

Allergy Testing and Immunotherapy

Atopic dermatitis and other allergy-related diseases can be among the most difficult and at times frustrating problems seen in veterinary medicine. Some studies suggest that atopy occurs in about 10% of the canine population making it the second most common hypersensitivity disorder after Flea Allergic Dermatitis FAD.

Atopy, allergic inhalant dermatitis, or atopic disease is an inherited predisposition to the development of antibodies to environmental allergens resulting in allergic disease

The most common causes of atopic dermatitis are inhaled or percutaneously absorbed allergens including weed, grass and tree pollens; moulds; house dust or house dust mites; animal dander as well as many other miscellaneous allergens. It is very common to have multiple causes and this must be taken into consideration when undertaking diagnostic testing and subsequent treatment. Animals will frequently have multiple allergies – FAD and food hypersensitivity as well as atopic disease.

Pathogenesis can involve an inherited predisposition to develop immediate hypersensitivity reactions to antigens during which a skin-sensitising antibody IgE becomes fixed to tissue mast cells. Subsequent specific antigen exposure couples with the sensitised mast cells causing degranulation and release of inflammatory mediators (histamine, enzymes, etc). With alterations in cell mediated immunity comes the likelihood of secondary conditions developing. In the dog the absorption of allergens predominantly occurs via the skin leading to the typical distribution pattern in this species. Allergens are presented to T-lymphocytes in the regional lymph nodes and cause subsequent activation of B-lymphocytes to produce IgE. In unaffected animals there is a suppressive effect of subsets of T-cells and other factors which keep the immune response within reasonable boundaries. This is thought to be depressed in atopic animals. The *threshold for pruritus* depends on the individual animal and can be influenced by other factors – nutrition, infection, systemic disease, etc. Breed predilections have been found in many studies with Labrador Retrievers, Golden Retrievers, West Highland White Terriers, Cocker Spaniels and German Shepherd Dogs consistently being present as the most common breeds affected. This does not rule out other pure breeds and cross breeds having allergic disease.

The **diagnosis** of atopy must be made after a full clinical examination and detailed history with the exclusion of other causes of skin disease, often involving multiple diagnostic tests. Allergy testing only identifies the potential offending allergens; it *DOES NOT* make the diagnosis.

Clinical signs:

commonly first seen in young **dogs** and **cats** between the ages of 6 months and 3 years.

- acute or chronic, localised or generalised
- appropriate distribution – in dogs - periorbitally, on feet, ear pinnae, flank, perineum, ventral abdomen, axillae.
 - in cats - the face, neck and pinnae are most affected
- most lesions occur secondary to pruritus with varying amounts of crusting, papules and pustules
- acute – erythema and oedema of skin and ears
- chronic- thickening of skin, hyperpigmentation, lichenification, pyoderma, malassezia infection
- alopecia is variable
- otitis externa may be the only manifestation of atopy
- other clinical signs may include rhinitis, asthma and gastrointestinal problems
- atopic cats can exhibit self induced often symmetrical alopecia without any skin lesions or eosinophilic granuloma complex
- cats may also have peripheral lymphadenopathy

In **horses** signs can also be very variable

- equine insect hypersensitivity (also known as sweet itch, summer seasonal recurrent dermatitis) is an immune-mediated hypersensitivity to the saliva of *Culicoides* spp. midges and is the most common cause of summer pruritus. There is a strong seasonal relationship with the occurrence of *Culicoides* midges. The

condition occurs only from late spring to late autumn and usually resolves in colder weather. The hypersensitivity appears to take some time to develop with horses rarely affected until 4-5 years of age and then showing progressive deterioration over time. Some breeds appear to be predisposed, for example pony breeds including the Welsh pony and the Icelandic pony, and the Shire horse, suggesting a possible genetic basis.

