EQUINE DISEASE QUARTERLY

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COMMENTARY

IN THIS ISSUE

Late-term abortion is one of the most devastating issues horse breeders face. Every pregnancy represents a labor of love, with a substantial amount of time, energy and money put into achieving the perfect foal. Every pregnancy loss raises questions concerning our ability to have prevented that loss and whether we could have done *more*.

In this issue, Dr. Alan Loynachan addresses the underlying causes of the 898 equine abortions examined by the UK Veterinary Diagnostic Laboratory over the 2016 and 2017 breeding seasons. This retrospective look is important to help us identify areas where we can improve management techniques and where we should focus our future research efforts to best benefit horse owners and breeders. As such, it's critical that breeding farms send their aborted foals to a veterinary diagnostic laboratory, even if the cause of abortion appears obvious.

Approximately 50% of the abortions evaluated were deemed non-infectious. Of these, most are not likely to be management related with the exception of twin pregnancies; however, twins did not comprise a large percentage of the abortions submitted. This is likely due to better management techniques, namely identification and reduction of twin pregnancies early in gestation, but also likely reflects the failure of owners to submit abortions with an obvious cause to the diagnostic laboratory. While this is understandable, it also makes it difficult to accurately measure the frequency of these losses.

Infectious abortions comprised the other 50% of submitted abortions, with placentitis representing the majority of these cases. Unfortunately, we know little about what predisposes a mare to develop placentitis, and still have trouble with early, accurate and specific diagnosis. Even so, there are steps that owners can take to aid in early diagnosis, including endocrine monitoring, regular ultrasound evaluation of the placenta as well as daily checks for premature mammary gland development, premature lactation, and purulent vulvar discharge. If anything out of the ordinary is noted, a veterinarian should be called to examine the mare and start treatment if indicated.

As placentitis comprises the majority of the infectious abortions seen, the laboratory of Dr. Barry Ball at the Gluck Equine Research Center has been focusing on better understanding the causes and progression of placentitis. By utilizing state-of-the-art techniques to look at changing gene expression, we have identified several potential targets which we believe will function as diagnostic aids and/or treatment options. Although more work is still needed to confirm our findings, we are optimistic that better options for dealing with placentitis will be available soon.

Again, I cannot stress enough the importance of sending all aborted foals, including fetal membranes and maternal serum, to a veterinary diagnostic laboratory. When breeders fail to submit abortions, it becomes more difficult to spot trends and, in turn, becomes more difficult to identify and respond to emerging threats. It's easy to justify only submitting abortions without an obvious cause; however, the overall health of the equine breeding industry relies on the submission of every abortion, every time.

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LLOYD'S

INTERNATIONAL

Third Quarter 2018

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

The final four cases of African horse sickness to be reported by the Republic of South Africa (RSA) this season occurred during the first half of July; two were in Eastern Cape Province, one in Free State Province and one in KwaZulu-Natal.

An outbreak of glanders was reported by P.R. China. The disease was confirmed in 17 horses at an equestrian club, one of which died.

Equine influenza was confirmed in Colombia, Germany and the USA. The disease occurred in 16 of 32 departments in Colombia, with over 2,700 recorded cases including one death. The German outbreak involved five unvaccinated horses. Equine influenza is endemic in the USA with evidence of infection identified in three states.

Belgium, France, Germany, Ireland, Switzerland, the UK, and the USA reported multiple outbreaks of strangles. The number of confirmed outbreaks ranged from two in Germany and Switzerland, three in Belgium, 17 in France, 60 in Ireland, and 154 in the USA. The disease is endemic in the UK and the USA.

Equine herpesvirus 1 related diseases were recorded by Argentina, Belgium, Canada, France, Germany, Japan, RSA, Switzerland, and the USA. Respiratory disease was diagnosed in Belgium (11 outbreaks), France (two outbreaks), RSA (one outbreak), and the USA (outbreaks in numerous states). Cases of EHV-1 abortion were reported by Argentina (one outbreak involving 15 cases in Thoroughbreds, all with incomplete vaccination histories), Japan, and RSA (single case in each country). EHV-1 neurologic disease was confirmed in Canada (two outbreaks), Germany and Switzerland (single case in each country), and the USA (six outbreaks involving single cases of the disease).

