

## **The Food Reaction Test (FRT)** **CANINE & FELINE**

### **SUMMARY**

Adverse food reactions (AFR), may induce a dysfunction of the intestine's mucosal barrier, disturb the normal protein digestion process and lead to mucosa permeation.

Normal digestion of the glycoproteins contained in food results in the production of amino acids. In patients with adverse food reactions, non-completely digested glycoproteins can permeate through the intestinal wall and elicit local inflammatory responses.

These responses may be cellular as well as humoral. In this last case hypersensitive reactions of type-I and type-III can play a role.

The FRT test identifies immune reactions to food components. It is important to identify and address potential food problems at the early stage of dermatology consultations since the symptoms associated are close and can be confounded with those of atopy. FRT may point out potential problems with food and suggest which food sources may be best suited for the control of adverse food reactions.

### **Prevalence of adverse food reactions**

Adverse food reaction is defined as a reaction to dietary components (1). The incidence of food allergy, with production of IgE is estimated at 5-8% in allergic dogs and 12% in allergic cats. However, adverse food reactions may affect 20 to 35% of atopic dogs and cats. Due to the complex nature of AFRs, clinicians may differ in the reported prevalence frequency. Their prevalence is increasing.

### **Clinical aspects related to Adverse Food Reactions**

The period between the food ingestion and the appearance of symptoms depend on the type of the reaction involved, the degree of patient sensitivity and the time of exposition.

In the dog, the most common clinical sign is non-seasonal pruritus (2,3,4) with presence of urticaria and dermatitis. In the cat, there are no recognized clinical criteria to distinguish cats with food allergy from those with environmental allergy (5).

Gastrointestinal symptoms like loss of appetite, weight loss, abdominal pain, vomiting, persistent diarrhoea and/or constipation, flatulence, borborygmus, etc. may also be indication of adverse food reactions.

Planning elimination diets and challenge to confirm the diagnosis of a food adverse reaction is problematic and their rate of success is somewhat deceptive.

### **Most common clinical signs related to AFR**

- Non-seasonal generalized pruritus
- Gastrointestinal symptoms: loss of appetite, weight loss, abdominal pain and borborygmus, vomiting, persistent diarrhoea/constipation, flatulence, etc.

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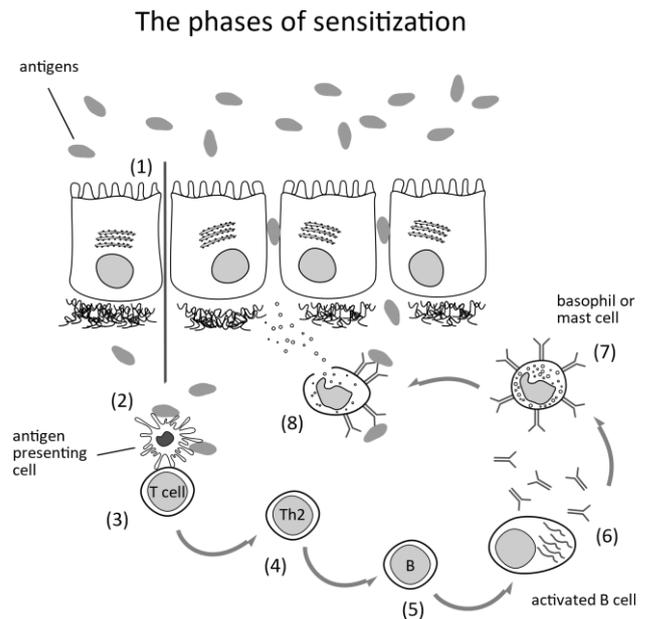
### The inflammatory mechanism of the intestinal wall

Adverse food reactions are susceptible to weaken and damage the microvilli and cell junctions of the intestinal mucosa allowing the transit of undigested proteins, food particles and microorganisms from the intestine to the basal membrane. The illustration shows a comparative of the normal and a damaged intestine mucosa.

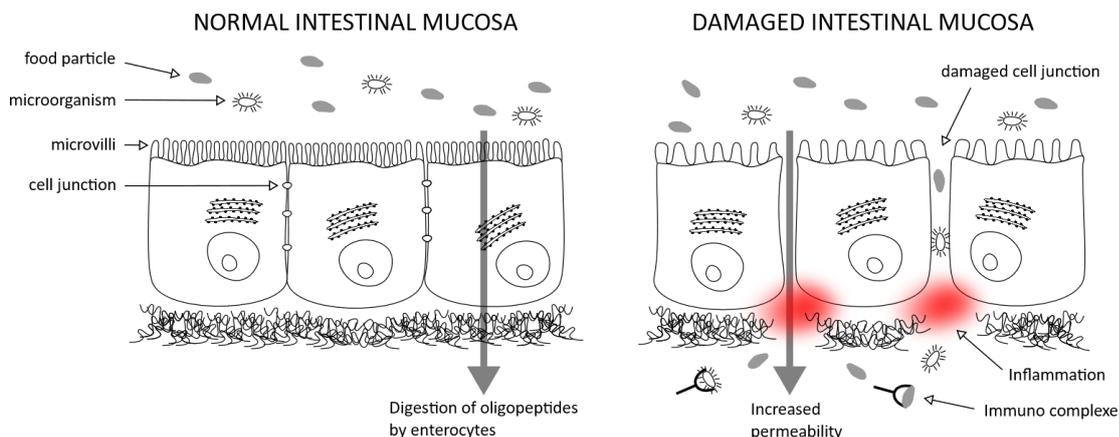
### The immunopathogenesis of the humoral responses

The sensitization phases:

- (1) The antigens penetrate through the weakened intestinal mucosa.
- (2) The allergens encounter resident dendritic cells (allergen presenting cells, APC)
- (3) APCs migrate to the regional lymph node where they meet naïve T cells which recognize the antigen (non-self) through the major histocompatibility system.
- (4) T cells become stimulated to a Th2 phenotype.
- (5) Stimulated Th2 lymphocytes develop into allergen specific activated B cells.
- (6) Activated B cells differentiate into plasma cells which start the production of IgE and IgG immunoglobulins.
- (7) Antigen specific IgE and IgG bind through their specific receptors to circulating basophil and mast cells.
- (8) During successive antigen stimulations, they release factors which initiate and maintain the inflammatory process.



