I. Diagnosis and Treatment of the Pruritic Horse

Pyoderma (Bacterial Skin Infections)

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1. Introduction

Bacterial folliculitis (superficial pyoderma) is usually caused by a coagulase positive *Staphylococcus* species. Both *S. aureus* and *S. intermedius* have been isolated. In one study, *S. aureus* accounted for twice as many isolates as *S. intermedius*; the same study isolated some strains of *S. hyicus* as well. Interestingly, in another study, lysozymes from equine neutrophils were only slightly bactericidal for *S. aureus*. Many isolates are resistant to penicillin G. Occurrence of pyoderma has been linked to poor nutrition and husbandry in some cases. Clinical signs of staphylococcal pyoderma are most often crusts, usually in a circular pattern suggestive of dermatophytosis (this may be the reason that equine pyoderma is underdiagnosed), epidermal collarettes (circular skin lesions with an exfoliative border as seen in dogs with superficial pyoderma; Figs. 1 and 2), or encrusted papules similar to the miliary dermatitis reaction pattern in cats. These infections tend to be variable in their intensity of pruritus. Histology usually shows folliculitis and/or furunculosis, but bacterial colonies are not always seen. A truncal form of bacterial folliculitis (contagious acne, contagious pustular dermatitis, or Canadian horsepox) is often associated with poor grooming, trauma from tack and saddle, warm wet weather, and heavy work. It is painful and interferes with working and riding. It is usually caused by a coagulase positive *Staphylococcus* species but may also be caused by *Corynebacterium pseudotuberculosis*. This organism is more commonly a cause of deep pyoderma, as discussed below (Fig. 3). In horses, folliculitis often develops in the saddle and lumbar region, particularly in the summer. The affected area initially may be swollen and very sensitive; this is followed by formation of follicular papules and pustules. These may become confluent or rupture, forming...
plagues and crusts. Deep pyoderma followed by ulceration may develop over large areas of the body, especially on the neck, sides of the thorax, inner surface of the thighs, or the prepuce.

A pastern bacterial infection (pastern folliculitis) is often seen. Again, the causative agent is usually a coagulase positive Staphylococcus species. As with most “primary pyodermas,” the mechanism(s) whereby the organism gains its foothold is unknown (not contagion and not poor sanitary conditions). The lesions are usually limited to the posterior aspect of the pastern and fetlock regions; one or more limbs may be involved. The initial lesions consist of papules and pustules (Fig. 4). If left untreated, the lesions coalesce and may produce large areas of ulceration and suppuration, which may be quite painful. The disease is usually not associated with systemic signs, and the general health of the horse is not affected.

A relatively uncommon nodular disease termed “botryomycosis” mimics actinomycosis or a deep fungal infection, but it is most often caused by Staphylococcus species in the horse. These may require surgical excision as well as long-term antibiotics.


In a 2000 study, methicillin-resistant coagulase-negative staphyloccal species were cultured from healthy horses in Japan; Yusada et al.\(^8\) concluded that “[t]hese organisms must be considered a potential threat to horses and veterinarians who care for them.” In a 2006 study from the Netherlands, methicillin-resistant coagulase-negative staphylococci were found frequently.\(^9\) The organism was usually S. sciuri, not S. epidermidis, which was found in the humans in close contact with these horses. No methicillin-resistant S. aureus (MRSA) was found in healthy horses.

In contrast, a single strain of MRSA was isolated from both humans (13%) and horses (4.7%) on horse farms in Canada and New York state.\(^10\) In looking at horses admitted to a university teaching hospital (Ontario Veterinary College, University of Guelph, Guelph, Ontario, Canada), MRSA was isolated from 120 (5.3%) of 2,283 horses. Of these 120 horses, 50.8% were positive at the time of admission, and clinical infections attributable to MRSA were present or developed in 14 horses. Horses colonized at admission were more likely to develop clinical MRSA infection. Administration of ceftiofur or aminoglycosides during hospitalization was the only risk factor associated with nosocomial MRSA colonization. Another strain of MRSA was isolated from a small number of horses at the Veterinary University in Vienna, Austria.\(^11\)
Of most concern is the finding of humans reporting skin lesions after contact with a community MRSA-positive affected foal, despite short-term contact with standard protective barriers. The isolates from the foal were indistinguishable from the ones from the humans.12

3. Treatment of Equine Pyoderma

The antibiotic usually used for many bacterial skin infections in the horse is trimethoprim sulfa orally (30 mg/kg, q 12 h for 2–6 wk, longer for deep infections).13 Interestingly, dosing intervals for IV administration of trimethoprim-sulfamethoxazole in horses may not be appropriate for use in donkeys or mules. Donkeys eliminate the drugs rapidly compared with horses.13 In cases of Staphylococcus sp. resistance to trimethoprim-sulfa drugs, enrofloxacin may be used. Use of enrofloxacin in young horses (<2 yr old) should be avoided because of concerns of damage to the articular cartilage.14 A recent report15 on the use of an oral-gel formulation of enrofloxacin (100 mg/ml of gel) showed good clinical efficacy for infections in several organs; however, almost one-third of the horses had some diarrhea, and 10% had oral lesions. Epstein et al.15 felt that this latter side effect could be overcome with administration of tap water rinse of the oral cavity. Interestingly, enrofloxacin binds to melanin in equine hair, although the clinical implication is unknown.16 In one report of 15 horses, vancomycin was used, alone or in combination with an aminoglycoside, to treat MRSA and enterococcal infections. The average vancomycin dosage was 7.5 mg/kg, q 8 h, IV over 30 min. The antibiotic, alone or in combination with an aminoglycoside, was safe and effective. Because of the problems with emerging resistance, Orsini et al.17 recommended that the use of vancomycin in horses be limited to cases in which culture and susceptibility indicate effectiveness and no reasonable alternative treatment is available.

For localized lesions, generic mupirocin ointment 2% or silver sulfadiazine creama may be effective. Shampoos such as ethyl lactateb or chlorhexidine (2%–4%) are helpful.

Dermatophilosis is caused by an actinomycete bacteria Dermatophilus congolensis. Three conditions must be present for Dermatophilus to manifest itself: a carrier animal, moisture, and skin abrasions. Chronically affected animals are the primary source of infection. However, they only become a serious source of infection when their lesions are moistened. This results in the release of zoospores, the infective stage of the organism. Mechanical transmission of the disease occurs by both biting and non-biting flies and possibly, fomites. Because normal healthy skin is quite impervious to infection with D. congolensis, some pre-disposing factor that results in decreased resistance of the skin is necessary for infection to occur; prolonged wetting of the skin by rain is one of the most prevalent causes.

The disease is usually seen during the fall and winter months with the dorsal surface of the animal most commonly affected. Occasionally, the lesions involve the lower extremities when the dorsal surface of the animal is wet or “wet pastures” (“dew poisoning”) or if horses are left in the stall while the stall is cleaned with high-pressure water hoses. In the early stages of the disease, the lesions can be felt better than they can be seen. Thick crusts can be palpated under hair coat (Fig. 5). Removing the crusts and attached hair exposes a pink, moist skin surface with both the removed hair and the exposed skin assuming the shape of a “paintbrush.” The under surface of the crusts are usually concave with the roots of the hairs protruding.
Diagnosis is made by the “railroad track” cocci on impression smears: a portion of one of the crusts should be minced and mixed with a few drops of sterile water on a glass slide, gram stained, and examined microscopically (Fig. 6). Alternatively, bacterial culture or histopathology may be used for diagnosis. A thick crust composed of alternating layers of parakeratotic stratum corneum, dried serum, and degenerating neutrophils is the most characteristic change. A superficial folliculitis may be a prominent feature of the disease. In sections stained with gram stain, the branching, filamentous organisms can be observed in the crusts and in the follicles. Treatment is removal from the wet environment, removal of crusts (with care because these may be painful), washing with iodophors or lime sulfur, and use of antibiotics (penicillin at 22,000 mg/kg procaine pen G, q 12 h, IM or trimethoprim sulfa orally with the same dosage used for staphylococcal pyoderma) for 7 days. As the crusts are important in contagion, these should be disposed of rather than brushed on to the ground.

4. Dermatophytes and Malassezia
Dermatophyte infections, like pyoderma, can be variably pruritic. The most common equine dermatophyte species isolated from horses are Trichophyton equinum, M. equinum, T. mentagrophytes, and T. verrucosum. Tack (bridles, halters, and saddle blankets) often act as fomites. The lesions usually appear first on the axillary/girth area and may spread over the trunk, rump, neck, head, and limbs (Fig. 7). Initial lesions may be urticarial in nature and can progress to multi-focal, sharply demarcated scaling and crusting areas (Figs. 8 and 9). Lesions may be superficial or deep. Superficial infections are more common and are manifested by the development of thick crusts or more generally, a diffuse moth-eaten appearance with desquamation and alopecia. Less commonly, deeper structures are infected through the hair follicles, which causes small foci of inflammation and suppuration. A small crust forms over the follicle, and the hair is lost. However, extensive alopecia and crust formation do not occur; some irritation and itching may be caused by this type. Rarely, dermatophytosis may be limited to the coronary band (Fig. 10).
Diagnosis is by fungal culture; biopsy is less reliable (*Trichophyton* species may cause acantholysis, which mimics pemphigus on histopathology). Hair is the specimen most commonly collected for the isolation of dermatophytes. Using forceps, hairs should be selected that appear broken, especially at the advancing periphery of an active, non-medicated lesion. In addition, surface keratin may be gathered by forceps or skin scrapings from similar areas and inoculated onto the culture medium.

The hair and surface keratin of large animals have large numbers of saprophytic fungi and bacteria. Therefore, it is recommended by some clinicians to cleanse the skin before taking samples for culture. This may be done by gently cleansing the area to be sampled with water and allowing it to air dry, although the authors do not routinely do this.

Sabouraud’s dextrose agar has been used traditionally in veterinary mycology for the isolation of fungi; however, other media are available with bacterial and fungal inhibitors, such as dermatophyte test medium (DTM). DTM is essentially Sabouraud’s dextrose agar containing cycloheximide, gentamicin, and chlorotetracycline as antifungal and antibacterial agents and to which the pH indicator phenol red has been added. Dermatophytes use protein in the medium first, and alkaline metabolites turn a medium red. Most other fungi use carbohydrates first and give off acid metabolites, which do not produce a red color change. These saprophytic fungi will later use the protein in the medium, resulting in a red color change. However, this usually occurs only after a prolonged incubation (10–14 days or more). Consequently, DTM cultures should be examined daily for the first 10 days. Some *Aspergillus* species and others cause a red color change in DTM, and therefore, microscopic examination is essential to avoid an erroneous presumptive diagnosis. It has been recommended that 1–2 drops of a sterile injectable B complex vitamin preparation be added to culture plates when culturing horses, because one strain of *T. equinum* (*T. equinum* var. *equinum*) has a unique niacin requirement.

**Fig. 8.** Dermatophytosis: urticarial lesions caused by *Trichophyton mentagrophytes* infection. (Courtesy of Elsevier Publishing.)

**Fig. 9.** Dermatophytosis: urticarial lesion caused by *Trichophyton mentagrophytes* infection that transitions into a circular area of alopecia. (Courtesy of Elsevier Publishing.)

**Fig. 10.** Dermatophytosis: scaling of the coronary band caused by *Microsporum gypseum* infection. (Courtesy of Dr. V. Fadok and Elsevier Publishing.)
However, the authors do not routinely do this. Skin scrapings and hair should be inoculated onto Sabouraud's dextrose agar and/or DTM and incubated at 30°C with 30% humidity. A pan of water in the incubator will usually provide enough humidity. Cultures should be checked every day for growth. DTM may be incubated for 21 days, but cultures on Sabouraud's agar should be allowed 30 days to develop. The authors usually use Derm-Duet, which has DTM on one side, rapid sporulating media (RSM) on the other side, and a well of water in the center. It is routinely incubated at room temperature. *T. verrucosum* has been reported not to grow on DTM.21

Topical treatment alone is often curative. Although 50% captan (2 tablespoons of the powder in 1 gallon of water) has been touted in the past, and while certainly safe for tack, its effectiveness has been questioned. Lime Sulfur (1 cup to 1 gallon of water) or bleach (1:10 with water) are both effective but messy and odiferous. Miconazole or ketoconazole veterinary shampoos are becoming more widely used and may be as effective. In Europe and Canada, an enilconazole rinse is highly effective.

Systemic treatment is occasionally needed. Griseofulvin's efficacy in horses (as well as an effective dose) has not been thoroughly researched. However, a dosage of 100 mg/kg daily for 7–10 days has been advocated and has been used with good success on a small number of horses by the authors. Griseofulvin is a teratogen and should not be used in pregnant mares. Additionally, it is no longer available. Alternatively, 20% NaI may be given IV (250 ml/500 kg horse every 7 days, 1–2 times). This also is contraindicated in pregnant mares, because it may cause abortion. Although medications such as itaconazole and fluconazole have been used to treat horses with systemic mycotic infections such as coccidiodomycosis and aspergillosis, there have not been any studies on their effectiveness in dermatophytosis. However, the safety record in horses in the face of the doses used (2–5 mg/kg, q 80%) of *Malassezia* sp. from intermammary debris from a healthy mare. (Courtesy of Elsevier Publishing.)

culture as *Malassezia* species (Fig. 11). Treatment with a topical 2% miconazole/chlorhexidine shampoo was curative. The authors are aware of other similar cases. However, healthy non-pruritic mares may also have large numbers of yeasts in the intramammary area.25

Fig. 11. Cytology of *Malassezia* sp. from intermammary debris from a healthy mare. (Courtesy of Elsevier Publishing.)

References and Footnotes

IN-DEPTH: SELECTED TOPICS IN DERMATOLOGY
Insect Hypersensitivity

Anthony A. Yu, DVM, MS, Diplomate ACVD

1. Introduction

Insect hypersensitivity is the most common cause of equine pruritus. There are four contributing causes of pruritus.

