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Improving allergy outcomes

IgE and IgG_4 food serology in a Gastroenterology Practice

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IgE and IgG4 food serology in a gastroenterology practice

The following study was conducted on consecutive patients from a gastroenterologist practice that utilized a test panel of 95 foods (assayed for both IgE and IgG_4). Test results were correlated back to patient history and symptoms and used in guiding exclusion diets for their patients

Allermetrix specific IgE and IgG_4 serology assays

The Allermetrix specific IgE assay is calibrated to the 2nd IRP WHO IgE standard and has a reporting range of 0.01 to 100 kU/L. Samples are considered positive to a specific allergen at a concentration of 0.05 kU/L. Based on QC performed every day and multiple times each day, a specific IgE concentration of 0.10 kU/L has a functional CV of about 25%. Therefore selecting 0.10 kU/L as a conservative positive cutoff would ensure that results would repeat as positive, >0.05 kU/L, 97.5 % of the time, and ensure few if any false positive results due to precision of the assay. In the following analysis the cutoff for a positive IgE response to an allergen was selected to be 0.10 kU/L.

The Allermetrix specific IgG_4 assay is calibrated using beekeeper plasma that has a high concentration of honey bee venom specific IgG_4. The reporting range is 0.81 – 128 units of specific IgG_4 and the cutoff for a positive response is 1.0 unit. Functional precision is about 30% at 0.3 units and 14% at 5 units. The use of 1.60 units as a cutoff for positive is conservative and ensures a repeated test will repeat positive, >1.0 unit, 97.5 % of the time. The 1.6 unit cutoff ensures few false positive results due to assay precision.

Results of testing

The conservative cutoffs for specific IgE and IgG_4 were used to evaluate 9,500 tests performed for 50 consecutive patients. Eight patients, representing 16% of the study, were non-reactive for both IgE and IgG_4 to the 95 food allergens tested. Table 1 shows that 48% of the patients were positive to at least one food by IgE serology and 80% of the patients were reactive to at least one food by IgG_4 serology.

Table 1 Samples were tested with 95 different foods for IgE and IgG_4 reactivity. Numbers in the "+" categories have at least one positive serology for the antibody. Numbers in the "-" categories had all negative serology results for the antibody type.

9,500 tests	IgG_4 "-"	IgG_4 "+"	Total
IgE "-"	8 **(16%)**	18 **(36%)**	26
IgE "+"	2 **(4%)**	22 **(44%)**	24
Total	10	40	50

One of the allergens included in the 95 food panel is oyster, and we have found the rate of IgE positive reactivity using the 0.10 kU/L cutoff to be 30% in this population of patients. This rate of reactivity is much higher than expected and 10 fold higher than the next closest food positivity rate. This very high rate of reactivity could be in part due to cross reactivity with other allergens, especially other invertebrate allergens. This very high rate of positivity at the conservative cutoff of 0.10 kU/L seems unlikely to be caused by cross reactive inhalant allergens. We did not test these same patients for inhalant allergens, and it is possible although we believe unlikely. It also seems unlikely that all these patients actively eat oysters as it is an acquired taste and not a common food. We do think another explanation may be the presence of parasites in the oysters that are commonly found in drinking water[i].

There have been a number of studies of IgG_4 serology for food allergens, especially in the pediatric population[ii] that have demonstrated specific IgG_4 to milk and egg are relatively common compared to IgG_4 responses to other foods. In addition, the presence of specific IgG_4 to milk and egg were not always associated with food allergy to those foods. As with all laboratory tests, results are only useful when interpreted with the clinical presentation.