The production of immune complexes activate cell responses leading to the release of histamine and inflammatory factors. The blood complement system also contribute to maintain the inflammatory process.



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With the progression of the lesions, the normal absorption processes become distressed. Normally during the digestion process, oligopeptides pass through the enterocytes which cleave them into amino acids which are released in the basal membrane. The protein fragments are very small (1 to 4 amino acid sequences) which transfer into blood vessels and are transported. Small oligopeptide sizes do not have the capacity of triggering an immune response.

### **The Food Reaction Test (FRT)**

FRT is a serum test, ELISA based designed to identify immune reactions to food components it measures a combination of IgE, IgG (1 to 4 subclasses) antibody reactions against food components.

### **What is tested with the Food Reaction Test?**

The FRT detects a combination of Type-I and Type-III reactions related to local inflammation of the intestinal mucosa.

#### Type-I reaction

Characterized by an IgE reaction. The response is rapid, occurring shortly after food intake (immediate to few hours).

#### Type-III

Characterized by the IgG 1 to 4 subclass and IgA reactions. The presence of high levels of antibodies indicate the formation of immune complexes which activate the complement and attract leucocytes (macrophages, basophils and eosinophils). A cascade of reactions leading to inflammation starts (5). Type-III reactions could manifest days after intake of the food making in some cases difficult to identify the cause(s); delayed reactions.

### **Use of the FRT test**

The results of the FRT identify immune reactivity against food components. As a result the results may indicate if a diet change might be necessary.

### **Do Cross Reactive Carbohydrate Determinants (CCDs) interfere with food testing?**

CCDs are carbohydrate structures in plants that can elicit immune reactions in pets (6). CCDs are present in most plant foods and they affect the measurement of humoral immune reactions. Studies demonstrate the presence of anti-CCD antibodies in foods (7).

In dogs, it is observed that 60-75% of patients show CCD reactions against food plants. The CCD reactions must be blocked before testing to obtain accurate results (8).

### **Can CCDs reactions be controlled?**

Yes, the anti-CCD reactions are controlled in FRT.

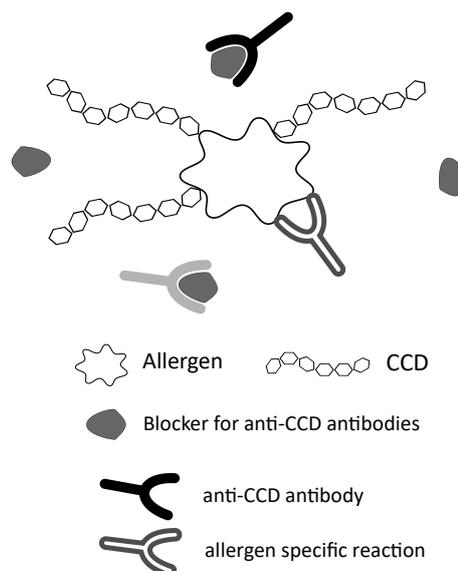
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To identify allergen specific reactions, the Heska FRT test benefits from an anti-CCD reaction blocking reagent.

The illustration (right), shows the specific reaction after blocking anti-CCD antibodies.

If anti-CCD reactions are not blocked, false-positive reactions are measured.

The FRT test uses a proprietary CCD specific blocker.



### When improvement may be expected?

The intestinal mucosa has a high regenerative capacity. Extensive damage to the intestinal mucosa of the canine intestine after 24 hr of cold preservation and transplantation recovers functionally within 3–7 days in the jejunum and 7–14 days in the ileum, whereas morphological recovery takes around 28 days (9).

Based on the results of the FRT, the first signs of improvement should be perceptible within 2 to 4 weeks of diet change. It is recommended maintaining the patient for at least one month on the new diet composition to allow the intestinal mucosa to fully recover its structure and function. After, it is possible start introducing progressively other food components if needed to find out an adequate long term and effective diet for the patient.

### Food Reaction Test allergen panel

The FRT tests the reactions for 12 animal and 12 plant food components.

| <b><i>Animal proteins</i></b> | <b><i>Carbohydrate components</i></b> |
|-------------------------------|---------------------------------------|
| <i>Chicken egg</i>            | <i>Corn</i>                           |
| <i>Fish-mix</i>               | <i>Wheat</i>                          |
| <i>Rabbit</i>                 | <i>White Potato</i>                   |
| <i>Trout, lake</i>            | <i>Rice</i>                           |
| <i>Lamb</i>                   | <i>Sweet Potato</i>                   |
| <i>Cow milk</i>               | <i>Barley</i>                         |
| <i>Beef</i>                   | <i>Carrot</i>                         |
| <i>Turkey</i>                 | <i>Soybean</i>                        |
| <i>Tuna</i>                   | <i>Green Bean</i>                     |
| <i>Salmon</i>                 | <i>Oat</i>                            |
| <i>Chicken</i>                | <i>Pea</i>                            |
| <i>Pork</i>                   | <i>Brewer's yeast</i>                 |

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