DIFFERENTIAL DIAGNOSIS OF NODULAR SKIN DISEASE

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The first thing to remember is that:

‘A lump is just a lump, and a bump is just a bump, until you biopsy’ (Dr. Danny Scott, Cornell University)

This does not mean that one has to biopsy every nodule to do a decent job in equine practice. It does mean that a biopsy should be recommended if empirical treatments have not been effective or have made the lesion worse. Recall that suspected sarcoids should only be biopsied if the owners are informed about treatment options should the lesion become more ‘aggressive’.

Neoplasms of the Skin

Equine Sarcoid
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Epidemiology and Pathogenesis
The equine sarcoid was first reported by Jackson in 1936.1 It is the most common tumor in equidae (horses, mules, and donkeys) worldwide and accounts for > 50% of cutaneous tumors. It has also been reported in zebras and tapirs.1a,b

Sarcoids are locally aggressive, non-regressing, fibroblastic tumors of the dermis and subcutis with a variable proliferative epithelial component. This dual involvement of the epidermis and the dermis is the hallmark of sarcoids and explains the multiple and evolving clinical appearance of the tumor. The epidermal component of sarcoids shares features of a benign papilloma and the fibroblastic component is consistent with a low grade fibrosarcoma.2 These characteristics lead to an incorrect histological diagnosis of fibrosarcoma or nerve sheath tumors when the surrounding skin is not included in the tissue analyzed.3

In spite of numerous clinical reports on sarcoids, the clinical and epidemiologic data are still puzzling. The inconsistent and sometimes conflicting data do not support any gender, breed, age and genetic predispositions or any anatomic predilection.4 These data reflect in part the frequent lack of histological confirmation of the disease in reported studies and may represent regional or national variations of the clinical characteristics of sarcoids.

Epidemiologic evidence of a causative agent comes from the fact that age is not a risk factor unlike spontaneous tumors, affected horses are likely to have a synchronous or metachronous lesions and anecdotal sarcoid outbreaks have been reported.4,5 Although papillomaviruses are strictly species specific, it is widely accepted that Bovine Papillomavirus (BPV) types 1 and 2 are associated with the pathogenesis of sarcoid disease; BPV1 more commonly found in Europe and type 2 in western US. However, full viral life cycle has never been demonstrated in equidae and viral particles have never been detected in lesions. Hence, the disease is understood as the result of an abortive infection where BPV gene sequences exists episomally (as free genetic material in a cell) or integrated in host DNA.8-10 The presence of viral genetic material is apparently necessary for tumor development. It is always BPV DNA...
sequences that are always found in sarcoids. Equine sarcoids can be transformed in vitro following BPV-1 infection. Detection of sequences of early-expressed genes of the viral genome including E5, E6, E7 and occasionally E2 is consistently found in sarcoïd tumors and surrounding normal cutaneous margins but not in other tumor types. Both the epithelial and fibroblastic components of the tumor contain unique viral gene sequences that are actively transcribed. However, it is not sufficient to produce the disease and its role in the etiology of sarcoïds continues to be questioned. BPV DNA sequences have been detected in healthy skins of horses not known to have ever been in contact with a source of BPV and in some cases of dermatitis. In addition, the presence of viral DNA sequences has also been reported in skin swabs of unaffected horses and PBMC of horses with unrelated skin lesions (abscess, carcinoma and hoof canker).

Experimental transmission studies of sarcoïds have been unsuccessful. Inoculation of sarcoïd cell-free extract in cows does not induce warts nor does it induce sarcoïds in unaffected horses. Experimental cutaneous infection with the bovine papilloma virus induces fibropapillomas clinically similar to sarcoïds. The lesions, however, regress spontaneously with production of neutralizing antibodies to the virus and viral DNA sequences in white blood cells. The infection in horses is considered abortive because the BPV virus cannot replicate in horses nor be serially passaged from BPV-induced fibropapillomas. An alternative theory is that an equine variant of BPV may be the cause of sarcoïds.

