Sarcoids are locally aggressive non-malignant fibroblastic tumors of equid skin and are the most common cutaneous tumor of horses. Sarcoids occur most frequently on the head, legs and ventrum of horses, donkeys and mules. Nearly 1/3 of affected equids have multiple tumors; classic tumors do not metastasize but commonly recur after excision. Sarcoids appear in areas subject to trauma and may occur at the site of a previous wound. Current information on etiology suggests sarcoids are virally induced by bovine papilloma viruses (BPV) 1 and 2, or a variant there of, in horses that are genetically predisposed (certain alleles of MCH class II are considered "sarcoid susceptible"). Infectious viral particles are not produced, but BPV episomal DNA is found in fibroblasts and express an oncoprotein that downregulates MCH class I expression. Transmission via flies is suspected as episomal proteins have been found in flies and in the skin of unaffected donkeys when housed with donkeys with sarcoids. Strong familial susceptibility to sarcoids has been described. Although sarcoids occur in all breeds, Appaloosas, QHs and Arabians are over represented. Although common, sarcoids occur in <1 in 1000 horses.

Clinical signs are highly variable. Tumors may be 1 cm or less to enormous in diameter and are poorly circumscribed. The over lying skin may be normal, alopecic, hyperkeratotic, hyperpigmented, ulcerated or a combination of these. Six clinical classifications have been described:  

**Occult:** flat, alopecic, circular lesion, often with small milliary papules or nodules  
**Verrucous:** wart like with a rough hyperkeratotic surface with scales similar to a papilloma or fibroma. Tumors may be sessile (flat) or pedunculated with a narrow neck. These tumors are often slow growing, may become aggressive if injured.  
**Nodular:** firm, well defined subcutaneous spherical nodules  
  - **Type A:** No clinically detectable dermal involvement, the skin moves freely over the surface of the mass and the mass moves freely over the subcutaneous tissue  
  - **Type B:** Obvious dermal involvement, may become ulcerated and more grow more aggressively  
**Fibroblastic:** flesh like, often ulcerated and ooze serum. These tumors resemble granulation tissue and are often found in wounds.  
  - **Type A:** pedunculated. In Type a the pedicle is narrow and usually consists of skin and subcutaneous tissue. Type 1b have a dumbbell shape with a deep mass connected by a narrow neck to a superficial mass.  
  - **Type B:** sessile: broadly based locally invasive  
**Mixed** (occult, verrucous, nodular and fibroblastic): may be pedunculated or sessile  
**Malignant/Malevolent:** may invade lymphatics and be found at multiple sites, often multiple extremely large tumors

Diagnosis is often made by visual inspection. Biopsy and histopathological evaluation confirm the diagnosis. It is best to include normal and abnormal skin in the biopsy as the characteristic findings are most often present at the junction of the two. Incise deep into the dermis when obtaining a biopsy to avoid obtaining only superficial inflammation and/or granulation tissue. Suspected occult sarcoids are usually very slow growing and may remain static for years. Biopsy of these is not recommended, as biopsy may increase the rate of growth and change them to a more aggressive tumor.

No treatment is uniformly satisfactory. Ten to 70% of treated tumors reoccur within one year. Often previously treated tumors become more aggressive and are more difficult to treat once reoccurrence has occurred. Choice of treatment depends on location and size of the tumor,
equipment available, experience of the clinician, previous treatment and economic considerations.

Surgical removal alone is the least satisfactory treatment but is often used to debulk tumors prior to using other treatment modalities. Carbon dioxide laser ablation is believed to result in less contamination of surrounding tissue with malignant cells compared to scalpel removal due to thermal killing and vaporization of virus particles. Outcome is improved when laser ablation is combined with chemotherapy or other treatment. Cryotherapy (using at least 2-3 freeze–thaw cycles monitored with tissue temperature probes) has been used with reasonable success by different clinicians. Multiple treatments are usually required. Cryotherapy is less successful in periorbital sarcoids than in other regions of the body.

