

Specific IgG Antibodies as Markers of Adverse Reactions to Foods

Vincent Marinkovich

Menlo Park, Calif., USA

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Introduction

It is widely acknowledged that non-IgE-mediated immunopathology is an important element in human illness [1]. Generally, these mechanisms are recognized for certain infectious processes, organ transplantation, and in a variety of inflammatory conditions, some with attendant autoimmune components. The most thoroughly studied disease in which immune complexes are involved is serum sickness, which occurs following the injection of heterologous antisera (fig. 1) given to treat various toxic infections [2]. Such studies show beyond doubt that the presence of foreign protein in the tissues of an individual will provoke a forceful immune response producing illness of varying degrees of severity involving all the body's organs (fig. 2). If such foreign protein exposure becomes chronic, the illness will become chronic and eventually life-threatening.

It is logical that such intrusion of foreign protein can occur across a damaged mucosa and that if significant transmucosal antigen uptake persists, it can overwhelm the more benign monoclonal IgA response of the mucosal immune system and the mechanisms of oral tolerance by which an immune response is suppressed when antigen is given orally. The most supportive recent studies of what can happen with large oral doses of antigen are those reports which demonstrate successful immunotherapy for certain pollen allergies with production of blocking antibodies via the oral route [3]. Surely this is a relatively common occurrence with high exposure antigens such as food, mold spores, and other organic dusts in occupational exposures. It must not be ignored as a possible basis for many adverse food reactions reported by patients who do not satisfy the criteria for IgE-mediated reactions.

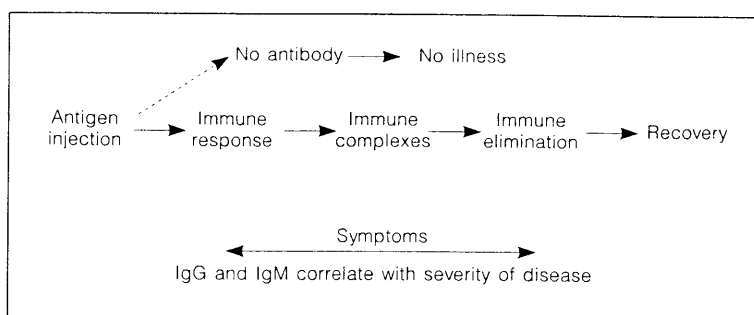


Fig. 1. Classical serum sickness.

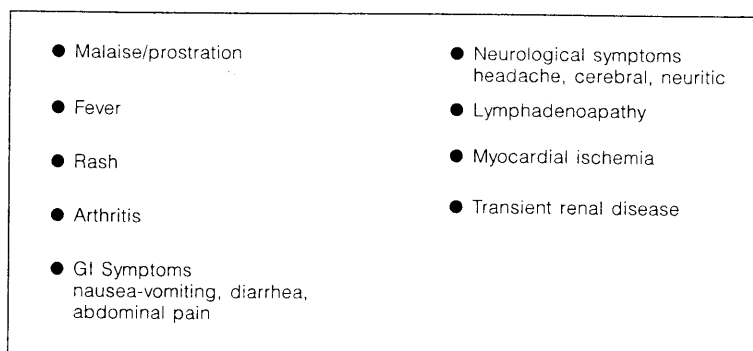


Fig. 2. Classical serum sickness.

If transmucosal antigen uptake can trigger an immune response, continued uptake of those antigens will lead to immune complex formation. When the macrophage system is saturated and/or complement is unable to prevent the build-up of large immune complexes, these complexes will circulate and cause inflammatory changes in the vascular space and tissues of deposit. The single most accurate measure of a general immune response is IgG antibody. Specific IgG antibodies would serve as markers of inflammation-associated antigens. Avoidance of these antigens could be clinically useful.

A recent separate, double-blind, placebo-diet-controlled study in which patients were tested for food-specific IgG antibodies and then monitored clinically while on IgG-based and sham diets showed highly significant symptom reduction on the IgG-based diets ($p < 0.00029$) [4]. This is to report a similar result in a retrospective analysis of 55 patients placed on elimination diets based on specific IgG antibody tests for foods.

Materials and Methods

An FDA-cleared method for simultaneously testing serum for specific IgE antibodies to each of 36 allergens, previously described [5], was adapted to the measurement of specific IgG antibody [6]. The IgE technique was modified by diluting serum 300-fold to avoid 'normal' IgG antibody levels to foods, and by reducing incubation time to 1 h for serum and 2 h for specific anti-IgG conjugate.

