



Sarcoid information

The sarcoid affects all members of the equid family worldwide; this includes horses, mules, donkeys, zebra, Przewalski Horse and exotic asses. It has several implications, and is a form of cancer. Affecting between 2-8% of horses, it is a common disease. Sarcoids can occur almost anywhere on the skin, although there are some regions that are more liable to their development.



Sarcoids are likely to multiply on a horse, and may enlarge quickly or slowly; especially when the sarcoid is traumatised or otherwise interfered with! Some sarcoids can remain static/quiescent for many months/years. Trauma can trigger the development of the most aggressive forms of aggressive sarcoid, from even the earliest, mildest and smallest lesions. The tumours may 'spread' across the horse, meaning that more will develop over time. On any one horse there may be different types and ages of sarcoid due to the fact that sarcoid continues to spread over the life of the equine at an unpredictable rate.

Further research has been devoted to the investigation of the sarcoid, both microscopically and genetically. There are still large 'unknown black holes' in our knowledge.

Ways that sarcoids affect horses

- They can become ulcerated and/or infected.
 - This may be debilitating and metabolically exhausting; and can become a serious welfare issue.
 - Some horses are so badly affected that they develop systemic effects; including low blood proteins, and anaemia. Such cases are sometimes destroyed on humane grounds.
- They can cause severe functional problems when they develop at highly dangerous body sites.
 - These sites include the eyelids, over joints, and coronary bands.
 - Treatment at these sites is usually restricted, and more problematic.
 - Eyelid sarcoids can be very aggressive and difficult, with extensive roots penetrating the muscles that control eyelid movement.



- Cosmetic difficulties.
- Location of the sarcoid can make it difficult/impossible to wear tack/rugs.
- Flies are attracted to sarcoids.
 - Particularly in the summer months. This can be highly distressing for the horse.
- Some horses perform less well with sarcoids than without them.
 - Sarcoids may limit the working life of horses.
- The price of a horse with sarcoids on the open market is usually less than the same horse without sarcoids
 - They may also be unsellable.
 - Sarcoid is a common cause of loss of commercial value, even in high performance horses.

Common areas

Sarcoids occur at all body sites, but there are some areas where the disease is more common:

- At sites where flies attack and can feed without difficulty.
- Where the skin is thin.
- Where there is little/no hair.
- Where there is a propensity for sweating.
- At wound sites where the skin has been broken (the wound may not have been recent)
 - We know that sarcoid formation is a common cause for incipient wound healing failure. If a wound fails to heal it should be tested for the presence of sarcoid.
 - Wounding is a very important factor in the development of sarcoid at abnormal locations such as the neck, upper body, and distal parts of the legs.



A sarcoid in the stifle where the skin is thin and there is little/no hair

Sarcoids never develop in internal organs and do not spread to these from cutaneous sites even when they are extremely aggressive or extensive; this means that affected horses are not usually 'sick'. They are rare on the upper trunk, back, and neck – when they do occur it tends to be where there has been skin damage (injection sites, rub marks or injury sites).



Sarcoid should be viewed as a form of skin cancer

There are several features of sarcoid that are consistent with the clinical principles of a genuine neoplastic (cancerous) disease:

- The behaviour of the tumours.
- The difficulties encountered in treatment.
- The tendency to recurrence.
 - There are very few cases which spontaneously resolve.
- The spread across the body from site-to-site.
 - Some sarcoid lesions are small and have a benign clinical behaviour. They may remain static for many months or even years.

The sarcoid is a tumour of fibroblasts – the cells that provide support and structure to tissues. The skin and the tissues directly underneath seems to be the only place where this tumour can exist. It does not spread to the internal organs. Sarcoid can infiltrate between muscles and can sometimes be very extensive and aggressive locally. Pathologists recognise it immediately, even in very small samples!

Stop and think before you apply anything to a sarcoid. It is cancer and should be treated with respect.

Susceptibility

Geographical influence

Sarcoids occur worldwide. There are some regional differences in the types, locations, and average number of tumours per horse. For example, in continental Europe it is estimated that the prevalence [1] is around 2.5%, but in the UK this is up to 6-7%. In Australia and Ireland, fibroblastic lesions are commoner on the leg than in other sites. The malignant form is rare in all countries but appears to be more common in the UK.

