Identifying Food Allergies: Why Serum IgE Testing is a Valuable Tool

Food allergy is an important component of allergic dermatitis. Identification of offending foods is an important factor in evaluating a pet's overall allergic exposure, and appropriate diet changes can often result in immediate relief from symptoms. While traditional elimination/provocation dietary trials have long been considered the "gold standard" for the diagnosis of food allergies, they are time-consuming and demand strict owner adherence to a rigorous protocol. Many owners find it extremely difficult to comply with the restrictions and lengthiness (minimum of six to eight weeks) of a properly conducted food trial, especially in households with multiple pets. Intradermal testing to identify food allergies is not safe due to the risk of inducing an anaphylactic reaction.

Serum IgE testing is a valuable and safe tool for the reliable identification of food allergens. Serum IgE food testing is routinely used in human medicine by primary care physicians for the evaluation of food allergies.[1] Numerous studies have documented a direct correlation between serum levels of food allergen-specific IgE and clinical reactivity to food: as IgE increases, so does the likelihood that a person will react to an ingested food.[2-5]

Food Allergy vs. Food Intolerance

Food allergy is an adverse IgE-mediated immune response to a food ingredient, characterized by rapid onset of symptoms following ingestion of the food. Food allergy is distinct from food intolerance, which is commonly a non-immune reaction to food. Onset of symptoms (bloating, gas or diarrhea) is slower, usually occurring over a period of days. Causes of food intolerance can be metabolic (defective digestive enzymes) or bacterial toxins. Common examples of food intolerance in humans are lactose intolerance and wheat gluten intolerance.

Incidence and Symptoms of Food Allergy (Canines and Felines)

Food allergy accounts for approximately 5-10% of all skin disorders in cats and dogs and 31% of non-seasonal canine dermatitis cases.[6] Symptoms occur in dogs as young as four months, up to 12 years of age; 50% of food-allergic dogs are younger than one year of age when diagnosed.[7]

Many animals with food allergies also have concurrent atopy due to environmental allergens. The most common symptom found in a food-allergic dog or cat is very itchy skin. Symptoms also include chronic or recurrent ear infections (generally caused by secondary yeast infection), seborrhea, hot spots, face rubbing, hair loss and secondary staphylococcal infections that respond to antibiotic treatment but recur after treatment has ended. Food-allergic dogs engage in excessive licking and chewing of the feet and tail areas, likely due to intense pruritus. Gastrointestinal (GI) symptoms can also occur in food-allergic animals, most commonly vomiting and diarrhea. In 15-20% of food allergic animals, dermatological and GI symptoms occur concurrently.[8]

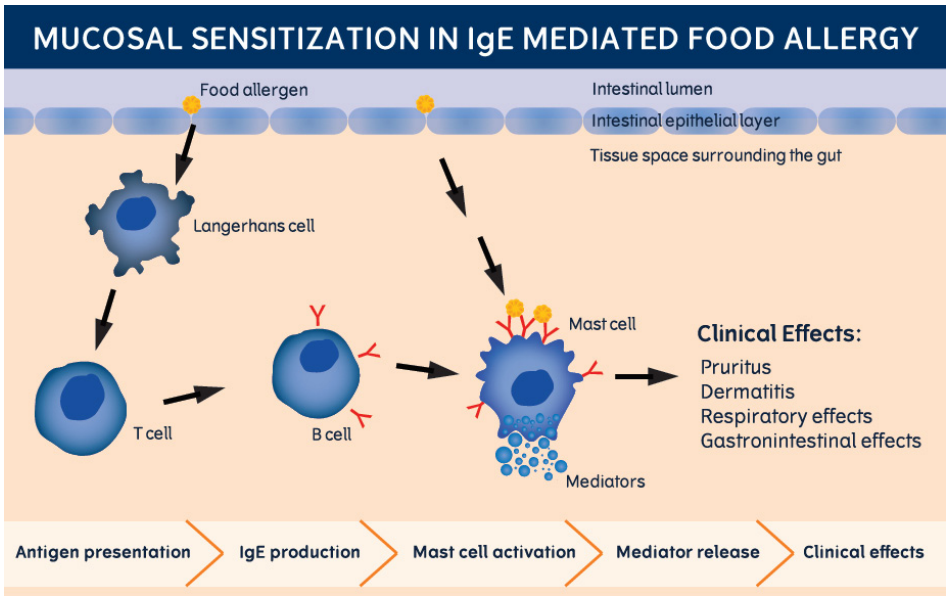
Though typical clinical symptoms of food allergy are sometimes difficult to distinguish from atopy or flea bite hypersensitivity, a few important discriminating features can help to make a proper diagnosis:

