

Equine urticaria: a clinical guide to management



Alison Diesel

Alison Diesel is a veterinary dermatologist in the Department of Small Animal Clinical Sciences in the College of Veterinary Medicine and Biomedical Sciences at Texas A&M University, USA. She graduated from Kansas State University College of Veterinary Medicine in 2005 and went on to pass the American College of Veterinary Dermatology (ACVD) Certifying Examination in 2010. She is a diplomate of the ACVD.

Urticaria (hives) is a fairly common clinical reaction pattern in horses. Although often attributed to allergic causes, several other aetiologies can lead to the manifestation of the condition. A thorough and complete history, specifically as it relates to dermatological disease, is the practitioner's most powerful tool in successful diagnosis and management. Advanced diagnostics such as allergen-specific immunoglobulin E serum or intradermal allergen tests are only helpful when an allergic aetiology has been confirmed based on appropriate history. This article discusses the various causes and appearances of urticaria in the horse, and aims to help guide the practitioner in determining when additional diagnostics and therapeutics are indicated.

OWNERS often consult practitioners about horses with urticaria (hives). Other than people, the horse appears to be the species most at risk for development of hives as part of a common skin reaction pattern. Although not always detrimental towards the health or comfort of the animal, urticaria can be frustrating to manage for both the client and the veterinarian. Management is crucial as persistent urticaria can negatively impact the horse's ability to perform in the show or work arena. As with other dermatological abnormalities, a complete, accurate and thorough history is the practitioner's most powerful tool for determining an underlying cause for hives and developing an appropriate management strategy tailored to both the patient's and the owner's specific needs.

Causes and pathogenesis

The formation of a hive results from degranulation of mast cells and/or basophils; release of various inflammatory mediators from the granules causes dilation of blood vessels, leakage of plasma into the surrounding dermis and subsequent dermal oedema. This combination leads to the classic 'wheal and flare' reaction seen in our patients (although the erythematous 'flare' can be difficult to appreciate on equine skin). This mast cell degranulation can be triggered by either immunological or non-immunological causes (Table 1). Immunological reactions are caused by either type I or type III hypersensitivity reactions. Type I hypersensitivities, or immediate hypersensitivities, are mediated by immunoglobulin E (IgE) and caused by allergic reactions. Acute inflammation results when previously sensitised IgE molecules on mast cells and eosinophils encounter an allergen, leading to cross-linking of the IgE molecules and subsequent degranulation. Release of vasoactive and inflammatory mediators in mast cell granules (eg, histamine, kallikreins, leukotrienes) and production of inflammatory cytokines (interleukin (IL)-4, 5, 13) from activated T lymphocytes involved in antigen processing manifests as urticaria formation in this immediate hypersensitivity reaction. Type III hypersensitivities on

the other hand are caused by antigen-antibody complex deposition leading to production of various inflammatory mediators and cell recruitment into affected tissue. With type III hypersensitivities, immune complexes form at sites of antigen-antibody contact, as well as in circulation. Complex deposition incites inflammation by activating complement, macrophages and mast cells. As with type I hypersensitivity reactions, degranulation of mast cells can lead to urticaria development. Additionally, chemotactic factors from complement activation (particularly C5a) call in more inflammatory cells (including neutrophils and eosinophils) which contribute to urticaria development. Immunological reactions are believed to be the most common triggers for urticaria in the equine patient, with type I hypersensitivities probably accounting for the bulk of cases reported. Non-immunological reactions are less common, although they are possible in the equine patient. Mast cell degranulation and urticaria formation may be triggered by factors including temperature (heat or cold), pressure, physiological changes with stress or exercise, or underlying genetic abnormalities. Although the lesions appear clinically identical, keys in the history will allow the practitioner to more accurately identify potential underlying causes.

