

HEALTH ZONE

Playing for the Long Haul

BY AMANDA DUCKWORTH

THE MAJORITY OF future racehorses have a relatively routine start to life, both when it comes to foaling and growing up next to their mothers. Part of that is a credit to Mother Nature, and part is the result of the care and management farms dedicate to the process.

Of course, for all of the best intentions, sometimes things do go wrong. How much that impacts each foal's future as a racehorse depends on both the issue at hand and the foal in question.

In its November 2019 issue, *Equine Veterinary Journal* published research looking into the outcome of sick foals titled "Factors associated with long-term athletic outcome in Thoroughbred neonates admitted to an intensive care unit."

"Limited information exists on the long-term outcome of foals that survive following hospitalization for disease as a neonate," explains the study. "Significant financial investment is required to raise foals to racing age; therefore, improved understanding of factors that affect long-term outcome and future athletic performance is important."

For the retrospective cohort study,

researchers analyzed the racing performance of Thoroughbred foals hospitalized as neonates when compared to their maternal siblings. The medical records of Thoroughbreds admitted to a neonatal intensive care unit between 1982-

Understanding factors that affect sick foals later in their careers

2008 served as the basis of the study, and multivariable logistic regression was used to identify disorders associated with failure to race and decreased racing performance.

Of hospitalized foals, the study found that 269 of the 454, or 59%, went on to race. From that group of 454, 394 of the foals were registered, which means 68% of the registered foals from that group raced. For comparison, 697 of 880, or 79%, of their registered siblings had racing careers.

"Foals with prematurity/dysmaturity and those with orthopaedic disease were significantly less likely to race than their siblings," the study found. "Premature/

dysmature foals also had significantly fewer starts and wins and lower earnings than their siblings. Foals with orthopaedic disorders had a lower percentage of wins, relative to their siblings. There was no significant association between racing performance and other disease categories."

A study named "Prematurity and Dysmaturity Are Associated with Reduced Height and Shorter Distal Limb Length in Horses" published in the August 2020 issue of the *Journal of Equine Veterinary Science* looked specifically at what happens to foals that are born early or small.

"The long-term effects of gestational immaturity in the premature (defined as <320 days gestation) and dysmature (normal term but showing some signs of prematurity) foal have not been thoroughly investigated," explains the study. "Studies have reported that a high percentage of gestationally immature foals with related orthopedic issues such as incomplete ossification may fail to fulfill their intended athletic purpose, particularly in Thoroughbred racing.

"In humans, premature birth is associated with shorter stature at maturity and variations in anatomical ratios, linked to alterations in metabolism and timing of physeal closure in the long bones. We hypothesized that gestational immaturity in horses might similarly be associated with reduced height and different anatomical ratios at maturity."

The skeletal ratios of horses with a history of gestational immaturity were compared with those of unaffected but closely related horses for this preliminary study. This information was determined through veterinary and breeder records. To make the comparisons, external measurements were taken from conformation photographs of 19 cases and 28 related horses. These were combined into indices to evaluate and compare metric



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MESSAGE FROM THE GRAYSON-JOCKEY CLUB RESEARCH FOUNDATION

RESEARCH UPDATE: NOCARDIOFORM PLACENTITIS

BY DR. BARRY A. BALL



Grayson-Jockey Club
Research Foundation

Nocardioform placentitis remains an enigmatic and poorly understood disease that was first diagnosed in central Kentucky in 1986. Since that time, nocardioform placentitis has occurred episodically with outbreaks in 1998, 1999, 2011, 2017 and 2020.

Cases of nocardioform placentitis have also been reported in South Africa, Italy, Australia, and New Zealand with anecdotal reports of the disease in eight other U.S. states during 2020. Nocardioform placentitis is characterized by late-term abortions, premature foals, neonatal deaths, and weak, stunted foals at term associated with an apparent fetal growth retardation due to placental insufficiency.

The resulting placental insufficiency and fetal growth retardation are related to the size of the lesion on the placenta. The distribution of the placental lesion is distinct from ascending bacterial placentitis with lesions of nocardioform placentitis distributed along the bottom portion of the placenta near the junction of the uterine horns and body. The lesion is often sharply demarcated from the surrounding normal placenta, and the affected placenta is covered with a thick, tan mucoid material. Although the placenta shows inflammatory changes, the infection with nocardioform placentitis seems limited to the placenta and does not involve the fetus in contrast to other forms of bacterial placentitis.

