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Clinical Evidence Article

What is the likelihood that Thoroughbred foals treated for septic arthritis will race?

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Summary

Reasons for performing study: **Septic arthritis is a serious problem in the neonate, with a poor prognosis being reported for recovery. The impact of neonatal septic arthritis on the likelihood that Thoroughbred (TB) foals will start on a racecourse is not known.**

Hypothesis: **The development of septic arthritis in a TB foal significantly reduces the likelihood that it will race when compared to foals from the same dam.**

Methods: **Medical records of 69 foals treated for septic arthritis were reviewed. The dam's foaling records were reviewed and lifetime racing records were then retrieved for both the affected foals and at least one of their siblings (controls). Outcomes that were statistically evaluated included discharge from the hospital and whether the foal eventually raced. Univariate analyses of categorical variables were conducted for each outcome. The number of affected and unaffected foals that raced at least once were compared using regression analysis. Survival analysis was used to compare age at first race between the study and comparison groups.**

Results: **Foals with septic arthritis were less likely to start on a racecourse compared to controls (odds ratio [OR] 0.28; 95% confidence interval [CI] 0.12–0.62, P = 0.001), while those foals that were discharged from the hospital were also less likely to start on a racecourse compared to controls (OR 0.36; CI 0.15–0.83, P = 0.008). The presence of multisystem disease was associated with a decreased likelihood of surviving to be discharged (OR 0.13; 95% CI 0.02–0.90; P = 0.005), but did not affect the likelihood that they would start in at least one race if discharged successfully (OR 0.45; 95% CI 0.04–2.81; P = 0.34) compared to the other foals with septic arthritis. Log-rank comparison of survival curves confirmed that foals discharged following treatment for septic arthritis took significantly longer to start in their first race compared to the sibling population (mean age of study group 1757 days, CI 1604–1909; mean age of sibling group 1273 days, CI 1197–1349; P = 0.0006).**

Conclusions: **The development of septic arthritis in a TB foal significantly reduces the likelihood that it will start on a racecourse when compared to controls.**

Potential relevance: **Accurate figures allowing a realistic assessment of the athletic future of a foal following treatment for septic arthritis are of significance for both owner and treating veterinarian.**

Introduction

In the neonate, septic arthritis is part of the septic arthritis/osteomyelitis syndrome (Martens and Auer 1980; Firth 1983; Steel *et al.* 1999; Meijer *et al.* 2000) and occurs with (Martens and Auer 1980; Schneider *et al.* 1992) and without (van Pelt and Riley 1969; Martens and Auer 1980; Carter and Martens 1986) infection of other body systems. In some cases, it is associated with failure of passive transfer of immunity (Platt 1973, 1977; Martens and Auer 1980; Stoneham 1997). Septic arthritis in foals has the potential to cause permanent degenerative joint disease, irreversible cartilage damage, fibrosis and unsoundness if the infection is not rapidly eliminated from the synovial space (Martens and Auer 1980; Stoneham 1997; Steel *et al.* 1999). The prognosis for recovery from septic arthritis in foals has been described as poor or unfavourable (Platt 1977; Martens and Auer 1980; Schneider *et al.* 1992; Steel *et al.* 1999; Meijer *et al.* 2000), although this is often due to complications attributed to underlying disease (Schneider *et al.* 1992; Steel *et al.* 1999; Meijer *et al.* 2000), as opposed to failure to resolve the joint sepsis (Steel *et al.* 1999; Meijer *et al.* 2000). Previous studies have reported that between 45% (Schneider *et al.* 1992) and 78% (Steel *et al.* 1999) of foals are successfully discharged from hospital following resolution of sepsis. Most previous studies on prognosis associated with septic arthritis have been restricted to short-term follow-up (Schneider *et al.* 1992; Meijer *et al.* 2000), with end-points such as discharge from hospital. Data on the long-term outcome in cases of septic arthritis are lacking, and there have been no previous studies comparing outcome of cases with a control population. It has been estimated that only 65% of Thoroughbred (TB) foals born annually in the UK enter training with the purpose of becoming a racehorse

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and start on a racecourse at least once (data from Weatherbys stud book and racing records). We hypothesised that the occurrence of septic arthritis in TB foals would significantly reduce the likelihood of the foals starting racing, when compared to their siblings. The aim of this study was to test this hypothesis in a case-control study.