Clinical signs and presentations

Equine urticarial lesions can have a rather variable appearance and may be mistaken for other dermatological abnormalities under certain conditions. Table 2 outlines differential diagnoses for urticaria based on clinical appearance, as well as recommended diagnostic tests to help differentiate the possibilities. Hives are classically well defined; they are raised lesions with steep sides and a flat top. The hair coat may appear raised over the top of the hives. Alopecia is not a feature with urticaria alone, but may occur secondarily when pruritus is present. Urticarial lesions are often moderately fluctuant and may 'pit' when pressure is applied to the centre of the lesion. In other cases, however, the wheals will be firmer and in this situation need to be differentiated from other nodular diseases including

Table 1: Immunological and non-immunological causes of urticaria in the equine patient

Immunological causes	Non-immunological causes
Allergic reactions (atopic dermatitis, food allergy, contact allergy)	Cold-induced
Stinging/biting insects (bee, wasp, hornet, mosquito, blackfly, spider, ant)	Cholinergic: exercise-induced, sunlight, heat
Snake bite	Stress/psychogenic
Infections and infestations (bacterial, viral, fungal, protozoal, parasitic – including intestinal parasites or ectoparasites)	Dermatographism (pressure induced)
Drug reaction (antibiotics, phenylbutazone, narcotics, guaifenesin, dewormers, hormones)	Genetic abnormality
Antisera, bacterins, vaccines	Idiopathic
Plants (nettle, buttercup)	
Transfusion reaction	
Vasculitis (several causes; drugs, purpura haemorrhagica)	

infections and neoplasia. Lesion size generally ranges from a few millimetres to about 5 centimetres in diameter (Fig 1). Papular hives are small, approximately 3 to 6 millimetres in diameter and may only be apparent by visualising the raised hairs along the skin surface. Often attributed to insect bite hypersensitivity, papular urticaria must be differentiated from folliculitis lesions. The latter are generally associated with concurrent scaling or crust formation and easily epilated hair. On the opposite end of the spectrum, giant urticaria may also be noted; these wheals will often form plaques of oedema of up to about 40 centimetres diameter.

Urticaria may also present in more bizarre forms as opposed to the classical circular wheal. Coalescing hives may form serpiginous (snake-like), gyrate or annular lesions, occasionally with a more indented centre giving the appearance of a doughnut (Fig 2). These lesions can resemble erythema multiforme (an immune-mediated skin disease) in the horse. Less commonly, urticaria will form in a linear fashion, giving the skin a corrugated appearance (Fig 3). Urticarial lesions generally remain intact; however, if a large amount of oedema is present,

surface serum exudation may be present leading to matting of the overlying hair coat.

Urticaria can present in horses of any age. No breed or sex predilections have been documented. There is some speculation that urticaria may be more common in thoroughbred, Arabian, and other racehorse breeds; however, this has not been confirmed or well documented. Suspected stress, physiological responses associated with racing and a higher prevalence of atopic dermatitis in these breeds have been proposed as possibilities for overrepresentation in these horses.

Most commonly, urticaria presents acutely and resolves fairly rapidly. However, in other situations, chronic or persistent urticaria is seen. While individual lesions are present for 24 to 48 hours, chronic urticaria episodes can last for at least six to eight weeks. In these cases, identification of an underlying trigger is especially important. With either acute or chronic urticaria, pruritus may or may not be a feature of the condition. When pruritus is present, secondary bacterial infection should be evaluated and addressed.

Table 2: Differential diagnoses for urticaria based on clinical appearance

Type of lesion	Differential diagnoses	Appearance – tests
Papular	Bacterial folliculitis	Crusts present – cytology (bacterial organisms +/- neutrophils) (crusts present)
	Dermatophytosis	Often crusting, scale and alopecia – fungal culture
	Demodicosis	Skin scrape – deep for mites (often crusting and alopecia)
	Pemphigus foliaceus	Moderate-marked crusting typically present – biopsy (acantholytic keratinocytes)
Classical	Cutaneous lymphoma	Biopsy
	Amyloidosis	Biopsy
	Vasculitis	Biopsy
	Sarcoid	Biopsy
Exudative	Bacterial infection (deep pyoderma)	Cytology, bacterial culture (deep tissue)
	Fungal infection (systemic mycoses, opportunistic infections)	Cytology, fungal culture
	Protozoal infection (pythiosis)	Cytology, serology
Giant	Vasculitis	Biopsy
	Oedema	Biopsy, bloodwork (assess protein/albumin status)
Gyrate/annular	Erythema multiforme	Biopsy
	Vasculitis	Biopsy