Nocardioform placentitis is associated with gram-positive, branching actinomycetes including *Amycolatopsis spp.*, and *Crossiella equi* along with more recently characterized isolates of *Streptomyces atiruber* and *Streptomyces silaceus*. Characterization of actinomycetes during the 2020 outbreak of nocardioform placentitis in Central Kentucky revealed that *Amycolatopsis spp.* was most common with *Crossiella equi* as the next most frequent isolate.

The ecology of these bacteria remains poorly understood as they have only been isolated from placental lesions and not from environmental sources. Attempts to induce the infection in mares by intrauterine inoculation of *Crossiella equi* at breeding and in pregnant mares via oral, intravenous, and intranasal routes have been unsuccessful. Therefore, the pathogenesis of nocardioform placentitis remains obscure.

Nocardioform placentitis abortions occur between November and June with a peak incidence in January, February, and March. The majority of affected fetuses are in the last trimester of pregnancy, and the identification of nocardioform lesions on the placenta of term pregnancies is a common presentation. Retrospective evaluation of monthly climate data (precipitation and average temperature) for Central Kentucky and the number of nocardioform placentitis cases seen by the University of Kentucky Veterinary Diagnostic Laboratory for the period between 1990-2020 was conducted. This analysis demonstrated a moderately strong negative association ($\rho = -0.60$; $P = 0.0004$) between August and September rainfall and the number of nocardioform placentitis cases submitted for the subsequent foaling season. Likewise, there was a moderately strong positive association ($\rho = 0.52$; $P = 0.003$) between mean temperatures in August and September and the number of nocardioform placentitis cases submitted in the subsequent foaling season. The strong association between a hot and dry August and September preceding

an increase in nocardioform cases is strongly suggestive of an environmental factor in this disease.

It is worth considering that the actinomycetes responsible for nocardioform placentitis might originate as soil-born organisms, despite the failure thus far to isolate these organisms from environmental sources. Related members of *Amycolatopsis* and *Streptomyces* are well characterized as soil-associated microorganisms.

Clinically, diagnosis of nocardioform placentitis before foaling remains difficult. Late in the disease, affected mares might show signs of premature lactation and mammary development but typically do not show a vulvar discharge. Evaluation of the uterus and placenta by transrectal ultrasound exam is often normal unless the disease has progressed extensively. Imaging the lesion with nocardioform placentitis requires examining the pregnant uterus with ultrasound through the body wall, a time consuming and diagnostically challenging procedure.

The true incidence of nocardioform placentitis remains unknown. Although cases with severe neonatal outcome (dead or very poorly developed neonates) are likely submitted to the UKVDL for pathologic workup, births that have lesions of nocardioform placentitis without effects on the fetus are much less likely to be submitted and remain uncounted.

This is supported by careful screening of all placentas on one farm that revealed frequent and often small lesions consistent with nocardioform placentitis without obvious neonatal effects during the 2020 foaling season. Accurately determining the impact of nocardioform placentitis is further complicated by incorrect diagnosis of the disease on farm.

During the 2020 outbreak, 171 placentas from affected mares and normal control mares were evaluated. Upward of 25% of the submitted placentas were incorrectly identified on the farm as normal or as nocar-

dioform placentitis, which emphasizes the importance of submitting these materials to a veterinary diagnostic lab for definitive diagnosis.

During the 2020 outbreak of nocardioform placentitis, a variety of clinical, epidemiologic, and pathology findings were generated from 264 pregnant mares with either nocardioform placentitis or normal control mares. Highlights from these data indicate that mares with nocardioform placentitis were older, had shorter gestational lengths, more dead neonates, and reduced foal birthweights compared to control mares without placentitis. Furthermore, neonatal weights were related to the size of the placental lesion (larger lesions had smaller neonates and were more likely associated with dead neonates). Interestingly, mares with nocardioform placentitis appeared to have no reduction in their fertility after foaling compared to controls.

