

Controversial Treatment Procedures

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Oral Desensitization with Cow's Milk in IgE-Mediated Cow's Milk Allergy. Contra!

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The gut-associated lymphoid tissue constitutes an important system for both local and systemic immunity against ingested antigens [1, 2]. Related to the immunologic defense mechanisms of the gastrointestinal tract are two phenomena that will be briefly discussed here. First, *tolerance* which can be naturally occurring or artificially induced. And second, *desensitization* which is primarily artificially induced in subjects who are already sensitized.

Oral Tolerance

Tolerance is a state of immunologic hyporesponsiveness. Using special protocols, orally-induced tolerance to certain particulate or soluble antigens, including food proteins, could be achieved in experimental animals [3]. This seems to be the result of enhancement of local suppressor T cells in Peyer's patches [4, 5]. Tolerance in mice could be achieved against T-dependent antigens (e.g., ovalbumin, bovine serum albumin, and aggregated human γ -globulin) but not against T-independent antigens (e.g., polyvinylpyrrolidone, lipopolysaccharide, and dinitrophenylate) [6]. The age of the animal and the dose of the fed antigen are critical for induction of tolerance. The neonatal period seems to be the optimal time [2]. The larger the dose of antigen or the more frequent the feeding, the more likely for tolerance to be achieved and for IgE response to be suppressed [7].

Oral tolerance has been demonstrated in man [8], but the information is very limited, particularly on inducing tolerance to food in infants. In one retrospective study on breast-fed infants at high risk of atopy, the incidence of atopy by 18 months of age was lower in those who received significant supplements of milk formula early in the neonatal period than those who were exclusively breast-fed

[9]. This area is far from being clear and can have major implications on infant feeding practices. Recent data from animal studies indicate that neonatal administration of high doses of foreign antigen induces a state of T- and B-cell anergy that is short lived and might be followed by impaired development of active suppression or tolerance [2].

Oral Desensitization

As an extension of the phenomenon of oral tolerance, is the potential for oral desensitization. Desensitization is a process of inducing refractoriness to a particular antigen to which the subject has been already sensitized. In humans it has been actually possible to achieve rapid oral desensitization in subjects with immediate-type allergic reactions to certain drugs such as penicillin, sulfonamides, and aspirin [10]. Various degrees of success have been also reported in trials of oral immunotherapy with specific inhalants (house-dust mite and certain pollens) causing IgE-mediated respiratory allergy [11].

On the other hand, trials of oral immunotherapy with food protein were very few and showed inconsistent results. Oral immunization with ovalbumin in previously sensitized guinea pigs was associated with decreased specific IgE antibody synthesis and prevented anaphylaxis to subsequent parenteral administration of ovalbumin [12]. Very little information has been published, at least in the English literature, on the role of oral immunotherapy with foods, including cow's milk [13].

Proponents of oral food immunotherapy claim that desensitization can be achieved by repeated oral administration of the offending food. Initially, the food is given, often in the form of a diluted extract, in very small quantities that do not provoke symptoms and is administered daily in gradually increasing quantities. In the meantime, the patient is required to avoid eating that food from another source, until desensitization is attained through the procedure, which may take several months. At present, the accumulated information indicates that the procedure does not have sufficient reliability [13, 14]. The few claims of some success of oral food desensitization are subject to one or more of the following limitations: (1) The inclusion of patients with subjective symptoms that cannot be documented with sufficient certainty. (2) The symptoms are not all classic IgE-mediated reactions. (3) Appropriate blind, placebo-controlled challenges were not always used to confirm the diagnosis or to evaluate the response to desensitization. (4) Lack of documentation of any associated immunologic changes as a result of the desensitization procedure. (5) A placebo treatment is not always included. (6) The duration of avoidance of natural exposure to the offending food can by itself be responsible for the development of spontaneous tolerance. This is particularly true for milk allergy in children [15, 16].

Nevertheless, since strict dietary elimination may not be feasible, there is a definite need for appropriately designed trials of oral food desensitization. Certain trials are revealing some promising results [17]. In carrying out such trials, exercising extra caution cannot be overemphasized since an error may result in a life-threatening reaction and any bias would affect the validity of the results.

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