Fig 1: (a, b) Conventional appearance of urticaria. Lesions are well defined and can vary in size from a few millimetres to 5 cm

Diagnostic considerations

As with any dermatological patient, a thorough history is imperative to enable the practitioner to arrive at the most likely reason for the development of urticaria. This will aid in the elucidation of a successful management plan for the horse and owner. General history regarding husbandry, environment, diet and systemic health should be evaluated, along with more specific dermatological history. Box 1 outlines pertinent questions to consider when obtaining information on the equine patient. Once the history has been obtained, the practitioner should critically evaluate the information provided by the owner and determine whether any patterns are readily identifiable. For example, does the horse seem to develop urticaria following administration of any specific therapeutic, feedstuff or supplement? Do the episodes of urticaria appear to be seasonal in nature, perhaps relating to the presence of biting flies or environmental allergens? Does urticaria develop in relation to exercise or work? Answers to these questions will help guide management strategy recommendations.

Along with a detailed history, a thorough physical examination is essential as part of the dermatological diagnostic process. Lesions should be evaluated for

size, firmness, presence of scale, crust and alopecia. In addition, the distribution of urticarial lesions should be noted. Particularly, the horse should be evaluated to determine whether lesions are associated with tack placement, whether they are restricted to haired skin, or whether mucous membranes and/or coronary bands have abnormalities present. The latter could indicate the presence of vasculitis related to drug reactions and/or systemic illness. Horses typically do not develop angio-oedema as part of an urticarial eruption; however, this should be noted if it is present. Although a complete physical examination of body systems other than the skin should be performed, particular attention should be paid to thoracic auscultation to determine whether wheezes or other evidence of recurrent airway obstruction is apparent.

When scaling and/or exudate is present with the lesions, impression cytology should be evaluated. This may be accomplished using either acetate tape or glass slides. Sample should be obtained from under crusts or scale to obtain a more diagnostic sample. Bacterial folliculitis in horses is often accompanied by scaling and crust; this should be considered a differential diagnosis, particularly in the case of papular urticaria. In addition, secondary bacterial infection may occur in a pruritic horse with urticarial lesions and self trauma.



Fig 2: Urticaria can present in unconventional forms, such as serpiginous, gyrate and annular urticaria, as shown here



Fig 3: Urticaria can also present in a linear fashion, although this is uncommon

Box 1: Questions to ask when taking a history

General questions

- In what sort of environment does the horse live? Pasture? Stable? Bedding?
- General health history?
- Current or recent medications?
- Vaccination history and protocol?
- Deworming protocol?
- Fly control measures?
- Diet history? Supplements?
- Travel history?
- Other horses? Other animals?
- Activity/purpose (eg, show, endurance, work, etc)?
- Pedigree?

Dermatology-specific questions

- Age of onset?
- First episode of urticaria? Or recurrent? Frequency of recurrence?
- Duration of urticarial episode?
- Onset affected by exercise? Heat? Cold?
- Location of lesions? Associated with location of tack?
- Pruritus present?
- Medications/therapy administered? Response?
- Other horses affected? In contact? Relatives?
- Seasonality?
- Other dermatological or respiratory (eg, recurrent airway obstruction) abnormalities associated with urticaria?

Biopsy should be considered for urticarial lesions that are firmer than usual, when standard therapy has not provided beneficial results, and when concurrent vasculitis is a concern. Histopathology of classical urticarial lesions typically shows mild to moderate perivascular dermatitis involving the superficial and deep dermis. Interstitial dermatitis may also be reported. In addition, the presence of clear or empty space within the dermis may be reported, due to the presence of oedema. Infiltrate with large numbers of eosinophils is common, with variable numbers of lymphocytes concurrently present. Although mast cells are known to be involved in the development of urticaria in the horse, they can be difficult to identify on a biopsy sample without the addition of special stains (eg, Giemsa or toluidine blue) as they are frequently degranulated and do not readily take up normal haematoxylin and eosin stains. Dermal oedema may also be noted on histopathology of urticarial lesions; this may be severe, particularly when serum exudate is also noted.

