

Equine atopic dermatitis and allergen specific immunotherapy

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Allergic skin diseases in horses are common and they present with pruritus, urticaria or both, along with secondary lesions including alopecia, scaling, crusting, change in pigment of the skin and lichenification. The most common causes are insect bites and environmental allergens (atopic dermatitis), and these can co-exist. There are no definitive diagnostic tests for insect bite hypersensitivity or atopic dermatitis and the diagnosis is based on history, consistent clinical signs and exclusion of other pruritic diseases.

Insect bite hypersensitivity (IBH) is an allergic response to the bites of blood-feeding insects, most commonly midges in the Culicoides family but also Simulium (blackfly), Stomoxidae (stable flies), Culicidae (mosquitoes) and Phlebotominae (sandflies). We are fortunate to not have Culicoides midges in New Zealand, but we do have other biting insects, including blackflies which we call sandflies. IBH is an important differential to be considered with a horse presenting with pruritus and/or urticaria. IBH has also been associated with respiratory disease, which may reflect that many IBH horses are also atopic and may manifest their atopic disease with both skin and respiratory disease. Commonly affected areas often reflect the feeding sites of the biting insect involved and the distribution can be dorsal, ventral or a combination of both. The face, ears, mane, tail, chest, ventral abdomen and legs are commonly affected. Clinical signs include pruritus, which can be severe leading to self-trauma, alopecia, excoriations, crusting and lichenification. Pruritic papular eruptions, urticaria, eosinophilic granulomas and airway disease may also be noted. Secondary skin infections are very common and can significantly contribute to the pruritus and therefore must be identified and managed. The diagnosis of IBH is a clinical diagnosis based on compatible history, clinical signs, exclusion of other causes of pruritus and a positive response to insect avoidance. Effective insect avoidance measures include a combination of environmental management, physical barriers and chemical repellents. Allergy testing (intradermal or serological) is not considered a diagnostic test as positive results can occur in normal horses. The results of allergy testing need to be interpreted in light of the clinical history and presentation. There is currently not enough evidence to recommend allergen specific immunotherapy as a mode of therapy for horses with IBH. Studies using recombinant allergens is ongoing, as are studies into cytokine vaccinations (IL-5 and IL-31) so we are hopeful that there will be more treatment options in the near future.

Atopic dermatitis (AD) is an abnormal immunological response to environmental airborne allergens. There are many gaps in our understanding of the pathogenesis of AD, particularly in horses. Extrapolating from what we know about the pathogenesis of AD in humans and dogs and from studies on IBH it is likely that in the initial stages of the disease there is a Th2 response and the production of allergen-specific IgE as a Type I hypersensitivity. The role of IgE has been demonstrated by serological and intradermal allergy testing and positive responses to allergen specific immunotherapy. The cytokine IL-31 has been confirmed to be an inducer of pruritus in horses, as it is in dogs and humans, and is being investigated as a target for therapy. The presence of skin barrier dysfunction is emerging as an important part of the disease in other species and by extrapolation it may be part of the atopic presentation in horses too, but specific studies are lacking.

AD is common and it can present with seasonal or non-seasonal signs depending on the allergens an individual is sensitised to. The pattern can change with time, with a horse initially presenting with seasonal signs becoming non-seasonal as the disease progresses or with a change in geographical location. The common presentations of AD are urticaria, urticaria with pruritus or pruritus alone. Secondary lesions are common and include alopecia, excoriations, and scaling. The commonly affected pruritic areas are the face, trunk and flexural surfaces.

Horses can also present with respiratory symptoms of equine asthma/equine allergic airway disease. Food allergy has been demonstrated to be a trigger for urticaria and is also possibly a trigger for atopic flares and pruritus, but it appears to be uncommon.

As for IBH the diagnosis of equine AD is based on compatible clinical history, the clinical presentation, and the exclusion of other causes of pruritus. Keeping in mind that AD and IBH often coexist. Allergy testing is not utilised as a diagnostic test as horses without AD can have positive results.

There are no specific guidelines for the management of equine atopic dermatitis. The treatment options are glucocorticoids, antihistamines, topical therapy, environmental management, essential fatty acids, and allergen specific immunotherapy.

