EQUINE DISEASE QUARTERLY

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IN THIS ISSUE

COMMENTARY

The art of horse production is pattern recognition. The most obvious pattern is that offspring resemble their parents. These resemblances can be found in phenotypes such as size, conformation, durability, and performance. Using phenotypes and pedigrees, breeders have applied selection, resulting in profound changes in horses since their domestication 5,500 years ago. Today, hundreds of breed registries exist, reflecting diverse goals among horse breeders. These interests span divergent phenotypes related to racing, pulling, jumping, dressage, performing special gaits, and characteristics associated with coat color or size. The commonality among these traits is they have a large genetic component. Foundation Stock were identified exemplifying traits of interest. The path to improvement has been to identify quality breeding stock, cross them to Foundation horses and select the best for future breeding stock. As a result, Foundation Stock are represented many times in horse pedigrees and contribute to the distinctive phenotypic characteristics within those breeds.

Recently, a reference whole genome sequence of the horse was determined. Scientists identified genes for discrete traits such as coat colors and some hereditary diseases. However, despite a great deal of research, no single gene has been found responsible for complex traits such as racing, jumping, and gait. This is not surprising since athletic performance involves a combination of muscle strength, cardiovascular capability, competitiveness, and coordination. Yes, a few genes have been identified that influence performance (e.g., DMRT3 for gait and MSTN for sprinting); however the development of champions involves many other genes as well as the art of the trainer and skill of the rider. This relationship is remarkably complex since variation exists despite generations of selection. The resilience of genetic variation may reflect the diverse ways in which a horse can become a champion. Northern Dancer and Secretariat were champion Thoroughbred racehorses; however, while Northern Dancer was relatively small in stature, Secretariat was renowned for his large size and stride length. While the old breeding adage is "breed the best to the best and hope for the best," the skill of the successful breeder is to identify hereditary patterns among the best and make judicious choices. There is no single genetic test that will replace the skill of the breeder.

Genomic tools have the potential to improve the recognition of useful patterns. Horse genes are distributed among 32 pairs of chromosomes (see the image in the online version of this issue at http://gluck.ca.uky.edu/equine-disease-quarterly). These chromosomes contain the genetic material under selection. Genetic recombination occurs during production of eggs and sperm in each generation that divides these genetic blocks into subsets of chromosomes. It is possible to identify the specific block inherited from each parent and relate those blocks to blocks found in the grandparents. Likewise, one might even discern the blocks back to the Foundation Stock. Unfortunately, such a tool does not yet exist for horses, but a similar commercial application is used by people to identify the origin of their ancestors. We anticipate horse breeders may seek to use such a tool one day.

Today we can apply genomics to assess one of the concerns of horse breeders, namely inbreeding. As noted above, the establishment of breeds relies on the identification and use of Foundation Stock. An unintended consequence of this is inbreeding and the attendant risk of inbreeding depression and the appearance of deleterious hereditary diseases. The article in this issue, "Genomics and Inbreeding," describes the concern and identifies ways in which genomics can be used to monitor inbreeding and assist breed registries to anticipate problems.