Age

Sarcoids can develop at any age. Although most cases are first noticed between 2 and 10 years of age, individual cases can start at any age from weeks old to the late 30's. This probably reflects when a genetically susceptible horse is challenged by the disease and then succumbs. It is probably not age related.



Breed

There are genetic aspects to the disease and the liability to it. Although most breeds are susceptible, some appear to be highly resistant (Lipizzaner) while others are reported to be more susceptible (Arabian). Crosses involving Lipizzaner horses are more liable to the disease.



Some families of horses are very liable to the disease and future generations appear to contract the disease. However, many horses are apparently less susceptible. This appears to have a genetic basis and relates to a specific gene that appears to impart either greater resistance or greater susceptibility. A high proportion of the general horse population may be genetically liable to the disease, but only relatively few are actually affected. This implies that there are other factors involved but it is not clear what these are.



Breed susceptibility has been explored at length and there is still much doubt surrounding this. The heritability of the susceptibility or resistance to the disease is unknown.

Development and diagnosis

Development

Several facts about the development of sarcoid are well known. There is some involvement with the bovine papilloma virus. Although this is not a vegetative virus, it does appear to act as an oncogene (a genetic insertion which imparts the properties of a tumour to a particular cell type). This means that there is, in theory, the possibility that horses can be 'infected' with bovine papilloma virus from close proximity to cattle and therefore develop de novo sarcoid.

There are some major difficulties with the concept of bovine papilloma virus involvement:

- The involvement of fibroblasts (the cells that provide support and structure to tissues) is not likely with a superficial viral infection
- If it were as simple as being caused by bovine papilloma virus alone – given that papilloma virus can be found on normal horse skin and, in particular, inflamed skin on the majority of horses – we would expect more horses to develop the disease. We



would also expect at least some of them to develop antibodies to the virus – this does not happen.

- The next enigma is how the virus gets access to the tissue itself, and how it goes on to produce an entirely predictable tumour state that is instantly recognisable.
 - Why is it that the tumour can develop very quickly from a de novo introduction of a tumour cell into a site on the body? It would seem very unlikely that this was possible with an accidental viral challenge.



There is considerable debate as to the true pathogenesis of the sarcoid.

There are elements of transmission between animals involved; apart from the genetic predisposition of some individuals, families and breeds. We do know that sarcoid can transfer from horse to horse, provided that there are certain criteria fulfilled. It is not as simple as the transfer of a virus from one site to another – otherwise we would expect to find almost every horse with sarcoid, or if they did not have sarcoid almost every horse would have antibody to the virus. Transmission between horses is a very complex and rare process that researchers are still trying to understand.

The distribution of sarcoid, and the fact that it is largely a summer related disorder (at least in the United Kingdom where there is a strong fly seasonality) strongly suggest that flies are intimately involved in the epidemiology. Whether they are involved in the direct cause is another matter. If multiple species of flies are seen feeding at a particular site on a horse then due care should be taken to investigate why they are attacking this particular site.

The simple truth is that we do not understand this disease but as a general rule it should be assumed that flies are probably responsible for transmitting the disease either from cattle to horses (in the event that the virus hypothesis is believed) or from site to site on the same horse (this is not as a result of blood transmission) or from horse to horse (if the cell hypothesis is believed).

Sarcoid development in wounds

Sarcoids can occur in wound sites at any future time. If a wound fails to heal it should be tested for the presence of sarcoid. A sarcoid-affected wound can look very similar to ‘proud flesh’ or exuberant granulation tissue. The treatment for ‘proud flesh’ will exacerbate a sarcoid, whilst treatment of ‘proud flesh’ with anti-sarcoid medication will simply stop the



healing process. It is vital to know whether any granulating, non-healing wound has any component of sarcoid.



This sarcoid had been treated as proud flesh and was treated with AW5 once sarcoid had been confirmed when the wound failed to heal.

Mixtures of granulation tissue and sarcoid are very common so biopsies and tissue samples taken during wound management may not always reveal the true nature of the problem. Injuries on the body and neck usually develop into verrucous sarcoids while wounds on the distal limb usually develop into aggressive fibroblastic sarcoids. Long delays in the development of the sarcoid may be due to a slower growing tumour type that eventually emerges or later develops in the wound site.