It is important to remember that neither serum IgE nor intradermal allergen tests diagnose an allergic aetiology in horses or any other animal. Allergy is a diagnosis of exclusion; there is no test available which gives the answer to 'is this patient allergic?'. Rather, these tests become potentially useful when other causes for urticaria development have been ruled out. As discussed previously, a thorough history is imperative to help rule in and out possible reasons why hives are present in a particular patient. Additionally, serum IgE and intradermal allergen tests are not helpful for diagnosing food allergies; although technically available, serum testing for food allergens has not been shown to correlate clinically with the results of elimination diet trials, nor with clinical signs associated with provocative dietary challenges. Many veterinary dermatologists consider them to be a waste of clients' money. Favourable response to an elimination diet trial is the only way to truly diagnose food involvement in the development of urticaria. This involves feeding a single feedstuff for at least four weeks. A novel bulk food

(something which the horse has not been exposed to previously) should be used as the dietary base, making sure to withhold any additional supplements, concentrates and additives during the trial period. The novel bulk food may vary by region but can include a single-grass species of hay such as Timothy, or a wilted vacuum-packed grass product (haylage). If, however, other potential causes have been eliminated, the horse responds to standard medical therapy for urticaria and recurrent episodes are reported, then serum IgE and/or intradermal allergen testing may be useful. Most commercially available serum IgE allergen tests currently have not been well evaluated in the equine patient; their results should be considered in light of the clinical history and presentation. Intradermal allergen tests are best performed by specialists in veterinary dermatology due to the cost of acquisition and maintenance of allergen extracts, and interpretation of results. Again, these findings should be considered in light of the horse's clinical history. It is important to remember that previously published studies have shown little to no correlation between intradermal allergen and serologic allergen tests in horses (or other domestic animal species). Although impossible to predict, one type of allergen test may provide more 'meaningful' (eg, clinically relevant) results over another in an individual patient.

Clinical management

In an ideal world, a specific aetiology would be identified for every case of equine urticaria; unfortunately, this is often not the case. Since several contributing factors and underlying causes can manifest as urticarial lesions in the horse, identification of a specific trigger can be rather daunting for both the veterinary clinician and horse owner. In the case of a single urticarial episode, identifying an aetiology is often impossible, unless lesions developed following a specific identifiable change or event in the horse's management (eg, addition of a new supplement, medication, vaccination, topical therapy, etc). If identified or strongly suspected, avoidance of the offending agent should be recommended for the future. Medical therapy may not be necessary if the episode is fairly acute; individual lesions should disappear without intervention within 24 to 48 hours. Unless lesions continue to develop, or the patient is negatively impacted by the presence of hives (eg, pruritic), monitoring for resolution is reasonable. On the other hand, if lesions are chronic and recurrent, the practitioner should make a concerted effort to identify an underlying cause if possible. Directed questions as discussed previously, examination of the horse's environment and current management practices are helpful in filtering possible aetiological agents.

General medical management for urticaria typically consists of administration of corticosteroids and/or antihistamines. For localised lesions, topical glucocorticoid spray may be sufficient. However, in more generalised or widespread cases, systemic corticosteroid administration may be necessary. Many practitioners favour injectable dexamethasone in the horse (0.04 mg/kg intramuscularly or intravenously); however, prednisolone (2 mg/kg orally) may also be effective. For short-term administration, steroids are typically well-tolerated and effective; however, care must be taken in the equine patient with chronic or recurrent urticaria as risk for development of laminitis increases with continued corticosteroid administration. Antihistamines are reported to have a variable effect for urticaria; however, in my experience, administration has often been effective at managing either acute or chronic urticarial eruption. Table 3 lists antihistamine options and