The mode of transmission of the disease is unknown and does not require contact with cattle. Intradermal injection of primary sarcoïd fibroblasts containing viral episomes, naked full-length BPV-1 genome, or transforming genes (E5 and E7) does not induce sarcoïds in horses and donkeys. Because only complete BPV virions can induce transformation, contamination cannot occur by casual contact with contaminated fomites or affected horses, by BPV-infected insect bites or blood samples. As a result horses are considered to be nonpermissive hosts for BPV and horizontal BPV transmission remains to be documented.27

**Biologic behavior:** Sarcoïds represent a wide spectrum of fibroblastic tumors ranging from indolent apparently benign lesions to aggressive and invasive tumors. Clinically many sarcoïds behave initially as benign lesions because they are slow growing giving the false impression that the lesion is inactive. In addition, sarcoïds are frequently classified as biologically benign tumors because they do not metastasize to distant organs and regional lymphatic metastasis is rare and usually associated with multiple unsuccessful treatments. However, the equine sarcoïd is not a benign tumor because it is a progressive disease that invades and destroys surrounding normal tissue, does not regress spontaneously, and recurs predictably after surgical mass removal. Early lesions are restricted to the dermis and epidermis, but advanced lesions commonly invade the subcutis and may extend through fascia into deeper muscular structures. Considering sarcoïds as benign tumors leads to inappropriate management early in the course of the disease and thus to multiple recurrences, and results in unsatisfactory cosmetic and functional outcomes as well as unnecessary expenses to control the disease.

**Diagnosis**

Sarcoïds are recognized as having different multiple clinical manifestations including occult, verrucous and nodular clinical types. In addition approximately one-third of affected horses have multiple sarcoïds at different clinical stages at the time of diagnosis. The different clinical aspects represent stages of tumor progression and reflect the relative predominance of the dermal or epidermal component. Lesions with a predominant epidermal component include occult and verrucous sarcoïds. Occult sarcoïds appear as an almost circular area of alopecia with a grey scaly surface. Verrucous sarcoïds may be sessile (flat variety) or pedunculated (warty variety); the skin is thickened with a dry rough surface,
with partial or total alopecia. Nodular sarcoids, also called fibroblastic sarcoids, range in appearance from a dermal/subcutaneous nodule to a large exophytic mass with a skin surface that eventually ulcerates. The nodular type is locally invasive, destroying adjacent tissues and may ultimately infiltrate lymphatic vessels, and nerve sheaths and disseminate to form regional metastases. Mixed forms represent a transition from one type to another. The multiplicity of recognized clinical forms confirms the equivocal and progressive nature of the disease.

The polymorphic appearance of sarcoids and the diverse list of differentials make the clinical diagnosis of sarcoids unreliable. The diagnosis and treatment of sarcoids require a biopsy because they are often over-diagnosed clinically. In a review of 681 horses referred to the Equine Oncology Clinic at the University of California Veterinary Medical Teaching Hospital (UCD VMTH) for evaluation and treatment of clinically diagnosed sarcoids, 31% of lesions were found to be non-neoplastic dermatologic conditions. Conversely, a recent report showed an 80% chance of accuracy in judging such lesions solely on the basis of clinical presentation. After ruling out a non-neoplastic skin condition, any clinically suspicious lesion should be biopsied. As with any tumor, early recognition and treatment of a small lesion is always associated with a better prognosis. It is important to keep in mind that any large and invasive sarcode associated with a poor prognosis was, earlier in its evolution, an apparently inactive small lesion that was not recognized or was neglected. There is no contraindication for a biopsy of a suspicious skin lesion as long as definitive and effective treatment is instituted immediately after the diagnosis is made. There should not be any fear about performing a biopsy of a suspected sarcode because very effective treatments are available. However, a biopsy like any trauma can increase proliferation of a previously slow-growing tumor and may accelerate tumor progression. As a result, a biopsy should not be recommended if the owner is not willing to pursue treatment, if needed, because the process of biopsy without subsequent treatment has the same effect on overall prognosis as an unsuccessful attempt at treatment.