Precautions to avoid sarcoid spread into a wound:

- Very careful fly control – particularly for horses with lesions already present.
- Avoid contact between younger horses and severely affected older animals.
- Early treatment of every case to reduce the threat of site-to-site, and horse-to-horse transmission.
- Wound management on horses with sarcoid, and those who are in close contact/proximity to horses with sarcoid must be perfect – especially over the summer months.

Diagnosis

Sarcoid of all types (there are 6) can look like other conditions such as ringworm. The implications, management, treatment, and prognosis of these conditions is very different. The diagnosis is vitally important and can only be confirmed by a veterinarian, in some cases tissues samples (biopsies) have to be taken.



The pathological features of the sarcoid are very recognisable in most cases. Pathologists examining skin biopsies taken from sarcoid lesions will usually be able to categorise and define the sarcoid type in detail. Differentiation of sarcoid from proud flesh/granulation tissue and some other tumours is important because the treatment options for each type of condition are different. In some cases, the diagnosis is not certain!

It may be possible to remove a few cells from the suspected lesion using a fine needle aspiration technique, rather than a true tissue biopsy.

Some pathologists classify sarcoid as a low grade fibrosarcoma or a spindle cell tumour. This is a description of its cellular appearance and doesn't mean it is a benign lesion.

Treatment options

There are around 40 different treatments used worldwide. This suggests that no single method is universally effective. The treatments available have variable effects; some can be very successful on some occasions and ineffective on others. Lesions that look the same and are in the same anatomical region may respond differently to the same treatment type!

Failure of treatment is usually followed by the reappearance of a more aggressive tumour, and often in increased numbers. It is important to select the best possible treatment as the first option. Repeated failures bias the long term outcome to failure. Horses should be treated at an early stage in the disease when lesions are small. Effective treatment is more certain if lesions are treated early, and if the horse is under 4-6 years of age. A very neglected lesion will require an extensive and aggressive treatment protocol which may have a big impact on the horse.

There are various treatments available:

- Radiation : This gives by far the best results but is very expensive and restricted – there are only two or three centres worldwide where this treatment can be done. It is reserved for difficult lesions such as around the eye or over joints, and where owners can afford to invest the considerable sums involved.
 - In the UK the only centre doing this is the Animal Health Trust in Newmarket.
- Topical therapy: AW5, Bleomycin, Efudix (5-Fluoro-uracil cream), Aldara (Imiquimod), Exterra/Blood Root Ointment, Retinoid drugs (Zorac), Aciclovir.
- Surgical removal
- Intralesional chemotherapy
- Ligation
- Cryosurgery (freezing)
- Photodynamic therapy



- Immune methods: BCG injection

Topical Therapy

AW5 cream

This material is available only to veterinarians upon request for the treatment of individually named cases who are referred through Equine Medical Solutions Ltd and have been provided with a protocol from Prof. Knottenbelt. AW5 is veterinarian applied, usually involving multiple applications over a period of days, as it cannot be handled by a non-veterinarian. This cream probably carries the best balance for topical therapy, in terms of cost, practicality and efficacy.

Treatment with AW5 can be painful and treated horses often have significant swelling. After the course has been completed, the horse can be quite dull. This is a product of the penetrative quality of the material and the ability to reach the depths of a sarcoid and its roots. If there is a period of discomfort following application then painkillers may be required.

After treatment, the lesion usually turns black and hard, gradually separating from the underlying normal tissues. There are limitations to the use of the material in terms of location and type of lesion being dealt with. This method can be quite hard on the sarcoid and the local tissue support.

If your vet has prescribed this treatment, make sure you have read and understood the owner handouts on the health and safety precautions.

5-Fluoro-uracil cream (Efudix™)

Efudix can be effective for the milder forms of occult or verrucous sarcoid. It is particularly useful as a pre-treatment modality before another method is used. It is a prescription-only pharmaceutical product. This material is available through Equine Medical Solutions by prescription from Prof. Knottenbelt. Usually this requires treatment twice (sometimes three times) a day and the treated area can get very sore! This means that completion of the course can sometimes be quite challenging.

