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Equine Sarcoids. A Clinical and Epidemiological Study in Relation to Equine Leucocyte Antigens (ELA)

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Broström, H.: Equine sarcoids. A clinical and epidemiological study in relation to equine leucocyte antigens (ELA). Acta vet. scand. 1995, 36, 223-236. – Associations between clinical parameters of sarcoids and the equine leucocyte antigen system (ELA) were analysed for 120 Swedish horses. Median age of affected horses was 5.2 years, and the majority presented with solitary tumors between 2 and 5 cm in diameter and ventral abdomen was a predilection site. Clinical signs first appeared at a median age of 3.5 years, and sarcoids at different locations first appeared at different ages. Lesions at different sites differed in size, and multiple tumors, early onset, long duration, and older age all had an association with large size. Clinical manifestations of sarcoids and the association between certain ELA-specificities and early onset (A5) and increased recurrence rates after surgery (W13), in addition to increased prevalence (A3W13), strengthen further that some horses are inherently predisposed to sarcoid growth.
Unassociated with any clinical parameters, one third of the untreated horses became free of sarcoids due to "spontaneous" regression, perhaps as a result of immune responses against the tumors. Seventy percent of the horses were treated (mostly by excision), and large size was the main parameter promoting treatment. Excision had no significant effect on possibly remaining sarcoids. Recurrence rate after first treatment was about 35%, with the majority of tumors recurring within 4 months. Early onset, long duration, large size, and localization to distal limbs all appeared to increase risk of recurrence. Early treatment, performed under general anesthesia in recumbency which permits wide excision and measures to avoid autoinoculation, significantly reduced recurrence rates.

AAT/PBV system; tumors.

Introduction

Sarcoid is worldwide in distribution and comprises the most common tumor in equine practice *(Ragland et al.* 1970, *Cotchin* 1977, *Miller & Campbell* 1982, *Marti et al.* 1993). These fibroblastic skin tumors do not metastasise but show variable clinical manifestations, ranging from aggressive, infiltrative growth to "spontaneous" regression, which may be indicative of an ongoing immune response against the tumors *(Ragland et al.* 1970, *Lane* 1977). Immunotherapy has, however, met only variable success, and the tumors have a reputation for being notoriously difficult to treat due to locally aggressive growth, large size, multiple lesions, localization to sites compromising excision, and high rates of recurrence after treatment *(Ragland*

et al. 1970, *Fretz & Barber* 1980). Sarcoids sometimes appear at sites of previous wounds, and both epidemiology and clinical behaviour strongly suggest the involvement of an infectious agent *(Jackson* 1936, *Ragland* 1966, *Voss* 1969, *Marti et al.* 1993), the obvious candidate being a virus *(Cheevers et al.* 1986, *Lory et al.* 1993, *Otten et al.* 1993). Certain breeds or rather families are more affected than others *(James* 1968, *Angelos et al.* 1988, *Mohammed et al.* 1992), and there is a strong association between genes in or near the equine Major Histocompatibility Complex (MHC), as assessed by the equine leucocyte antigen (ELA) system, and susceptibility to sarcoid *(Lazary et al.* 1985, *Meridith et al.* 1986, *Broström et al.* 1988). Thus, the equine sarcoid may be considered a virus-induced tumor with a variety of manifestations as result of interactions between the etiologic agent, the environment, and the host genome.

The purpose of the present study was to assess if the most likely course of the disease could be predicted on the basis of clinical parameters and ELA, which, in extension, would provide rational decisions for therapy. Analytical epidemiology examined associations between total number, localization, size, and duration of the sarcoids as well as the relation to ELA, age at onset, age at first treatment, gender, and coat colour at the level of both affected horses and individual tumors. The incidence of "spontaneous" regression and possible parameters associated with these events were analysed as were factors promoting surgery and increased risk of recurrence.