1. The bite itself, which is painful because of the chewing mouthparts of these flies.

2. An immediate (i.e., type 1) hypersensitivity to salivary antigens of biting insects or inhalation of desiccated insects, which is supported by the increased immunohistochemical presence of IgE in skin of horses with insect hypersensitivity and detection of IgG and IgE serum antibodies to Culicoides salivary gland antigens in horses with insect dermal hypersensitivity.1,2

3. A delayed (i.e., type 4) and cutaneous basophil hypersensitivity reaction that is similar to flea-allergy dermatitis in dogs and cats.

4. Langerhans’ cells and T-lymphocytes cytokine production.3–5

Ultimately, all of the above cells interact to enhance release of inflammatory cytokines that result in eosinophil recruitment and activation. Culicoides spp., black flies, horn flies, and stable flies most commonly implicated, and occasionally, mosquitoes, deer flies, and horse flies are involved (Fig. 1).

2. Signalement

The tendency to develop insect hypersensitivity seems to be multifactorial (genes, major histocompatibility complex, and geography). Evidence exists that insect hypersensitivity reactions may be 35% inherited.9 Certain breeds (i.e., Welsh Ponies, Icelandics, Arabians, Connemaras, Quarter Horses, and German Shires) seem to be predisposed to developing insect hypersensitivity. Many horses start to develop clinical signs at a young age (i.e., 2–4 yr).3,6,7

3. Clinical Signs

Generally, most cases of insect hypersensitivity tend to be seasonal (in areas where colder weather affects insect development), be highly pruritic (somewhat steroid unresponsive depending on severity), and begin with primary papules or wheals involving a
dorsal or ventral distribution and a combination distribution pattern depending on the feeding habits of the insects involved (e.g., *Culicoides pusillus* [mane/tail], *C. lahillei* [ventral], *C. alachua* [dorsal], *C. insignis* [all of the above]; Table 1). Secondary alopecia, crusting, excoriations, hypopigmentation, and lichenification occur as a result of chronic irritation (Figs. 2 and 3). When pruritus involves the mane and tail, the horse will rub the areas until the hairs are broken or barbed, leaving a “buzzed mane” and “rat tail” appearance, respectively (Fig. 4). Secondary *Staphylococcus* infections are common and may exacerbate the pruritus.

Black flies are known to have a salivary toxin that, when injected repeatedly (i.e., multiple bites),

<table>
<thead>
<tr>
<th>Type of Insect</th>
<th>Feeding Location</th>
<th>Time of Feeding</th>
<th>Environmental Condition Necessary for Insect Reproductive Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Culicoides</em> spp</td>
<td>Depends on species</td>
<td>Sunrise and sunset</td>
<td>Standing water Decaying vegetation Manure</td>
</tr>
<tr>
<td>Blackflies</td>
<td>Face, Ears, Ventral abdomen, Groin, Medial forelegs, Thighs</td>
<td>Morning and evening</td>
<td>Running water</td>
</tr>
<tr>
<td>Stable flies</td>
<td>Legs, Abdomen, Thighs</td>
<td>Daytime, under shade trees, Prefer the early morning and late evening</td>
<td>Manure Decaying bedding</td>
</tr>
<tr>
<td>Horn flies</td>
<td>Focal midline (around the umbilicus)</td>
<td>Daytime</td>
<td>Cow manure</td>
</tr>
<tr>
<td>Mosquitoes</td>
<td>Lateral aspect of the body</td>
<td>Dusk, Immediately after sunset</td>
<td>Water</td>
</tr>
<tr>
<td>Deerflies</td>
<td>Sides of chest, Flanks and proximal legs</td>
<td>Daytime</td>
<td>Vegetation Water</td>
</tr>
<tr>
<td>Horseflies</td>
<td>Sides of chest, Flank and proximal legs</td>
<td>Daytime</td>
<td>Vegetation Water</td>
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Fig. 2. Classic distribution of a severe case of insect-bite hypersensitivity encompassing all described distribution patterns including mane/tail, dorsum, and ventrum.

Fig. 3. Severe case of insect bite hypersensitivity with crust and post-inflammatory hypopigmentation involving the inner thighs.
is capable of causing capillary permeability leading to shock and even death.\textsuperscript{6} Horsefly and deerfly bites differ from those of other insects in that they typically cause nodular lesions that ulcerate.\textsuperscript{3,6} Respiratory signs (i.e., recurrent airway obstruction that is similar to reactions noted in humans with asthma and arthropod hypersensitivity) have been associated with positive skin-test reactions to only Culicoides spp. and mosquitoes.\textsuperscript{7,9,10}

4. Differential Diagnoses
The primary differentials for insect hypersensitivity include atopy, food allergy, and a stable vice. Secondary bacterial infections are common. Primary or secondary dermatophytosis should always be considered, particularly if multiple horses are affected in the same environment. Some species (e.g., \textit{C. variipennis}) transmit the filarid parasite, Onchocerca cervicalis, which in itself may result in similar clinical signs with ventral crusting/pruritus. A regular deworming protocol with ivermectin would minimize the likelihood of onchocerciasis. Other ectoparasites such as lice, Chorioptes, and Psoroptes should be ruled out before pursuing extensive diagnostics.

5. Diagnosis
Diagnosis of insect hypersensitivity is based on history (single horse involvement and seasonality; e.g., spring \textit{[C. niger/alachua]}, summer \textit{[C. stellifer]}, and fall \textit{[C. insignis]} depending on the region), distribution pattern (e.g., horn flies focus on the umbilical region), and an inspection of the patient’s environment for evidence of insect breeding grounds (forested area or ponds/still water within a mile; Table 1). Skin scrapings are helpful in ruling out ectoparasite problems (e.g., Chorioptes and psoroptes). Skin cytologies and/or cultures are useful in determining whether a bacterial (\textit{Staphylococcus} or \textit{Dermatophilus}) and/or fungal infection (\textit{Trichophyton mentagrophytes}, \textit{Microsporum canis}, or \textit{Microsporum gypseum}) is present.

There are diagnostic tests for insect hypersensitivity.

1. A stringent ectoparasiticidal trial using Knockout L.A.\textsuperscript{a} up to every other day depending on the severity of the condition and parasite load in the environment. One study noted significant improvement with every other week application in cases of suspected Culicoides hypersensitivity.\textsuperscript{11}

2. Intradermal skin testing with several insects including \textit{Culicoides variipennis}, which crossreacts with other species of Culicoides, stable flies, mosquitoes, deer flies, horse flies, and black flies, because several types of insects can cause allergies in horses; however, many have cross-reactive antigens (Fig. 5).\textsuperscript{3,6,7,12–14}

3. In vitro testing is not reliable in horses.\textsuperscript{15}
6. Conclusion

Insect hypersensitivities can manifest as a single condition or as part of a spectrum of allergic conditions including atopy, food allergy, and contact hypersensitivity. To successfully manage any equine patient with allergies, every effort should be made to become familiar with the feeding habits and environmental requirements for reproduction for insects. This will help to successfully eliminate their contribution to the allergen load.

References and Footnote


Atopy

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1. Introduction

Manifestations of equine allergies include dermatoses (hives, pruritus, scale/crust, leukotrichia, or nodules) as well as respiratory conditions (recurrent airway obstruction [RAO]). Currently, the pathomechanism is not completely understood both in human and veterinary medicine. Allergies seem to be a multifactorial condition involving immunoglobulins, major histocompatibility complex (MHC-II), cytokines, chemokines, and the neuroendocrine system. The classic type I hypersensitivity pathway continues to play an intrinsic role in the production of an allergic response. The inherited predisposition to form sensitizing antibodies to environmental allergens such as molds, dust, and pollens of grasses, weeds, and trees results in the production of antigen-specific immunoglobulin E (IgE), which then fixes to tissue mast cells. Cross linking of mast cell bound IgE results in release of inflammatory mediators, which culminates in pruritus, urticaria, and an allergic bronchitis. Other genes, such as the beta chain of the high affinity IgE receptor found on mast cells and basophils, may also regulate susceptibility to atopy. We now realize that this traditional type-I allergic response is only the tip of the iceberg, and its role still remains controversial in the horse, especially in cases of RAO.1–13

In humans, the allergic response has been further elaborated to involve T lymphocytes, particularly the T helper cell paradigm. The T helper 2 cell (Th2), in fact, produces cytokines such as interleukins (IL) 4, 5, 6, 10, and 13, of which IL4 and IL13 are essential for the B-cell immunoglobulin class switching to IgE. In non-atopic individuals, the T helper 1 cell line (Th1) produces interferon (IFN) and IL2, which in turn suppress the proliferation of allergy promoting Th2 cells, and are responsible for the local immune defense system.

Recently, bronchoalveolar lavage fluid harvested from antigen challenged allergen induced RAO horses had increased numbers of Th2 cells that produced the classic allergic profile (increased IL4 and IL5 and decreased IFN).4 Many studies show the horse’s ability to react to allergens introduced intra-dermally; however, controversy surrounds the significance of these reactions.5–13 It is obvious that further studies are necessary to delineate the allergic behavior of the equine immune system.

2. Signalment

Two recent studies from California revealed a median age of onset of 5–6.5 yr of age with a range of 2–12 yr.14,15 Cannon cautions that horses are often sold during the “good” season and develop allergies their next “bad” season, which makes age of onset difficult to determine. As well, pre-disposed breeds
include Thoroughbreds, Quarter Horses, Warmbloods, Arabians, and Morgans, and males (usually geldings) were almost twice as likely as mares to have atopy. However, the study populations were small, regional, and potentially, socio-economically influenced. It will take a multicenter (general and referral practice) study or verifiable survey of thousands of allergic horses to get a true picture of the signalment of equine allergic dermatoses.

3. Clinical Signs
Pruritus with secondary lesions (alopecia, excoriations, lichenification, and hypopigmentation) of the face, ears, trunk, and distal legs is one presentation for equine atopy (Figs. 1–4).12–15 Horses may develop secondary pyoderma, which is characterized by excess scaling, small epidermal collarettes, or encrusted papules ("miliary dermatitis"). Chronic recurrent urticaria, which may or may not be pruritic, and allergic-based RAO, similar to that of asthma in humans and cats, may either present singly or in combination with the prurtic form. Some uncommon presenting signs suspected associated with allergies include laminitis and head tossing.16

4. Diagnosis
Diagnosis of atopic dermatitis is based on history, clinical signs, and the exclusion of other differentials. Skin testing should not be used to diagnose atopy. Rather, allergy testing is currently used to discern specific environmental reactants for incorporation into an avoidance program or inclusion into allergen-specific immunotherapy (ASIT). Positive reactions indicate that antigen-specific IgE is present in the patient; it does not indicate that the antigen in question caused the disease. Therefore, careful historical evaluation and correlation with reactions will improve avoidance and ASIT success rates.

5. Intradermal Allergy Test or Blood Test
If possible, intradermal allergy testing (IDT) is preferred over serologic allergy testing (SAT). Skin testing assesses tissue fixed IgE and the entire inflammatory cascade. Because mast cells have been found to produce IL4 and express the ligand for CD40, they can then augment B cell production of antigen specific IgE in tissues without systemic (blood) levels being significantly increased (previ-
ously activated B cells but not naive B cells). This increase in antigen specific IgE in tissue after allergen exposure is readily identified by IDT but not serum testing. In fact, comparison of allergen-specific IgE levels in the blood and bronchoalveolar lavage fluid (BALF) of asymptomatic and symptomatic RAO horses with those of normal horses revealed no difference in blood levels of allergen-specific IgE. RAO horses, however, had statistically significant increases of allergen specific IgE in their BALF compared with normal horses, which indicates a local amplification of IgE without a parallel representation in the serum.

Based on a series of studies, horses with atopic dermatitis, recurrent urticaria, and RAO generally have a higher incidence of positive reactions than healthy horses. That being said, several studies reveal that defining appropriate test concentrations of the allergen extracts still requires further study to uniformly standardize the IDT. Although appropriate withdrawal seems almost essential in dogs and cats to obtain reactions to test allergens, testing horses on shorter to no withdrawal times has, in most cases, still produced significant findings.

The IDT is typically performed under sedation using detomidine. An area for testing is shaved on the neck tailored to the amount of allergens being tested for the specific geographic region. Horses with short, summer coats may be circumvented if the owners are concerned about appearances during the show season. Allergens from a typical dog/cat profile along with several other insects and outdoor allergens are injected intradermally in a grid pattern avoiding any primary or secondary existing lesions. Skin test reactions are then assessed at 30 min and 4 h after inoculation. Reactions are compared with a positive and negative control based on the size and turgidity of wheals. Erythema as a criterion is limited to those horses with white skin on the neck.

As allergies become a more common presenting complaint in equine medicine and long-term control of symptoms using anti-inflammatory medication carries side effects, costs, and drug-testing liabilities, offering intradermal allergy testing and development of allergen-specific immunotherapy should be a serious consideration for large equine groups/centers. False positive/negative reactions can be minimized by the expertise of the allergist.

References and Footnotes


TREATMENT OF EQUINE ALLERGIES

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1. Introduction

One trend that is coming to light is the fact that horses, as well as humans, dogs, and cats, commonly have combination allergies (i.e., insect allergies, atopy, and drug and food hypersensitivities). It is, therefore, important to keep in mind key concepts such as “allergic threshold” and “summation of effect” when diagnosing and treating equine allergic dermatoses. That is, a successful therapeutic protocol must encompass the patient’s pre-disposing/environmental influences along with treating the secondary perpetuating factors (bacteria and Malassezia), all while specifically targeting the primary etiology. Regardless of which combination of therapeutic options is selected for the horse, the client must be educated regarding the chronicity of equine allergies, the workload involved in multimodal therapy, and the unrealistic expectations for control of the condition.

2. Environmental Control

Avoidance or reduced allergen exposure is the best treatment for all allergic forms. Although this option if often impractical, it must be offered and considered as an adjunct to systemic therapy by the owner in lieu of lifelong anti-inflammatory therapy. There are many recommendations of how to reduce/avoid allergen exposure.

1. Move from the current environment, which may include moving to a different part of the country, moving down the road, moving to a different barn (bank barn versus open air), or restricting indoor/outdoor activity depending on allergic reactions (put horses with mold spore and dust allergies to pasture and keep horses with summer pasture associated allergies indoors).