Materials and methods

Power of study

The number of foals required (n) for this study, using a significance level of 5% and study power of 80%, was calculated using the standard formula:

$$n = 7.84 * (P_0 * [1 - P_1] + P_1 * [1 - P_0])/(P_1 - P_0)^2$$

where P_0 is the proportion of TB foals that successfully start on a racetrack following treatment for septic arthritis and P_1 the proportion of TB siblings that start on a racetrack. With P_0 estimated to be 40%, based on previously published data (Steel *et al.* 1999) and P_1 estimated to be 65%, based on statistics published by Weatherbys, the required number of foals for the study was therefore 67.

Study subjects

The admission records for Beaufort Cottage Equine Hospital between 1988 and 2001 were reviewed to identify TB foals that had been admitted with suspected joint pathology, and medical histories were then retrieved. To be eligible for inclusion in the study, foals had to be TBs, intended for use as racehorses, and age <4 months at the time of admission. Any TB foals which were not intended solely as racehorses were excluded from the study. A diagnosis of septic arthritis was made when >2 of the following criteria were met: lameness; joint distention; synovial fluid white cell count >3 x 10^9 cells/l; >90% neutrophils in synovial fluid; and degenerative changes in polymorphonuclear leucocytes in synovial fluid. Information retrieved from the medical records included sex, evidence of multisystem disease, number of joints infected, anatomical location of the joint(s) involved, white cell count of the synovial fluid at the time of admission to the hospital, and details of antibiotic therapy and lavage procedures performed.

Controls

The foaling history of each foal's dam was then reviewed in order to obtain registration details of the affected foal, along with details of 2 foals from the same dam. Where mares had produced fewer than 2 live foals in the years prior to the affected foal being born, the closest siblings in age born after the affected foal were selected for comparison, provided that they had attained racing age within the study period, in order that each foal treated for septic arthritis might have 2 siblings as controls. In the case of mares that had failed to produce 2 other live foals of racing age in the study period (n = 8), only one control was available for comparison.

Outcome

Outcomes evaluated statistically included discharge from the hospital and whether the foal eventually raced. Outcome was determined by evaluation of medical records to determine whether the foals were successfully discharged from the hospital. Lifetime race records were then obtained for all control foals, and all those that had been successfully discharged following treatment for septic arthritis. Race records were obtained from when foals were age >2 years until 1 December 2003, and the time from birth until the first start and the number of starts were recorded.

Variables

Variables evaluated statistically included infection in more than one joint, presence of multisystemic disease, and the specific joint involved. Analyses of categorical variables were conducted for each outcome. Comparisons among groups of discreet data were initially made using univariate analyses of odds ratios (OR) and 95% confidence intervals (CI), along with a χ^2 test for independence. Data were analysed using combined regression analysis (Pairs etc, Version 0.86, WinPEPI)[1], which allows for matching of cases and their siblings, thereby clustering data by dam, to test the null hypothesis that septic arthritis as a foal did not affect the likelihood of that TB foal starting on a racetrack compared to controls. Kaplan-Meier survival curves were generated depicting age at first race of male and female foals in both the study group and control population, and age at first race of the study group and control population. Survival curves were compared using the log-rank test. Differences were considered significant at $P<0.05$.

Results

Sixty-nine TB foals (male n = 38; female n = 31) met the criteria for inclusion in the study. Of these, 5 had 2 affected joints at presentation and the remaining 64 had only one affected joint. The joint involved was recorded in 57 cases and included femoropatellar with or without involvement of the femorotibial joint (n = 17), tibiotarsal (n = 15), metacarpophalangeal or metatarsophalangeal (n = 10), radiocarpal (n = 6), humero-ulnar (n = 5), coxofemoral (n = 2), scapulohumeral (n = 1) and distal interphalangeal (n = 1) joints. In 4 of the 5 foals with >1 joint involved, it was the same joint in contralateral limbs. The specific joints affected were not recorded for the fifth foal. Results of cytology of synovial fluid collected at admission were available for 44 foals; nucleated cell counts (range 5.0–194 x 10^9 cells/l; median 38 x 10^9 cells/l) exceeded the reference limit (3.0 x 10^9 cells/l) in all cases. Duration of clinical signs prior to presentation at the hospital was recorded in 51 cases, with clinical signs first noticed <24 h prior to admission in 38 cases (74.5%).