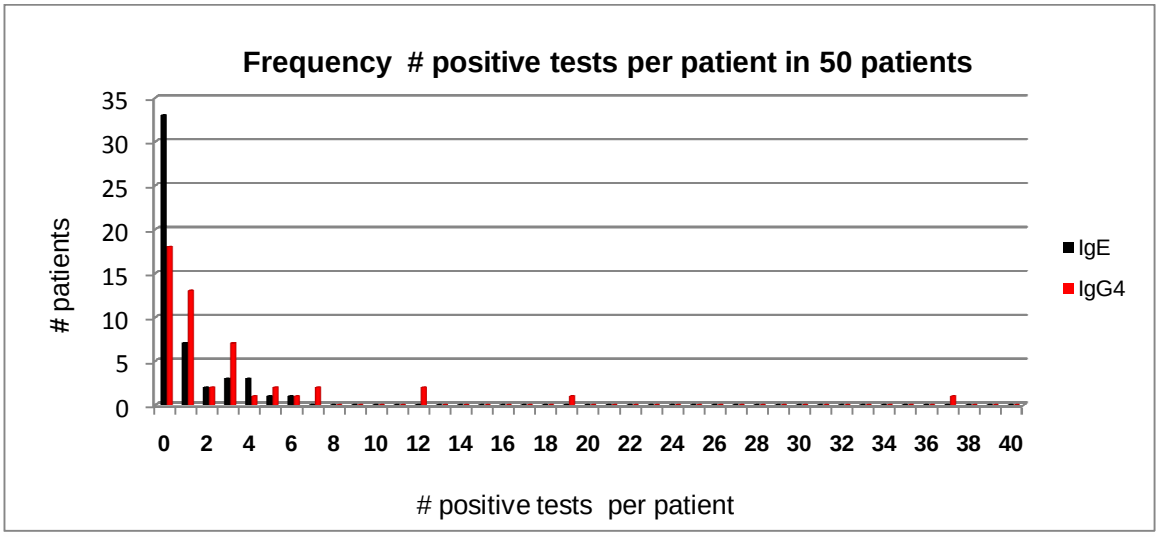
In the light of the oyster specific IgE prevalence and relatively common milk and egg specific IgG_4, we chose to eliminate results for specific IgE to oyster, and specific IgG_4 results to egg and dairy products which included egg white, egg yolk, milk, cheese, and yogurt. After elimination of these tests, the analysis, now including 9200 tests, presented in Table 2 demonstrates 16 patients negative to foods for both IgE and IgG_4 reactivity. Seventeen patients or 34% had a positive reaction with IgE, and 32, 64% were positive by IgG_4 serology.

Table 2 Samples were tested with 94 different foods for IgE and 90 for IgG4 reactivity. Numbers in the "+" categories have at least one positive serology for the antibody. Numbers in the "-" categories had all negative serology results for the antibody type.

9,200 tests	IgG_4 "-"	IgG_4 "+"	Total
IgE "-"	16 **(32%)**	17 **(34%)**	33
IgE "+"	2 **(4%)**	15 **(30%)**	17
Total	18	32	50

Analysis of the 9,200 test set demonstrates the number of positive results by antibody type, Figure 1, shows the majority of patients are reactive to only a few foods. There are 2 patients that have more than 4 specific IgE positive food results, and 9 that have more than 4 specific IgG_4. There are 3 patients that have more than 10 positive IgG_4 results. One of the patients with more than 10 positive IgG_4 results also had several positive specific IgE responses, one of the other 3 had only 2 positive specific IgE and the other 2 were negative for IgE.

Figure 1 Number of positive results for specific IgE to 94 foods, and specific IgG_4 serology for 90 foods for each patient sample tested. Results for oyster specific IgE and egg and dairy IgG_4 results were excluded from this analysis.



Analysis by strength of reaction for IgE and IgG_4 indicate that most assay responses are low, class 1 or class 2, with some high responses, Figures 2 and 3. Strong IgE responses, Class 3 and higher were seen for 6 results of the total 4,700 tested by IgE. It is clear that any positive IgE response is a relatively rare occurrence, 23 of 4,700 tests (0.5%) but specific IgE is important because it indicates a potential for strong clinical allergic responses. IgG_4 responses are less rare, but remain relatively rare, 201 of 4,450 tests (4.5%). Figure 3 indicates that Class 2 responses are more common that Class 1, which suggests that truncating the lower end of a Class 1 response by selecting 1.60 units as the cutoff for positive may have excluded many positive responses. However, when the cutoff is set to 1.0 units there are 110 positive responses, which are still fewer than the Class 2 responses. This demonstrates that positive IgG_4 responses tend to be strong when they occur.

Figure 2 Classification of positive IgE results to 94 food allergens. Class scores represent the strength of assay response. Class 1 is the weakest positive response and Class 6 the strongest.

