RVC OPEN ACCESS REPOSITORY - COPYRIGHT NOTICE

This author's accepted manuscript may be used for non-commercial purposes in accordance with Wiley Terms and Conditions for Self-Archiving.

The full details of the published version of the article are as follows:

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

AUTHORS: Loeffler, A; Errick, D; Allen, S; Littlewood, J D

JOURNAL: Veterinary Dermatology

PUBLISHER: Wiley

PUBLICATION DATE: 3 September 2018 (online)

DOI: http://dx.doi.org/10.1111/vde.12685



1 Long-term management of horses with atopic dermatitis in

the South East of England: owners' perceptions

- 3 Anette Loeffler*, Desiree Herrick*, Serena Allen*, Janet D. Littlewood†
- 4 *Department of Clinical Science and Services, Royal Veterinary College, Hawkshead
- 5 Lane, North Mymms, Hertfordshire, AL9 7TA, UK
- 6 †Veterinary Dermatology Referrals, 2 Waterbeach Road, Landbeach, Cambridge,
- 7 CB25 9FA, UK
- 8 Current address for:
- 9 *Desiree Herrick: Unit 1A Old Market Retail Park, High Street, Pitsea, Basildon,
- 10 Essex, SS13 3BY
- *Serena Allen: Haven Veterinary Practice, 35 Holland Road, Clacton-on-Sea, Essex,
- 12 CO15 6EH

13

- 14 Corresponding author: Anette Loeffler, Royal Veterinary College, Hawkshead
- 15 Lane, North Mymms, Hertfordshire, AL9 7TA, UK. Tel. +44 1707 666333, fax: +44
- 16 1707 666298. Email: aloeffler@rvc.ac.uk

17

- 18 Conflicts of interest: None
- 19 Sources of funding: Self-funded
- 20 **Running title:** Management of equine atopic dermatitis
- 21 **Acknowledgements:** The authors thank owners of horses for their willingness to be
- 22 involved in this study and their veterinary surgeons for referring the cases
- 23 An abstract with data from this study was presented at ESVD/ECVD congress in
- 24 Salzburg, Austria, 2014.

25

26

27

- 30 **Abstract**
- 31 **Background –** Allergic pruritus and urticaria in the horse are challenging for
- veterinarians and owners, and little is known about their long-term management.
- 33 **Objectives –** To summarise intradermal allergen test results (IDT), and to assess
- owners' perceptions of skin disease and of effects of medical treatment and
- 35 management changes in their atopic horses over time.
- 36 **Animals** Eighty-two horses with atopic dermatitis in the xxx referred for IDT
- 37 between 2006 and 2011.
- 38 **Methods –** IDT results were retrospectively reviewed. Owners completed telephone
- 39 questionnaires on skin changes, medication, effect of allergen-specific
- 40 immunotherapy (ASIT) and management.
- 41 **Results-** Sixty-one owners (74.4%) could be contacted, an average of 5.9 years
- 42 (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
- 47 horses (61.7%) still required medication to control skin disease although 25 (53.2%)
- 48 required less since referral. Owners reported benefit from ASIT in 9/14 horses
- 49 (64.3%), from glucocorticoids in 33/35 (94.3%) and from antihistamines in 17/28
- 50 (60.7%). Specific management changes were implemented for 22 horses and
- reported as beneficial in 9/22 (40.9%).
- 52 **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
- 54 changes.

Introduction

- The management of pruritus and urticaria due to allergic skin disease in the horse is
- 57 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,
- 64 pollens and epithelia. 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*
- 67 hypersensitivity and other insect bite hypersensitivities (IBH), and if possible adverse
- 68 food reactions.
- 69 Management strategies include allergen avoidance, topical therapy, and systemic
- 70 medications such as antihistamines, glucocorticoids and tricyclic antidepressants.⁹
- 71 Dust and moulds can be found in high concentrations in various feeds and bedding
- materials¹⁰ 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
- 74 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
- 76 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
- 79 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; 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.
- 85 Injectable or oral dexamethasone and oral prednisolone are the most commonly
- recommended, with long-term therapy aiming at lowest necessary doses given on
- 87 alternate days.9
- 88 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,
- 90 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
- 93 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
- 95 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
- 97 after one year.²⁴ In a placebo-controlled study of 28 horses with insect and
- 98 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,

- 102 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

111

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

114 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,
- 123 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
- 126 hypersensitivity was discussed with every owner and elimination diet trials
- recommended but IDT was performed irrespectively, based on suspected atopic
- 128 dermatitis.