Although all foals were treated with systemic, broad-spectrum antibiotic drugs and joint lavage, there was no standardised treatment protocol, with the specific antibiotics and lavage technique used varying with preference of the treating clinician. Affected joints were usually lavaged on alternate days until a clinical improvement was seen, with lavage being performed between 1 and 6 times in total (median = 1 lavage). Standard practice was to review the antibiotic regimen if antimicrobial sensitivity indicated that the organisms cultured were resistant to the initial antibiotic choice, or if there was a failure to respond to treatment. Foals were discharged from the hospital when clinical signs of infection had resolved, although all foals were still receiving antibiotic drugs at the time of discharge.

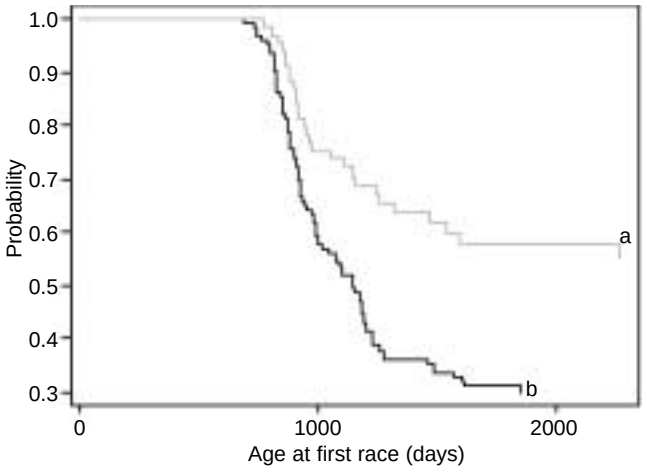

Fig 1: Kaplan-Meier plot of the probability of a Thoroughbred foal starting on a racecourse, for a) study and b) control groups.

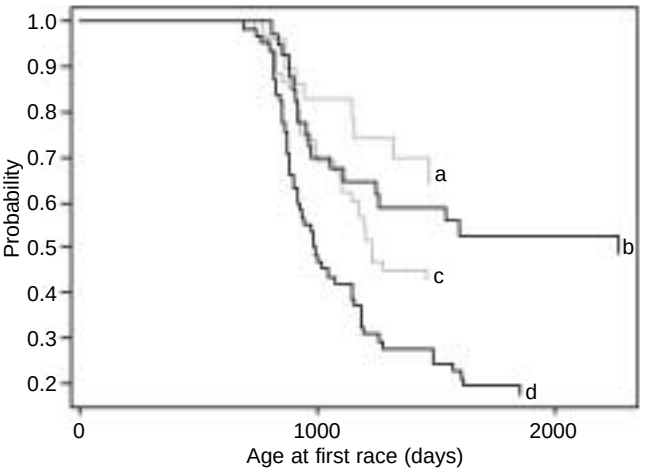

Fig 2: Kaplan-Meier plot of the probability of the control and study populations starting on a racecourse, for male and female foals. a = female cases; b = male cases; c = female controls; d = male controls.

Of the 69 foals admitted to the hospital for treatment of septic arthritis, 58/69 (84.1%) survived to be discharged from the hospital, with long-term follow-up available for all foals discharged. Of the 11 foals subjected to euthanasia prior to discharge, one foal was destroyed because of a disease process other than septic arthritis. The remaining 10 foals were all subjected to euthanasia because of failure of the septic arthritis to respond to treatment. Three of the 5 foals (60%) with more than one affected joint failed to survive to discharge from the hospital. The remaining 2 foals (40%) were discharged successfully, but did not race. However, statistical analysis of these limited numbers failed to demonstrate an association between the presence of infection in more than one joint and a reduced likelihood of foals either surviving to discharge or starting on a racecourse. Eight of 69 foals (11.6%) had evidence of a disease process outside the synovial cavity; concurrent osteomyelitis (n = 1), ruptured bladder (n = 1), pneumonia (n = 1) and infected umbilical remnants requiring surgical resection (n = 5). Of these 8 foals, 4 failed to survive until discharge (50%). Of the remaining 4 that were discharged, 2 (25%) failed to race. The presence of multisystemic disease was associated with a decreased likelihood of the affected foal surviving to be discharged successfully from the hospital (OR 0.13; 95% CI 0.02–0.90; P = 0.005). However, of those foals discharged successfully, the presence of multisystemic disease did not affect the likelihood that they would start in at least one race compared to foals treated for septic arthritis that were not affected with multisystemic disease (OR 0.45; 95% CI 0.04–2.81; P = 0.34).