Materials and methods

Horses

This epidemiologic study was based on retrospective data of 120 Swedish horses with clinically diagnosed sarcoids. In cases treated by conventional surgery (64 out of 74 treated horses), the sarcoids were confirmed histologically. The horses were selected from files of the Department of Surgery, Swedish University of Agricultural Sciences, Uppsala. Clinical cases were also collected from the Large Animal Clinic of Helsingborg, Helsingborg and Royal Lifeguard's Dragoons, Stockholm, and from stables in the Stockholm and Helsingborg area. Most of the cases were treated by the author, and surgery was usually performed under general anesthesia in recumbency since many of the horses referred to the University Clinic suffered from large and/or multiple lesions with difficult localizations. This procedure supplies adequate surgical exposure that permits wide excision and measures to avoid autoinoculation with tumor cells by the "non-touch" technique, and gloves and instruments were changed before wound closure. The total sample consisted of horses with sarcoids as well as animals with previously confirmed lesions that had regressed either "spontaneously" or as result of treatment. The horses were offsprings from 92 different sires and represented 92 Swedish Halfbreds, 13 Thoroughbreds, 9 Ponies of varying genetic background, 2 Anglo-Arabs, 2 Irish Hunters and 2 Standardbred horses. Apart from the tumors, all horses appeared healthy at the clinical examination.

Collection of data

Information was sought on 23 parameters. Due to the restrospective character of data collection and the involvement of several clinics, it was not possible to retrieve complete information on all parameters for each horse . Therefore, for each parameter, the number of horses for which data were available is given in brackets.

The parameters recorded were:

1. ELA specificity (78).

2. Breed (120).
3. Gender (119).
4. Coat colour (106); black, brown, bay, roan and others.
5. Onset (95); the age of the horse in years at first anamnestic signs of sarcoid.
6. Duration (96); number of years with sarcoid to a. first treatment or b. spontaneous regression of any sarcoid for untreated horses. For untreated cases with no regression of the tumors, duration was defined as the number of years with sarcoids to last observation.
7. Age of the horse at completion of the study (108).
8. Total number of sarcoids of each affected horse (112); groups defined by solitary, several (2-5) or multiple tumors.
9. Location of the sarcoids (112); head, neck, chest, upper abdomen, lower abdomen (including groin), proximal limbs, distal limbs (from carpal or hock joints), and urogenital area (prepuce, penis, udder and vulva).
10. Approximate size of the sarcoids at first veterinary inspection (104): small (<2 cm), medium (2-5 cm) or large (>5 cm). Maximal size defines the largest tumor of each horse during the disease period.
11. Treatment; treated (76) and untreated (34). Ten had unknown treatment.
12. Total number of treated sarcoids.
13. Location of treated sarcoids.
14. Size of treated sarcoids (i.e. size of largest, treated lesion in horses with multiple, treated lesions).
15. Information on recurring, treated sarcoids (total number, localization and size).
16. Total number of untreated sarcoids.
17. Localization of untreated sarcoids.
18. Size of untreated sarcoids (i.e. size of largest, untreated lesion during the observation period in horses with multiple, untreated lesions).
19. Information on regressing, untreated sarcoids (total number, localization and size).
20. Observation period without recurrence (72 out of 76 treated horses could be evaluated); number of months without recurrence after first treatment.
21. Total number of recurrencies of treated sarcoids for each horse (72 of 76 treated horses could be evaluated).
22. Clinical manifestations of the disease. Each of 107 horses could be included in 1 or more of the following categories: a) Remaining sarcoids (due to recurrence of treated or "spontaneously" regressed sarcoids, persistent, untreated lesions or development of new lesions); b) signs of "spontaneous" regression of any sarcoid; c) recurrence of treated lesions that later regressed; d) treatment associated with regression of additional, untreated sarcoids; e) totally free of sarcoids due to treatment and/or "spontaneous" regression; f) development of new sarcoids after treatment; g) more than 1 sarcoid with complex growth; h) extreme variability in clinical appearance.

Determination of ELA specificities

Clinical parameters of tumors were analysed for sarcoid horses expressing 1 of the frequent ELA specificities A2, A3, A5 or W13, respectively, relative to sarcoid horses lacking these particular specificities. Seventy eight of the sarcoid horses were typed for their ELA by methods earlier described *(Lazary et al.* 1985). The majority of these horses (69 Swedish halfbreds) were analysed in a previous study showing an association between equine sarcoids and certain ELA specificities *(Brostrom et al.* 1988). Briefly, the alloantisera

were obtained from primiparous mares and from alloimmunizations with leucocytes. Each horse was tested against a collection of 118 alloantisera recognizing the ELA specificities A1 to A10 and W11 and, in addition, 2 locally characterized specificities (Be22 and Be25). Furthermore, the panel of alloantisera identified ELA specificities W17, W18, and W20 and split the seemingly supertypic W11 specificity by the 3 new specificities A14, A15, and A19 *(Lazary et al.* 1988). Each specificity was defined by at least 2 antisera. All specificities represent allelic gene products, probably coded for by 1 single locus. The collection of alloantisera also identified the specificities W12 and W13 of a second locus and the specificity W21 that might be a product of an ELA-linked locus or of an ELA-independent locus. Each horse was also typed for the codominantly expressed non-MHC antigens ELY1.1 and ELY1.2 as well as for ELY2, an antigen that segregates independently from ELY1.

