

# Non-surgical management of sarcoids in the horse

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**The wide variety of treatments reported to be successful in the management of the equine sarcoid probably indicate that no one treatment is universally effective, writes Derek C Knottenbelt.**

The restrictions that apply in the management of sarcoid in terms of the variety of clinical / pathological type, the location and extent of individual tumours makes the choice of treatment somewhat easier. However, there are considerable limitations that apply in every case.

Suitable methods that can apply include radiation, which is widely regarded as the gold standard against which other methods can be compared. Beyond this a wide variety of topical and intralesional chemotherapy methods have been developed across the world.

Almost all reported methods of topical and intralesional chemotherapy have reported successes. Many of these have little evidence to support their use and many are patently useless. Immunological methods have been used for many years and these range from the illogical and inappropriate use of "autogenous vaccines" to the recently reported autografting of tissues. The induction of a strong local inflammatory and immunologic response through intralesional BCG administration has been used for many years with success, particularly around the eye regions.



This aggressive malignant periocular sarcoid was treated with iridium 192 interstitial brachytherapy. The outcome, below, was exceptionally good but it took over 12 months to reach the state shown and there were some side effects on the cornea and lens. These were, however, trivial to the horse and he was able to compete to the highest possible level.



The same horse after treatment.

Treatment selection must be considered very carefully and the best available method must be used on the first occasion. The problem with any treatment method is not the successes – these are accepted with gratitude of course, but failures of any treatment method results in a significant drop in the overall prognosis for the case.

Homeopathic methods are universally useless; these methods can be regarded as a direct exploitation of the vulnerable, the gullible and the disillusioned.

The treatment of the equine sarcoid remains a major challenge in equine practice since the prevalence of the tumour is high (up to 8% in some parts of the world). Furthermore, there are

around 40 described treatments and this simply suggests (as we know!) that no one treatment is universally effective.

Treatments seem to have a variable rate of success when carried out by different veterinarians. Few extensive case series have been published but those that have been put in the public domain (Knottenbelt and Kelly, 2000) have confirmed the ongoing difficulty of management and the variability of results from any single modality.

*There is nothing more expensive than a cheap treatment that does not work ... except of course an expensive treatment that does not work! A lack of research effort in oncology is possibly the largest single factor that constrains oncologic advances. In spite of the ease of access and diagnosis cutaneous oncology still receives little research effort or clinical interest. – Derek Knottenbelt*

Having a wide variety of treatments available provides the clinician with an opportunity to select the best possible option at the outset and where treatment selection can be based on published evidence-based clinical results the prospects of success should be higher.

In considering the options for an individual case or even an individual lesion on a horse, there are factors that affect the choice of treatment method and outcome. Some of the major constraining factors are:

1. **Tumour type and behaviour:** Some sarcoids are amenable to surgery for example whilst others are far less so. The clinical behaviour also matters enormously particularly because of the risks of interference and / or the risks of malignancy.
2. **Tumour location:** Anatomic constraints will inevitably affect the choice of treatment. Removal of skin on the face is difficult and any treatment that scars the upper eyelid will be contraindicated. For example surgical removal of a palpebral sarcoïd cutaneous carcinoma on the upper eyelid can result in loss of the eye because the eyelid becomes non-functional – even assuming the tumour CAN be removed in its entirety! For example an invasive sarcoïd on the pastern region on the coronary band provides a considerable challenge and indeed, in many such cases treatment is not possible.
3. **Tumour extent:** Large tumours also limit what can be done. Surgical removal of a large area of skin affected by sarcoïd is often impossible to close. Extensive squamous cell carcinoma of the mouth cannot be treated effectively without serious complication.
4. **Time between tumour development and presentation:** Typically of cancer therapy, early treatment is much more effective than late treatment. The failure of owners (and, unfortunately, all too often veterinarians) to address a relatively trivial matter in a timely fashion so that cases are presented late in the course when treatment is virtually impossible. However, sometimes the signs are either so benign or so subtle that even a caring owner may easily miss them or at least attribute less significance to them. This can also be complicated by application of irrational and inappropriate “treatments”.
5. **Owner and patient compliance:** In order to be successful a treatment needs to be used in the correct manner and where the application of the treatment is compromised either by the owners or the horse’s lack of compliance the outlook will inevitably be adversely affected. Painful treatments or those that require prolonged contact are often not well tolerated.
6. **Facilities and expertise:** Treating neoplastic disease is always problematic and it is clear that horses treated by experienced veterinarians under ideal conditions have a better overall prognosis. Where sophisticated facilities exist treatment options are necessarily wider and so a more focussed option may be applied. For example the