Twenty-eight foals (40.5%) with septic arthritis subsequently started in ≥1 race and 17 (24.6%) raced ≥5 times. Therefore, 28 of the 58 (48.3%) foals discharged from the hospital following treatment started in a race. Of the 130 foals in the control group, 86 (66.2%) subsequently started in ≥1 race and 69 (53.1%) raced ≥5 times. Data analysed using combined regression analysis[1] confirmed that the occurrence of septic arthritis as a neonate resulted in a TB foal being less likely to start on a racecourse compared to its siblings prior to the commencement of treatment (OR 0.28; 95% CI 0.12–0.62, P = 0.001). If the foal was successfully discharged from the hospital following resolution of joint sepsis, it would still be less likely to start on a racecourse compared to its siblings (OR 0.36; 95% CI 0.15–0.83, P = 0.008). Of foals that started on a racecourse at least once, those that had been treated for septic arthritis were as likely to start ≥5 times as the control (sibling) population (OR 0.38; 95% CI 0.14–1.08; P = 0.037).

Of the 130 foals in the control group, 64 were female and 66 were male. A significantly larger proportion of the male foals started on a racecourse compared to females (OR 2.82; 95% CI 1.24–6.49; P = 0.007). In comparison, no statistically significant difference was found between the number of male and female foals treated for septic arthritis that started on a racecourse (OR 1.89; 95% CI 0.64–5.74; P = 0.20). Overall, male foals treated for septic arthritis were less likely to start on a racecourse when compared to male foals in the control group (OR 0.26; 95% CI 0.10–0.68; P = 0.002). The same was true of female foals treated for septic arthritis, compared to the female population in the control group (OR 0.39; 95% CI 0.14–1.05; P = 0.04).

Kaplan-Meier survival curves were generated comparing age at first race with the sex of the foal, and comparing age at first race between the study and control groups. Data from foals that failed to start in a race were censored. Log-rank comparison of the survival curves confirmed that foals discharged successfully following treatment for septic arthritis took significantly longer to appear on a racetrack for the first time compared to the control population (mean age of study group 1757 days, CI 1604–1909; median age of sibling group 1148 days, mean age of sibling group 1273 days, CI 1197–1349; P = 0.0006; Fig 1).

Within the control population, male foals appeared on a racetrack at an earlier age than females (median age of male foals 987 days, mean age 1172 days, CI 1074–1270; median age of female foals 1225 days, mean age 1208 days, CI 1144–1273; P = 0.002; Fig 2). However, within the study group, sex was not statistically associated with age of the foal at its first race (mean age of male foals 1692 days, CI 1487–1896; mean age of female foals 1333 days, CI 1242–1424; P = 0.24; Fig 2).

Discussion

Survival rates reported here for foals treated for septic arthritis are higher than those in other reports (Schneider *et al.* 1992; Steel *et al.* 1999; Meijer *et al.* 2000), which may be the result of early recognition and treatment of joint sepsis. All foals were resident at large studfarms, where the awareness of the importance of adequate colostrum consumption, along with thorough daily

checks of foals, contributed to a better management regime. The majority of cases were admitted to the hospital by members of the practice rather than being a referral population as described by previous reports, where it might be expected that there is a bias towards more severely affected animals.

