

## Nutritional management of gastrointestinal disorders due to food sensitivities

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### WHAT ARE FOOD SENSITIVITIES OR 'ADVERSE REACTIONS TO FOOD'?

The most appropriate term for abnormal responses to an ingested food is 'Adverse Reactions to Food' (ARF). However, due to a lack of understanding of this term by pet owners, although technically not completely correct, the terms 'food allergy', 'food hypersensitivity' or 'food sensitivity' are often used by veterinarians to describe ARF. We will use the term ARF throughout this document. ARF can be classified as non-immunologic and immunologic (the latter being the true food allergies or hypersensitivities – see Table I).<sup>1,2</sup>

**Table I** – Classification of Adverse Reactions to Food\*

Category	Immunologic		Non-immunologic					
	Food anaphylaxis	Food allergy	Dietary indiscretion	Food intolerance				
Subcategory				Food toxicity	Metabolic food reaction	Food idiosyncrasy	Pharmacologic reactions to food	Nonspecific dietary sensitivity
Example	Peanut allergy in people	Mainly IgE mediated, but also with type II (cytotoxic), III (immune complex), and IV (cell-mediated) components	Garbage can, pica	Aflatoxins, enterotoxins	Lactose intolerance	Onions, grapes	Histamines	Loose faeces in large breeds

\*Adapted from Roudebush<sup>1</sup> and Cave<sup>2</sup>

In dogs and cats, the symptoms and signs of ARF involve the skin or gastrointestinal (GI) tract<sup>1</sup>, or both.<sup>3</sup> ARF may lead to a wide variety of skin lesions. Basically, ARF should be considered in the differential diagnosis of any pruritic disorder. The same holds true for GI disorders (see below). Signs may vary from a mildly increased defaecation frequency to severe vomiting and/or diarrhoea due to inflammatory bowel disease (IBD).

### HOW OFTEN DO WE SEE ADVERSE REACTIONS TO FOOD?

True prevalence figures for ARF in dogs and cats are not known. This is due to the fact that ARF often co-exists with other allergies (e.g., flea allergies and atopic dermatitis) and/or that the role of food in some diseases is still poorly understood.<sup>1</sup> Estimates of ARF constituting up to 50% of all dermatoses are made.<sup>3</sup> Prevalence data of ARF in GI disorders are even scarcer. In a study in cats with chronic GI problems, 49% of those cats improved on a novel protein diet.<sup>4</sup> In various studies (cited in<sup>1&5</sup>), clinical improvement in dogs with IBD in both the small and large bowel suggests a role of food sensitivity in their pathogenesis.

### TRUE FOOD ALLERGIES - ALLERGENS AND AETIOPATHOGENESIS

Food proteins and/or glycoproteins make up the vast majority of known food allergens<sup>1</sup> and most of them have a size of 10-70 kDa.<sup>6</sup> Carbohydrate and lipid allergies have not been described in dogs, and even in people these presumed allergies may have been due to contamination of these ingredients with (glyco)proteins (cited in<sup>2</sup>). The residual allergenicity of protein hydrolysate decreases with the decreased size of protein fractions. Since the alleged allergic mechanism in dogs and cats is mainly through IgE mediated mast cell degranulation<sup>2,7</sup> and since mast cell degranulation needs crosslinking between two IgE receptors, the assumed minimum polypeptide size limit for an allergen to elicit an allergic response is ~3 kDa.<sup>8</sup>

The most common ingredients reported to cause ARF with cutaneous (and possibly also GI) signs in dogs are listed in Table II. These data are from Roudebush<sup>9</sup>, who consolidated all available data in the literature published over the last four decades. Such data in GI disease are lacking, but one may presume that the same ingredients are also involved in ARF with GI signs. A unique food allergy similar to coeliac disease in people is the gluten-sensitive enteropathy in Irish Setters.<sup>10</sup> This gluten enteropathy, in which Irish Setters are allergic to the gliadin component of gluten from some cereal grains, has not been described in any other dog or cat breed.