- Allergic airway disease, urticaria or hives. These allergic diseases of equines appear to be common, with many of the same causal allergens as for cats and dogs with others more specific to their environment. Again this may be a familial problem in horses. Recurrent airway obstruction (RAO) or chronic obstructive pulmonary disease (COPD) is a common condition of horses characterized by small airway inflammation and obstruction following exposure of susceptible horses to moldy hay and straw.

Allergic disease confirmatory testing

Currently there are two methods of confirmatory testing to identify the allergens after a diagnosis of allergic disease – *in vivo* intradermal skin testing and *in vitro* serum IgE tests which measure allergen specific IgE. Synthesis of IgE after exposure to allergen is the instigator of the allergic process. While IgE exerts its effect after binding strongly to mast cell Fc receptors, the presence of free IgE in the serum can be used to quantify and determine the allergen specificity of the allergic disease.

Intradermal skin testing measures the ability of injected allergen to bind to allergen-specific immunoglobulin on the surface of mast cells and to cause actual mast cell degranulation.

- tests the skin's reaction to an injected allergen
- requires a lot of attention to detail with extensive patient preparation and usually a referral
- is time consuming,
- costly to perform on an individual basis
- can be affected by previous use of steroids and anti histamines
- existing skin conditions can interfere with the procedure
- is a subjective assessment and therefore requires skill to perform
- can produce false negatives

Although intradermal testing with allergen is a useful diagnostic tool for some species, skin testing frequently produces false positive results in horses.

Serum antibody testing:

- requires little patient preparation
- simple blood testing in the surgery
- occasional false positives
- standardised procedure
- not influenced by existing dermatological conditions
- not influenced by existing medication
- presence of antibody does not prove allergic disease

Management of animals with atopic disease includes the avoidance of allergens where possible, using topical or systemic medications, immunotherapy (or desensitisation/hyposensitisation) and also treating any concurrent conditions.

Taking into account the "allergic threshold" above which the animal cannot tolerate any further exposure without showing signs of disease, careful attention must be paid to other combined stresses which may

cause this threshold to be breached - for example infection, nutritional state, environment, parasites as well as increased allergen loading. Once all of these precipitating factors are removed as far as possible, it is often medication in some form which is required to control the remaining clinical symptoms. It is at this point that immunotherapy (or desensitisation) can be a consideration to avoid prolonged use of steroids.

Immunotherapy/desensitisation is defined as the practice of administering gradually increasing quantities of an allergen extract to an allergic subject to ameliorate the symptoms associated with the subsequent exposure to the causative allergen.

In

essence the allergens are given by subcutaneous injection in increasing doses up to a maintenance dose, which can vary in individual patients.

Immunotherapy "down regulates" the allergic response and is beneficial in a high proportion of cases requiring on average 4 – 12 months for the effects to be seen.

Recent research has shown that there is a balance of activity in two types of white blood cell (Th1 and Th2 lymphocytes) with over-activity of the Th2 type causing the symptoms of allergic disease. Immunotherapy is thought to either stimulate the Th1 cells, and/or reduce the activity of the Th2 cells. There is considerable on-going research in this area which will undoubtedly lead to a better understanding and treatment of allergic disease.

In order to get the most benefit from the use of immunotherapy it is very important to:

- choose the best candidates
- be specific in the choice of allergens
- pay particular attention to any other aggravating factors involved, for example concurrent infections
- instruct owners carefully in the procedure and time this method of treatment will take

Some animals will improve in a few weeks, but mostly it takes several months before the effects are known. Careful monitoring and reassessment is necessary during initial treatment to allow for adjustments in the injection protocol if required. If the therapy proves helpful it will need to be maintained for life. Not all animals will have a response which will relieve all the symptoms - some will have alleviation which allows for lower levels of steroids or antihistamines rather than complete cessation of treatment. Cases where there is no improvement should be re-evaluated for a missed alternative diagnosis. It must always be taken into account that it is not possible to test for every existing allergen in the environment, and therefore it is possible that some which are having a significant effect in an individual animal may be missed.

