

Food Allergy in Dogs and Cats: A Review

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Food allergy (FA) is defined as “all immune-mediated reactions following food intake,” in contrast with food intolerance (FI), which is non-immune-mediated. Impairment of the mucosal barrier and loss of oral tolerance are risk factors for the development of FA. Type I, III, and IV hypersensitivity reactions are the most likely immunologic mechanisms. Food allergens are (glyco-)proteins with a molecular weight from 10–70 kDa and are resistant to treatment with heat, acid, and proteases. The exact prevalence of FA in dogs and cats remains unknown. There is no breed, sex or age predilection, although some breeds are commonly affected. Before the onset of clinical signs, the animals have been fed the offending food components for at least two years, although some animals are less than a year old. FA is a non-seasonal disease with skin and/or gastrointestinal disorders. Pruritus is the main complaint and is mostly corticoid-resistant. In 20–30% of the cases, dogs and cats have concurrent allergic diseases (atopy/flea-allergic dermatitis). A reliable diagnosis can only be made with dietary elimination-challenge trials. Provocation testing is necessary for the identification of the causative food component(s). Therapy of FA consists of avoiding the offending food component(s).

Keywords adverse food reactions, clinical signs, diagnosis, hypoallergenic diet, therapy

INTRODUCTION

Food allergy (FA) is recognized as a potential cause of various dermatological and gastrointestinal (GI) signs in the dog and cat. The exact incidence of FA is unknown. However, the term “allergy” is often used indiscriminately. Acquaintance with exact terminology is important when dealing with FA. The aim of this review is to give a survey about the current knowledge of FA based on an extensive literature study. General information concerning the terminology, etiopathogenesis, underlying immunologic mechanisms, and occurrence of FA will be given. Next to it, practical aspects as clinical signs, differential diagnosis, diagnosis, management, and prognosis will be discussed.

TERMINOLOGY

The current terminology of adverse food reactions is advised by the “American Academy of Allergy and Immunology” and the “National Institute of Allergy and Infectious Disease.”^{2,37} Adverse food reactions (food sensitivity) are divided into two

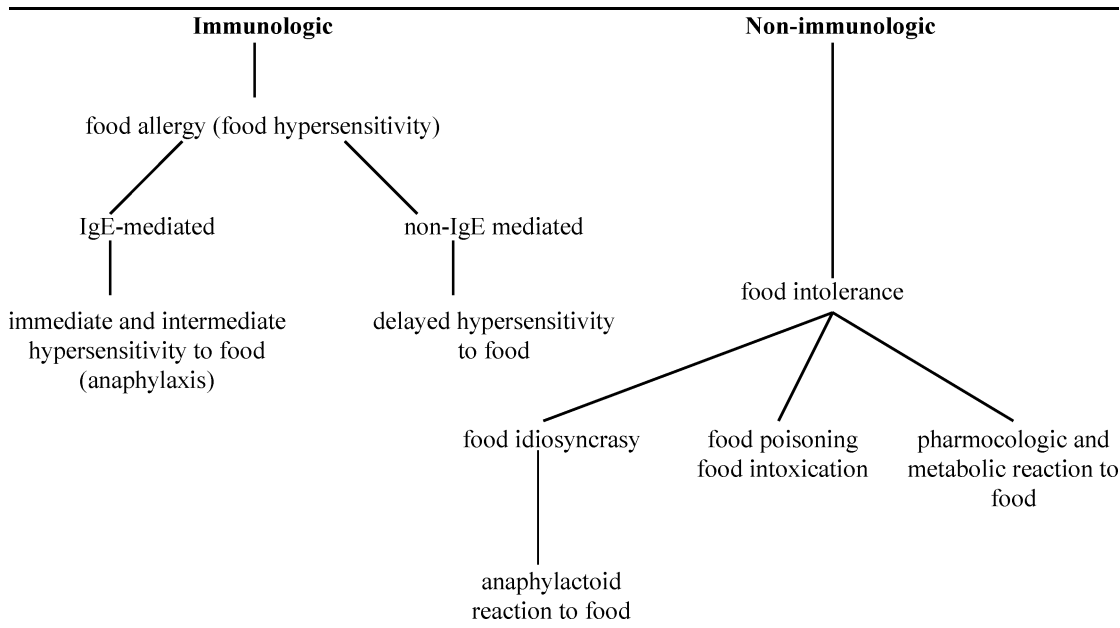
categories: immunological and non-immunological reactions (Table 1). Food allergy (food hypersensitivity) implies all immunological reactions following food intake. Non-immune mediated reactions are indicated as food intolerance (FI). Food idiosyncrasy, food toxicity, and food poisoning, anaphylactic food reaction, pharmacological and metabolic food reactions are all forms of FI. Overlap between the different types is possible, because a clear distinction is difficult.

Food idiosyncrasy describes a quantitatively abnormal response to a food substance or additive which resembles allergy but does not involve immune mechanisms.² Because previous sensitization is not required, a food idiosyncrasy can occur on the first exposure to the causative substance, which differs from FA. Most of the reactions on food additives are food idiosyncrasies.³⁹

Food intoxication and food poisoning are biological effects caused by an infection or the presence of toxins in foods. These toxins can be inherent to the food or are produced by parasites or micro-organisms.² Aflatoxicosis (aflatoxins) and botulism (exotoxins of *Clostridium botulinum*) are examples of food poisoning by micro-organisms.

Anaphylactoid reactions to food mimic real anaphylaxis, but are not mediated by an immunologic release of chemical mediators. These reactions are also part of FI, food idiosyncrasy, food toxicity, and food poisoning or pharmacological reaction to food.² Anaphylactoid reactions can occur after ingestion of

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Table 1 Classification of adverse reactions to food (adapted from Guilford, 1996a; Roudebush et al., 2000)

spoilt tuna which contains large amounts of histamine, resulting from decarboxylation of histidine by bacteria as *Proteus* and *Klebsiella*. A non-immunological release of histamine can also be influenced by endorphins in the brain^{11,86} and might explain why a dog becomes pruritic when he shows signs of euphoria.³⁷

A metabolic food reaction is related to the reaction of the metabolism of the host after food intake.² Reasons for susceptibility to a particular food include disease status, malnutrition, and inborn errors of metabolism.²¹ Lactose intolerance is a metabolic adverse reaction that can occur in dogs and cats.^{37,42,64} A form of primary lactose intolerance occurs in puppies.³⁷ When puppies are weaned, lactase activity falls to 10% of the levels found in the young. These pups can only tolerate small amounts of milk, and suffer from diarrhoea after excessive milk intake. In cases of FA, quantities of milk are smaller than those required to induce clinical signs in animals with a dietary intolerance.³⁷ Secondary lactose intolerance can affect adult animals with enteritis because of a reduced lactase activity.³⁷