Analyses of data

The different breeds were analysed together as a single sample. Due to the retrospective character of data collection, all parameters for each horse were not available. Therefore, the number of horses, that appear in statistical analyses comparing different parameters, will sometimes be less than the total number of horses registered for each parameter. The data were analysed by a statistical program package (IDA 800, Luxor Inc, Sweden). The data were evaluated using Student's t-test (unpaired), χ^2 analysis and One way analysis of variance. P values <0.05 were accepted for significance.

Results

The majority of the horses were geldings (58.5%) or mares (38.1%), and the predominant colours were brown (38.1%) and bay (30.4%). Gender had no significant impact on total number (112 horses), maximal size (104) or location (112) of sarcoids (χ^2 analyses, data not shown). Similarly, coat colour had no significant association to total number (106), maximal size (99) or location (106) of the tumors.

The total number of sarcoids and their location in affected horses

The total number of sarcoids and their locations were known for 112 horses. Solitary tumors were found in 66.1% of the horses, whereas 20.5% and 13.4% presented with several or multiple lesions, respectively (Table 1). The majority of solitary sarcoids was localized to the lower compartments of abdomen (32.4%), while the rest were evenly distributed to the different body regions (between 6.8% and 14.9% was found in each region), except for upper abdomen, where solitary sarcoids were rare (1.4%). In horses with several or multiple tumors, the lesions were scattered on the body surface with locations largely the same as the solitary tumors. Thus, the location of tumors did not differ significantly between horses carrying different total numbers of sarcoids (Table 1).

Parameters predictive of sarcoid size

The location of 68 solitary sarcoids had a significant relationship to their size (Table 2). Furthermore, sarcoids on the head were significantly smaller ($p<0.01$), and sarcoids on the extremities significantly larger ($p<0.05$) when compared to all other sites (2×2 table χ^2 analysis). For horses with several or multiple sarcoids, the situation was more complex, and location of all their individual sarcoids relative to their sizes was not assessed. The total number and size of sarcoids was known for 104 horses. The majority of the horses had

Table 1. Location of sarcoids in relation to total number in sarcoid horses.

	Number of sarcoids							
	Solitary (1)		Several (2-5)		Multiple (>5)		Total	
Localization	No. of horses	% of horses	No. of horses	% of horses	No. of horses	% of horses	No of horses	% of horses
Head	11	14.9	5	10.2	6	12.0	22	12.7
Neck	5	6.8	5	10.2	6	12.0	16	9.2
Chest	7	9.5	14	28.6	9	18.0	30	17.3
Upper abdomen	1	1.4	1	2.0	3	6.0	5	2.9
Lower abdomen	24	32.4	12	24.5	11	22.0	47	27.2
Prox. extremities	9	12.2	6	12.2	9	18.0	24	13.9
Distal extremities	8	10.8	1	2.0	2	4.0	11	6.4
Urogenital	9	12.2	5	10.2	4	8.0	18	10.4
Total No. of horses	74	66.1%	23	20.5%	15	13.4%	112	100%

3×8 table χ^2 analysis: Not significant.

medium-sized tumors (59.6%), 18.3% had small and 22.1% had large tumors (Table 3). In horses with solitary or several sarcoids, approximately 60% and 70%, respectively, of their largest sarcoids were medium-sized, and the rest comprised 2 equally sized groups of either small or large lesions. In contrast, among horses with multiple lesions, the majority (53.3%) presented with at least 1 large sarcoid, and horses with multiple, but exclusively small tumors, were less common (13.3%). This association between multiple lesions and large size (of at least 1 tumor) was statistically significant ($p<0.05$, Table 3).

The median age of 95 horses at first clinical signs of sarcoids was 3.5 years (range: 0.7 to 12.0 years). Median duration of the disease was 1.5 years (96 horses; range: 0.2 to 13.0 years) and median age at first clinical examination was 5.2 years (108 horses; range: 1.5 to 17.0 years). Analyses of 62 horses with solitary sarcoids showed that sarcoids of the head

Table 2. Location of sarcoids in relation to size in horses with solitary sarcoids.