**Treatment**

Sarcoids are low grade fibrosarcomas and share common features of soft tissue sarcomas. They are locally invasive and tend to infiltrate into surrounding normal tissues through and along fascial planes 2-4 cm from the palpable tumor mass. Treatments that are used can be broadly grouped into ablative (surgery, laser vaporization, cryotherapy, hyperthermia and caustic ointments), cytotoxic (radiation therapy, chemotherapy) and biologic (immunotherapy) modalities. The overall treatment goals are to 1) destroy all tumor cells in the gross tumor and also in the normal appearing surrounding tissues and 2) to minimize damage to healthy tissues. These goals are difficult to achieve with ablative treatment methods because they are not selective against tumor cells. A cuff of surrounding of normal tissue containing microscopic disease must be ablated to remove all tumor cells. Early complete surgical resection has a central role in the treatment of sarcoid. Alternate ablative modalities have no oncologic benefits over a well-planned conventional surgery and do not allow histopathological evaluation of surgical margins to assess the quality of the procedure. Topical applications of escharotics with zinc-chloride-based caustic ointments or 5-FU cream or retinoids are used empirically for treatment of sarcoids. Unfortunately, no evidence-based data have been published so far documenting treatment efficacy against only histologically confirmed sarcoids. As a result no evidence-based information on treatment protocol, efficacy, prognosis and toxicity is available.

Because tumor size and previous unsuccessful treatment attempts are the most important prognostic factors, early and histologically complete surgical resection is the mainstay of treatment of sarcoids. Failure to eliminate the disease results in regrowth of a tumor that is histologically and biologically more aggressive and requires wider excision than the primary lesion. As a result, it is critical
to submit the resected tissue specimen for histopathologic examination to determine the status of the surgical margins. As a rule, grossly or histologically incomplete resection (i.e., positive or close pathologic margins [≤ 5mm]) must be followed by a re-resection if possible or by effective adjuvant treatment. For non-invasive sarcoids resected with pathologic margin >5 mm, and invasive sarcoids resected with pathologic margin > 1cm, the risk of recurrence is low and no further treatment but observation at regular intervals for at least 1 year is recommended. For invasive sarcoids resected with surgical margins between 5 and 10 mm, the risk of recurrence is high and adjuvant treatment may be recommended particularly when tumor recurrence may be difficult to manage because of unfavorable anatomic location.

Among the non-surgical treatments, radiation therapy and intratumoral chemotherapy with a viscous-fluid slow-release formulation of cisplatin have well documented efficacy against biopsy confirmed sarcoïds of all clinical types and in any location. The selective effects of these treatments have the advantage of controlling the disease while avoiding disruption of anatomic structure and preserving function. When compared to radiation therapy, intratumoral chemotherapy with cisplatin is as effective but without long-term side-effects and does not require any special license. The overall cure rate (all stages and clinical types combined) after treatment with intratumoral cisplatin therapy used alone or as adjuvant to surgery has been reported to be as high as 96%. Treatment includes a series of 4 intratumoral administrations of cisplatin (approximately 1 mg / cm3 of tissue) given at 2-week intervals. Widely available and inexpensive compounded crystal is formulated in a water-sesame-seed-oil emulsion stabilized with Sorbitan monooleate (Span 80). Treatments are done on an outpatient basis under sedation and the methods of administration and safety precautions have been described.

Although other antineoplastic drugs and drug formulations for intratumoral chemotherapy have been evaluated, cisplatin in sesame seed oil emulsion remains the most effective drug. Attempts at increasing 1) cisplatin uptake in tumors cells by electroporation applied under general anesthesia or 2) drug exposure with cisplatin-containing biodegradable beads implanted intraoperatively require anesthesia and complex procedures but have not shown any improved therapeutic benefits. Systemic chemotherapy with doxorubicin has shown preliminary evidence of efficacy for fast growing fibroblastic sarcoïds but not for indolent verrucous sarcoïds.

BPV-associated equine sarcoïds are distinct from other equine tumors in that they express targetable viral foreign antigens, the expression of which is necessary to maintain the cancerous phenotype. While therapeutic vaccines aim to develop a strong cellular immune response to BPV antigens that are expressed in transformed cells, prophylactic vaccines aim to prevent a putative BPV infection by inducing a neutralizing antibody response. Immunotherapy has been evaluated for treatment of sarcoïds. Therapeutic humoral immunization has not been found effective for treatment of affected horses. Vaccination against BPV-1 virus-like particle in sarcoïd-bearing horses and donkeys resulted in BPV-1 neutralizing antibodies but was not therapeutically effective. As the vaccine was immunogenic, trials of protective vaccination are underway. Other vaccines may hold promise as well.