2. Minimize dust exposure in the barn, which may include switching to rubber mats and/or minimum dust generating bedding,1–4 or switching to grass silage, hydroponic or wet down hay, and/or pelleted rations.

3. Control insects in the environment by moving horses away from standing water, manure piles, compost, and cattle, stabilizing before dusk until after dawn, using fly sheets or masks sprayed with permethrin repellant, using a 1±32 × 32 per 2.5-cm grid meshing, placing box fans within the stall, using time-release insecticide sprays, or placing fly wasps in compost and manure areas and fish in ponds.

4. Use dietary trials to diagnose food hypersensitivity or intolerance. Current recommendations consist of a 4- to 6-wk trial using novel food sources like timothy, rolled oats,
alfalfa, or barley if not routinely fed. Previous alfalfa exposure through medications, treats, or hay cubes should be investigated, and unnecessary supplements, vitamins, and other drugs should be discontinued. To rechallenge, add one item back into feeding every 7 days; exacerbation of clinical signs usually occurs within 24–72 h.

5. Other allergens that owners might overlook include laundry detergent for the blanket/saddle pad/leg bandages, topically applied wound ointments, sprays, and powders, and regular dewormers and vitamin supplements.

In a study evaluating the positive effects of environment versus environment and anti-inflammatory therapy, a simple change to wood shavings and a pelleted diet for 2 wk from straw and hay resulted in improvement of recurrent airway obstruction (RAO) in 12 horses within 3 days and continued to 7 days.1 The addition of steroids in a crossover study induced a more rapid reduction in airway inflammation but not a more rapid improvement in airway function, which is most likely attributable to the use of prednisone (decreased bioavailability) versus prednisolone or dexamethasone. Overall, airway function was best after 30 days at pasture. The notable improvement in lung function within 3 days of an environmental modification emphasizes the need for allergen reduction as the cornerstone of treatment of RAO.1,4

Another study evaluated shredded cardboard as an appropriate minimum dust bedding. Pulmonary function tests (ventilatory mechanics, arterial blood gases, airway inflammation scoring, and bronchoalveolar cytology) were significantly different from those recorded in poor hygienic conditions.3 On basis of the in vitro and in vivo results, it was concluded that cardboard bedding, used in conjunction with low dust forage, might be appropriate in the provision of minimum dust management of heaves affected horses (Table 1).

Food allergens are another route by which clinicians can help minimize/eliminate allergen load by avoidance alone. In a study of 22 cases of recurrent or chronic urticaria in Thoroughbred racehorses during training season, food allergy seemed to exacerbate the clinical symptoms.5 Intradermal skin tests with fresh allergenic food potentiated syndromic reactions in some horses, and elimination of the suspect allergen brought about resolution of clinical signs such as urticaria and enteritis. In general, an elimination trial of high protein food items, supplements, flavored medications, and any molasses-containing products for a minimum of 4–6 wk is worthwhile when attempting to minimize the patient’s allergen load.

3. Topical Control

When treating horses with allergies, patient fly control is a mandatory part of any therapeutic regimen. A spray containing permethrin and an insect growth regulator (pyriproxyfen; Knockout L.A.6) was effective in treating horses with Culicoides spp. hypersensitivity.6 Other recommended repellants include Avon Skin-So-Soft Bath Oil diluted 50:50 with water and Skin-So-Soft Bug Guard Plus IR3535 lotion with sunscreen or an aqueous DEET (N,N-diethyl-m-toluamide) solution at a concentra-

<table>
<thead>
<tr>
<th>Feed/bedding</th>
<th>Respirable Dust (particles × 10^3/l)</th>
<th>A. fumigatus (CFU/l)</th>
<th>F. rectivirgula (CFU/l)</th>
<th>T. vulgaris (CFU/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good hay</td>
<td>63.0 (30.0)</td>
<td>20.1 (5.6)</td>
<td>3.1 (1.2)</td>
<td>3.3 (1.2)</td>
</tr>
<tr>
<td>Silage 78% D.M.</td>
<td>8.8 (2.5)</td>
<td>11.5 (6.5)</td>
<td>1.7 (1.2)</td>
<td>2.2 (0.7)</td>
</tr>
<tr>
<td>Silage ± 50% D.M.</td>
<td>4.5 (1.9)</td>
<td>4.5 (4.2)</td>
<td>0.4 (0.2)</td>
<td>1.2 (0.8)</td>
</tr>
<tr>
<td>Alfalfa pellets</td>
<td>9.5 (4.4)</td>
<td>2.6 (2.5)</td>
<td>0.1 (0.0)</td>
<td>0.4 (0.2)</td>
</tr>
<tr>
<td>Wood shavings</td>
<td>31.5 (12.9)</td>
<td>16.7 (2.9)</td>
<td>1.2 (0.7)</td>
<td>1.9 (1.4)</td>
</tr>
<tr>
<td>Cleanbox wood shavings</td>
<td>6.2 (0.1)</td>
<td>0.04 (0.05)</td>
<td>0.02 (0.04)</td>
<td>0.15 (0.09)</td>
</tr>
<tr>
<td>Good straw</td>
<td>11.6 (4.9)</td>
<td>9.5 (5.0)</td>
<td>0.4 (0.4)</td>
<td>0.8 (0.4)</td>
</tr>
<tr>
<td>Flax straw</td>
<td>9.3 (1.8)</td>
<td>2.4 (0.5)</td>
<td>0.2 (0.2)</td>
<td>1.4 (0.3)</td>
</tr>
<tr>
<td>Ecobed cardboard</td>
<td>5.7 (1.6)</td>
<td>0.03 (0.05)</td>
<td>0 (0)</td>
<td>0 (0.01)</td>
</tr>
<tr>
<td>Rolled grains</td>
<td>120.3 (30.6)</td>
<td>10.2 (0.6)</td>
<td>1.8 (1.6)</td>
<td>1.1 (1.1)</td>
</tr>
<tr>
<td>Whole grains</td>
<td>4.1 (0.9)</td>
<td>4.5 (1.5)</td>
<td>0.1 (0.0)</td>
<td>1.0 (0.1)</td>
</tr>
<tr>
<td>Molassed concentrates</td>
<td>2.1 (0.6)</td>
<td>0.8 (0.3)</td>
<td>0.3 (0.2)</td>
<td>3.0 (1.8)</td>
</tr>
</tbody>
</table>

Material was agitated in an air stream and particulates expressed per liter of air.
tion of 16.6% (a previously approved but recently discontinued equine product is Ceratex). Application frequency will depend on the product selection, geographic insect distribution, season of the year, and severity of the patient’s condition.

Shampoo therapy should not be overlooked in the treatment of equine allergies. The simple act of bathing with cool water rehydrates the skin, improves the integrity of the epidermal barrier, results in the vasoconstriction that decreases delivery of inflammatory mediators to the skin, helps to minimize percutaneous absorption of allergens, and finally, with appropriate ingredient selection, addresses secondary superficial infections. The selection of shampoos should be based on the patient’s skin condition and may include colloidal oatmeal products (shampoos, conditioners, and bath treatments) with or without a local anesthetic (promoxine HCl) or corticosteroids for pruritic dermatoses, sulfur/salicylic acid shampoos for horses with excess scale, antimicrobial shampoos (benzoyl peroxide, chlorhexidine or imidazoles) if secondary infections have been identified, or a combination of one or more of the above.

Lime sulfur (LymDyp) is a very effective multimodal topical therapeutic, because it provides not only ectoparasitic activity but also antipruritic, antiseborrheic, and antimicrobial effects in all animals. Although off label, it is a safe and proven treatment option that can be applied as a dip or spray on horses.

Topical steroids have also shown good efficacy when treating small animal patients. Unfortunately, most of these products are not labeled for use in equine medicine. I have used several topical steroid products for treatment of localized lesions.

Resicort is a mild 1% hydrocortisone, leave-on conditioner in a non-irritating base. Steroid ointments or creams (Aclovate [alclo-metasone 0.05%] or Elocon [mometasone 0.1%]) have different potencies (mild-moderate and high, respectively). Genesis Topical Spray is a 0.015% triamcinolone spray.

When choosing a topical steroid, one must strive for products with minimal side effects (i.e., minimal to no hematological and biochemical changes, suppression of the adrenal axis, and local cutaneous alterations [atrophy, alopecia, comedone formation, and secondary infections]).

4. Systemic Therapy

Along with the traditional immunoglobulin E (IgE)-mediated allergic reactions, it seems that the T-helper-1/T-helper-2 paradigm, along with all its cytokine alterations, exists in some form in the lung of horses with RAO. Similar to other domestic species, our focus on treatment of allergies should be directed at reestablishing the balance of T-cell inter-

5. Allergen Specific Immunotherapy

Allergen specific immunotherapy (ASIT) is a useful non-steroidal long-term treatment alternative in equine veterinary dermatology. It has been used to control insect hypersensitivities, urticaria secondary to atopy, and allergen induced RAO in horses with anticipated improvement in some cases as early as 2 mo. However, a minimum of 12 mo is necessary to determine ASIT’s efficacy in an allergic patient. ASIT may also be a consideration when treating allergy induced head shaking and laminitis.

Although the mechanism of action of immunotherapy is not clearly defined, there are several theories that have been proposed.

1. Induces immunoglobulin G (IgG) blocking antibody production in secretions, serum, and tissue.
2. Decreases circulating IgE by stimulating Tregulatory cells.
3. Decreases the number of mast cells and/or mast cell response to antigen.

When selecting allergens for inclusion into ASIT, historical correlation with the allergy test findings along with likelihood of allergen exposure is key. ASIT has shown mixed results for treatment of insect hypersensitivity, urticaria secondary to atopy, and RAO ranging from 16% to 90% efficacy. A recent report reflected the current consensus that 60–70% of atopic horses improve with ASIT. Although the exact reasons for inconsistencies in response to ASIT may be caused by individual response, a number of factors may contribute to the variable responses.

- Lack of allergen standardization.
- Selection of antigen (was it based on intradermal, serologic, or both) for allergen concentrations.
- Incorporation of non-specific immunostimulants (e.g., mycobacterial cell wall).
- Induction of immunotherapy and maintenance protocols.
- Administration of allergen (dose and route; i.e., SC or intradermal).
- Use of post-induction aftercare.
- Lack of objective data in a controlled environment.

Further studies with the standards set forth by the Canine Atopic Task Force need to be performed to reliably assess the efficacy of this treatment modality in horses.

However, based on the positive responses, minimal side effects (local injection reaction), decreased
dosing frequency/workload for the owner, and cost
efficacy (weight independent dosing), ASIT in horses
is a viable therapeutic modality for long-term con-
trol of insect hypersensitivity, recurrent urticaria/
pruritus, and RAO. Even in competitive trial and
show horses where concerns about the use of medi-
cation and drug testing arise, hyposensitization pro-
vides an alternative treatment modality that may
allow the horse to return to performance standards
and not compromise the rider’s ethics.

5. Polyunsaturated N-3 and N-6 Fatty Acids
Most mammalian cell membranes incorporate poly-
unsaturated N-3 and N-6 fatty acids (PUFAs), and they
are thought to create a shift in the production of
pro-inflammatory mediators to non- or anti-inflam-
atory mediators in the arachidonic acid cascade.
Other possible mechanisms by which PUFAs exert
their positive clinical benefit in atopic dermatitis are
still under investigation. Fatty acid supplements
have shown variable reported responses in horses.25–28
The difference in results is most likely attribu-
table to the variability of the research parameters.

1. Source and dose of fatty acid being given and
in food (linseed oil and flaxseed meal versus
oil and marine fish oils).
2. Type of allergic reaction being evaluated (in-
sect allergy versus atopy versus other).
3. Parameters being evaluated (intradermal test
reaction versus circulating plasma fatty acid or
inflammatory mediator concentrations).
4. Length of the study.
5. Number of horses in the study.
6. Study design (randomized double-blind pla-
cebo controlled ± crossover and 6-wk
washout).
7. Geographic location of the studies (Florida,
Oregon, United Kingdom, and Canada).

Currently, it is difficult to make any conclusions on
the efficacy of the essential fatty acids based on
current equine studies. Our knowledge of clinical
benefits of PUFAs in recent canine atopic dermatitis
studies along with the lack of significant adverse
reactions (mainly diarrhea) would prescribe its use
in equine dermatology as adjunct to any long-term
anti-inflammatory protocol. Typically, improve-
ment in pruritus and/or skin condition should be
noted within 2–8 wk after initiating therapy.10
A variety of PUFAs exist on the veterinary market
and are typically administered at their labeled dose
(Derm Caps 100s; 1 capsule per 100 lbs divided
twice daily).

7. Antihistamines and Tricyclic Antidepressants
Antihistamines and tricyclic antidepressants (TCA)
provide a non-steroidal alternative for long-term
control of allergic reactions in horses. The H1-re-
ceptor antagonist activity of these drugs is some-
times complemented by other mechanisms of action
including anti-serotonin-serotonin re-uptake inhibi-
tion. Exact dosing and recent pharmacokinetic
studies are lacking in the horse.29–32 The following
are the antihistamines and TCAs that are being
prescribed to horses (in my personal order of prefer-
ee).33

1. Hydroxyzine hydrochloride or pamoate (0.5–
1.0 mg/kg, q 8 h).
2. Doxepin hydrochloride (0.5–0.75 mg/kg, q
12 h).
3. Amitriptyline (1–2 mg/kg, q 12 h).
4. Chlorpheniramine (0.25 mg/kg, q 12 h).
5. Diphenhydramine (0.75–1 mg/kg, q 12 h).
6. Pyrilamine maleate (1 mg/kg, q 12 h).

Similar to humans and other domestic species, there
is tremendous variation in response to antihista-
mines/TCAs. It is sometimes necessary to try sev-
eral different classes of antihistamines at 2-wk
intervals before finding the most effective option.
Despite the paucity of synergy between antihista-
mines/TCAs and other anti-inflammatory therapies
in the horse, it is worthwhile to combine therapies
based on the numerous positive studies in dogs and
cats. Although antihistamines and TCAs have
fewer reported side effects (light sedation and occa-
sional personality changes) than corticosteroids, one
must always keep in mind the anticholinergic prop-
erties of these medications, particularly in patients
with glaucoma, gastrointestinal atony, cardiac arr-
hythmias, or urinary retention problems. Lastly,
advise owners to contact show authorities regarding
drug restrictions/withdrawals at least 14 days
before the event.