	Tumor size			
Location	Small (<2 cm)	Medium (2-5 cm)	Large (>5 cm)	Total
Head	6	4	1	11
Neck and chest	2	7	2	11
Abdomen	5	15	2	23
Extremities	0	10	6	16
Urogenital	1	6	1	8
Total No. of horses	14	42	12	68

3×5 table χ^2 analysis: $p<0.05$.

Table 3. Total number of sarcoids in relation to maximal size in sarcoid horses.

		Maximal size*							
		Small (<2 cm)		Medium (2-5 cm)		Large (>5 cm)		Total	
Total Number		No of horses	% of horses	No. of horses	% of horses	No. of horses	% of horses	No. of horses	% of horses
Solitary	(1)	14	20.6	42	61.8	12	17.6	68	100
Several	(2-5)	3	14.3	15	71.4	3	14.3	21	100
Multiple	(>5)	2	13.3	5	33.3	8	53.3	15	100
Total		19	18.3	62	59.6	23	22.1	104	100

3×3 table χ^2 analysis: $p<0.05$. *Maximal size is defined by the largest tumour of each horse.

tended to have an earlier onset (2.9 ± 1.5 years; mean ± SD) and to be found on younger horses (5.4 ± 2.7 years) as compared to animals with sarcoids of other locations, whereas horses with tumors on ventral abdomen were slightly older (7.9 ± 3.9 years) than the average. None of these differences were, however, statistically significant (one way analysis of variance). Small to medium-sized, solitary sarcoids first appeared at a significantly younger age (46 horses; 3.6 ± 1.8 years, mean ± SD) and had a shorter duration (47 horses; 1.9 ± 1.9 years) as compared to large tumors (11 horses; 4.8 ± 3.4 years and 3.7 ± 3.9 years, respectively) (Student's t-test; $p = 0.043$ and $p = 0.015$, respectively).

Parameters inducing treatment

The analysed group comprised 76 treated (69.1%) and 34 (30.9%) untreated horses, (10 horses were excluded because complete information was not available). Sarcoids were treated by excision in 64 horses, by thermocautery in 4 horses, by cryosurgery in 1 horse, and by the layman procedure of "ligation" in 7 horses.

Clinical parameters of the 68 horses treated by excision or thermocautery were compared with the corresponding parameters of the 34 untreated horses. Horses subjected to treatment presented with significantly larger lesions as compared to untreated (Table 4), and this difference was increased further at the level of individual, treated tumors. When small tumors were designated 1, medium-sized 2 and large 3, the maximal size of 68 treated and 47 untreated tumors was 2.22 ± 0.57 and 1.81 ± 0.54 (mean ± SD), respectively ($p = 0.0002$; Student's t-test, unpaired). Other clinical parameters had no significant impact on promotion of treatment.

Result of treatment

Results of treatment were available for 72 horses, of which 26 (36.1%) had between 1 and 6 recurrences (1.7 ± 1.5, mean ± SD). The time period from first treatment to first clinical signs of recurrence ranged from 0.5 to 24.0

Table 4. Maximal size of sarcoids for treated and untreated horses.

		No. of horses	
Maximal size		Treated	Untreated
Small	(<2 cm)	5	12
Medium	(2-5 cm)	43	19
Large	(>5 cm)	20	3
Total No.		68	34

3×2 table χ^2 analysis: $p = 0.001$.

Table 5. Size, onset and duration of treated sarcoids of horses with or without recurrences.

	Recurrences		
	None		Yes
Size* (mean ± SD)	2.12 ± 0.56		2.42 ± 0.58
Range	1 - 3		1 - 3
Significance**		P = 0.024	
Onset*** (mean ± SD)	4.3 ± 2.6		3.1 ± 1.5
Range	0.7 - 12.0		1.0 - 8.0
Significance**		P = 0.022	
Duration*** (mean ± SD)	1.6 ± 1.3		2.8 ± 3.1
Range	0.2 - 5.5		0.5 - 13.0
Significance**		P = 0.017	

* Size: 1 = small (2<2 cm), 2 = medium (2-5 cm), 3 = large (>5 cm).
** Student's t-test, unpaired. *** Onset and duration in years.

