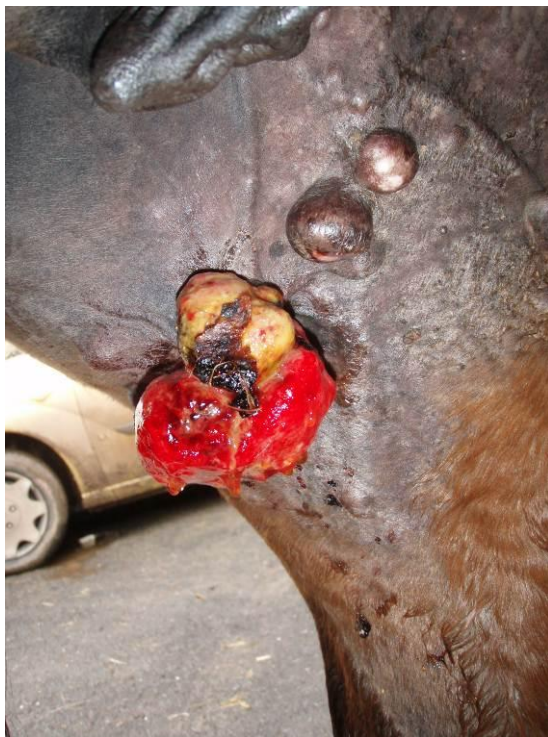


## THE EQUINE SARCOID: AN UPDATE

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### Introduction

The equine sarcoid is by far the commonest cutaneous neoplasm of horses and the risk factors that predispose to its development in an individual have only partially been identified. The disease is becoming more prevalent and yet there is still little interest in advancing research efforts. It affects horses of all ages, although the majority of cases are first presented between 2 and 9 years of age. Sex appears to play no significant role although again there have been suggestions that geldings are over represented. Almost all breeds of horse, mules, donkeys and zebra, are susceptible although there is some suggestion of an increased prevalence in 'thin skinned horses'. The Quarterhorse and the Lipizzaner are reported to be less susceptible.



*The equine sarcoid is unique in respect of its aetiology and its epidemiology. It also occurs in several distinct forms and individual animal may have several or many lesions and these may be very varied in appearance.*

A genetic basis for the disease has been established. Several genetic lines have known predisposition but individuals within those lines may not get sarcoids at all while others may be severely affected. While this may superficially suggest that there is some heritable aspect of the disease it is very important to realize that there are other factors that need to be present for a particular animal to get the disease. It is easy to propose that horses with sarcoids should not be used for breeding but the genetic tendency to the disease probably exists in a far higher number of horses than actually show overt sarcoid skin disease. The suggested autosomal recessive gene responsible for imparting a susceptibility to the condition probably has an influence on the number type and severity of lesions,

and the tendency to recurrence and exacerbation in an individual. Realistically therefore we are not in any position at this time to advise that affected horses should not be used for breeding but I think it is reasonable to try to exert breeding pressure against the disease by avoiding the breeding of two affected horses.

For many years researchers have been trying to find a cause for the disease but we are still some way from a definitive answer. The role of papilloma viruses is uncertain - no patent virus particle has yet been conclusively demonstrated but a very high proportion of sarcoids have genetic material that is identical or very similar to that found in some papilloma viruses. The distribution of lesions and the epidemiology of sarcoids strongly suggest that flies are significant but how the fly and the 'virus' are linked has yet to be established.