The underlying etiology of nocardioform placentitis remains unknown despite the disease's being first identified more than 30 years ago. It appears likely the pathogenesis of nocardioform placentitis is mul-

tifactorial with a strong environmental association (hot, dry periods in late summer preceding the next foaling season). A number of related bacteria are isolated from nocardioform placentitis lesions, and many of these bacteria are from groups that are often associated with soil. This suggests that there is likely some upstream, common environmental factor involved with the development of nocardioform placentitis. The nature of this factor remains speculative.

Ongoing studies at the Gluck Center funded by the Grayson-Jockey Club Research Foundation, the Koller Priority Response Fund, and the Albert G. Clay Endowment are examining multiple aspects of this disease. These studies will examine possible markers in blood of pregnant mares, including steroid hormones, cytokines, alpha-fetoprotein and transcripts for inflammatory signaling.

Other studies will examine the role of the mare's immune response and antibody formation to bacteria associated with nocardioform placentitis. Data collected during the 2020 outbreak will also be used for a more detailed epidemiologic investigation of the

disease. High-throughput RNA sequencing will be used to examine the interaction of the pathogenic bacteria with the placenta in order to understand how these organisms induce disease and the response of the mare to the infection. Work is also underway to develop better in vitro models for the disease, which to date has not been successfully induced experimentally.

These studies will provide a better grasp of the causes, outcomes and possible preventions and treatments for this enigmatic disease. **BH**

In September 2020, a half-day virtual workshop on nocardioform placentitis was held at the University of Kentucky. Presentations from this workshop and the associated white paper can be found at this web address:

<https://gluck.ca.uky.edu/nocardioform-sept2020>

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properties of conformation.

"A principal component analysis showed that the first two principal components account for 43.8% of the total conformational variation of the horses' external features, separating horses with a rectangular conformation from those that are more square," the study found. "Varimax rotation of PC1 and analysis of different gestational groups showed a significant effect of gestational immaturity, with the premature group being more affected than the dysmature group.

"Mean values for the four dominant indices showed that these groups have significantly lower distal limb to body length relationships than controls. The observed differences suggest that gestational immaturity may affect anatomical ratios at maturity, which, in combination with orthopedic issues arising from incomplete ossification, may have a further impact on long-term athletic potential."

In the January 2018 issue of the *Equine Veterinary Journal*, the study "Gestation length and racing performance in 115 Thoroughbred foals with incomplete tarsal ossification" also explored the impact of gestation lengths on the health of foals.

"Incomplete ossification of the cuboidal bones of the carpus and tarsus in foals has the potential for significant consequences, including chronic lameness and decreased athletic ability," explains the study. "The objective is to determine if the degree of ossification of the cuboidal bones is associated with gestational length, and if the diagnosis of incomplete ossification is a predictor of performance in Thoroughbred racehorses."

The retrospective cohort study examined the medical records of Thoroughbred foals less than 90 days of age from 1994-2011 and records containing tarsal radiographs were identified.

"Radiographs of the tarsus were exam-

ined for signs of incomplete ossification and those that were incompletely ossified graded on a scale of 1-4 using a modification of a previously reported index, with grade 1 being the least ossified and grade 4 being the most," explains the study. "Gestational length was determined by examining breeding records and foaling dates reported to The Jockey Club. Race records for 2- and 3-year-old affected foals and their maternal siblings were obtained and compared."

The study found that foals with grades 1 and 2 ossification were usually premature; however, grades 3 and 4 were not. Foals with grades 2 and 3 ossification were significantly less likely to race than their siblings, and all four categories earned less money than their family members.

"A larger sample size of foals with grade 1 ossification would increase the power of the study," the study notes. "Foals radiographed at an older age may

have had lower ossification scores if radiographed earlier.

“Incomplete ossification, especially grades 1 and 2, is associated with a short gestation length. Foals with grades 2 and 3 incomplete ossification were less likely to race and grades 1, 2 and 3 earned around \$30,000 less than their maternal siblings.”

Another issue that can greatly affect a foal is septic arthritis, which usually presents itself when the foal is younger than one month old. In November 2020, *Equine Veterinary Journal* published the study “Factors associated with survival and racing performance of 114 Thoroughbred foals with septic arthritis compared with maternal siblings (2009-15).”

