, generally being performed in a hospital setting, to very slow up dosing, which in some cases is performed at home. In a recent article for *Annals*, Pajno et al¹⁰ add to the growing literature regarding OIT in patients with CMA by examining a pilot study using a more "practical and patient-friendly" protocol. This is achieved by performing a weekly outpatient dose-increasing protocol comprising 28 visits during approximately 4 months. Thirty children with confirmed CMA via double-blind placebo-controlled food challenge (DBPCFC) were randomized to receive active therapy or sham protocol with the use of soy. Note that unlike other protocols, there were no "home doses" between clinic visits for up dosing. The primary outcome was the reduction in clinical sensitivity as demonstrated by change in threshold dose via DBPCFC, and the secondary outcome was immunologic change associated with the procedure. The OIT was effective, with the "full" DBPCFC milk dose (200 mL) tolerated in 10 of 13 individuals, partial tolerance in 1, and 2 who required discontinuation owing to severe reactions associated with the OIT protocol. Regarding immunologic variables, as is seen in other studies, there is no change in specific IgE

levels; however, in the actively treated group, there is a rise in IgG4 levels to cow's milk.³

Allergists should be greatly encouraged by this study because it adds to a growing literature that intimates future hope for food-allergic patients. This work needs to be replicated with larger numbers; however, should continued safety with this approach be seen, it is potentially a procedure that can be performed in the outpatient setting. Note, however, that this study was not performed in a classic outpatient setting because the authors' clinic was the allergy unit of a university with "full resuscitation facilities immediately available."

As demonstrated in this study, OIT is by no means perfect because not all the participants achieved the desensitized state and there is potential for adverse events. This is reinforced in the CMA OIT study by Skripak et al,³ who demonstrated reaction rates higher than would be expected for conventional immunotherapy for pollen and environmental allergy, with approximately 1 in 100 doses of active therapy resulting in a multisystem reaction and 1 in 600 requiring epinephrine use.¹¹ One may question whether the future use of peptide microarray immunoassays may help in stratifying prospective patients undergoing OIT regarding the likelihood of reaction.¹² Last, note that Pajno et al¹⁰ actually explored desensitization, not tolerance, to cow's milk. Further research regarding what is necessary to convert from a desensitized state (continued uninterrupted ingestions) to the tolerant state (where cessation of ingestion is not followed by resensitization) is needed. The importance in distinguishing these 2 states is exemplified in a study by Staden and colleagues,⁹ who performed a double-blind placebo-controlled trial comparing OIT to egg or milk vs placebo. Sixty-four percent of actively treated individuals were found to demonstrate a "good or at least partial response" after a median of 21 months; however, when they then underwent 2 months of elimination of the relevant food allergen and were rechallenged, they demonstrated a likelihood of protection that was similar to that seen in the control group. Despite these concerns, Pajno et al¹⁰ provide hope that we may someday be able to offer food-allergic patients a cure for their ailment.

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REFERENCES

1. Chapman JA, Bernstein IL, Lee RE, et al. Food allergy: a practice parameter. *Ann Asthma Allergy Immunol.* 2006;96:S1–S68.
 2. LeBovidge JS, Strauch H, Kalish L, Schneider LC. Assessment of psychological distress among children and adolescents with food allergy. *J Allergy Clin Immunol.* 2009;124:1282–1288.
 3. Skripak JM, Matsui EC, Mudd K, Wood RA. The natural history of IgE-mediated cow's milk allergy. *J Allergy Clin Immunol.* 2008;121:1331–1336.
 4. Freeman J. "Rush" inoculation. *Lancet.* 1930;1:744.
 5. Oppenheimer JJ, Bock SA, Christensen F, et al. Treatment of peanut allergy with rush immunotherapy. *J Allergy Clin Immunol.* 1992;90:256–262.
 6. Longo G, Barbi E, Berti I, et al. Specific oral tolerance induction in children with very severe cow's milk-induced reactions. *J Allergy Clin Immunol.* 2008;121:343–347.
 7. Meglio P, Bartone E, Plantanura M, et al. A protocol for oral desensitization in children with IgE-mediated cow's allergy. *Allergy.* 2004;59:980–987.
 8. Morisset M, Moneret-Vautrin DA, Guenard L, et al. Oral desensitization in children with milk and egg allergies obtains recovery in a significant proportion of cases: a randomized study in 60 children with cow's milk allergy and 90 children with egg allergy. *Eur Ann Allergy Clin Immunol.* 2007;39:12–19.
 9. Staden U, Rolinck-Werninghaus C, Brewe F, Wahn U, Niggemann B, Beyer K. Specific oral tolerance induction in food allergy in children: efficacy and clinical patterns of reaction. *Allergy.* 2007;62:1261–1269.
 10. Pajno GP, Caminiti L, Ruggeri P, et al. Oral immunotherapy for cow's milk allergy with a weekly updosing regimen: a randomized single-blind controlled study. *Ann Allergy Asthma Immunol.* 2010;105:376–381.
 11. Moreno C, Cuesta-Herranz J, Fernandez-Tavora L, Alvarez-Cuesta E. Immunotherapy safety: a prospective multi-centric monitoring study of biologically standardized therapeutic vaccines for allergic diseases. *Clin Exp Allergy.* 2004;34:527–531.
 12. Cerecedo I, Zamora J, Shreffler WG, et al. Mapping of the IgE and IgG4 sequential epitopes of milk allergens with a peptide microarray-based immunoassay. *J Allergy Clin Immunol.* 2008;122:589–594.
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