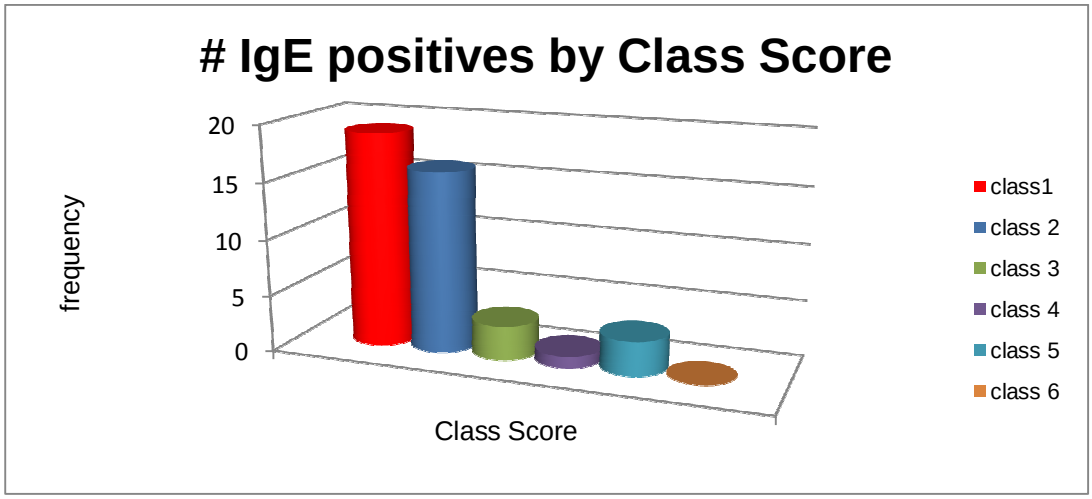
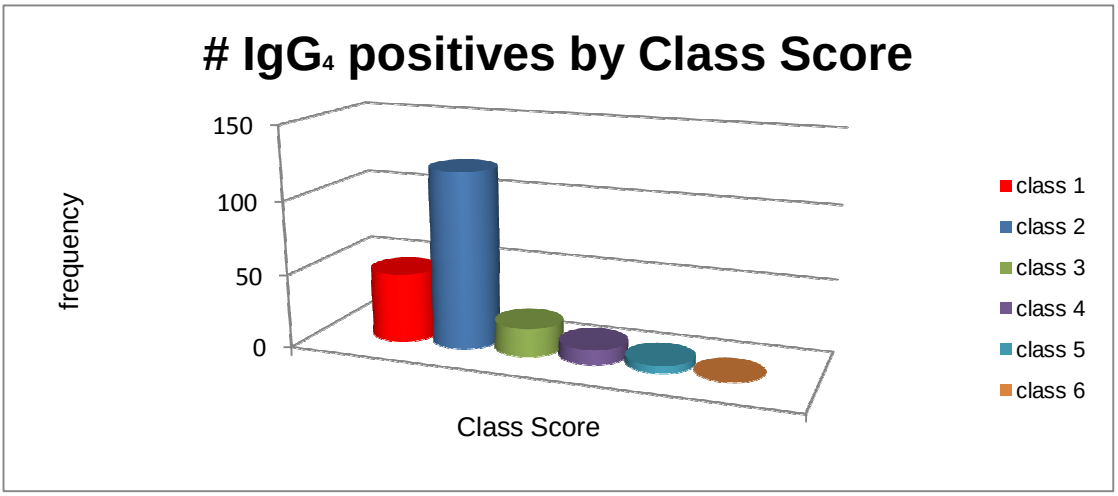


Figure 3 Classification of positive IgG_4 results to 90 food allergens. Class scores represent the strength of assay response. Class 1 is the weakest positive response and Class 6 the strongest.