This method is usually used to treat or part-treat superficial verrucous or occult sarcoid. It can work very effectively if the course can be completed. Sometimes repeated courses are required. It is particularly useful for areas around the face and eyes but can be used over wider areas on any other body part. It can be used as an adjunct to surgical excision and to laser surgery as well as cryosurgery.



If your vet has prescribed this treatment make sure you have read and understood the health and safety precautions you should take.

Imiquimod (Aldara™, 3M USA)

This cream modulates the immune system and may only be used in superficial sarcoids. It has specific antiviral and anticancer properties and is available for topical human use in most countries. The drug has a specific anti-viral and anticancer function and as such it is an entirely logical approach to the sarcoid problem. It is usually restricted to areas of very small sarcoid because the material is difficult to manage, expensive and is supplied in very small sachets. It can be used in some areas of the body but on superficial sarcoids only. This material is available through Equine Medical Solutions by prescription from Prof. Knottenbelt on cases submitted through our portal. If your vet has prescribed this treatment make sure you have read and understood the health and safety precautions you should take.

Other topical adjunctive agents

- Bleomycin: this is supplied by us on a case-by-case basis and doesn't illicit an inflammatory response
- Exterra™/Blood Root Ointment/Newmarket Blood Root is an extract of plants and an escharotic chemical that is available in USA on prescription only (via veterinary surgeons). There are reports of effective treatments being performed.
- Retinoid drugs such as tazarotene (ZORAC™) have been trialled on over 500 cases. It is a useful adjunctive treatment in some forms of the sarcoid (especially verrucous and occult lesions) but it seldom results in a cure. This is a very useful way of eliminating all the secondary change resulting from the sarcoid. It is not usually a treatment in itself but there have been some reports of successful outcomes following its use alone.
- Aciclovir – an anti-HERPESVIRUS cream that is used to treat 'cold sores' in humans. It has a weak 'bystander effect' on suicide gene expression in some tumours and has been shown to help treatment on small superficial sarcoids over an extended application period.

Surgical removal

Surgical removal can be effective for small lesions in safe areas but carries a relatively high failure rate in terms of recurrence. Special surgical precautions can be taken to reduce (but not eliminate) the risk of recurrence. The best prognosis is achieved by selecting the most



amenable lesions (i.e. small, well defined, localised lesions in convenient sites). The prognosis for surgical removal can be improved by protecting the site from contact with cells from the active sarcoid lesion. This is achieved with plasticised dressings or surgical dressings placed over the lesion before surgery commences.

Nodular lesions in the groin and thigh areas are sometimes amenable to this method provided that the lesions have no skin involvement. Nodules round the eye should not be treated surgically without careful consideration. In some circumstances however it can work reasonably well but absolute care has to be taken and smart surgical principles have to be applied in all cases. In all cases furthermore the excised sample of tissue must be submitted to the laboratory for histological confirmation of the diagnosis and confirmation of the safety of the exceptional margin. It is the last cell that we seek to destroy!

Laser surgery may be effective in some cases but it is not simple to perform and is not widely available; special licensed equipment is required and special training is very wise (and may become a statutory requirement). There is a time and place for this method and when used correctly carries an excellent chance of success and in most circumstances is better than conventional surgery.

Smart surgery is a 'one-cut, one-blade' principle where no instrument is returned to the surgical site following a single use also helps. This may add to the cost of surgery but it is money well spent! We offer an information leaflet on this type of surgery.

Surgery is thought to be better if the wound site is not sutured afterwards. The open site could be at risk of reintroduction of sarcoids or infection and will be both slow to heal and in some sites highly problematic. If surgical treatment is followed with other adjunctive treatments it has higher rate of success.

Intralesional Chemotherapy

Injection of cytotoxic drugs such as cisplatin, mitomycin C or 5-fluoro-uracil into the centre of lesions is a useful method of treatment but is restricted to certain types of sarcoid. Sometimes aqueous solutions are injected and these will usually be washed out of the lesion within 3 to 5 minutes – sometimes it is enough to do this and sometimes this is combined with mechanisms to slow down the washout process of the drug – obviously the longer it stays inside the lesion the better the result will be. The chemicals are usually incorporated into a stable emulsion or wax form to ensure that the drug stays within the lesion.