Therapeutic vaccines aim to control tumors by activating the patient’s own cellular immune response to recognize and kill cancer cells. Non-specific cell-mediated immunotherapy uses immune stimulatory agents that act nonspecifically to elicit both innate or adaptive immunity and results in the induction of proinflammatory cytokines, chemokines and other immune mediators. This in turn leads to the generation of a Th1-biased cell-mediated immune response and a concomitant generation of cytotoxic effector cells against antigens in the tumor. Bacillus Calmette-Guérin (BCG) cell wall derivatives and imiquimod are 2 non-specific immunostimulants that have been reported for treatment of sarcoïds. BCG cell wall derivatives administered intralesionally has been shown to be effective only for periocular
sarcoids. The number of treatments depends on the rate of tumor regression, and the treatment schedule is dependent on normal tissue toxicity; most sarcoids require 2 to 9 treatments over several weeks. Encouraging results have been reported with a biological response modifier used topically (5% imiquimod cream). The ointment is recommended for the treatment of viral warts and basal cell carcinomas in people. It is applied as a thin layer to the tumor surface three times a week on nonconsecutive days up to 32 weeks until resolution. The reported 60% response rate suggests that topical imiquimod may be a therapeutic option for specific equine sarcoids. However, the data must be confirmed in a larger series of horses with sarcoids of all types and adequate long-term follow-up. In this author’s experience, imiquimod has been effective only for treatment of occult sarcoids and persistent papillomas in adult horses. Treatment did not prevent progression of verrucous or fibroblastic sarcoids. In all cases, treatment was associated with severe and painful skin inflammation.

Footnotes
a. Nomagen™, Fort Dodge Laboratories, Inc., Fort Dodge, Iowa
b. Aldara®, 3M Pharmaceuticals, Minneapolis, MN
c. Indian Mud, Original cream company, Magnolia, AK
d. XXTERRA™, Larson Laboratories, Inc. Fort Collins, CO
e. Animex™, NIES, Las Vegas, NV
f. Efudex® 5% fluorouracil, Hoffmann La Roche Inc, Nutley, NJ

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Melanoma

Melanomas occur in all domestic animals, but of the large domesticated species, they are most important in the horse. Excessive exposure to sunlight has not been definitively proven to predispose
horses to the development of melanoma. A disturbance in melanin metabolism associated with graying has been hypothesized to stimulate formation of new melanoblasts or to stimulate their activity, resulting in focal areas of overproduction in the dermis and epidermis, with subsequent tumor formation. A higher incidence is observed in the Arabian, Lipizzaner, and Percheron breeds, probably because gray coat color occurs more often in these breeds. There is no gender predilection.

Melanocytic skin tumors of horses traditionally have been described in aging gray horses, in typical locations: the ventral tail, perineum, external genitalia, lip, udder, and periocular and parotid gland regions. These tumors have been the subject of several classification schemes in attempting to correlate histopathologic appearance with clinical behavior (i.e., benign or malignant). One study distinguished three basic types of melanocytic skin tumors, as discussed next.

Melanocytic nevi (melanocytoma) occur in the superficial dermis or at the epidermal-dermal junction and frequently have epithelial involvement, with nests of relatively large, mildly to moderately pleomorphic cells showing variable cytoplasmic pigmentation and occasional mitoses. More than 70% of these occur in horses less than 6 years of age and may occur in horses of any color (not just gray). Most of these tumors occurred in atypical locations. Of 28 melanocytic nevi, only one became invasive; the rest exhibited benign behavior.

Dermal melanomas are found in the deep dermis and are composed of small, homogenous, indistinct tumor cells, either round or dendritic, with no mitoses. (If there are multiple, confluent dermal melanomas, this is referred to as dermal melanomatosis). About 80% of these tumors are in horses older than 6 years or between 5 and 15 years and are much more common in gray horses. Most of these tumors occurred in typical locations. Of 14 cases available for follow-up in one study, eight had malignant behavior, as demonstrated by metastases.

