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REVIEW OF THERAPEUTICAL MANAGEMENT OF EQUINE SARCOID

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Abstract

Sarcoids are reported as the most common tumour of the horse, localized of the skin, that do not metastasize and rarely regress spontaneously. Treatment described in veterinary literature includes surgical excision, cryotherapy, radiotherapy (low-dose-rate or high dose rate brachytherapy with iridium, strontium; external beam radiotherapy), chemotherapy (topical, intralesional injection, electrochemotherapy, photodynamic therapy, drug-matrix implants), hyperthermia, laser therapy, immunotherapy. The purpose of this reviewer study was to evaluate the success of various treatment methods. The information was collected from 75 scientific papers, published between of 1977-2020 and indexed in international databases (Google scholar, Web of Science - Clarivatics, Cabi). Treatments options depend by many variables, including sarcoid tumour type and location, aggressiveness of the tumour, clinical experience, client compliance, treatment costs, patient behaviour, and the availability of services, equipment, and facilities. Recent updates of the success of treatment and recurrence rate of tumour after different treatment methods are presented and discussed. Despite the many treatment options available for equine sarcoids, there is no way 100% effective in achieving healing.

Key words*: sarcoid, equine, treatment.*

INTRODUCTION

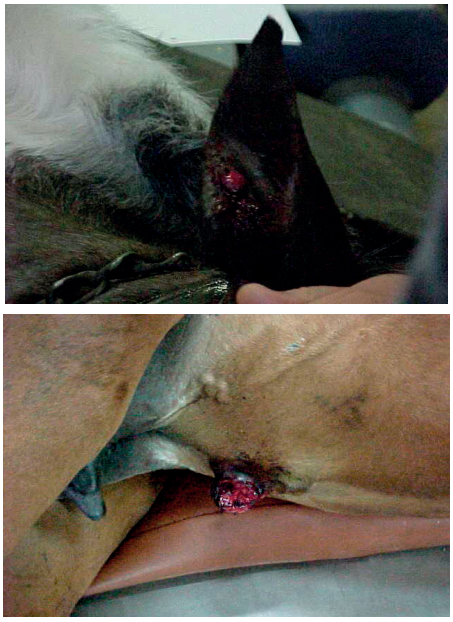
Sarcoids are reported as the most common tumour of the horse. The sarcoids are classified in six different groups according to their clinical appearance: fibroplastic, mixed, maleovant, nodular, occult and verrucous types of lesions. Common locations for these sarcoids include the periocular region, lips, ear pinnae and ventral abdomen - Figure 1. (Knottenbelt, 2005; Marti et al., 1993).

Olson and Cook (1951) identified pathological effect of papillomaviruses (PVs) at sarcoids occurring in horses could be caused by persistent infection with bovine papillomavirus (BPV). BPVs infection predominantly involves the dermis and is episomal but also affects the epidermis of equine sarcoids (Brandt et al., 2011). In studies that aimed to elucidate the pathogenesis of PV-associated sarcoids in equines, the equine cell lines were specifically transformed with BPV 1 and 2 (Gobeil et al., 2009; Kaynarcalidan and Oguzoglu, 2021).

While not life threating, sarcoids adversely affect the horse's aspect.

In the report of first international workshop on equine sarcoid Marti et al. (1993) concluded "no therapy has been found which is effective in all cases of equine sarcoids". The treatment described in veterinary literature includes more methods, permanently actualised.

The purpose of this review study was to evaluate the success of various treatment methods.



a)

b)

Figure 1. Fibroblastic sarcoids: a- nodular on the ear pinnae; b - ulcerative on the ventral abdomen (original)

MATERIALS AND METHODS

The information about the sarcoid's treatment was collected from 75 scientific papers, published between of 1977-2020 period and indexed in international databases (Google scholar, Web of Science - Clarivatics, Cabi).
For data analysis, we aimed to identify treatment methods, the factors that influenced the choice of treatment and the effectiveness of treatment.

RESULTS AND DISCUSSIONS

Equine sarcoids are challenging to treat. There are multiple treatment modalities reported, with a variety of levels of evidence to support their use. Treatment described in veterinary literature include: surgical excision, cryotherapy, radiotherapy (low-dose-rate or high dose rate brachytherapy with iridium, strontium; external beam radiotherapy), chemotherapy (topical, intralesional injection, electrochemotherapy, photodynamic therapy, drug-matrix implants), hyperthermia, laser therapy, immunotherapy etc, with variable degrees of success. The therapeutic potential of the different methods is presented in Table 1.

Immunotherapy is a treatment modality for equine sarcoid that relies on local immune stimulation to attack and kill tumour cells. The most common immunomodulator used is Bacillus Calmette and Guerin (BCG), an attenuated strain of *Mycobacterium bovis*. Success rates from 83 to 100% have been observed for periorbital sarcoids but for sarcoids found elsewhere on the body, success rates have only been approximately 50% (Caston et al., 2020; Goodrich et al., 1998; Klein et al., 1986, 1991; Knottenbelt and Kelly 2000; Lavach et al., 1985; Martens et al., 2001; McConaghy et al., 1994; Murphy et al., 1979; Newton 2000; Owen and Jagger 1987; Schwartzman et al., 1984; Vanselow et al., 1988). Severe complications, including death, anaphylaxis, severe local inflammatory reactions and septic arthritis have been reported with the use of BCG. The tumour regression may require several months of weekly therapy (Klein et al., 1986; Lavach et al., 1985; Vanselow et al., 1988).

