The allervet® handbook

The answer to allergy
In the beginning...

In 1906 a Viennese paediatrician named Clemens von Pirquet noted that some of his patients were hypersensitive to usually innocuous entities such as pollen, dust and certain foods. He called this phenomenon “allergy”, a word derived from the Ancient Greek words *allos*, meaning “other” and *ergon*, meaning “work” and historically all types of hypersensitivity were classified as allergies, thought to result from inappropriate activation of the immune system.
Canine allergic disease

Canine allergic disease manifests most frequently as skin disease or gastrointestinal disease. Some individuals will have clinical signs involving both systems.

Allergic skin disease:

Canine pruritic dermatoses which are associated with hypersensitivity include:

- Flea allergic dermatitis (FAD)
- Atopic dermatitis (AD)
- Allergic and irritant contact dermatitis

Gastrointestinal disease

Adverse reactions to food may reflect food allergy or intolerance. Clinical signs include anorexia, weight loss, flatulence, vomiting, diarrhoea and borborygmus.

What is Canine Atopic Dermatitis?

The International Task Force on Canine Atopic Dermatitis definition is as follows: "A genetically predisposed inflammatory and pruritic allergic skin disease with characteristic clinical features associated with IgE antibodies most commonly directed against environmental allergens" (Halliwell 2006).

It is currently accepted, based on clinical experience, that dogs with AD may be hypersensitive to environmental allergens, food allergens (food induced AD) or both.

Certain breeds are recognised as being at increased risk of developing AD; these include the terriers (West Highland White, Cairn, Fox, Yorkshire), Chinese Shar Pei, Cocker Spaniel, Dalmatian, Bulldog, Boxer, Labrador and Golden Retriever.

The currently favoured route for allergen exposure is via percutaneous penetration, facilitated by a defective epidermal barrier and irregularities in cell mediated immunity.

The classical sign of AD is pruritus. The incidence of canine AD in the general population is unclear - studies quote between 3.3% - 30% - but this appears to be increasing, possibly due to the changing lifestyle of dogs; proposed risk factors include spending more time indoors, increased uptake of routine vaccination and ecto/endoparasite control (Hillier, Griffin 2001).

Clinical signs are rarely seen in dogs less than 6 months old, except perhaps in the Shar Pei. Most become symptomatic between the age of 6 months and 3 years. Late onset disease is less common and is rare in dogs over seven years of age.

Dogs may present with the “triad” of facial rubbing, axillary pruritus and paw-licking but lesions can be found anywhere on the body. Initially pruritus may be seasonal, depending on the inciting cause, but may become perennial as an increasingly wide range of allergens become problematic. Secondary (Staphylococcal) pyoderma and Malassezia dermatitis are common complications. Otitis externa may accompany generalised pruritus but can be the major, or only, presenting sign.
Feline allergic disease

Feline allergic disease may present as skin, respiratory, GI disease or a combination of these.

Feline pruritic dermatoses which are associated with hypersensitivity include:

- Flea allergic dermatitis (FAD)
- Atopic dermatitis
- Allergic and irritant contact dermatitis
- (Feline eosinophilic granuloma complex)
- (Feline psychogenic alopecia)

Feline atopic dermatitis is less well characterised than its canine counterpart. The pathogenesis of disease is unclear and there are no recognised breed associations.

Disease usually manifests between 6 months – 3 years of age as a chronic pruritic, usually corticosteroid responsive dermatosis.

Lesions include miliary dermatitis, over-grooming/barbering, non-lesional alopecia or eosinophilic granuloma complex. These are not pathognomonic for atopy; FAD, cutaneous adverse food reactions, neurological and behavioural problems may have a similar presentation.

Respiratory disease. Feline asthma is a chronic respiratory disease affecting the small airways. The aetiology is imperfectly understood however studies have demonstrated high levels of allergen-specific IgE in cats diagnosed with asthma, suggesting the pathogenesis involves a hypersensitivity response (Halliwell 1993) (Caro, Rodriguez, Gonzalez 2002).

A study to investigate the efficacy of allergen specific immunotherapy (ASIT) in cats with eosinophilic bronchitis, diagnosed on clinical findings and tracheal wash cytology and utilising the allervet® serological assay for allergen identification, demonstrated an excellent clinical response in 62.5% of cats (became asymptomatic), with a good response in 25% (significant clinical improvement but required sporadic supplementation with inhalation therapy). A further 12.5% improved but required additional oral therapy (Caro Vadillo et al 2010).

The results provide strong support for a hypersensitivity disorder which includes a type 1 component, and demonstrate the potential of ASIT as a management tool for feline asthma.

Gastrointestinal disease. Feline eosinophilic enteritis is one example of an adverse food reaction; other histological patterns of inflammatory bowel disease may also represent adverse reactions to food. Clinical signs include anorexia, weight loss, chronic vomiting/diarrhoea and increased frequency of defecation.
Equine allergic disease

Equine allergic disease may present as skin or respiratory disease, headshaking or a combination of these.

Equine pruritic dermatoses which are associated with hypersensitivity include:

- Atopic dermatitis
- Insect bite hypersensitivity (*Culicoides spp.*, *Simulidae spp.*)
- Urticaria
- Cutaneous adverse food reactions

Genetic influences are recognised as a strong predisposing factor in the development of equine allergic dermatoses. Pruritus is often the primary presenting sign - frequently involving the mane, withers or tail. Lesions include a papular rash, hair loss, urticaria and facial/periorbital oedema. A diagnosis may not be possible based on the clinical presentation alone - findings are rarely specific.

The pathogenesis of equine atopy is incompletely understood; as in other species it is thought to involve a predisposition to develop IgE antibodies against environmental allergens and may result in dermatological or respiratory disease.

Age of onset of atopic dermatitis is variable, typically between 18 months and 6 years. Clinical signs commonly involve chronic relapsing pruritus and urticaria with scaling, hyperpigmentation, alopecia and secondary trauma. Lesions may develop anywhere on the body but frequently involve the head, mane and tail.

Insect bite hypersensitivity (sweet-itch) is an allergic reaction to the saliva of biting flies including midges, black flies, stable flies, horse flies and mosquitoes, thought to be mediated by both type 1 and type IV hypersensitivity reactions. Signs develop in young adults with a peak incidence around 3 years and are seasonal (during the fly season); the severity and duration of signs may intensify with time. Lesions usually affect the dorsal midline (mane, rump and tail) and predominantly reflect self-trauma (papular rash, scaling, alopecia, hyperpigmentation, urticaria). Sweet-itch is often a severely irritating and potentially debilitating disease; horses may show behavioural changes or loose weight due to constant discomfort.