months, but the majority (95%) recurred within a few months after treatment (3.8 ± 4.9 months). A significant association existed between size of the treated tumors and recurrence rates (Table 5). Horses with recurring sarcoids also had a significantly earlier onset and longer duration of their tumors before first treatment when compared to that of horses without recurrences (Table 5). Furthermore, the 10 treated tumors localized to the lower parts of the limbs had significantly higher numbers of recurrences (1.7 ± 1.8, mean ± SD) as compared to 99 treated sarcoids of all other locations (0.5 ± 0.9, mean ± SD) (Student's t-test, unpaired, p = 0.0005). The total number of sarcoids per se in treated horses had no significant relation to recurrence rates. Nevertheless, due to repeated treatments and "spontaneous" regression, the apparent success rate of treated sarcoids was approximately 92% at completion of the study. However, 16 of the treated horses (22.2%) still carried sarcoids, not only as result of recurrence of treated lesions (6 cases), but also due to persisting, untreated lesions and the development of new tumors.

The detailed circumstances by which excision was performed had a significant impact on recurrence rates. Among 30 horses submitted to excision in recumbency under general anesthesia at the University Clinic, 6 had recurring tumors. In contrast, out of 17 horses, where the tumors were excised in standing position after administration of a tranquilizer supplemented with local anesthesia and usually under field conditions, 13 had at least 1 recurrence and several had multiple recurrences making a total of 30 recurrences among these 17 horses (p = 0.0001; 2×2 table χ^2 analysis). Horses treated by other methods than excision were too few to allow any real conclusions, but some details may be of interest. Among the 4 horses, that were treated by thermocautery, 2 became free of tumors, 1 showed 2 recurrences and another had a recurrence that regressed "spontaneously" within 6 months. The case treated by cryosurgery was successful, but healing took 1 year. Six out of the 7 horses with solitary, pedunculated sarcoids at various localizations, that were "ligated" by the owner, became tumor-free within 0.5 to 1 year.

Table 6. ELA specificity in relation to onset of sarcoids.

	ELA specificity precent (+) or absent (–)							
	A2+	A2–	A3+	A3–	A5+	A5–	W13+	W13–
Onset (mean ± SD)	4.1 ± 1.7	3.6 ± 2.0	3.6 ± 2.1	3.8 ± 1.8	2.9 ± 1.1	4.2 ± 2.1	3.4 ± 1.8	4.1 ± 2.1
No. of horses	16	46	29	33	24	38	31	31
Significance*	ns		ns		p = 0.009		ns	

* Student's t-test, unpaired. Onset in years of age. Not significant = ns.

Predictive effects of ELA specificities on onset, total number, localization, maximal size and recurrence rates of sarcoids

Clinical parameters were compared for 62 houses expressing or lacking either of the common ELA-specificities A2, A3, A5 or W13. A5 was significantly associated with an earlier onset compared to animals lacking that specificity (Table 6), whereas the other clinical parameters appeared unassociated with any of the ELA specificities analysed (χ^2 table analyses; data not shown).

Clinical parameters and ELA of 26 horses with recurring tumors were analysed in relation to a control group of 46 treated horses without recurrences during a mean observation period that was significantly longer (47.9 ± 38.5 months; range: 3.0 to 144.0 months) than that to first recurrence (3.8 ± 4.9 months; range: 0.5 to 24.0 months) ($p<0.0001$, Student's t-test, unpaired). Horses lacking ELA-specificity W13 had a significantly lower risk of recurrence of their treated sarcoids compared to horses expressing this specificity (Table 7). None of the other ELA-specificities analysed had any significant association with recurrence rates (Table 7).

"Spontaneous" regression of sarcoids

Among 72 treated and 34 untreated horses, 29 (27.4%) showed "spontaneous" regression of 1 or more sarcoids during the observation period. Thus, almost 1 third of the untreated horses (10 horses) became free of tumors after 0.5 to 7 years of disease (2.2 ± 1.8 years, mean ± SD). All of these horses had solitary sarcoids. Five of the untreated horses (14.7%) presented with sarcoids of very variable clinical manifestations, including regression and recurrence of tumors or development of new sarcoids. The rest of the untreated horses (55.9%) showed more or less static lesions during a disease period ranging from 0.2 to 9.0 years (2.3 ± 2.6 years, mean ± SD). Untreated horses had no significant associations between "spontaneous" regression and total number, localization, size, onset, and duration of their sarcoids or in ELA, gender, coat colour, and age of the affected horses (data not shown).