Other immunomodulators used to treat equine sarcoid include Baypamun - inactivated parapoxovis virus (Studer et al., 1997). Topical immune modulators have also been used to treat equine sarcoid. After treatment with the immunomodulator imiquimod 5% cream (Nogueira et al., 2006; Torres et al., 2010; Pettersson et al., 2020) reported 60-80% success rate and 12,5% recurrence rate. Complications included alopecia, erythema, erosions and depigmentation of the tumour and periphery (Nogueira et al., 2006).

Vaccination with autologous vaccine (Espy 2008; Dutka, 2008; Kinnunen et al., 1999; Rothacker et al., 2015) or vaccines composed of chimeric virus-like particles (Ashrafi et al. 2008; Mattil-Fritz et al. 2008) has a complete resolution tumour rate of 50-80%, but recurrence rate is high (40-50%).

Conventional surgical excision alone has success rates of 30-50%, with most tumours recurring within 6 months (Genetzky et al., 1983; McConaghy et al., 1994; Knottenbelt and Kelly 2000). Recurrent tumours are often aggressive and regrow more rapidly than the initial tumour (Tarwid et al., 1985; McConaghy et al., 1994; Hewes and Sullins, 2009). A success rate of 20-64% has been reported (Bogaert et al., 2008; Carstanjen et al., 1997; Dutka, 2008; Funiciello et al., 2020; Genetzky et al., 1983; McCauley et al., 2002; McConaghy et al., 1994; Knottenbelt and Kelly 2000; Hewes and Sullins 2009; Ragland et al., 1970; Sala et al., 2010; Semieka et al., 2012; Tarwid et al., 1985; Taylor and Haldorson, 2013). The overall success rate was 74,9-86,8% by ***electrosurgical excision*** resulted in the highest surgical treatment success rate (Haspeslagh et al., 2016).

Laser surgical excision. A CO_2 laser or diode laser are surgical instruments that cuts and vaporises soft tissue with minimal intraoperative haemorrhage and less post-operative oedema and pain compared to scalpel blades (Taylor and Haldorson, 2013). A success rate of 60-80% has been reported (Compston et al., 2013, 2016; Carstanjen et al., 1997; Martens et al., 2001; McCauley et al., 2002). Laser surgical excision is simple to perform, suitable in majority of locations, especially where lesions are early and well circumscribed. The recurrences rate is higher

for verrucous lesions and those on head and neck.

Regardless of surgical method, the difficulty incompletely resecting sarcoid tumours, especially those in the periorbital region, often necessitates other treatment options for primary or adjunctive therapy (Taylor and Haldorson, 2013; Hollis, 2020).

Cryotherapy involves application of liquid nitrogen at -196°C, either by spray or probe, to destroy tumour cells through the formation of intracellular ice and subsequent rupture of cell membranes (Taylor and Haldorson, 2013). Three freeze-thaw cycles that decrease the tissue temperature to -20° to -30°C should be applied to each tumour (Hewes and Sullins, 2009).

The success rate of 49-100% has been reported (Lane et al., 1977; Fretz and Barber 1980; Joyce, 1976; Klein et al., 1986; Martens et al., 2001; Munroe, 1986; Newton, 2000). The highly tumour recurrence (25-60%) is more likely for periorbital sarcoids (Knottenbelt and Kelly, 2000).

Hyperthermia has been reported to induce regression for at least 7 months in 3 cases of equine sarcoid (Hoffman et al., 1983). Because of the limited reports of hyperthermia for the treatment of sarcoid tumours, it is difficult to make recommendations regarding its use (Goodrich et al., 1988; Taylor and Haldorson, 2013).

Radiotherapy has long time been considered the "*gold standard*" for the treatment of periocular sarcoids in the horse, and there are various techniques of delivering this treatment : Low-dose rate interstitial brachytherapy (LDR) iridium wires/seeds, strontium plesiotherapy, high-dose rate brachytherapy (HDR), teletherapy, and electronic brachytherapy (Byam-Cook et al. 2006; de Groot and de Groot, 1984; Hollis, 2016, 2018, 2019, 2020; Hollis and Berlato, 2018; Lewis, 1964; Theon and Pascoe, 1995; Turrel et al., 1985; Walker et al., 1991; Wyn‐Jones, 1983).

The most commonly used technique is interstitial brachytherapy. Low-dose rate interstitial brachytherapy has reported success rates of between 74 and 100%. Electronic brachytherapy is a technique which may provide an alternative to high-dose rate brachytherapy (Hollis, 2019, 2020). The requirement for general anesthesia, carefull case selection, possibility of late cataract formation and high cost and limited availability of any of the techniques are significant disadvantages.