Urticaria is a common condition in horses with no age, breed or sex predilection. Classical lesions are flat topped wheals with pitting oedema or angio-oedema. Lesions are transient, should pit under digital pressure and resolve in 24-48 hours although new lesions may develop close by. It may be useful to demarcate lesions in waterproof marker to monitor their progress.

Urticaria describes a clinical manifestation and is not a diagnosis. It has been associated with drug eruptions (penicillin, tetracycline, sulphonamide, PBZ, flunixin, phenothiazine, vermectin, moxidectin, vaccines), foods, topically applied products (shampoos, ectoparasiticides, rugs, tack), allergic disease (atopy, sweet-itch, contact or irritant dermatitis), systemic disease, stress/excitement and mechanical effects (cold, heat or pressure). In approximately half of all cases there is no identifiable cause.

Cutaneous adverse food reactions have been reported anecdotally in horses. It is a relatively common belief that high protein foods can cause papular eruptions, so called “protein bumps”. Whilst this cannot be explained by our current understanding of hypersensitivity reactions it is possible that plane of nutrition and level of training may modify immune responses and unmask sub-clinical atopy. As with many diseases stress can play a significant role. Horses suspected of suffering from “food allergy” may subsequently be diagnosed with atopy (Littlewood 2001); could this be the equine equivalent of food-induced atopic dermatitis?
Respiratory disease. Recurrent airway obstruction (RAO)/Chronic obstructive pulmonary disease or “heaves” is a chronic condition of horses involving an allergic bronchitis characterised by wheezing, coughing and laboured breathing. Affected horses show a marked increase in respiratory effort and may become increasingly dyspnoeic in response to exercise. A productive soft cough may be induced by feeding and exercise. With long standing disease there may be hypertrophy of the extrinsic respiratory muscles causing the classic “heave line”. Horses with RAO may present in acute respiratory failure as a veterinary emergency.

Allergens precipitating bouts of RAO include mould spores, mites, pollens, hay and grain mill dust.

In a 2006 study [Monreal et al] serum samples from 23 horses with confirmed RAO, 11 horses with non-allergic airway disease and 23 control horses were blindly tested for IgE against various environmental allergens using the allervet® equine serological assay and a serological test performed by a major commercial competitor.

Results from the allervet® test demonstrated excellent sensitivity and negative predictive values (95.7% and 96.0% respectively), with acceptable specificity and positive predictive values (72.7% and 71.0% respectively). The main allergen detected was grain mill dust, followed by mites, grass pollens and moulds.

In comparison the results from the competitor’s test showed lower sensitivity and negative predictive values (69.6% and 66.7% respectively), with poor specificity and positive predictive values (42.4% and 45.7% respectively). Mites were the major allergens detected, followed by tree and weed pollens.

Differences in test performance may be explained in part by the type of allergens included in the panels; the allervet® panel includes grain mill dust, the competitor’s panel does not. allervet® results in clinically confirmed cases of RAO suggest that for some horses grain mill dust is a significant allergen.

These findings support a Type 1 hypersensitivity component in the development of RAO (although the pathogenesis also involves neutrophil mediated inflammation) and indicate that serum IgE evaluation can be a useful tool when investigating the inciting cause of allergic respiratory disease.

Studies are ongoing to evaluate concentrations of allergen specific IgE in bronchoalveolar lavage fluids from horses with respiratory disease.

Headshaking and other head vices are thought to be manifestations of hypersensitivity in some horses. In an allervet® study from 2009 we found that 30% of horses undergoing serological evaluation for allergic disease presented with a combination of respiratory signs and head shaking.

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Pathophysiology of allergic skin disease

Whilst classical allergy usually involves type 1 (immediate and late phase – see figures 1 and 2) or type 1V (cell mediated) hypersensitivity reactions this is a gross oversimplification. Dysfunction of the epidermal barrier may increase permeability to allergens, irritants and microbes. Decreased production of antimicrobial proteins can increase susceptibility to pyoderma, and environmental factors may modify allergic responses in genetically predisposed individuals.

T helper 2 lymphocytes drive humoral immunity and result in IgE production. Studies have detected Th2 polarisation in the skin of human atopics and IL-4 expression is thought to be a hallmark of human AD. The importance of IL-4 in canine and feline atopic disease is less consistent. IL-5 expression may be more common in atopic compared to healthy canine skin. Many other cytokines have been associated with atopic dermatitis including the newly described IL-31, also produced (not exclusively) by sensitised Th2 cells.

Binding of IL-31 to its receptor triggers the Janus kinase/signal transducer and activator of transcription (JAK/STAT) pathway, resulting in an unrelenting cycle of pruritus and neuroimmune stimulation. The ability to block JAK/STAT could act at many levels of the itch-scratch cycle to block the pruritic response.

IgE is present in serum in minute quantities compared to other immunoglobulins. Most is bound irreversibly to mast cells or basophils, via the high-affinity receptor (see fig 2).

Antigen (allergen) is presented by dendritic antigen presenting cells, to Th2 lymphocytes (see fig 1).

Figure 1: Pathogenesis of Type 1 Hypersensitivity

Figure 2: IgE/Mast Cell Receptor Complex

Th2 cells produce a variety of cytokines including IL-3, IL-4, IL-5 and GM-CSF. IL-4 is instrumental in “turning on” IgE-producing B cells, sustaining development of Th2 cells and triggering IgE synthesis. IL-3, IL-5 and GM-CSF (also produced by activated mast cells) promote survival of eosinophils, important effectors of type 1 hypersensitivity. Activated B lymphocytes develop into plasma cells and up-regulate IgE production.

IgE binding results in mast cell sensitisation. If specific antigen subsequently cross-links two mast-cell-bound IgE molecules, a message is transmitted into the cell (signal transduction) initiating a series of reactions which ultimately lead to both mast cell degranulation, with discharge of potent pre-formed inflammatory mediators (histamine, heparin, tryptase, chemotactic factors, TNF) and de novo synthesis of secondary mediators (prostaglandins, leukotrienes, cytokines, PAF). These mediators are responsible for initial (immediate) signs of type 1 hypersensitivity and initiate events leading to the late-phase response.
Over the years various workers have developed and published criteria for diagnosing canine AD (Willemse 1986, Prelaud et al 1988). These criteria were further refined by Claude Favrot and his colleagues following a large study involving over 1000 dogs, published in 2009 and clarified by Olivry in 2010. They are recommended for use in general practice to aid in the diagnosis of AD.

The 2009 Favrot Diagnostic Criteria for Canine Atopic Dermatitis

1. Onset of signs under 3 years of age
2. Dog living mostly indoors
3. Glucocorticoid-responsive pruritus
4. Pruritus sine materia at onset (i.e. pruritus without lesions at onset)
5. Affected front feet
6. Affected ear pinnae
7. Non-affected ear margins
8. Non-affected dorso-lumbar area.