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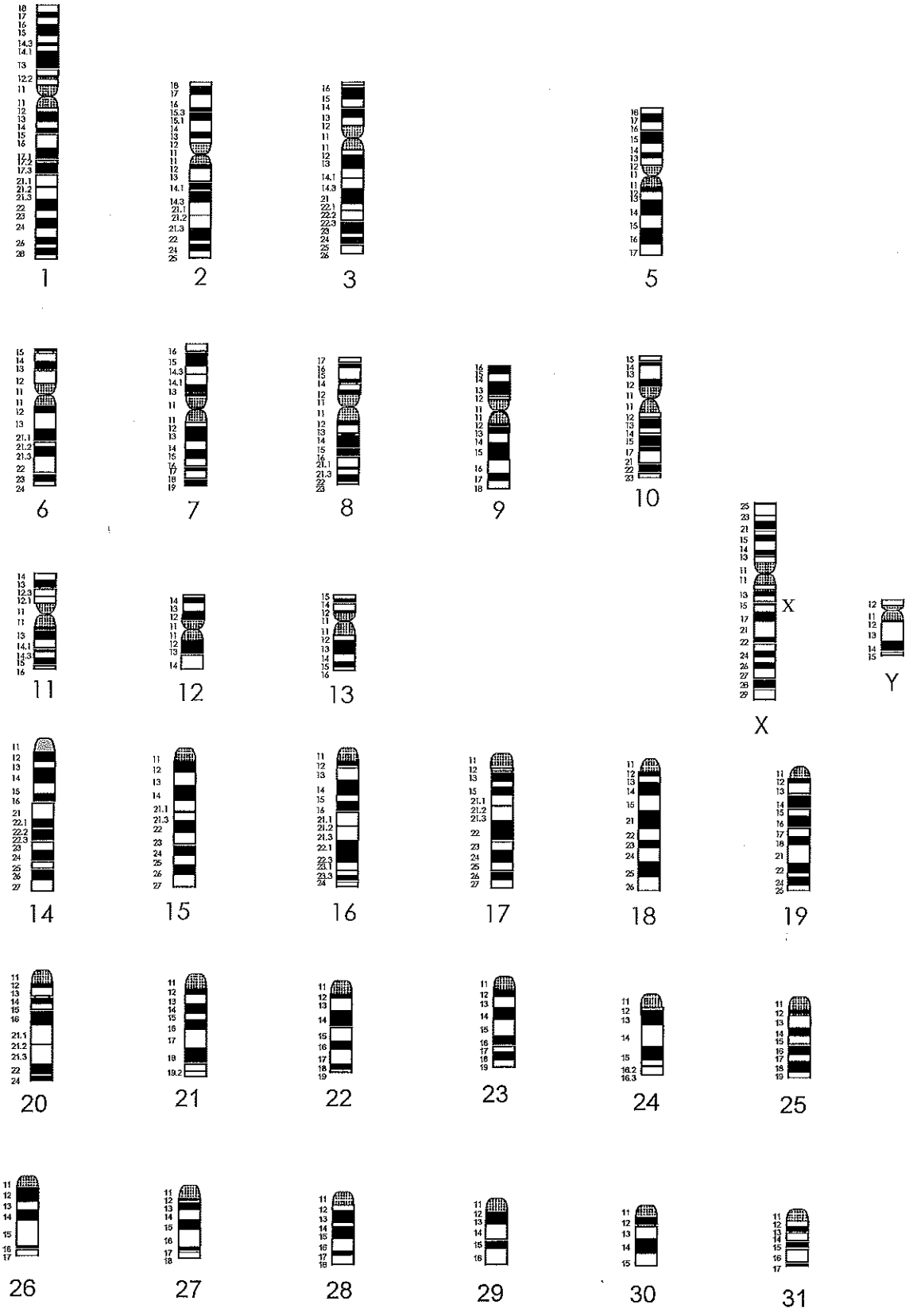
A banded representation of the 31 autosomal chromosomes as well as chromosomes X and Y for the domestic horse.



INTERNATIONAL

Third Quarter 2019

The International Collating Centre, Newmarket, United Kingdom, and other sources reported the following equine disease outbreaks.

Cases of African horse sickness decreased substantially in the Republic of South Africa (RSA) during the period under review. Fewer than five cases occurred in the Eastern Cape Province, Mpumalanga and KwaZulu Natal; no cases were reported in the Western Cape Province.

Kuwait confirmed three subclinical cases of glanders on pre-export testing.

Equine influenza was recorded in Belgium, Denmark, France, Germany, Sudan, the UK, and the USA. The number of outbreaks/cases varied with fewer than five cases reported by Belgium, Denmark, and Germany, to six outbreaks in France, four of which involved multiple cases. Sudan reported 700 cases with 107 deaths; cases spread from south Darfur to east Darfur. The UK recorded 59 outbreaks. The disease was reported as endemic in the USA with outbreaks confirmed in six states.

France, Germany, the Netherlands, Switzerland, the UK, and the USA reported outbreaks of strangles. The number of confirmed outbreaks ranged from two in Switzerland, three in Germany, 15 in the Netherlands, and 27 in France. The UK and the USA reported the disease as endemic, with the USA recording strangles in 14 states.

Equine herpesvirus 1 (EHV-1) related diseases were recorded by Belgium, Denmark, France, Germany, Ireland, Switzerland, the Netherlands, the UK, and the USA. Respiratory disease was diagnosed in Belgium (two outbreaks), Denmark (one outbreak), France (four outbreaks), Germany (one outbreak), Ireland (two outbreaks), the Netherlands (one outbreak) and the USA (numerous outbreaks). Denmark reported one outbreak involving four cases of EHV-1 abortion. EHV-1 myeloencephalopathy was confirmed by France (three outbreaks, one involving five cases of the disease), Switzerland and the Netherlands (one outbreak apiece), and the USA (three outbreaks each involving single cases).