Chemotherapy is commonly used to treat equine sarcoid (Theon et al., 1993, 1999; Hewes and Sullins, 2006; Hewes and Sullins, 2009; Funiciello and Roccabianca, 2020; Jaglan et al., 2018; Knottenbelt et al., 2018; Knottenbelt, 2019; Knottenbelt et al., 2020; Knottenbelt and Walker, 1994; Newton, 2000; Souza et al., 2017; Spoormakers et al., 2002; Tamzali et al., 2001, 2012; Tozon et al., 2016).

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Cisplatin - two approaches are available for controlled-release administration: percutaneous injection (water solution or mixing with sesame seed oil) and implantation of biodegradable beads. A retrospective analysis of long-term outcome after cisplatin injections revealed that overall tumour resolution at 4 years was 80-90% for sarcoids (Theon et al., 1993, 1999, 2007). Knottenbelt and Kelly (2000) reported a 33% success rate using injectable cisplatin and Spoormakers et al. (2002) of 78% after injectable cisplatin mixing with sesame seed oil. Intratumorally cisplatin beads have also been effective in treating sarcoids with a cure rate of 91% (Hewes and Sullins, 2006). Cisplatin electrochemotherapy (ECT) is a novel therapy, for equine sarcoid that utilises electrical field pulses to increase cell membrane permeability and thus increase cisplatin delivery to the tumour. Tamzali et al. (2001, 2012) and Tozon et al. (2016) reported a 93% success rate.

Intra-lesional *mitomycin C* are available, but 100% success rate was obtained only in a study of small case series of periocular lesions (Hollis, 2020).

Table 1. The therapeutic potential of the different methods

Treatment typs	Sarcoid localisation		Cases number	Complete resolution Time/%	Recurrence	Adverse effects	Source
	perio cular	other					
Immunotherapy imiquimod 5% cream	x	x	31	12 months/ 60-80%	12.5 %	local inflammation, exudation, alopecia, erythema, erosions, depigmentation, pain	Torres et al., 2010; Nogueira et al. 2006; Pettersson et al., 2020
Baypamun (inactivated parapoxovis virus)	unn		10	3 months/ 60%	unn	unn	Studer et all (1997)
Bacillus Calmette and Guerin (BCG)	x	x	202	8 months/ 50-100%	17-20%	Fatal and nonfatal anaphylaxis, severe local inflammatory reactions, septic arthritis	Caston et al., 2020; Goodrich et al., 1998; Klein et al., 1986, 1991; Knottenbelt and Kelly, 2000; Lavach et al. 1985; Martens et al., 2001; McConaghy et al. 1994; Murphy et al., 1979; Newton, 2000; Owen and Jagger, 1987; Schwartzman et al., 1984; Vanselow et al., 1988;
Vaccination autologous vaccine	x	x	74	90-180 days/ 59-80%	40-50%	edema and hyperemia of underlying tissue, swelling, alopecia, erythema and exudation	Espy 2008; Dutka (2008); Kinnunen et al., 1999; Rothacker et al., 2015
vaccines composed of chimeric virus-like particles	x	x	30	50%	7-30%	unn	Ashrafi *et al*. 2008; Mattil-Fritz *et al*. 2008
Surgical excision conventional	x	x	261	6-12 months/ 20-64%	40 to 72 %	dehiscence, scar	Bogaert et al., 2008; Carstanjen *et al*., 1997; Dutka, 2008; Funiciello et al., 2020; Genetzky *et al*. 1983; McCauley *et al*. 2002; McConaghy *et al*. 1994; Knottenbelt and Kelly 2000; Hewes and Sullins 2009; Ragland et al., 1970; Sala et al., 2010; Semieka et al., 2012; Tarwid et al. 1985; Taylor and Haldorson, 2013;
Electrosurgical excision	x	x	230	6 months/ 87%	unn	unn	Haspeslagh et al., 2016;
Laser removal - CO2 laser - Diode laser	x	x	172	5 months/ 60-80%	9-30 %	burns, prolonged healing, scar, corneal damage leukotrichia	Compston et al., 2013, 2016; Carstanjen et al. 1997; Martens et al. 2001; McCauley et al. 2002; Taylor and Haldorson, 2013
Cryotherapy - application of liquid nitrogen at -196°C,	x	x	68	7 months/ 49–100%	25-60%	Edema, scarring	Lane et al., 1977; Fretz and Barber 1980; Joyce, 1976; Klein et al., 1986; Martens et al., 2001; Munroe, 1986; Newton, 2000;
Hyperthermia radiofrequency 50°C	unn		3	7 months / 100%	-	na	Goodrich et al. 1988; Taylor and Haldorson, 2013; Hoffman et al., 1983;
Radiotherapy -teletherapy cobalt	unn		4	60 to 100 % success rate	unn	unn	Lewis, 1964; de Groot and de Groot, 1984;
Radiotherapy - brachytherapy iridium-192	x	x	92	12-36 months/ 60-94%		no acute adverse effect	Byam-Cook et al. 2006; Hollis and Berlato, 2018; Theon and Pascoe, 1995; Turrel et al. 1985; Walker et al. 1991; Wyn - Jones, 1983;
Plesiotherapy Strontium	x	-	8	6 - 30 months /100%	unn	No significant short or long - term adverse effects	Hollis, 2016, 2020;
Intratumorally chemotherapy – Cisplatin intratumorally injections	x	x	437	48 months/ 80-90 %	87 %	corneal damage	Theon et al. 1993, 1999; Hewes and Sullins 2009; Funiciello and Roccabianca, 2020; Souza et al., 2017
Cisplatin bed implants		x		91%	unn	unn	Hewes and Sullins 2006;
Cisplatin Oil	unn			unn / 78	unn	no systemic side-effects	Spoormakers et al., 2002;
Cisplatin electrochemotherapy	x	x	334	48 months/ 92-98%	0%	ulceration tumor	Tamzali et al., 2001, 2012; Tozon et al/. 2016;
Bleomycin	x	x	118	12 months /44%	unn	unn	Knottenbelt et al., 2018; Knottenbelt et al.,2020; Souza et al., 2017
Fluorouracil (5-FU intratumoural	x	x	14	36 months/ 61%			Stewart et al. 2006
AW3/4-LUDES % fluorouracil cream	unn		146	35%	unn	unn	Knottenbelt and Kelly 2000; Knottenbelt and Walker 1994; Newton, 2000;
Anthiomaline (lithium antimony thiomalate) + vincristine	-	x	6	50%	unn	unn	Jaglan et al., 2018;
Antiviral therapy 5% acyclovir cream	x	x	37	3 months/ 68-95%	0%	unn	Haspeslagh et al., 2016, 2017; Stadler et al. 2011;
tricyclodecan - 9 - yl - xa nthogenate	x	x	6	50%	30%	temporary oedema at the injection site	Otten et al., 1994;
Photodynamic therapy Hypericine intratumoural	unn		4	92.3%	39%	hyperaemia, edema, cyanosis and pruritus	Martens et al., 2000;
Plant extract *Viscum album* subcutaneous injections	x	x	42	12 months/ 37%	unn	edema	Christen-Clottu e al., 2010;
bloodroot ointment	x	x	49	42 moths/ 86.5%	9%	unn	Wilford et al., 2014;