In another study, clinicopathologic 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 Lipizzaner breed. Of the 296 horses, dermal melanomas were present in 148 horses (50%), 68 of which were older than 15 years; 51 of these were melanoma bearing. In 75.6% of cases, melanotic tumors were detected underneath the tail. None of the affected individuals had any severe clinical effect or was handicapped in performance. The authors concluded that in contrast to melanomas in solid-colored horses characterized by early metastases, melanomas in gray horses showed less malignancy. Affected individuals often had encapsulated nodules or structures similar to human blue nevi. This finding at least partially reflects confusion in terminology between true malignant melanomas and dermal melanomas.

Anaplastic malignant melanomas are composed of sheets of extremely pleomorphic epithelioid cells with poor pigmentation and many mitoses. These are usually seen in horses older than 20 years of age and occur in horses of any color. Metastasis usually occurs first to the regional lymph nodes, then to the lungs, spleen, and liver. Hematogenous spread may also occur. Metastatic growths may be larger than the primary lesions and softer in consistency.
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 PO q8h) was shown to decrease the number and size of melanoma growth. However, another study of 10 horses found that cimetidine had no consistent effects on either the number of tumors or the tumor surface area over the 16 weeks of treatment at 5 mg/kg PO q12h. Another article noted a cure rate of 81% for melanomas treated with intratumoral injections of cisplatin. A recent article reported significant tumor regression when injecting interleukin-18- and interleukin-12-encoding plasmid DNA into the tumors of horses with metastatic melanomas.

References

Cutaneous lymphoma
Cutaneous lymphoma has occasionally been reported in horses. Both T-cell and B-cell forms have been reported. Lesions present as nodules, either cutaneous or subcutaneous. Diagnosis is made by biopsy and, ideally, immunohistochemistry to determine cell type. In one horse, progesterone receptors were demonstrated on the lymphoma (B) cells, and the lesions regressed after removal of an estrogen-secreting ovarian tumor. This horse also had a history of partial regression of its tumor after administration of a synthetic progestin, altrenogest (0.044 mg/kg PO once daily for 10 days). Another horse demonstrated reduction in tumor size after administration of another synthetic progestagen, megestrol acetate (0.2 mg/kg PO once daily for 8 days) as well as a local injection of 20 mg betamethasone into a mass. Clearly, treatment is far from standardized, but the progesterone drugs may offer a reasonable treatment modality. Topical retinoids such as tazarotene (marketed as Tazorac cream or gel (at 0.05% and 0.1% concentrations) have been anecdotally reported as having efficacy against smaller lesions. Retinoid products are often expensive, and may cause skin irritation. A recent report describes a horse that responded to incomplete surgical removal plus lomustine and prednisolone.

References
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Mastocytosis

In horses, mastocytosis (mast cell tumors, mastocytomas) occur in animals 1 to 18 years old (average, 9 years), with no breed predilection. A predilection for males has been proposed but is not always sustained. In addition, multiple mast cell tumors resembling urticaria pigmentosa of humans may occur in newborn foals; these spontaneously appear and regress. Mastocytosis is usually solitary and occurs most often on the head and trunk, although occasionally multiple tumors may be seen. Lesions are 0.5 to 20 cm in diameter, well to poorly circumscribed, firm to fluctuant, dermal or subcutaneous, 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 sections showing both sheets of mast cells with numerous eosinophils and collagen degranulation. Ultrastructural features are similar to those noted in mastocytomas of other species.

Clinically, most mast cell tumors in horses do not recur after being excised (22 of 25 in one study). In 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 years later. There is some debate as to whether equine mastocytomas are benign neoplasias or focal dysplasias of mast cells.

