TITLE: Long-term management of horses with atopic dermatitis in southeastern England: a retrospective questionnaire study of owners' perceptions

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Long-term management of horses with atopic dermatitis in the South East of England: owners' perceptions

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Abstract

Background – Allergic pruritus and urticaria in the horse are challenging for veterinarians and owners, and little is known about their long-term management.

Objectives – To summarise intradermal allergen test results (IDT), and to assess owners' perceptions of skin disease and of effects of medical treatment and management changes in their atopic horses over time.

Animals – Eighty-two horses with atopic dermatitis in the xxx referred for IDT between 2006 and 2011.

Methods – IDT results were retrospectively reviewed. Owners completed telephone questionnaires on skin changes, medication, effect of allergen-specific immunotherapy (ASIT) and management.

Results- Sixty-one owners (74.4%) could be contacted, an average of 5.9 years (range 28-88 months) after IDT; of those, three could not be enrolled. Of the 58 remaining horses, eleven (19%) were deceased at time of owner interview, including four (6.9%) euthanised due to uncontrollable skin disease. The remaining 47 owners reported that signs of skin disease had not been seen for at least two years in 18 horses (38.3%), including two that only flared with known triggers. Twenty-nine horses (61.7%) still required medication to control skin disease although 25 (53.2%) required less since referral. Owners reported benefit from ASIT in 9/14 horses (64.3%), from glucocorticoids in 33/35 (94.3%) and from antihistamines in 17/28 (60.7%). Specific management changes were implemented for 22 horses and reported as beneficial in 9/22 (40.9%).

Conclusions- Equine atopic dermatitis may not always be chronic but severe cases appear difficult to control. IDT helps to formulate ASIT and can guide management changes.

Introduction

The management of pruritus and urticaria due to allergic skin disease in the horse is challenging for veterinary surgeons and owners, and little is known about the long-term treatment requirements and progression of disease over time.

In the horse, atopic dermatitis, as a hypersensitivity reaction to environmental allergens and food, presents with pruritus or urticaria or both.[1-8] It is typically described as a lifelong condition requiring ongoing treatment interventions, but signs may be seasonal or perennial, depending on the causal allergens.[9] Allergens commonly implicated in many reports include house dust and storage mites, insects, pollens and epithelia.[6] As for other veterinary species, the diagnosis of equine atopic dermatitis is a clinical diagnosis based on compatible history, clinical signs and exclusion of other differential diagnoses such as ectoparasite infestations, *Culicoides* hypersensitivity and other insect bite hypersensitivities (IBH), and if possible adverse food reactions.

Management strategies include allergen avoidance, topical therapy, and systemic medications such as antihistamines, glucocorticoids and tricyclic antidepressants.[9] Dust and moulds can be found in high concentrations in various feeds and bedding materials[10] and implementation of allergen reduction measures has been shown to be beneficial in some equine patients with recurrent airway disease[11,12] and in 18 of 19 horses with non-summer seasonal and perennial pruritus with or without urticaria.[13] Many topical therapies are likely used but there is little published evidence regarding their use or efficacy. Hydrocortisone aceponate spray (Cortavance, Virbac Limited, Bury St Edmunds, UK) has been found to be useful anecdotally, did not seem to result in detectable levels of drug in the blood[14] and may only have a weak skin-thinning effect compared to other glucocorticoids.[15] There are few data regarding the efficacy of antihistamines in the management of equine allergic skin disease. Antihistamines used in horses include hydroxyzine and diphenhydramine, with anecdotal reports of greater benefit in urticaria than pruritus;[9] cetirizine was shown to be ineffective in the management of IBH.[16] Systemic glucocorticoids are often required in horses with atopic dermatitis to control pruritus and limit self-trauma. Injectable or oral dexamethasone and oral prednisolone are the most commonly recommended, with long-term therapy aiming at lowest necessary doses given on alternate days.[9]

