



## Food allergy, hypersensitivity (delayed allergy) and intolerance testing

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What do the following disorders have in common?

Acid reflux	Irritable Bowel Syndrome	Asthma	Skin disorders/rashes
Fatigue	Obesity	Bloating/Gas	Inability to lose weight
Joint/muscle pain	Migraines/headaches	Depression	Anxiety

Give up? It's food hypersensitivity, also called delayed food allergies.

There is a lot of confusion regarding what constitutes a 'food allergy', what the different types of reactions to foods (or other potential allergens) involves and/or what tests are available to determine a person's specific immune reactions to foods or other allergens. This brief overview should provide some clarity.

### **Immune system = Defender and Mechanic**

The immune system plays a number of roles in the body; it identifies foreign substances and seeks to neutralize/eliminate them, and is also responsible for repair due to wear and tear on the body. When repair deficits accumulate, inflammation occurs, and when this becomes chronic, immune dysfunction and autoimmune conditions emerge.

When healthy, the immune system is very tolerant. This means that foreign antigens (i.e., substances the immune system recognizes as 'not self') are soaked up, neutralized, and recycled without burdening the body or provoking symptoms. Healthy people have a natural 'rebalancing' system that allows the immune system to process, recycle, repair and protect the body. However, when immune dysfunction occurs, the body begins to inappropriately react to many substances, which can lead to a host of unpleasant symptoms.

### **Tests of immune system responses: What is measured and what use is it?**

There are three main types of reactions typically discussed in relation to foods or environmental allergens:

1. **Tests of classic allergy** measure IgE (Immunoglobulin E) either by RAST (radioallergosorbent test) blood tests or by in-office skin prick tests. These are also called Type 1 hypersensitivity (or immediate hypersensitivity) reactions and can be quite severe. These tests can be (and are usually the only ones) conducted by medical clinics/hospitals.

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2. **Tests of hypersensitivity** measure delayed immune responses, also known as delayed allergies. There are three mechanisms for delayed hypersensitivity reactions:
  - a. Reactive antibodies (i.e., IgM, IgG)
  - b. Immune complexes
  - c. T-cell mediated responses

These reactions occur several hours to several weeks after exposure; this delay in symptoms makes clinical management (and allergy determination) difficult. However, these types of hypersensitivity reactions are usually the most clinically relevant and useful to help in the healing process.

3. **Intolerances** measure non-immune adverse events primarily centered on digestion, assimilation, and elimination of intestinal contents. Lactose intolerance is the best studied example: A lack of digestive competence for lactose causes intestinal irritation that can elicit alternating constipation and diarrhea, often with bloating or gas. Intolerance testing often requires stool testing or biopsy to confirm.

### **Hypersensitivity tests: all are not equal**

There are several methods that are used to measure delayed hypersensitivity reactions to foods and/or environmental allergens; the most common are serum tests of immune system memory, particle size tests and functional immune system assays.

### **Serum Tests of Immune System Memory**

These tests measure the physical presence of a substance – typically an IgG antibody or IgG antibody subtype (i.e., IgG4). ELISA, IgG, IgG EIA and all tests of immunoglobulin G are of this type. Measurement of antibody reveals that at some time the immune system mounted a response to the tested substance. (The same mechanism operates when we recover from an infection.) Antibodies are formed as a result of these reactions, and they may either *protect* the body or *provoke* reactions. Said differently, IgG tests do not distinguish helpful neutralizing antibodies from harmful reactive antibodies, and therefore may identify foods that may not necessarily be offending agents. In addition, IgG antibodies incorporate only one class of delayed hypersensitivity reactions (albeit the largest one – about 70% of delayed hypersensitivity reactions are caused by IgG antibodies) and therefore, could miss offending foods or environmental agents.

Many places offer IgG serum tests, including Genova, Metamatrix, Doctor's Data, and Quest Diagnostics. If a blood draw is not possible, the IgG4 Bloodstick test by Metamatrix offers a viable

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alternative to gather useful information about hypersensitivities; otherwise, the functional immune system assays are a better choice.

### Particle Size Tests

These tests measure particles of a specific size, typically ten microns. Lymphocytes are memory white blood cells with a typical size of ten microns, and the theory is that by measuring particles within this size range, one can predict the immune response to specific substances. However, clumps of platelets, stacks of red cells, and granulocytes remnants (i.e., pieces of old white blood cells) are also measured because they too can be ten microns. This makes the test much less accurate, and can lead to results that are unnecessarily restrictive. ALCAT and SAGE are labs that offer tests of particle cell size.

### Functional Immune System Assays (also known as Lymphocyte Response Assays (LRAs))

These tests identify the full range of delayed immune responses, including reactive (provoking/harmful) antibodies, immune complexes, and direct T-cell responses to potential food and environmental agents. These tests measure every functionally relevant immune reaction to potential allergens, making them the most comprehensive and clinically relevant tests available. Other true lymphocyte response assays, such as MELISA measure responses through a different mechanism and only measure T-cell responses, making them less clinically relevant.

### Summary

The Lymphocyte Response Assay (LRA) by ELISA/ACT Technologies is the most comprehensive and clinically relevant hypersensitivity test available today. It measures all hypersensitivity pathways with high precision and clinical significance and requires a blood draw.

If a blood draw is not possible, the IgG4 Bloodstick test by Metamatrix is the best choice to help determine possible food allergens.

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