8. Phosphodiesterase Inhibitors
Pentoxifylline (PTX) is a synthetic xanthine deriva-
tive related to caffeine and theophylline. Its phos-
dodiesterase inhibition imparts three major
therapeutic benefits.34–42

1. It improves wound healing and connective-
tissue disorders by increasing fibroblast colla-
genases, decreasing fibroblast collagen,
fibroblast fibronectin, and fibroblast glyco-
aminglycans, and decreasing response to
 tumour necrosis factor (TNF)-alpha.
2. Rheologic agents decrease platelet aggrega-
tion and adhesion, increase red cell deform-
ability, decrease vasoconstriction, increase
plasminogen activator, plasmin, and anti-
thrombin III, and decrease fibrinogen, alpha 2
ti-plasmin, alpha 1 antitrypsin, and alpha 2
macroglobulin modulating effects.
3. Immunomodulators inhibit T- and B-cell ac-
tivation and proliferation, increase leukocyte
def ormability and chemotaxis, decrease leu-
kocyte adhesion and aggregation, decrease
neutrophil superoxide release and neutrophil
degranulation, decrease monocyte TNF-alpha production, leukocyte response to TNF-alpha, lymphotoksin, and interferon-gamma, decrease production of interferon-gamma, and IL-2, increased production of IL-10 and PGE2, and decrease natural killer cell activity.

By one or many of the mechanisms above, PTX potentiates the effectiveness of many medications including steroids (steroid sparing effect).43–48 For this reason as well as the fact that PTX’s rheologic activity potentially minimizes the risk of laminitis,49 I tend to use pentoxifylline (8–10 mg/kg, q 12–24 h)10,50 in conjunction with steroids. This provides a non-steroidal alternative with minimal side effects (hyperecitzability and sweats) for the purpose of tapering or eliminating the need for glucocorticoids in immune-mediated and allergic dermatoses. This medication should not be used in conjunction with anticoagulants or in patients with hemorrhagic disorders.

9. Corticosteroids
Corticosteroids have long been a standard therapy for allergies in the horse. Corticosteroids work primarily by gene repression and inhibition of nuclear factor kappa B, which directly or indirectly prevents the production of cytokines, chemokines, cell adhesion molecules, complement factors, and prostaglandin and leukotriene synthesis involved in the allergic response. Unfortunately, aggressive use of corticosteroids in horses may cause various adverse effects, including steroid hepatopathy, laminitis, and iatrogenic hyperadrenocorticism.51–53 Individual sensitivity to glucocorticoids may be directly related to Type 1:Type 2 11-β-hydroxysteroid dehydrogenase ratio. Judicious use, appropriate amounts, and intervals are key to minimizing adverse reactions. The following are the two most commonly used glucocorticoids used for the short-term treatment of equine allergies.

1. Prednisolone: syrup compounded or tablets at 0.5–1.5 mg/kg/day for 7–14 days and then tapering to 0.2–0.5 mg/kg, q 48 h over 2–5 wk for maintenance. If cost is an issue, prednisone may be substituted for prednisolone; the latter has been shown to have greater bioavailability in horses.54

2. Dexamethasone: powder or tablets. Injectable dexamethasone solution given orally is 60–70% bioavailable compared with the IV route.11 The initial loading oral or IV pulse dose is 0.05–0.1 mg/kg daily for 3–7 days and then tapering to 0.01–0.02 mg/kg every 48–72 h for maintenance. This regime is particularly helpful in more refractory cases.

Lastly, when addressing allergy induced RAO, the use of locally dispersed steroids through metered-dose inhalers (MDI) may help minimize concerns regarding glucocorticoid side effects while dispersing maximal concentration of drug at the effector sites.55,56 Masks have been designed for use with MDIs to improve drug delivery. Beclomethasone dipropionate and fluticasone propionate are both efficacious and well tolerated by horses, but sometimes these MDI steroids have a delayed response of ≥ 4 days; this necessitates combining them with faster acting drugs such as bronchodilators and systemic corticosteroids. As well, MDI steroids have few residual effects after treatment is discontinued.56

10. Cyclosporine
Cyclosporine has been used in the management of human, feline, and canine atopic dermatitis. However, the lack of pharmacokinetic data in horses and moreover, the cost of the medication limits its use in equine medicine at this time.

11. Other Treatment Options
Methylsulfonylmethane (MSM)5 can be used in conjunction with other anti-inflammatory therapies for its antioxidant properties. Controlled studies are lacking regarding its efficacy in equine allergies; however, because of the absence of significant side effects, I continue to use the product initially at 10–12 gm/500 kg q 12 h and then taper to a once daily dose.

Some of the earlier and more recent research of anti-inflammatory modalities is focused on receptor antagonists (platelet-activating factor receptor antagonist57 and eotaxin receptor [CCR3] antagonists58), protein kinase-C inhibitors and its subsequent effects on eosinophils,59 and monoclonal antibodies directed against cytokines (anti-IL-4 monoclonal antibody [pascolizumab]60). With each study, we hope to learn more about the pathogenesis of allergies and ultimately, find the key to turn off the allergic response with minimal side effects and cost.

References and Footnotes


II. Nodules, Lumps, and Bumps

Nodules—Infectious

Stephen D. White, DVM, Diplomate ACVD

1. Infectious

A serious yeast-caused disease is sporotrichosis (Sporothrix schencki), which presents as a nodular to ulcerative lymphatic cording disease (Fig. 1). Diagnosis is made when the organism is detected on histopathology, immunofluorescent antibody testing on affected tissues, impression smears, and/or culture.1 This is a zoonosis, and therefore, care should be taken in handling suspected samples. Successful therapy with a number of different systemic iodine preparations (NaI or KI) has been reported. The organic iodides have proven to be superior in efficacy to the inorganic iodides in the treatment of equine sporotrichosis, and ethylene diamine dihydroiodide (organic iodide powdera or EDDI 20 Gr. Dextrose baseb) is the drug of choice. This product is in the form of a feed additive. It can be mixed with a small amount of grain and administered at a dosage of 1–2 mg/kg of the active ingredient once or twice daily for the first week. The dosage is then reduced to 0.5–1.0 mg/kg once daily for the remainder of the treatment. In general, lesions will begin to regress during the first month of treatment, and treatment should be continued for at least 1 mo beyond the complete resolution of all cutaneous nodules and healing of any ulcerated lesions. Discontinuing therapy prematurely will invariably result in an unnecessary relapse of the disease. During treatment, the horse should be closely observed for any evidence of iodide toxicity (iodism), which includes excess scaling and alopecia, a serous ocular or nasal discharge, excess salivation, anorexia, depression, coughing, nervousness, or cardiovascular abnormalities. Should any of these signs develop, the treatment should be discontinued for 1 wk and resumed at three-quarters of the dosage at which the iodism was noted. In most instances, the treatment is subsequently well tolerated.2 Although both itraconazole and terbinafine have been shown to be effective in vitro against the organism isolated from a horse, the author is unaware of any clinical reports in this species.3

Habronemiasis (summer sore) is a granulomatous disease caused by the deposition of Habronema majus, Habronema muscae, or Draschia megastoma larvae by flies at the site of wounds or natural body moisture (sheath or eyes).4,5 Diagnosis is based on

aKnockout L.A., Virbac, Peakhurst, NSW 2210, Australia.
bCeratex, Vet Genix, Coral Gables, FL 33134.
cLymDyp, DVM Pharmaceuticals, Miami, FL 33137.
dResicort, Virbac, Peakhurst, NSW 2210, Australia.
eAclovate, GlaxoSmithKline Consumer Healthcare LP, Pittsburgh, PA 15230.
fElocon, Schering Corporation, Kenilworth, NJ 07033.
gGenesis Topical Spray, Virbac AH, Inc., Fort Worth, TX 76137.
hDerm Caps 100s, DVM Pharmaceuticals, Miami, FL 33137.
jMSM, Vita-Flex Nutrition Co, Council Bluffs, IA 51501.
clinical signs, history, and presence of calcified concretions (sulfur granules), and it is confirmed by biopsy. Arabians, gray horses, and horses with a dilute haircoat are over-represented. The medial canthus of the eye, male genitalia, third eyelid, and distal extremities are the most common parts of the body affected (Fig. 2). Treatment in the past has been either corticosteroids or organophosphates, topically or systemic; ivermectin (0.3 mg/kg) has been shown to be effective and is considered the treatment of choice by many clinicians. Moxidectin (0.4 mg/kg orally) may also be used. Systemic (prednisolone administered at 1 mg/kg once daily for 10–14 days and then tapered over a 2-wk period) or intralesional/topical corticosteroids often are also used because of the hypersensitivity reaction nature of the disease process. In severe cases, surgical removal or debulking of the lesion should be considered. It should be noted that the author and others have seen this disease in horses that were routinely given ivermectin as part of their deworming program.

Corynebacterium pseudotuberculosis infections are usually present as solitary or multiple abscesses or nodules with many draining tracks that progress to diffuse cellulites. When this process affects the pectoral region, it is often termed “pigeon fever” in the United States. Some observations about this type of deep Corynebacterium infection are that it may occur where caseous lymphadenitis is common in sheep, although proximity to sheep is not a requirement, and that it may be seen seasonally when insect population and activity are maximal. Insect vectors seem probable, especially stable, horn, and house flies. The draining nodules or abscesses are especially common in the pectoral region (Fig. 3), and occasionally, they affect the face, neck, axilla, groin, and limbs. They begin deep and enlarge, often with much edema; they rupture in 1–4 wk and discharge viscid, creamy purulent exudates, which is a major source of contamination. Abscesses most often rupture externally. Treatment depends on location. For example, if the abscess is in the axilla and painful on movement and/or preventing locomotion, establishment of drainage is very important, and antibiotics are indicated. Antibiotics most commonly used are procaine penicillin (20,000–50,000 IU/kg/day) with rifampin (3–5 mg/kg, PO); alternatively, trimethoprim sulfa (TMS; 30 mg/kg, q 12 h) may be used. Treating with TMS and rifampin concurrently may lead to a greater incidence of colitis and is to be avoided. If the decision is made to use antibiotics but drainage cannot be easily established...
(for example, an axillary abscess where the owner is unwilling to allow the veterinarian to use a trocar and drain), the antibiotics must be used for a minimum of 1 mo. If the abscess is solitary and not causing pain or fever, antibiotics are usually not necessary, but bringing the abscess to a head with hot packs or heat-inducing agents (ichthammol) is important. After any abscess has drained, gentle cleaning with tamed iodines or chlorhexidine is indicated.

2. Neoplasms

Mastocytosis (mast cell tumors) occurs in horses 1–18 yr of age (mean = 9 yr), and there is no breed predilection. A predilection for males has been proposed but is not always substantiated. There is one report in a donkey. In addition, multiple mast cell tumors resembling urticaria pigmentosa of humans may occur in newborn foals; these spontaneously appear and regress. Equine mastocytosis is usually solitary and occurs most commonly on the head and trunk. Lesions are 0.5–20.0 cm in diameter, well to poorly circumscribed, firm to fluctuant, dermal or SC, and may or may not be alopecic, ulcerated, and hyperpigmented. Lesions on the legs tend to be very firm and immovable.

Histology may vary from sheets of mast cells with few eosinophils (presumably early lesions) to those showing both the sheets of mast cells with numerous eosinophils and collagen degranulation. Ultrastructural features are similar to those noted in mast cell tumors of other species. Clinically, most mast cell tumors in horses do not recur after being excised (22 of 25 in one study). The author knows of one anecdotal case of metastasis from a tumor on the muzzle to regional lymph nodes; the tumor and the nodes were removed, and the horse was clinically sound 3 yr later. There is some debate as to whether equine mast cell tumors are benign neoplasias or focal dysplasias of mast cells.

Melanocytic skin tumors of horses traditionally have been described in aging grey horses and on the ventral tail, perineum, external genitalia, lip, udder, periorcular, and parotid gland regions. They have been the subject of several classification schemes in attempt to correlate histopathologic appearance with clinical behavior (i.e., is it benign or malignant?). One study distinguished three basic types of melanocytic skin tumors. Melanocytic nevi (melanocytoma) occurs in the superficial dermis or at the epidermal-dermal junction, and it frequently has epithelial involvement with nests of relatively large, mildly to moderately pleomorphic cells showing variable cytoplasmic pigmentation and occasional mitoses (Fig. 4). More than 70% of these occur in horses <6 yr of age and may occur in horses of any color (not just grey). Most of these tumors occurred in atypical locations. Of 28 melanocytic nevi, only one became invasive, and the rest exhibited benign behavior.

Dermal melanomas are found in the deep dermis and are composed of small homogeneous, indistinct tumor cells, either round or dendritic, with no mitoses. (If there are multiple, confluent dermal melanomas, this is referred to as dermal melanomatosis). Eighty percent of these tumors are in horses >6 yr of age or between 5 and 15 yr, and it is much more common in grey horses. Most of these tumors occurred in typical locations. Of 14 cases available for follow-up in one study, 8 had malignant behavior as shown by metastases.

In another study, the clinical and pathological characteristics of cutaneous melanomas occurring in 83 Camargue-type gray-skinned horses showed that the tumors occurred most frequently underneath the tail (93.9%) and at high rates in the perianal region (43.0%), the lips (33.0%), and the eyelids (24.0%) but rarely in the vulva (3.8%). Microscopic examination indicated that these tumors were composed mostly of melanocytes and numerous melanophages and that these cells manifested a remarkable cellular atypia. Early stages of the tumors occurred in close association with apocrine sweat glands but not at the dermal-epidermal junction.