*Why do flies feed preferentially on sarcoids and what does this imply for the epidemiology of the disease? BPV particles have been found in flies associated with horses and this has been suggested as means of induction of de novo sarcoids. It is unlikely that the epidemiology of sarcoid is as simple as that.*

The equine sarcoid is a fibroblastic tumour and the clinical behaviour of the transformed cells is typical of a slow growing fibrosarcoma / spindle cell sarcoma/ fibroma. A wide variety of morphological pathological descriptions are applied to the disease and it is quite likely that these are individually correct in terms of the histological appearance. The term sarcoid was first used by Jackson (1936) to depict its generally sarcomatous appearance. It is used to encompass a spectrum of fibroblastic neoplasms. Furthermore, the verrucose "wart-like" appearance of many sarcoids, which is manifest by a hyperkeratotic, exfoliative and acanthotic nature, cannot be accounted for simply in terms of the behaviour of fibroblasts. Fibroblasts have no mechanism for the production of keratin and should therefore have no influence on the behaviour of the overlying or adjacent epidermis. The role of the papillomavirus DNA in the behaviour of the overlying and surrounding keratinocytes and in the consequent clinical appearance of the "typical sarcoid" is an interesting new development. Some pathologists are not prepared to make a diagnosis of sarcoid if there are no epithelial changes or if there is no epithelium on the biopsy specimen. Given that the sarcoid is a primary tumour of

fibroblasts this is somewhat surprising and it seems that the definition given by Jackson on 1936 has been taken as the definitive description. However, he stated that the sarcoid had a variable dermal component implying that it need not have any at all. Furthermore, all transmission experiments that have been performed identify that the “danger cell” is indeed the fibroblast. It is now clear that the keratinocytic responses are secondary to growth factors expressed in the fibroblasts by the viral genome and this is a plausible and adequate explanation for the clinical appearance of the disease.

The location of the typical sarcoid gives significant clues on the true nature of the disease. The most susceptible regions of the body appear to be thin-skinned, hairless areas where sweating occurs. The common feature of these areas is of course that flies can and do feed. This explains why superficial sarcoids on the distal limb and body trunk are much less common and when they do occur they invariably relate to small or large wounds. The role of wounds in the pathogenesis is an important new concept in the understanding of the disease. If we accept that flies are in some way involved in the pathogenesis of sarcoid then we need to establish how this is the case. Does the fly transmit the “papilloma virus” as a vegetative virus or is the hypothesis that it is in fact the cells that are translocated across the horse and between horses enough to explain the distribution and epidemiology of the disease. The latter appears to be a genuine possibility and it may explain in part at least why some horses get many more than others and why some individuals are never affected. Here it may be a matter of the relationship between the host and the “imported transformed cell”.

Sarcoids commonly multiply on the individual horse; sometimes very rapidly while some others remain relatively, or even completely, static for years (or even for life).

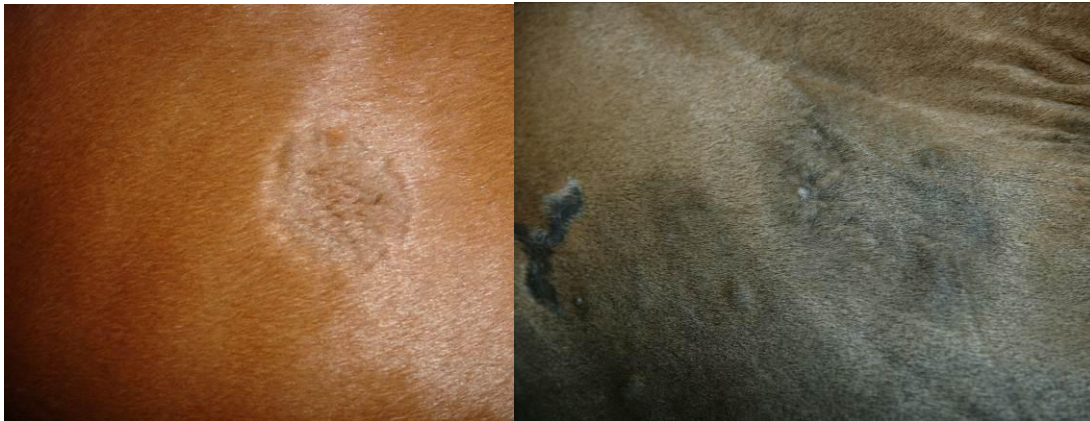
### **New Perspectives on Clinical Recognition**

Clinically and pathologically, sarcoids present most of the features of a true neoplasm; indeed it is best regarded as a form of skin cancer. Although this may not be strictly true in pathological terms it does at least suggest that the behaviour of the tumour is unpredictable and that treatment may be problematical. It is however clear that it is not a wart

Six distinct clinical entities, which are noticeably different, can be recognized with individuals being affected by any combination of these. These forms can be correlated with the histological features but all have central fibroblastic component comprised of transformed fibroblasts. The keratinocyte and hair changes (pigment, density and hair shaft quality) are likely to be secondary changes arising as a result of gene expression for mediators that affect keratinocyte behavior and keratin production.