133

- 129 Information on signalment (age, sex, breed or type), cutaneous signs relevant for
- referral for IDT (pruritus, urticaria, both, seasonality), previous therapy including
- 131 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 described⁶ 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
- 138 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
- 143 ArtuVet, Lelystad, Netherlands) with concentrations and dilutions available in the
- supplementary table (Supplementary table S1).
- 145 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
- 148 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
- 155 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

160

171

- 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

- 172 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).
- 179 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
- 184 had improved skin problems.
- Thirdly, owners were asked about their horses' current management and on
- implementation of management changes recommended at time of IDT
- 187 (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
- 190 extent) and ectoparasite and fly control measures. For each question, owners were
- 191 asked whether they considered those changes beneficial to their horse's skin
- 192 problem.

- An option to answer 'unsure' or 'unknown' was included where appropriate. The
- 194 questionnaire was trialled in six pilot calls and adjusted based on feedback. Each
- 195 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.

198 Data analysis

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

201202

Results

Enrolled horses and owners

- 203 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
- 206 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
- 210 (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
- 214 (23.2%) showed seasonal flares during spring or summer.
- Owners of 61 (74.4%) horses were contacted by telephone. For the remainder, either
- 216 contact details were not available or attempts to make contact as described above
- 217 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
- 219 questionnaire for the 58 horses ranged between 28 and 88 months (mean 71 months
- 220 or 5.9 years).

227

- 221 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
- 223 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
- 230 (SD 8.1). Two horses had shown no positive wheal and flare reactions to any of the
- 231 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
- 235 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

237 (3.9%), distributed over all allergen groups, that had not been recorded at earlier time

238 points.

239

258

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

245 problems at the time of telephone contact had been lesion-free since the time of IDT

246 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)

248 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

250 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-

256 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

259 Systemic glucocorticoids had been used in 35/47 horses (74.5%) to control skin

260 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

262 (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

264 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

266 flares of pre-existing laminitis, and one each with drowsiness, weight gain, or

267 behaviour changes.

268 Twelve owners reported using topical glucocorticoid preparations (hydrocortisone

aceponate spray (Cortavance): n=6, fusidic acid/bethamethasone combination

270 (Fuciderm, now Isaderm, Dechra Veterinary Products, Shrewsbury, UK): n=4,

271 unknown human eczema cream: n=1), and all but one owner observed a beneficial

effect when the product was applied at least daily.

273 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

275 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

277 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

282 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 283 284 signs relapsed after immunotherapy had been discontinued following completion of injections with the initial vial. Restarting ASIT was perceived as helpful again in both 285 cases. The remaining nine horses no longer received ASIT at the time of telephone 286 287 contact. Six owners stated they thought they had finished the treatment after the 288 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 289 vial due to lack of effect and one owner stated expense as the reason for stopping. 290 291 Twelve owners reported administering the maintenance injections themselves (injections by the veterinarian as default administration type). No systemic adverse 292 293 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 294 295 attention.

296 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 297 the aim to control their skin disease since IDT. These included systemic antimicrobial 298 therapy (n=1), shampoo therapy used at least weekly (n=18) with seven owners 299 300 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 301 302 a beneficial effect). Skin-related, non-prescription food supplements (various, unknown) had been given by 30 owners (65.2%) without adverse effects reported. 303

Management changes

304

316

Twenty-two owners (46.8%) had implemented recommended changes to stables. 305 306 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 307 additional medication had been needed since. Skin disease was reported to have 308 improved in three horses after they had been relocated to a different yard, in another 309 three following dietary changes (treats removed from diet), one horse improved when 310 311 shavings were removed from its stable, and in the remaining two horses multiple changes had been made concurrently. 312

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 317 reporting interval greater than two years was available for all. While information 318 319 derived from owner interviews was collected retrospectively and is inevitably 320 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 321 322 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 323 324 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 325 exacerbation in autumn, suggesting that the impact of seasonality may be less 326 327 relevant.

- 328 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
- 330 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
- 332 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.
- 338 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
- 348 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
- 358 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 guestionnaire 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
- 365 skin disease and the financial burden associated with chronic skin disease. Other
- 366 horse-specific factors may also have played a role and need to be investigated
- 367 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 375 effect. To date, despite their wide use, only review articles describe the use of both 376 377 medications in the treatment of allergic skin disease in horses and provide some pharmacokinetic information and dose recommendations. 9,23 Further study is needed 378 on which therapies or combinations help atopic horses most and if there is a 379 380 difference in response to therapies between pruritic and urticarial horses which was 381 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 382 to contribute to clinical signs. 28 Concerns over glucocorticoid use as a risk factor in 383 384 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 385 recent studies seem to show that such a link may have been overestimated. 33,34 but 386 due to the critical consequences of laminitis, further research is still needed. In light 387 388 of the relatively high number of atopic horses in this study which were euthanised 389 due to uncontrolled disease, and none due to laminitis caused by glucocorticoid therapy, concerns over the potential risk of laminitis need to be balanced 390 against welfare considerations due to uncontrolled atopic dermatitis. In the authors' 391 392 opinion, glucocorticoids have an important role to play in the management of atopic 393 horses, and prednisolone at low doses given on alternate days to horses not predisposed to laminitis would be a recommended strategy.9 394 395 The benefit of ASIT reported in 64% of horses in this study was lower than the 84% 396 owner-reported efficacy from a recent North American study on 41 horses receiving 397 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. 398 399 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 400 401 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.