ETIOPATHOGENESIS

The wall of the digestive tract is the largest surface of the body exposed to the environment. The GI tract has to differentiate between nutrients on the one hand and potential harmful substances (bacteria, viruses, parasites) on the other hand, which have to be tolerated and expelled (immunity) respectively.⁸⁰ The Gut Associated Lymphoid Tissue (GALT) accomplishes this double function. GALT is composed of four distinct lymphoid compartments: Peyer's patches (PP) and aggregates of lymphoid follicles throughout the intestinal mucosa, lymphocytes and plasma cells scattered throughout the lamina propria, enterocytes with intraepithelial lymphocytes (IELs), and mesenteric lymph nodes.⁸⁰ The nature of GALT in the dog and cat is now

becoming clearly defined. Canine PP have classical follicular (B lymphocyte) and parafollicular (T lymphocyte) zones and an overlying dome epithelium that constitutively expresses MHC class II molecules, which suggests that enterocytes (in addition to M cells) may be important in the transfer of luminal antigen to the underlying lymphoid tissue.²³ Plasma cells in the dome of the canine PP predominantly express IgG, but isolated cells produce mostly IgA in the proximal intestine and IgM in the ileum.^{45,46} The small intestinal lamina propria of the dog contains a mixture of plasma cells (IgA > IgG > IgM), T lymphocytes and MHC II macrophages and dendritic cells, in addition to eosinophils and IgE-bearing mast cells.^{24,25} Recent studies of the feline small intestinal mucosa have identified several differences to the dog: a much larger population of IELs, a lack of constitutive expression of MHC II by enterocytes, and a higher concentration of lamina propria plasma cells in the ileum compared to the duodenum.^{72,96}

Four mechanisms ensure the conflicting functions of tolerance and exclusion of antigens: (1) the mucosal barrier, (2) regulation of the immune response, (3) elimination and (4) tolerance of antigens reaching the mucosa.³¹ Impairment of this GI defence predisposes patients to FA.

Mucosal Barrier

Exclusion of substances from the lumen is ensured by components of the mucosal barrier, which is composed of different interrelated immunologic and non-immunologic components (Table 2). The rate of intact protein absorption depends on the integrity of the mucosal barrier, to which different factors contribute: morphology and functionality of the enterocytes, presence of IgA, effective digestion, quality and composition of the food and presence of inflammation.³⁰

Table 2 Components of the mucosal barrier (adapted from Sampson, 1991)

Nonimmunologic barriers	
Block penetration of ingested antigens	
–	intestinal peristalsis
–	intestinal mucus coat (glycocalyx)
–	intestinal microvillous membrane composition
–	intact mucosa
Breakdown ingested antigens	
–	gastric acid and pepsins
–	pancreatic enzymes, intestinal enzymes
–	intestinal epithelial cell lysozyme activity
Immunologic barriers	
Block penetration of ingested antigens	
–	antigen-specific secretory IgA (sIgA) in gut lumen: elicited at the Gut Associated Lymphoid Tissue (GALT)

According to available data in man, the maturation of the enterocyte depends on the age and the stage of development along the crypt-villus axis.⁸⁵ The uptake of antigen by the enterocytes depends on the content of proteins and phospholipids of the cell membrane. A change in composition and function of the enterocytes occurs at a young age.⁸³ The larger neonatal permeability of enterocytes enhances the absorption of food molecules and colostral antibodies. During the development of the enterocyte along the crypt-villus axis, the composition of the cell membrane also changes: immature crypt cells have twice the endocytotic capacity (i.e. protein absorption) of mature crypt cells.⁸⁵ Recent research in dogs concerning postnatal development of nutrient transport in the intestine of dogs, revealed a decreased absorption for most nutrients between birth and adulthood.¹⁰

IgA is an important immunologic component of the mucosal barrier.⁸³ In the intestinal secretions, IgA is mainly present in the secretory form (sIgA): two monomeric IgA molecules are covalently bound by a peptide (J-chain) synthesised by IgA-producing plasma cells. This dimeric form of IgA is transported actively through the epithelia of the gut mucosa and is added to a secretory component of the epithelial cell. Owing to this, sIgA is formed, which is resistant to enzymatic degradation. IgA may complex with food antigens thereby preventing their transport through the mucosa. After attachment to the glycocalyx, the antigen-IgA complex is more sensitive to proteolytic digestion than the free antigen in the gut lumen.

An effective digestion of proteins results in free amino acids and small peptides which are poor antigens, whilst incomplete digestion leads to exposure of larger polypeptides with residual antigenic properties which can still elicit an allergic reaction.⁸⁰

Malnutrition increases intestinal permeability to macromolecules by changing the morphology and activity of the enterocytes.⁸⁵ More proteins can pass the mucosal barrier because of incomplete digestion and enhanced possibility of protein absorption.

Diet composition can influence protein absorption in two ways: consuming a protein along with other proteins decreases individual absorption rates of the proteins, whereas protein absorption will increase when ingesting a protein with glucose.⁸⁵

Regulation of the Immune Response

Penetration of the epithelium by an antigen evokes an immune response. This happens constantly, but the organism differentiates between “good” and “bad” antigens to prevent a continuous immune reaction. M-cells (specialised epithelial cells for antigen presentation in the Peyer’s patches)³¹ take up small amounts of antigen, and present it to the underlying lymphoid tissue.⁸³ Immune reactions can be prevented by T-cell suppression, which leads to tolerance. In cases of FA however, an antigen-specific immune reaction with formation of IgM, IgG, or IgE occurs.⁸⁴

Elimination of Antigens

In spite of the defence, the mucosal barrier is not totally impermeable to macromolecules even in normal circumstances. Small but immunologic significant amounts of dietary proteins cross the intact mucosa and reach the systemic immune system. Formed immune complexes are removed by the mononuclear phagocytic system of the liver and the mesenteric lymph nodes.³¹ The consequences of increased mucosal permeability and increased circulating immune complexes against food components are unpredictable. Contributing factors are species, age of the animal, type and quantity of the antigen absorbed, location of the absorption, pathophysiological state and genetic make-up of the host.⁸⁵ In some cases, oral tolerance to the absorbed antigen is maintained, whilst in other situations the suppressor response of the GALT is by-passed and local inflammation results. Hypersensitivity rather than tolerance to the absorbed protein develops (see also regulation of the immune response and oral tolerance).

Oral Tolerance

Oral tolerance is the phenomenon whereby prior exposure to an antigen by the enteric route induces a specific immunological unresponsiveness (locally and systemically) on subsequent systemic exposure to the same antigen.¹⁶ The suppressor function of the GALT (cellular immunity) is the basis of oral tolerance. In addition to the suppressor response, the gut-associated humoral immune system generates IgA, which is secreted on the mucosal surface. Although oral tolerance is essential to life, animals are not born with it. It develops at a young age, but the exact time is unknown. When animals are weaned and start eating new foods, they have to be able to develop oral tolerance. It is estimated that puppies and kittens have this potential from 6 weeks on.⁸⁹ If new food components are consumed before that age, it is likely that oral tolerance will not develop, which can result in an allergy to that food. Induction of oral tolerance is more effective after repetitive contact with smaller amounts of protein during several weeks.³¹ Without new exposure to the antigen, oral tolerance will be reduced. A study carried out by Zemmann et al. (2003) describes a successful protocol for tolerance induction

in atopic dogs. Oral tolerance was induced by means of a 28-day treatment with ovalbumin dissolved in cow's milk starting at the age of 9 weeks.

IMMUNOLOGIC MECHANISMS

The most common studied and best defined allergic reactions to food in man are IgE-mediated reactions (Type I hypersensitivity) that lead to clinical symptoms of immediate hypersensitivity (within a few minutes to hours after food intake). IgE-activated mast cells can release cytokines that cause a delayed hypersensitivity reaction (within a few hours to days). Type II (cytotoxic reactions), Type III (mediated by immune complexes) and Type IV (cell mediated) hypersensitivity reactions have been implicated in food-allergic disorders in people and other animals, but their involvement in FA in the dog and cat has not been clearly established.⁸⁰ In dogs and cats, Type I, Type III, and Type IV hypersensitivity are possible immunologic mechanisms.⁶³ Table 3 gives an overview of the different types of hypersensitivity reactions.