*Occult sarcoid:* The predilection sites include the skin around the mouth and eyes, the neck and other relatively hairless areas of the body including the inside of the forearm, armpit and thigh. Lesions show as hairless areas, often roughly circular. They usually contain one or more small cutaneous nodules (2-5 mm diameter) or roughened areas with a mild hyperkeratotic appearance but these may or may not be present or obvious in every case. An area of changed/altered, slightly thickened skin with thin hair coat and slight changes in hair pigment may be encountered and may be difficult to identify in winter-coated animals. The lesions are characteristically slow growing; they may progress to “wart” verrucose growths or if injured may develop rapidly into fibroblastic lesions. While the lesion remains as a static/quiescent hairless patch showing no evidence of growth in size or number of nodules, it may be wise not to interfere.

Cases have existed for over 15 years without treatment or acceleration; however extensive development of verrucous sarcoid or conversion into fibroblastic type sarcoid, usually demand immediate attention. This can occur at any time with or without apparent insult.



*Typical occult sarcoids - it is easy to overlook these, but you do so at your peril since they invariably become worse with time!*



*Verrucous or "warty" sarcoid. It is easy to understand why the term wart is applied to these lesions but it does not impart the right message concerning its danger.*

**Verrucous (warty) sarcoid:** These lesions have a rough hyperkeratotic appearance and scaling over limited or wider areas of the body. Most often this type is seen on the face, body and groin/sheath areas. Extensive areas can be affected and are often surrounded by an area of slightly thickened

/changed skin (possibly reflecting a surrounding area of early occult sarcoid) with altered, thin hair-growth pattern.

Individual lesions may be sessile (flat-based) or pedunculated (with a narrow neck) giving a true wart like appearance - indeed this type is probably the source of the name "wart" on horses. The name is of course misleadingly benign for a potentially dangerous condition. The lesions are most often slow growing and not very aggressive until injured/insulted. However, small nodules may appear at any stage or over any area of the affected skin. These may develop a true fibroblastic character whether or not they are insulted or traumatised. Rubbing, biopsy, partial excision or minor or major trauma to the surface commonly results in a dramatic change to fibroblastic sarcoid over variable areas of the lesion.

The verrucose sarcoid can be mistaken for papillomatosis (true warts), chronic blistering, severe chronic rubbing or irritation such as can be seen in a few cases of sweet itch for example.

*Nodular sarcoid:* The lesions are easily recognisable, as firm, well-defined subcutaneous, spherical nodules of 5-20 mm diameter but can be much larger. Most often this type can be found in the groin, sheath or eyelid areas. The number of nodules varies widely - single, few, several or hundreds are common. The nodules usually lie under apparently normal skin and then may be freely movable. However, sometimes there are dermal and deep attachments, which prevent independent movement of the overlying skin and /or movement of the tumour mass relative to deeper tissue. The overlying skin may become thin over larger nodules and when these ulcerate they quickly become more aggressive fibroblastic type tumors. A similar aggressive fibroblastic response commonly follows iatrogenic or accidental or iatrogenic damage.

*Fibroblastic sarcoid:* These tumours have a characteristic fleshy sarcomatous appearance. Predilection sites include the groin, eyelid, lower limbs and coronet, sites of skin wounds at any location and sites of any other types of sarcoid subjected to trauma or insult. Both pedunculated (Type 1 fibroblastic sarcoid) and extensive sessile tumours (Type 2 Fibroblastic sarcoid) with prominent ulceration and serum exudation are commonly encountered. The latter may reflect single or repeated insults to the "lesser" forms but may develop spontaneously.