402

403

404 405

406

407

408

409

References

411

- Fadok VA. Overview of equine pruritus. *Vet Clin North Am Equine Pract* 1995; 11:
 1-10.
- Littlewood JD, Paterson S, Shaw SC. Atopy-like skin disease in the horse. In: Kwochka KW, Willemse T, von Tscharner C, eds. *Advances in Veterinary Dermatology 3*. Butterworth Heinemann 1998; 563-564.
- Lorch G, Hillier A, Kwochka KW *et al.* Results of intradermal tests in horses without atopy and horses with atopic dermatitis or recurrent urticaria. *Am J Vet Res* 2001a; 62: 1051-1059.
- 420 4. Rees CA. Response to immunotherapy in six related horses with urticaria secondary to atopy. *J Am Vet Med Assoc* 2001; 218: 753-755.
- White SD. Advances in equine atopic dermatitis, serologic and intradermal allergy testing. *Clinical Techniques in Equine Practice* 2005; 4: 311-313.
- 6. Rendle DI, Durham AE, Wylie CE *et al.* Results of intradermal testing for the investigation of atopic dermatitis and recurrent urticaria in 50 horses in the south of England. *Equine Vet Educ* 2010; 22: 616-622.
- 7. Scott DW, Miller WH. Skin immune system and allergic skin disease. In: Merchant T, ed. *Equine Dermatology*, 2nd edition. St. Louis: Saunders Elsevier; 2011: 263-311.
- 430 8. Stepnik CT, Outerbridge CA, White SD *et al.* Equine atopic skin disease and 431 response to allergen-specific immunotherapy: a retrospective study at the 432 University of California-Davis (1991-2008). *Vet Dermatol* 2011; 23: 29-35.
- 433 9. Rosenkrantz W, White S. Equine atopic disease symptomatic therapy and allergen-specific immunotherapy. In: Noli C, Foster A, Rosenkrantz W, eds. *Veterinary Allergy*. 1st edition. Chichester: Wiley Blackwell, 2014; 360-370.
- 436 10. Vandenput S, Istasse L, Nicks B *et al.* Airborne dust and aeroallergen
 437 concentrations in different sources of feed and bedding for horses. *Vet Q* 1997;
 438 19: 154-158.
- 439 11. Woods PSA, Robinson NE, Swanson MC *et al.* Airborne dust and aeroallergen 440 concentration in a horse stable under two different management systems. *Equine* 441 *Vet J* 1993; 25: 208-213.
- Jackson CA, Berney C, Jefcoat AM *et al*. Environment and prednisone
 interactions in the treatment of recurrent airway obstruction (heaves). *Equine Vet* J 2000; 32: 432-438.
- Littlewood JD. Incidence of recurrent seasonal pruritus ('sweet itch') in British and German shire horses. *Vet Rec* 1998b; 142: 66-67.
- 14. De Pater M, van Ree M, Sloet van Oldruitenborgh-Oosterbaan M. Topical hydrocortisone aceponate spray in the horse: unauthorised medication?
 Proceedings of the European Veterinary Conference-Voorjaarsdagen, 2009, Amsterdam, Netherlands. 4.
- 451 15. Kietzmann M, Kemmet, S. Skin thinning effects of topically administered glucocorticoids in dogs and horses. *Vet Dermatol* 2012; 32 (Suppl 1): 42.
- 453 16. Olsén L, Bondesson U, Broström H *et al.* Pharmacokinetics and effects of cetirizine in horses with insect bite hypersensitivity. *Vet J* 2011; 187: 347-351.
- Lorch G, Hillier A, Kwochka KW *et al.* Comparison of immediate intradermal test reactivity with serum IgE quantitation by use of a radioallergosorbent test and two ELISA in horses with and without atopy. *J Am Vet Med Assoc* 2001; 218: 1314-1322.

18. Lebis C, Bourdeau P, Marzin-Keller F. Intradermal skin tests in equine dermatology: a study of 83 horses. *Equine Vet J* 2002; 34: 666-672.