Allergen specific immunotherapy should be considered for the safe and effective long-term management of atopic horses. It is usually considered when looking for an alternative to systemic glucocorticoids and antihistamines, often because of side effects, ineffectiveness, or when there is a need to withdraw medications prior to competition.

ASIT involves the administration of gradually increasing amounts of allergens to the horse either subcutaneously or sublingually. The goal of successful therapy is to provide clinical benefit with improvement of clinical signs by equal to or greater than 50% as well as reducing the requirement for medication by the same margin. This is done by inducing immune tolerance. The current understanding of how ASIT induces immune tolerance is that it promotes a shift from a Th2 response towards a Th1 and Regulatory T cell (Treg) response. Treg cells produce regulatory cytokines (e.g. IL-10, TGF- β and IL-35) and suppress Th2 cells, eosinophils, and basophils. These effects along with generation of blocking allergen-specific antibodies contribute to the development of allergen tolerance (Kucuksezer 2020).

Allergy testing is required first and there are two methods of allergy testing – an intradermal test or a serological test. The intradermal test measures cutaneous mast cell activity via surface bound allergen-specific IgE. The serological test measures allergen-specific IgE in serum. Intradermal testing is generally considered to be the gold standard, but interpretation of the test takes considerable experience to become confident in. Intradermal testing does have several advantages including testing the allergic pathway in the affected organ, testing for a larger panel of allergens and immediate results. However, when travel or access to a dermatologist is not possible then testing with IgE serology is a valid option and the tests available have improved considerably in their accuracy and reliability. Importantly, from the information we have to date, the response of the patient to ASIT does not appear to be related to the allergy test utilised (Gershwin 2015). The main factors influencing successful response to ASIT are a correct diagnosis, regular monitoring and experienced clinical multi-modal management.

Allergy test results are correlated with the clinical history including seasonality of symptoms, allergenicity of positive allergens, exposure to allergens and considering cross-reactivity between allergens. The number of allergens included in an ASIT formulation is not standardised but is generally between 10–14.

ASIT is not a quick fix, and it does take several months before a response is noted – at least 3–4 months and out to 12–18 months. Immunotherapy is often required to be given for the duration of a patient's lifetime, or at least several years, although there is some evidence that unlike dogs, horses that have had a positive response to ASIT are more likely to remain in remission after cessation of therapy (Stepnik 2012).

When starting ASIT there is an induction phase until the maintenance dose is reached, which is then continued long term. The injections are administered every second day for 25 days, every 10 days for 30 days and then every 2–4 weeks ongoing. The maximum injection volume given is 1ml and the allergens for injection are in an aqueous base and need to be refrigerated. The expected maintenance injection frequency is every 2–4 weeks, but this may need to be adjusted depending on the individual's response. Oral immunotherapy is formulated in a glycerine base and is administered via a pump-action dropper. The dose is given under the tongue or into the cheek pouch once daily for one week, then twice daily as maintenance.

There have been two recent publications which have helped with our understanding and management of equine allergic diseases. The first is the Clinical consensus guidelines of the World Association for Veterinary Dermatology on equine allergic skin diseases (Marsella 2022) and the other is a comprehensive review spanning studies over 40 years of the efficacy and safety of ASIT in horses (Herrmann 2023). These publications have reviewed the available evidence, and the results show a beneficial response to ASIT in 75% of horses with allergic respiratory disease, 88% with urticaria and 59–70% with atopic dermatitis.

The most common adverse events reported are local reactions with wheals, swelling and pruritus at the site of injection (Herrmann 2023). Most are mild reactions and self-limiting but should prompt a review of the allergen schedule. Systemic signs consistent with IgE-mediated reactions are rare (Herrmann 2023) but can be serious, including anaphylaxis, and these potential risks need to be discussed with owners prior to starting to ensure that any signs are detected early and promptly managed.

Patient and client selection and compliance is essential to the success of ASIT, and allergy testing should only be performed in allergic horses where the owner understands and is committed to pursuing immunotherapy for at least 12 months. ASIT is the only therapy for atopic dermatitis and equine asthma with the potential to prevent progression of the disease and should be considered as an important part of the long-term management, especially in horses where options for anti-allergy medications are so limited.

References

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