Immediate Hypersensitivity

Immediate hypersensitivities to food occur within a few minutes to several hours after ingestion of the offending antigen. These responses are mediated by IgE bound on mast cells.¹⁶ In all probability this is also true for cats and dogs.^{47,48,66,100} Without oral tolerance, an individual develops an IgE response to a certain food antigen instead of an IgA response.¹⁶ IgE binds on GI and peripheric mast cells, which leads to sensitization for the causative food antigen. On subsequent contact with the antigen, mast cell degranulation occurs. This releases a range of inflammatory mediators. When the sensitized mast cells are limited to the GI tract, a local and intestinal Type I hypersensitivity reaction causes loss of fluid, plasma proteins, and blood through the capillaries of the gut into the lumen.¹⁶ The stimulated secretion of mucus and chloride disturbs motility and disaccharidase activity. These changes lead to clinical symptoms of vomiting, diarrhoea, and weight loss. In some cases, repeated degranulation of mast cells leads eventually to accumulation of eosinophils in the gut wall, resulting in eosinophilic

gastroenteritis.⁶¹ The increase in absorption of macromolecules following gastrointestinal hypersensitivity can deteriorate the allergic reaction or may even lead to multiple hypersensitivities.¹⁶ More general reactions occur when the antigen escapes from the gut and reaches sensitized basophils or IgE-bearing mast cells in the skin. Extra-gastrointestinal effects are also possible after the release of gastrointestinal mast cell mediators in the systemic circulation.⁸³

Intermediate Hypersensitivity

When judging the reported timing of occurrence of adverse reactions after food challenge, intermediate hypersensitivities to food appear frequently in dogs and cats.^{51,95,98} They occur several hours after antigen ingestion and are probably the result of a late-phase response to IgE-mediated mast cell degranulation and/or type III hypersensitivity response to immune complexes. Activated mast cells release a great number of cytokines, which attract neutrophils, eosinophils, and in smaller amounts also lymphocytes. These cells also release other mediators, evoking chronic inflammation.⁸³ In man, IgA complexes dominate the lamina propria of normal people. These are non-inflammatory and are quickly eliminated by the liver. In food-allergic people, IgE and IgG complexes are thought to accumulate in the gastrointestinal mucosa.⁸³ This leads to an inflammatory response by the fixation of complement and the attraction of phagocytes. Moreover, IgG and IgE complexes are another stimulus for mast cell degranulation and eosinophil migration and may contribute to the eosinophilic infiltration seen in some cases of FA.¹⁶

Delayed Hypersensitivity

In man, delayed type hypersensitivity (DTH) reactions appear several hours to 2–3 days after ingestion of the allergen and are probably mediated by Type III and Type IV reactions.^{16,83} Non-specific symptoms such as recurrent abdominal pain, fatigue, arthropathies, oral ulcers and GI upsets can be seen. The prevalence of DTH responses to food in the canine and feline population is unknown, but clinical experiences indicate their occurrence.^{51,95,97}

Table 3 Comparison of different types of hypersensitivity reactions (Roitt, 1991)

Hypersensitivity reaction	Type I anaphylaxis	Type II cytotoxic	Type III immune complex mediated	Type IV cell-mediated
Antibody	IgE bound to mast cell	IgM and IgG ± CF*	Humoral antibodies ± CF*	T-cell receptor
Origin of antigen	Exogenous	Cell surface	Extracellular	Associated with MHC-molecule on macrophage or target cell
Response to intradermal antigen				
– Maximal reaction	After 30 minutes	—	After 3–8 h.	After 24–48 h.
– Form of appearance	Urticaria	—	Erythema en oedema	Erythema and induration
– Histology	Degranulation of mast cells Oedema	—	Acute inflammation Mainly polymorphonuclear cells	Perivascular inflammation Mainly monomorphonuclear cells

*CF: complement fixation.

Table 4 Common food allergens in the dog

	Beef	Dairy	Wheat	Lamb & mutton	Egg	Chicken	Soy	Pork	Rabbit	Fish	Canned foods ¹	Dry foods ¹	Diverse ²	Number of animals
Walton (1967)	13	22	11	6	3			4	1	2	17		5	82
Jeffers et al. (1991)	12	5	4		2	3	3					2		13
Harvey (1993)	6	11	8	1	4	1							1	25
Denis and Paradis (1994)	8	4	1	1	2	2		1	1				2	14
Paterson (1995)	13	2		5	4	2	1	2					6	20
Jeffers et al. (1996)	15	7	6		5	7	8						3	25
Chesney (2002)	5	4			4			1				10	3	19
	72	55	30	13	20	19	12	8	2	2	17	12	20	198
%	36	28	15	6,6	10	9,6	6	4	1	1	8,6	6	10	

¹Canned foods and dry foods: commercial foods in which the exact causative food allergen was not identified.

²Diverse: corn, rice, "biscuit," chocolate, gluten.

FOOD ALLERGENS

General Characteristics

Although all food proteins are antigenic (foreign to the body), only a small component of the total protein content of a food is allergenic: the capacity of a protein to induce an allergic reaction is influenced by the immunogenicity and the permeability of the gut for the protein.⁹⁰ Allergen immunogenicity depends on stimulation of IgE production and histamine release of mast cells after bridging of the allergen between two IgE molecules on the surface of the mast cell membrane.⁹⁰ This requirement places a minimum size limit on molecules that can stimulate IgE production. The maximum size limit is related to the absorption capacity of the enteric mucosa for the protein. In man, food allergens are almost exclusively glycoproteins with a molecular weight (MW) of 10–70 kDa.⁹⁰ In dogs and cats no data are available on the exact MWs of food allergens.

Factors that determine which proteins are the most important allergens are incompletely understood. Immunogenicity and stability of the protein play an important role.⁹⁰ Food allergens maintain their immunogenicity in spite of different treatments: a lot of allergens are partially resistant to influence of heat and acid and can resist the digestion process. However, it seems that

allergenicity can be influenced by food processing: protein denaturation can destroy old epitopes (antigenic determinants) or expose new ones, with a decrease or increase of allergenicity respectively.³⁰ The importance of this phenomenon in FA is under debate, but it appears that the allergenicity of most foods is either unchanged or reduced by cooking or partial digestion.^{4,51} Maillard reactant products are formed when proteins are cooked with carbohydrate. They can increase or decrease the allergenicity of proteins, depending on the food component. This phenomenon may explain the apparent increase in allergenicity of proteins in canned pet foods compared to fresh proteins.³⁰

Common Food Allergens in Dogs and Cats

There are a lot of potential food allergens and because of the multiple ingredient content in commercial pet food, it is difficult to detect the specific causative food allergens. Several publications have been analyzed in which the allergen has been identified by elimination and single ingredient challenge trials yields in dogs,^{13,19,40,51,52,68,95} and cats^{28,32,33,60,70,88,95} with FA. The allergens are presented in Tables 4 and 5, for dogs and cats respectively. Veterinarians believe that food additives (dyes and preservatives) are common food allergens.⁷⁶ However, not one

Table 5 Common food allergens in the cat

	Beef	Dairy	Fish	Poultry	Rabbit	Commercial foods ¹ (D/C)	Egg	Lamb	Barley/Wheat	Additives	Diverse ²	Number of animals
Walton (1967)	5	7	1	1	1	1C					2	18
Stogdale et al. (1982)	1		1	1								1
Medleau et al. (1986)						1C						1
White and Sequoia (1989)		2	6			4*		1				13
Guaguère (1993)	4	3	2				1					17
Reedy (1994)								1				1
Guilford et al. (1998)	5		1	1		4C 6D		3		1	3	22
Guilford et al. (2001)	3	1	1	1		1C 5D		1	4	1	5	16
	18	13	12	4	1	22	1	6	4	2	10	89
%	20	14,6	13	4,5	1	24,8	1	6,7	4,5	2,2	11	

¹Commercial foods (D = dry foods, C = canned foods): the exact food allergen was not identified.