Table 3: Dosing in the horse

	Drug	Dose and frequency
H1 antihistamine receptor blockers	Chlorpheniramine	0.25 to 0.5 mg/kg every 12 hours
	Diphenhydramine	1 to 2 mg/kg every 8-12 hours
	Hydroxyzine	1 to 2 mg/kg every 8-12 hours
	Cetirizine	0.2 to 0.4 mg/kg every 12 hours
Centrally acting tricyclic drugs	Amitriptyline	1 mg/kg every 12 hours
	Doxepin	0.5 to 0.75 mg/kg every 12 hours
	Trimeprazine	1 to 2 mg/kg every 12 hours

dosing for the equine patient; hydroxyzine is favoured by many practitioners. In more severe cases of urticaria, or in the case of concurrent angio-oedema, administration of adrenaline (epinephrine) (1:1000 dilution; 5 to 10 ml per 450 kg subcutaneously or intramuscularly) may be necessary to control clinical signs.

For cases of chronic and/or recurrent urticaria, management should focus on the causative agent if identified. If temperature factors or exercise are implicated in urticaria development, husbandry and use issues may have to be addressed with the owner. Fly control should be critically evaluated in horses with seasonality of urticaria corresponding with the presence of biting flies and other insects. Use of fans, fly masks, sheets and topical preventatives (frequent application of pyrethrin- or permethrin-containing products) should be recommended. Alteration in the horse's environment (eg, removal of standing water, manure, rotting vegetation, relocation of horse away from cattle, changes in times during the day when the horse is on pasture versus stalled) can be highly beneficial for urticaria caused by insect bite hypersensitivity reactions, if possible to implement. Although strict dietary trials in the horse can be difficult, dietary change may be beneficial in certain patients. It is uncertain what the true prevalence of cutaneous adverse reactions to food is in the equine species. This aetiology is commonly suspected by practitioners; however, it is rarely confirmed with dietary challenges. Only an occasional case has been reported in the peer-reviewed literature, lending to the uncertainty of how frequently food is involved in urticaria development. However, if a feedstuff or additive is indeed determined to be a causative agent, avoidance should be recommended as primary therapy.

When other causes have been ruled out and an allergic aetiology is determined to be the most likely reason for urticaria, a meaningful and fitting intradermal allergen test or serum IgE test (eg, one that identifies allergens present during the times of year that the horse develops urticaria and is relevant to the horse's regional environment) is helpful for formulating immunotherapy. Allergic/atopic urticaria can be fairly well controlled with injectable immunotherapy in the horse. Although veterinary sources cite variable reports of efficacy for immunotherapy in the management of atopic dermatitis and/or urticaria attributed to underlying environmental allergy, horses appear to be a species which show an overall favourable response to immunotherapy compared to other domestic animals. Efficacy of 70 to 85 per cent with regards to management of atopic urticaria is probably reasonable. In my experience, allergen-specific immunotherapy injections have been very beneficial for managing these patients. Whether horses will show a similar response to oral/sublingual immunotherapy for atopic urticaria is as yet unknown.

Summary

Urticaria can be a very frustrating management condition for owners and veterinarians alike, although may be relatively innocuous to the equine patient. That said, chronic and persistent hive development can negatively impact the horse's ability to perform the desired function. Attention to a detailed history is the practitioner's best diagnostic tool for determining possible aetiologies and developing a management plan. Choosing appropriate diagnostics (and not just running an 'allergy test' on every horse with hives) will guide the practising veterinarian in identification of secondary problems, allow for identification of 'look-a-like' dermatological conditions, and, when allergen testing is indicated, guide appropriate immunotherapy formulation. Reminding owners that this is a condition of 'management' as opposed to 'cure' will help set reasonable expectations before owners set them on their own.