A clinical study was conducted on 296 gray horses of the Lipizzane breed. Of the 296 horses, dermal melanomas were present in 148 horses (50%), 68 of which were >15 yr of age; 51 of these were melanoma bearing. In 75.6% of cases, melanotic tumors were detected underneath the tail. None of the affected individuals suffered any severe clinical effect or were handicapped in performance. Seltenhammer et al. concluded that in contrast to melanomas in solid colored horses characterized by early metastases, melanomas in grey horses showed less malignancy. Affected individuals often had encapsulated nodules or structures similar to human blue nevi. Probably, this finding at least partially reflects confu-
sion in terminology between true malignant melanomas and dermal melanomas.

Anaplastic malignant melanomas were composed of sheets of extremely pleomorphic epithelioid cells with poor pigmentmentation and many mitoses. These are usually seen in horses >20 yr of age and in horses of any color.

In regard to treatment, one study reported good success with excising dermal melanomatosis from the perineal, perianal, perirectal, or ventral tail regions. In a study of three horses, cimetidine (2.5 mg/kg, q 8 h, PO) was shown to decrease the number and size of melanomas tumor growth. However, a more recent study of 10 horses found that cimetidine had no consistent effects on either the number of tumors or tumor surface area over the 16-wk treatment at a dose of 5mg/kg, q 12 h, PO.

References and Footnotes

Sarcoids
Anthony A. Yu, DVM, MS, Diplomate ACVD

1. Introduction
Sarcoids are one of the most common causes of locally aggressive, non-metastatic fibroblastic nodular neoplastic lesions in horses, and they account for 35–90% of dermatological neoplasms.

2. Proposed Viral Etiology
Papillomaviridae (animal and human viruses) infect epithelial cells and cause hyperproliferation, warts, papillomas, or condylomas. Bovine papillomavirus (BPV) is currently categorized into six subtypes and two groups (A or B). Subgroup A transforms fibroblast and epithelial cells, whereas subgroup B transforms epithelial cells only. It is believed that BPV types 1 and 2 (subgroup A) are associated with the genesis of sarcoid disease. Polymerase chain reaction methods have been able to detect viral DNA and RNA from most sarcoids and recently, expression of the major transforming oncoprotein, E5, of BPV types 1 and 2. BPV types 1 and 2 do not seem to produce infectious virions but rather persistence and disease pathogenesis by downregulating major histocompatibility complex (MHC) class I expression.

3. Signalment
Sarcoids are more often noted in donkeys and mules than horses. Most affected individuals are geldings, and the age of onset is between 1 and 7 yr. Thoroughbreds, Warmbloods, and those horses that often work cattle, such as Appaloosas, Arabians, and Quarter Horses, seem predisposed to sarcoid formation. Standardbreds seem unlikely to develop sarcoids, possibly because of a decreased expression of the MHC class II antigen W13 ELA alleles; however, the aforementioned breeds tend to have an increased expression.

4. Clinical Findings
Multiple lesions are noted in 14–84% of affected individuals (Fig. 1). Sarcoids tend to occur in areas of previous trauma or irritation by insects or tack, including the chest, legs, girth, and base of the ears along with areas of thin skin such as the periccular, muzzle, and ventral abdomen (Fig. 2). Geographical variation seems to result in differing distribution (e.g., the trunk in the United Kingdom and Switzerland) potentially associated with feeding patterns of...
different flies and therefore, transmission of the virus to different sites.\(^1\) The fly vector transmission hypothesis is also supported by the lack of equine sarcoids in Norway, a country without biting insects.

5. Sarcoid Types

There are multiple publications with various classifications of equine sarcoids. Recently, a classification has been put forth by Knottenbelt,\(^7\) and a brief summary follows.

**Occult (Superficial) Type**

- Presents alopecia, scaling, and skin thickening.
- Presents sarcoids that are flat, annular, slightly thickened, scaly, hyperkeratotic, and hyperpigmented.
- Affects neck, face, peri-oral, sheath, medial thigh, and shoulder.

**Verrucous Form**

- Presents sarcoids that are \(<6\) cm and dry with a horny surface and a cauliflower-like appearance.
- Presents a prominent warty or verrucous appearance.
- Affects the head, neck, axillae, and groin.

**Nodular Form**

- Presents sarcoids that are entirely SC with normal overlying skin and haircoat.
- Affects eyelids, groin, and sheath.

**Fibroblastic Form**

- Presents fleshy fibrovascular appearance.
- Often closely resembles granulation tissue/proud flesh.
- Presents rapid growth along with ulceration, bleeding, and interference with function.
- Affects axillae, groin, legs, periocular, and previous wound sites.
- Also affects sites of other sarcoid type subject to trauma.
- Type 1 is pedunculated.
- Type 2 has a broad locally invasive base.

**Malignant/Malevolent Sarcoid**

- Is an aggressive locally invasive form.
- Extends widely into adjacent skin and subcutis.
Is invasive with infiltrated lymphatic vessels.
- Has multiple cords of tumor mass.
- Elbow and jaw.

Mixed Forms
Common with components of two or more types.

6. Diagnosis
Although it has been suggested that as high as 50% of flat or verrucous type sarcoids that are biopsied will transform into the more aggressive fibroblastic type, a recent roundtable discussion at the North American Veterinary Dermatology Forum (NAVDF) in 2006 among dermatologists and dermatopathologists from various parts of the world recommended that biopsies be taken to confirm your diagnosis so that appropriate therapy can be pursued. If transformation is noted (typically within 2 wk), then consider applying imiquimod to the affected lesion (see below) to prevent transformation and provide potential resolution. Also, the attendees at the roundtable did not find such a high incidence of transformation; however, it could be that the specialists are seeing a skewed population. That being said, when possible, the entire tumor should be removed.

When sampling tissue for dermatohistopathologic evaluation, it is advised to take large (6–8 mm) and deep biopsies, because small and superficial biopsies may read out as granulation tissue over the top of a chronic ulcerated sarcoid. Also, some sarcoids may initially appear consistent with insect bites (eosinophils with reactive appearing fibrosis) and are subsequently rebiopsied to be consistent with equine sarcoid. Perhaps these cases are truly insect bites that later become equine sarcoids. As a general rule, all well differentiated spindle cell proliferations appear very similar on histopathology. This includes granulation tissue, equine sarcoïd, amelanotic melanocytic tumors, nerve sheath tumors, and non-transmissible, non-sarcoïdal well differentiated fibrosarcoma. Classic equine sarcoid is fairly recognizable; however, it is not terribly dissimilar from the other listed differentials. The classic appearance consists of overlying epidermal hyperplasia and perpendicular arrangement of some spindle cells with surface epithelium creating a picket fence pattern. Problems in diagnosis arise when there is no surface epithelium, when the lesion is traumatized with overlying granulation tissue as mentioned above, or when the mass is in the deep dermis to subcutis without the overlying typical changes. In cases where dermatohistopathology does not support the clinical diagnosis, polymerase chain reaction analysis for BPV may be of value.

7. Management/Treatment
Lesions may progress if they are handled and rarely, may regress spontaneously. The general rule of thumb is if it is flat, leave it alone, but if it is fibroblastic, treat aggressively or refer. To date, there is no one treatment option that has proved universally successful. Surgical excision, cryosurgery, carbon dioxide LASER, radiofrequency hyperthermia, radiotherapy, chemotherapy, immunotherapy, or combinations thereof are summarized below.

8. Surgical Approaches
Surgical excision has met with 50–64% recurrence within 6 mo. Thus, surgery is used more often to debulk the mass and improve combination treatment. Typically, 0.5–1 cm margins have been described; however, in the NAVDF roundtable, the group felt that 3–10 cm margins were more appropriate in an attempt to decrease recurrence. Surgical excision, therefore, should be performed under general anesthesia (not local anesthesia) to perform thorough extirpation. To close such a defect, pinch or split thickness graft can be used. One should anticipate increased healing time and excess granulation tissue. In general, a cosmetic outcome can be achieved.

Cryotherapy has achieved up to 70% success with no recurrence. The procedure involves applying probes cooled to −20–30°C directly on the sarcoid with 2–3 freeze/thaw cycles. Thermocouple needles are used to monitor depth and degree of freezing. Hyperemia, hemorrhage, swelling, and local edema follow, resulting in damaged epithelium and viral particles at the site. Average healing time is 2.4 mo. The hair follicles are damaged or destroyed, and hair regrows white or not at all. Facial nerve paralysis, septic arthritis, loss of upper eyelid, and eviscerated globe are some of the complications to discuss with the owner before embarking on this treatment modality. Regression of multiple tumors (when only a select few are treated) has been reported inconsistently and is likely the result of a cryimmune response to sarcoid-cell components.

Carbon dioxide LASER cuts and evaporates tumor tissue with accurate dissection and excellent cosmetic results. The advantages include decreased to no post-operation swelling, no post-operation pain on palpation, primary wound closure or second intention healing without hypergranulation, and superior cosmesis. It has been reported that 81% of 59 horses with sarcoids treated by CO₂ laser were free from recurrence after 12 mo. In the same study, 60% of 35 horses in which sarcoids were treated by cryosurgery and 64% of 14 horses in which sarcoids were treated by conventional surgery were sarcoïd free after 12 mo. The improved success rates may be caused by the extension of the thermal-killing effects and vaporization of viral particles with CO₂ LASER, thus extending the margins and minimizing recontamination, respectively. Regardless of the technique, animals with multiple sarcoids were more predisposed to recurrence, and donkeys showed a significantly lower recurrence rate than horses.
9. IntraleSIONAL Approaches

Radiofrequency (orthovoltage) current induced hyperthermia\(^2\) involves heating sarcoids to 50\(^\circ\)C for 30 s (2 MHz current) with a thermoprobe every 1–3 wk. Hyperthermia is often combined with radiotherapy, immunotherapy, and chemotherapy. Limited reports on success of use in three cases resulted in regression with no recurrence 7–12 mo after the last treatment.

Interstitial brachytherapy\(^4,14\) using various isotopes (e.g., permanently implanted seeds of radon-222 or gold-198, removable needles of radium-226, cobalt-60, or iridium-192, and 192Ir seeds using an after loading technique) has been used to treat equine sarcoids. Responses range from 50% to 100% sarcoi free for 1 yr, alone or in combination with surgical debulking and/or hyperthermia, especially when the peri-orbital is involved. Fortunately, the treatment radiates the tumor locally and spares adjacent healthy tissue. Disadvantages include exposure for the surgeon, need for special equipment, size of the tumor limiting its application, poor local cosmesis (alopecia and leukotrichia), and patient containment in a radiation safety approved area that increases costs.

Intratumoral cisplatin\(^15–20\) (an emulsion of 10 mg of powdered cisplatin, 1 ml of sterile saline, and 2 ml of patient’s serum, medical grade sesame or peanut oil [resultant solution contains 3.3 mg of cisplatin per milliliter], or aqueous cisplatin [Platinol\(^a\) at 1 mg/ml]) has proven successful as a sole chemotherapeutic treatment or when performed after debulking the tumor. The procedure involves pre-treating the area with local anesthetic and then injecting the mixture into multiple planes no further than 0.6–1 cm apart at the base of the tumor and surrounding tissue at a dose rate of 0.97 mg of cisplatin/cm\(^2\) of tissue every 2 wk through four injections using Luer locked small gauge needles (22–25 gauge). It has been reported that 87% of these horses have not relapsed after one year. Disadvantages include need for safety precautions (chemotherapy gear, Luer lock syringes, latex gloves, protective eyewear, surgical masks, and biohazard disposal), potential for secondary peri-injectional infections, and occurrence of some degree of tissue sloughing and perilesional swelling. A serious human health concern is the potential for carcinogenicity and teratogenicity of all those handling treated horses, including extruded drug and the patient’s sweat, urine, and/or feces. At this time, post-chemotherapeutic treatment quarantine times have not been addressed. Recently, cisplatin injections have been combined with adjunctive therapies to try to improve responses. Thus far, the addition of a single high dose of interleukin-2 has not improved efficacy over cisplatin injections alone (~80%). However, cisplatin intraleSIONal injections followed by electropulsation (improves diffusion of chemotherapeutics through tumors) of sarcoids resulted in regression after only two to three electrochemotherapies in 100% of the treated lesions. No adverse effect from the electric pulses was observed, and no regrowth was observed in the 18-mo follow-up period.

10. Topical Cytotoxic Approach

XXTerra,\(^b\) a caustic agent containing zinc chloride, has anecdotally had some benefit. The product also contains water and bloodroot (Sanguineria canadensis). XXTerra is proposed to alter the tumor antigens of sarcoids in vivo, apparently stimulating the immune system to recognize them as foreign and mount a response quite similar to the host versus graft rejection. It can become quite sore to the touch, but this sensitivity lasts only a few days. According to the manufacturer, XXTerra has been effective in >95% of the sarcoids treated. Total failures have been observed in rare instances and have been attributed to a non-functional immune system. XXTerra seems safe on normal skin. The product is applied 0.125- to 0.25-in thick over affected areas and then covered with a non-adherent Telfa pad and bandage. The procedure is repeated every 4–6 days until the tumor is ready to slough (i.e., purulent debris and blood is noted). For sarcoids located where a bandage cannot be used, the product is topically applied daily for 4–6 days and then repeated at 4-day intervals until the tumor sloughs.

AW–3–LUDES,\(^21,c\) a topical proprietary ointment containing a variety of heavy metals and the antimitotic compounds 5-fluorouracil and thiouracil, is administered on successive or alternate days for 3–5 treatments. Within 5–10 wk, preferential necrosis and sloughing of the sarcoid tissues should be noted.

11. Immunomodulatory Approach

Bacillus of Calmette and Guerin (BCG; Regressin-V\(^d\))\(^,9,22\) cell wall fractions of an attenuated strain of Mycobacterium bovis, acts as an immunomodulator that stimulates host lymphocyte and natural killer cells. Optimal results are obtained if this product is used in an immunocompetent host with limited tumor burden or post-debulking in the periocular region. An 83.5% (10 of 12) rate of remission has been achieved with periorcular sarcoids, whereas use on all other body regions resulted in a 48.5% rate of remission. After two or more injections, swelling occurs within minutes or hours and may be extensive. Inflammation progresses to necrosis and ulceration of the tumor along with pyrexia, leukocytosis, non-fatal anaphylaxis, severe local inflammatory reactions (including lymphangitis), septic arthritis, and general malaise in some cases. Complete resolution of the process and tumor takes months (6 wk to 1 yr or more). Complications can include death from anaphylactic shock after two or more injections. Therefore, pre-medication with flunixin meglumine and corticosteroids has been recommended. An advantage is tumor specificity
whereby only sarcoïd cell necrosis is noted on histopathologic post-BCG evaluation.