X – yes; unn -unnamed

Bleomycin, non-permanent cytotoxic drug, induces DNA stand break is used in electrochemotheraphy or as intralesional injection (Knottenbelt et al., 2018; Knottenbelt et al., 2020; Souza et al., 2017). May be more effective when combined with other agents (tazarotene or 5-FU), probably due to improved penetration of bleomycin into cells (Hollis, 2020).

Five-fluorouracil (5-FU) is a topical chemotherapeutic drug. Intratumoural injection of 5-FU resulted in complete resolution of sarcoids in 61% of horses for up to 3 years (Stewart et al., 2006).

AW3/4-LUDES2 are compounded topical chemotherapy creams that contain 5% fluorouracil, heavy metals and thiouracil. Knottenbelt and Kelly (2000), Knottenbelt and Walker (1994) and Newton (2000) reported a success rate of 35% in 149 horses with sarcoids.

Antiviral therapy is a controversial method with 53-68% success rates reported for early, very superficial lesions (Haspeslagh et al., 2016, 2017; Stadler et al., 2011).

Plant extract use (*Viscum album* subcutaneous injections or Blood root ointment - extract of *Sanguinaria canadensis*) is cheap, but there are minor scientific success rates reported (Christen‐Clottu et al., 2010; Wilford et al., 2014).

To choose a proper therapeutic plan, some considerations must be evaluate: each lesion can require a specific treatment and can react in a different way compared to other sarcoids even on the same horse; the extent and location of the tumour greatly affect therapeutical response; the duration of the lesion is important as early intervention usually requires less aggressive treatments; sarcoid-affected animals can never be considered free of the disease, even after successful treatment (Funicello and Roccabianca, 2020; Hollis, 2020; Knottenbelt, 2019; Melkamu et al., 2018; Taylor and Haldorson, 2013).

From all references analysed conquered that treatments options depend by many variables: tumour type, location, aggressiveness, clinical experience, client compliance, treatment costs, patient behaviour, and the availability of services, equipment, and facilities.

CONCLUSIONS

Treatments options depend by many variables, including sarcoid type, location, and aggressiveness of the tumour.

Despite the many treatment options available for equine sarcoids, there is still no way 100% effective in achieving healing.

REFERENCES

Ashrafi, G.H., Piuko, K., Burden, F., Yuan, Z., Gault, E.A., Muller, M., Trawford, A., Reid, S.W., Nasir, L., Campo, M.S. (2008) Vaccination of sarcoid-bearing donkeys with chimeric virus-like particles of bovine papillomavirus type 1. *J. Gen. Virol.* **89**, 148-157.