Equine herpesvirus 4 respiratory disease was diagnosed in France (20 outbreaks), Germany (three cases involving two premises), and the UK (seven outbreaks, most of which represented single cases of infection in unvaccinated horses).

Germany reported equine arteritis virus infection in a stallion.

Equine infectious anemia was confirmed in Canada, France, and the USA. Two outbreaks involving single cases of asymptomatic infection were recorded by Canada. France diagnosed a single case, and the USA identified 17 cases involving horses in five states, the preponderance in Texas.

The RSA reported equine piroplasmosis as occurring in four provinces, with the majority of confirmed cases in Gauteng Province.

Contagious equine metritis was confirmed in France (single clinical case in a mare) and Germany (10 cases, all in non-Thoroughbreds, the majority were Icelandic horses; nine premises were involved.)

Ireland and the USA reported outbreaks of salmonellosis. A total of 14 mares and foals were involved in an outbreak in Ireland. Of 11 cases diagnosed in the USA, nine were associated with *Salmonella* serogroup B isolates.

Equine neorickettsiosis was reported by the USA. The disease was confirmed in five states, with the highest number of cases (26) recorded in Kentucky, of which six died.

Clostridial enterocolitis was diagnosed in a limited number of cases in the USA, all associated with *Clostridium perfringens* infection of undetermined toxin type.

The USA reported one case of proliferative enteropathy (*Lawsonia intracellularis* infection).

The third quarter of 2018 saw cases of Eastern equine encephalomyelitis confirmed in Canada (9) and the USA (39), the majority of which were in unvaccinated horses. Florida and Georgia were the most severely affected states in the USA.

West Nile virus infection was reported by Canada (14 cases), France (6 cases), Greece (one case), Germany (one case), Italy (105 cases), Romania (one case), RSA (one case), and the USA (140 cases, many in the state of Ohio).

Australia confirmed one case of Hendra virus infection in an unvaccinated horse on a premises in New South Wales.

A single case of equine encephalosis was diagnosed in a horse in the RSA Province of Gauteng.

Equine Disease Quarterly

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Biofilm-Associated Endometritis

Bacterial endometritis (infection of the uterine mucosa) that is refractory to traditional antimicrobial treatment is a significant challenge to the equine breeding industry. A common survival strategy employed by bacterial pathogens is the formation of a biofilm, which is a complex and dynamic structure composed of aggregates of bacteria surrounded by a thick protective layer of exopolysaccharide. Biofilms confer resistance to immune mediated clearance by reducing the host's ability to recognize infection. Additionally, biofilms protect bacteria from antibiotics by providing a diffusion barrier and creating a microenvironment that slows down bacterial metabolism and replication, which makes them more tolerant to antimicrobial agents.Using a model of equine infectious endometritis, we have clearly identified the ability of the bacterium *Pseudomonas aeruginosa* to form a biofilm within the uterus of the mare. The biofilm forms in multiple locations with the greatest amount of adherent bacteria occurring between the tissue folds and in the uterine horns. This suggests that a traditional guarded culture swab may not be ideal for detecting biofilm-associated infections and a low volume lavage may be a better diagnostic tool. The bacteria are in greater numbers deep within the endometrial glands as compared to the luminal surface. To be successful in clearing these infections, treatment options will need to be capable of penetrating deeper into the glands and tissue. For microscopic visualization of biofilms within endometrial biopsies, Bouin's solution provides significantly better preservation of the biofilm matrix on the surface of the endometrium as compared to traditional formalin fixation.

Bacteria residing in a biofilm can be up to 1,000 times more refractive to treatment with antibiotics as compared to free-living (planktonic) bacteria. The simple administration of more or a higher concentration of antibiotics has failed to eliminate chronic biofilm infections in both human and veterinary medicine. The goal in treating a biofilm-associated infection is to disrupt the biofilm material and kill the bacteria residing within the biofilm.