*Not specified commercial food.

²Diverse: penicilline, 'Brand's essence', gluten, viscera.

case was found in literature for dogs and only two cases for cats.^{32,33} Moreover, most reactions on food additives are types of FI.³⁹

Multiple Food Hypersensitivities

According to Walton (1967), multiple hypersensitivities are uncommon in dogs and cats. However, Harvey (1993) and Paterson (1995) showed that 35–48% of the dogs were allergic to more than one food component. According to Jeffers et al. (1996), the average number of allergic reactions per dog is 2.4. A study in cats with chronic gastrointestinal problems,³³ revealed 50% of the cats with FA allergic to more than one food component. These findings show the importance of systematic introduction of specific food components to the elimination diet to identify a food allergen. Moreover, testing other ingredients should not be neglected when one causative substance has already been identified (see diagnosis).

Cross-Reactivity

In some groups of food, allergy for one member of the group can result in a variable degree of allergy for the other members of the same group, because of antigenic similarity between food allergens.⁷ In man, this cross-reactivity is sometimes seen with sea foods, vegetables, and cereals. Cross reactivity in other foods is far less seen, even when the origin is the same species. Research in man has shown that FA usually is specific.⁷ and that dietary restrictions of entire food families are rarely needed. Also in dogs, cross-reactivity among products of the same animal species or between different vegetable products has not been demonstrated. Jeffers et al. (1996) showed that there was a significant difference between the number of dogs allergic to beef versus milk, and for soy versus wheat. This refutes a possible cross-reactivity between proteins from bovine origin and to soy and wheat. Hence, a dog allergic to cow milk usually can tolerate beef.^{51,95}

CLINICAL SIGNS

Occurrence

Dogs

Veterinary literature is equivocal on the incidence of FA. Most authors agree that diagnosis of FA is uncommon.⁶³ FA would be responsible for 1% of all skin diseases in dogs.^{1,95} According to Muller et al. (1989), 10% of all allergic skin diseases (excluding parasitic allergies) are due to FA. FA is the third most common occurring skin allergy after flea-allergy and atopy. There is no clarity about the incidence of GI symptoms of FA. According to Walton (1967), GI symptoms rarely occur. Others,^{19,63} mention GI symptoms are present in 10–15% of the cases. FA can occur more frequently than believed, because

it is difficult to entirely carry out the extensive test procedure for diagnosing FA.^{8,81} GI symptoms of FA are less frequently seen than dermatological symptoms. The reported simultaneous incidence of GI and dermatological symptoms varies with the author.^{19,28,32,58,63,68} However, the connection between dermatologic and GI symptoms is not pathognomonic for FA. A study carried out by Guilford et al. (2001) showed that 20% of the cats with concurrent chronic GI and skin problems, had no FA. On the other hand, 75% of the cats with FA had GI problems only. In dogs, no data were found concerning GI symptoms as only presentation of FA.

A recent literature study, carried out to determine the exact incidence of FA, mentions a lot of problems that make it difficult to determine the accurate incidence of FA.¹² Published studies generally do not state the size of the population from which the dogs were drawn, and so the frequency of FA cannot be deduced. Many of the reports give less information than would have been useful: inclusion criteria to suspect dogs for FA, criteria by which the result of the elimination diet is evaluated and information about animals where FA was not diagnosed are important elements. The variety of clinical signs is also an important stumbling-block. Pruritus is an important symptom in evaluating the elimination diet, but objective judgment of a reduction in pruritus is difficult. The person who evaluates the effect of the elimination diet also plays a role. Relying on several authors,^{19,54,94} Chesney (2001) concluded that 17.4% of the dogs that were submitted to a food test had FA.

There are no sex, breed or age predilections for FA in the dog.^{19,40,74,95,97} A higher risk is reported for certain breeds: Boxers, Cocker and Springer Spaniels, Collies, Dalmatians, German Shepherds, Lhasa Apsos, Miniature Schnauzers, Retrievers, Shar-Peis, Soft-Coated Wheaten Terriers, dachhunds and West Highland White Terriers.^{19,40,74,91,94,99} However, this could not be confirmed statistically. Harvey (1993) reports a lower risk for crossbreeds, but also without statistical significant differences. FA can occur at any age: Most of the authors report a range of 4 months to 14 years age.⁸⁰ The average age varies with the study consulted: 15 months,¹³ 2 years⁷⁴ and 4–6 years.⁴⁰ The first symptoms often arise before the age of one year: 33% with Rosser (1993), 51% with Harvey (1993), 48% with Denis and Paradis (1994) and 36% with White (1998). On the other hand, some authors,^{19,95,97} report a contact with the offending food allergen during 1–2 years before the first symptoms occur.

Cats

FA seems to be rarely diagnosed in the cat.^{60,87,98} According to Muller et al. (1989), FA is -as in dogs- responsible for 1% of all skin diseases in the cat. It is the main but one cause of allergic dermatitis in the cat, after flea-allergy. FA represents 11% of the cases of miliary dermatitis.⁸⁷ Cats with chronic pruritus, chronic vomiting or simultaneous pruritus and vomiting or diarrhoea have FA in 17% of the cases.³² GI symptoms are present in only 10–15% of the cases.⁶³ It is difficult to evaluate the exact

prevalence, because skin injuries are multifactorial (FA, flea-allergy dermatitis and atopy) and symptoms often disappear after control of one of these causes.²⁸

There is no sex, breed, or age predilection for FA in cats.^{19,28,95,98} However, a few studies report a higher risk for the Siamese and the Birman cat.^{19,74} The age on first appearance of symptoms varies between 6 months to 11 years.^{28,95,98} There seems to be no connection between the onset of clinical signs and a recent change of food: in most of the cases the offending food component was given during more than 2 years.^{70,98} Therefore, FA seems to have a long period of sensitisation (6 months to 2 years) and would be rare in the young animal. However in 38.5% of the cases, clinical symptoms are seen before the age of 2 years.²⁸

Symptoms

FA is usually non-seasonal and often occurs suddenly after months or years of consuming the diet containing the inciting foodstuff. The occurrence of symptoms is usually consistent with subsequent challenges: each intake of the allergen causes symptoms. An inconsequent response can be explained by a variation in dose of the allergen ingested (more important with FI because a small dose of allergen is sufficient for an allergic reaction), interference with food ingested simultaneously or an altered method of food preparation.³⁰

FA may cause dermatologic and GI symptoms.³⁰ Affection of other organ systems occurs in man, but little in dogs and cats. However, clinical experience suggests that adverse reactions to food (and maybe FA) occasionally are responsible for different symptoms such as anorexia, rhinitis, conjunctivitis, bronchoconstriction, seizures, malaise, FLUTD (Feline Lower Urinary Tract Disease), urinary incontinence, and glomerulonephritis.^{1,74,91,95,97,98}

Dermatologic Signs

Dogs

The most common symptom of FA in dogs is pruritus. In general, the pruritus is present constantly, but the intensity can be variable. Pruritus can be either generalized or limited to face, ears, paws, axillae, inguinal or perineal region.^{19,40,58,74,95,97} This presentation resembles atopy.⁴⁴ The response of pruritus after administration of corticosteroids arouses controversy in literature. In contrast with atopy, FA mostly reacts poorly on a systemic treatment with corticosteroids. However, studies report patients with a total response of pruritus following treatment with corticosteroids.^{19,40,74} (Table 6).