If 5 criteria are met the sensitivity is 85% with a specificity of 79%. If 6 criteria are met the sensitivity falls to 58% and specificity increases to 89%. Whilst these criteria could lead to a misdiagnosis in 20% of cases, by ruling out ectoparasitic disease and pyoderma, the specificity can be increased considerably.

All animals should be evaluated for ectoparasites by skin scraping. Therapeutic trials for fleas and sarcoptic mange (dogs) should be undertaken.

A combination of systematic and topical treatment for pyoderma and Malassezia should be employed if micro-organisms are contributing to the level of pruritus. Specific culture for dermatophytes should be performed when indicated.

In 2011 Dr Favrot and his colleagues produced a set of criteria to help identify cats with non-flea induced allergic dermatitis:

1. Presence of at least two body sites affected.
2. Presence of at least two of the four clinical patterns:
   - Symmetrical alopecia
   - Miliary dermatitis
   - Eosinophilic dermatitis
   - Head and neck erosions/ulcers
3. Presence of symmetrical alopecia
4. Presence of any lesions on the lips
5. Presence of erosions or ulcerations on the chin or neck
6. Absence of lesions on the rump
7. Absence of non-symmetrical alopecia on the rump or tail
8. Absence of nodules or tumours

If 5 of the 8 criteria are met a diagnosis of allergic dermatitis is likely although similarly presenting dermatoses (FAD, dermatophytosis, adverse food reaction, neurological and behavioural factors) must be ruled out.

As for dogs, these feline criteria may be useful and practical but it remains essential to eliminate other cause of pruritus to reduce the likelihood of a misdiagnosis.

Similar diagnostic criteria have not, as yet, been established for horses.

Serological testing and intradermal skin testing have no role to play in diagnosing atopic disease or other hypersensitivity disorders. Once the clinical diagnosis has been established, testing for IgE may be appropriate to assist in allergen avoidance or to permit the use of allergen specific immunotherapy as a treatment modality.
Methods of IgE detection

Intradermal skin testing (IDST):
This method is generally acknowledged as the “gold standard” for allergen identification.

Drawbacks of IDST include the lack of standardisation:

- Reproducibility between tests and antigen manufacturers is poor. The test is operator-dependent in terms of technique and interpretation making results subjective.
- Patients must be sedated and extensively clipped.
- Existing skin disease may preclude testing
- There is a small but significant risk of an adverse reaction including anaphylaxis.
- Anti-allergic drug therapy may need to be withdrawn for an appropriate period of time - see table summary for Optimal and Minimal withdrawal times (Olivry and Saridomichelakis 2013).

Serological testing:
In-vitro diagnostic test methods have some major advantages over IDST.

- Testing is standardised and objective.
- A single blood sample is all that is required; the patient is spared extensive clipping and any discomfort associated with intradermal injection.
- There is no risk of adverse reactions.
- Existing skin pathology does not preclude testing.
- Withdrawal of drugs to control pruritus is often unnecessary (Miller, Scott et al 1992) and see table summary for Optimal and Minimal withdrawal times.

Following antigenic exposure, IgG is produced in far higher concentrations than IgE. The inadvertent detection of IgG has, in the past, contributed to the under performance of some serological tests.

It is more than twenty years since the development of the first commercially available in-vitro allergen specific IgE assay. Currently there are many assays which employ either polyclonal or monoclonal anti-IgE antibodies, or recombinant human high-affinity IgE receptor fragment to detect canine IgE. Although comparative studies have attempted to demonstrate the superiority of one method over another advances in technology have led to improved reagents and procedures making previous comparisons obsolete.

A study to define the performance characteristics of a commercially available monoclonal antibody based (mac) ELISA for detection of canine IgE and comparison with a high affinity IgE receptor based ELISA demonstrated that the [mac] ELISA is reproducible and results are comparable to the high affinity IgE receptor based ELISA within and between laboratories (Lee et al 2009).

It would be unrealistic to expect perfect correlation between the results of serological and IDST; serology demonstrates “free” rather than “mast cell bound” IgE. There may be merit in certain cases of combining the results from both test methods when determining the content of an immunotherapy vaccine.

There are animals who fulfil diagnostic criteria for atopic dermatitis but are persistently negative for IgE on serological and intradermal skin testing – this has given rise to the syndrome of “atopic-like dermatitis”, defined as “an inflammatory and pruritic skin disease with clinical features identical to those seen in canine atopic dermatitis in which an IgE response to environmental allergens cannot be detected” (Halliwell 2006).

The incidence is thought to be between 20-25% of clinically diagnosed canine cases; the incidence in felines and equines is not currently known. Failure to identify IgE does not affect the diagnosis (which is clinical) but precludes the use of allergen avoidance and immunotherapy as management tools.
Animals suffering from atopy or other hypersensitivity disorders frequently receive anti-inflammatory or antipruritic medications and there may be concern that such drugs could influence the results or interpretation of specific tests for IgE. In 2013 Thierry Olivry and Manolis Saridomichelakis, on behalf of the International Committee on Atopic Diseases of Animals, produced evidence based guidelines for antihistamine drug withdrawal times:

Summary of optimal (OWT) and minimal withdrawal times (MWT) before intradermal and serological tests in dogs

<table>
<thead>
<tr>
<th>Drug example</th>
<th>OWT</th>
<th>MWT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intradermal tests</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antihistamines (oral)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydroxyzine, cetirizine</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Glucocorticoids (short acting, oral)</td>
<td>14</td>
<td>Unknown</td>
</tr>
<tr>
<td>Prednisone, prednisolone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucocorticoids (long acting, injectable)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methylprednisolone acetate</td>
<td>Unknown</td>
<td>28</td>
</tr>
<tr>
<td>Glucocorticoids (topical)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrocortisone, triamcinolone</td>
<td>14 (high potency)</td>
<td>0 (low potency)</td>
</tr>
<tr>
<td>Glucocorticoids (otic)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betamethasone, mometasone</td>
<td>14</td>
<td>Unknown</td>
</tr>
<tr>
<td>Ciclosporin (oral)</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Pentoxifylline (oral)</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Ketoconazole (oral)</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Essential fatty acids (oral)</td>
<td></td>
<td>0</td>
</tr>
</tbody>
</table>

| **IgE serological tests**                        |     |       |
| Antihistamines (oral)                            |     |       |
| Not tested                                       | Unknown | 0 |
| Glucocorticoids (short acting, oral)             |     |       |
| Prednisone, prednisolone                        | 0   | 0     |
| Glucocorticoids (long acting, injectable)        |     |       |
| Methylprednisolone acetate                      | <28 | Unknown|
| Glucocorticoids (topical or otic)                |     |       |
| Not tested                                       | Unknown | 0 |
| Ciclosporin (oral)                               |     | 0     |

*For intradermal tests, withdrawal times mentioned are those for the determination of the immediate phase reactions.