- Non-seasonal; year-round symptoms
- Symptoms occurring before one year of age
- Intense pruritus; tail-rubbing and feet-licking
- Primary focal areas affected: ears, base of tail and feet ("ears, rears and feet")
- Recurrent ear infections (yeast otitis)
- Poor response to antihistamines and steroids

The Pathogenesis of Food Allergy

The gastrointestinal (GI) tract is one of the largest organs in the body. Commonly referred to as the "gut," the GI tract includes the gastrointestinal lumen and the gut-associated lymphoid tissue (GALT). The GI lumen is lined by the gastrointestinal mucosa, which serves four critical functions: 1) to process ingested food for energy and growth, 2) to protect the host from harmful pathogens, 3) to serve as a physical barrier, preventing the transport of food antigens from the GI lumen to mast cells in the GALT, and 4) to develop oral tolerance to foods that are needed for survival.

As food antigens pass through the GI tract, they are introduced to the gastrointestinal mucosa, which contains more lymphoid cells and produces more antibodies than any other site in the body. It is here that oral tolerance to foods is developed. Failure to develop oral tolerance leads to food allergy. In healthy individuals, up to 2% of ingested food antigens, (small amounts of intact proteins and large peptides) can make it through the intestinal mucosal barrier to be rapidly absorbed and transported throughout the body, without causing an unhealthy immune response.[9]



The seven most common food allergies in dogs:

1. Beef
2. Chicken
3. Milk
4. Eggs
5. Corn
6. Wheat
7. Soybean

For food allergy to occur, food antigens must breach the intestinal barrier in order to be exposed to the mucosal immune system. Increased transmission of food antigens through the GI mucosa contributes to the development of food allergy by increasing the rate of exposure. Allergic sensitization to ingested food antigens occurs in the GALT, where allergen-specific IgE binds to high affinity IgE receptors on the surface of mast cells and basophils.[10] Upon subsequent exposure to the same food, cross-linking of antibody-primed IgE receptors leads to mast cell degranulation, the release of inflammatory mediators and the accumulation of clinical symptoms.

In food-allergic patients, barrier defects in the mucosal lining create increased permeability. In such individuals, larger protein antigens can be absorbed before digestion to smaller peptides is complete, allowing hypersensitivity to develop.

In a 2009 study of food-allergic infants, intestinal permeability was significantly increased when compared with healthy, non food-allergic young children. Furthermore, intestinal permeability remained elevated in the food-allergic infants even after 6 months of consuming an allergen-free diet.[11]

In a study of immune responses to food antigens in dogs, atopic dogs had higher levels of food allergen-specific IgE when compared to normal dogs, consistent with a Th2 (allergenic T cell) phenotype.[12] In another study of cutaneous adverse food reactions in canines, elevated Th2-related gene and immune T cell expression was demonstrated in the skin of food-allergic animals fed a provocation diet. Dogs selected for study were identified by a food provocation/food elimination dietary trial. Despite resolution of clinical symptoms when fed an elimination diet, the Th2 immune phenotype persisted in skin biopsies of food-allergic animals, suggesting a continuing "pre-activated immune status" in dogs previously sensitized to food allergens.[13]

Three Important Considerations When Interpreting Serum IgE Food Test Results:

1. Serum IgE testing for foods should always be interpreted in the context of the patient's clinical history, symptoms, and relevant allergen exposure.
2. The presence of IgE indicates sensitization to a food, but is not always equivalent to clinical allergy. A positive score may be reported as the result of antibody cross-reactivity to other allergens with a similar protein structure. It is important to consider possible cross-reactivity within allergen families when selecting the foods to eliminate from the pet's diet.
3. A negative IgE score indicates that no IgE sensitization was found for that ingredient in the patient.

Serum IgE food testing can provide crucial support to veterinarians by identifying target allergens to avoid for a food trial. When selecting an appropriate diet for a patient, we recommend avoidance of food ingredients scoring positively in the test, reflecting elevated IgE.

In some cases, a patient may show elevated IgE to numerous foods, which limits the number of available diets and makes dietary restrictions more difficult. With these patients, more consideration is given to allergen cross-reactivity to ensure that unnecessary foods are not removed from the pet's diet. In either case, it is safer to remove ingredients from a pet's diet than to continue feeding sensitizing ingredients. Therefore, a reputable and specific serum allergy test is important. Negative scores are just as clinically relevant as positive scores when making diet recommendations.