Among 14 treated horses, "spontaneous" regression contributed to the tumor-free state. Thus, in 8 cases (2 ligations, 1 thermo- and 5 excisions) the lesions recurred, but regressed "spontaneously" within 1 year. Four more horses showed "spontaneous" regression of remaining, untreated sarcoids after excision. In addition, 1 horse had a previous history of "spontaneous" regression, and 1 horse had 5 excisions with 5 recurrences, of which the last regressed "spontaneously" or perhaps as a result of repeated, local treatments with a Mycobacterial cell wall preparation (Regressin®: Ribi ImmunoChem Res, Inc, Hamilton, Montana) (*Schwartzman et al.* 1984).

Table 7. ELA specificity relative to recurrence of sarcoids.

ELA	No. of horses with recurrence	No. of horses without recurrence	Significance*
W13+	14	11	
W13–	5	14	p = 0.049
A3+/W13+	12	10	
A3–/W13–	5	14	ns
A5+	9	7	
A5–	10	18	ns
A2+	3	8	
A2–	16	17	ns

* 2×2 table χ^2 analysis. Not significant = ns.
All A3+ were also W13+; three W13+ were A3–.

Discussion

Equine sarcoids have a variety of clinical manifestations, and the present study analysed their statistical associations. Like most other reports on sarcoids, the study was mainly based on clinical cases actively brought to veterinary attention, whereas sarcoids incidently found were less frequent. Thus, the study neither determines prevalence and incidence rate of sarcoids in the normal population, nor the effect of gender, breed or coat colour. In equine practice, diagnosis of sarcoid is often based on distinctive clinical features like gross morphology, multiple appearance, elevated incidence at certain ages, contagious character and predilection for certain sites *(Ragland et al.* 1970, *Lane* 1977, *Pascoe* 1990), rather than on the typical histopathological picture *(Jackson* 1936, *Baker & Leyland* 1975). In the present study, diagnosis was based on histopathology in cases subjected to excision, and on clinical history and gross morphology. The majority of sarcoids subjected to excision were of fibroblastic type, but, as result of the preoperative disinfection routines, also many originally mixed or verrucous sarcoids gained the appearance of the fibroblastic type, and therefore the different types of sarcoids were not classified in detail *(Pascoe* 1990).

Among the presented Swedish horses, descriptions of size and total number of sarcoids and their localizations were largely similar to previous reports from other countries, although horses with multiple sarcoids may predominate in files of special clinics *(Ragland et al.* 1970, *Lane* 1977, *Fretz & Barber* 1980, *Miller & Campbell* 1982, *Bastianello* 1983, *Laursen* 1987). Statistical analyses revealed that localizations of sarcoids were similar for horses with different total numbers of tumors. However, localization of a sarcoid had a significant impact on its size, with the largest lesions generally found on distal limbs. This probably reflects that certain sites are more frequently exposed to mechanical irritation that both initiates wounds and stimulates growth of the tumors *(Jackson* 1936, *Ragland et al.* 1970, *Madewell & Theilen* 1987). In this context, sarcoids in Denmark *(Laursen* 1987) and in some studies from Great Britain *(Lane* 1977) display similar predilection sites as in Sweden, whereas reports from USA, Australia and South Africa describe head and partic-

ularly distal limbs as the most common localizations of sarcoids *(Jackson* 1936, *Ragland et al. 1970, Sundberg et al.* 1977, *Miller & Campbell* 1982, *Bastianello* 1983). While the existence of predilection sites may point to a viral etiology itself *(Jackson* 1936, *Sundberg et al.* 1977), the variations in predilection sites between different reports may also reflect geographical variations due to differences in horse husbandry. Animals used for hard work in rough country are more likely to get injuries on their lower legs than horses mainly used for activities on riding grounds.

Median age of affected horses was 5.2 years, which confirms that sarcoid is a disease mainly affecting young, adult horses *(Klein et al.* 1986, *Laursen* 1987), or donkeys during their first 5 years *(Reid et al.* 1994). These findings might, however, also reflect a bias for younger age in veterinary files, since Swedish horses subjected to therapy had a shorter median duration of disease to first treatment (1.0 years; 2.1 ± 2.2, mean ± SD) as compared with that of untreated horses, either to "spontaneous" regression (2.0 years; 2.2 ± 1.8) or to last observation (2.0; 2.4 ± 2.4) *(Broström,* unpublished). Median age at first clinical sign of sarcoids was 3.5 years, and tumors at different sites tended to have somewhat different onsets. Whether this reflects age dependent site-differences in exposure to frequent mechanical injuries, such as the head in younger horses and ventral abdomen, including girth region, in the older riding horse, is unknown.