Advantages of immunotherapy:

- low frequency of administration
- low risk of long term side effects
- possibility of altering the course of the disease
- more cost effective than symptomatic therapy
- reduction or cessation in the need for steroid administration

Disadvantages:

- initial high cost of therapy
- repeated injections may need to be made in surgery
- poor patient compliance to repeated injections
- very low risk of anaphylaxis

Efficacy of the treatment varies with the studies performed but general results suggest approximately 75% of cases treated show good response with either no further need for steroids or reduced need. The age of commencement, severity of clinical signs, duration of clinical signs, breed and type of allergens involved all have a bearing on the success of immunotherapy.

Concurrent therapy: both glucocorticoids and cyclosporin have multiple effects on the immune system and their concurrent use should be avoided wherever possible. However it may be necessary in some severe cases to continue their use at a very reduced dose to keep the animal comfortable, but allowing for a longer period of time for the full effects of the therapy to be appreciated.

Adverse Reactions to Food

These can be divided broadly into

food intolerance – clinical symptoms due to the ingestion of food with or without an immune response
food allergy - clinical symptoms due to a hypersensitivity reaction from an ingested protein
metabolic intolerance – enzymatic deficiency, for example lactose intolerance, pancreatic insufficiency

These reactions may begin at an early age and are more frequently seen in young animals but can develop at any age. Injured mucosa or defects in local immunity allows for the penetration of antigens across the G I mucosa and an increased immunoglobulin (mostly IgE) synthesis which on subsequent exposure induces degranulation of mast cells.

Symptoms of food allergy include:

- pruritus
- erythema
- bilateral otitis
- pododermatitis
- recurrent pyoderma
- (gastro intestinal symptoms)
- secondary manifestations of concurrent infection as with atopy
- cats may have peripheral lymphadenopathy and eosinophilia

Food trials and selective dietary avoidance are the only method of treatment available. The food trial can be started whilst awaiting the results of the blood sample with selective foods being individually reintroduced using the test results obtained for guidance.

Allergy Management Programme

Greendale Veterinary Diagnostics has an allergy management programme utilising techniques which have proved successful in more than 250,000 dogs, cats and equines since 1985. Our programme uses a company with ongoing commitment to research, development and quality control. Single allergen test panels and rigorous quality control measures maximise assay specificity.

We require 4 – 6 ml serum for testing – more if multiple panels are requested. Serum cannot be tested if haemolysed.

Steroid and anti-histamine therapy do not interfere with the test

Use our order form to select from the following options:

Canine/Feline

Inhalant screen – panel contains 54 tree, weed, grass, mould, mite and flea antigens.

Trees	Grasses	Weeds	Moulds/Other
Beech, American Box elder/maple mix Elm Mix Olive Pollen Pine Mix Cottonwood (Poplar) Birch Mix Cedar Mix Alder Mix Ash Mix Mulberry, White Walnut, Black Hazelnut Pollen Sycamore Mix Oak Mix	Bahia grass Rye/Fescue Bluegrass Timothy Orchard Grass Brome Grass Reed/Sweet vernal Johnson Grass Bermuda Grass	Ragweed tall/short English Plantain Lamb's Quarter Dandelion Russian Thistle Dock mix/Sheep Sorrel Goldenrod Pigweed mix Cocklebur Mugwort, Common Nettle Mustard Pollen Dog Fennel Daisy	Grass Smut Mix Aspergillus Mix Alternaria tenuis Cladosporium Penicillium, Mixed Rhizopus nigricans Fusarium Pullularia pullulans Helminthosporium Candida Cat Epithelia
	Mites Dust Mite Mix Acarus Siro T. putrescentiae Blomia tropicalis Flea		

Food screen – 21 food allergens commonly found in commercial pet foods. Results include diet recommendations from a database of available diets. We also have a 'Speciality' food panel.

Insect screen – 10 common household and stinging insects, including flea.

Indoor screen – 11 indoor environmental allergens, including carpet fibres, fabrics and epithelia.