Optimal withdrawal times (OWT’s) are those that have been shown, or are very likely based on mechanism of action, to be associated with no interference on test results.

Minimal withdrawal times (MWT’s), which are shorter than OWT’s are defined as those that might, at most, be associated with a small inhibitory effect that should not affect the interpretation of most test results.

The effect of type 1 antihistamines on serological testing has not been studied; in theory blockade of the type 1 antihistamine receptor should not impact on the measurement of IgE in patient serum and no withdrawal time is required.

Study data was based on use of oral corticosteroids at anti-inflammatory/antipruritic rather than immunosuppressive doses; therapy for up to 2 months was found to be unlikely to affect serological testing and required no withdrawal period. Extrapolating from this data it has been proposed that use of topical or otic corticosteroids should also not incur any withdrawal period.

The duration of Ciclosporin studies was 6-8 weeks; when used at doses recommended for atopic dermatitis this did not affect serological testing and no withdrawal period is required. The effects of longer courses of ciclosporin on serum IgE levels are unknown. Anecdotally we have experience of a small numbers of cases where prolonged therapy appears to have suppressed the IgE response. In the absence of specific data, it may be prudent to delay testing animals that have been on medication for more than 8 weeks until therapy has been withdrawn for 4-6 weeks.
Allergenic triggers in the environment:
Aeroallergens  •  Arthropod allergens  •  Microbial allergens

**Aeroallergens**

- House dust and storage mite proteins
- Pollens from grasses, weeds and trees
- Fungal spores

**House dust mites**

Dermatophagoides farinae, the American house dust mite, and Dermatophagoides pteronyssinus, the European house dust mite, are the most commonly encountered species.

House dust mites feed on human and animal dander, thriving in warm, humid conditions. Large numbers are found in mattresses, bedding, carpets and soft furnishings. Both live and dead mites and their faeces can be allergenic. Several mite allergens are proteolytic enzymes; proteolytic activity may directly contribute to allergenicity by facilitating penetration through mucosal surfaces (Arruda et al 2001).

Acaricidals, used to decrease numbers of viable mites, may not significantly reduce the allergenic load. Additional control measures include regularly hoovering mattresses, carpets, floors and soft furnishings. Frequent washing of, or replacing, cushions, quilts and other types of soft pet bedding.

Controlling humidity is of major importance, mite populations stop growing and die out when the relative humidity is <60%.

Clinically normal, as well as hypersensitive, animals may test positive to house dust mites, therefore serological results must be evaluated in conjunction with clinical signs.

**Storage mites**

Commonly encountered storage mites in the UK include Acarus siro, Tyrophagus putrescentiae and Lepidoglyphus destructor. As for the house dust mites, storage mites and their faeces are highly allergenic; many dogs, cats and horses have raised levels of IgE to storage mites. Mite-sensitive individuals frequently show co-sensitisation to house dust and storage mites. In some cases this may reflect parallel sensitisation however, ELISA cross-inhibition studies have demonstrated extensive cross reactivity between the house dust mites, between D. farinae and the storage mites T. putrescentiae and Acarus siro and between the latter two mites (Saridomichelakis et al 2008).

Cross reactivity may explain positive reactions in dust mites sensitised patients where exposure to storage mites is thought to be unlikely.

Whether or not there is also in-vivo cross reactivity to the mites is unclear; the results of both serology and intradermal skin testing support the possibility of developing clinical signs following exposure to a novel but cross-reacting antigen (Saridomichelakis et al 2008).

Storage mites are found in cereal based foods; their presence will eventually result in significant spoilage. Populations expand rapidly in warm humid conditions in contaminated food.

Methods to decrease exposure include changing from a dry to a tinned or fresh food diet. If this is not practical dried food should be purchased in small quantities and stored in dry, airtight containers that are thoroughly washed and dried once emptied. Food residue in the bottom of the container may be heavily contaminated and should be discarded.

After feeding it may be helpful to wipe clean the animal’s face or muzzle.

Cockroach allergy is common in man; although less of a problem in domestic animals positive serological reactions may occur and reflect either exposure or cross reactivity with dust mites. The structural protein tropomyosin, which is common to some species of cockroach, mites including the Dermatophagoides spp. and shell fish, may be responsible for this cross reactivity (Eggleston, Arruda 2001).
**The significance of airborne particle size**

The size of airborne particles determines both the time taken for them to “settle out” in still air, and their destination within the respiratory tract following inhalation.

Small particles, up to 2 microns, are airborne for up to 6 hours, following inhalation they may reach the alveoli.

Particles between 2-10 microns may settle in as little as 1.5 minutes, following inhalation some reach the bronchi/bronchioles. Examples include fungal spores, dander, smoke and diesel particles.

Particles between 10-20 microns settle in 4-15 minutes in still air. They are filtered out in the nasal cavity and do not reach the bronchi. Examples include small pollen grains, mite droppings, certain cockroach allergens and some fungal spores.

Particles larger than 40 microns settle rapidly and are rarely inhaled.

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**Fungal spores**

Fungal spores are microscopic particles released by moulds in their thousands into the atmosphere. Moulds favour damp, musty conditions; rotting vegetation (grass cuttings, leaves, compost heaps) are a prime environment for mould growth.

*Cladosporium* is the most frequently encountered mould in air. Indoor concentrations reflect the outdoor concentration of the airborne spores. Levels of this mould rise in the spring and peak in late summer and autumn.

*Alternaria* is also an outdoor mould which blooms during warm weather.

Higher concentrations of spores from outdoor moulds are found in rural compared to urban environments.

Indoor moulds can be found on spoiled food (stale bread, cheese, fruit), behind wallpaper, on walls suffering from damp, around and within refrigerators.

*Aspergillus* and *Penicillium* are two of the most commonly encountered moulds found indoors; they are present all year round although spore concentrations peak during winter and spring.

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**Pollens**

Almost all pollens that are allergens are from anemophilous species (pollinated by wind). Anemophilous pollen grains are light and non-sticky, so that they can be transported by air currents. Grasses (*Poaceae*) are the most important producers of aeroallergens in most temperate regions, with lowland or meadow species producing more pollen than upland or moorland species.