For allergen-specific immunotherapy (ASIT), allergen-specific IgE can be detected by intradermal testing (IDT) and serological methods.[3,7,17-21] However, results from IDT, considered to be the gold standard test, and from serological tests correlated poorly or not at all in two equine studies.[17,20] Positive IDT reactions may occur in normal horses, but atopic horses show more numerous and stronger positive reactions.[3,22] A few studies have evaluated the efficacy of ASIT in equine atopic dermatitis. Most authors report a 60-71% good to excellent response to ASIT based on the results of intradermal testing,[1,4,8,23] but higher response rates have also been described. In one study, 13 of 15 horses with urticaria showed an excellent response to immunotherapy after one year.[24] In a placebo-controlled study of 28 horses with insect and environmental hypersensitivities, 64% of the horses treated with ASIT showed a 50% or greater improvement compared to 23% with placebo,[25] but more recently an overall response rate of 84%, as perceived by the owners, was reported in a large retrospective study.[8] However, of those where glucocorticoids could be discontinued,

59% were well controlled with ASIT as the sole treatment and 9% of the partial responders needed doxepin in addition to ASIT. In 44% of cases, ASIT was discontinued due to resolution of clinical signs, with two thirds of these reporting no recurrence of disease, but recurrence of clinical signs occurred within 1-12 years of stopping ASIT in the remaining one third.

The aims of this study were to investigate the progression of atopic dermatitis in horses after IDT and to summarise their IDT results. Owners' perceptions and reports on their horses' skin disease, on medical treatment utilised and on effects of management changes over time were investigated through telephone questionnaires.

Methods

The study had been approved by the Royal Veterinary College Ethics and Welfare committee (R349).

Study population

Horses with suspected atopic dermatitis which had been referred for intradermal testing to one of two dermatology referral centres in the South East of England between 2006 and 2011 were enrolled. Patients had been diagnosed initially with allergic skin disease by their referring veterinary surgeon. At referral, allergic dermatitis was confirmed clinically based on a history and presenting signs of pruritus and/or urticaria after ectoparasite infestations and microbial infections had been ruled out. Dermatological examination was performed combined with microscopic examination of skin scrapings, coat brushings and/or with anti-ectoparasite therapy, cytological examination of lesions, and fungal or bacterial culture or antimicrobial therapy when indicated. Insect-bite hypersensitivities were ruled out by confirming non-summer seasonal or perennial disease from the medical records. Food hypersensitivity was discussed with every owner and elimination diet trials recommended but IDT was performed irrespectively, based on suspected atopic dermatitis.

Information on signalment (age, sex, breed or type), cutaneous signs relevant for referral for IDT (pruritus, urticaria, both, seasonality), previous therapy including response (glucocorticoids, antihistamines) and elimination diet trials was collected from electronic or paper medical histories as far as available.

Intradermal testing

All horses were tested using procedures as previously described[6] against allergens considered relevant for allergic skin disease in Europe such as environmental mites, epithelia including feathers, and pollens (grasses, weeds and flowers, trees). In addition, allergen solutions of insects, fungi, grain crop pollens, house dust and grain mill dust and smut were included when available. Allergen test kits varied minimally in their composition over the six-year duration of the study due to availability of allergen solutions and between referral centres. Allergens used were recorded for each horse from the medical records. Allergen solutions had been sourced over time from one of two manufacturers (Greer Laboratories, Lenoir, North Carolina, U.S.A. or ArtuVet, Lelystad, Netherlands) with concentrations and dilutions available in the supplementary table (Supplementary table S1).

Reactions were considered positive if the diameter of the wheal was greater than the mean of the positive and negative controls measured at 30 minutes. Wheal sizes

were assessed at 30 minutes and 2-4 hours (considered immediate and late-phase IgE-mediated reactions). Additional observations were made at 12-24 hours to assess delayed reactions. ASIT was offered for all horses showing positive reactions to allergens suitable for inclusion (indoor allergens, epithelia, pollens) but not for horses only showing reactions to fungi and insects.

Management changes were recommended for all horses, depending on groups of allergens implicated by IDT (indoor allergens and dusts, epithelia, pollens, insects), to reduce exposure (Supplementary tables S1, S2). At Veterinary Dermatology Referrals, specific changes recommended included use of rubber matting in stables with minimal or no loose bedding, feeding of vacuum-packed, wilted grass products to replace hay and feeding of pelleted concentrate foods stored for only short periods in original packaging, frequent rug laundering and quarterly pressure cleaning of stables, removal of bird nests and use of selective weed killer, if relevant.