Intralesional treatments: Radio frequency hyperthermia (orthovoltage at 2MHz to heat the tumor to $50^\circ$C for 30 sec) by clinicians experienced with this technique has been reported to have good success in long term resolution of sarcoids.\(^a\) Tumors greater than 1 cm in diameter should be debulked prior to treatment.

Intratumoral cisplatin emulsion in sesame oil (with or without SPAN 80 to aid in emulsion of cisplatin) given every 2 weeks for 3-4 injections has proven to be successful in a wide variety of tumors either alone or after debulking of larger masses (87% success in sarcoids).\(^3,4\) Disadvantages of cisplatin injections are the necessary safety precautions of handling the drug due to serious human health concerns. Cisplatin biodegradable beads (Royer Biomedical, 301-696-2177) have eliminated some of the drug handling concerns and have shown 83% success rate in resolution of tumors for 2 years.\(^5,6\) Beads are placed within the tumor at 1.5 cm intervals. Lesions are re-evaluated in 1 month and retreated of necessary. Electrical field pulses, which increase cell permeability, has been used in conjunction with cisplatin. Cisplatin (1 mg/ml aqueous solution) injected in a grid pattern followed by electrical field pulses has shown a 99% to 100% (when combined with surgery) regression rate.\(^7\) Cisplatin has also been used in combination with IL-2.\(^8\)

Interstitial brachytherapy using iridium-192 implants is particularly useful in periorbital sarcoids as the radiation affects the tumor while sparing adjacent healthy tissue. 100% successful resolution of periorbital sarcoids has been reported using this technique.\(^9,10\) Disadvantages of this technique is the need for special equipment, licensing for use, and patient confinement in a radiation safety approved facility. Thus it is usually available only in referral centers and is an expensive option.

Intralesional 5-fluorouracil has approximately 60% success rate when used in small tumors and those not previously treated.\(^11\)

Topical cytotoxic therapy: A paste containing extracts of Bloodroot (Sanunieria Canadensis) and ZnCl (Xxterra® Larson Laboratories, Inc) purportedly alters "sarcoid antigens" and stimulates the immune system. The compound is also cytotoxic and results in inflammation and soreness. No evidence based studies on its effectiveness are available although there are many anecdotal reports of success.

Five percent acyclovir used topically for 60 days has shown complete regression of 68% of sarcoids and partial regression of 32% in one study.\(^12\) Slow growing occult tumors seemed to respond most favorably. Some tumors required longer treatment; surgical debulking of larger tumors improved response.

Immunomodulatory therapy: Imiquimod 5% (Aldara®, 3M Pharmaceuticals) modifies the immune response and has antiviral and antitumor activity in animal models and humans. In a preliminary study approximately 60% of sarcoids treated completely resolved and 75% showed reduction in tumor size.\(^13\) Adverse affects include erythema, alopecia, exudates, and erosions. Imiquimod may be a good therapy to prevent tumor transformation post-biopsy.\(^14\)
Intralesional injections of preparations made from cell wall fractions of BCG, an attenuated strain of Mycobacterium bovis, (Regressin-V®) stimulate host lymphocyte and natural t-killer cells. Reaction in the tumor is apparent after the second or subsequent injection and may occur very rapidly. The tumor eventually undergoes ulceration and necrosis. Systemic signs of inflammation including pyrexia, leukocytosis and, in rare cases, anaphylaxis (nonfatal and rarely fatal) may occur. Consequently premedication with flunixin and/or corticosteroids has been recommended.

EquiStim® (nonviable Propionibacterium acnes; Neogen) is a non-specific immune stimulant that activates macrophages and lymphokine production. It may also increase natural killer cell activity and enhance cell-mediated immunity. No evidence-based reports are available on success.

**Vaccination as a Treatment:** Autogenous vaccine made from frozen pieces of a sarcoid tumor have been reported to induce regression in 12 of 15 sarcoids within 90-180 days.15

Because of the large number of treatment regimens it is apparent that no one treatment has emerged as the preferred one. Prognosis for regression depends on size, aggressiveness, location and number of tumors. The most valuable aid in the successful long term resolution of sarcoids is regular re-examination at intervals no less than 10 days or grater than 3 weeks with prompt treatment of any reoccurrence. The success of all treatment modalities decreases with the number of attempts to treat a sarcoid, particularly when multiple modalities are used.