FA can mimic other common skin disorders, including pyoderma, pruritic exsudative dermatoses or "hot spots" (injuries which are caused by self-trauma in response to pruritus or pain), folliculitis and ectoparasites.⁸⁰ A variety of primary and secondary skin lesions occur and include papules, erythema,

Table 6 Response of patients with FA following treatment with corticosteroids

	Total response (%)	Partial response (%)	No response (%)
Harvey (1993)	48	24	0.04
Rosser (1993)	39	44	17
Denis and Paradis (1994) Dogs	58.3	27.1	14.6
Cats	50.0	50	0

excoriations, epidermal collarettes, hyperpigmentation, pododermatitis, seborrhea, and otitis externa.^{19,40,74,95,97} The presence of otitis externa is an important indication for FA. In some animals it may be the only presentation for FA.^{40,74}

Some dogs only show recurrent bacterial pyoderma (with or without pruritus). All clinical symptoms disappear temporarily after treatment with antibiotics, but reappear after finishing the treatment.^{19,40,74,97} Recurrent pyoderma is a common finding in allergic dermatoses, especially in atopy.^{44,63}

In 20–30% of the cases of FA, simultaneous allergic skin diseases are present.⁸⁰ The combination of atopy, FA and flea-allergic dermatitis is well known.^{19,68,74} Relying on the history and clinical symptoms, it is difficult to differentiate between atopy and FA. The age at onset of symptoms can possibly help to distinguish between both: atopy occurs in young adults (1–3 years), while FA is sometimes seen in animals younger than one year of age.⁵ In contrast with FA, atopy can occur seasonally.

Cats

Different clinical reaction patterns are associated with FA in the cat: severe, generalized pruritus without lesions, miliary dermatitis, localised pruritus with self trauma (especially around the head, neck and ears), traumatic alopecia, eosinophilic plaque and rodent ulcer, exsudative dermatitis and scaling dermatosis. Different combinations are possible.⁸ Otitis externa can occur as only clinical sign or in combination with others. Pruritus is the most frequent symptom of FA in the cat and is mainly localized on head, neck, and ears.^{19,28,60,88,95,98} Spreading to other locations as the limbs, the ventral abdomen and the inguinal region is also possible. Primary lesions as maculae, erythema, papules, eosinophilic plaques occur.^{19,28,60,98} However, secondary lesions (alopecia, excoriations, encrusting) by self-trauma following pruritus are more frequently seen.^{19,28,60,88,95,98} Eosinophilia is seen in 20–50% of the cases.^{60,88} In 30% of the cats with dermatologic signs of FA, a moderate to marked peripheral lymphadenomegaly is found.^{8,80} Concurrent flea-allergy or atopy can also be present.^{8,19}

GI Signs

Although there is no sex, breed, or age predilection for the occurrence of GI symptoms of FA, the German Shephard, Irish Setter, and Shar-Pei would be more frequently affected.⁸⁰ GI

symptoms of FA are non specific: vomiting, diarrhoea (varying from profuse and watery to mucoid or hemorrhagic), intermittent abdominal pain or an increased fecal frequency can be seen.^{13,19,28,33,65,68,88,95,97,98} FA is not unlikely in dogs with pruritus and increased defecation behavior (more than 3 times a day).^{58,68} Acute onset of diarrhoea and/or vomiting are often wrongly attributed to FA, whilst these are rather cases of FI. It is difficult to determine the true incidence of this phenomenon because the association is often made by the owner and the help of the veterinarian is not sought.³⁸ FA can be a possible cause of chronic diseases of the GI tract manifested as an intermittent or persistent period of diarrhoea and/or vomiting.^{6,33}

The Role of FA in Some GI Diseases

Inflammatory Bowel Disease (IBD). The most frequent forms of IBD in dogs and cats are lymphocytic-plasmocytic and eosinophilic enteritis,⁸⁰ which can be distinguished by infiltration of lymphocytes and plasma cells or eosinophils respectively.^{6,65} The exact cause of these entities is mostly unknown, but in some cases FA might be the underlying problem. Hence it appears that a food change might be beneficial. In patients with IBD it is significant to carry out a food trial before starting a treatment with immunosuppressive medicaments.³⁶

Gluten-Sensitive Enteropathy (GSE). GSE is an important chronic inflammatory disease of the small intestine of people. An analogical disorder affects the Irish Setter and is genetically determined.^{22,35} Clinical signs occur between 4–7 months of age.⁶ “Gluten” is a crude mixture of gliadin and glutenin (two peptides that form part of the protein fraction in wheat) and is normally digested by pancreatic enzymes in the gut lumen, and completed by brush border and intracellular enzymes of the mucosa.³⁰ Completely hydrolyzed gliadin is not toxic. The cause of GSE is unknown. Initially, a defective mucosal digestion was suggested as the underlying primary cause.³⁰ However, changes in enzyme activity are rather a secondary problem because the enzyme activity of the brush border is normal in GSE dogs raised on a gluten free diet.³⁴ Increase of intestinal permeability was determined in Irish Setters with GSE.³⁵ GSE in humans may be caused by Type IV hypersensitivity for gluten.³⁰ Dogs with GSE have an increased number of lymphocytes in the mucosa and the level of total IgA in the serum is also raised.³⁵ In contrast to man, anti-gliadin IgG in the serum is lower in dogs with GSE than in healthy age-matched controls. This proves that GSE is not caused by a systemic immune response, but does not rule out a mucosal delayed hypersensitivity response.

Protein-Loosing Enteropathy (PLEP) and Protein-Loosing Nephropathy (PLNP) in the Soft Coated Wheaten Terrier (SCWT). The syndrome of PLEP and PLNP is rare, and can occur in the SCWT. FA is the underlying cause.⁹¹ Allergic reactions in the affected dogs probably cause enteritis that proceeds to enteropathy. Deposition of circulating immune complexes (Type III hypersensitivity) can cause glomerulonephritis, leading to nephropathy.

Table 7 Differential diagnosis of food allergy in dogs (Muller et al., 1989; Vroom, 1994b)

Ectoparasitic causes	Mites	Lice
	<i>Cheyletiellose</i>	Flea-allergy
	<i>Demodicose</i> <i>Scabies</i>	
Immunologic causes	Atopy	Drug-reaction
	Contact allergy	Auto-immune disease
	Dermatomycoze	Zinc deficiency
Other causes	Primary pyoderma	Hypothyroidy
	Seborrhea	Leishmaniosis
	Granulomatous	Bacterial otitis
	sebumglandadenitis	

DIFFERENTIAL DIAGNOSIS

Because FA has a large variety of symptoms, the list of potential differential diagnoses is very comprehensive. In Tables 7 and 8, the main differential diagnoses of the dermatologic form of FA in dogs and cats respectively, can be consulted.