Not surprisingly, duration of tumors influenced their size *(Miller & Campbell* 1982), and horses with large (solitary) tumors were significantly older (12 horses; 8.5 ± 4.3 years) as compared to horses with small and medium sized lesions (5.7 ± 2.6 years) ($p = 0.002$) *(Broström,* unpublished). However, onset and duration of the disease as well as age of the affected horses had no major impact on the total number of sarcoids, which may suggest that horses that develop several or multiple tumors do so during a rather short period of time rather than gradually over several years. This could be the result of infection of susceptible animals due to environmental influences, such as possible vector transmission during the summer *(Laursen* 1987), autoinoculation (*Ivascu et al.* 1974), immunosuppression (*Onion* 1987), or the fact that some horses are also more predisposed to sarcoid growth than others. This is supported by the finding that horses with large numbers of sarcoids had a significantly higher risk of developing large lesions, as also reported elsewhere *(Diehl et al.* 1988). In fact, at least 40% of the risk of developing sarcoids in Swedish Halfbreds is associated with the genetic background of the horse, expressed as an association between certain ELA-specificities (A3W13 or W13) and the prevalence of sarcoids *(Broström et al.* 1988). The present study found that also early onset and risk of recurrence after surgery was significantly associated with the ELA-system (specificities A5 and W13, respectively), whereas other clinical parameters, like total number, localization and size, had no significant relation to any of the common ELA-specificities (A2, A3, A5 or W13) analysed.

Sarcoids have been attributed both to retroviruses *(England et al.* 1973, *Cheevers et al.* 1986) and to papillomaviruses *(Lory et al.* 1993, *Otten et al.* 1993). It is well established that tumors caused by oncogenic viruses possess novel antigens that are virus-specific and shared by tumors induced by the same virus. Such tumors are subject to a variety of surveillance processes, where the antigens are recognized by the immune system and may also function as target structures in the subsequent destruction of the tumor cells *(Onion* 1987). Untreated sarcoids have variable clinical

manifestations, and although no direct estimations have been made of the incidence of "spontaneous" resolution of the tumors, some authors claim, in contrast to others, that a large fraction of sarcoids do regress after several years, which might be indicative of an immune response against the tumors *(Roberts* 1970, *Stannard and Pulley* 1978, *Nilcock* 1993). Thus, like in the present report, increased incidence has been noted in adult horses up to 7 years of age with a definitive decrease in prevalence with advancing age *(Lane* 1977, *Sundberg et al.* 1977, *Fretz & Barber* 1980, *Miller & Campbell 1982, Klein et al.* 1986, *Laursen* 1987). Sarcoids are also rare in reports based on abbatoir carcasses, which are dominated by older horses *(Cotchin & Baker-Smith* 1975). The relevance of immune responses against sarcoids is also supported by the effects of immunomodulators like BCG on tumor growth *(Klein et al.* 1986), and by observations of both cell mediated and humoral immunity in sarcoid horses against sarcoid cells *in vitro (Watson et al.* 1974, *Broström et al.* 1979). In the present study, almost 30% of all horses showed signs of "spontaneous" regression (with or without recurrence) of 1 or more of their sarcoids. Moreover, among the untreated horses, about one third became totally free of sarcoids due to "spontaneous" regression, but also among treated horses, a significant fraction became finally sarcoid-free due to "spontaneous" regression of recurring or remaining untreated lesions. However, "spontaneous" regression appeared unassociated with ELA and any of the clinical parameters analysed.

The major problem associated with sarcoids in equine practice is the high incidence of recurrence after surgery. In the present study, approximately 70% of the sarcoid horses were subjected to treatment, mostly excision. The recurrence rate was 36.1% after first treatment, and the majority of tumors recurred within 4 months, and then often in a more malignant form with infiltrative, rapid growth *(Roberts* 1970). Others have reported a recurrence rate of approximately 50% within 3 years after surgery, the majority of which recurred within 6 months *(Ragland et al.* 1970). Clinical parameters associated with increased risk of recurrence after surgery were early onset, long duration, large size and localization to distal limbs. On the other hand, excision performed under general anesthesia, which permits wide excision and measures to avoid autoinoculation, significantly reduced recurrence rates when compared to tranquilized animals operated under local anesthesia in standing position. This finding was even more significant, since the majority of tumors excised in recumbency were the more aggressive, large tumors, and/or lesions with difficult locations. The only significant parameter promoting treatment was large size, which was associated with both long duration and increased risk of recurrence. Therefore, particularly aggressively growing sarcoids are best treated by early excision under optimal surgical conditions.