Conclusion

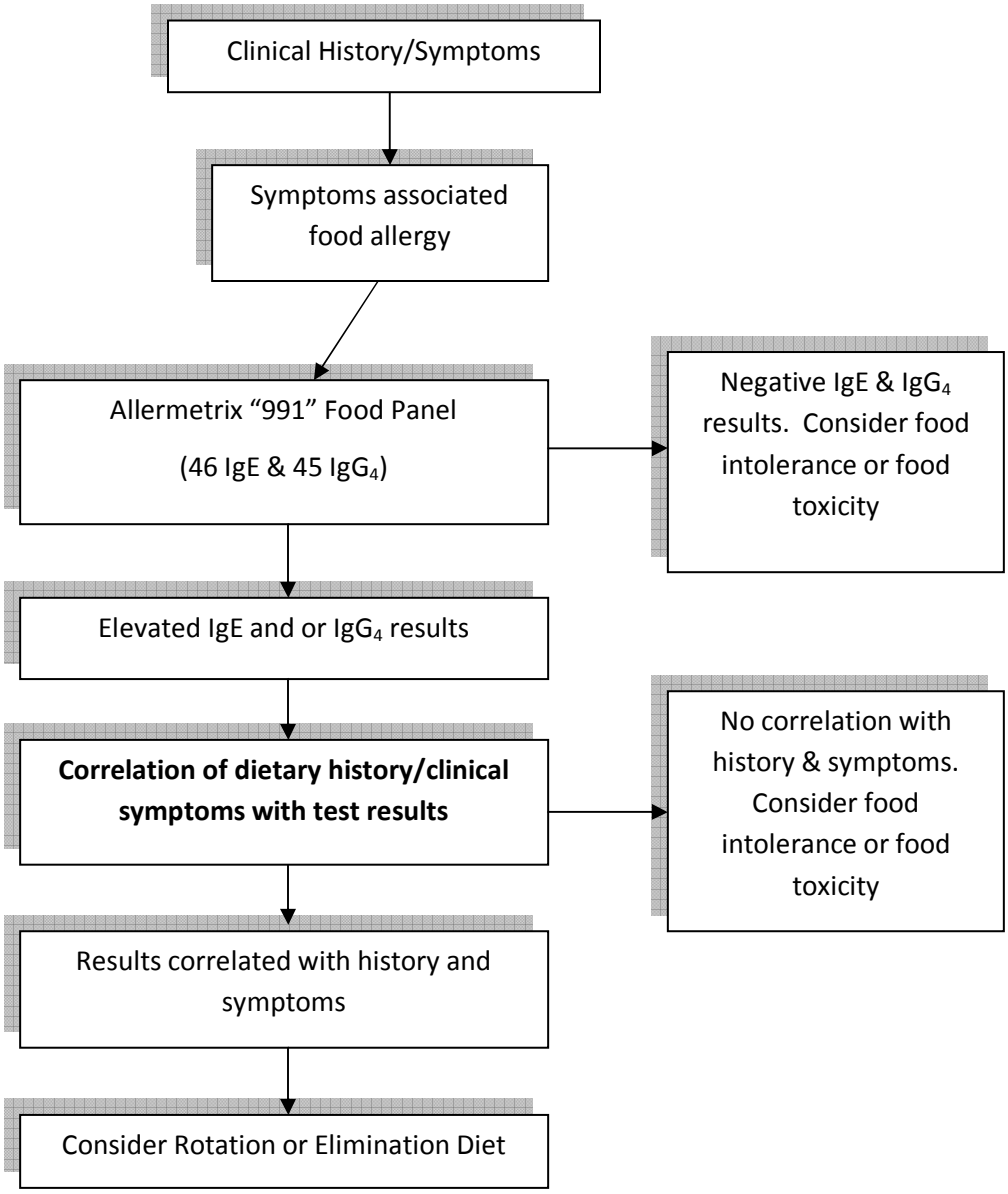
The high rate for specific IgE positive results in this patient population (as compared to patients seen in a non-gastroenterologist practice) suggests that gastroenteritis patients may have a high prevalence of food allergy. It would be interesting to evaluate these results in the context of the clinical diagnosis to determine whether the number of positive allergens and type of antibody response correlate with any diagnostic groups. Additionally, correlation of the strength of the assay response and the clinical diagnosis may open many new questions. Clearly there are several questions that can be investigated from the study presented. Importantly, the IgE and IgG_4 positive serology were found in about 2/3^{rds} of the patients and it has been shown that using such laboratory results to guide elimination diets in IBS patients can ameliorate symptoms.

Food Allergy Testing Strategy for a Gastroenterology Practice >>>

A Strategy to Identify the Food Allergic Patient

When developing a strategy to identify food allergy, various factors must be taken into effect; dietary history, clinical symptoms, IgE mediated responses, non-IgE mediated responses (IgG or IgG_4), allergen antigenicity and hidden foods. Approximately 90% of food allergy is found in the following foods/food groupings; tree nuts, milk, peanuts, milk, eggs, soy, wheat, fish and shellfish.