Diagnosis

A food trial is the most important diagnostic tool in dogs and cats with suspected adverse reactions to food. In vitro testing, biopsies, intradermal skin testing and gastroscopic food sensitivity testing are not reliable for diagnosing FA.^{1,29,50,51,54,62} However, food testing gives no information about the underlying immunologic mechanism. Although FI can also be identified with an elimination diet and following challenge, it is generally accepted that most of the animals with adverse reactions to food do suffer from FA when symptoms reappear after challenge with their former food.⁵⁴

Food Trial

The diagnosis of an adverse food reaction is confirmed by a food trial. The first step is the introduction of an elimination

Table 8 Differential diagnosis of food allergy in cats (Wills, 1992; Guagère, 1993; Vroom, 1994b)

Ectoparasitic causes	Mites	Flea-allergy
	<i>Cheyletiellose</i>	Reaction to tick bites
	<i>Demodicose</i>	Lice
	<i>Notoedres</i>	
	<i>Otodectes</i>	
	<i>Thrombiculiasse</i>	
Immunologic causes	Eosinophilic granulome complex	Allergy to intestinal parasites
	Contact dermatitis	Pemphigus foliaceus
	Drug reaction	Systemic lupus erythematosus
Viral causes	Atopy	Discoid lupus erythematosus
	Pox virus	Calici virus
	Herpes virus	Pseudorabies
Other causes	Dermatophytosis	Feline acné
	Neurodermatitis	Other causes of miliary dermatitis
	Cat bite	Causes of generalised alopecia
	Pyoderma	Deficiency of biotine or fatty acids

diet, followed by challenging the patient's former food. When symptoms recur on the former diet and disappear again on the elimination diet, diagnosis of FA is made. With a provocation test, the causative food component(s) must be identified. Table 9 gives an overview for a step-to-step approach in diagnosing and treating FA in dogs and cats.

Elimination Diet

Composition and Properties

Removal of the previous diet and introduction of a novel protein "hypoallergenic" diet is advised by many authors.^{1,19,60,63,93,100} Yet, the concept of such a diet is not entirely correct: a "hypoallergenic" diet does not really exist.⁹ Food itself is antigenic (foreign to the body, capable of binding to specific antibodies) and the treatment of an allergy for a certain component consists of switching it to an alternative with a different set of antigens. A diet can only be "hypoallergenic" if the animal was never exposed to the food components before. The identification of what is truly a novel protein for any given individual is entirely dependent on the accuracy and extent of the dietary history obtained. Because of the enhanced complexity of pet foods, it has become more difficult to compose a suitable elimination diet.³⁶

The ideal elimination diet should reply to some criteria:⁷⁸ contain a limited number of new, highly digestible proteins or exist on hydrolyzed protein, have a lower protein content than the usual foods, avoidance of additives and vasoactive amines, and be nutritionally adequate for the animal's life-stage and condition. The importance of a low protein content demands a little nuance: low protein content is only beneficial in non-allergic reactions (FI) because in cases of FA, small amounts of protein already evoke clinical responses. Though, it is hypothesized that limitation of protein can be useful in delayed type III reactions by limitation of immune complex formation (Guilford, unpublished data, 1994).

Choice

Home Made Diets (HMDs). HMDs are generally recommended as initial test diet for dogs and cats with suspected FA.^{40,43,63,97} Veterinarians in North-America prescribed HMDs in 72% of dogs and 86% of cats with suspected FA.⁷⁶ A HMD consists of one protein and one carbohydrate source. The most recommended food components in dogs are lamb, chicken, fish, rabbit, venison, rice, potatoes, and tofu.^{19,40,76,97} In cats, the use of baby food with lamb, rabbit, and rice is recommended.^{19,55,76,98} In contrast with previous years, the traditional elimination diet based on lamb and rice cannot be used in a number of cases due to different commercial foods based on lamb and rice which enlarges the possibility that animals with FA have already been exposed to these food components.⁹ HMDs should not include other supplements but butter, margarine, vegetable oils, salt, or spices.¹⁸

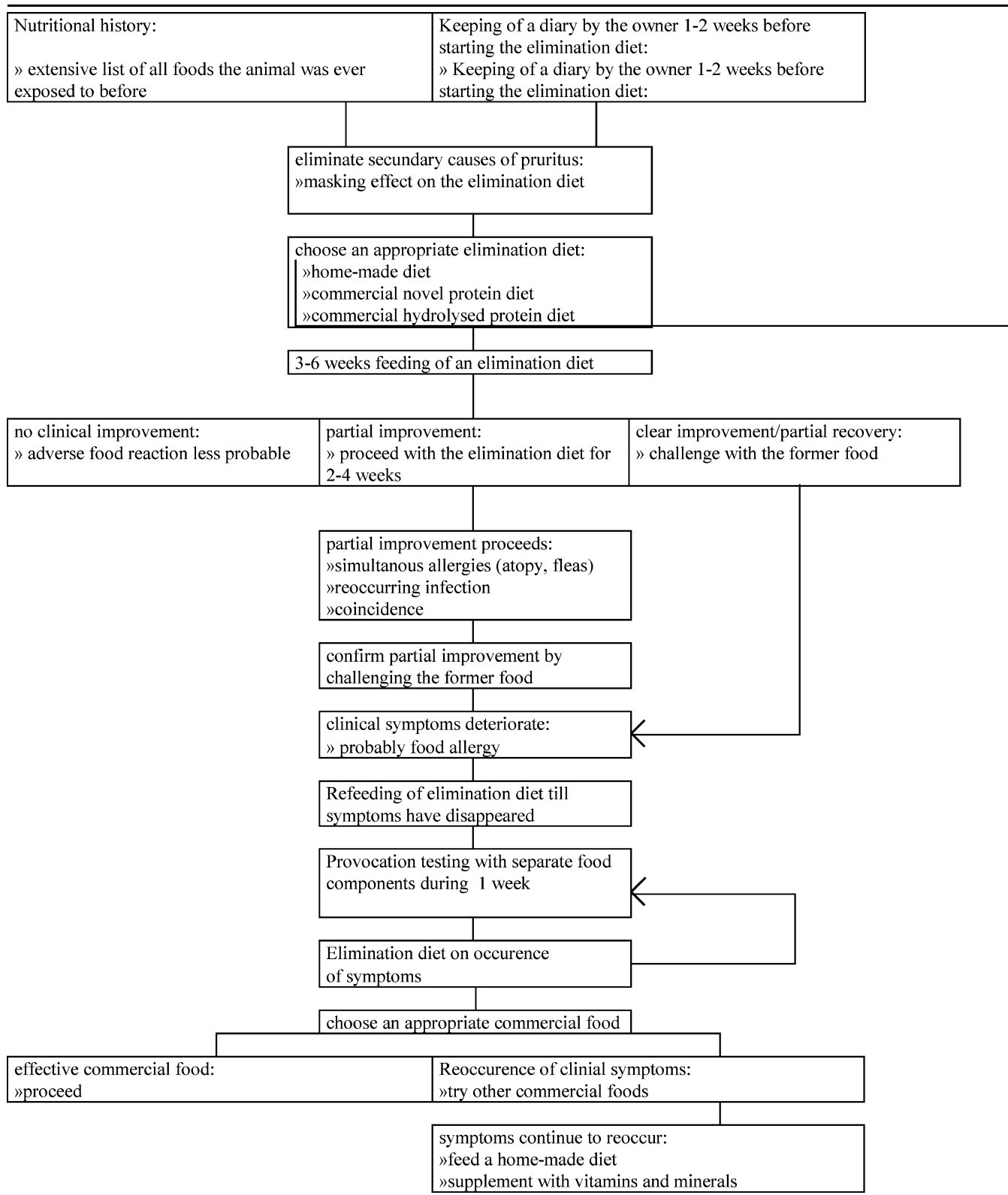
Advantages of HMDs are the ease of replying to a patient's specific needs⁷¹ and to compose a diet based on the individual nutritional history.⁴³ Owners also feel more involved and have the feeling that they can do something for their pet. It is disadvantageous that preparation of HMDs can be expensive and (especially in large breeds) time consuming.^{43,51} Distastefulness and initial digestive upsets.⁴³ are also possible problems. Gradually introducing the HMD can limit initial digestive upsets as vomiting, diarrhoea, colitis or flatulence.