**Squamous cell carcinoma (SCC)** is a malignant neoplasm and may occur as an invasive ulcer or an ulcerated mass. Lesions are frequently accompanied by inflammation and fibroplasia. SCCs occur with the greatest frequency at mucocutaneous junctions of the head and genitalia and are most common in animals without skin pigmentation, but may occur on any animal. Solar radiation, body secretions (smegma) and chronic contact dermatitis have been incriminated as causal agents. Lesions may be ulcerated and necrotic or proliferative. Proliferative lesions, particularly around the eye, may have a "cauliflower" appearance. Proliferative lesions may be traumatized resulting in intermittent hemorrhage and secondary infections. SCCs are locally invasive and destructive but do not metastasize widely throughout body. They do, however, spread to regional lymph nodes. Advanced tumors of the head with grossly affected submandibular and retropharyngeal lymph nodes may have metastasis to the lung.

Because of the ulcerative surface, a small biopsy may sample only inflammation and/or fibrosis thus missing the diagnosis. Treatment for SCC depends on the location and size of the tumor. Early diagnosis and treatment is essential for success and the best response is seen in tumors < 1 cm in diameter. Documented treatments include surgical excision, cryotherapy, radiofrequency hyperthermia, carbon dioxide laser ablation, chemotherapy, immunotherapy, or combinations of these. Surgical excision should be followed by ancillary treatment such as cryotherapy, intralesional cisplatin or radiation therapy if tumor margins have not been removed, as evaluated by histopathology. Success for combined therapy in early lesions can range from 75-100%. Treatment success after metastasis to regional or internal lymph nodes is poor.

**Scleral or corneal surface SCC treatment:** Complete surgical removal, verified by histological evaluation of tumor margins, is successful. However complete removal is often not practical and/or difficult. SCCs may be treated with surface brachytherapy (strontium 90 probe) following surgical removal. Success rate is good with careful coverage of affected area and lesion margins. Superficial keratectomy/conjunctivectomy may also be followed by CO2 laser ablation. A 92% success rate has been reported, although granulation tissue at surgical site may occur in ~25% cases.16

Topical treatment with Mitomycin C, an antibiotic produced by Streptomyces caesiptosu that has cytotoxic effects dependent on the availability of oxygen, has been used in ocular
surgery to prevent scarring. In one study 6 of 8 eyes with SCC treated with Mitomycin C (0.04% ocular solution instilled in eye once daily for 7 days then 7 days off to a maximum of 4 courses) alone resolved and 7 of 9 eyes treated with Mitomycin C and surgery resolved. Mitomycin C therapy initiated immediately after surgery may have complications (minor complications- granulation tissue, blepharospasm, conjunctival necrosis; major complications-ulcerative/non-ulcerative blepharitis, stromal ulcer, bullous keratopathy and descemetocele) which are diminished if treatment with MC is delayed until corneal epithelialization is complete.

Photodynamic treatment of ocular SCC resulted in regression without reoccurrence in 7/9 treated horses. The 2 cases with tumor reoccurrence were tumors that had been previously treated. Both resolved with additional treatment. In this treatment a light sensitive compound that reacts to a certain wave length of light is injected into the tumor. When the tumor is subsequently treated with the appropriate light the photodynamic compound causes tissue necrosis.

Periocular tumors, surgically debulked if necessary, are most successfully treated with iodiridum 192 implants and usually result in functional and cosmetically acceptable outcomes. Intratumoral chemotherapy with cisplatin has been reviewed. In this report 88% of 151 tumors on 144 horses were successfully treated with intratumoral cisplatin either alone or following debulking. Cisplatin (7%) containing biodegradable beads have also been used successfully. External megavoltage radiation (cobalt-60) has been used successfully at the University of Georgia for larger tumors of the perineal and head region with a success rate of 80%.

Disadvantages of chemotherapy is the need for care in contamination of humans (cisplatin) and the need for special licensing and containment housing for the use of any form of radiation therapy.