Despite the large number of publications in the literature on septic arthritis, limited data are available on the prognosis for neonatal septic arthritis (Schneider *et al.* 1992; Steel *et al.* 1999; Meijer *et al.* 2000), particularly in an athletic breed such as the TB, with only 2 studies extending follow-up beyond discharge from the hospital (Platt 1977; Steel *et al.* 1999). Although many studies have examined the efficacy of different treatment regimes in the management of septic arthritis, no study has focused on such a specific study group, or compared the long-term outcome following treatment for septic arthritis to a suitable control group. The purpose of this study was not to compare specific treatment regimes used and their effect on long-term prognosis, but to assess whether a TB foal treated successfully for septic arthritis would be less likely to race compared to its siblings. All foals admitted to the hospital for treatment of septic arthritis were matched with 2 siblings of racing age as controls, for comparison of the number of starts achieved in their career (Mitten *et al.* 1995). Statistics published by Weatherbys suggest that approximately 65% of TB foals born in one year start at least once on a racecourse, a figure that has not changed over the past decade. Our figures showed that 66.2% of controls started successfully in at least one race, an almost identical result to the predicted average. In comparison, only 48.3% of all foals discharged successfully following treatment for septic arthritis started in at least one race in their career. This result is higher than 2 previous studies reporting the long-term outcome of TB foals treated for septic arthritis, where only 30% (Platt 1977) and 37% (Steel *et al.* 1999) of foals subsequently raced.

The potential exists to cause permanent degenerative joint disease, irreversible cartilage damage, fibrosis and unsoundness if infection is not eliminated rapidly from the synovial space (Martens and Auer 1980; McIlwraith 1983; Stoneham 1997; Steel *et al.* 1999). Once bacteria have entered the joint, they localise in the synovial membrane and provoke a profound inflammatory reaction (Martens and Auer 1980; Bertone *et al.* 1987). Release of cellular enzymes leads to depletion of proteoglycans from the cartilage (Martens and Auer 1980; McIlwraith 1983; Bertone *et al.* 1987), alteration in cartilage pliability and subsequent collagen breakdown from increased vulnerability to mechanical forces (McIlwraith 1983; Bertone *et al.* 1987). The nutritional capacity of the synovial fluid is diminished due to the inflammatory changes occurring, resulting in further articular cartilage destruction (Martens and Auer 1980; McIlwraith 1983). Although young animals have a greater capacity for regeneration of articular cartilage than mature individuals (Martens and Auer 1980; McIlwraith 1983), the degenerative changes that occur subsequent to infection are likely to have contributed to the higher number of foals that failed to race following successful resolution of sepsis, compared to the control population.

Unlike in previous studies (Martens and Auer 1980; Steel *et al.* 1999), infection of multiple joints was not associated with either a reduced likelihood of foals surviving to discharge, or a reduced likelihood of racing. However, the total number of foals treated with multiple joint involvement was very low (5/69; 7%) compared with previous studies, where a significantly higher incidence of multiple joint involvement was recorded; 50% (Schneider *et al.* 1992) and 50.6% (Steel *et al.* 1999). The affected joint (femoropatellar, tibiotarsal or metacarpo/metatarsophalangeal joints) did not have a significant effect on either survival to discharge or long-term prognosis. Other joints were not affected in sufficient number to allow for accurate evaluation. The presence of multisystemic disease was associated with an increased likelihood of the affected foal not surviving to be discharged successfully from the hospital. However, of those foals discharged successfully, the presence of multisystemic disease did not affect the likelihood that they would start in at least one race.

Despite the large number of foals in the study, the retrospective study design, coupled with the fact that many foals received more than one antimicrobial and lavage technique, precludes any conclusions being drawn regarding the relative efficacy of specific treatment modalities. However, the aim of the study was not to compare the relative success associated with one specific treatment, but to look at the long-term prognosis of foals that had survived until discharge from the hospital and whether the occurrence of septic arthritis as a neonate would affect the likelihood of starting on a racecourse. Studies adopting a retrospective, controlled design are required in order to be able to draw any conclusions on the efficacy of specific treatment regimens. Similarly, attempts to examine the effects of the joint involved, number of joints and existence of concurrent pathology on survival and long-term prognosis should be viewed with caution, as this study relies on retrospective analysis of medical records. When attempting to draw conclusions from the effects of multiple joint involvement or multisystemic disease, the low numbers of foals in each of these categories reduces the power of that component of the study.

The prognosis for survival following early identification and treatment of septic arthritis in this particular population of TB neonates is favourable, although it is reduced by the presence of multisystemic disease. If the infection was eliminated from the synovial space before irreversible damage occurred, then almost 50% of foals successfully discharged started in at least one race. However, the prognosis for starting in a race, compared to their siblings, is less good.

Manufacturer's address

[1]Sagebrush Press, Salt Lake City, Utah, USA.

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