Owner recruitment

Owners were telephoned between September 2013 and March 2014 and asked for their participation in a telephone questionnaire study on their horse's skin disease, medication, effect of allergen-specific immunotherapy (ASIT) and implementation of management changes since IDT. Owners were called from known telephone numbers (number not withheld by the caller) by the same investigator (DH) up to three times if there was no reply and no answering machine and up to two messages were left on answering machines before the case was excluded due to failed contact. Owners of horses who were known to be dead since IDT were not contacted. For horses reported deceased by their owner during the telephone contact, the cause of death was recorded, but they were not asked to complete the questionnaire.

Questionnaires

Questions were divided into three broad topics. Firstly, owners were asked to assess their horse's skin problem at the time of the telephone questionnaire and at the time of IDT. They were asked to describe skin signs as pruritic, urticarial, both or other, whether changes in type or distribution of problems had been observed since IDT and whether other skin problems had been diagnosed by their veterinarian since IDT. Owners were asked to assess the severity of itching and/or urticaria on analogue scales of 0-10 (0 for normal/never and 10 for severe/present all the time).

Secondly, questions on medication and other treatments, specifically glucocorticoids, antihistamines, ASIT, antidepressants, nutritional supplements and washes, were asked. Sub-questions for each treatment were whether the horse had ever received it, was currently receiving it and how frequently (seasonally, throughout the year), whether the treatment was tolerated and whether the owner thought the treatment had improved skin problems.

Thirdly, owners were asked about their horses' current management and on implementation of management changes recommended at time of IDT (Supplementary information S2), including whether they had changed barn or paddock, where the horse spent most of its time, type of bedding used, rugging (type, time spent wearing rugs and frequency of laundering), clipping (frequency and extent) and ectoparasite and fly control measures. For each question, owners were asked whether they considered those changes beneficial to their horse's skin problem.

An option to answer ‘unsure’ or ‘unknown’ was included where appropriate. The questionnaire was trialled in six pilot calls and adjusted based on feedback. Each questionnaire was estimated to take 20 minutes including a short introduction outlining the study purpose, confidentiality provisions and the option to decline. At the end of the questionnaires, owners were offered contact details of investigators.

Data analysis

Microsoft Excel (Microsoft, version 15.38, 2017) was used for data collection and analysis.

Results

Enrolled horses and owners

Eighty-two horses had undergone IDT for suspected atopic dermatitis during the study period, 15 from the RVC, 67 from Veterinary Dermatology Referrals (original starting population). Ages at time of IDT ranged between one and 25 years (mean 9.9 years). There were 40 mares, 40 geldings, one stallion and one horse of unknown sex. Breeds or types varied, with 23 recorded as cob or pony, mostly Welsh cob, 21 as thoroughbred including thoroughbred crosses, 7 Irish sports horses, 8 warmbloods and 23 other types. Pruritus was the presenting complaint in 36 horses (43.9%), urticaria in 34 horses (41.5%) and 12 (14.6%) presented with both. In most horses (67/82, 81.7%), lesions were reported as generalised. Of the 15 horses with localised lesions, eight showed signs only on the trunk, six on the head and one on the legs. All animals suffered from skin disease during the winter months but 19 (23.2%) showed seasonal flares during spring or summer.

Owners of 61 (74.4%) horses were contacted by telephone. For the remainder, either contact details were not available or attempts to make contact as described above had failed. One owner declined participation and two could not provide answers as the horses had been sold soon after IDT. The time between IDT and telephone questionnaire for the 58 horses ranged between 28 and 88 months (mean 71 months or 5.9 years).

At the time of telephone contact, eleven of the 58 (19.0%) horses were reported dead, including four (6.9%) euthanised due to uncontrollable skin disease (three with pruritus, one with urticaria). One had died a spontaneous death of unconfirmed cause, five had been euthanised for known diagnoses (brain tumour, lymphoma, colic, lameness (investigated and confirmed as non-laminitic), kissing spines) and one horse for old age-related reasons.