An important drawback of most HMDs is that they are nutritionally inadequate for growth and maintenance. HMDs recommended by veterinarians in North-America were nutritionally inadequate for 89% of dogs and 92% of cats.⁷⁶ These foods contained excessive amounts of protein and lacked calcium, essential fatty acids, certain vitamins, and other micro-elements. Evaluation of several HMDs.⁴¹ confirms these findings. The feeding of nutritionally inadequate HMDs to young animals during a period of 3 weeks or longer, can lead to nutritional disease.⁸⁰ Foods deficient in thiamin (vitamin B₁) lead to anorexia and bad growth in pups within 10–20 days. Cats develop anorexia and vomiting within 1–2 weeks because of a lack of thiamin. Foods with a severe imbalance of minerals can cause skeletal diseases in young dogs within 4 weeks and may not be fed longer than 3 weeks. In theory, a deficiency of taurin is a concern in cats, but usually it is not necessary to supply during the food test.^{1,55} Although a HMD is not nutritionally balanced nor complete, supplements are not necessary during the short test period. When a HMD is given during a prolonged time, it has to be balanced with essential ingredients.⁴³

Commercial Novel Protein Diets (NPDs). Most of the NPDs are recommended for long term maintenance treatment for dogs and cats with FA,^{76,92} because they are supposed to be nutritionally adequate and balanced. A variety of NPDs are available for dogs and cats.⁹ NPDs are easy to obtain and practical in use,¹⁸ but are not always tested on animals with FA.⁸⁰ Several studies were conducted concerning the efficacy of NPDs in patients with FA.^{51,77,79,92} in the early 90s: NPDs used as long term maintenance treatment had an efficacy of 70–80%. The lack of individual dietary history can explain why the diet was not effective in some of the dogs. The presence of additives in commercial foods or alteration of antigenic properties during food processing can be other possible explanations.⁴³ Jeffers et al. (1991) described a case of a dog that had an allergic reaction following a commercial diet based on egg and rice, although oral provocation with chicken eggs was tolerated. Although the NPD cannot replace the HMD as a test diet (only elimination diets which are 100% effective are reliable in diagnosing FA), it can be useful in a number of cases: large breed dogs where HMDs are very expensive and time consuming, owners who are not prepared to cook for their pet, animals which do not tolerate HMDs, owners that refuse to do a challenge or when the dog is allergic to multiple food components.

Commercial Hydrolyzed Protein Diets (HPDs). The recent use of HPDs, allows real hypoallergenic diets. Hydrolysis of

Table 9 Algorhythm for diagnostic steps and treatment of food allergy in the dog and cat (adapted from de Jaham, 2000; Roudebush et al., 2000)



proteins to smaller peptides and amino acids (AA) reduces the MW of the original protein, by which the antigenicity and allergenicity of the protein are reduced. This means that the molecules are too small to evoke a cross binding between IgE on the surface of the mast cell.¹⁵ This prevents degranulation of the mast cell and IgE-mediated (Type I) hypersensitivity. Hence, it does not influence non-IgE-mediated forms of FA. HPDs are multicomponent, nutritionally complete formulas with well-defined chemical compositions.⁶⁰ The optimal MW of a protein hydrolysate varies with the type of protein used and the species involved. In humans, a reduction of allergenicity can only be reached when peptides are smaller than 15AA, which corresponds with a MW of 3500–5000Da.^{27,59} In the dog, peptides with a MW higher than 4500Da could still be capable of starting the immunologic reaction which contributes to the allergic reaction.¹⁸ Free AA are not allergenic, but are not suitable in foods because of their bitter taste and high osmolarity.^{59,66} Hyperosmolar products attract large amounts of water, causing severe diarrhoea. HPDs are composed with different sources of protein with different degrees of hydrolysis. In man, certain protein fractions of cow milk (whey and casein) and soy protein are used as basic protein sources.^{14,59} The efficacy of HPDs depends on the degree of hydrolysis and the protein material used. According to Olson et al. (2000), a degree of hydrolysis of 50% is required to prevent allergic reactions in dogs. Less is known about the diagnostic value of HPDs. A prospective study carried out by Groh and Moser (1998) with casein and liver HPDs showed clinical improvement in 20 of the 29 dogs (69%) suspected from FA.

Duration

The duration of an elimination diet is subject of discussion for patients with dermatologic symptoms and owing to the contradictory data in literature, it is difficult to give clear recommendations. Many older publications and text books recommend a period of 3 weeks.^{1,51,63,95,97,98} Rosser (1993) suggested that in some cases the duration of the elimination diet had to be prolonged to 10 weeks: following a 3-week period only 25% of the dogs were diagnosed and dogs that did not show any progression after 3 weeks had partial or total recovery after 6–10 weeks. In a study from Denis and Paradis (1994), certain cases required 13 weeks to detect improvement of symptoms. Other studies report a response for most of the dogs within 3–4 weeks.^{20,40,68} However, challenge can be done when the animal shows any response on the elimination diet, even if this occurs within the first 3 weeks. When there is no response during this period, it is recommended to maintain the test for another period of 3 weeks.⁴³

In patients with GI symptoms, a shorter elimination period of 2–4 weeks is sufficient.⁸⁰ There is no explanation known for this. Cats with lymphocytic-plasmocytic enteritis showed a clinical progression within 2 weeks on the elimination diet.⁶⁵ An appropriate elimination diet fed to cats with chronic GI problems, reduced symptoms within 4 days.³³ With chronic

Table 10 Pruritus score (Paterson, 1995)

Score	Severity of pruritus
1	Dog not pruritic at all, or scratches occasionally like a normal dog
2	Dog scratches/bites occasionally, and is generally comfortable
3	Dog scratches and bites frequently, but not excessively
4	Dog scratches and bites very frequently, often seems uncomfortable
5	Dog scratches and bites almost constantly, in a lot of discomfort

relapsing problems, the elimination period has to be longer than the normal symptom free period of the patient, to obtain a reliable judgement of the attribution of FA in the patient's symptoms.⁴

Interpretation of the Response on the Diet

Dermatologic Signs. In patients with dermatologic signs, pruritus is the most important symptom that is evaluated during the elimination diet. Evaluation of pruritus is rather subjective and criteria for reduction of pruritus differ according to the studies consulted, varying from 50%.⁵¹ to 80–100%.^{97,98} Only Paterson (1995) made an objective evaluation of pruritus by the use of a pruritus score (Table 10): at the end of the elimination test, almost all dogs showed a reduction to a score of 3 or less.