prognosis with surgical excision may be improved by use of laser instruments or by concurrent chemotherapy. Radiation treatment is the gold standard but it is only available in a few centres and in any case is also only applicable to relatively small tumours in suitable sites.

- 7. Cost of treatment:** The cost of treatment is often of major concern to owners and the more so when the relative value of the horse is low. The size of the patient means that all methods of treatment whether topical, surgical or systemically are likely to be expensive. Furthermore the physiology and nature of the horse may add to the complications. Often the best treatments are the most expensive but the benefit has to be weighed against the financial sacrifice. It might be better in some cases to encourage the expensive option because the lesser ones may carry a much poorer prognosis. Nevertheless, there are times when a cheaper less sophisticated method will work adequately; this will depend largely on the tumour type, its extent and nature and the skill and experience of the veterinarian.

## Reported treatment methods include:

### 1. Surgical

**excision:** This is always an attractive option for accessible benign, well-defined tumours at convenient sites with good surgical access. It is relatively simple and uses basic principles of surgery. The benefits and constraints are discussed elsewhere. Quite often surgery is used in combination with other methods such as radiation and intratumoral chemotherapy.



Fig 1: A chronic fibroblastic sarcoid treated successfully with topical AW4. It required three different courses of treatment. The pictures on the right show the start of the second course and below the final position after the three courses.

**2. Cryonecrosis:** This has similar constraints to surgery and in many studies the results are very similar. The destruction of tissue tends to be indiscriminate and so during the procedure surrounding normal tissues are almost inevitably damaged. Failure occurs when either the margins of the mass cannot be defined or the true extent of the tumour cannot be defined, but there are reports of its successful use in various sites including the eyelid and mouth.

**3. Laser excision:** The availability of CO<sub>2</sub>-YAG and diode laser units is increasing and there are clear advantages in its use but the selection of the cases is critical (Vingerhoets et al., 1988). The advantages of laser surgery lie in the bloodless surgical field, the fine control that is possible and the "cautery" of the incision edges.

4. **Ligation:** Since all tumours rely on blood supply for their growth, ligation can be successful provided that the margins of the tumour are included in the consequent necrosis. This can be effectively combined with some forms of topical and intralesional chemotherapy.

5. **Hyperthermia (radiofrequency):** The author has limited experience with this method but there are reports of successful treatment of superficial verrucose or occult sarcoids. Its effects are due to the increased sensitivity of neoplastic cells to temperatures of 42°C – 46°C, which can be lethal to neoplastic cells. In theory at least, the method is reasonably selective in its effect and so it is a pity that it has not been more widely tested.

6. **Chemotherapy (direct and chemical cautery / antimetabolic effects):** Topical and intralesional chemotherapy using antimetabolic and cytotoxic chemicals have been used for many years in a variety of forms mainly in the management of sarcoid. Topical or intralesional 5-Fluorouracil, intralesional cisplatin (either as a solution, emulsion (Theon, 1997) or biodegradable beads «Matrix II Cisplatin beads, Royer Inc, USA», topical retinoids (such as tazarotene), podophylin. Silver nitrate and topical AW4 (which is based on a combination of heavy metal salts, natural oils and 5-fluorouracil) have been used with some success (Knottenbelt and Walker, 1994; Knottenbelt 2009) (see Figure 1).

Systemic antimetabolic and cytotoxic drugs are used widely in other species but there seems little benefit from their use in horses for management of sarcoids and there are no reported studies using these methods.

