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TEN DIFFICULT CLINICAL CONCEPTS WHEN DEALING WITH THE ALLERGIC DOG

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IS THIS SCABIES OR ATOPIC DERMATITIS?

The clinical signs of scabies and atopic dermatitis should be distinguishable if dogs would only read the textbooks. The lesion distribution is usually the first clue in differentiating between them. The key differences are that atopic dermatitis affects predominantly the distal limbs and feet whereas scabies affects the elbows and hocks, and atopic dermatitis affects the medial pinna and external auditory meatus whereas scabies affects the outer edge of the pinna. However, cases occasionally arise in which one disease may mimic the other. Unfortunately, negative skin scrapings will not distinguish the two because the test is not 100% sensitive. If the clinician is still in doubt, blood can be submitted for detection of anti-scabies IgG. However, this test, although very good, is also not 100% sensitive or 100% specific. Trial therapy is the final method of ruling out scabies but clinicians should be aware that some cases of scabies have been resistant to selamectin therapy. If there is still any doubt, a second therapeutic trial should be initiated (lime sulfur, ivermectin, amitraz) before embarking on long term management of atopic dermatitis.

I SUSPECTED ATOPIC DERMATITIS BUT ALL THE ALLERGY TESTS WERE NEGATIVE

The diagnosis of atopic dermatitis is primarily based on the presence of a consistent history and clinical signs, and ruling out other pruritic skin diseases that could look similar. Allergy tests are primarily used to document allergens that could be used for treatment with allergen-specific immunotherapy. In some dogs, it is possible to make a clinical diagnosis of atopic dermatitis and yet have negative allergy tests, either with intradermal tests or in-vitro assay of allergen-specific IgE. There are two main possibilities as to why this may arise. The first is false negative reactions. In other words, allergy tests are not 100% sensitive. False negative reactions can occur due to technical reasons such as the allergens being out of date and no longer potent, the appropriate allergens not being tested for, or the allergens are too dilute. False negative reactions can also occur due to biological reasons such as the skin reactivity having been suppressed by prior therapy, or failing to detect serum IgE when the skin would have been hyper-reactive. The second possibility is that a state of "intrinsic" atopic dermatitis might exist in dogs as is thought to occur in humans. In this condition, there are no detectable changes in serum or skin-bound IgE, but all the other clinical signs are identical. In this case, the pathogenesis may involve other mechanisms such as direct damage to the epidermis and defective regulation of cellular function. When faced with a negative allergy test result in a classically atopic dog, the first step is to perform an alternative allergy test (if a skin test was performed, an in-vitro blood test should be performed and vice versa). If both tests prove to be negative, and there are no other possible diagnoses, the dog should be managed symptomatically for "intrinsic" atopic dermatitis with glucocorticoids, antihistamines, essential fatty acids, cyclosporine, topical therapy or some combination thereof.

I GOT A POSITIVE IGE BLOOD TEST BUT THE DOG RESPONDED TO PARASITICIDAL TREATMENT

In vitro allergy tests are not 100% specific. In other words, they can generate false positive results. A false positive result can occur in two ways. First, a "technical" false positive result can arise if the reagents in the assay are not specific and measure other things in addition to IgE. This type of false positive result is less likely with assays that use Fcε receptor technology. A "biological" false positive reaction occurs when elevated concentrations of allergen-specific IgE are genuinely detected in clinically normal dogs. This can occur with any in-vitro test, regardless of the reagents used, and merely indicates that demonstration of increased levels of allergen-specific serum IgE is not sufficient to distinguish between normal dogs and those with atopic dermatitis. Hence, clinicians should not rely on a positive blood test result to make a diagnosis of atopic dermatitis.

I GOT A POSITIVE INTRADERMAL SKIN TEST RESULT BUT THE DOG ENDED UP HAVING HYPOTHYROIDISM

Intradermal skin tests are not 100% specific and can give false positive results. False positive reactions may arise due to the presence of irritants in the testing solutions, or allergens that are too concentrated. Also, clinically irrelevant reactions can occur in dogs that have mast cell-bound IgE that leads to degranulation during skin testing but no signs of atopic dermatitis. This could indicate previous sensitisation without current exposure, a sub-clinical state of hypersensitivity, or the necessity of factors other than mast cell bound IgE to cause atopic dermatitis (such as defects in barrier function, abnormal mast cell function, mutations in IgE receptor subunits, up-regulated cytokine pathways, the presence of particular subtypes of IgE etc.). Such false positive or clinically irrelevant reactions have been demonstrated in studies on clinically normal dogs and indicate that the intradermal skin test cannot be used as a sole measure to distinguish between atopic and normal dogs. Hence, clinicians should not rely on a positive intradermal test result to make a diagnosis of atopic dermatitis. The history and clinical signs must be considered first and other diseases investigated and ruled out.