A series of *in vitro* (within a laboratory setting, such as in a test tube) studies were conducted to assess biofilm dispersal and/or bacterial killing by antibiotics and non-antibiotic agents alone or in combination against Gram-negative bacteria (*E. coli, K. pneumoniae* and *P. aeruginosa*). Data would indicate that antibiotics and non-antibiotic agents are more effective against biofilms if administered concurrently. When dealing with bacterial infections protected in biofilms, the treatment period should be at least 72 hours in duration, with repeated treatments every 24 hours (i.e. a uterine infusion of the selected combination once every 24 hours for three consecutive days). Following this treatment protocol, the biofilm was completed disrupted and bacterial killing ensued. Assessment of antibiotic sensitivity of the offending pathogen(s) is still important as inherent genetic resistance of the bacteria involved will not be overcome solely by the addition of the non-antibiotic compounds.

A recent *in vivo* study evaluated the intrauterine treatment of a preformed *Pseudomonas aeruginosa* biofilm with a combination of ceftiofur and tris-EDTA or ceftiofur and tris-EDTA alone. Of five mares treated with a combination of ceftiofur and tris-EDTA, all effectively cleared the infection. This contrasted with only two of five mares treated with ceftiofur and one of five mares with tris-EDTA. The findings confirmed greater efficiency in killing preformed biofilm within the uterus by using a combination of antibiotic (ceftiofur) and non-antibiotic (tris-EDTA) agents.

Advances in our understanding of the significance of biofilms in human and veterinary medicine will in time lead to improved diagnostics and more effective treatment modalities. Fortunately several therapeutic options are currently available to clinicians for the treatment of biofilm-associated equine bacterial endometritis.

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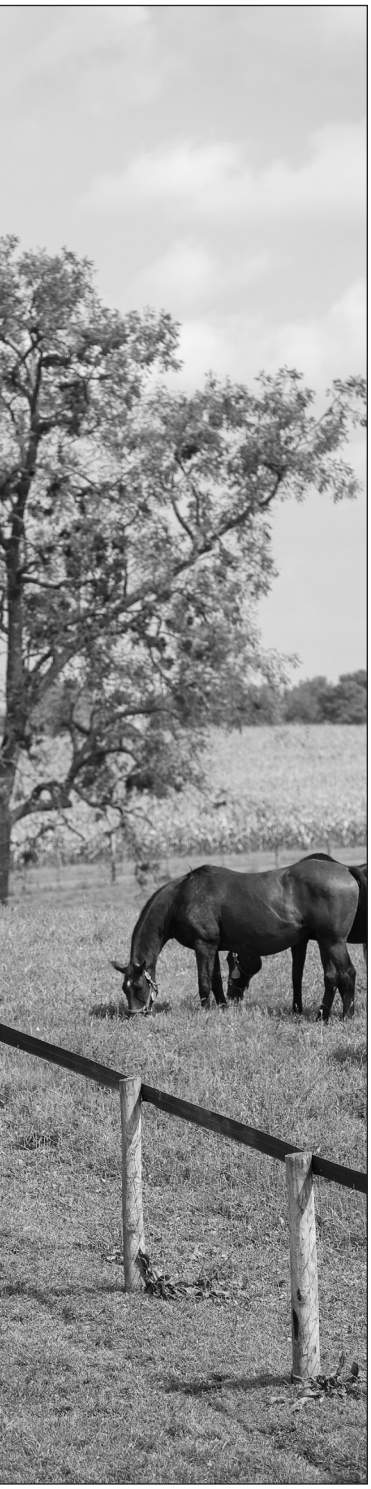
Tall Fescues – Endophyte-infected, Endophyte-free, and Novel Endophyte