*Sarcoid Transformation at wound sites:* One of the most dangerous problems that occur with the sarcoid relates to those that develop at sites of wounds (including surgical wounds). Accidental wounds that fail to heal may contain significant sarcoid components in the wound margins and admixed with granulation tissue. Even a small wound on the distal limb can become a very troublesome sarcoid with a complete or partial failure of the wound to heal. While the clinical appearance of proud flesh can be remarkably similar, treatments for the two conditions are very different. Indeed treatment that is suitable for proud flesh (cutting back and grafting) serve only to make the sarcoid even more aggressive and even more impossible to treat effectively. Thus, wound management in all horses, and those with sarcoid skin tumours at other sites (and those with no sarcoids that are genetically susceptible to the disease) are particularly important.

The fibroblastic proliferation at a wound site can be very extensive but an interesting feature of sarcoid transformation at wound sites is that lesions on the body trunk (that might normally expect to

heal well by contraction) develop a verrucous sarcoid while those lesions that develop at the site of limb wounds (where healing is notoriously slow and difficult and where exuberant granulation tissue develops) develop a fibroblastic lesion. Whilst there are exceptions to this rule it is a significant pathophysiological aspect.



*A typical fibroblastic sarcoid. Note that this horse had been treated using radiation for a similar sarcoid on its upper eyelid. The residual scar and white haired area is evidence for all to see. The case was successfully treated on both occasions.*

In spite of their aggressive appearance fibroblastic sarcoids do not metastasise but can spread locally in dermis by local invasion/extension. Repeated insult (accidental or iatrogenic) encourages local sub-dermal and dermal invasion. The other major complication is the attraction that flies have to ulcerated and bleeding sarcoids. This simply provides a relatively direct and easy means of spread of sarcoid to other sites on the body and possibly even to other horses.

*Mixed (Verrucous, Nodular and Fibroblastic) Sarcoid:* This type of sarcoid probably represents a progressive/transient state between the verrucous / occult types and fibroblastic / nodular types. Variations in proportion of the several types of sarcoid is infinite and complex mixtures of any or all of the above types (containing both verrucous and fibroblastic elements) are common in long standing lesions or those subjected to repeated minor trauma (such as rubbing by tack or harness). They become progressively more aggressive as more fibroblastic transformation takes place - a common consequence of biopsy or injury.

*Malignant / Malevolent Sarcoid:* This is a recently described variation with predilection sites in the jaw, face, elbow and medial thigh areas in particular. A particularly dangerous form occurs in the immediate area around the eye. A history of repeated trauma to other types of sarcoid e.g. surgical interference is commonly described. Some cases have no such history with spontaneous development of typical multiple, locally invasive sarcoids. Others show extensive infiltration of

lymphatics (cords of tumour are commonly palpable) with numerous ulcerative nodules and surface involvement as well as possible extension to local lymph nodes.

The malevolent form of sarcoid is particularly dangerous, not least because there is no current treatment for it. Its appearance is not easily mistaken for other skin diseases but again the presence of several different types of sarcoid elsewhere on the body makes the diagnosis relatively simple.

Sarcoids generally (not only the malignant form) have a high capacity for local tissue invasion into the surrounding skin and other tissues. This is particularly dangerous in the eyelid. This local spread makes treatment very difficult and may explain why sarcoids have a bad reputation for recurrences following surgical excision or other interference.

### **New diagnostic approaches**

The tendency to exacerbation and recurrence following biopsy, treatment or other interference means that “first presentation” diagnosis needs to be as accurate as possible. There is a general and understandable fear of biopsy – we know that over 80% of lesions that are subjected to biopsy or partial surgical removal without any further therapeutic intervention will be significantly exacerbated. Although tis exacerbation is often marked, the process of biopsy is much less liable (5%) to cause remote exacerbation i.e. there is little risk of sarcoids at other sites being exacerbated by the process of biopsy or partial removal.