The interpretation of a patient's response to the elimination diet can be hampered by (1) a partial or accidental response, (2) the influence of infections (bacterial, mycotic) or (3) a simultaneous started treatment for pruritus.⁴³ A *partial response* occurs when concurrent allergies are present or in atopic patients that go through a fluctuation in severity.⁴³ This allows a false diagnosis of FA. To prevent this problem, it is necessary to repeat the food trial several times, until both the owner and the veterinarian are fully convinced that the diet is the determining factor in preventing the symptoms. Unfortunately, it is very time-consuming to repeat this cycle (first response to the elimination diet, relapse after challenge, second response to elimination diet) and this may lead to problems with the owner's cooperation. Until recently, no cases were reported with this approach. *Secondary infections* occur frequently in dogs with FA and a treatment is often prescribed simultaneously with the start of the elimination diet.^{20,55,92} It is important to maintain the treatment during challenge testing, because otherwise infections can reappear and wrongly suggest that the patient relapsed on the food. Related problems are the cases of recurrent pyoderma following FA in dogs.⁴³ Pruritus in these patients is only caused by the lesions of staphylococci and completely disappears after treatment with antibiotics. Diagnosis of this non-pruritic form of FA with secondary pruritic pyoderma is very difficult, especially if the period between the relapses is greater than 3 weeks. In this situation, the veterinarian has to determine if the elimination diet prevents the relapse of pyoderma, but this can demand several weeks. Moreover, more weeks may pass before the pyoderma reappears after challenge. This makes it very difficult to maintain the cooperation of the

Table 11 Disorders that can progress clinically with an elimination diet/hypoallergenic diet (Hall, 2002)

Food allergy	Pancreatitis
Food intolerance	Exocrine pancreas insufficiency
Small intestine bacterial overgrowth (SIBO)	Chronic gastritis
Idiopathic IBD	Gastro-oesophageal reflux
Lymphangiectasy	Emptying disturbances of the stomach
	Portosystemic shunts

owner during the repeated periods of challenge and treatment with antibiotics. *Pruritus treatment* with corticosteroids is only advised when absolutely necessary (eg. in dogs and cats with self-mutilation) and only for a short period (1–3 weeks).⁴³ After finishing the treatment, the elimination diet must be continued for another 2 weeks to evaluate the effect of the diet itself.^{99,100}

Finally, when there is no progression with the elimination diet, pruritus can possibly be maintained by another cause (no FA), presence of another allergy (besides FA) or another allergen in the elimination diet.¹⁰⁰

GI Signs. Remission of GI symptoms following elimination diet is indicative for a FA, but is no proof.³⁶ A number of GI disorders can react to a change of food (Table 11). With the change of the protein source, factors as digestibility and contents of fat and carbohydrate are altered, that can improve certain GI diseases.

Challenge Test

In patients with FA, the re-introduction of the original food will cause clinical problems following reduction or disappearance of symptoms on the elimination diet, which confirms diagnosis of FA. Depending on the underlying immunologic mechanism, symptoms are detected within a few hours to 3 days, but if the allergen was excluded from the diet longer than one month, it can also last up to 7 days.^{20,28,51,74,95,98,100} Some owners will refuse to do a challenge with the former food after reduction of clinical signs, but it is important to underline the importance of the challenge test, because a significant placebo effect can occur in 20% of the cases.⁴³ This means that continuing the elimination diet will be useless in some patients. These are cases of FI which cure spontaneously (eg. after intake of fish with a high amount of histamine) or patients without FA in which a simultaneous treatment (eg. antiparasitic or antibacterial) was started. Ferguson underlines the importance of the challenge test (cited by Rosser and White, 1998): “an unchallenged case is an unconfirmed case.”

Provocation Test

Because dogs and cats are exposed to a number of dietary proteins, it is very important to carry out extensive provocation tests with specific food components, to determine the allergen.⁵² First of all, the animal is fed the elimination diet until a maximal progression of clinical signs is reached. Afterwards a set

of different challenges with specific food components can be carried out. One protein or carbohydrate source is added to the elimination diet for a period of 1–2 weeks.^{40,43,52} If no symptoms are detected, the first food component can be changed by a second for another period of 1–2 weeks. This cycle is repeated until the animal is exposed to all possible sources of its former food. If symptoms occur on one specific food component, the patient must be fed the elimination diet again, until maximal progression of symptoms is reached. Afterwards, a following food component can be tested. This procedure is very time-consuming, but gives the veterinarian and the owner information which permits to plan the long term treatment of the patient.⁴³

Provocation testing can be carried out in several ways.^{8,80} In an “open” food challenge, the owner and the veterinarian know which specific food component is fed. In a “single-blind” food challenge, only the veterinarian is informed. “Double-blind” challenges are done in a way that neither the veterinarian, nor the owner know which food component is fed to the animal. Practical concerns limit the use of single- and double-blind challenge tests in veterinary medicine. This can be regretted as in humans the placebo effect is important in food trials. The owner or the veterinarian might be influenced during the observation of clinical symptoms in dogs and cats.³⁰ However, several authors believe that open challenges are reliable for the routine clinical work in veterinary medicine.^{51,98} Only two studies reported double-blind challenge tests.^{56,57}

TREATMENT-MANAGEMENT

The principle for treating FA is very simple: avoidance of the offending food allergen,^{63,80} hence the importance to do provocation testing with separate food components.⁵¹ Concurrent allergies can influence the threshold for clinical symptoms in some animals.⁸⁰ Prevention of fleas and other causes of pruritus must be carried out.⁵⁵

Diet Manipulation

The aim of the treatment is feeding of a diet that is balanced and on which the patient stays asymptomatic. Both HMDs and commercial foods (NPDs and HPDs) can be used.⁸⁰ The use of mixtures of vitamins and minerals based on pure chemical substances is advised for supplementation of macrominerals and trace elements in HMDs.⁵³

Medicamental Treatment

Corticosteroids can be used in cases of FA with insufficient cooperation of the owner or in rare occasions where multiple food allergies hamper the composition of a suitable

hypoallergenic diet.³⁸ Chronic GI diseases with FA are often treated with relatively high doses of corticosteroids, sometimes combined with a cytostaticum.³⁸ Antihistaminica can be beneficial in cases of FA with urticaria.³⁸ On presentation of other symptoms, they are probably of little help. Treatment with antibiotics is started when secondary bacterial infections are present.^{20,55,93}

PROGNOSIS

The prognosis of FA is very good when the offending food allergen is identified. The way the diet is followed accurately influences the prognosis to a great extent. Correct instruction of the owner and attention from the veterinarian are of great importance.⁶³ A relapse is possible when the animal becomes allergic to another food component. Some patients become allergic to the new protein in their diet after 2–3 years.²⁰ When this happens, a new food trial has to be carried out to identify the new allergen and to compose a new hypoallergenic diet.¹⁸ Identification of the new allergen is not difficult when the animal receives a commercial hypoallergenic diet, because of the limited number of ingredients. When the animal is fed a normal commercial food without the causative (primary) food allergen, identification of the new allergen will demand more effort because of the larger amount of food ingredients. Strict avoidance of food allergens can allow that oral tolerance recovers, by which the allergy subsides.⁸⁹ The persistence of antibodies to the causative food component prohibits the recovery of oral tolerance when it is ingested again. Several months are necessary before antibodies have disappeared. Some medicaments can prevent the regain of oral tolerance: immunosuppressiva such as corticosteroids can suppress the production of sIgA on the mucosa or inhibit the suppressor function of the GALT.⁸⁹ One-third of the persons that strictly avoided the offending food component during 1–2 years, tolerated new exposure to the food allergen.⁶⁷ For dogs and cats, there are no data available on this subject. According to Muller et al. (1989) natural hyposensitisation rarely occurs.

CONCLUSIONS

The exact prevalence of FA in dogs and cats remains unknown, but is probably underestimated because of the difficulties to make a reliable diagnosis of FA. The lack of a reliable diagnostic test is a big concern and would be a great step forward in determining the exact prevalence of FA in suspected patients. Up to now, an extensive food trial is the only way to diagnose FA. Unfortunately, the correct performance of the different phases of this test (elimination diet, challenge and provocation testing) is a very time-consuming activity. For a successful outcome of the food trial, the choice of an appropriate elimination diet is of great importance. The recent development of HPDs can be a helpful alternative for HMDs and NPDs. However, clinical

studies are required to evaluate the nutritional value and the efficacy of these HPDs in treating dogs and cats with FA.

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