Pollens show seasonal as well as geographic variation in prevalence in the environment. Patients suffering from pollen allergies may initially have seasonal disease with clinical signs over the spring and summer months, coincident with high environmental levels of the particular pollen(s) to which they are sensitised. Over time seasonal disease may become perennial. The peak pollen season extends from March to September but can begin in January and end as late as November. Horses may be exposed to pollen throughout the year depending on the type and quality of hay offered.
**Avoiding fungal spores:**

Moulds flourish in damp places, ventilation is key to preventing growth.

- Keep animals away from compost heaps, piles of rotting leaves, dead and decaying wood.
- Avoid walking through woodland in warm damp conditions.
- Damp areas such as kitchens, bathrooms should be kept clean and ventilated after cooking, showering etc.
- Windows prone to condensation should be thoroughly dried and cleaned.
- Avoid drying clothes indoors and vent tumble driers to the outside.
- Keep houseplants to a minimum and change soil regularly, or avoid altogether.
- Dry wet clothing, rugs or tack in a well ventilated, dedicated place.
- Hay and grain should be stored in a dry, well ventilated area.
- Do not feed spoiled hay.
- Ensure stables and kennels are adequately ventilated.

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**Arthropod bite hypersensitivity**

**Flea allergic dermatitis (FAD):** This is the most common form of allergic skin disease seen in the dog and cat in flea-endemic regions. Type 1 and type IV hypersensitivity reactions to allergens in flea saliva are involved in the pathogenesis in dogs; mechanisms of FAD in the cat are unclear.

This pruritic skin condition shows a classical distribution affecting the back, dorsal lumbosacral region, perineum, tail, caudal/medial thighs and abdomen. Unlike flea infestation, the severity of clinical signs is independent of the numbers of fleas on the animal.

**Sweet-itch:** Biting flies such as midges, black flies, mosquitoes, horse and stable flies can be highly problematic for some horses. In most cases this is due to a hypersensitivity reaction to insect saliva which is inoculated during feeding.

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**Microbial allergens**

*Staphylococci* and *Malassezia* are commensals at various sites on canine skin including the nares, axilla, groin and perineum. If the epidermal barrier is breached (trauma, epidermal barrier dysfunction, endocrine disease) colonisation and infection may occur. Some patients develop hypersensitivity to these organisms which exacerbates pruritus. Serological testing may identify affected animals and direct therapy.
Reactions to ingested foods are rare (adverse food reactions or AFR); generally the incidence is cited as between 1 - 5% of dermatological disease in dogs and cats and around 10 - 15% of non-seasonal, non-parasitic, allergic dermatitis in dogs (Muller et al, 2001).

No breed or sex predisposition is recognised. Although a significant proportion of cases occur in dogs less than 12 months of age (Harvey, 1993; Rosser 1993), most dermatologists agree that there is no true age predisposition. Risk factors have not been identified for cats and little is known about the prevalence of AFR in horses.

Clinical disease most frequently affects the skin, typically causing non-seasonal pruritus (Carlotti et al 1990; Tizzard 2000), which may predispose to recurrent pyoderma and acral lick dermatitis. Less commonly the gastrointestinal tract is involved and signs may include one or a combination of the following: vomiting, diarrhoea, abdominal pain, flatus, barbarygmus and weight loss.

When clarifying the diagnostic criteria for Canine Atopic Dermatitis (2009) Favrot’s group attempted to differentiate between cases of food induced and non-food induced disease in recognition of the fact that dogs suffering from adverse food reactions may be clinically indistinguishable from those with classical AD.

Concurrent dermatological and gastrointestinal disease is recognised and may be more likely in cases of food-induced AD where disease is also more likely to be non-seasonal and poorly responsive to corticosteroid therapy.

In the cat eosinophilic enteritis and inflammatory bowel disease have been associated with AFR. There is some evidence to suggest that food reactions may rarely manifest as respiratory, neurological, musculo-skeletal or urinary tract disease (Day 1999).

Otitis externa may accompany generalised skin disease but can be the only clinical sign (Rosser 1990).

Adverse food reactions may be intermittent or episodic if the offending foods are given sporadically, and may also be non-pruritic unless aggravated by concurrent disease (Scott 1995).

Adverse reactions to food encompass dietary hypersensitivity, which has an immunological basis and dietary intolerance which is a non-immunological, physiological response to a food. Clinically these conditions are indistinguishable (Scott 1995) and can only be diagnosed based on the response to a strictly controlled elimination diet followed by food provocation.

**Dietary hypersensitivity**

The antigenic components of food are usually heat, acid and enzyme stable proteins and glycoproteins (Tizzard 1999). In some cases, however, the immunogenic substance may be a product of digestion, for example successive pepsin hydrolysis of cow’s milk yields several novel protein allergens (Bahna 1985).

The immunological basis of dietary hypersensitivity is not fully understood; reactions may be mediated by any of types 1–1V hypersensitivity, however, type 1 hypersensitivity, resulting in IgE mediated, mast cell dependent reactions are thought to be largely responsible for clinical signs of disease (Day 1999; Halliwell 1992).

The presence of IgE antibodies is considered significant (Johansson et al 1994) as a marker of systemic exposure to dietary components but does not confirm type 1 hypersensitivity as the cause of clinical signs or permit a diagnosis of “food allergy”.

Factors such as gastro-intestinal inflammation or selective IgA deficiency may favour exposure of allergens to gut-associated lymphoid tissue, resulting in elevated serum concentrations of antibodies to dietary components. Under normal conditions secretory IgA binds dietary allergens ensuring they are shed into the bowel lumen or, if absorbed, are removed by the liver without provoking an inflammatory response (Batt et al 1999).
Dietary intolerance

The American Academy of Allergy and Immunology have defined dietary intolerance as those adverse reactions to food that are not immunologically mediated.

There are several proposed mechanisms:

Food idiosyncrasies, where an animal responds abnormally to a food. Examples include gluten enteropathy and lactose intolerance.

Metabolic reactions, where a food component affects the animal’s metabolism.

Examples include tyramine and histamine:

- Tyramine is present in liver, sausage, fermented cheese, pickled fish and chocolate and leads to release of noradrenaline from tissue stores, resulting in hypertension and other sympathetic effects.
- Histamine is present in pig’s liver, sausage, tinned fish and some commercial canned pet foods, but will only be absorbed from the gastrointestinal tract if there is a defective mucosal barrier with increased permeability.
- Pharmacological reactions, where certain food components act like drugs. Examples include caffeine, theobromine and food additives such as tartrazine.
- Food poisoning, where the adverse reaction is caused by a toxin, microbial protein or organism.

If dietary intolerance leads to gastro-intestinal inflammation and/or altered gut permeability there may be elevated serum concentrations of non-IgE antibodies to food components (effect rather than cause).