The development of modern PCR methods to detect the smallest amounts of genetic material has recently been used to identify the BPV virus genome in swabs simply taken from the surface of a suspected sarcoid. This is certainly helpful particularly in the differentiation of other clinically similar conditions. Otherwise there is little new in the diagnosis. We continue to rely largely upon intuitive supposition or standard biopsy techniques; the former may be unreliable for less experienced clinicians and the latter may be problematical unless a treatment method is available immediately.

There remains a real need for a greater consensus amongst pathologists and this could provide real progress in both diagnosis and treatment.

### **New perspectives in therapy:**

Interestingly, a few individuals show spontaneous full and permanent self-cure and in my experience, spontaneous full remission (self-cure) usually means that the horse will not develop further lesions. This is the one group of horses that can probably be assumed to totally resistant. It is likely that this response has some immunological basis and this might be a very interesting line of research. There is no apparent correlation between the number of lesions and the likelihood of spontaneous regression / self-cure or indeed the tendency to develop multiple lesions. The course of the condition is entirely unpredictable and it is probably unwise to assume that there any invariable rules about the disorder: even the most benign-looking small lesion can erupt into a potentially catastrophic mass in a short time. The value of small interfering MRNA (siMRNA) and targeting methods for E5 gene expression appears to be increasingly positive.

Notwithstanding the self-cure cases, and the hope of some immunologic / genetic therapy in the future, treatment should follow as soon after diagnosis as possible. Suspicious lesions can justifiably be treated immediately after biopsy using a suitable regimen. There are ten or more recognized treatment methods for the disease and this suggests that no one treatment is invariably effective. Indeed with the possible exception of radiation (which is largely impractical for most cases) treatments are all inadequate in some respect. What works for one vet may not work for others and so each veterinarian needs to be careful about the treatment modality selected. It is imperative however that the best possible treatment method is applied first time. The selection of an inadequate (compromise) treatment will inevitably lead to later complications and possibly even acrimony between vet and owner. It may be better to leave the lesion untreated than to interfere with an inadequate method that has little or no chance of resolving the lesion. Failure to resolve the lesion results in a drop in the prognosis of 40% for each failed attempt! Bearing in mind the rather poor prognosis from which most lesions start, failure is a disaster.

New treatment methods have focused on the use of photodynamic therapy mediators and on the restoration of keratinocyte function so that the extent of treatment (of any sort) involves less surface area.

1. Photodynamic therapy is an attractive option that limits the damage to the area of the tumour only but it is clearly only applicable to single small tumours in convenient locations.
2. Mediator approaches: These are in their earliest stages of development and rely upon the mechanisms to encourage an auto-rejection of abnormal cells. So far Interleukin –12 and IL-18 have been tested in limited numbers with encouraging results. The prospect of immunological or cytokine mediated recognition of tumor cells is exciting but are both expensive and so far unquantified. There may be unwanted effects from this approach also.
3. Alterations of the keratinocyte function with retinoid topical medications. The realization that the keratinocyte related changes in equine sarcoid introduced the concept of a two-phase treatment method. The first involves the use of a retinoid cream to exfoliate the keratinocytes and restore their normal function so that the focus(es) of sarcoid could be identified and treated by surgery, topical chemotherapy, cryosurgery or radiation.

Apart from the above the time-honored range of treatment methods is available although many of these have been refined to the point where results are considerably better. Judicious selection of the treatment should enable cure rates (for treated lesions) of around 70% or more. Radiation methods clearly provide the best outlook but they are very expensive in either teletherapy or interstitial brachytherapy methods. There are also logistic problems and the facilities are becoming more difficult not less so!

There is an increasing desire, quite understandably, to seek treatments that do not require the expense of veterinary attention. Usually this is VERY counterproductive. Sarcoid is cancer and when the local pet shop or tack shop or charlatan is consulted on human cancers then they will be in a position to proffer “advice” on horses. Homeopathy and other herbal remedies simply do not work.