In all cases of confirmed SCC frequent thorough post treatment examinations should be performed to detect recurrence. SCC commonly reoccur at the original site but may also occur at sites distant to the original tumor and or may occur in regional lymph nodes 2-5 years after resolution of the original tumor.

**Melanocytic neoplasms** There are multiple names and synonyms for tumors of melanin containing cells. Current nomenclature suggests the use of melanocytoma for all noncongenital benign proliferations of melanocytes and melanoma for malignant proliferations of melanocytes. Melanomas are thought to develop from genetic mutations in the melanin metabolism molecular pathway and are related to the grey coat color.

Melanocytomas are uncommon and usually occur in horses ≤ 2 years of age with no breed, sex or coat color predilection. They most commonly occur as solitary lesions on the legs and trunk and are usually firm, well circumscribed and 1 - 5.5 cm in diameter. Surgical excision is curative. Melanocytomas are histologically distinct from melanomas.

Melanomas are common tumors, especially in older grey horses, comprising 3.85% to 15% of all skin tumors. Classically these tumors are multiple (but may be solitary) and are found under the tail, in the perianal region, and on or near the head (periorbital, lips, parotid region, guttural pouch) but may be found anywhere. The tumors may coalesce and discharge a thick black substance. Three growth patterns have been described: 1) slow growth for years without metastasis, 2) slow growth for years with sudden rapid growth and metastasis, and 3) rapid growth and malignancy from the onset. Many horses have metastasis to internal organs at necropsy that were not associated with clinical signs.

Diagnosis can be made from aspiration of the tumor and cytologic examination, which reveals pleomorphic and atypical melanocytes. Preferred diagnosis in early lesions is histopathology of a biopsy. If weight loss, inappetence, chronic colic, neurologic deficits and/or lameness are concurrent other diagnostic procedures are indicated. Metastatic melanomas may spread via the lymphatics or hematogenously. Common sites include the serosal surface of the
spleen, liver and lung, however any region of the body may be affected.

Local treatment: Although excision of solitary lesions in total is curative, in many instances surgical excision is not attempted because of the location and shear numbers of tumors. Intratumoral chemotherapy with either cisplatin or carboplatin has been used successfully in some tumors. Response is generally inversely related to tumor size, thus surgical debulking prior to treatment is advisable. Therapy with biodegradable beads (Royer BioMedical, Inc) has also been successful in small tumors or following surgical debulking.

Brachytherapy may also be a viable option. A new system by Xoft, Inc (San Jose, CA), Axxeat Controller) uses a electronically generated miniaturized high dose rate of x-rays to apply radiation directly to the tumor. This methodology, similar in action to Iridium 192, does not require radioactive isotopes or heavy shielding. It was designed to be used in human medicine, allowing health care workers to remain in the room during treatment. Hyperthermia and electrochemotherapy can be used to increase the tumor cell penetration by cytotoxic drugs. A new system utilizing microwave energy (Thermofield® System, Parmenides Inc, Franklin, TN) has been shown to be effective in treating advanced local disease when combined with intratumoral chemotherapy.

Systemic therapy: Cimetidine (2.5 mg/kg PO q 8 hrs for at least 3 months) is an histamine (H2) receptor antagonist that has been reported to limit or stop the progression of melanomas that are increasing in size. The antitumor effect of cimetidine may be from the inhibition of H2 receptors on tumor cells, thus blocking the activation of immunosuppressive regulatory T cells and/or increasing the activity of natural killer cells. Anitumor vaccines target tumor specific antigens (proteins) and thus spare normal tissue. A whole tumor cell autogenous vaccine has ben available for a number of years. When used with other therapeutic modalities tumor regression and subjective improvement in well being has been reported. DNA vaccines are made by utilizing DNA sequences that encode for a tumor specific protein. The DNA sequence is cloned into a molecular vector which allows production of the tumor protein. Additionally the vectors may have an immunostimulating effect. Tyrosinase, an enzyme necessary for the production of melanin, is limited to melanocytes and is produced in higher concentration in neoplastic melanocytes than normal cells. A USDA approved vaccine encoding human tyrosinase is available for the treatment of dogs with melanoma (Oncept; Merial, Inc, Athens, GA). The use of this vaccine with other treatment modalities markedly increased the survival rate in dogs. Dogs share 90% DNA homology with human tyrosinase; horses share 90% homology. Recent studies of the use of this vaccine (off label) in a large group of horses found tumor shrinkage (some dramatic) in the majority of horses.