Similarly, *Propionibacterium acnes* is a non-specific immunostimulant that may induce macrophage activation and lymphokine production, increase natural killer cell activity, and enhance cell mediated immunity against immunogenic components of equine sarcoïds. Protocols vary from intralosomal to IV injections once weekly for 6–8 wk. Susceptible lesions generally show improvement after two to three treatments, and eventually, they necrose and slough.

Autogenous vaccination,23 using autogenous polymerized tumor tissue combined with tuberculin purified protein derivative as an adjuvant, resulted in complete regression in nine horses with refractory sarcoïds. However, because the risks include tumor production and transmission of other diseases, this procedure should only be attempted in the most refractory of cases and with individual patients known to be negative for equine infectious anemia.

Imiquimod 5%24 is an immune-response modifier that was shown to have potent antiviral and antitumor activity in animal models and humans. Until recently, the successful use of topical imiquimod in the treatment of equine sarcoïds has been anecdotally reported. An open label study evaluating the efficacy of topically applied imiquimod 5% cream (3 times per week) for the treatment of various equine sarcoïds revealed a 75% reduction in tumor size in 13 of 16 (81.3%) tumors in the study over 8–24 wk; 9 of them (56.2%) showed complete resolution. The most common adverse effects included exudate, erythema, erosions, and alopecia, which were limited to the tumor and adjacent areas. Based on these results, topical imiquimod seems to be a good therapeutic option for the treatment of equine sarcoïds and to prevent tumor transformation post-biopsy.

12. Future Therapeutic Direction

The positive response to the immunomodulator Alldara supports the hypothesis of a viral component to the etiology of sarcoïds. Based on these findings and the response to non-specific immunomodulatory agents, perhaps we should focus our treatment direction toward specific anti-viral agents (e.g., ribavirin) and/or other specific anti-viral immune-response modifiers (e.g., interferon), as opposed to toxic chemotherapeutic agents and expensive surgical extirpation.

13. Client Education

Prognosis depends on many variables such as site, size, aggressiveness, number of lesions, number of treatment attempts, and location (legs and axillae = aggressive; periocular = vulnerable). Failure to resolve the lesions frequently results in regrowth of the tumor, which may be more aggressive with extensive local infiltration and faster growth.8 Combined therapy may provide fewer chances of relapse. If sarcoïds are noted on a pre-purchase examination, the lesion(s) should be recorded, and owners should be made aware of their location along with the potential risk that even flat sarcoïds may become malignant.

References and Footnotes

Aural Plaques

Anthony A. Yu, DVM, MS, Diplomate ACVD

1. Introduction

Papilloma virus has been shown through electron-microscopy and immunohistochemical techniques from lesions of aural plaques. It is suspected that biting insects may transmit the virus. Interestingly, biopsies of aural plaques may stimulate reduction or resolution of lesions; however, this may only be temporary (6–12 mo). Possibly, it is caused by a release of “papilloma antigens” into the blood stream, which prompts an immune response against the plaques.

2. Signalment

There is no sex or breed prevalence, and horses of any age can be affected; however, the disease is rarely seen in horses <1 yr of age. A study reported that 48 of 214 (22%) randomly examined horses were diagnosed with aural plaques.

3. Clinical Findings

Single to multiple, smooth or raised (up to 10 mm) depigmented plaques (1–30 mm diameter) can be located bilaterally on the inner surface of the pinnae (Fig. 1). The lesions tend to coalesce and can affect up to 40% of one or both ear-pinnae surfaces. Horses can be asymptomatic unless severely irritated by biting flies, particularly black flies. Rarely, plaques may be seen around the anus, penis, and vulva. Horses with this condition tend to be 1 yr of age or older.

4. Diagnosis

Diagnosis in practice is based on a classic clinical appearance. Dermatopathology is pursued primarily to rule out pre-cancerous stages of squamous cell carcinoma. Histopathology of aural plaques have features consistent with papilloma virus infection, such as papillated epidermal hyperplasia, koilocytosis, and increased numbers and sizes of keratohyalin granules. Other non-specific findings include orthokeratotic hyperkeratosis and epidermal hypomelanosis.

5. Treatment

Aural plaques do not spontaneously regress. The response to topical application of tretinoin (Retin-A: 0.025%, 0.05%, or 0.1% cream and 0.01% or 0.025% gel) has been variable. Treatment is typically directed at insect transmitted viruses. Therefore, it includes interferon alpha-2a orally (1000 IU/ml) and/or topically, topical iodine applications (Xenodine), and fly repellants (2% permethrin/pyriproxyfen [Knockout L.A.]). Griseofulvin, as an immune modulator, has been anecdotally helpful in some cases. Trauma to the area (i.e., biopsies or scraping with a dull scalpel blade) may prompt an immune response against the plaque(s).

Imiquimod, an immune response modifier, shows potent antiviral and antitumor activity in animal models and humans. It has been used with great efficacy in the treatment of external genital and perianal warts caused by papilloma virus in humans as well as other cutaneous viral infections, such as molluscum contagiosum, and skin tumors, such as basal cell carcinoma, actinic keratosis, and recently, squamous cell carcinoma in situ. Imiquimod is currently recommended as a treatment modality for papillomas and herpes virus as well as Bowen’s dis-
ease (squamous cell carcinoma in situ) in small animal dermatology. More recently, research into the use of imiquimod to treat equine sarcoïds, also suspected to have a papillomavirus viral etiology, revealed 13 of 16 (81.3%) had a 75% reduction in size within 8–24 wk. Based on the effects of imiquimod along with the similar pathogenesis of human warts and equine aural plaques, a multi-center investigation of imiquimod as a treatment for horses with aural plaques is underway.

6. Prognosis
Aural plaques tend to be persistent and rarely undergo spontaneous regression.

References and Footnotes

*Retin-A, Ortho, Marysville, OH 43040.
*Xenodine, Veterinary Products Laboratories, Phoenix, AZ 85067-4820.

Eosinophilic Granuloma (Nodular Necrobiosis)
Anthony A. Yu, DVM, MS, Diplomate ACVD

1. Introduction
Eosinophilic granulomas are the most common non-neoplastic nodular disease in horses and are characterized by intense eosinophilic infiltrates. The collagen degeneration that accompanies this condition is most likely caused by release of toxic eosinophilic contents such as major basic protein.

2. Pathogenesis
A large subset of affected horses represents hypersensitivity reactions to insect bites. There is evidence to support this hypothesis.

1. Many affected horses have been diagnosed with *Cuticoides* hypersensitivity.
2. Nodules recur each year with the onset of pruritus and the insect season and tend to resolve in the winter or with insect control.
3. Lesions occur at body sites on which insect feeding has been documented.

Other groups of affected horses were intradermal allergy test positive for inhalants but not insects, whereby allergen specific immunotherapy (ASIT) resulted in resolution of clinical signs. This suggests that atopic dermatitis is a potential underlying etiology. Food allergies have also been proposed; dietary trials have resulted in resolution of clinical signs, and rechallenge resulted in relapse. Overall, similar to cats, eosinophilic granulomas tend to be a reaction pattern attributable to an allergic etiology.

In fact, injection site granulomas were reported in response to the silicone coating on hypodermic needles (Fig. 1). Future reactions were avoided by using uncoated stainless steel needles.

3. Clinical Findings
As mentioned previously, nodules usually appear in the warmer months of the year, although geographic variations exist, and males are more frequently affected.

1. One or multiple lesions, which vary in size from 1–10 cm, typically are round and firm with no hyperpigmentation, alopecia, or ulceration noted (Fig. 2). Atypical lesions may ulcerate and drain, whereas some may be cystic or plaque-like with a central caseous or calcified core. The neck, withers, saddle, and girth are the most affected areas. Multiple lesions (sometimes hundreds) on one side of the body only have been rarely reported.

4. Diagnosis
History, palpation, and clinical appearance are very suggestive. Confirming the diagnosis requires dermatopathologic evidence of a granulomatous reaction and the appearance of flame figures around collagen bundles consisting of eosinophils and eosinophilic granules or “mush.” Calcification can be observed in older lesions. Notably, the equine eosinophilic granuloma is histologically similar in appearance to the linear granuloma lesions in cats.

5. Treatment
Glucocorticoids are the principal means of treating these lesions. If a single lesion is noted, intraleisional or sublesional injection of 5 mg triamcinolone acetonide for 2 wk with 3 treatments provides a
non-surgical alternative. If an incomplete resolution is noted with this protocol or if concern regarding laminitis and other adverse effects associated with the use of glucocorticoid exists, surgical extirpation or CO₂ LASER ablation should be considered. When multiple lesions are present, prednisolone 1–2 mg/kg/day for 7–10 days with tapering completely off medication within 3–4 wk is likely with this condition, especially if the underlying etiology is addressed (i.e., ectoparasite control, dietary trial, and ASIT).

References

Urticaria
Anthony A. Yu, DVM, MS, Diplomate ACVD

1. Introduction
Of all domestic animals, horses show the greatest incidence of urticaria and angioedema. Similar to the eosinophilic granuloma complex in cats, urticaria and angioedema in horses are symptoms but not a diagnosis. The real challenge is to identify and eliminate/address the underlying etiology of this condition. For this reason, urticaria and angioedema are some of the most common dermatologic conditions referred to a veterinary equine dermatology practice.

Urticaria and angioedema occur as a result of mast cell and basophil degranulation in response to either an immunologic or non-immunologic stimulus. Immunologic reactions, typically type immunoglobulin E (IgE) associated or type-III hypersensitivity, may result from allergens that are ingested (food allergy), inhaled (atopy), injected (insect hypersensitivity), or percutaneously absorbed (contact allergy or drug reaction). Non-immunologic factors that may intensify reactions in horses include psychologic stresses, genetic abnormalities, various drugs and chemicals (e.g., aspirin, narcotics, foods, or food additives), temperature related urticaria (heat, cold, or sunlight), physical urticaria (pressure or dermatographism), and exercise-induced urticaria. Regardless of the inciting factor, basophil and mast cell release of inflammatory mediators (histamine, platelet activating factor, and prostaglandins) cause increased vascular smooth muscle cell relaxation and endothelial cell retraction, which allows plasma to extravasate and form cutaneous wheals or angioedema.
2. Signalment
There seems to be no characteristic signalment associated with the development of urticaria or angioedema. Thoroughbred and Arabian horses between 1 and 10 yr of age seem to be affected frequently because of their increased predisposition to allergic dermatitis.

3. Clinical Findings
Pitting edema is the key clinical feature of urticaria and angioedema, although some hives can be quite firm on palpation. Inflammatory lesions, tumors, and fluid filled swellings do not pit on compression. The onset of clinical lesions can be acute or peracute within minutes to hours post challenge from exposure to the inciting factor. Pruritus is variable. The overlying skin is normal, and there is no alopecia. Lesions vary in shape and size and may present as papular, annular, giant, or gyrate (serpiginous, linear, or arciform) wheals (Figs. 1 and 2; Table 1). In cases with severe dermal edema, oozing of serum from the skin surface and possibly, cracking and superficial sloughing of the hair and skin that resembles pyoderma and vasculitis may be noted. Angioedematous reactions are SC, localized to generalized, gravity dependent fluid swellings that are variably pruritic, and may have serum leakage or hemorrhage. The pattern of distribution includes the head, extremities, and, ventral abdomen and thorax. Angioedema may be a cutaneous manifestation of systemic and/or serious disease.

4. Underlying Etiologies
Urticaria and angioedema are symptoms rather than specific disease entities. It is often seen just before races (perhaps psychogenic) or in association with insect or arthropod envenomation, various infections (strangles, dermatophytosis, dermatophillosis, dourine, babesiasis, surra, horse pox, or mal de caderas), intestinal parasitism (Cyathostomosis), topical applications (especially parasiticidal sprays, dips, and pour-ons), systemic medicaments (especially trimethoprim potentiated sulfonamides, penicillin, phenylbutazone, ivermectin, aspirin, guaiphenesin, phenothiazine, streptomycin, oxytetracycline, gas anesthesia, or iron dextran), feedstuffs (pasture plants or concentrates), contactants (saddle soaps, leather conditioners, or tack), various biologicals (strangles, encephalomyelitis, and salmonellosis vaccines or botulinum and tetanus toxoids), snake bites, hypodermiasis, erythema multiforme, inhalants (pollens, molds, or chemicals), purpura hemorrhagica, plants (stinging nettle), hematoma (especially hemophilias), lymphangitis, abscess/pyoderma, cellulitis, vasculitis (immune mediated and photoactivated), lymphoreticular neoplasia, mast cell tumor, or amyloidosis.1,2,4–10

5. Diagnosis
Based on the extensive list of potential causes, a veterinarian’s task can seem ominous. Careful examination of the horse’s history and environment are key to establishing a possible etiology. For instance, the sudden onset of wheals associated with the administration of a drug renders the cause readily apparent. A protracted history may be more difficult to decipher, because eruptions wax and wane, environmental challenges occur daily, and medications are often used concurrently with feed supplements.
Physical urticaria (dermatographism) is easily distinguished by drawing a pattern on the skin with a blunt object. Within 10–15 min, a positive reaction is denoted by marked edematous swelling of the inscribed pattern. Historical evidence of dermatographism includes swelling involving areas of light pressure such as under the saddle, bridle, or girth. Temperature sensitive urticaria will similarly develop edematous swelling within 15 min of cold (ice cube) or heat (hot pack hand warmers) application to the skin. Exercise-induced urticaria and cholinergic urticaria are easily confused. Cholinergic urticaria results from an increase, either active (exercise related) or passive (hot bath), in body core temperature, whereas exercise-induced urticaria requires the active stimulus of exercise.4,11

Skin scrapings, fungal cultures, impression smears, and serology are valuable diagnostic tools if an infectious etiology is suspected. Biopsies may help to rule out other potential etiologies. Biopsies are recommended when the lesions are firmer than expected or when the disease has been ongoing (>2 mo). A dermatopathologist with an interest in equine dermatology is advised, especially if secondary self-inflicted trauma is involved. Typical histopathologic findings of urticaria or angioedema vary from a simple vascular dilatation and edema in the superficial and middle dermis to pure perivascular dermatitis with varying numbers of mononuclear cells, neutrophils, mast cells, and eosinophils.2

In challenging cases, immunohistochemical evaluation of IgE bearing cells may distinguish between common clinical differentials, such as insect bite hypersensitivity, and pemphigus.12 Laboratory tests may provide confusing results when evaluating urticaria and angioedema. This is exemplified by a case of a Paso Fino stallion that was cultured dermatophyte positive (Trichophyton mentagrophytes) and histologically diagnosed with urticaria; however, the horse had negative findings on special stains.4 Successful treatment was achieved with antifungal therapy for the dermatophytosis and IV dexamethasone for the urticaria. It was suspected that the ringworm infection resulted in an "id" reaction, an immunologic response of the skin to systematically absorbed fungal antigens.