Food Screen		
Traditional		Speciality
Chicken Lamb Beef Pork Egg Turkey Peanut Rabbit Fish mixed Milk/Cow's Yeast Corn Carrot	Barley Wheat Oats Beets Potato Soy Beans Sweet potato Rice	Apple Berry mix Duck Green pea Green bean Salmon Shellfish mixed Spinach Tomato Venison

Environment Screen - Indoor
Mouse epithelium Human epithelium Cat epithelium Dog epithelium Cotton lintens Jute Sheep Epithelia/Wool House Dust Pyrethrum Kapok Tobacco Leaf

Environmental Screen - Insects
Flea Mosquito Cockroach Mix Moth Housefly Fire Ant Yellow Jacket/Hornet Honey Bee Wasp Ant, Black

Equine

Panel contains approximately 70 allergens including weed, tree, grass, mould, mite, insect, Culicoides and feed ingredients.

Inhalant	Weeds	Other
<p>Trees</p> <p>Beech, American Box Elder/maple Mix Elm Mix Olive Pollen Pine Mix Cottonwood (Poplar) Birch Mix Cedar Mix Alder Mix Ash Mix Mulberry, White Walnut, black Hazelnut Pollen Sycamore Mix Oak Mix</p> <p>Grasses</p> <p>Rye/Fescue Bluegrass Timothy Orchard Grass Brome Grass Reed Canary Johnson Grass Bermuda Grass</p>	<p>Ragweed tall/short English Plantain Lamb's Quarter Dandelion Russian Thistle Dock mix/Sheep Sorrel Goldenrod Pigweed mix Cocklebur Mugwort, Common Nettle Mustard Pollen Dog Fennel Clover, red Alfalfa pollen Daisy</p> <p>Moulds</p> <p>Grass Smut Mix Aspergillus Mix Alternaria tenuis Cladosporium Penicillium, Mixed Rhizopus nigricans Fusarium Pullularia pullulans Helminthosporium Candida Cephalosporium Epicoccum Mucor Botyrtis cinera Aspergillus fumigatus</p>	<p>Cat epithelium Grain mill dust Mouse epithelia Flaxseed Pyrethrum Cockroach mix</p> <p>Environmental Screen – Insects</p> <p>Dust Mite Mix Acarus Siro T. putrescentiae Blomia tropicalis Culicoides Deer Fly Caddisfly Horsefly Ant, Black Mosquito Housefly Ant, fire Wasp Yellow jacket/hornet</p> <p>Food Screen</p> <p>Apple Oats Wheat Carrot Barley Molasses Beets Corns</p>

Equine food and insect screens can be ordered separately, or as part of the comprehensive Equine Allergy Screen

Culicoides can be tested on an individual basis, but frequently there will be multiple allergens involved which may be missed and subsequently affect the response to immunotherapy.

Please note:- allergens included in the panels are constantly under review and may change from those stated above

Results and interpretation

These are sent out in the form of 'scores' which enable veterinarians to make up individual treatment sets for immunotherapy. Competent advice is available if required on result interpretation, with regard to the animal's clinical history, to ensure the correct allergens are incorporated in the treatment sets. Greendale staff pride themselves in giving individual advice and guidance on all aspects of the interpretation and ordering of treatment sets to make the process as easy as possible. VMD authorisation is now required on all treatment sets and we have partially completed forms for your convenience. Full instructions on injection schedules are provided with each treatment set, and for the more challenging case special regimes can be produced upon discussion of patient response.

Please see our current brochure for a list of prices and contact the laboratory for any further information.

Recent Survey Results On The Response to Desensitisation

We have recently conducted a survey amongst our existing clients on the response, in their opinion, to the use of desensitisation. The replies have proved very encouraging and are detailed in the table below.

	Small Animal	Equine
Very good	17%	40%
Good	60%	47%
Acceptable/Promising	14%	6%
Variable	9%	7%