ARTON, UK AGRICULTURAL COMMUNICATIONS

Tall fescue (*Lolium arundinaceum)* is one of the most widely grown perennial grasses in the world and covers approximately 37 million acres in the United States alone. It can be infected with an endophytic fungus (*Epichloë coenophiala),* which in a symbiotic relationship with the plant produces chemicals called alkaloids that confer benefits to the plant. This tall fescue, native to Europe, was introduced into the United States in the 1800s. In 1931, E.N. Fergus, a University of Kentucky agronomist, collected tall fescue seed from the Suiter farm in Menifee County, KY, on the basis of winter hardiness, persistence in high traffic areas, and drought resistance, giving rise to the cultivar of fescue known as Kentucky 31 (KY31). However, some of the alkaloids, primarily the ergot alkaloids produced by infected plants, are detrimental to grazing animals, including horses.

Historically, the endocrine hallmark of fescue toxicosis in several animal species is a decrease in the circulating concentration of the hormone prolactin. Prolactin is secreted by the pituitary gland, and control of its secretion is complex and not completely understood. Prolactin exerts effects on a variety of systems including milk production, steroidogenesis (estrogens, progesterone and testosterone), hair growth and shedding, libido, and synthesis of surfactant by the fetal lungs. Importantly, prolactin may also exert an effect on the feto-placental unit by altering steroid synthesis and/or metabolism and maturation of the fetal adrenal-pituitary axis, which is necessary for parturition. One major regulator of prolactin secretion is dopamine, a hormone produced by the hypothalamus. Dopamine, interacts with receptors in the pituitary gland and inhibits the secretion of prolactin.

Ergovaline is the most abundant ergot alkaloid in tall fescue. Ergovaline, and several other alkaloids from fescue, have similar chemical structures to dopamine and can bind to dopamine receptors, thereby causing a decrease in prolactin secretion, resulting in partial or complete agalactia (the inability to produce milk) in foaling mares. Additional problems associated with KY31 fescue consumption in foaling mares include altered hormone concentrations, extended gestation, thickened placenta, placental retention, dystocia, birth of dysmature foals, and increased foal and placental weights. Dopamine receptors have been found in tissues other than the pituitary, including ovarian tissues and the corpus luteum, but the roles of those receptors in fescue toxicosis, if any, have not been fully elucidated. The drug domperidone is frequently used in broodmares that are exposed to KY31 fescue and prevents or reverses the adverse reactions of ergovaline. Domperidone functions by binding to dopamine receptors, but rather than suppressing prolactin production, it competes with dopamine and allows for normal prolactin secretion.

Because of the adverse health effects of common endophyte infected fescue in grazing animals, varieties of tall fescue which do not contain the fungal endophyte have been identified. Even though these endophyte-free varieties do not produce ergot alkaloids, animal performance is excellent. However, the plants do not persist well in pastures or compete well with other pasture grasses. More recently, endophyte strains that do not produce the alkaloids that are harmful to animals but still confer vigor and persistence to the plant, have been identified and inserted into tall fescue. These are called novel endophyte varieties of fescue, and some of these are commercially marketed as "Jesup Max Q," "Texoma Max QII," and "Baroptima Plus E34." More recently, "Lacefield Max QII" was released by Dr. Tim Phillips in the Department of Plant and Soil Sciences at the University of Kentucky. The Alliance for Grassland Renewal is an association of seed companies, universities, and government agencies that regulate themselves by establishing certain quality control standards for novel endophyte tall fescues. For example, all seeds sold under the Alliance tag must be 95% pure, have 70% live (viable) endophyte, and have independent confirmation that the fescue variety does not cause fescue toxicosis in animals and will persist well under conventional grazing conditions.

Although this article emphasizes the effects of

ergot alkaloids on a dopaminergic receptor, it is important to remember that some of the alkaloids also bind to other receptor types, including adrenergic and serotonergic receptors, and thus may affect additional body systems.