Intradermal tests

The average number of allergens each horse was tested against was 54.2 (standard deviation (SD) 10) and the average number of positive reactions per horse was 13 (SD 8.1). Two horses had shown no positive wheal and flare reactions to any of the allergens despite strong histamine injection reaction. The allergens tested in at least 50 horses and which resulted in positive reactions in at least 25% of horses are listed in Table 1. Most (1247, 96.1%) of the 1297 positive reactions recorded in total occurred at the early readings considered compatible with immediate and late-phase hypersensitivity reactions. At the later time points, compatible with delayed reactions, 122 (9.4%) positive reactions were recorded, 72 at sites of earlier readings, 50

(3.9%), distributed over all allergen groups, that had not been recorded at earlier time points.

Skin disease - owner assessment

Of the 47 horses for which follow up information was available, (14 RVC, 33 Veterinary Dermatology Referrals), owners considered their horse's skin disease at the time of telephone contact as resolved without medication in 18 cases (38.3%), as improved with treatment in 25 cases (53.2%) and as unchanged or worse despite medication in four cases (8.5%). Six of the 18 horses that no longer had skin problems at the time of telephone contact had been lesion-free since the time of IDT while another ten had not had skin disease for at least the previous two years. Four of these horses had had management changes implemented after IDT (see below) and two further horses only showed skin disease after known triggers (cereal-based food or treats, shavings). The remaining 29 horses were still receiving either glucocorticoids or antihistamines throughout the year or at least three times a year during flares. Six owners reported that their horses had been diagnosed with pituitary pars intermedia dysfunction since IDT and that new, different skin lesions had developed (crusting papules, urticaria in previously pruritic horses and vice versa).

Owners' assessment of pruritus, irrespective of medication or management used, on a 1-10 scale gave a median of 9 (range 3-10) at the time of IDT and of 1.5 (range 0-6) at the time of telephone contact. Median scores for the frequency of urticaria flares were 8 (range 2-10) at the time of IDT and 2 (range 0-7) at telephone contact.

Medication and immunotherapy - owner assessment

Systemic glucocorticoids had been used in 35/47 horses (74.5%) to control skin disease since IDT, including seven still receiving treatment at the time of telephone contact. Good response to glucocorticoid therapy was reported in 94.3% of horses (33/35) after IDT. Adverse effects of glucocorticoid therapy were reported by owners in 7/35 (20%) including laminitis in one heavy draft horse (which according to the medical records was recorded as a foot abscess and without further mention of laminitis in the medical records during the subsequent two years), two horses with flares of pre-existing laminitis, and one each with drowsiness, weight gain, or behaviour changes.

Twelve owners reported using topical glucocorticoid preparations (hydrocortisone aceponate spray (Cortavance): n=6, fusidic acid/bethamethasone combination (Fuciderm, now Isaderm, Dechra Veterinary Products, Shrewsbury, UK): n=4, unknown human eczema cream: n=1), and all but one owner observed a beneficial effect when the product was applied at least daily.

Twenty-eight horses (59.6%) had received antihistamines (type unknown) at some stage since IDT to control their cutaneous signs and good response was reported in 17 of these 28 horses (60.7%). Eight horses were still maintained on antihistamines as the sole medication at the time of telephone contact. Drowsiness was the only adverse effect reported in three horses.

ASIT had been ordered for 27 horses (57.5%) but its use was only reported by owners of 14/47 horses (29.8%) with nine owners of these 14 horses (64.3%) reporting a beneficial effect including eight reporting a 75-100% improvement. In only three horses was immunotherapy continued beyond the first prescribed

immunotherapy vial of at least nine months; in one of them antihistamines were given concurrently throughout. A further two horses were restarted on ASIT when clinical signs relapsed after immunotherapy had been discontinued following completion of injections with the initial vial. Restarting ASIT was perceived as helpful again in both cases. The remaining nine horses no longer received ASIT at the time of telephone contact. Six owners stated they thought they had finished the treatment after the initial vial (typically nine months), including three in which treatment was thought to have had no effect. Another two owners stopped ASIT before completing the initial vial due to lack of effect and one owner stated expense as the reason for stopping. Twelve owners reported administering the maintenance injections themselves (injections by the veterinarian as default administration type). No systemic adverse effects were reported, localised injection site reactions were seen by owners in 6/14 horses (42.9%) on individual occasions, none persisted or required veterinary attention.