Equine herpesvirus 4 respiratory disease was reported by Belgium, Germany, and the Netherlands (three outbreaks apiece); France (11 outbreaks); Ireland, Japan, and Switzerland (one outbreak apiece); the UK (six outbreaks); and the USA (numerous outbreaks).

France, Poland, and the UK recorded cases of equine arteritis virus infection. Two outbreaks were confirmed by France, represented by single cases of abortion and two cases of equine viral arteritis in one of the outbreaks. Poland recorded one outbreak involving three cases of equine viral arteritis. The UK confirmed infection in a subclinical carrier stallion.

Equine infectious anemia was reported by Canada (three outbreaks involving single cases, one of which was clinical), France (two outbreaks, each involving single cases), and the USA (14 outbreaks, one of which involved 17 horses).

The USA confirmed five outbreaks of anthrax, all in a high-risk region of Texas.RSA reported that equine piroplasmosis was endemic in the country, with 29 cases recorded during the period under review.

Contagious equine metritis was confirmed by Denmark (case in a stallion), France (two outbreaks, one involving a carrier stallion and another causing metritis and abortion in a mare), and Germany (infection in a mare).

Three outbreaks of salmonellosis were recorded in the USA.

The USA reported 25 cases of equine neorickettsiosis involving three states. The vast majority were in July and August in Kentucky.

Clostridial enterocolitis was recorded in the USA, with confirmation of 13 cases of *Clostridium perfringens* Type A toxin genotype and 15 cases of *C. difficile*.

France reported eight outbreaks of rotavirus infection, six involving single cases and two with two cases. The USA confirmed 22 cases of infection, principally in Kentucky, the preponderance associated with the G14 virus genotype and a few involving both G3 and G14 genotypes.

A single case of *Lawsonia intracellularis* infection was reported by the USA.

Eastern equine encephalomyelitis was recorded in the USA with 76 cases confirmed in the third quarter, the majority in Florida and Michigan.

West Nile encephalitis was reported by Austria (two cases), Brazil (three cases), Canada (one case), France (four cases), Germany (eight cases), Greece

Equine Disease Quarterly

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(two cases), Italy (one case), and the USA (34 cases, of which 14 were in California).

RSA confirmed three cases of equine encephalosis.

Vesicular stomatitis (Indiana serogroup) was confirmed on premises in seven states in the USA: Colorado, Nebraska, New Mexico, Oklahoma, Texas, Utah and Wyoming. A total of 1095 affected premises were identified during the period under review.

Rhodococcal-related disease was reported by Belgium (one case) and the USA, in which the disease is endemic. Twenty cases were diagnosed in Kentucky; this is considered a significant underestimate of the actual incidence.

Germany and Switzerland reported single cases of ehrlichiosis.