In this author’s opinion, allergy testing for urticaria is warranted if the history coincides with a clinical case that is recurrent or persists for >8 wk. Allergy testing should not be used to diagnose atopy. Rather, it is a means of confirming your clinical suspicions and formulating a treatment plan involving both avoidance and allergen specific immunotherapy. Positive reactions indicate that antigen specific IgE is present in the patient; it does not indicate that the antigen in question caused the disease. Therefore, careful historical evaluation and correlation with reactions is important for hyposensitization success. Serologic testing is available through Greer Laboratories,a Spectrum Laboratories,b Heska Corporation,c and Bio-Medical Services.d Serologic testing can be quite expensive; however, recent series of studies from the Ohio State University concurred with previous findings that intradermal allergy testing is more reliable than serologic testing.13–16

Intradermal allergy testing (IDT) does require sedation, shaving, withdrawal from essential fatty acids, antihistamines, and topical steroids for 7–14 days, and withdrawal from oral/injectable glucocorticoids for 7–28 days. This author has performed IDT on cases that have received injectable diphenhydramine and glucocorticoids shortly before allergy testing, and significant results were still obtained (Fig. 3). Therefore, withdrawal from anti-inflammatory medications does not seem as crucial in horses as it does in dogs and cats. A detailed review of the testing method has recently been reviewed.13–16 The tests are tailored to specific geographic regions using small animal test concentrations/allergens with additional insects and outdoor allergens to account for the horse’s exposure. This author tends to read test reactions at 30 min and 4 h after inoculation and omits the 24-m and 48-h reactions because of the questionable value of the delayed responses for immunotherapy and feasibility in practice. Evaluating size and especially turgidity of the wheals is very important, and it requires the expertise of an allergist to minimize false positive/negative reactions.17

Dietary trials are the only way to diagnose food hypersensitivity or intolerance. The author’s current approach consists of a 4–6-wk trial with novel food sources such as timothy, rolled oats, alfalfa, or barley, if not routinely fed, because these items are easily obtainable single source foods. Discontinuation of unnecessary supplements, vitamins, and other drugs is mandatory throughout the trial period. After the urticaria has resolved, confirmation of food allergy is achieved by challenging with one
item weekly and monitoring for exacerbation of clinical signs (typically 24–72 h).

Unless a specific etiology is identified, treatment is often frustrating, because recurrences are common. Acute cases of idiopathic urticaria can be treated successfully with antihistamines, glucocorticoids, and/or epinephrine. The optimal treatment involves avoidance or reduced allergen exposure. Unfortunately, this is often impractical but may include moving to a different part of the country or simply down the road to another stable, restricting indoor/outdoor activity (depending on IDT reactions), and/or providing rubber mats and pelleted rations to decrease dust. Short-term symptomatic therapy includes antihistamines, essential fatty acids, and glucocorticoids (Table 2). For chronic cases where an allergic dermatitis is suspected, allergen specific immunotherapy (ASIT) provides optimal responses, and it can be used to address not only urticaria but also pruritus and recurrent airway obstruction (RAO) cases. ASIT carries the fewest long-term side effects, provides more rapid responses than those seen in dogs and cats, and provides the most cost-effective and least treatment intensive option compared with symptomatic therapy in horses. ASIT also provides an alternative treatment modality that precludes drug testing and allows competitive horses to re-

<table>
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<tr>
<th>Table 1. Clinical Classification of Urticaria/Angioedema</th>
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<tr>
<td>I. Conventional urticaria:</td>
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<tr>
<td>a. Papules and wheals that vary from 2 mm to 5 cm in diameter.</td>
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<tr>
<td>II. Papular urticaria:</td>
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<tr>
<td>a. Small, 3 to 6-mm-diameter papules</td>
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<td>b. Most often associated with stinging insects, especially mosquitoes and culicoides.</td>
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<tr>
<td>III. Giant urticaria:</td>
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<tr>
<td>a. Large wheals up to 20–40 cm in diameter</td>
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<tr>
<td>b. Consider vasculitis a serious differential/complication</td>
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<td>IV. Exudative urticaria:</td>
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<tr>
<td>a. Severe dermal edema oozes from the skin, mats the hairs, and eventually causes alopecia.</td>
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<tr>
<td>b. Often mistaken for pyoderma or pemphigus</td>
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<tr>
<td>V. Gyrate (polycyclic) urticaria:</td>
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<tr>
<td>a. Arciform, serpiginous, or doughnut shaped</td>
</tr>
<tr>
<td>b. Often associated with drug reactions</td>
</tr>
<tr>
<td>c. Can persist for months</td>
</tr>
<tr>
<td>d. Major differential is erythema multiforme that typically do not exhibit pitting with digital pressure.</td>
</tr>
<tr>
<td>VI. Angioedema (angioneurotic edema):</td>
</tr>
<tr>
<td>a. Involves large areas of subcutaneous tissues</td>
</tr>
<tr>
<td>b. More diffuse and involves the head and/or gravity dependent extremities</td>
</tr>
<tr>
<td>c. Cutaneous marker for a more systemic and serious disease than urticaria.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2. Symptomatic Treatment of Urticaria/Angioedema</th>
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<tbody>
<tr>
<td>Epinephrine</td>
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<tr>
<td>3 to 5 ml of a 1:100 solution, SQ or IM</td>
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<tr>
<td>Lifesaving for severe angioedematous reactions</td>
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<tr>
<td>Antihistamines</td>
</tr>
<tr>
<td>Hydroxyzine hydrochloride @ 1–1.5 mg/kg q 8 h</td>
</tr>
<tr>
<td>Doxepin hydrochloride @ 0.5–0.75 mg/kg q 12 h</td>
</tr>
<tr>
<td>Diphenhydramine @ 0.75–1 mg/kg q 12 h</td>
</tr>
<tr>
<td>Chlorpheniramine @ 0.25 mg/kg q 12 h</td>
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<tr>
<td>Side effects include light sedation, occasional personality changes, +/+ teratogenicity</td>
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<tr>
<td>AQHA recommended withdrawal is 10 days before any show or competition</td>
</tr>
<tr>
<td>Corticosteroids</td>
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<tr>
<td>Prednisolone</td>
</tr>
<tr>
<td>0.5–1.5 mg/kg/day 7–14 days, then taper to 0.2–0.5 mg/kg q 48 h over 2–5 wk</td>
</tr>
<tr>
<td>Dexamethasone</td>
</tr>
<tr>
<td>Loading/pulse dose at 0.02–0.1 mg/kg/day IV for 2–3 days, then oral maintenance dose of 0.01–0.02 mg/kg q 48–72 h</td>
</tr>
<tr>
<td>This regimen is particularly helpful in more refractory cases</td>
</tr>
<tr>
<td>Fatty acid supplementation</td>
</tr>
<tr>
<td>DVMs Derm Caps or 3VCaps Liquid Econo @ double the dose/day</td>
</tr>
<tr>
<td>Allerderms EFA Caps HP @ double the dose/day</td>
</tr>
<tr>
<td>Vet Solutions EFA @ 2 2/3 pumps per 50 kg/day</td>
</tr>
</tbody>
</table>
turn to performance standards without jeopardizing the owner’s ethics.

6. Prognosis

The prognosis for urticarial reactions is good, because general health is not usually affected. The prognosis for angioedema varies with the severity and location. Angioedematous reactions involving the nasal passages, pharynx, and larynx may be fatal if not immediately addressed.

References and Footnotes


*Greer Laboratories, Lenoir, NC 28645.
†Spectrum Laboratories, Mesa, AZ 85204.
‡Heska Corporation, Fort Collins, CO 80525.
§Bio-Medical Services, Austin, TX 78759.
III. Crusting and Ulcerative Lesions

Cutaneous Equine Sarcoidosis (a Subset of Equine Idiopathic Granulomatous Disease [IGD])

Anthony A. Yu, DVM, MS, Diplomate ACVD

1. Introduction

Cutaneous equine sarcoidosis (CES) is a subset of equine idiopathic granulomatous disease (IGD). Also referred to as systemic granulomatous disease, generalized granulomatous disease, equine histiocytic disease, and equine histiocytic dermatitis, CES is a rare condition in horses. CES is an idiopathic scaling and crusting disorder that histopathologically resembles the condition described in humans, which is believed to be an aberrant reaction to an infectious agent/antigen. A similar reaction occurs in the lungs (granulomatous pneumonia [GP]) and gastrointestinal system (granulomatous enteritis [GE]) in horses. In a recent review of nine horses with CES, skin lesions were found on horses with GE and GP, and 5 of 9 CES cases also had lung involvement. It has been proposed to classify the three subsets under an encompassing term of equine IGD.

Hairy vetch (Vicia villosa) has been reported to produce a similar reaction pattern in cattle and horses; however, many subsequent cases have not had this risk factor. Thus far, an infectious etiology for CES, including *Mycobacteria, Borrelia, Coccidioides, Cryptococcus*, and *Corynebacteria* has not been determined using histopathology, immunohistochemistry, or polymerase chain. A response to steroids would mean that CES is caused by an immune mediated reaction rather than infectious etiology.

2. Signalment

Although no age, sex, or breed predisposition has been cited in literature, a recent study did reveal a predisposition in gelding Thoroughbreds when nine cases were reviewed over 16 yr. Ages ranged from 5 to 21 yr.

3. Clinical Findings

Cutaneous lesions typically start with crusts, scales, alopecia, and pruritus involving the limbs (legs, thighs, and elbows), thorax, neck, head/face, ventral abdomen, back, and ears and spread gradually to cause a generalized exfoliative dermatitis sparing the mane and tail (Figs. 1 and 2). Although reported, nodular lesions are quite rare. Peripheral lymphadenopathy, however, is quite common. Recognition of the cutaneous lesions prompts the clinician to investigate other organ involvement, particularly the respiratory and gastrointestinal systems and to a lesser extent, the liver and kidneys. Weight loss, intractable diarrhea, exercise intolerance, dyspnea, diminished appetite, ventral edema,
If malabsorption/GE is present, it is recommended that medications be given parenterally where possible. Also included in my initial protocol are the use of essential fatty acids, shampooy therapy, and pentoxifylline. Adding essential fatty acids at the recommended daily dose may help reduce the scaling by replenishing the corneal lipid envelope and providing membrane stabilizing effects. Shampoo therapy (Universal Medicated Shampoo or Sebolux) enhances keratolysis and keratoplasty and provides topical antimicrobial protection. Pentoxifylline (10 mg/kg, q 8–12 h) has rheologic activity that may improve drug delivery into granulomatous tissue and minimize the risk of laminitis while administering steroids. Additionally, pentoxifylline has anti-inflammatory properties, namely anti-tumor necrosis factor-α, which potentially allows for a synergistic tapering of steroids. Some cases of CES have spontaneously resolved, and therefore, tapering of medications to the lowest dose possible or in total is always advised.6,7

If minimal response is noted to the above protocol, adding azathioprine (3 mg/kg daily) for 30–60 days and then tapering to every other day alternating with steroids may provide some benefit. Systemic antibiotics should always be considered in severe generalized cases (trimethoprim sulfa, 15–30 mg/kg, q 12 h for 30 days) where a primary or secondary infection may be suspected.

7. Prognosis
The prognosis for cases limited to cutaneous involvement tends to be better (>12 yr) than those with concurrent internal organ disease, especially if signs of weight loss/wasting exist.6 As spontaneous remission has been reported, treatment should be attempted in all cases.6,7 Most horses with internal involvement, however, tend to decline over several months and are eventually humanely euthanized.

References and Footnotes

Fig. 2. Close-up of horse in Fig 1. with sarcoidosis. Note the sheets of scale emanating from the skin and caught in the hairs, characteristic of an advanced case of sarcoidosis.
Pemphigus
Anthony A. Yu, DVM, MS, Diplomate ACVD

1. Introduction
Pemphigus foliaceus, first described in this species in 1981, is the most common autoimmune skin disease in the horse. Several forms of pemphigus exist including pemphigus foliaceus, pemphigus vulgaris (very rare), drug-induced pemphigus, and paraneoplastic pemphigus. The most commonly reported form is that of pemphigus foliaceus. Pemphigus foliaceus in humans is a result of the production of autoantibodies directed against cell adhesion proteins, particularly the desmosomal antigens (desmoglein 1 [DSG1] in pemphigus foliaceus and DSG3 in pemphigus vulgaris) of the stratified squamous epithelium. The antibody antigen complex moves through multiple pathways and then incites acantholysis. A similar pathway is hypothesized for the dog and horse based on the detection of DSG1 in immunoblotting/immunoprecipitation studies. Several trigger factors have been proposed including drugs, systemic disease, neoplasia, stressful situations, and lastly, allergies (foods, inhalants, insects) based on the presence of case clusters and seasonality (Figs. 1–5).

2. Signalment
Pemphigus presents in both adult horses (≥5 yr of age) and foals (<yr of age). This age dichotomy may not be obvious in all populations. Younger horses often carry a better prognosis and potential for spontaneous remission without relapses. Of the specific horse breeds, Appaloosas, Quarter Horses, and Thoroughbreds seem to be at greater risk, although this may have some geographic variability. At this time, there does not seem to be any evidence of sex predilection. Pemphigus has been known to have a waxing and waning course, and there may also be a seasonal incidence of the condition, potentially caused by allergen load (pollens, insects) and/or the increased use of preventative medications (dewormers, vaccines, supplements, etc.).