Further reading

- CORNICK, J. L. & BRUMBAUGH, G. W. (1989) Dermatographism in a horse. *Cornell Veterinarian* **79**, 109-116
- FADOK, V. A. (1990) Of horses and men: Urticaria. *Veterinary Dermatology* **1**, 103-111
- FADOK, V. A. (1995) Overview of equine papular and nodular dermatoses. *Veterinary Clinics of North America - Equine Practice* **11**, 61-74
- HINDEN, S., KLUKOWSKA-RÖTZLER, J., JANDA, J., MARTI, E. I., GERBER, V. & ROOSJE, P. J. (2012) Characterization of the inflammatory infiltrate and cytokine expression in the skin of horses with recurrent urticaria. *Veterinary Dermatology* **23**, 503-e99
- KNOTTENBELT, D. C. (2009) Pascoe's Principles and Practice of Equine Dermatology. 2nd edn. Saunders Elsevier
- MATTHEWS, N. S., LIGHT, G. S., SANDERS, E. A., HARTSFIELD, S. M. & HUSTEAD, D. R. (1994) Urticarial response during anaesthesia in a horse. *Equine Veterinary Journal* **25**, 555-556
- MIYAZAWA, K., ITO, M. & OHSAKI, K. (1991) An equine case of urticaria associated with dry garlic feeding. *Journal of Veterinary Medical Science* **53**, 747-748
- PATERSON, S. (2000) Investigation of skin disease and urticaria in the horse. *In Practice* **22**, 446-455
- PATERSON, S. & BALL, C. (2013) A practical approach to equine dermatology. *In Practice* **35**, 190-196
- POLLARD, R. E. & PUCHALSKI, S. M. (2011) Reaction to intraarterial ionic iodinated contrast medium administration in anaesthetised horses. *Veterinary Radiology and Ultrasound* **52**, 441-443
- RÜFENACHT, S., MARTI, E., VON TSCHARNER, C., DOHERR, M. G., FORSTER, U., WELLE, M. & ROOSJE, P. J. (2005) Immunoglobulin E-bearing cells and mast cells in skin biopsies of horses with urticaria. *Veterinary Dermatology* **16**, 94-101
- SCOTT, D. W. & MILLER, W. H. JR. (2011) Equine Dermatology. 2nd edn. Saunders Elsevier
- VOLLAND-FRANCQUEVILLE, M. & SABBAH, A. (2004) Recurrent or chronic urticaria in Thoroughbred race horses: clinical observations. *European Annals of Allergy and Clinical Immunology* **36**, 9-12

Quiz: Equine urticaria

- (1) With regards to immunological causes of urticaria, which hypersensitivity types have been implicated in the development of urticarial lesions in the horse?
- Type I
 - Type II
 - Type III
 - Type IV
 - a. and c.
 - All of the above
- (2) Which clinical presentation of urticaria is often attributed to insect bite hypersensitivity in the horse?
- Gyrate
 - Linear
 - Giant
 - Papular
- (3) What is the practitioner's most important diagnostic tool as part of the work up for equine urticaria?
- History
 - Intradermal allergen testing
 - Serum IgE allergen testing
 - Cytology
 - Biopsy
- (4) How long should an individual urticaria lesion persist without therapeutic intervention?
- 4-6 hours
 - 12-28 hours
 - 24-48 hours
 - 72-96 hours
- (5) A horse presents with a history of chronic urticarial lesions. On thorough questioning of the owner, it is noted that lesions are typically present during the spring and summer months and only rarely during other times of the year. Which is the incorrect answer for the 'next step' in this particular patient?
- Administering a serum IgE or intradermal allergen test
 - Discussing current fly control practices with the owner
 - Discussing the presence or absence of particular plants in the horse's pasture with the owner
 - Discussing any dietary changes made during the spring and summer as compared to the rest of the year
 - Discussing deworming and vaccination schedules with the owner as it relates to the time of the year

Answers
(1) e, (2) d, (3) a, (4) c, (5) a



Equine urticaria: a clinical guide to management

Alison Diesel

In Practice 2014 36: 295-300

doi: 10.1136/inp.g3116

Updated information and services can be found at:

<http://inpractice.bmj.com/content/36/6/295.full.html>

These include:

References

This article cites 9 articles, 2 of which can be accessed free at:

<http://inpractice.bmj.com/content/36/6/295.full.html#ref-list-1>

Email alerting service

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:

<http://group.bmj.com/group/rights-licensing/permissions>

To order reprints go to:

<http://journals.bmj.com/cgi/reprintform>

To subscribe to BMJ go to:

<http://group.bmj.com/subscribe/>