Adverse food reaction and the gastrointestinal tract

The small intestine (SI) mucosa has a general barrier function but must also be protective. Thereby an immune response against pathogens takes place while harmless environmental antigens (bacteria, food components) must be tolerated. Despite recent advances in understanding the immune system, it is still unclear what prompts the SI to respond to or to become tolerant of a particular antigen.

The mucosal immune system is extremely complex, here just a very few highlights should be outlined:

1. In the intestinal mucosa IgA is synthesised by B lymphoid lineage and then transported into the intestinal lumen, where its main function is immune exclusion (binding the antigen and neutralising it). Immune exclusion limits the amount of antigen absorbed into the intestinal mucosa and thus the amount available to stimulate active immune responses. This helps maintain tolerance and protects the mucosa from antigen invasion.

2. Response to parasites occurs through IgE which is bound on mucosal mast cells. Inappropriate IgE responses to food antigens also can be generated, providing a potential mechanism for food allergy.

3. The mucosal immune system can either generate specific immune responses (e.g., toward a pathogen) or remain tolerant (e.g., to commensal bacteria or food components). The best current hypothesis which effect occurs is the “danger theory”: the type of response depends on the context in which the antigen in presented. The normal intestinal mucosa has an intact mucosal barrier and an environment dominated by down-regulatory cytokines, who in addition encourage IgA response (which again limits mucosal antigen exposure through immune exclusion). Therefore most immune responses that develop are tolerance responses. However, when the mucosa is invaded by a pathogen or toxin, cell damage leads to the release of “danger signals” (inflammatory mediators, cytokines, chemokines). Thus, a tolerance immune response is changed into an active immune response. This can be either Th1 dominated (cytotoxic or IgG response) or Th2 dominated (IgE response). If the danger signals persist this may lead to a breakdown in tolerance to harmless environmental antigens.

Sensitization of a patient to a dietary antigen may provoke an IgE-mediated allergic reaction when the animal is exposed to the antigen next time. The release of numerous mediators may have effects like pruritus, urticaria, or even anaphylaxis, or on the intestine they may induce changes in absorption, secretion, permeability and gut motility, causing vomiting and diarrhoea.

Theoretically, any intestinal disease may predispose the animal to the development of food sensitivity; therefore feeding of a novel protein source during these periods may preclude the development of sensitivity to the diet. Allergies acquired as a result of GI disease will not respond 100% during the elimination trial.

Adverse reaction to food components

An adverse reaction to food is a repeatable, unpleasant response to a dietary component. Thereby we have to distinguish between a manifestation of an immunologic reaction to a dietary antigen (a true food allergy or hypersensitivity) and a non-immunologic reaction (food intolerance). In view of the number of diverse foods that are ingested by animals, it is not surprising that adverse reactions develop to dietary substances. The fact that food-related reactions appear relatively infrequently is testimony to the effectiveness of the intestinal mucosal barrier. Although different pathogenetic mechanisms are responsible for the two groups, the food allergy and the food intolerance, the clinical signs are similar, and the approach to treatment is the same, usually involving exclusion of the offending food component. Food intolerance may be associated with a single ingredient of a prepared food (lactose, preserv-
Food allergy

This hypersensitivity reaction includes all immunological reactions which become manifest in dermatological and/or gastrointestinal (GI) symptoms. Food allergy with GI signs may be more difficult to prove than cases in which dermatologic signs exist. The management of food allergy is simple: “feed any food that does not contain the allergen, and the animal will be healthy”. The difficulty for the clinician lies in the recognition of food allergy and the identification of foods that must be excluded. Food sensitivity reactions were suspected or documented in 49% of cats presented because of gastrointestinal problems in a prospective study. The authors concluded that adverse reactions to dietary ingredients are common in cats with chronic GI problems. It was also documented by other studies that gastrointestinal clinical signs were significantly improved by the feeding of selected protein diets.

Dietary hypersensitivity may involve a variety of mechanisms, including type I (IgE mediated), type II (immune complex mediated), and type IV (delayed) reactions.