In many cases of AFR a single component of the diet is implicated. Foods are usually protein rich and in dogs and cats, cereals, dairy products and beef are most frequently involved (Carlotti et al 1990; Harvey 1993) along with fish, chicken and eggs.

In the horse wild oats, clover and alfalfa have been recognised as antigens (Tizzard 1999).

A definitive diagnosis of AFR requires the use of an elimination diet followed by test meal investigation. This process involves exclusively feeding a novel protein and carbohydrate diet for up to 13 weeks, although a significant degree of improvement should occur within 4-6 weeks, (Muller et al 2001).

Traditionally, simple diets such as home prepared lamb/chicken/turkey and rice have been recommended, without any investigation into the suitability of such diets.

Evaluation of the immunogenic compounds in milk and beef has identified bovine IgG and phosphoglucomutase as major allergens and implicated them as major allergens in lamb. These allergens could play an important role in cross reactivity between beef, milk and lamb, suggesting that lamb is not a suitable source of dietary protein for dogs allergic to bovine products (Martin et al 2004).

Studies have demonstrated that some dogs proven to suffer from AFR (diagnosed following elimination diet and challenge exposure) produce high levels of IgE and IgG to antigens present in the food(s) responsible for their clinical signs. (Halliwell 2004) (Gonzalez et al 2004).

Serological testing may be useful as follows:

- To identify suitable patients for a limited-antigen dietary trial.
- To aid in selection of the most appropriate ingredients for an elimination diet.
- To emphasise to the owners the importance of adhering to the elimination diet.

A diagnosis of AFR can only be made retrospectively based on the response to an appropriate elimination diet followed by provocative testing.
Research and development scientists at allergen® have produced an oligoclonal assay based on canine recombinant IgE (rIgE), see fig 3. This incorporates 3 monoclonal antibodies raised against known epitopes on the heavy chain domains (2, 3 and 4) of the rIgE molecule. Oligoclonal technology combines the advantages of monoclonal specificity with polyclonal sensitivity resulting in enhanced performance of the assay (Alvarez et Zalve 2010).

The test is an indirect ELISA; the enzymatic reaction produces a colour change measured as the optical density using a densitometer. The optical density reading is directly proportional to the patient’s serum concentration of allergen specific IgE. Results are reported as negative, borderline, positive or high positive, rather than numerically - whilst the OD reflects the serum concentration of IgE the presence and quantity of allergen specific serum IgE does not necessarily correlate with the severity of clinical signs (Lee et al 2009).

Figure 3: Production of a Recombinant Canine IgE Molecule

Immunoglobulin E (IgE) is a key molecule in immediate allergic reactions in dogs, and it is used in-vitro for detection of allergen-specific IgE employing anticanine IgE antibodies. Usually, these reagents are developed against IgE purified from sera that frequently are contaminated with other immunoglobulins, cross-reaction with which could produce false positives. Molecular biology techniques now allow the production of immunoglobulins free of contamination with other isotypes. The aim of this study was to produce recombinant canine IgE (rIgE) using the known sequence of its gene that comprises the domains CH2-CH3-CH4 of the constant heavy chain region.

A mammalian cell system was employed in order to maintain the glycosylation motifs of the molecule. rIgE was affinity purified and characterized in order to check its molecular weight and structure in SDS-PAGE and immunoblotting assays. The rIgE represented a minority protein in the supernatant of transfected cells. The purification needed several washing steps, and the elution required a high concentration of imidazole (500mM). rIgE was specifically recognized by an anti-canine IgE-peroxidase polyclonal antibody, showing an apparent molecular weight of 50 kDa in the presence of beta-2-mercaptoethanol and a molecular weight of 100 kDa in non-reducing conditions consistent with the predicted molecular weight for mono and dimeric forms. The rIgE maintains native IgE epitopes and can be used to produce new monoclonal antibodies against the Fc region of canine IgE that are free of contamination and cross-reaction with other immunoglobulins.
Canine, feline and equine test options

Canine and feline screen

The canine and feline environmental screen incorporates the entire panel of environmental allergens assigned to five categories: grasses, weeds, trees, indoor and mites. The screen and panel contents are tailored to include the most relevant allergens (in terms of frequency of detection and degree of allergenicity). Panel contents are reviewed periodically to embrace shifts in allergen prevalence.

Flea and Malassezia are tested and reported individually making this screen an extremely cost-effective option.

A food screen is also available for dogs and cats and is reported as either positive (IgE/IgG present) or negative (IgE/IgG not detected).

When screen results are positive individual allergens within that group (or groups) can be tested.

Negative screens do not rule out a diagnosis of a hypersensitivity disorder or adverse food reaction, these are clinical diagnoses. Testing individual allergens, however, is not appropriate for these cases thus avoiding unnecessary expense.

Screen tests are offered to increase flexibility; if preferred it is possible to test full environmental and food panels at the outset.

Panels can be requested individually or in combination.

Canine and feline environmental panel

Allergens included in the screening categories are shown below and make up the full environmental panel.

<table>
<thead>
<tr>
<th>Grasses</th>
<th>Ryegrass, Cocksfoot, Bermuda grass, Timothy, Oat, Rye</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weeds</td>
<td>Mugwort, Ragweed, Goosefoot, Russian thistle, Sorrel, Rape, Plantain</td>
</tr>
<tr>
<td>Trees</td>
<td>Birch, Privet, Pine, Beech, Ash, Willow, Cypress, Oak</td>
</tr>
<tr>
<td>Indoor</td>
<td>Alternaria spp., Aspergillus spp., Cockroach, Flea, Malassezia</td>
</tr>
<tr>
<td>Mites</td>
<td>House dust mites: Dermatophagoides pteronyssinus, Dermatophagoides farinae</td>
</tr>
<tr>
<td></td>
<td>Storage mites: Tyrophagus putrescentiae, Acarus siro, Lepidoglyphus destructor</td>
</tr>
</tbody>
</table>

Canine and feline food panel

Food panel

| Beef, Milk, Lamb, Venison, Chicken, Egg, Turkey, Pork, White fish, Blue (oily) fish, Soya bean, Corn, Wheat, Rice, Potato, Sugar beet, Carrot, Pea, Yeast, Oat |

3ml of serum is recommended for canine and feline tests.
Equine environmental panel

<table>
<thead>
<tr>
<th>Grasses</th>
<th>Ryegrass, Timothy, Bermuda grass, Oat, Rye</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weeds</td>
<td>Plantain, Mugwort, Goosefoot, Ragweed, Rape, Russian thistle, Sorrel</td>
</tr>
<tr>
<td>Trees mix</td>
<td>Birch, Alder, Hazel</td>
</tr>
<tr>
<td>Trees</td>
<td>Privet, Cypress, Poplar, Oak, Willow, Beech, Elm, Ash</td>
</tr>
<tr>
<td>Mites</td>
<td>House dust mites: Dermatophagoides pteronyssinus, Dermatophagoides farinae, Storage mites: Tyrophagus putресcentiae, Lepidoglyphus destructor, Acarus siro, Glycophagus destructor, Cockroach</td>
</tr>
<tr>
<td>Dusts</td>
<td>Hay dust, Grain mill dust</td>
</tr>
</tbody>
</table>

Equine food panel:

| Food panel       | Wheat, Oat, Barley, Rye, Corn, Alfalfa, Carrot, Carob, Sugar beet, Soya bean, Molasses |

Equine insect panel:

| Insect panel     | Culicoides Spp. (Midges), Black Fly, Mosquito, Horse Fly, Stable Fly |

Insect testing

Levels of serum IgE appear to increase rapidly in response to fly bites and decrease quickly when there are no flies in the environment. When testing horses to support a diagnosis of “sweet-itch” sampling during the fly-biting season (May – October) is recommended.