**Table II – Ingredients reported to cause AFR in dogs (330 cases)\***

Beef	32%
Dairy	18%
Chicken	15%
Wheat	13%
Chicken egg	7%
Soy	5%
Lamb	5%
Pork	4%
Fish	4%
Corn	3%
Turkey	2%
Rice	2%
Duck	1%

\*Adapted from Roudebush<sup>9</sup>

The GI tract is confronted with two very conflicting tasks: providing an effective barrier against pathogenic microorganisms and foreign substances versus preventing an adverse immune response against the massive load of foreign antigens represented by the food. The gastrointestinal mucosal barrier and oral tolerance by the gut-associated lymphoid tissue (GALT) are two effective mechanisms in the defense against hypersensitivity to food antigens.<sup>1</sup>

An effective mucosal barrier prevents the vast majority of food antigens from reaching the GALT. Certain carbohydrate compounds in the mucosal layer and IgA play an important role in this barrier function.<sup>1</sup> Complete digestion of the food (leading to small particles, like peptides and single amino acids, which are presumed non-allergenic) is another important component of this defense. Despite this, some food antigens will cross this barrier and reach the GALT. An effective tolerance mechanism to these GALT-presented antigens is generated by a subtle interplay of T-cell deletion and anergy, as well as the induction of regulatory and immunosuppressor T-cell effects and IgA production.<sup>2</sup>

Although the exact mechanisms which lead to the development of food allergies are poorly understood, any disruption in the above defence mechanisms may predispose to food allergies. These events may include a loss in mucosal barrier function (e.g., by severe viral enteritis or bacterial enterotoxins), intestinal parasites or altered intestinal flora.<sup>2</sup> Currently, the influence of the gut microbiota on the development of food allergies and immunity in general is a hot topic in human and comparative biomedical research.<sup>11</sup>

## IN WHAT GI DISORDERS MAY FOOD SENSITIVITIES PLAY A ROLE?

As described before, food plays a very important role in the development of many GI disorders. Besides the 'mundane' dietary indiscretions, which typically lead to acute, self-limiting and short bouts of vomiting and diarrhoea, and food intolerance such as lactose intolerance, food seems to play an important role in the pathogenesis, as well as the management of the following chronic gastrointestinal disorders.<sup>5,12,13,14</sup>

- Chronic gastritis
- Inflammatory bowel disease (IBD), incl. lymphocytic-plasmacytic enteritis and eosinophilic colitis
- Chronic idiopathic intestinal disorders (CIID)
- Constipation

Nowadays, the typical work-up of a case with chronic gastrointestinal disease after excluding parasites, pancreatic disease and other extraintestinal causes is to start a food trial first.<sup>2</sup> Many cases of IBD/CIID respond favourably to a dietary change, typically with a highly digestible food, either with novel protein and carbohydrate sources or with a hydrolysed animal protein source.<sup>2,5</sup> It is unclear whether the favourable response to this dietary change is due to a true food allergy as primary inciting cause, or that a food allergy is a secondary event due to the mucosal inflammation (and loss of mucosal barrier), which predisposes to the development of food allergies.

## DIAGNOSIS

Several diagnostic procedures have been suggested to diagnose food allergies in dogs with GI and skin disease. The measurement of food-specific antibodies (typically by ELISA or RAST) in plasma has been shown to be of limited diagnostic value.<sup>15</sup> Endoscopic food sensitivity testing has been shown to have more diagnostic value. During this test, individual food ingredient solutions are applied to the gastric mucosa during an endoscopy and the mucosa is observed for mucosal changes like oedema for 5 minutes.<sup>16</sup> It has been shown that ~10% of dogs with IBD are positive on this test.<sup>1</sup> Despite its diagnostic value, the costs and the invasiveness of the procedure have prevented its widespread use in daily clinical practice. Recently, a new 'patch test' tool was developed showing high sensitivity and negative predictability. This test may be used to select the most appropriate elimination trial food in dogs with suspected ARF.<sup>17</sup>

The standard for the diagnosis of food sensitivities is still a dietary elimination trial with either a commercial hydrolysed or a novel protein diet<sup>2</sup>, ideally followed by a dietary challenge with the suspected offending ingredient(s) or foods. Home-made elimination foods offer the flexibility in choosing unique protein and carbohydrate sources.<sup>2</sup> However, the risk for nutritional deficiencies with these foods is significant.<sup>18,19</sup>

## NUTRITIONAL MANAGEMENT OF FOOD SENSITIVITIES

It is clear from the foregoing that food plays a very important role in the management of many chronic GI disorders, including IBD. As cited from Hall<sup>5</sup>: “Most clinicians agree that dietary management is a key component in the successful treatment of IBD, ...”. In case of a strong suspicion of a true food allergy, a strict dietary elimination trial should be started with a hydrolysed or a novel protein diet.<sup>2</sup> However, in many patients with mild uncomplicated IBD or CIID, dietary management with a highly digestible food with some other key characteristics may be beneficial.