References

Squamous cell carcinoma

Squamous cell carcinomas (SCCs) are tumors composed of squamous epithelial cells. They occur in all domestic species and are the second most common tumor recognized in the horse. Although their gross appearance may vary, these tumors are usually slightly raised, broad based, and white to pink and have a cobbled or cauliflower-like surface. SCCs frequently occur on the penis and sheath of aged stallions and geldings. They also occur on the lips, nose, eyelids, eyes, and ears of horses. Diagnosis is by biopsy. There is increasing evidence that SCC in horses is associated with papillomavirus infection.
The treatment of choice is wide surgical excision.\textsuperscript{4,5} Solar elastosis (aggregates of thick, wavy, interwoven elastic fibers, mixed with areas of degenerated collagen), when seen histologically with SCC, may lend a more favorable prognosis after complete surgical removal of lesions.\textsuperscript{6} Other treatment modalities reported as successful include cryosurgery, radiofrequency hyperthermia, and radiation therapy.\textsuperscript{7} Another study showed topical application of 5-fluorouracil (5-FU) and intralesional cisplatin were shown to be effective in horses with SCC.\textsuperscript{8-11} Piroxicam was successful in the long-term control of SCC with metastases in one horse.\textsuperscript{12}

References


Papilloma virus and papillomas

At least 2 or more papilloma viruses have been recognized in horses, and others in donkeys. These may present on the face in young horses, or on the genitalia of older horses.\textsuperscript{1,2} Penile papillomas may be associated with a transformation to squamous cell carcinoma.\textsuperscript{3} Treatment for the condition in young horses may include benign neglect, biopsy (in theory to release viral antigens and thus stimulate the horse’s own immune system to attack the virus) or autogenous vaccine administration.

Aural plaques may be a form of viral papilloma that often affects the inner pinna. Nonpruritic, these plaques may also occur on the genitalia and mammary glands. The color varies from pink to grayish-white. Plaques do not resolve spontaneously, as do the “classic” papillomas seen in young horses. Biopsy or “shaving off” aural papillomas may stimulate reduction or resolution of the masses, although in some horses, this may only be temporary (6 to 12 months). This has been theorized to be due to the release of “papilloma antigens” into the bloodstream during the surgical procedure, prompting an immune response against the tumor. Imiquimod (Aldara-3M, Minneapolis, Minn.), a nonsteroidal local immune response–modifier cream, has been helpful in some cases, used 3 times weekly, every other week, for 2 to 4 months.\textsuperscript{3} Owners should wear gloves and should be forewarned that there is frequently an impressive inflammatory reaction to the cream in the initial weeks of treatment. A papillomavirus has
been demonstrated in aural plaques on electron microscopy and with immunohistochemical techniques.\textsuperscript{4}

**Pox virus**

Molluscum contagiosum has been reported in donkeys.\textsuperscript{5} Treatment is uncertain, but single lesions may be surgically removed.

**References**


**Non-neoplastic nodules**

**Equine Eosinophilic Granuloma (EEG)**

*(Nodular Necrobiosis, Equine Collagenolytic Granuloma)*

This is the most common equine nodular skin disease. It is seen throughout the world. There is no apparent breed, age, or sex predilection. The most prominent feature of the disease has classically been termed collagenolysis (necrobiosis, degeneration of collagen). However, it has now been shown that in fact the skin changes are actually the result of the eosinophils, and that the collagen is not abnormal or degenerating but rather coated with material from the eosinophils. Although the etiology is not known, the pathogenesis probably involves a hypersensitivity reaction. Insect bites have been suggested as a possible cause, but this is still probably only one of several etiologies.

In rare cases, the development of equine eosinophilic granulomas (EEG) has been noted in areas of previous injections using standard silicone-coated stainless steel hypodermic needles.\textsuperscript{1} The reaction may occur at sites of intravenous as well as intramuscular injections. The lesions consist of nonpainful, cool, raised papules or nodules 0.25 to 1 cm in diameter at sites of previous injection. The nodule appears 24 to 48 hours after the injection and the subsequent eosinophilic granuloma can persist for months to years. Affected horses do not develop a lesion at the site of injection if non-disposable, non-coated needles are used. The use of the non-coated needles is recommended for any horse that develops injection-site collagenolytic granulomas. EEG has a tendency to occur during the warmer months of the year.\textsuperscript{2} The lesions consist of one to multiple firm nodules situated in the dermis. The nodules usually vary from 0.5 to 5 cm in diameter. Occasionally very large lesions are present. The nodules usually occur on the withers, back and sides of the neck but may occur anywhere. Unless traumatized, the overlying skin surface and hair coat is usually normal in appearance. If the areas of ‘coated collagen’ are extensive and involve the superficial dermis there may be "transepidermal elimination" which results in ulcerated lesions containing a "necrotic plug" of tissue. There is no pruritus and usually no pain associated with the lesions.