5ml of serum is recommended for equine tests.

Equine screen

The equine screen includes the allergens from the environmental panel, separated into outdoor and stable groups. The outdoor group contains common grasses, weeds and trees.

The stable group includes mites, moulds and dusts.

When screen results are positive individual allergens within that group (or groups) can be tested.

Negative screen results do not rule out a diagnosis of atopy or a hypersensitivity disorder - this is a clinical diagnosis. Testing individual allergens, however, is not appropriate for these cases thus avoiding unnecessary expense.

Allergens from the outdoor and stable groups are combined in the full environmental panel. Whilst the screen tests is offered to increase flexibility it is possible to choose the full environmental panel at the outset.

Equine food and insect panels are also available.
Interpretation of results and treatment

Interpretation of results
Results are reported as negative, borderline, positive or high positive rather than numerically since the presence and quantity of allergen specific serum IgE does not necessarily correlate with the severity of clinical signs (Lee et al 2009) and is not an indication of the significance of the allergen. Negative results do not rule out a diagnosis of atopy or a hypersensitivity disorder but preclude the use of allergen avoidance or allergen specific immunotherapy as disease management tools.

Cross reactivity
Significant cross reactivity exists between some common allergens and has important implications in terms of diagnosis and treatment:

Alder and Hazel are closely related taxonomically to Birch; all are members of the Betulaceae family and share a major antigen, Bet v 1. Patients who are Bet v 1 sensitised are usually sensitised to pollen from all three trees. In terms of both diagnosis and treatment, Birch is sufficient to represent other members of this family.

Birch also contains the allergen Bet v 2; this is a pan-allergen (a highly conserved allergen found in almost all extracts of vegetable origin). Patients who are Bet v 2 sensitised are polysensitised to many plant species.

Cocksfoot shares major antigens with Meadow grass and Meadow fescue, Rye shares antigens with Wheat and Barley, Timothy shares antigens with Bent grass. Therefore, Cocksfoot, Rye and Timothy are sufficient to diagnose and treat patients sensitised to these other grasses (Festucaeae).

Patients with positive reactions to certain pollens may have positive food results due to cross-reactivity. For example, IgE raised against pollen from Festucaeae may cross react with Soya bean, Corn, Wheat and Pea. IgE raised against pollen from Betulaceae may cross react with carrot.

Treatment options - environmental testing
When faced with positive serology results, options include:
- Allergen avoidance
- Allergen specific immunotherapy (desensitisation)

Allergen avoidance
Allergen avoidance should always be attempted. In situations where it is practical it may alleviate or, at least, significantly improve clinical signs. For example, horses allergic to Culicoides spp. should be stabled at dawn/dusk when midges are most active and fly screens should be fitted over stable doors. Ceiling fans, to create a draught, should be used alongside fly repellents and anti-fly rugs.

Pocket-sized botanical illustrations are provided for owners when serology results indicate pollen sensitisation; the cards help owners to identify, therefore avoid, the relevant grasses, weeds or trees, in their own garden and when out walking.

We have produced a unique pollen calendar which indicates the average pattern of pollen release for the UK. This is issued with veterinary results for patients who are pollen sensitised, and helps to predict periods of high allergenic load (which may be associated with clinical deterioration).

When mite results indicate sensitisation we provide information cards containing practical advice regarding the source of mite allergens and strategies to reduce the level of environmental contamination.

The effect of age on test results
Serology results from patients less than 12 months old are associated with an increased risk of both false negative and false (temporarily) positive results (allervet®, unpublished data).

Although atopy may be recognised clinically in dogs less than a year old, these patients are immunologically immature; the results of serology may change if they are tested prior to, then after, 12-18 months of age when there may be evidence of/further sensitisation, or apparent desensitisation.

If a young animal is sensitised but all of the IgE is mast cell bound, IgE will not be detected in serum. In addition, animals less than 12 months old have not experienced a “full calendar year” of allergens and there is the possibility of further sensitisation with exposure to novel antigens.

Positive results in immature dogs may subsequently become negative due to improved protection at mucosal surfaces. The primary effector molecule of the mucosal immune system is secretory IgA (an IgA dimer). Serum IgA concentrations do not reach normal adult levels until 12-18 months of age; this transient IgA deficiency may manifest clinically as upper respiratory tract infection, otitis externa, Staphylococcal and atopic dermatitis (Schalm’s Veterinary Haematology).

To summarise: evidence of sensitisation in juveniles may be present, however, retesting when animals are over 12 months old is always recommended prior to embarking on immunotherapy. Atopic phenotypes who initially test negative should also be retested at a later date if immunotherapy is a potential therapeutic option.
Allergen specific immunotherapy

Immunotherapy may be more effective than allergen avoidance for animals sensitised to a wide range of environmental allergens.

The concept of immunotherapy is not new; empirically derived protocols have been practised for many years. As a direct result of wide and successful use of immunotherapy in the human field, the World Health Organisation now advocates this as the most appropriate rationale for treating human allergy.

The objective of immunotherapy is to administer increasing doses of allergen to a point where the patient’s immune system becomes “tolerant”. Moderating the immune response reduces the frequency and severity of hypersensitivity reactions.

Immunotherapy requires commitment and will not work for all patients, however, studies show a positive response to immunotherapy in 81% of pets with atopic dermatitis (Gonzalez, Yuste et al 2003), (Gonzalez et al 2004).

Immunotherapy is not a “quick-fix” for atopic disease; if successful, maintenance therapy is usually required for several years. In some cases immunotherapy may actually cure atopic disease, rather than promoting clinical remission.

Animals suffering from atopy may become sensitised to an increasing number of allergens over time and in some cases it may be necessary to repeat diagnostic procedures and review immunotherapy accordingly.