Fly prevention was used in 22 (46.8%) horses regularly during the spring and summer. In total, 38 horses (82.1%) were receiving or had received other agents with the aim to control their skin disease since IDT. These included systemic antimicrobial therapy (n=1), shampoo therapy used at least weekly (n=18) with seven owners using chlorhexidine-based products, and 11 using products of unknown composition but with claims of alleviating allergic skin signs (and 12/38 owners (31.6%) perceiving a beneficial effect). Skin-related, non-prescription food supplements (various, unknown) had been given by 30 owners (65.2%) without adverse effects reported.

Management changes

Twenty-two owners (46.8%) had implemented recommended changes to stables, bedding, feed or rugs, and nine of those (40.9%) reported a perceived subsequent improvement in their horse's skin disease, including four horses for which no additional medication had been needed since. Skin disease was reported to have improved in three horses after they had been relocated to a different yard, in another three following dietary changes (treats removed from diet), one horse improved when shavings were removed from its stable, and in the remaining two horses multiple changes had been made concurrently.

Almost all horses (45, 97.8%) were reported to wear rugs at some time during the year with 34 wearing the rug all day during the cooler months. Thirty-five of 47 (74.5%) horses were regularly clipped.

Discussion

This is the first study to report on the management of atopic horses over time, and a reporting interval greater than two years was available for all. While information derived from owner interviews was collected retrospectively and is inevitably associated with a high degree of subjectivity, it still provides a realistic insight into the burden of allergic skin disease on horses and their owners, and may help to stimulate future research and improvements in clinical management. In addition, questionnaire data were collected during the colder months of the year in the UK which may have biased reporting. However, in the UK, clinical signs and onset of atopic dermatitis in the horse have been reported throughout the year,[2] and including onset and exacerbation in autumn, suggesting that the impact of seasonality may be less relevant.

The data on clinical signs and IDT results collected from medical records were broadly in line with similar previously published work,[8,16] including one study in the South of England.[6] Positive reactions to house dust mites, storage mites and insects predominated, likely reflecting exposure to such allergens through a largely stabled lifestyle and management, including frequent use of house dust mite-harbouring rugs,[26] and exposure to biting insects when at pasture.

Results from this study on disease outcome at least two years after referral were highly surprising, firstly with regard to the substantial proportion of horses for which owners reported that skin disease had resolved and treatment had not been required for at least two years and secondly, with regard to the number of deceased horses.

These findings challenge the widely accepted anecdotal belief that atopic dermatitis in the horse is chronic and requires lifelong treatment.[5,7,9] Unfortunately, our data do not allow conclusions to be made on duration of disease before resolution in these horses, and so predictions cannot be made on how long signs might persist in horses with potentially transient presentations. However, the results suggest that, at least in some horses, the prognosis for atopic dermatitis can be excellent and they further corroborate previous advice that it is best to perform allergen tests if the disease is recurrent or persistent for more than six to eight weeks.[27] Whether resolution of skin signs without medication was spontaneous or due to management changes, which were perceived to help by almost half of the owners, remains unknown. The role of allergen load rather than exposure is less clear for atopic dermatitis compared to respiratory lower airway disease in the horse.[28] However, in the absence of such data, the benign nature of recommendations on management changes warrant inclusion in the management plan for every atopic horse presented for IDT.

In contrast, the finding that 19% of horses were dead at the time of telephone interview, including 7% (four horses) where owners reported that the animals had been euthanised due to uncontrollable skin disease, is concerning. While research on the pathomechanisms and treatment options on allergic diseases has progressed substantially over the past decades, the social implications of chronic allergic diseases are only slowly starting to receive attention. Initial results of a survey on health-related quality of life in atopic dogs and on quality of life in their owners showed that the disease had a deeply negative impact on both measures but only 1% of owners stated they had contemplated euthanasia.[29] In addition, treatment was considered a major financial burden by a third of dog owners and 40% stated that they had to limit other expenses as a consequence. The questionnaire in our study was not designed to further explore reasons for euthanasia but the results are likely to reflect some degree of welfare concerns, implications on the use of a horse with skin disease and the financial burden associated with chronic skin disease. Other horse-specific factors may also have played a role and need to be investigated further.