For this study, researchers investigated factors associated with survival and then analyzed the racing performance of foals with septic arthritis compared with their maternal siblings.

“There is little consensus on factors associated with survival in foals with septic arthritis and limited data on long-term racing performance of Thoroughbred foals treated for septic arthritis,” explains the study. “A more thorough understanding of short- and long-term outcome is necessary to help inform owners and subsequently guide treatment.”

To explore this topic, the veterinary records were reviewed of Thoroughbred foals less than 181 days old that underwent arthroscopic *cannulae*, or through-and-through needle lavage for the treatment of septic arthritis between 2009-15. Additionally, the foaling record of the dam and the lifetime racing records of two of each foal’s siblings were reviewed to make comparisons between treated foals and their brothers and sisters.

“Ninety (78%) of 115 foals diagnosed with septic arthritis were discharged alive,” the study found. “Foals less than 26 days old at the time of admission were five times less likely and foals with concurrent multisystemic disease were six times less likely to be discharged alive. Sixty (67%) foals discharged alive started in ≥ 1 race, and there was no difference in the proportion of foals that started in a race or racing performance between

foals treated for septic arthritis and their maternal siblings.

“Foals treated for septic arthritis at the Scone Equine Hospital, New South Wales, Australia, had a good prognosis for survival, and for this cohort, foals that survived to discharge had a similar ability to race as their maternal siblings.”

Another recent study in Australia, “Barriers to entering race training before 4 years of age for Thoroughbred horses born in the 2014 Australian foal crop,” was published in August 2020 by *PLoS One* and examined the reasons Thoroughbreds failed to make it to the races.

“The most frequent reason identified by respondents for horses not participating in the racing industry was that the horse had died before it entered training,” researchers found. “The period of greatest mortality risk was the period from birth to 12 months of age.

“Of the 125 deaths that occurred before one year of age, 47% occurred during the neonatal period (less than one month of age), 38% occurred between one and six months of age, and the remaining 14% occurred from six to 12 months of age. In the neonatal period the most critical period was the first week, with 76% of these foals dying within seven days of birth.”

The number of horses in the study that died before training was 239, or 38% of the 633 horses enrolled in the survey. From those 239 horses, 125 of them, or 52%, died before they were a year old, and congenital malformation was the most common cause of death in this age group.

“Mortality was the most frequent barrier preventing foals (beginning) training, with the majority of these deaths occurring before these foals reached one year of age,” the study concluded. “A large proportion of foal deaths occurred in the first month of life.”

Across the variety of studies about a foal’s future performance as a racehorse, how that performance is measured can and does vary. That very concept led to the review published in the May 2018 *Equine Veterinary Journal* titled “A systematic literature search to identify performance measure outcomes used in


clinical studies of racehorses.”

“Racing performance is often used as a measurable outcome variable in research studies investigating clinical diagnoses or interventions,” the review explains. “However, the use of many different performance measures largely precludes conduct of meaningful comparative studies and, to date, those being used have not been collated.”

For the review, 217 studies that described racing performance were identified, and they contributed 117 different performance measures.

“No one performance measure was used in all studies, despite 90.3% using more than one variable,” researchers found. “Data regarding race starts and earnings were used most commonly, with 88.0% and 54.4% of studies including at least one measure of starts and earnings, respectively. Seventeen variables were used 10 times or more, with the top five comprising return to racing, number of starts, days to first start, earnings per period of time, and earnings per start.

“Performance indices have been developed to improve assessment of interventions; however, they are not widely adopted in the scientific literature. Use of the two most commonly identified measures, whether the horse returned to racing and number of starts over a defined period of time, would best facilitate future systematic reviews and meta-analyses in advance of the development of a gold-standard measure of race performance outcome.”

A healthy, happy foal is the goal of all breeding farms for every mating that is planned, but the scientific reality is that it will never be achievable in every case. How much a rough first year of life impacts a foal’s ability to be a productive racehorse depends on what went wrong, and while it certainly does not preclude a horse from a fruitful career, odds are the foal will have a harder time succeeding in the future than its healthier paddock mates. 

Amanda Duckworth is a freelance writer based in Lexington.