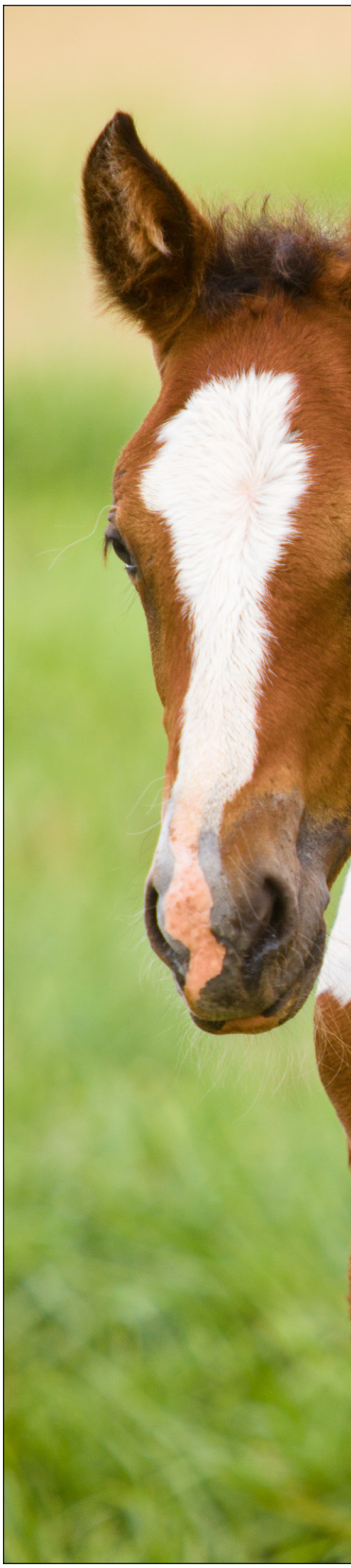
Inbreeding and Genomics

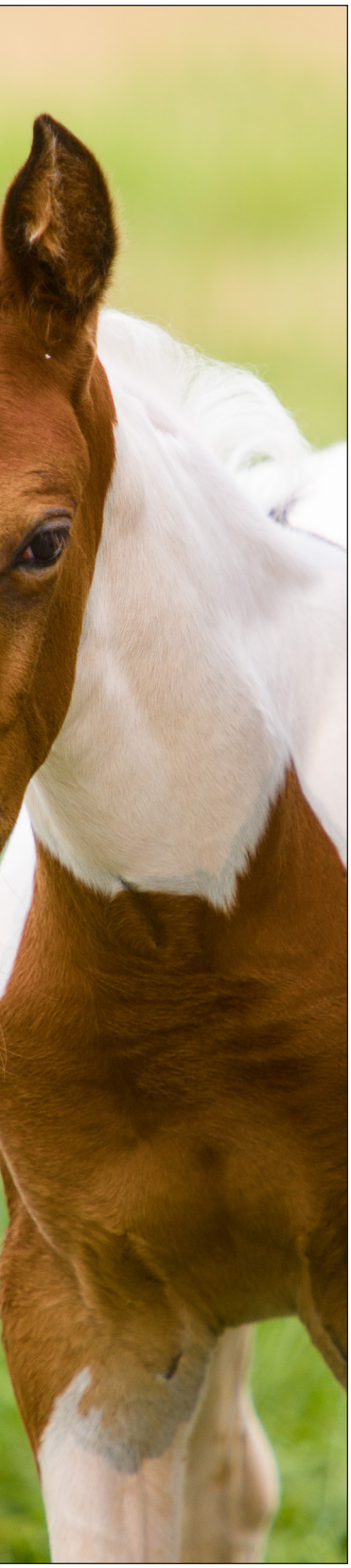
Inbreeding has played a key role in the improvement of livestock breeds, resulting in more uniform populations with highly specialized performance traits. Selection for desirable traits entails identifying individuals with superior performance and often mating them to relatives (inbreeding) who possess the same superior traits. The goal of this practice is to increase the frequency of the desired characteristics and thus of the beneficial genes in the offspring. At the same time, negative consequences of inbreeding are well known. In small populations such as captive bred species, the loss of diversity associated with inbreeding is a major concern, and significant losses of diversity may lead to extinction. The increased expression of recessive deleterious genotypes can also lead to embryonic loss or other defects, some of which can be fatal. Furthermore, inbreeding can lead to a phenomenon called inbreeding depression. Inbreeding depression is commonly manifest in poor performance of traits that are complex (due to contributions of many different genes), such as fertility and athleticism. Mindful of the dangers inherent with inbreeding, breeders traditionally balance the benefits and dangers of inbreeding by monitoring their breeding stock, culling poor performers and avoiding matings of closely related individuals.

Recently, genetic tools have become available that provide an alternative approach to unambiguously quantify and manage inbreeding relative to the traditional use of pedigrees. Today, a genomic survey of a horse's DNA may cost $70 to $180. A comprehensive whole genome sequence, including analyses, may cost $1,000 to $2,500. So far, over 1,000 horses have had their entire DNA sequenced in connection with research projects. Those genome sequences have been used to identify the genetic bases of diseases, coat colors and even some performance traits. Nevertheless, the overall performance of horses is complex, involving over 20,000 genes and probably millions of other functional elements. Studying genes one at a time is unlikely to be effective to significantly improve performance. Genomic tools, however, make it possible to identify associations between the genome and traits that contribute to success or which may cause problems.