Bogaert, L., Martens, A., Depoorter, P., Gasthuys, F. (2008). Equine sarcoids, part 2: current treatment modalities. *Vlaams Diergeneeskundig Tijdschrift*, *77*(2), 62-67.

Brandt, S., Tober, R., Corteggio, A., Burger, S., Sabitzer, S., Walter, I., Kainzbauer, C., Steinborn, R., Nasir, L Borzacchiello, G. (2011). BPV-1 infection is not confined to the dermis but also involves the epidermis of equine sarcoids. *Veterinary microbiology*, *150*(1-2), 35-40.

Byam-Cook, K.L., Henson, F.M. D., Slater, J.D. (2006). Treatment of periocular and non-ocular sarcoids in 18 horses by interstitial brachytherapy with iridium-192. *Veterinary record*, *159*(11), 337-341.

Carstanjen, B., Jordan, P., Lepage, O. M. (1997). Carbon dioxide laser as a surgical instrument for sarcoid therapy- a retrospective study on 60 cases. *The Canadian Veterinary Journal*, *38*(12), 773.

Caston, S.S., Sponseller, B.A., Dembek, K.A., Hostetter, J.M. (2020). Evaluation of locally injected Mycobacterium cell wall fraction in horses with sarcoids. *Journal of Equine Veterinary Science*, 103102.

Christen‐Clottu, O., Klocke, P., Burger, D., Straub, R., Gerber, V. (2010). Treatment of clinically diagnosed equine sarcoid with a mistletoe extract (Viscum album austriacus). *Journal of veterinary internal medicine*, *24*(6), 1483-1489.

Compston, P.C., Turner, T., Wylie, C.E., Payne, R.J. (2016). Laser surgery as a treatment for histologically confirmed sarcoids in the horse. *Equine veterinary journal*, *48*(4), 451-456.

Compston, P.C., Turner, T.G., Payne, R. J. (2013). Laser surgery as a sole treatment of histologically confirmed equine sarcoids: outcome and risk factors for recurrence. *Equine Veterinary Journal*, *45*, 2-2.

de Groot R, de Groot E (1984) – Radiotherapy for Equine sarcoid and other superficial lesions in the horse, *Veterinary Radiology* **25**, 92.

Dutka, A. (2008). *Equine Sarcoids in Lipizzaner horses*. PhD thesis, Veterinarmedizinischen Univ. Wien

Espy, B.M. (2008, December). How to treat equine sarcoids by autologous implantation. In *Proceedings* AEEP (pp. 68-73).

Fretz, P.B. Barber, S.M. (1980) Prospective analysis cryosurgery as the sole treatment for equine sarcoids. *Vet. Clin. N. Am.: Small Anim. Pract.* **10**, 847-859.

Funiciello, B., Roccabianca, P. (2020). Equine Sarcoid. In *Equine Science*. IntechOpen.

Genetzky, R.M., Biwer, R.D. and Myers, R.K. (1983) Equine sarcoids, causes, diagnosis, and treatment. *Comp. Cont. Educ. Pract. Vet.* **5**, S416.

Gobeil, P.A., Yuan, Z., Gault, E.A., Morgan, I.M., Campo, M.S., Nasir, L. (2009). Small interfering RNA targeting bovine papillomavirus type 1 E2 induces apoptosis in equine sarcoid transformed fibroblasts. *Virus research*, *145*(1), 162-165.

Goodrich, L., Gerber, H., Marti, E., Antczak, D.F. (1998). Equine sarcoids. *Veterinary Clinics of North America: Equine Practice*, *14*(3), 607-623.

Haspeslagh, M., Garcia, M.J., Vlaminck, L.E., Martens, A.M. (2017). Topical use of 5% acyclovir cream for the treatment of occult and verrucous equine sarcoids: a double-blinded placebo-controlled study. *BMC veterinary research*, *13*(1), 1-6.

Haspeslagh, M., Taevernier, L., Maes, A.A., Vlaminck, L.E.M., De Spiegeleer, B., Croubels, S.M., Martens, A.M. (2016). Topical distribution of acyclovir in normal equine skin and equine Sarcoids: an in vitro study. *Research in Veterinary Science*, *106*, 107-111.

Haspeslagh, M., Vlaminck, L.E., Martens, A.M. (2016). Treatment of sarcoids in equids: 230 cases (2008–2013). *Journal of the American Veterinary Medical Association*, *249*(3), 311-318.

Hewes, C. A., Sullins, K. E. (2006). Use of cisplatin-containing biodegradable beads for treatment of cutaneous neoplasia in equidae: 59 cases (2000–2004). *Journal of the American Veterinary Medical Association*, *229*(10), 1617-1622.

Hewes, C.A., Sullins, K. E. (2009). Review of the treatment of equine cutaneous neoplasia. In *Proceedings of the 55th Annual Convention of the American Association of Equine Practitioners, Las Vegas, Nevada, USA* (Vol. 55, pp. 387-393).

Hoffman, K.D., Kainer, R.A. and Shideler, R.K. (1983) Radio-frequency current-induced hyperthermia for the treatment of equine sarcoid. *Equine Pract.* **5**, 28-31.