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KENTUCKY

Equine Abortion: A Review of the 2016 and 2017 Breeding Seasons in Kentucky

The loss of a developing fetus during pregnancy can be a frustrating, emotional, and costly experience for horse owners, farm workers, veterinarians, and the public. A thorough evaluation of the aborted fetoplacental unit (fetus and placenta) by a veterinary pathologist can help determine the cause of abortion, identify new, unusual, or foreign causes of fetal loss, rule out involvement by infectious agents, and aid in the epidemiologic monitoring of abortifacients (factors that can result in abortion). A two-year review of equine abortions, from the 2016 and 2017 breeding seasons, was conducted at the University of Kentucky Veterinary Diagnostic Laboratory to evaluate current abortion trends.

Dates listed below indicate data for the respective breeding season, not calendar year.

A total of 898 cases of equine abortion, 570 from 2016 and 328 from 2017, were evaluated. The majority of cases were considered sporadic and unrelated, except for one equine herpesvirus 1 abortion storm that was identified during the 2016 breeding season. Abortions during early gestation began in May of the 2016 breeding season and June of 2017 breeding season. The highest number of abortions occurred in March of both years, and the last abortions occurred in July of 2017 (2016 breeding season) and May of 2018 (2017 breeding season). Abortions were categorized into infectious (2016= 55% and 2017= 38%) and non-infectious causes (2016= 45% and 2017= 62%).

Infectious causes of fetal death were attributed to bacterial, viral, fungal, and unidentified (presumably bacterial) agents that resulted in placentitis and/or systemic infections. Placentitis was the most common cause of infectious disease and was identified in 280 cases (24.6%) in 2016 and 102 cases (20.2%) in 2017. Approximately 5% of abortions each year were attributed to ascending placental infections through the mare's cervix by bacteria such as *Streptococcus zooepidemicus* and *Escherichia coli.* Nocardioform/mucoid placentitis was diagnosed in 145 (12.7%) and 27 (5.3%) cases during 2016 and 2017, respectfully. Three cases of mycotic placentitis were diagnosed in 2016, and one case was diagnosed in 2017. Placentitis due to unidentified agents occurred in 79 (6.9%) cases in 2016 and 47 (9.3%) cases during 2017. Agents were not identified, presumably, due to the use of antimicrobial therapy, chronic resolved infections, or overgrowth by environmental organisms. Leptospiral abortion or perinatal death was identified in five cases (0.4%) during 2016 and 11 cases (2.2%) in 2017. Abortion due to fetal bacterial septicemia or pneumonia was diagnosed in 4.4% of cases in 2016 and 1.6% of cases in 2017. Equine herpesvirus 1 was the only viral agent identified in fetuses over the two-year period, and it was responsible for 16 (1.4%) abortions or perinatal deaths in the 2016 breeding season and 10 (2.0%) in the 2017 breeding season.

Non-infectious causes of abortion are considered sporadic events. They included abortion associated with umbilical cord torsion (2016= 3.9% and 2017= 7.9%), fetal stress (2016= 1.8% and 2017= 2.0%), placental "cervical pole" necrosis (2016= 0.5% and 2017= 0.4%), twin pregnancy (2016= 0% and 2017= 0.6%), miscellaneous causes (hydrops, tissue necrosis of unknown etiology, and maternal stress and disease; 2016= 1.2% and 2017= 2.0%), and abortion of undetermined cause (2016= 14.9% and 2017= 27.5%).

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Abortion of undetermined cause occurs quite regularly and is frustrating to both clients and diagnosticians. Based on the human and veterinary literature, many of these occur due to physiologic abnormalities (e.g. fetal cardiovascular disease, hypoxia), stress and disease in the pregnant mare, autoimmune disorders, genetic irregularities, environmental exposures, and endocrine abnormalities; all of which cannot be easily assessed or tested for in the aborted fetoplacental units. A diagnosis of abortion of undetermined etiology isn't completely without value, because infectious diseases and other possible causes of abortion storms can be readily ruled out.

In conclusion, equine abortion remains to be unfortunately common. Both infectious and non-infectious causes are frequently responsible. Evaluation of the aborted fetoplacental unit by your local veterinary diagnostic laboratory can aid in determining the cause of abortion, help to monitor and track known abortifacients, and identify new and possibly emerging causes of abortion.

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