## WHAT WOULD A FOOD FOR UNCOMPLICATED CASES OF CHRONIC GI DISEASE LOOK LIKE?

### Egg

Egg contains a protein of the highest bioavailability, so the likelihood of undigested protein eliciting an allergic reaction is low. It is not a common dietary allergen (Table II)<sup>9</sup> so it is very well suited as single intact animal protein source for uncomplicated IBD/CIID cases. A study conducted in hypersensitive dogs evaluated the efficacy of feeding foods whose single source of intact protein was chicken egg. These foods were well tolerated by these dogs: they did not have clinical signs of food allergy while on this food.<sup>20</sup> Another study in 13 dogs with idiopathic chronic colitis showed that these dogs were successfully managed long-term with a commercial dry food with egg as sole source of animal protein.<sup>21</sup>



### High digestibility

It is imperative to use highly digestible foods in dogs with food sensitivities, especially those that are anorectic and are losing weight. In these patients it is paramount to ensure that the components of the food (macro and micronutrients), are of the best quality and can be readily assimilated when digestive functions are suboptimal. A highly digestible food minimises the substrate available for metabolism by intestinal bacteria and remaining undigested substrate (which may elicit an allergic response and increases osmotic pressure in the gut, which may further exacerbate diarrhoea).<sup>22</sup>

### Prebiotics and probiotics

Soluble or fermentable fibres (also known as prebiotics), such as found in beet pulp, flax seed, barley and oats are not digested in the small intestines, but are fermented by enteric bacteria to form short-chain fatty acids. Prebiotic fibres benefit gut flora, motility and stool quality and provide fuel for colonic wall health.<sup>23, 24</sup> Probiotics (live intestinal bacterial strains, such as *Lactobacillus* and *Bifidobacter spp.*) could theoretically contribute to a healthy gut microbiota, but objective data in dogs and many other species are lacking.<sup>5</sup>

### Fat restriction needed?

Fat restriction was traditionally recommended in patients with many GI diseases because of concerns over fat maldigestion and malabsorption in these patients. However, the need for fat restriction has been challenged recently because low-fat diets make it difficult to correct weight loss deficits.<sup>5</sup> Furthermore, due to the fact that fat has an osmolality close to plasma, the undigested fat does not contribute to osmotic diarrhoea. So a higher fat content in the food is appropriate for many patients with GI disorders. Providing  $\omega$ -3 fatty acids may also help break the cycle of gastrointestinal inflammation. The only diseases for which fat restriction is necessary are hypertriglyceridemia, pancreatitis and protein losing enteropathy/lymphangiectasia.<sup>22</sup>

## Other nutrients and ingredients

Antioxidants, such as vitamin E, vitamin C,  $\beta$ -carotene, taurine and others, help maintain health and vitality. Antioxidants neutralise the free radicals produced during inflammation and even during normal body metabolism. Ongoing studies are exploring potential roles for specific nutrients and food-derived compounds (including arginine, glutamate, glutamine, glutathione, glycine, vitamin A, zinc, and specific lipids) in gut mucosal turnover, repair, and barrier function.<sup>25</sup>

Recently, hypovitaminosis D has been described in chronic GI disease in dogs.<sup>26</sup> Hence sufficient supply of dietary vitamin D, and probably also other vitamins (such as vitamin B<sub>12</sub> which is reported to be low in dogs with GI disease as well<sup>27</sup>), is warranted in chronic GI disease. Natural ingredients, such as ginger, have been implicated to help improve GI motility and health.<sup>28</sup>

## CONCLUSION

Food is a cornerstone in the management of many chronic GI disorders in dogs, including IBD and other chronic idiopathic intestinal disorders. This may be due to primary food allergies or food intolerances. For the diagnosis and management of true food allergies, a hydrolysed or novel protein food is warranted. In milder cases, highly digestible, single protein foods with prebiotics, antioxidants and anti-inflammatory  $\omega$ -3 fatty acids have been shown to be beneficial.

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