Cutaneous lymphoma (synonym: lymphosarcoma, malignant lymphoma) is an uncommon malignant tumor of lymphocytes. Cutaneous lymphosarcoma occurs as two separate entities: primary cutaneous lymphosarcoma (epitheliotropic) which develop from T lymphocytes (of which mycosis fungoides is a subtype) and systemic lymphosarcoma with cutaneous involvement. The later tumors are often of B-cell origin with many T lymphocytes (believed to drawn by cytokine release from neoplastic B cells; T-cell rich B-cell lymphomas) affect the dermis and subcutis and contain a heterogeneous group of lymphocytes. Nonepitheliotropic lymphoma occurs in adult to aged horses. Some horses will be systemically ill and have increased circulating lymphocytes (10,000-30,000/ul). Horses with a histiolympocytic phenotype (a mixture of pleomorphic lymphocytic and histiocytic cells) may have multiple skin lesions without concurrent illness for months to years. Tumors are generally subcutaneous. Epitheliotropic lymphoma is characterized by multifocal to generalized
exfoliative dermatitis with or without pruritus and focal areas of nodules with or without ulceration.

Diagnosis is best made with a surgical biopsy. Excision of the entire nodule or a significant wedge of tissue is preferred.

Most horses with systemic lymphoma are sick and will die within weeks to months. Horse with the histiolymphocytic form often remain healthy for years before they become ill or are lost to follow up. Some horses have lesions which regress and reoccur without therapy. Palliative therapy with steroids will provide a temporary reduction in tumor size. Anecdotal information indicates some horses respond to therapy with progesterone, however a recent study found neither estrogen nor progesterone in most tumors.\textsuperscript{25} Chemotherapy has been used to treat horses with cutaneous lymphoma. One treatment regimen that has been used is a protocol of cyclophosphamide, doxorubicin, vincristine and prednisone.\textsuperscript{c} Another protocol utilizes cyclophosphamide, cytosine, arabinoside plus life-long prednisolone.\textsuperscript{d} Drugs are given per meters squared of body surface. The formula to determine this in the horse is:

\[ M^2 = 4(\text{wt in kg}) + 7/(\text{wt in kg} + 90). \]

To date there is no evidence based data to indicate efficacy of chemotherapy.

**Cutaneous mast cells tumors** (cutaneous mastocytomas) are single (usually) or multiple benign nodular dermal lesions that occur in mature animals. Multiple congenital tumors may occur in horses which regress spontaneously. Tumors are usually raised, firm, fairly well demarcated and 0.5 to 20 cm in diameter. Aspirates of the tumor are often diagnostic. Cytologic examination reveals well differentiated mast cells. Histopathological confirmation is desirable, especially if eosinophils are also observed.

Complete surgical excision is curative. If surgical removal is not possible sublesional injections of steroids, cryotherapy or radiotherapy may be effective. There are rare reports of spontaneous regression.

**Equine collagenolytic granuloma** is a fairly common disease of horses, also known as “nodular necrobiosis” or “eosinophilic granuloma.” Hypersensitivity to insect bites is suspected as the cause. Grossly, they are single to multiple, firm, non-pruritic cutaneous nodules on the back, withers, and neck. Histologically the nodules consist of collagen degeneration with associated eosinophilic/granulomatous inflammatory response. Established lesions may have calcified centers.

Most lesions are innocuous but persistence and growth of nodules under tack may interfere with the use of the horse. Because of the location (on the back, under tack) surgical removal is often not practical. Intrallesional injection of steroids or the systemic administration of steroids if the lesions are numerous may help resolve lesions and prevent new ones from occurring. It is important to eliminate the chronic irritation of the nodules under the saddle. The use of orthopedic closed cell foam with "cut outs" over the affected area may alleviate pain and prevent further growth or calcification of lesions.

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Suggested Reading


References