One of the areas in which genomics excels is in determining levels of inbreeding. An animal's inbreeding coefficient is the likelihood that both parents transmitted the same piece of DNA to their offspring that they each inherited from a common ancestor. Traditionally, we measured inbreeding by identifying all common ancestors – those that appear in the paternal and maternal sides of an individual's pedigree. After common ancestors are identified, the relationship between the parents of the individual in question can be calculated. Using this method, on average, pedigree-based inbreeding coefficients for Thoroughbred horses are reported to be between 12.5%-13.5%, however individual horses may have values that range from less than 5% to over 20%. When genomic measures have been made in other species, geneticists discovered that inbreeding levels calculated from pedigrees are poorly correlated (50%-80%) with genomic measures of inbreeding. This is not surprising since pedigrees inaccurately assume a random and equal transmission of genes each generation. Which variant of each gene is inherited, however, is not predictable. For example, full-siblings share, on average, 50% of their genes; however, at any particular part of the genome they may share 0, 50, or 100%. Further, genes are not randomly distributed in a breed since selection practices are applied in mating horses. If we are good breeders, the genetic constitution of our current generation is not a random representation of the ancestors, but rather, a selection of the genes contributing to their success.

There are other ways to apply genomics to horse breeding. As noted above, both the genome and the traits we value are complex. Our genomic tools are





Matt Barton, Agricultural Communications

powerful, and we can begin to seek genetic patterns correlated with measures valued by horse owners. The limitation for such studies is the quality and availability of data for traits related to fertility, conformation, durability and athleticism. Collecting these data and using genomics to identify genes associated with these complex traits would be a more sensible way to improve performance rather than simply seeking to limit inbreeding.

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NATIONAL

Besnoitiosis in Donkeys

Besnoitiosis is a protozoan infection caused by *Besnoitia* spp., which are cyst-forming coccidian parasites that affect multiple host species worldwide. *Besnoitia bennetti* is the species known to infect equids and has been reported in horses and donkeys in Africa, Asia, and more recently, the United States and Europe. Equine besnoitiosis was first reported in 1927 in four horses from Sudan. The only reported cases of equine besnoitiosis in North America have been in donkeys.

The life cycle of *Besnoitia* species involves both a definitive (predator) and intermediate (prey) host. Although a feline definitive host has been identified for *Besnoitia* species known to infect several types of wildlife, attempts to demonstrate a cat as the definitive host of *B. bennetti* have been unsuccessful, thus precluding researchers from elucidating the parasite's life cycle and mode of disease transmission in donkeys. Clinical disease is characterized by a miliary dermatitis caused by pinpoint parasitic cysts in the skin, mucous membranes, and conjunctiva. The skin over the muzzle, nostrils, ears, perineum, and medial thigh appears to be preferentially affected. One of the most unique features of besnoitiosis is the development of "scleral pearls," which are cysts on the sclera of the eye (Figure 1). Cysts have also been infrequently identified in the testicles, nasopharynx, larynx, trachea, and esophagus of infected donkeys. Infected donkeys may also have generalized crusting dermatitis, poor hair coat, and/or focal areas of alopecia. Often affected donkeys have a history of chronic dermatitis non-responsive to treatment with antibiotics, ointments, medicated baths, etc.

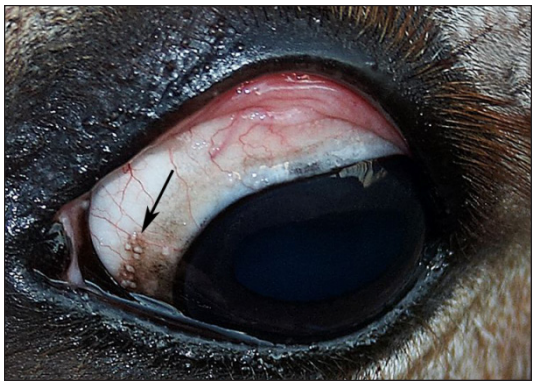

Figure 1. Scleral pearls (arrow) in an infected donkey.

In an epidemiologic investigation of besnoitiosis in donkey herds across the United States, young animals (average age 2 years) were at increased risk of infection when compared to older individuals. Sex and breed were not associated with developing besnoitiosis. The most common lesions in infected donkeys were cysts in the nostrils (94%), perineum (69%) and sclera (81%). Some infected animals remain seemingly otherwise healthy, while others become cachexic and debilitated as a result of the disease. The reason for this difference in host response to infection is unknown, but similar clinical subtypes are observed with bovine besnoitiosis in European cattle herds.