Immunotherapy using polymerised allergens

**allervet**® offers a novel approach to allergen specific immunotherapy using Vet-Goid, a polymerised allergen vaccine.

**How is Vet-Goid different from previous immunotherapies?**

Vet-Goid is a chemically and physically modified allergen preparation; it is glutaraldehyde polymerised and adjuvanted, benefiting from decreased allergenicity with enhanced immunogenicity. These properties allow it to overcome some of the major drawbacks associated with traditional immunotherapies.

**What are the problems associated with traditional immunotherapy?**

Two major drawbacks are the potential for immunotherapy to trigger a systemic allergic reaction including anaphylactic shock and the length of time it takes to achieve the maximum dose therefore a clinical response.

**How does polymerisation lead to decreased allergenicity?**

A type 1 hypersensitivity response is triggered when epitopes on the surface of an allergen cross link two molecules of IgE on the membrane of a sensitised mast cell.

A polymer comprising multiple allergens has a smaller surface area than the same number of allergen monomers, with fewer exposed epitopes which are able to cross link mast cell bound IgE.

In addition, the molecular weight and shape of the polymerised allergen results in cross linking of fewer IgE pairs on tissue mast cells than would occur with individual allergen monomers.

Finally, following subcutaneous injection, high molecular weight polymerised allergens diffuse more slowly towards sensitised mast cells than allergen monomers. Their progress is more likely to be interrupted by antigen processing and presenting cells (APCs) in the tissues, reducing their opportunity to react with sensitised mast cells.

These properties all contribute to decreased allergenicity and permit higher staring doses of immunotherapy and achievement of the maximal dose after just 1 week, which translates into a more rapid clinical response. There is no prolonged or complicated initial stage of treatment.
How is immunogenicity enhanced?
Allergens incorporated into immunotherapy vaccines diffuse from the site of injection, are detected and phagocytosed by surveillance APCs. APCs exposed to high doses of allergen release IL10 which in turn activates T reg cells. T reg cells dampen down the activity of allergen reactive Th2 cells, decreasing B cell IgE production, and initiate antigen switching to IgG class 4 antibodies. IgG4 antibodies are “blocking” antibodies which capture allergen, preventing mast cell activation. It is these changes which ultimately result in immune tolerance. The use of polymerised allergens provides a safe mechanism to quickly deliver the high concentrations of allergen required to initiate immune modification, resulting in a shorter time to clinical improvement.

Immunotherapy is available for the majority of the allergens in the environmental panels with the exception of flea, Malassezia, hay dust and grain mill dust.
Up to five allergens or allergen groups can be included; when patients are polysensitised those allergens which are most likely to be significant are selected [determined by allergenicity and prevalence].
Therapy using polymerised allergens (allergoids) has been shown to be safe and efficacious with an excellent or good clinical response in 78% of cases. Clinical improvement was observed more rapidly than with traditional immunotherapy. Mild reactions (increased pruritus) was observed following <1% of injections (Gonzalez, Bravo 2012).

Vet-Goid Summary:
- Decreased allergenicity, increased immunogenicity
- Safe and efficacious
- Requires an SIC rather than an STC
- Simple dosing schedule (see opposite)
- No complicated or prolonged initial treatment phase
- Cost effective

Dosage schedule:
- 0.2ml - Day 1
- 0.5ml - Day 7
- 0.5ml - Every month thereafter
Treatment options - food testing

Positive results are used to assist in selection of an appropriate diet for a food elimination trial. Such a trial should be conducted for a minimum of 6-8 weeks; if there is a good clinical response test ingredients from the previous diet are introduced gradually until the patient relapses at which point the elimination diet is used to “rescue” the patient. This strategy is the basis of an elimination/provocation diet. In reality few owners wish to challenge their animal if clinical signs have resolved and choose to feed an elimination, or limited antigen, diet long term.

Negative food serology does not rule out the possibility of an adverse food reaction in which either serum antibodies are not detectable, or the pathogenesis is non-immunological. It is still worth conducting a well controlled dietary trial to determine the likelihood of an adverse food reaction causing or contributing to the clinical presentation. With negative test results this could be a home prepared diet using novel proteins, following careful questioning of the owner regarding previous dietary history, or a commercial hypoallergenic or hydrolysed protein diet.

**allervet® Food Guidance List**

When canine and feline food panels are positive details of a selection of proprietary diets are provided with the results. These diets are, to the best of our knowledge, free from all of the ingredients (proteins) to which there are positive reactions. Diets appropriate for life stage, and treats are included when suitable.

**Food guidance list example:** Lady Penelope, a 3yo F/N DSH tested positive for IgE and IgG to white fish and corn; based on these results the following diets would be suitable for a dietary trial:

<table>
<thead>
<tr>
<th>Diet</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dechra Specific FDW Food Allergy Management</td>
<td>Wet</td>
</tr>
<tr>
<td>Dechra Specific FODHY Allergy Management Plus</td>
<td>Dry</td>
</tr>
<tr>
<td>Hills Pet Nutrition d/d Venison Formula</td>
<td>Wet</td>
</tr>
<tr>
<td>Hills Pet Nutrition d/d Venison &amp; Green Pea</td>
<td>Dry</td>
</tr>
<tr>
<td>Hills Pet Nutrition z/d Low Allergen</td>
<td>Dry</td>
</tr>
<tr>
<td>Purina HA Hypo Allergenic</td>
<td>Dry</td>
</tr>
<tr>
<td>Royal Canin Hypoallergenic DR 25</td>
<td>Dry</td>
</tr>
<tr>
<td>Royal Canin Sensitivity Control Chicken with Rice</td>
<td>Wet Pouch</td>
</tr>
<tr>
<td>Royal Canin Sensitivity Control S/O Duck with Rice</td>
<td>Alutray Tray</td>
</tr>
<tr>
<td>Royal Canin Sensitivity Control S/O Chicken with Rice</td>
<td>Alutray Tray</td>
</tr>
</tbody>
</table>

The **food guidance list** aims to indicate a broad selection of suitable, proprietary diets but is obviously not exhaustive. It remains the responsibility of the submitting veterinary surgeon to check the suitability of any suggested diet or product prior to its use.
References


Caro Vadillo, A.; Rodriguez, J.L. (2002) Identifying specific IgE when exposed to environmental allergens: a complementary test for the diagnosis of feline asthma. AMAC.


Olivery T., Saridomichelakis M. and for the International Committee on Atopic Dermatitis. (2013) Evidence-based guidelines for anti-allergic drug withdrawal times before allergen-specific intradermal and IgE serological tests in dogs. ECEIM.


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If you would like more information regarding any aspect of allergy testing please contact the laboratory.