Histologically, the primary change consists of one to several foci of ‘altered collagen’ in which the collagen fibers have an amorphous, granular appearance and elicit a granulomatous host response.
There is tremendous infiltration of the surrounding connective tissue with eosinophils. In older lesions, mineralization may be seen.

Diagnosis is often visual; important differential diagnoses are Hypoderma infestation (in which case a breathing pore will usually develop) and habronemiasis. Biopsy of a lesion for histopathology is necessary to make a definitive diagnosis.

Therapy consists of corticosteroids and/or surgical removal. In the case of a single lesion, surgical removal is frequently performed. Care should be given, however, if the lesion is in the saddle area, as these may take a long time to heal if surgically removed. Corticosteroid therapy is the only non-surgical treatment. The corticosteroids may be administered systemically or intralesionally. For intralesional use, triamcinolone acetonide or methylprednisolone acetate are the corticosteroids of choice. Due to the dense nature of the nodules, the drug is usually injected perilesionally rather than intralesionally. The injections may be repeated at 2 week intervals if necessary. Any lesions remaining after 3 injections will probably have to be surgically removed. When large numbers of nodules are present, systemic corticosteroid therapy is used. The usual regime consists of 1 mg/kg prednisolone orally per day for 10-14 days followed by 0.5 mg/kg/day for an additional 10-14 days. If a few lesions persist following systemic corticosteroid therapy, these may be treated with intralesional therapy (not if in saddle area) and/or surgically removed.

References

Sterile Nodular Panniculitis
This is a rare, idiopathic inflammatory condition of the subcutaneous fat in horses. Its importance is related to differential diagnoses:
1. Clinically, equine eosinophilic granuloma
2. Histologically, infectious panniculitis

The etiology of ANY panniculitis seen on histopathology has to include infections and drug eruptions. Thus ‘sterile nodular panniculitis’ refers to sterile subcutaneous inflammatory nodules and is a descriptive term representing clinically the end result of unknown etiologic factors.

The disease presents as deep-seated cutaneous nodules and plaques, which may be single, multiple or generalized, and vary in size from a few millimeters to several centimeters in diameter. Nodules may be firm and well circumscribed or soft and ill defined. They are initially subcutaneous but may fix to the overlying skin as they progress. The lesions may become cystic, ulcerate and develop draining tracts that discharge an oily, yellowish-brown to bloody substance; may or may not be painful and may heal with depressed scars. Concurrent constitutional signs (anorexia, depression, lethargy and pyrexia) may be present.

Diagnosis is primarily based on skin biopsy which will show granulomatous to pyogranulomatous inflammation of the sub-cutis fat and have negative results for both special stains for bacteria, mycobacteria, and fungi as well as culture for these organisms as well.
Treatment of sterile nodular panniculitis is prednisolone, given orally at 1.1-2.2 mg/kg/day, or 20-30 mg dexamethasone/500 kg/day orally. Lesions usually subside within 7 to 14 days. Relapses may occur and require long-term alternate day prednisolone maintenance therapy.

References

Unilateral papular dermatosis
Another uncommon equine dermatosis of unknown cause; no age or gender predilections. There may be a genetic predisposition in quarter horses. Lesions occur in spring and summer, with the outstanding clinical feature being multiple (30 to 300) papules and nodules limited to one side of the trunk. The lesions are usually rounded, well circumscribed, firm and nonpainful.

Cytology shows numerous eosinophils and skin biopsy shows eosinophilic folliculitis (mural and/or luminal) and furunculosis. A hypersensitivity to a flying arthropod has been hypothesized; the unilateral nature of the disease being explained as the parasite’s location vis-à-vis the wind (?!?).