Laboratory Algorithm for Food Testing



The Allermetrix-Food Panel (#991)

Food allergies are difficult to diagnose and often the allergens causing disease are not obvious. The literature indicates there are a number of foods that are most often identified. Allermetrix has constructed a comprehensive food allergy panel that incorporates data from published clinical studies and our in-house testing results from a gastroenterology practice. For the best diagnostic efficiency, both IgE and selective IgG_4 antibodies must be tested to identify the offending allergen(s). Often, food allergy is not IgE mediated requiring the need to assay for IgG_4 reactivity (believed to be involved in delayed reactions).

Allermetrix reviewed over **23,370** food tests and identified the most commonly positive allergens. The rate of positive results is highest for IgE to Oyster (see note below) and IgG_4 to both milk and egg reactions, but, other groups of food also demonstrate high rates of reactivity for both IgE and IgG_4. After analysis of individual allergens, 46 IgE and 45 IgG_4 foods were selected for the "991" food panel.

The allergens included in the "991" panel are grouped below:

- **Legumes:** Peanut (IgE& IgG_4), Pinto Bean (IgG_4), Soybean (IgG_4) Wax String Bean (IgE& IgG_4), White/Navy Bean (IgE& IgG_4)
- **Tree nuts:** Almond (IgE& IgG_4), Brazil Nut(IgE& IgG_4), Cacao (IgE& IgG_4), Cashew (IgE& IgG_4), Coconut (IgE& IgG_4), Cola Nut (IgE), English Walnut (IgE& IgG_4), Hazelnut (IgE&IgG_4), Pecan (IgE& IgG_4), Pine Nut (IgE),Pistachio (IgE& IgG_4)
- **Fish:** Codfish (IgE), Salmon (IgE), Trout (IgE)
- **Shellfish:** Clam (IgE, IgG_4), Oyster (IgE& IgG_4), Scallop (IgE& IgG_4), Shrimp (IgE)
- **Dairy:** Cow's Milk (IgE& IgG_4)
- **Animal:** Beef (IgG_4), Egg White (IgE& IgG_4), Egg Yolk (IgE& IgG_4), Turkey (IgE)
- **Fruits:** Apple (IgG_4), Banana (IgE), Blueberry (IgE), Cantaloupe (IgE& IgG_4), Grape/Raisin (IgG_4), Lemon (IgE& IgG_4), Honeydew Melon (IgE& IgG_4), Orange (IgE& IgG_4), Peach (IgE), Plum/Prune (IgE), Strawberry (IgE), Tangerine (IgE), Tomato (IgE& IgG_4), Watermelon (IgE& IgG_4)
- **Seeds/Spices:** Cumin (IgE),Mustard (IgE& IgG_4), Nutmeg (IgE), Vanilla (IgG_4)
- **Grains:** Barley (IgG_4), Buckwheat (IgE& IgG_4), Gluten (IgE& IgG_4), Malt (IgE& IgG_4),Oat (IgG_4), Rice (IgG_4), Rye(IgG_4), Wheat (IgG_4)
- **Vegetables:** Bell Pepper (IgG_4), Black/White Pepper (IgE), Garlic (IgG_4), Red Pepper (IgE& IgG_4), Summer/Yellow Squash (IgG_4), White Potato (IgE& IgG_4)
- **Yeast:** Yeast/Baker's (IgG_4)

(**Note:** Often times egg and milk IgG_4 results are elevated in normal patients. Additionally, oyster IgE positivity rates are substantially elevated compared to all other foods analyzed. This high rate may be due to cross-reacting allergens rather than exposure to oyster itself. Naturally occurring contaminants in the oyster may also be an explanation).

Improving Allergy Outcomes Through "Applied Science"

By incorporating the best information available in the literature, the practical experience of years of food testing and detailed statistical analysis of test results, Allermetrix continues to evolve better testing strategies. We refer to this strategy as "**Applied Science"**. Only with continuous review and reevaluation can laboratories help physicians identify causes of food allergy and ultimately help those who suffer.

It is clear that physicians must correlate all results back to the patient clinical symptoms and history in order to obtain the correct diagnosis .

Individualized elimination/rotation diets are available at Allermetrix (based on your food selections). Additionally, individualized patient information for how to avoid any hidden food testing positive (e.g. egg, wheat etc. which are contained unknowingly in many food preparations) is provided.

References

[i] Schets FM et al., Int. J. Food Microbiol. 113(2) 189, 2007.
[ii] Calkhoven PG et al., Clinical and Experimental Allergy 21 901, 1991