465

466 467

- 462 19. Kalina WV, Pettigrew HD, Gershwin LJ. IgE ELISA using antisera derived from
 463 epsilon chain antigenic peptides detects allergen-specific IgE in allergic horses.
 464 *Vet Immunol Immunopathol* 2003; 92: 137-147.
 - 20. Morgan EE, Miller WH, Wagner B. A comparison of intradermal testing and detection of allergen-specific immunoglobulin E in serum by enzyme-linked immunosorbent assay in horses with skin hypersensitivity. *Vet Immunol Immunopathol* 2007; 120: 160-167.
- 469 21. Peterson A, Schott HD. Effects of dexamethasone and hydroxyzine treatment on intradermal testing and allergen-specific IgE serum testing results in horses. *Vet Dermatol* 2009; 20: 615-622.
- 472 22. Evans AG, Paradis, MR, O'Callaghan M. Intradermal testing of horses with
 473 chronic obstructive pulmonary disease and recurrent urticaria. *Am J Vet Res* 474 1992; 53: 203-208.
- 475 23. Marsella R. Equine Allergy Therapy: Update on the treatment of environmental, 476 insect bite hypersensitivity, and food allergies. *Vet Clin Equine* 2013; 29:551-557.
- Tallarico NJ, Tallarico CM. Results of intradermal allergy testing and treatment by
 hyposensitization of 64 horses with chronic obstructive pulmonary disease,
 urticaria, headshaking, and/or reactive airway disease. *Vet Allergy Clin Immunol* 1998; 6: 25-35.
- Rosenkrantz WS, Griffin CE, Esh RE *et al.* Responses in horses to intradermal challenge of insects and environmental allergens with specific immunotherapy. In:
 Kwochka KW, Willemse T, von Tscharner C, eds. *Advances in Veterinary Dermatology 3.* Butterworth Heinemann, 1998; 192-200.
- 485 26. Wallace JC, Vogelnest LJ. Evaluation of the presence of house dust mites in horse rugs. *Vet Dermatol* 2010; 21: 602-607.
- 487 27. Fadok VA. Of horses and men: urticaria. Vet Dermatol 1990; 1: 103-112.
- 28. Couëtil LL, Cardwell JM, Gerber V *et al.* Inflammatory airway disease of horses--Revised Consensus Statement. *J Vet Intern Med* 2016; 30: 503-515.
- 490 29. Linek M, Favrot C. Impact of canine atopic dermatitis on the health-related quality of life of affected dogs and quality of life of their owners. *Vet Dermatol* 2010; 21: 456-462.
- 493 30. Eyre P, Elmes PJ, Strickland S. Corticosteroid-potentiated vascular responses of 494 the equine digit: a possible pharmacologic basis for laminitis. *Am J Vet Res* 1979; 495 40: 135-138.
- 496 31. Johnson PJ, Slight SH, Ganjam VK *et al.* Glucocorticoids and laminitis in the horse. Review. *Vet Clin North Am Equine Pract* 2002; 18: 219-236.
- 498 32. Bailey SR, Elliott J. The corticosteroid laminitis story: 2. Science of if, when and how. Review. *Equine Vet J* 2007; 39: 7-11.
- Jordan VJ, Ireland JL, Rendle DI. Does oral prednisolone treatment increase the incidence of acute laminitis? *Equine Vet J* 2017; 49: 19-25.
- 502 34. Welsh CE, Duz M, Parkin TDH *et al.* Disease and pharmacologic risk factors for 503 first and subsequent episodes of equine laminitis: A cohort study of free-text 504 electronic medical records. *Prev Vet Med* 2017; 136: 11-18.
- 505 35. Thomsett LR. Differential diagnosis of skin diseases of the horse. *Equine Vet J* 1970: 2: 46-51.

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 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 Artı
Controls	Histamine phosphate	1:10000 w/v	1:10000 w/v	0.1 mg/ml
	Saline	n/a	n/a	n/a
Indoor	Dermatophagoides farina (farina mite)	1:10	1:10	100 NU/ml
allergens and dusts	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	v	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 (<i>Anas platyrhynca</i>)	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	Kentucky blue (meadow) grass (<i>Poa pratensis</i>)	1:20	1:20	1000 NU/m
pollens	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
1	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	Sheep sorrel (Rumex acetosella)	1:20	1:20	1000 NU/m
pollens	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
	• ,	1:20		1000 NU/m
	Daisy (Leucanthemum vulgare)	1.20	1.20	1000 110/111
	Daisy (Leucanthemum vulgare) Stinging nettle (Urtica diodica)	1:20	1:20 1:20	1000 110/111

	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 &	Aspergillus fumigatus	1:20	1:20	n/i
fungi	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

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

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