The current gold standard for diagnosing besnoitiosis in donkeys is histologic identification of *Besnoitia* cysts within the skin of individuals displaying clinical lesions, generally achieved via skin biopsy. *B. bennetti* can be detected in blood via western blot and indirect fluorescent antibody testing (IFAT), and antibody titers in donkeys have been shown to be effective for identifying infected donkeys. While these assays are not yet

available in the United States, they represent an effective and non-invasive method for screening individual donkeys and herd populations and would undoubtedly further our understanding of the epidemiology and transmission of besnoitiosis in the United States.

There are no known effective treatments for equine besnoitiosis. Treatment with anti-protozoal medications ponazuril, trimethoprim-sulfamethozazole, and nitazoxanide have not been effective. The potential for natural recovery from besnoitiosis and the long-term prognosis for infected animals remains unknown. The author has followed several infected donkeys for the past 5 years, none of which have spontaneously resolved. Although besnoitiosis has not yet been reported in horses in North America, cases have been described in Africa, and the potential for similar infections in the United States cannot be excluded as a possibility.

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KENTUCKY

Peripartum Death in Mares

Complications associated with foaling are a significant cause of morbidity and mortality in both foals and mares. Even apparently normal births can result in significant internal and external injury to the mare. In extreme cases, these injuries can be severe and result in death or require humane euthanasia of the dam.

A review of diagnostic case submissions to the University of Kentucky Veterinary Diagnostic Laboratory was conducted to assess equine peripartum deaths during the 2017 and 2018 foaling seasons. Mares that died secondary to foaling complications or were humanely euthanized due to significant parturition associated injury were included.

During the two-year period, 121 cases of peripartum death were identified out of approximately 3,000 equine necropsy submissions. Cases were categorized into five groups (gastrointestinal, musculoskeletal, reproductive, vascular, and miscellaneous) based on the primary organ system associated with the cause of death. Submissions began in December and extended into June of both years. Deaths occurred in multiple breeds, but Thoroughbreds predominated.

Fatal lesions associated with the gastrointestinal tract were most common and occurred in 52 (43%) cases. Diseases with the highest incidence included cecal rupture (12%), colonic torsion (7%), colonic rupture (4%), rectal prolapse (3%), cecal impaction (3%), gastric rupture (3%), rectal tear (3%), and non-infectious inflammatory processes (3%). One to two cases of small intestinal perforation, mesenteric rents and tears, and colonic displacement were also identified.

Fatal vascular lesions accounted for 24% of peripartum deaths and included the No. 1 cause of death during the review period, rupture of the uterine artery. Ruptures of the uterine artery were by far the most common vascular lesion (17%), frequently resulted in secondary hematoma formation in the broad ligament, a connective tissue structure that supports the uterus, and hemoperitoneum. Infrequent ruptures were also associated with the internal iliac artery (3%), circumiliac artery (1%), ovarian artery (1%), and aorta (1%). Two cases of broad ligament hematoma were recorded, in which the exact location of the vascular rupture could not be determined.Direct injury to the mare's reproductive tract occurred in 22% of the cases and frequently resulted in humane euthanasia. Uterine tear/rupture was most frequent in this category and occurred in 12% of the cases. Less common reproductive injuries included uterine prolapse and vaginal lacerations, each of which occurred in 3% of mares. Single cases of hydrops pregnancy, uterine adhesions, uterine torsion, and significant vaginal hemorrhage were also noted.

Surprisingly, injuries to the musculoskeletal system resulted in euthanasia of 10 (8%) mares. Fractures (5%) were most common followed by individual cases of hip joint luxation, diaphragmatic hernia, significant muscle trauma, and peripheral nerve damage. Fractures were specifically associated with the pelvis, tibia, and femur and were noted to occur in mares during dystocia events,

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suffering post-foaling pain, and being transported to a veterinary clinic.

The miscellaneous group included four sporadic and individual cases that occurred in the peripartum time period. These cases included death or euthanasia due to uncontrollable post-dystocia pain, a presumed cardiovascular event following dystocia, an anaphylactic drug reaction, and liver disease of unknown cause.

Dystocia was specifically mentioned in the clinical history of 19% of the 121 cases. Although the accuracy of this self-reported number is not definitive, it does emphasize that many injuries during the foaling period are not associated with difficult births.

In summary, equine death associated with the foaling period is unfortunately common. The underlying causes likely include a mixture of diseases associated with birthing trauma, pain, fetal movement and positioning, and vascular changes associated with gestation. Evaluation of mares during and following parturition is essential to rapidly identify and treat this unique group of diseases.

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