7. **Immunological methods:** These methods rely upon the alteration of the immunological relationship between the host and the tumour cells. Interestingly equine sarcoids spontaneously disappear in some horses (possibly less than 0.5% but in Sweden this proportion is reported to be over 15% (Brostrom, 1995). The mechanism for this is unknown but it certainly provides a direction for future research. Any method that can establish a normal rejection mechanism will result in a dramatic and satisfactory resolution of the sarcoids from the whole body surface.

Current oncologic research is focusing on alteration of the immune mechanisms to allow immunologic recognition of the abnormal cells or alteration of the tumour cells to make them more recognisable.

- **Autogenous vaccines** made from sarcoid cells is an entirely inappropriate approach (Knottenbelt, Edwards and Daniell, 1995; Knottenbelt, 2009). However, efforts at producing an effective vaccine are ongoing in several centres and there are preliminary reports of some successes (Kinnunen et al., 1999). Attempts to produce a vaccine for the equine sarcoid similar to that used in human cervical cancer prevention have understandably failed since the tumour – virus relationship is very different.
- **Immunomodulatory therapy:** Interestingly around the eye the results of local injection of purified protein derivatives or live freeze dried bacilli of BCG are really good (Knottenbelt and Kelly, 2004)! The protocol for use appears to be important and repeated injections of a protein material are not without hazard.

BCG therapy is far less effective for occult and verrucose sarcoids and any situated away from the periorbital region. Use of this method and on the distal limb is specifically contraindicated because of possible / probable exacerbation of the tumour.

The antiviral, anti-tumour compound imiquimod is an interesting alternative method of treatment for sarcoid. The material is marketed as a 5% cream (Aldara, 3M) for the treatment of external genital warts, various skin tumours including precancerous dysplastic changes and

squamous cell and basal cell carcinoma in humans. The material has a potent antiviral and anti-tumour compound that is reported to modulate the local immune processes. The efficacy against tumour and virally induced papillomas in various species makes it difficult to interpret its method of action. However, in a single publication on sarcoid, a very impressive result was obtained. The published study by Nogueira et al., (2006) reported spectacular success and this is certainly a modality that deserves more research and further development. The author has limited experience of its use and those that we have treated have usually been improved somewhat in the short term, without any long term benefits. This may be a result of different regimens of treatment and different cases selected for treatment. In common with other agents applied topically there are failures and difficulties with the course of treatment but it seems more likely that its effects are due to the specific mediator-induced inhibition of the tumour rather than the putative virus that is possibly involved in sarcoid pathogenesis.

- **Homeopathy:** These methods are consistently useless in the management of neoplastic disease; whilst they may do no specific harm, it delays the application of appropriate interventions. All sensible, informed scientific opinion and all trials conducted into the use of homeopathy have failed to show anything beyond a placebo effect. It is hard to see how a horse can demonstrate a placebo effect!

Until proper scientific proof of efficacy and a plausible scientific explanation for the effects are produced it is probably dishonest to exploit the fear of cancer in owners simply to obtain financial reward.

- **Radiation:** The use of ionising radiation represents the gold standard treatment for the equine sarcoid. The techniques have significant advantages in minimising scarring and distortion due to cicatrization in an area where the function of the organs involved is of vital importance.

The basic principle of the technique arises because ionising radiation (electromagnetic radiation) and high energy particles (helium, high energy electrons) ionise tissues through which they are directed. It is assumed that the major effect of the radiation is on DNA but it is likely that a wide range of cell proteins and lipids are affected within the cell and in the cell membrane.

It is important to remember that the response to a radiation dose may be slow to develop. This is because the cells may survive in the absence of effective DNA but are unable to reproduce and therefore the natural ageing process of the cell type reflects the delay in clinical effect, which is characteristic of radiation therapy.

Following a course / dose of radiation the tissues are indiscriminately destroyed (after a variable period) and followed by local tissue repair from natural stem cells.



Radiation treatment can be successful as show in the above case, and below. It is whether it is worth the personal risks that is the major question.