Of the 29 horses for which management of skin disease was still required after IDT, different combinations of antihistamines, glucocorticoids, ASIT and management changes were reported to achieve acceptable levels of control with tolerable adverse effects for most patients and owners. Results on drug efficacy need to be interpreted with care as these were based on owner impressions over time rather than on veterinary assessment following a defined intervention period. However, the high frequencies of beneficial effects reported for glucocorticoids (94.3%), mainly as oral

prednisolone, and for antihistamines (60.7%) provide some assurance on treatment effect. To date, despite their wide use, only review articles describe the use of both medications in the treatment of allergic skin disease in horses and provide some pharmacokinetic information and dose recommendations.[9,23] Further study is needed on which therapies or combinations help atopic horses most and if there is a difference in response to therapies between pruritic and urticarial horses which was not the focus of this study. Slightly more information is available on the use of glucocorticoids for non-infectious lower airway disease where inflammation is thought to contribute to clinical signs.[28] Concerns over glucocorticoid use as a risk factor in the development of laminitis are widespread, but the scientific basis for this association is sparse, at least for non-predisposed horses.[30-32] Results from two recent studies seem to show that such a link may have been overestimated,[33,34] but due to the critical consequences of laminitis, further research is still needed. In light of the relatively high number of atopic horses in this study which were euthanised due to uncontrolled disease, and none due to laminitis caused by glucocorticoid therapy, concerns over the potential risk of laminitis need to be balanced against welfare considerations due to uncontrolled atopic dermatitis. In the authors' opinion, glucocorticoids have an important role to play in the management of atopic horses, and prednisolone at low doses given on alternate days to horses not predisposed to laminitis would be a recommended strategy.[9]
The benefit of ASIT reported in 64% of horses in this study was lower than the 84% owner-reported efficacy from a recent North American study on 41 horses receiving ASIT,[8] but comparable to those found by Rosenkrantz *et al*. in horses.[25] However, the low uptake of ASIT following IDT in this study was surprising and disappointing. Reasons for not starting or at least not pursuing therapy were not explored as these findings had been unexpected. Measures have been taken since to extend discussion with owners and strengthen recommendations towards ASIT.

While "much folklore still remains in respect of certain equine skin diseases" as stated in 1970 by the late L.R. Thomsett,[35] the results from this study on long-term management of allergic horses from an owner perspective indicate that atopic dermatitis may have a better prognosis than in other companion animals and may not always be chronic. Still of concern though, the high number of euthanised horses in this study suggests that severe cases may be difficult to control and that the burden of chronic skin disease for owners should not be underestimated. Management changes, following identification of relevant allergens by IDT, in combination with medication and sometimes ASIT, may help provide effective control of clinical signs.

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Tables

Table 1. Allergens tested in at least 50 of the 82 horses and resulting in positive reactions in 25% or more of horses

Allergen	No. of positive reactions / horses tested	% Positive	Kit (Greer Laboratories or Artu Biologicals)
Dermatophagoides farinae (farina mite)	76/85	89.4	Both
Dermatophagoides pteronyssinus (house dust mite)	74/85	87.1	Both
Moth	55/65	84.6	Greer
Aedes communis (mosquito)	45/65	69.2	Greer
Tyrophagus putrescentiae (copra mite)	53/78	68.0	Both
Tabanid (horse fly)	43/65	66.2	Greer
Lepidoglyphus destructor (hay mite)	52/84	61.9	Both
Acarus siro (flour mite)	51/85	60.0	Both
Grain mill dust	39/65	60.0	Greer
Culicoides (midge)	34/64	53.1	Greer
Trifolium pratense (red clover)	43/84	51.2	Both
Grain mill smut	33/65	50.8	Greer
Mixed feathers (chicken, goose, duck)	42/84	50.0	Both
Urtica dioica (stinging nettle)	32/64	50.0	Greer
Cockroach, German	29/65	44.62	Greer
Avena sativa (cultivated oat)	21/55	38.18	Greer
Leucanthemum vulgare (daisy)	31/84	36.90	Both
Rumex crispus (yellow dock)	23/64	35.94	Greer
Soldiago virgaurea (golden rod)	30/84	35.71	Both
Taraxacum officinale (common dandelion)	22/62	35.48	Both
Sheep epithelia	22/63	34.92	Greer
Salix viminalis (pussy / black willow)	22/64	34.38	Greer
Aspergillus fumigatus	22/64	34.38	Greer
Artemisia vulgaris (common mugwort)	23/84	27.38	Both
Rhizopus nigricans	14/55	25.45	Greer

Note: House dust and black ant also showed reactions in 71.5% and 70%, respectively, but were only tested in 14 and in 30 horses, respectively.