Hollis A. (2020) Management of equine sarcoids. Retrived in December 9, 2020, from https://www.thewebinarvet.com/webinar/management-of-equine-sarcoids

Hollis, A.R. (2018). Managing periocular sarcoids. *UK-Vet Equine*, *2*(5), 145-152.

Hollis, A.R. (2020). Strontium plesiotherapy for the treatment of sarcoids in the horse. *Equine Veterinary Education*, *32*, 7-11.

Hollis, A.R., Berlato, D. (2018). Initial experience with high dose rate brachytherapy of periorbital sarcoids in the horse. *Equine Veterinary Education*, *30*(8), 444-449.

Jaglan, V., Singh, P., Punia, M., Lather, D., Saharan, S. (2018). Pathological studies and therapeutic management of equine cutaneous neoplasms suspected of sarcoids. *The Pharma Innovation Journal*, *7*(9), 96-100.

Joyce J. R. (1976). Cryosurgical treatment of tumors of horses and cattle. *Journal of the American Veterinary Medical Association*, ***168*(3),** 226–229.

Kaynarcalidan O, Oguzoglu T.C. (2021). The oncogenic pathways of papillomaviruses. *Vet Comp Oncol*., 19, 7–16, 2021 from https://doi.org/10.1111/vco.12659

Kinnunen, R.E., Tallberg, T., Stenbäck, H., Sarna, S. (1999). Equine sarcoid tumour treated by autogenous tumour vaccine. *Anticancer research*, *19*(4C), 3367

Kinnunen, R.E., Tallberg, T., Stenbäck, H., Sarna, S. (1999). Equine sarcoid tumour treated by autogenous tumour vaccine. *Anticancer research*, *19*(4C), 3367-3374.

Klein, W. R., Rutten, V. P., Steerenberg, P. A., Ruitenberg, E. J. (1991). The present status of BCG treatment in the veterinary practice. *In vivo (Athens, Greece)*, *5*(6), 605-608

Klein, W.R., Bras, G.E., Misdorp, W., Steerenberg, P.A., de Jong, W.H., Tiesjema, R.H., Ruitenberg, E.J. (1986). Equine sarcoid: BCG immunotherapy compared to cryosurgery in a prospective randomised clinical trial. *Cancer Immunology, Immunotherapy*, *21*(2), 133-140.

Knottenbelt, D. C., Watson, A. H., Hotchkiss, J. W., Chopra, S., & Higgins, A. J. (2020). A pilot study on the use of ultra‐deformable liposomes containing bleomycin in the treatment of equine sarcoid. *Equine Veterinary Education*, *32*(5), 258-263.

Knottenbelt, D.C. (2005). A suggested clinical classification for the equine sarcoid. *Clinical Techniques in Equine Practice*, *4*(4), 278-295.

Knottenbelt, D.C., Kelly, D.F. (2000). The diagnosis and treatment of periorbital sarcoid in the horse: 445 cases from 1974 to 1999. *Veterinary ophthalmology*, *3*(2‐3), 169-191.

Knottenbelt, D. C. (2019). The equine sarcoid: why are there so many treatment options?. *Veterinary Clinics: Equine Practice*, *35*(2), 243-262.

Lane, J. G. (1977). The treatment of equine sarcoids by cryosurgery. *Equine veterinary journal*, *9*(3), 127-133.

Lavach, J. D., Sullins, K. E., Roberts, S. M., Severin, G. A., Wheeler, C. A., Lueker, D. C. (1985). BCG treatment of periocular sarcoid. *Equine veterinary journal*, *17*(6), 445-448.

Lewis RE (1964) Radon implant therapy of squamous cell carcinoma and equine sarcoid. *Proceedings of the American Association of Equine Practitioners* **10**, 217-20.

Martens, A., De Moor, A., Vlaminck, L., Pile, F., Steenhaut, M. (2001). Evaluation of excision, cryosurgery and local BCG vaccination for the treatment of equine sarcoids. *Veterinary Record*, *149*(22), 665-669.

Martens, A., Moor, A.D.E., Waelkens, E., Merlevede, W., de Witte, P. (2000). In vitro and in vivo evaluation of hypericin for photodynamic therapy of equine sarcoids. *The Veterinary Journal*, *159*(1), 77-84.

Marti, E., Lazary, S., Antczak, D. F., Gerber, H. (1993). Report of the first international workshop on equine sarcoid. *Equine veterinary journal*, *25*(5), 397-407.

Mattil-Fritz, S., Scharner, D., Piuko, K., Thones, N., Gissmann, L., Muller, H. and Muller, M. (2008) Immunotherapy of equine sarcoid: dose-escalation trial for the use of chimeric papillomavirus-like particles. *J. Gen. Virol.* **89**, 138-147.

McCauley, C.T., Hawkins, J.F., Adams, S.B. and Fessler, J.F. (2002) Use of a carbon dioxide laser for surgical management of cutaneous masses in horses: 32 cases (1993-2000). *J. Am. Vet. Med. Ass.* **220**, 1192-1197.