Unilateral papular dermatosis usually undergoes spontaneous remission within several weeks to months. Because of this and the lack of other clinical signs, treatment is not usually attempted. However, oral prednisolone at 1 mg/kg once a day for two to three weeks is an effective treatment. Occasionally the condition recurs.

Reference

Cutaneous amyloidosis
Yet another uncommon nodular dermatosis of unknown etiology. The condition appears to be a primary form of amyloidosis: concurrent inflammatory processes are not present, and amyloid deposition is usually restricted to the skin and occasionally the regional lymphatics, regional lymph nodes, and upper respiratory mucosa. One case report in one horse showed amyloidosis concurrent with lymphoma.

The course of cutaneous amyloidosis is progressive and prolonged; megestrol acetate may be an effective treatment (0.2 mg/kg per os q24h until lesions resolve). Because certain forms of primary amyloidosis in humans have a genetic basis, it may be advisable not to use affected horses for breeding until more is learned about the genetics of the equine disorder.

References

Cutaneous Habronemiasis
(Summer Sores)
This is a disease fairly specific to equids. The prevalence is highest in regions with a temperate/tropical climate worldwide. It is caused by any of the three species of Habronema that parasitize the horse: H muscae, H microstoma, and H megastoma. The adult worms reside in the stomach where they cause little
reaction with the exception of *H. megastoma* which produces varying sized nodules that usually occur near the margo plicatus. The females are viviparous and the larvae are passed in the feces where they are ingested by the maggots of flies which serve as the intermediate host. *H. muscae* and *H. megastoma* develop in the house fly, *Musca domestica*. *H. microstoma* develops in the stable fly, *Stomoxys calcitrans*. The normal life cycle is completed when the infective larvae are deposited by flies around the horse’s lips where they are subsequently swallowed.

Cutaneous habronemiasis is a form of aberrant parasitism when the larvae gain access to the deeper layers of the skin in a presumably hypersensitive host. It is important to remember that infective larvae of *Habronema spp* cannot penetrate normal healthy skin. Thus, for cutaneous habronemiasis to develop, the larvae must be deposited in previously damaged skin or mucous membranes. In a retrospective study from UC Davis of 63 cases, Arabians, gray horses, and horses with diluted coat colors were overrepresented; Thoroughbreds were underrepresented.1

The disease is seasonal, first appearing in the spring and in most cases spontaneously regressing in the winter months. As the occurrence of the disease is sporadic, with only a few horses in any given area being affected, a hypersensitivity reaction is suspected. Once the disease develops in a horse it usually will recur each succeeding summer unless stringent preventative measures are taken. The usual locations for the lesions are the medial canthus of the eye, conjunctiva, the male genitalia (especially the urethral process), and the lower extremities. The lesions themselves consist of areas of ulceration with or without granulation tissue and usually containing small gritty yellow nodules. Biopsy of the lesions consist of granulation tissue, a diffuse infiltration of eosinophils, and foci of coagulation necrosis of eosinophils surrounded by a granulomatous response. In less than half the cases, often in the areas of coagulation necrosis cross sections of dead larva can usually be found.1

Diagnosis is often based on the basis of the history and the location and appearance of the lesions. The three major differential diagnoses include exuberant granulation tissue (‘proud flesh’), fibroblastic types of equine sarcoid and squamous cell carcinoma. All three of these may be secondarily infected with *Habronema*. Thus if the lesions do not respond to habronemiasis treatment, or if there is any reason to suspect that there is an underlying neoplasm, a biopsy should be obtained for histopathology. (Scrapings of the lesions are usually unrewarding as far as demonstrating the larvae.)

In the retrospective report from UCD, treatment consisted of surgical removal (7 horses) or medical treatment (56) consisting of debulking granulation tissue and topical, intraliesional, or systemic treatment with corticosteroids. All horses were treated with ivermectin. Thus treatment should be aimed at decreasing the size of the lesion, reducing inflammation, and preventing recurrence. Fly control and regular deworming with ivermectin are recommended to reduce the incidence of habronemiasis.

References