3. Clinical Signs
Classic clinical findings of vesicles and pustules are rarely noted in the horse, because lesions of pemphigus progress rapidly to crusts, exfoliation, erosions, alopecia, and scaling (Fig. 6). In fact,
Transient, persistent, or recurrent urticaria may precede actual crusts. Pruritus, pain, and edema resulting in a stiff gaited lameness are variable. Lesions tend to begin on the face or limbs and spread to the rest of the body in days to weeks (Figs. 7–12). A localized form restricted to the coronary bands can also be seen. Mucosal lesions are extremely rare. Although internal organs are not involved, systemic signs including depression, poor appetite, weight loss, fever, and lethargy are often noted and expressed in the complete blood count (CBC) and serum chemistry profile changes including anemia, leukocytosis, neutrophilia, hyperglobulinemia, and hypoalbuminemia.

4. Differential Diagnosis
Differential diagnoses include dermatophilosis, dermatophytosis, *Staphylococcal* folliculitis, sys-
5. Diagnosis

Diagnosis is based on history, clinical findings, skin cytology, and dermatohistopathologic findings. Cytologic sampling is ideally performed from intact pustules; however, impression smears from both the skin and under the surface of a teased crust will often be rewarding. Single or rafts of acantholytic cells that are 10–20 times the size of surrounding neutrophils can be found on cytologic evaluation using a Diff-Quik stain (Fig. 13). Characteristically, there is little to no evidence of bacteria, and neutrophils/eosinophils have a healthy appearance (no evidence of toxic changes). Based on these findings, multiple skin biopsies should be taken to confirm the diagnosis. Primary vesicles or pustules, if present, are ideal, and crusted sites are the next best choice for multiple biopsies. Surgical preparation of biopsy sites is not recommended, because the crusts may contain the acantholytic cells necessary for diagnosis. Dermatopathologic findings include subcorneal and/or intraepidermal pustules, spanning multiple hair follicles associated with marked acantholysis, neutrophils, and occasionally, eosinophils. As *Trichophyton equinum* may mimic the clinical and histological appearance of pemphigus (crusts and acantholytic cells), fungal stains should be performed on all biopsies suggestive of pemphigus. Immunohistochemical staining has taken precedence over immunofluores-
cence because of the ability of the former method to detect autoantibodies within formalin fixed tissues (e.g., immunoperoxidase) rather than the need for special handling of skin samples for direct immunofluorescence. The use of immunoprecipitation has been reported in one horse with paraneoplastic pemphigus. This technology is currently available for use in human dermatology to confirm the diagnosis and act as a prognosticating tool when evaluating response to therapy. Species specific tests are being investigated for the dog and hopefully, for the horse in the near future.

6. Treatment

Before starting therapy, baseline and follow-up bloodwork (CBC and biochemical profile) are recommended to monitor the effect of the immunosuppressive regimen. Multimodal therapy is often necessary for the treatment of pemphigus in horses and includes the following treatment.

- Essential fatty acids: DermCaps 100s, 1 capsule/50–100 kg, q 12 h.
- Vitamin E: 13 IU/kg/day.
- Decreased exposure to sun (photoaggravated disorder).
- High doses of corticosteroids.
- Dexamethasone at an induction dose of 0.02–0.1 mg/kg/day PO or IV for 7–10 days and then tapering to 0.01–0.02 mg/kg, q 48–72 h.
- Prednisolone at 1.5–2.5 mg/kg/day for a 7–10 day period and then tapering over several weeks to a maintenance dose of 0.5–1 mg/kg, q 48 h. This is preferred if low albumin is detected.
- Pentoxifylline at 8–10 mg/kg, 2–3 times/day and then tapering after steroids have been minimized.
- Azathioprine at 2–3 mg/kg, q 24 h, PO for 3–4 wk and then tapering to every other day. Therefore, low (1–7%) bioavailability can be costly to maintain.
- Injectable gold salts: aurothioglucose (no longer available) or aurothiomalate. Test doses of 20 and 50 mg at weekly intervals. If no abnormal reactions, 1 mg/kg, IM weekly for 6–12 wk and then tapering to every 2- to 3-wk injections until weaned off entirely. This is often used in conjunction with steroids during the initial induction phase.
- Monitor CBC for bone marrow suppression (thrombocytopenia), drug reactions (eosinophilia), and glomerulonephritis (proteinuria).
Eliminate inciting factor (i.e., tumor extirpation in paraneoplastic pemphigus).

7. Prognosis
Management in horses may take weeks or months to control. It is not without complications including hepatopathies and reported laminitis when using glucocorticoids, bone marrow suppression, and adverse drug reactions with adjunctive immunosuppressive therapy. Typically, an initial response is noted within 7–14 days, and then medication can be tapered 20% every 1–2 wk based on individual responses. Young horses have an excellent prognosis for remission and little chance of relapse, whereas mature horses tend to have a less favorable prognosis (46%); typically, lifelong therapy is necessary for control of the condition. If a trigger factor can be identified and eliminated, therapy should be tapered and potentially discontinued.

Fig. 10.

Fig. 11.

Fig. 12.

Fig. 13. Cytology from crust of an equine pemphigus foliaceus case shows acantholytic cells 10–20 times the size of surrounding neutrophils, and deep blue staining cytoplasm, and a central nucleus. Note that there is no evidence of bacteria, and neutrophils/eosinophils have a healthy appearance (no evidence of toxic changes).
References and Footnotes


Hereditary Diseases

Stephen D. White, DVM, Diplomate ACVD

1. Introduction

Epidermolysis bullosa (EB) includes a number of diseases typified in humans by the common finding of blister formation after minor trauma. Most forms are congenital and apparent soon after birth. In animals and humans, subsets of EB are classified by the histologic location of the blister or cleft. These subtypes (and respective cleft locations) are termed EB simplex (basal cell layer of the epidermis), junctional EB (intralamina lucida or basal cell layer), and dystrophic EB (sublamina densa).

Junctional EB has been reported in Belgian foals of both sexes as well as other breeds and a donkey.1–4 Lesions are usually noted within 3 days of birth and include multiple asymmetrical irregular skin erosions and ulcers that are often encrusted. Lesions may be especially prominent around the coronary bands (causing the hoof to crack and slough) and on the oral, anal, and genital mucosa. Histology and ultrastructural findings point to a cleft in the intralamina lucida of the basement membrane zone. This is presumably caused by a defect in the anchoring filaments that connect the basement membrane to filaments in the superficial dermis.2 A laminin-5 defect has been shown in Belgians and in two French draft breeds (Trait Breton and Trait Comtois); the mutation is a cytosine insertion in exon 10 of the LAMC2 gene.1,7–7 Because of this knowledge, the Veterinary Genetics Laboratory at the University of California at Davis offers a diagnostic test to determine carrier status (available online at www.vgl.ucdavis.edu/service/horse/index.html) in Belgian Draft horses and related breeds.

Clinical presentation and the age of the foal are highly suggestive of the diagnosis. Histology and ideally, electron microscopy are required to confirm the diagnosis. There is no known treatment, and affected horses, as well as the sires and dams of affected horses, should not be bred; the mode of inheritance is autosomal recessive.

This disease differs from epitheliogenesis imperfecta (see below). At first, EB does not present large areas of the skin are devoid of epidermis, but rather, the skin is later lost because of the fibril defect.

Epitheliogenesis imperfecta (aplasia cutis) is an inherited, congenital discontinuity of squamous epithelium. It is thought to be an autosomal recessive trait, and it has been reported in several breeds. Lesions are most common on the limbs, head, and tongue. Hooves may slough in severe cases. Clinical presentation is usually diagnostic.5 In moderately to severely affected animals, the disease is fatal within a few days, because the foal usually dies of septicemia or other developmental abnormalities. Mildly affected areas may heal by scar formation. More recent reports would suggest that some of these horses with epitheliogenesis imperfecta (Saddlebreds) may, in fact, have a condition similar to the junctional EB common in Belgian foals.9–11

Hereditary equine regional dermal asthenia (HERDA; “hyperelastosis cutis”) is a disease that occurs early in life in horses. Most affected horses are Quarter Horses, but registered Paint Horses and Appaloosas with Quarter Horse lineage have been afflicted with this disease.12,13 Many of the Quarter Horses are from high-quality cutting lines. The disease (or something very similar) has also been reported in a cross-bred Arabian mare, a Thoroughbred gelding, a Hanoverian foal, and a Hafflinger horse.14–17

The working hypothesis is that these horses have a defect in their collagen fibers or in the way those fibers are structurally organized in the mid to deep dermis. Typically, these areas are over the back and sides of the neck (Fig. 1). The skin in these areas may seem to be easily torn or stretched, and it often develops seromas and hematomas (“blisters” filled with either serum or blood) (Fig. 2). Healing per se is usually adequate but often leaves rather unsightly scars. Diagnosis is often based on the
clinical signs alone; histologic findings are sometimes subtle, but “clumped” or poorly organized collagen fibers below the level of the hair follicles may be seen. A zone of mid- to deep-dermal separation has been reported in two horses, and it has been present in some of the biopsy samples that the author has seen. Poorly oriented” collagen fibers are sometimes seen on electron microscopy. There is no blood test to confirm the disease.

This condition is almost certainly present at birth; however, it is often not noticed until ~2 yr of age when horses start being trained with tack, and the friction/trauma of this induces the typical lesions. As with many genetic diseases, there is no effective treatment or cure, but some of these horses have been maintained as “pasture pets.”

This disease follows an autosomal recessive mode of inheritance; therefore, for the foal to be affected, both the sire and the dam must carry the gene, and if they were bred again, there would be ~25% chance that the next foal would also be affected. At the present time, there is no test available to verify carriers. Obviously, clinically affected horses with the disease should be removed from breeding programs.

Progressive chronic lymphedema is the tentative term for a condition seen in Shires, Clydesdales, and Belgians. It is characterized by progressive swelling, hyperkeratosis (thickening), and fibrosis (hardening) of the skin on the lower legs. This chronic progressive disease starts at an early age, progresses throughout the life of the horse, and often ends in disfigurement and disability of the limbs. Inevitably, this condition leads to the horse’s premature death. In the Belgian draft horse, it has reduced the average life expectancy of a stallion from 20 to 6 yr.

The pathologic changes and clinical signs closely resemble a condition known in humans as chronic lymphedema or elephantiasis nostras verrucosa. The lower leg swelling is caused by abnormal functioning of the lymphatic system in the skin, which results in chronic lymphedema (swelling), fibrosis, a compromised immune system, and subsequent secondary infections of the skin. Based on preliminary research, it seems that a similar pathogenic
mechanism is involved in the disease that affects these specific draft horse breeds.

The clinical signs of this disease are highly variable. The earliest lesions are characterized by skin thickening and crusting; both are often visible only after clipping the long feathering. Secondary infections develop very easily in these horse’s legs and usually consist of either chorioptic mange or bacterial infections. Both dark and white skin on the lower legs are equally affected. These lesions are consistent with pastern dermatitis, which is certainly seen in other breeds. In Shires, Clydesdales, and Belgians, however, these lesions do not respond well to therapy.

As the disease progresses, 1–2 thick skin folds and sometimes multiple small, well-demarcated ulcerations develop predominantly in the rear of the pastern region. The ulcerations are covered with adherent crusts. Manual removal of the crusts and even movement during exercise results in bleeding. These small sores may seem to respond initially to various topical medications, but they often reverse course, only to progress in severity and multiply in number. Small lesions tend to coalesce into larger and more intractable (resistant to cure) areas of skin ulceration. Over time, the lesions extend up the leg, often affecting the skin as high as the knees or hocks. These lesions are, at the very least, irritating and bothersome to the horses and at times, can be quite painful. Severely affected individuals often exhibit generalized swelling in all four legs.

This condition is thought to be primarily a lymph-system disease, and the pastern dermatitis in these draft horses is a secondary result caused by the body’s inability to properly supply fluids and oxygenate the skin of the lower leg. The lymphatics break down over time, and protein-rich fluid leaks into the tissues of the lower leg, which results in fibrosis of the tissues under the skin and thickening of the skin itself. The tissue fibrosis leads to even more blockage of fluid within the legs, thereby inhibiting proper circulatory flow. This results in neovascularization; this is a process by which the body develops new blood vessels in a futile attempt to provide oxygen to its tissues.

Researchers suspect that a deficiency or abnormality in a connective tissue component known as elastin is the underlying element and perhaps, the cause of the lymphatic degeneration in these horses. In affected animals, the lymph vessels and deep tissues of the skin do not have sufficient amounts or proper configuration of elastin. The lack of this critical tissue element apparently instigates the progression of disease and the chronic progression of clinical signs.

As the condition becomes more chronic, the lower leg enlargement becomes permanent, and the swelling is firm on palpation. More thick skin folds and large, poorly defined, firm nodules develop. The nodules may become quite large and are often described as “golf ball” or even “baseball” in size. Both skin folds and nodules first develop in the back of the pastern area. With progression, they may extend and encircle the entire lower leg. The nodules become a mechanical problem, because they interfere with free movement and are frequently injured during exercise. This disease often progresses to include massive secondary infections that produce copious amounts of foul-smelling exudates, generalized illness, debilitation, and even death.20,21

In a recent report on what may be the same condition in several draft breeds, the authors found a perivascular dermatitis dominated by T lymphocytes with an increase in major histocompatibility complex (MHC) class II–positive dendritic-like cells. Immunohistochemical labeling for cytokeratins (CK) 5/6, CK10, and CK14 indicated a change in their expression pattern. This correlated with the degree of epidermal hyperplasia, indicating abnormal differentiation of keratinocytes. There was a statistically significant correlation between the severity of skin lesions and several other factors including increasing age, increasing cannon circumference, prominence of anatomical structures such as fetlock tufts of hairs, ergots, and chestnuts, and bulges in the fetlock region.22

References