McConaghy, F.F., Davis, R.E., Reppas, G.P., Rawlinson, R.J., McClintock, S.A., Hutchins, D.R., Hodgson, D.R. (1994). Management of equine sarcoids: 1975–93. *New Zealand Veterinary Journal*, *42*(5), 180-184.

Melkamu, S., Chanie, M., Asrat, M. (2018). A Review on Equine Sarcoid: Current Techniques Employed in Sciences for Diagnosis, Prevention and Control. *Journal of Animal Research*, *8*(3), 513-519.

Munroe GA (1986) Cryosurgery in the horse, Equine Veterinary Journal **18**, 14-7

Murphy, J.M., Severin, G.A., Lavach, J.D., Hepler, D.I., Lueker, D. C. (1979). Immunotherapy in ocular equine sarcoid. *Journal of the American Veterinary Medical Association*, *174*(3), 269-272.

Newton, S.A. (2000) Periocular sarcoids in the horse: three cases of successful treatment. *Equine Vet. Educ. 12,* 137-143.

Nogueira, S.A., Torres, S.M., Malone, E.D., Diaz, S.F., Jessen, C., Gilbert, S. (2006). Efficacy of imiquimod 5% cream in the treatment of equine sarcoids: a pilot study. *Veterinary dermatology*, *17*(4), 259-265.

Olson C, Cook R.H. (1951). Cutaneous sarcoma-like lesions of the horse caused by the agent of bovine papilloma. *Proc Soc Exp Biol Med.,* 77, 281-284.

Otten, N., Marti, E., Söderström, C., Amtmann, E., Burger, D., Gerber, H., Lazary, S. (1994). Experimental treatment of equine sarcoid using a xanthate compound and recombinant human tumour necrosis factor alpha. *Journal of Veterinary Medicine Series A*, *41*(1‐10), 757-765.

Owen, R.A., Jagger, D.W. (1987). Clinical observations on the use of BCG cell wall fraction for treatment of periocular and other equine sarcoids. *The Veterinary Record*, *120*(23), 548.

Pettersson, C.M., Broström, H., Humblot, P., Bergvall, K.E. (2020). Topical treatment of equine sarcoids with imiquimod 5% cream or Sanguinaria canadensis and zinc chloride–an open prospective study. *Veterinary Dermatology*, *31*(6), 471-e126.

Ragland III, W. L., Keown, G.H., Spencer, G.R. (1970). Equine sarcoid. *Equine Veterinary Journal*, *2*(1), 2-11.

Rothacker, C. C., Boyle, A. G., Levine, D. G. (2015). Autologous vaccination for the treatment of equine sarcoids: 18 cases (2009–2014). *The Canadian Veterinary Journal*, *56*(7), 709.

Sala, A., Schüszler, L., Sabău, M., Luca, C., Igna, C., Dascălu, R., Brezovan, D. (2010) horse sarcoids: a morphoclinical and therapeutical experience on ten cases. *Lucrări Ştiinţifice Medicină Veterinară* vol. XLIII (2), 109-118.

Schwartzman, S.M., Cantrell, J.L., Ribi, E. and Ward, J. (1984) Immunotherapy of equine sarcoid with cell wall skeleton (CWS)-trehalose dimycolate (TDM) biologic. *Equine Pract.* **6,** 13-23.

Semieka, M.A., Ali, M.M., Al-Lethie, A.A. (2012). Sarcoids in donkeys: common types and available treatment. *Journal of Advanced Veterinary Research*, *2*(4), 276-283.

Souza, C., Villarino, N. F., Farnsworth, K., Black, M. E. (2017). Enhanced cytotoxicity of bleomycin, cisplatin, and carboplatin on equine sarcoid cells following electroporation‐mediated delivery in vitro. *Journal of Veterinary Pharmacology and Therapeutics*, *40*(1), 97-100.

Spoormakers, T..P., Klein, W.R., Jacobs, J.J.L., Van Den Ingh, T.S., Koten, J.W., Den Otter, W. (2003). Comparison of the efficacy of local treatment of equine sarcoids with IL-2 or cisplatin/IL-2. *Cancer Immunology, Immunotherapy*, *52*(3), 179-184.

Spoormakers, T.J., Klein, W.R., van Weeren, P.R. (2002). Treatment of equine sarcoids with cisplatin in arachid oil: a useful alternative?. *Tijdschrift voor diergeneeskunde*, *127*(11), 350.

Stadler, S., Kainzbauer, C., Haralambus, R., Brehm, W., Hainisch, E., Brandt, S. (2011). Successful treatment of equine sarcoids by topical aciclovir application. *Veterinary Record*.

Stewart, A.A., Rush, B., Davis, E. (2006). The efficacy of intratumoural 5‐fluorouracil for the treatment of equine sarcoids. *Australian veterinary journal*, *84*(3), 101-106.