Symptoms:
Clinical signs of food allergy generally involve the skin and GI tract. The major sign of skin disease is pruritus (anywhere, but often face, paws, rear or ears). Skin lesions and secondary infections arise through self-trauma. In cats, food allergy may result in miliary dermatitis, self induced alopecia, eosinophilic granuloma complex, or even more often in self induced ulcerations of head and neck.

Signs of food-allergic gastrointestinal disease are not pathognomonic and include vomiting, diarrhea, abdominal pain, flatulence, borborygmi, increased bowel movements, weight loss or failure to thrive. Every level of the GI tract can be damaged by adverse food reaction. The clinical signs usually relate to gastric and small bowel dysfunction, but colitis can also occur. The role of food allergy in canine or feline inflammatory bowel disease (IBD) is unknown. However, hydrolyzed or selected protein diets may be useful in the management of IBD.

Diagnosis:
Clinical signs should resolve on exclusion of the offending dietary component and return with rechallenging. Dietary trial is the golden standard to confirm the presence of dietary sensitivity, although such trials do not distinguish food intolerance from allergy.

Skin testing has been proved unreliable in the diagnosis of food-allergic disease. Alternatively the ELISA (blood test) can be used to measure antigen-specific serum antibodies to food components in vitro. In most cases IgG and IgE responses to different food components are assessed. But, like in other laboratory tests too, several limiting factors have to be considered:

- First, antibodies to food components can be found in normal or subclinically effected animals (the same with allergy testing for environmental allergens for Atopic dermatitis – the diagnosis must be a clinical diagnosis and the tests are performed to learn which allergens are involved).
- Second, because many vaccines may contain bovine serum albumine, animals may develop antibodies to beef antigens.
- Third, food allergy in not only triggered by IgE but also by IgG thus if only one of those antibodies is tested the other response is missed.
- Fourth, one food protein contains various allergens. If the in vitro antigen is not related it may not react at all.
- Fifth, the antibodies may have arisen secondary to another underlying intestinal disease (see above discussion about danger theory).

Food Intolerance

Most of the mechanisms of food intolerance are complex.

- Food poisoning caused by a toxin or toxin-producing organism or organisms that have multiplied in the food and cause acute GI symptoms.
- Pharmacologic intolerance caused by pharmacologically active compounds (e.g. chocolate poisoning through methylxanthines or through vasoactive amines)
- Pseudoallergic mechanisms histamine mediated; high in histamine content is e.g. some fish and some commercial dog foods or because of histamine producing bacteria. Strawberries or food additives can cause histamine release from mast cells without IgE mediation.
- Metabolic reactions intolerance to lactose associated with lactase deficiency.
- Food idiosyncrasy an abnormal response that resembles food allergy but that does not involve immune mechanisms (e.g. to food additives).
- Intolerance to disaccharides commonly occurs secondary to enteritis or rapid food changes.

The clinical signs are not distinguishable from food allergy, thus see food allergy.

Dietary Trials

The principle of an exclusion (elimination) diet is to feed dietary components to which the animal has not previously been exposed. This diet should be the sole source of nutrition for the duration of the trial. Complete owner compliance is essential, and it must be stressed that all treats and supplements must be withheld.

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Due to the fact that food intolerance following an unsuccessful symptomatic treatment,
the dog showed massive flatulence in the same evening. However, the owner could not
detect any connection between these symptoms, in fact, he wasn’t aware that there could
be a connection at all. The previous veterinarian already prescribed several diets, always using
commercial hypoallergenic products. Also different antibiotics, cortisone and antifungal
shampoo were tried without success.

**Cases**

**“Don Carlos”**
Rottweiler, male dog, 9 months old

**History:** Diarrhoea and massive flatulence from 3 months old, general behaviour is O.K. He is regularly wormed, the intensity of diarrhoea changes, sometimes heavy sometimes slight. Dog goes to a training school, where he is incentivised by food (different treats), generally he is fed commercial supermarket-feed.