513 S1: Supplementary table 1: Allergen solutions and dilutions used for intradermal
514 testing of horses during the study period

	Allergen	Dilutions Greer from 20.000 PNU stock solutions up to 2008	Dilutions Greer from 20.000 PNU stock solutions from 2008	Dilution Artu
Controls	Histamine phosphate	1:10000 w/v	1:10000 w/v	0.1 mg/ml
	Saline	n/a	n/a	n/a
Indoor allergens and dusts	*Dermatophagoides farina* (farina mite)	1:10	1:10	100 NU/ml
	D. pteronyssinus (house dust mite)	1:1000 w/v	1:1000 w/v	100 NU/ml
	Acarus siro (flour mite)	1:20	1:20	100 NU/ml
	Tyrophagus putrescentiae (copra mite)	1:20	1:20	100 NU/ml
	Lepidoglyphus destructor (hay mite)	1:20	1:20	100 NU/ml
	Euroglyphus maynai	n/i	n/i	100 NU/ml
	House dust	1:20	n/i	n/i
	Grain mill dust	1:20	1:20	n/i
	Grain mill smut	1:1000 w/v	1:1000 w/v	n/i
Epithelia	Horse dander	n/i	1:20	n/i
	Dog epithelium	n/i		100 µg/ml
	Mouse dander	n/i	1:20	
	Cat dander (*Felis domesticus*)	1:20	1:20	100 µg/ml
	Mixed feathers (chicken, goose, duck)	1:20	1:20	
	Duck feathers (*Anas platyrhynca*)	n/i	n/i	100 µg/ml
	Goose feathers (*Anas anser*)	n/i	n/i	100 µg/ml
	Chicken feathers (*Pullus gallinaceus*)	n/i	n/i	100 µg/ml
	Sheep epithelia	1:20	1:20	
	Epithelial mix 1 (guinea pig, dog, cat, hamster, rabbit)	n/i	n/i	100 µg/ml
Grass pollens	Kentucky blue (meadow) grass (*Poa pratensis*)	1:20	1:20	1000 NU/m
	Red top (bent grass, *Agrotis gigantean*)	1:20	1:20	1000 NU/m
	Couch grass	1:20	1:20	n/i
	Orchard grass (cocksfoot, *Dactylis glomerata*)	1:20	1:20	1000 NU/m
	Sweet vernal (*Anthoxanthum odoratum*)	1:20	1:20	1000 NU/m
	Velvet grass (Yorkshire fog, *Holcus lanatus*)	1:20	1:20	1000 NU/m
	Timothy (*Pheleum pratense*)	1:20	1:20	1000 NU/m
	Meadow fescue (*Festuca pratensis*)	1:20	1:20	1000 NU/m
	Perennial rye grass (*Lolium perenne*)	1:20	1:20	1000 NU/m
	Couch grass	1:20	1:20	n/i
	Brome grass	1:20	n/i	n/i
	Avena sativa (cultivated oat)	n/i	n/i	1000 NU/m
	Bermuda grass (*Cynodon dactylon*)	n/i	n/i	1000 NU/m
	Grass pollen mixture (Bermuda, orchard, sweet vernal, Timothy, velvet)	n/i	n/i	1000 NU/m
Weed pollens	Sheep sorrel (*Rumex acetosella*)	1:20	1:20	1000 NU/m
	Ragweed (*Ambrosia elatior*)	n/i	1:20	1000 NU/m
	Golden rod (*Soldiago virgaurea*)	n/i	1:20	1000 NU/m
	Yellow dock (*Rumex crispus*)	1:20	1:20	n/i
	Common dandelion (*Taraxacum officinale*)	1:20	1:20	1000 NU/m
	Red clover (*Trifolium pratense*)	1:20	1:20	1000 NU/m
	Common mugwort (*Artemisia vulgaris*)	1:20	1:20	1000 NU/m
	Daisy (*Leucanthemum vulgare*)	1:20	1:20	1000 NU/m
	Stinging nettle (*Urtica diodica*)	1:20	1:20	
	English plantain (*Plantago laceolata*)	1:20	1:20	1000 NU/m