Studer, U., Marti, E., Stornetta, D., Lazary, S., Gerber, H. (1997). The therapy of equine sarcoid with a non-specific immunostimulator--the epidemiology and spontaneous regression of sarcoids. *Schweizer Archiv fur Tierheilkunde*, *139*(9), 385.

Tamzali, Y., Borde, L., Rols, M. P., Golzio, M., Lyazrhi, F., & Teissie, J. (2012). Successful treatment of equine sarcoids with cisplatin electrochemotherapy: a retrospective study of 48 cases. *Equine veterinary journal*, *44*(2), 214-220.

Tamzali, Y., Teissie, J., Rols, M. P. (2001). Cutaneous tumor treatment by electrochemotherapy: preliminary clinical results in horse sarcoids. *Revue de Medecine Veterinaire*, *152*(8/9), 605-610.

Tarwid, J.N., Fretz, P.B. and Clark, E.G. (1985) Equine sarcoids: a study with emphasis on pathologic diagnosis. *Comp. Cont. Educ. Pract. Vet.* **7**, 293.

Taylor, S., Haldorson, G. (2013). A review of equine sarcoid. *Equine Veterinary Education*, *25*(4), 210-216.

Taylor, S.D., Toth, B., Baseler, L.J., Charney, V.A., Miller, M.A. (2014). Lack of correlation between papillomaviral DNA in surgical margins and recurrence of equine sarcoids. *Journal of Equine Veterinary Science*, *34*(5), 722-725.

Théon, A. P., Galuppo, L. D., Snyder, J. R., Wilson, W. D. (2006). Intratumoral administration of cisplatin for treatment of sarcoids in 378 horses. In *AAEP proceedings*. Vol. 52, 337-339.

Theon, A. P., Pascoe, J. R. (1995). Iridium‐192 interstitial brachytherapy for equine periocular tumours: treatment results and prognostic factors in 115 horses. *Equine Veterinary Journal*, *27*(2), 117-121.

Theon, A. P., Pascoe, J. R., Carlson, G. P., Krag, D. N. (1993). Intratumoral chemotherapy with cisplatin in oily emulsion in horses. *Journal of the American Veterinary Medical Association*, *202*(2), 261-267.

Théon, A. P., Wilson, W. D., Magdesian, K. G., Pusterla, N., Snyder, J. R., Galuppo, L. D. (2007). Long-term outcome associated with intratumoral chemotherapy with cisplatin for cutaneous tumors in equidae: 573 cases (1995–2004). *Journal of the American Veterinary Medical Association*, *230*(10), 1506-1513.

Theon, A.P., Pascoe, J.R., Galuppo, L.D., Fisher, P.E., Griffey, S.M. and Madigan, J.E. (1999) Comparison of perioperative versus postoperative intratumoral administration of cisplatin for treatment of cutaneous sarcoids and squamous cell carcinomas in horses. *J. Am. Vet. Med. Ass.* ***215,*** 1655-1660.

Thoresen, A. S. (2011). Outcome of Horses with Sarcoids Treated with Acupuncture at a Single Ting Point: 18 cases (1995-2009). *American Journal of Traditional Chinese Veterinary Medicine*, *6*(2).

Torres, S.M., Malone, E.D., White, S.D., Koch, S.N., Watson, J.L. (2010). The efficacy of imiquimod 5% cream (Aldara®) in the treatment of aural plaque in horses: a pilot open‐label clinical trial. *Veterinary dermatology*, *21*(5), 503-509.

Tozon, N., Kramaric, P., Kadunc, V. K., Sersa, G., Cemazar, M. (2016). Electrochemotherapy as a single or adjuvant treatment to surgery of cutaneous sarcoid tumours in horses: a 31-case retrospective study. *Veterinary Record*. *179*(24), 627-627.

Turrel, J.M., Stover, S.M., Gyorgyfalvy, J. (1985). Iridium‐192 interstitial brachytherapy of equine sarcoid. *Veterinary Radiology*, *26*(1), 20-24.

Vanselow, B. A., Abetz, I., Jackson, A. R. B. (1988). BCG emulsion immunotherapy of equine sarcoid. *Equine veterinary journal*, *20*(6), 444-447.

Vingerhoets, M., Diehl, M., Gerber, H., Stornetta, D. and Rausis, C. (1988) [The treatment of equine sarcoidosis by carbon dioxide laser]. *Schweiz. Arch. Tierheilkd.* **130**, 113-126.

Walker, M., Adams, W., Hoskinson, J., Held, J. P., Blackford, J., Geiser, D., Henton, J. (1991). Iridium‐192 brachytherapy for equine sarcoid, one and two year remission rates. *Veterinary Radiology*, *32*(4), 206-208.

Wilford, S., Woodward, E., Dunkel, B. (2014). Owners' perception of the efficacy of newmarket bloodroot ointment in treating equine sarcoids. *The Canadian Veterinary Journal*, *55*(7), 683.

Wyn‐Jones, G. (1983). Treatment of equine cutaneous neoplasia by radiotherapy using iridium 192 linear sources. *Equine Veterinary Journal*, *15*(4), 361-365.