> "Serology may be helpful in the management of dogs with suspected adverse food reactions by identifying suitable candidates for limited-antigen dietary trials, and in the selection of the most appropriate diet."
>
> Dr. Richard E.W. Hallwell
> Professor Emeritus, University of Edinburgh
> Royal (Dick) School of Veterinary Studies
> Edinburgh, UK

Case Study:
In a 2012 study, sensitivity and specificity of serum IgE testing was compared with patch (skin) testing in a group of dogs with cutaneous adverse food reactions, identified by dietary provocation/elimination trials. Specificity of the serum IgE test was high (91.4%), and was equivalent to the specificity of food antigen patch testing, indicating that serum IgE testing is reliable and can be helpful in selecting non-sensitizing food ingredients.[14]

Allergen Cross-Reactivity

Veterinarians and pet owners should be aware of possible cross-reactivity between plant allergens and foods. Cross-reactivity occurs when IgE antibodies to specific allergens (plant, insect, epidermal, mold, dust mite or foods) are capable of identifying similar allergens from different sources. Cross-reactive antigenic structures recognized by the antibody are identical, even if they are members of different plant or animal families. Cross-reactions are frequently seen between certain pollen types and foods.

Some examples:

- Antibodies targeting a birch pollen allergen detect a similar protein found in apple and avocado.
- Antibodies to short ragweed pollen cross-react with similar proteins in cantaloupe and bananas.
- Grasses commonly cross-react with cereal grains, which are cultivated grasses: Timothy grass and Bluegrass cross-react with wheat; Crowngrass and Johnson grass cross-react with corn.
- Antibodies to tropomyosin (a muscle protein), found in the exoskeletons of dust mites and cockroach, show cross-reactivity to the same protein found in shrimp and other shellfish.

Cross-Reaction Can Occur in Two Ways:

1. Antigenic cross-reactivity among families (related species)

   Timothy Grass → Wheat

2. Pan-allergen cross-reactivity (unrelated species/families)

   Birch Tree → Apple

   Short Ragweed → Cantaloupe

A clear understanding of allergen cross-reactivity plays an important role in the successful management of your patient's allergies. ALK has researched allergen cross-reactivity thoroughly. We believe it is vital that our veterinary partners understand how we arrive at our treatment and dietary recommendations, and why your test results may, at times, look different than expected.

Pan-Allergens

Pan-allergens are protein antigens that are widely distributed throughout nature. The structure of these "universal" proteins is highly conserved across plant and animal species so that vital protein functions remain stable and unchanged. Pan-allergens are responsible for many IgE cross-reactions, even between unrelated pollen and plant food allergen sources.

A well-known pan-allergen is profilin, the primary allergen found in birch, grass and many other plant pollens. Profilin is an essential protein component of all eukaryotic cells, and its structure is highly conserved. Profilin is found in many plant foods. The following chart illustrates some common pan-allergen and other cross-reactive antigens detected by serum IgE testing. The nature of immunological relationships between allergens is particularly important in the understanding of IgE food test results, when pollen and food allergens cross-react.

PAN-ALLERGENS AND OTHER ANTIGENIC CROSS-REACTIONS BETWEEN FOOD AND POLLENS

If your pet is allergic to:	Your pet could also be allergic to:
Beef, cow's milk, chicken, turkey, duck, egg, lamb, pork, rabbit, venison	Albumin (pan-allergen)
Tomato, potato, tobacco leaf	Mugwort / sagebush (pan-allergen)
Apple, pear, potato, tobacco, carrot, kiwi, hazelnut, plum, banana, peach, parsley, cherry	Birch (pan-allergen)
Barley, corn, oats, wheat, rice	Grass pollens (cereal grains are cultivated grasses)
Green pea, green bean, peanut, soybean	Mesquite, alfalfa pollen, red clover (cross-reactive members of the legume family)
Beets, spinach	Kochia, lambsquarters, russian thistle (cross-reactive members of the goosefoot family)

IgG and Food Allergy

In recent years, some laboratories have begun to promote serological testing for food antigen-specific IgG to diagnose food-induced hypersensitivity. Based upon a review of evidence-based medicine in humans, there is no credible evidence that measuring IgG antibodies is useful for diagnosing food allergy, nor that IgG antibodies cause symptoms.[15,16] IgG antibodies to foods are commonly found in healthy adults and children. The presence of IgG reflects exposure to allergen but not the presence of disease. The exception is anti-gliadin (a wheat protein) IgG antibodies, which are elevated in human patients with histologically confirmed celiac disease (a form of wheat gluten intolerance). IgG antibodies against foods are part of the body's normal physiological response to repeated exposure to food components. Additionally, a convincing case has not been made that IgG can induce histamine release, a hallmark of antibody-induced hypersensitivity.[15] Because IgG serum concentrations are a thousand-fold higher than IgE, using an IgG test for foods greatly increases the risk of making inappropriate dietary restrictions, which could have a negative nutritional impact upon the patient.

Additional Readings and Information

Food allergies are a complex issue. For further information on hydrolyzed protein diets and grain storage mites and their relationship to food allergy, please contact Customer Service: 1-800-444-2370.

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