**Progress:** The owner had already suspected the feed was causing the problems; a food-change was carried out in accordance with the serological food allergy test. The results showed IgE reactions against beef, pork, and lamb, and IgG reactions against fish. Consequently, he administers a diet which does not contain anything of the positively responding substances and instructs the owners to follow this elimination-diet rigorously. The dog is already more lively within 2 weeks and vomiting does not reoccur.

**“Charly”**
European domestic cat, male castrated, 3 years old

**History:** Cat was an orphan and was bottle fed by the previous veterinarian, positive IgE and IgG reactions were found against beef, lamb, chicken, duck and fish. Based on this test results and knowing that the cat is very fussy the veterinarian chooses an elimination-diet containing ostrich meat. Within one month, the ulceration at the head had vanished without additional therapy, and the nutritional condition was satisfying within 3 months.

**“Meggy”**
European domestic cat, female spayed, 7 years old

**History:** For 5 years she had suffered from chronic diarrhoea. Different veterinarians prescribed antibiotics, antihelminthic therapy or other regimes, however always without success.

**Progress:** Due to the fact that food intolerance was suspected, a serological food allergy test was performed. The test results showed positive IgG antibodies against nearly all substances which were tested and allergen specific IgE antibodies were detected against beef, lamb, chicken, fish and soy protein. Based on this test results the cat was strictly fed a diet containing hydrolysed antigens. The cat started to improve within feeding this diet from the 2nd month. After 2 months the diarrhoea had disappeared. After being fed with the conventional food, diarrhoea occurred again.

**“Tesso”**
Malinois, female spayed, 6.5 years old

**History:** For approximately 3 months, the dog has been increasingly weaker and vomits daily.

**Progress:** following an unsuccessful symptomatic treatment the veterinarian decides to carry out a food allergy test. The results showed IgE reactions against beef, pork, and lamb, and IgG reactions against fish. Consequently, he administers a diet which contains nothing of the positively responding substances and instructs the owners to follow this elimination-diet rigorously. The dog is already more lively within 2 weeks and vomiting does not reoccur.

**Literature:**

"Sheila"
Dachshund, female spayed, 4 years old
History: The dog is “always” suffering from soft poos and occasionally the whole body is pruritic. The second dog living in the household doesn’t show any symptoms. Several different diets were fed. In fact the fur of the dog became more beautiful on that occasion; however a very strong itch and diarrhea occurred. The owner blamed the food for it.
Clinic: No abnormality detected.
Progress: Since the pruritic episodes might not be linked to the feeding as there also seemed to be seasonal fluctuations, a serological allergy test was performed. One was carried out to detect allergen specific antibodies against seasonal and perennial allergens and additional a food allergy test was conducted. The first showed positive reactions against some pollens, house dust mites and storage mites; the second detected positive IgE reactions against lamb, chicken duck and wheat, and IgG antibodies against lamb, wheat, soy, rice and oat. The feeding was rearranged immediately choosing a commercial food, which contains none of the positive tested substances. The faeces were moulded soon afterwards, but the itchy episodes had only slightly improved. Therefore an allergen specific immunotherapy was started, and after approximately 3 months, the pruritus gradually improved.

"Larissa"
White shepherd, female, 3 years old
History: Started as puppy licking the stomach and immediately got diarrhoea. She was previously fed a specific “dermatological” food for 2-3 months and is now fed a product based on “lamb and rice” however, without success. The conclusion was that the food is not the reason for the problem.
Clinic: Only slight erythema of the skin was seen at the clinical examination.
Progress: A home cooked elimination diet with horse meat and potato was carried out. Because of the application of cortisone which was necessary from time to time the veterinarian did not perform a food allergy test. After 2 months still no improvement of the symptoms was perceived, and the owner was close to giving up. However with some persuasion, the diet was continued and after 3 months the dog was free of complaints. Since the owner didn’t want to do any further experiments with the feeding, a ration including a sufficient amount of mineral nutrients mixture was included.