THE ALLERGY TESTS WERE POSITIVE BUT THE PRURITUS RESPONDS COMPLETELY TO ANTIBIOTICS AND THEN RELAPSES

There are two explanations for this phenomenon. The first is that the dog has sub-clinical atopic dermatitis that leads to secondary staphylococcal pyoderma. When the pyoderma is controlled, the dog is no longer pruritic but the underlying atopic disease leads to frequent relapses. The second explanation is that the allergy test results were clinically irrelevant and the pyoderma is either due to another underlying disease or is idiopathic. The distribution of the lesions is most important here. If the dog has lesions that fit with the distribution of atopic dermatitis (facial, ears, pedal, axillae, ventrum), then that is a more likely underlying cause. However, if the lesions are restricted to the trunk and there is no involvement of the head or extremities, atopic dermatitis is less likely. In the first scenario, management of the underlying atopic dermatitis may lead to control of the recurrent pyoderma. In the second scenario, other underlying causes should be investigated. If none can be found, long term management of the recurrent pyoderma

may be more appropriate (pulse antibiotic therapy, autogenous bacterins).

FALSE FOOD ALLERGIES

Many animals appear to show a response to restricted diets. Many also seem to get worse when fed their original diet. Unfortunately, this does not confirm a diagnosis of food allergy. Some of the pitfalls in interpreting food trials include:

OWNER COMPLIANCE: SOME OWNERS CANNOT ACTUALLY COMPLETE A FOOD TRIAL PROPERLY BUT INDICATE THAT THEY CAN. THEY MAY ALSO REPORT PLACEBO EFFECTS.

Failure to Re-Challenge: If the diet is not rechallenged, many false diagnoses of food allergy will be made.

Partial or Coincidental Responses: Partial responses to diet trials may occur in animals that have atopic dermatitis and food allergy at the same time, but can also occur when another disease undergoes spontaneous fluctuations in severity (waxing and waning).

Influence of Secondary Bacterial and Yeast Infections: A major problem encountered when assessing dietary trials is the development and control of secondary infections such as staphylococcal pyoderma and *Malassezia* dermatitis. These infections are common in dogs with cutaneous hypersensitivities and specific treatment for them is often prescribed at the same time as the restricted diet trial. When the animal returns for re-examination, there may have been a dramatic response and a significant or complete reduction in pruritus. It is critical when faced with this situation that the antimicrobial therapies are continued throughout the challenge phase of the diet trial. If they are not, it is likely that the secondary infections will recur and give the impression that the dog has relapsed on reintroduction of the normal diet, again leading to an erroneous diagnosis of food allergy.

Concurrent Anti-Pruritic Therapy: The use of anti-pruritic therapy such as glucocorticoids at the same time as the food trial can greatly complicate the assessment of the patient's progress. It is critical, therefore, that glucocorticoids are used only when absolutely necessary (for example, in dogs or cats that are so pruritic that they are self-mutilating themselves). In this case, the glucocorticoids must be given orally and for the shortest possible time (1-3 weeks). They must then be withdrawn completely so that the effects of the diet trial can be assessed.

I CAN SEE LOTS OF BACTERIA ON CYTOLOGY BUT NO NEUTROPHILS

The skin of dogs contains bacteria as part of the normal flora. However, the numbers are sufficiently low so as to be

only seen occasionally on cytology. Hence, when looking at stained tape strips, only sporadic bacteria can be seen adhering to the corneocytes. In some cases of pruritus, it is possible to find large numbers of bacterial colonies on stained tape strips in the absence of a neutrophilic response. This is usually referred to as bacterial overgrowth rather than infection. However, it is thought that these organisms might be clinically significant because they may be able to secrete irritant substances or allergens. Hence, if this cytological picture is seen, topical antibacterial therapy would be indicated, although systemic antibiotics would not be required.

I HAVE DIAGNOSED ATOPIC DERMATITIS BUT THE DOG ALSO HAS DEMODICOSIS

This poses considerable clinical problems. The demodicosis may pre-date or be concurrent to the atopic dermatitis, or it may have been caused by glucocorticoid therapy. In any case, further glucocorticoids should be avoided at all costs. Alternative methods of management should be found for the atopic dermatitis (immunotherapy, antihistamines, essential fatty acids, topical therapy or possibly cyclosporine). The demodicosis should be treated with either amitraz or daily ivermectin. If it is absolutely impossible to manage the dog without glucocorticoids, life-long maintenance therapy with amitraz or ivermectin may be required.

THIS LOOKS WEIRD

The vast majority of cases of pruritus are caused by parasites, infections or allergies. However, if it isn't any of these, or if it looks unusual compared to the cases seen every day, the following uncommon or rare skin diseases should be considered: epitheliotropic lymphoma, pemphigus foliaceus, intestinal parasite hypersensitivity, drug eruption, sterile eosinophilic pustulosis, syringo-hydromelia in Cavalier King Charles Spaniels, zinc-responsive dermatosis, acral mutilation syndrome, pseudorabies.

THE PRURITUS WON'T RESPOND TO ANY OF MY TREATMENTS

If an allergic dog fails to respond to anti-pruritic therapy, clinicians should first establish that the diagnosis is correct. Failure to respond could be due to the presence of a disease that doesn't normally respond to anti-pruritic medication. In particular, scabies, *Malassezia* dermatitis, food intolerance and the diseases listed under point 9 should be considered. If the dog genuinely has atopic dermatitis, the vast majority will respond to glucocorticoids and cyclosporine, some will respond to allergen-specific immunotherapy and a few will respond to antihistamines and essential fatty acids. If none of the above treatments work, clinicians can consider pentoxifylline, misoprostol, Chinese herbal therapy and in intractable cases, azathioprine.