The use of thermo- or cryosurgery, and radio- or chemotherapy, in place of or as complement to excision, have sometimes increased the success rate *(Lane* 1977, *Fretz & Barber* 1980, *Turell et al.* 1985, *Theon et al.* 1993, *Knottenbelt & Walker* 1994). In addition, several immunotherapeutic approaches have also been applied, including tumor vaccines and Mycobacterium bovis (BCG) preparations *(Roberts* 1970, *Schwartzmann et al.* 1984, *Klein et al.* 1986, *Tallberg et al.* 1994). Cases subjected to thermo- or cryosurgery in the present study were too few for any conclusions. Similarly, vaccination procedures with autologous tumor material or Regressin® *(Schwartzmann et al.* 1984) were few and re-

sults unreliable. In preliminary studies, 5 cases of excision were combined with intramuscular administration of autologous tumor vaccines (National Veterinary Institute, Uppsala), that produced 5 different clinical responses, including regression of remining sarcoids, recurrence of treated sarcoids or the development of new tumors during the course of vaccination *(Broström,* unpublished). Similarly, 1 out of 2 horses was sucessfully treated with local injections of Mycobacterial extracts (Regressin®). Of note is that ligation performed by untrained personnel appeared to be effective in the treatment of some solitary, pedunculated sarcoids as earlier reported *(Pascoe* 1973).

Sarcoids of the present study represented lesions largely amenable to excision. Here, recurrence appeared as a problem, largely surmountable by an adequate, serious approach. However, sarcoids at difficult sites, such as the eyelids and coronet *(Raphel* 1982), or lesions affecting larger areas present special problems that may need therapeutical modalities other than excision. Since sarcoids have a variety of manifestations as result of interactions between the virus, the environment, the host genome, and the mode of therapy, surgeons await the identification of the aetiological agent(s) and of the genetic mechanisms (in or outside MHC) participating in tumor growth, and the possibility to induce/amplify specific immune responses against the tumors.

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Sammanfattning

Sarcoider hos hast. En klinisk och epidemiologisk studie i relation till hastens leukocyt antigen system (ELA).

Studien beskriver sarkoider (inkar) hos 120 svenska hastar och analyserar samband mellan tumorernas kliniska parametrar och specificiteter inom hastens leukocyt antigen (ELA) system. Hastarnas medianålder var 5,2 år och majoriteten uppvisade solitara tumorer mellan 2 – 5 cm i diameter med ventrala abdomen som predilektionsstalle. Median åldern vid sjukdomsdebut var 3,5 år, men debutåldern varierade beroende på tumorernas lokalisation. Storleken av en tumor hade ett samband med dess lokalisation, och multipla sarcoider, tidig sjukdomsdebut, lång duration och hog ålder hade alla ett positivt samband med storlek. Tumorernas kliniska beteende och samband mellan vissa ELA-specificiteter och tidig debutålder (A5), okad recidivrisk efter excision (W13) och tidigare visad forhojd prevalens (A3W13) indikerar att vissa hastar ar mer disponerade for tumorvaxt an andra.

Oberoende av kliniska parametrar, så blev en tredjedel av de obehandlade hastarna fria från sarcoider till foljd av "spontan" regression, vilket kan indikera ett immunsvar mot tumorerna. Sjuttio procent av hastarna behandlades, vilket framforallt initierades av tumorstorlek. Behandlingen (vanligen excision) hade inte någon significant effekt på eventuellt kvarvarande sarcoider. Andelen recidiv var 35% efter forsta behandling, och majoriteten recidiverade inom 4 månader. Tidig debut, lång duration, betydande storlek och lokalisation till distala extremiteterna innebar okad recidivrisk. Tidig behandling under allman anestesi, vilket tillåter omfattande excision och battre mojligheter att undvika autoinokulation visade sig drastiskt sanka recidivrisken.

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