Patients were seen in a private clinic. They each complained of symptoms suggestive of adverse reaction to foods (fig. 2) and were negative by all specific IgE tests. Each showed elevated antibody titers to one or more foods on the specific IgG test. All patients were instructed in dieting to avoid or minimize exposure to those foods to which they showed antibody. They were followed clinically for a year and then re-evaluated. Of the original 55 patients who were followed for a year, 24 chose not to follow the diet for a number of reasons, but all continued to be seen and were otherwise under treatment. The two groups were compared for clinical improvement and changes in specific IgG levels at the 1 year re-evaluation.

Results

The patients who remained on the diets for the full year showed significant drops in specific IgG levels to the foods avoided. Those not dieting did not ($p < 0.001$). The value of serial specific IgG levels to foods to measure dietary compliance is well known and supported by this study. More significantly, the 31 patients who dieted were much more often clinically improved than the non-dieters (28 of 31 dieters versus 7 of 24 nondieters, $p < 0.01$). The criteria for clinical change used were largely derived from patient interviews. The patients were referred back to their original list of symptoms and asked to judge their relative status 1 year later by both subjective and objective measures.

The patients who chose not to diet were largely skeptical of the dietary approach or did not wish to trade dietary constraints for symptom amelioration. Some did improve without diet, presumably because of better use of medications, control of environmental allergen exposure, and generally taking better care of themselves.

Discussion

It is necessary to acknowledge that neither specific IgE nor specific IgG testing alone is diagnostic. One possible exception is seen in anaphylactic-level, food-reactive individuals who can show an enormous specific IgE antibody titer to their allergenic food. Likewise, in this study, all patients with very high specific IgG titers to one or a few foods were clinically benefited by a diet eliminating those foods. Nevertheless, all positive sIgE and sIgG results to foods must be

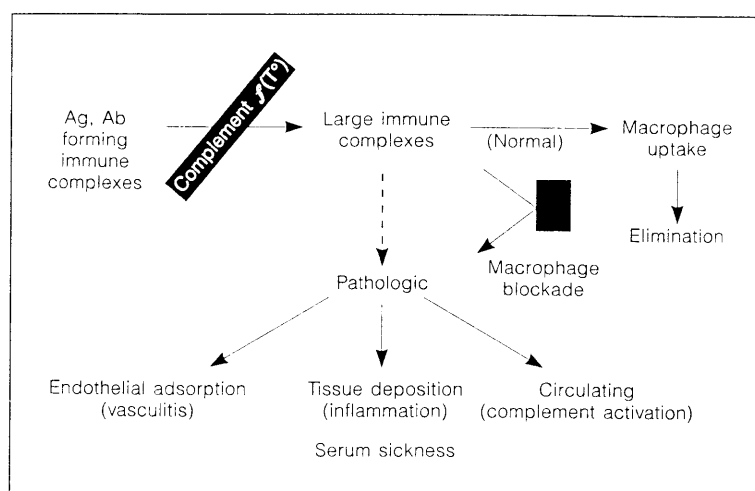


Fig. 3. Type III immunopathology.

evaluated along with clinical history and oral challenge to arrive at accurate diagnoses. Even these will fade as antibody levels change.

It is generally agreed that non-IgE immunological hypersensitivity to foods exists [7] and is able to cause considerable morbidity. The immune complexes deposited in areas of tissue inflammatory reactions cannot be entirely secondary phenomena. The central question is whether specific IgG antibody titers, found in serum, reflect exposure levels to that antigen (amount consumed and taken up) and parallel the inflammatory potential of continual antigen ingestion.

The present study strongly supports the value of specific IgG antibody determinations to foods as a helpful clinical tool to reduce illness. It does not address the issue of how much the IgG-derived immune complexes are central to the pathology. They could certainly be secondary phenomena which nonetheless can point the way for effective, symptom-reducing dietary management of patients with a variety of clinical patterns. One possible scheme of immunopathogenesis (fig.3) requires that failure of the temperature-dependent complement function to reduce complex formation and macrophage blockade exist in some way to allow the clinical disease state. Since these functions are independent of each other and of antigen uptake and antibody production, such a scheme becomes very difficult to measure and define. In clinical practice the approach can be simple. One presumes that the patient with appropriate history and symptoms has satisfied the necessary steps, and that if one can identify the antigen, its removal would result in clinical improvement.

In our hands, serum-specific IgG antibody titers to high exposure allergens such as foods and molds have been very helpful in formulating trial elimination diets which seem highly beneficial in reducing symptoms. These phenomena may far surpass in incidence the IgE-mediated food reactions generally thought to represent 'true' food allergy. Certainly more work is needed to test this hypothesis.

References

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V. Marinkovich, MD, 90 Middlefield Road, Suite 100,
Menlo Park, CA 94025 (USA)