## **Radiation is used in two basic ways:**

1. **Brachytherapy:** This technique is used primarily for the treatment of superficial sarcoids which are either situated in areas which are not amenable to other modalities, or which have recurred after previous attempts to remove them (by whatever means).

Radiation sources are applied directly onto or into the mass. The most frequent methods for this include a number of sources of beta and gamma radiation which are implanted into the tumour mass or are applied directly to the surface. In the former case (eg, iridium 192, gold 198) gamma radiation is continuously emitted through the target tissue and the relative emissions and lengths of source can be adjusted. In the latter (e.g. strontium 90 plaque) the radiation is applied in fractionated doses calculated to deliver the required "lethal" overall dose. Iridium 192 sources are expensive and requires specialised facilities for stabling and care over the period of treatment which may be up to 10 days or more. Strontium 90 plaques are much easier/safer to handle but require fractionation and therefore repeated potential operator exposure.

2. **Teletherapy (External Beam Radiotherapy):** This is performed far less frequently in equine medicine, mainly for logistic and capital cost reasons but facilities are being developed in the UK and Germany and it is expected that sarcoid will form a major part of the case loads in these centres.

Radiation brachytherapy is largely restricted to ophthalmic oncology and it is most frequently applied by brachytherapy in the treatment of squamous cell carcinoma, neurofibroma and nodular and fibroblastic sarcoid around the eye. There are few reports of the use of teletherapy for any other equine problems (Coumbe, 1994). Radiation has a considerable advantage over most other tumour treatments in having a very acceptable cosmetic consequence. Scarring is minimal and the slower rate of resolution allows local tissues to adapt to changing cell types more easily. For this reason and because the procedure carries both cost and safety implications (no matter how it is applied) the technique is usually restricted to small tumours in difficult sites such as the eye and periorbital skin and over joints. There is the added advantage that radiation can be used as "fail-safe" technique – previous less expensive techniques which have not succeeded may still be treated by this method with good prospects of success. Radiation therapy carries a better overall prognosis than most other methods and can be combined with surgical debulking so that less radiation needs to be applied. As the clinical effects of radiation depend heavily on the replication rate of the cells involved tumours growing fast are more responsive than old, long-standing tumours – the effects of the treatment on sarcoid are not usually maximal until 12 – 14 months after treatment has been completed. The effects of radiation often take up to 12 – 14 months to develop and some cases have distressing periods off tissue sloughing during this time.

## Novel therapies for equine sarcoids:

These include:

- Electrochemotherapy: a therapeutic approach providing delivery into cell interior of non-permeant drugs with intracellular targets.
- Photodynamic therapy: Photodynamic therapy is currently being explored for some cutaneous tumours. Photo activated chemicals such as hypericin, are introduced to the tumour (either topically or systemically via labelled antibody) and the lesion is then subjected to intense U/V light. This causes massive mediator release and cell damage. There are few reports of the results of this but it is an attractive option.
- Autografting (with cryo-preparation of the donor grafts): This is a recently revisited technique that was first used in the 1940s (where it failed to bring convincing results) that involves the subcutaneous implantation of frozen cubes of tumour tissue derived from a sarcoid on the horse. The results reported of late are incredibly impressive but involve very few cases so far. There is no apparent material difference in the new technique so it is hard to understand what the improved outcome is due to!



There is no doubt that many sarcoid lesions can be treated by one means or another. As is always the case, the successes are not the problem – it's the failures! Failure of any treatment has to be viewed as a potential disaster since the prognosis for subsequent treatments falls dramatically (by around 40%).

Any claims for 100% effective treatment should be viewed with scepticism; either the cases are so carefully selected or the results are interpreted constructively.

**It remains singularly disappointing that owners and regrettably some veterinarians apply irrational interferences and cause significant exacerbations or at least a serious drop in the prognosis by so doing.**

**The advertisements in the lay press peddling “dietary supplements”, creams and lotions are simply irresponsible and should be stopped; they simply set out to exploit the gullible, vulnerable and disillusioned owner.**

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