	Lamb's quarter (*Chenopodium album*)	1:20	1:20	1000 NU/m
	Weed pollen mixture 1 (mugwort and nettle)	n/i	n/i	1000 NU/m
	Weed pollen mixture 2 (mugwort, nettle, dandelion, plantain)	n/i	n/i	1000 NU/m
Tree pollens	Alder (*Sambucus nigra*)	n/i	1:20	1000 NU/m
	American elm	n/i	1:20	n/i
	Red oak	1:20	1:20	n/i
	Black/pussy willow *(Salix viminalis)*	n/i	1:20	n/i
	American beech (*Fagus sylvatica*)	1:20	1:20	1000 NU/m
	Eastern sycamore (*Plantanus occidentalis*)	1:20	1:20	1000 NU/m
	White poplar	1:20	1:20	n/i
	White ash	1:20	1:20	n/i
	American hazelnut (*Corylus avellana*)	n/i	1:20	1000 NU/m
	White birch (*Betule pendula*)	1:20	1:20	1000 NU/m
	Horse chestnut (Buckeye, *Aesculus hippocastanum*)	n/i	n/i	1000 NU/m
	Hawthorn (*Crataegus*)	n/i	n/i	1000 NU/m
	Linden (*Tilia cordata*)	n/i	n/i	1000 NU/m
	Tree pollen mix 1 (birch, alder, hazel)	n/i	n/i	1000 NU/m
	Tree pollen mix 2 (English oak, European beech, American elm)	n/i	n/i	1000 NU/m
Moulds & fungi	*Aspergillus fumigatus*	1:20	1:20	n/i
	Aureobasidium pullulans	1:20	1:20	n/i
	Alternaria alternata	1:20	1:20	n/i
	Phoma beta	1:20	1:20	n/i
	Penicillium notatum	1:20	1:20	n/i
	Cladosporium herbarium	1:20	1:20	n/i
	Fusarium moniliforme	1:20	1:20	n/i
	Mucor racemosus	1:20	1:20	n/i
	Rhizopus nigricans	1:20	1:20	n/i
	Trichoderma spp.	1:20	1:20	n/i
	Malassezia pachydermatis	1:20	1:20	n/i
	Fungus mixture 1 (*Alternaria alternate, Aspergillus fumigatus, Cladosporium herbarum*)	n/i	n/i	100 ng/ml
Insects	Flea (*Ctenocephalides* spp.)	1:1000 w/v	1:10	1000 NU/m
	Cockroach, German	n/i	1:20	n/i
	Horse fly (*Tabanus* spp.)	1:20	1:20	n/i
	Moth	1:40	1:40	n/i
	Aedes communis (mosquito)	1:20	1:20	n/i
	Culicoides (midge)	1:5	1:5	n/i
	Culicoides (midge)	1:10	1:10	n/i
	House fly	1:20	n/i	n/i
	Black ant	1:20	n/i	n/i

515 n/i: not included. NU: nitrogen unit

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518 Supplementary table 2: Suggestions on management changes provided to horse
519 owners to reduce exposure to environmental mites in atopic horses. Owners were
520 informed that recommendations were based on anecdote rather than evidence for
521 efficacy and that measures should be tailored to each horse depending on practicality
522 and intradermal test result

Stable	Foodstuff	Rugs	Other
Replace loose bedding with rubber matting	Storage in clean, sealed containers	Avoid excessive rugging	Maintain horse at pasture for extended periods
Quarterly vacuuming and pressure hosing of stable walls, ceiling, floor	Replace hay with wilted, vacuum-packed grass products	Launder rugs frequently at high temperatures or freeze for 2-3 days after laundry	Use of broad-leaf weed-killer
Reduce exposure to birds and poultry (remove nests before eggs are laid)	Replace loose with cubed concentrate	Add human anti-allergy duvets (in polycotton cover) between skin and rugs to provide a barrier to dust mite allergens	Insect prophylaxis with frequent applications of permethrin-containing products as per data sheet or manufacturer's recommendations

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