They frequently delay the application of proper treatment beyond the time when success is possible. That means the failure is then blamed on the conventional medical approaches.



*Examples of mistreated sarcoids that have become irretrievable!  
Homeopathy and quackery simply do NOT WORK*

No matter how identical two lesions may appear to be, the response to treatment can be very different - no two cases respond in an identical fashion to a single treatment method.

There will be a financial commitment at some point in the large majority of cases. There is a strong likelihood that prolonged or repeated treatments will be required. We are all looking for a “sure-fire” treatment for cancers but this is a long way off yet for the equine sarcoid. No case of sarcoid can be considered to be free of the disease even following apparently successful treatment. Recurrences may take up to 25 years to occur and of course the affected horse remains liable to further sarcoid development regardless of the methods used to cure them (excepting of course the self-curing cases which remain solidly immune).

Homeopathic remedies are often used to treat sarcoids but remain very disappointing. It is unwise to conclude that none of these will ever treat cases because certain natural medicines including Alo Vera, Rosemary Oil and Teetree Oil have however, been found to help a few cases. Recently ‘Exterra’ (Indian Mud) has been used widely and has some efficacy in a limited number and types of sarcoid. A material known as *Camrosa* (which has no defined components) is probably dangerous and should

not be used – any material that will treat almost any disease in almost any animal must be viewed with some skepticism! It is also important to know that in some cases application of remedies of various natural and homeopathic types have resulted in considerable exacerbation of the tumours. This is probably more a property of the fact that the tumours have been interfered with rather than any directly harmful effect of the remedy.

**Prognosis:**

The prognosis is always very guarded and owners should be made aware of the possible serious complications, which can arise both from the disease itself and from the treatment. A diagnosis of equine sarcoid has a very serious effect on the value of the horse and the likely enjoyment that the owner will get out of it.

**Summary:**

Whatever is said about the equine sarcoid in folk-lore and in the largely ill-informed lay press, it should undoubtedly be regarded as a form of skin cancer. It should therefore be treated with the respect deserving of any neoplastic state; early veterinary consultation will help to ensure that the condition is held in check and not allowed to run rampant through the skin of a horse. Whenever a horse is found to have a sarcoid lesion it needs to be put into the proper perspective. The condition is unpredictable and before a purchaser parts with their money he/she should be sure of the insurance implications and the likelihood that treatment will be required. A single small lesion may remain identical until the horse dies of old age but it could erupt at any time or it may herald the development of more lesions as time passes; the difficulty is deciding which is which... there is no clinical indicator which helps to predict which lesions will take on an aggressive form and which will not! It is clear that the fewer lesions that are present at any one time the fewer it will get and this may link to the feeding habits of flies during summer months. Horses should be as sarcoid free as they can be over the summer months when flies are a problem.

The correct choice of treatment method is critical. The best possible method should be used for each individual lesion taking into account the type, anatomical location, duration, and previous treatment history and owners resources. Each factor will influence the decision but no method is universally effective. Resorting to homeopathic rubbish or other witch-doctoring is not what cancer deserves. Unless and until there is a wider appreciation of what the disease is and how it can develop into an irretrievable situation, we will continue to destroy horses. We should do for our horses as we would wish to be done ourselves!

The prospects for successful treatment are far better if the lesions are small, early and the horse is under 4-5 years of age. None of the treatment methods are cheap and none of them are certain of success. Sarcoids around the face and on the legs are particularly dangerous in almost every aspect of the disease and owners should not be unduly surprised when any selected treatment fails to help: indeed you should not be surprised if the treatment makes matters worse! Furthermore there is no current method for treating microscopic lesions – we can only treat those we can actually see. We would hope of course that eventually we might be able to find a way of making the immune processes of the patient recognize the presence of abnormal cells and reject them – this way every single cell could be detected and destroyed; there would be no more sarcoids. This is some way off yet – if it were as simple as this then we would have an answer to every cancer and disease in every

species of animal! We are in desperate need of more effective treatments and some form of prophylaxis if we are to rid the horse of this distressing and expensive disease.

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