These materials are very dangerous to the surgeon; special precautions must be taken to ensure operator safety. There are also safety issues regarding these materials in respect of the handling of the horse – usually the amount of chemical that is used is minute compared



to the size of the horse but there are still sensible precautions that need to be taken. The site of the injection should not be touched under any circumstances and advice from your vet will allow you to manage the case safely.

They are not available in all countries. In some countries there are restrictions on the use of these materials and in any case course they are all strictly drugs and cannot be applied by owners. Typically of course there are withdrawal times as well which may affect the use of the horse and any use of any of these drugs will immediately mean that the horse has to be signed out of the food chain for the rest of its life.

Ligation

Application Application of a strangulating band around the base of a nodular sarcoid may be effective if the lesion has no roots. **This can be extremely dangerous if there is a root structure** and should only be performed by a veterinary surgeon.

Ligation is most applicable to conveniently sized and situated Type A1 and B1 nodular lesions and some small pedunculated (Type 1a) fibroblastic lesions. The tumour will die slowly over some weeks and will eventually fall off leaving an open wound. This may in some cases be much larger than expected due to elastic recoil in the skin.

Attempts at ligation by owners with tail hairs or string are counterproductive and make matters worse!

Cryosurgery (freezing)

Cryosurgery involves using a liquid nitrogen spray at -196°C on a tumour site. This is only effective for lesions that are relatively small and not very deep. Where other methods are not feasible it can be used with other chemotherapy agents and can be repeated until success is achieved. Each lesion must be frozen quickly and thawed slowly at least three times (this is known as a cryosurgical cycle). It is time consuming and tedious if many lesions are to be treated. To be effective freezing needs to be aggressive and it may cause extensive damage to surrounding structures and consequent extensive scarring. There is a high rate of recurrence.

Cryosurgery is commonly performed in conjunction with surgical excision of the bulk of the lesion. This results in a minor (probably insignificant) improvement in the prognosis. A similar method involving surgical removal followed by application of heat cautery is used in some parts of the world to good effect. It is likely that this works by cauterising/killing any seeding



cells that are deposited back into the wound site during surgery. When it is used adjunctively on a surgical site after the tumour has been removed it adds benefit to the prognosis.

Photodynamic therapy

This method relies on the ability of cells to absorb a photodynamic chemical. The chemical is delivered into the lesion via the blood stream through injection, or delivered directly to the tumour site by applying it topically. The agent is activated by a specific wavelength of light so that when this type of light is applied it causes significant cell damage. The method is only applicable to limited lesions in convenient sites.

The photodynamic agents will react to sunlight so this can cause severe side effects in normal skin when the horse is exposed to sunlight.

Immune methods: BCG injection

BCG is a human TB vaccine that can be used for certain types of sarcoid. It is injected carefully into the sarcoid itself this minimises the risks and maximises the effect. Because the tumours are often very solid a 'pressure syringe' should be used. This method works reasonably well for nodular and fibroblastic lesions around the eyes but is much less effective elsewhere. It should not be used on sarcoids on the limbs – they will often become much worse!

The method carries significant risks and so careful supportive medication is required at the time of each injection. The horse could have an allergic reaction to the protein in the injection. The vet administering the injections will monitor the swelling that normally occurs shortly after the injections have been given. Usually the swelling that follows is a good sign rather than about one and this should have subsided or nearly subsided by the time the next injection is given. The interval between the injections is very strictly defined. Whilst most horses respond to 3-5 procedures some require up to 9 injections given every 1–4 weeks according to a strict treatment plan.

Prior to the injection the vet will administer medications to try to prevent the potential for anaphylaxis. Although these add to the cost of the procedure, it is not an option to avoid them. Following the injection, the vet will remain with the horse usually for up to 30 or 45 minutes to ensure that there is no adverse reaction. It is important to point out that adverse reactions and anaphylactic collapse is an extremely rare event. Many thousands of cases are treated with this method and there are only a handful of reported cases of side effects.

This material is currently restricted to human use and is unavailable for equine use.