Session 1

Field and Clinical Observations on Mare Reproductive Loss Syndrome

Chairperson: Dr. Bill Bernard, Rood and Riddle Equine Hospital, Lexington, Kentucky

Clinical Observations Associated with Early Fetal Loss in Mare Reproductive Loss Syndrome during the 2001 and 2002 Breeding Seasons

W. T. Riddle

I WOULD LIKE TO BEGIN WITH A BRIEF HISTORY OF THE early fetal loss (EFL) syndrome associated with Mare Reproductive Loss Syndrome (MRLS). On April 26, 2001, I ultrasounded six mares on one farm to determine the sex of their fetuses. All mares were between 60 and 70 days of pregnancy. Two of these mares (at 63 and 65 days) were found to have dead fetuses surrounded by allantoic and amniotic fluids containing hyperechoic material. These would be my first cases of MRLS and the beginning of an unprecedented number of early abortions in Central Kentucky. A report released by the Governor's office estimated the number of Thoroughbred EFL caused by MRLS in 2001 to be 2,998 (1).

These large numbers had never before been reported in Central Kentucky nor anywhere in the world. The only comparable experience was in 1980 and 1981 when smaller numbers of EFL were seen in Central Kentucky. Estimates were 256 in 1980 and 162 in 1981 (2). It is difficult to make exact comparisons because ultrasound was not in use at that time, but the breeding dates and the gestational ages were similar. Another similarity was the occasional recovery of fetuses and membranes from the reproductive tract. This is an uncommon finding for abortions at this stage of gestation. No cause was ever determined for the losses in 1980 and 1981.

Mares experiencing EFL from MRLS typically present with no outward signs. Occasionally the mare will present with a sero-sanguinous or purulent vulvar discharge. Some mares may be found with membranes protruding from their vulvas with the fetus located either in the vagina or uterus. A small percentage (estimated at less than 5%) may exhibit mild colic signs, abdominal straining, or low-grade fevers (101-101.5°F) 1 to 3 days before EFL occurs.

Often with MRLS losses, rectal palpation will indicate the mare is pregnant. The uterus may have normal to slightly less fluid distension expected for the stage of gestation, and it is only on ultrasound examination that the mare is found to have a compromised or dead fetus. Prior to the appearance of MRLS in 2001, most mares were not ultrasounded after 30 days of gestation unless fetal sexing was requested. It has now become standard practice for most veterinarians in Central Kentucky to continue ultrasounding through the 60- to 90-day pregnancy examinations. The typical appearance on ultrasound for an MRLS loss is a dead fetus surrounded by an echogenic allantoic fluid and a more echogenic amniotic fluid.

The majority of losses in my practice have occurred between 40 and 80 days of gestation, with a range of 32 to 140 days (Table 1). In 2001, these mares were bred between February 10 and April 10, while in 2002 breeding dates ranged from February 15 to April 1. In 2001, losses began on April 26 and ended on July 2, while losses in 2002 began on April 29 and ended on June 3. This summer I have had four additional EFL that may have been caused by MRLS, the most recent of which was a mare bred on May 6 that aborted on August 17 at 101 days.

Table 1. Gestational ages represented.

Days	2001	2002
30 - 39	3	0
40 - 49	8	5
50 - 59	11	0
60 - 69	12	5
70 - 79	11	6
80 - 89	4	0
90 - 99	4	1
100 - 140	3	1

The majority of losses in 2001 were concentrated over a three-week period beginning April 26, while losses in 2002 were more evenly distributed over a five-week period beginning April 29. In 2001, I had 56 losses on the seven farms that I service. In 2002, I had 18 losses that occurred on only two of the seven farms. These figures indicate a 68% decrease in MRLS losses from 2001 to 2002. The majority of equine practitioners in Central Kentucky experienced a similar decrease.

Conception rates in 2001 and 2002 were not adversely affected by MRLS. Mares that were less than 30 days pregnant during the period of exposure were apparently not affected. There was no increase in the normal pregnancy loss rate between 15 and 30 days gestation.

In 2001, the status of the mares that aborted in my practice was as follows: barren, 19 (34%); maiden, 20 (36%); and foaling, 17 (30%). Thus barren, maiden, and foaling mares were roughly equally represented. In 2002, the status of the mares that aborted was as follows: barren/aborted, 5 (28%); maiden, 10 (56%); and foaling, 3 (16%). Maidens represented 56% of losses in 2002, which is likely the result of heavy eastern tent caterpillar (ETC) loads in fields containing maiden mares on one farm.

In 2001, serum progesterone levels measured by enzyme linked immunosorbent assay (ELISA) from 10 mares taken when EFL was found averaged greater than 4 ng/ml.

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In 2002, serum progesterone levels from six mares at the time of loss averaged 5.9 ng/ml. Therefore, progesterone levels were adequate to maintain the pregnancies at the time of the abortions.

During 2001 and 2002, uterine cultures were taken on all mares following abortion. Results included *alpha Streptococcus*, *beta Streptococcus*, *Escherichia coli*, *Enterobacter cloacae,* and no growth.

Uterine cytologies taken within 7 days of abortion from five mares in 2001 showed moderate to severe inflammation. This inflammation is consistent with recent abortion and is not unique to MRLS. Following abortion, all mares were lavaged and treated for 5 days with the appropriate antibiotic based on culture and sensitivity. On subsequent heats, most mares had normal cytologies and no growth on uterine culture. In 2001, uterine biopsies performed on 10 mares one to three months after MRLS abortion showed no significant pathology. There were no changes on biopsies that could be related to MRLS.

Of the 56 mares that aborted from MRLS in 2001, 31 remained in my care in 2002. Thirty of these 31 conceived, and one mare remained barren. Two of the 30 pregnant mares were again affected by MRLS on their subsequent pregnancy in 2002.

In 2001, aspirates of allantoic fluid were taken by pipette through the cervix from three mares with dead fetuses *in utero*. Cultures of this fluid grew *alpha Streptococcus* in two cases and *E. coli* in the third. Cytologies of these fluids showed sheets of squamous epithelial cells, cocci in chains, and a rare neutrophil. Based on this finding, it is likely that the hyperechoic material seen on ultrasound is squamous epithelial cells.

Complete blood counts and chemistries taken from three mares at the time of abortion in 2001 showed no significant abnormalities.

The appearance of hyperechoic allantoic and amniotic fluids in mares affected by MRLS has been a consistent finding. Prior to 2001, during thousands of fetal sexing ultrasounds of pregnancies between 58 and 75 days, the presence of echogenic fluids was not reported. In 2001 and 2002, all mares in which the dead fetus was found *in utero* had hyperechoic fluids. Many other mares were also found to have echogenic fluids with a live fetus. In 2001, the appearance of this fluid prior to day 80 was associated with a greater risk of loss. A review of May 2001 records in my practice shows 29 mares that were less than 80 days of gestation with live fetuses and echogenic fluids. Of these 29 mares, eight (27.5%) aborted within 30 days. This can be compared to May 2002 records that show 69 mares less than 80 days with live fetuses and echogenic fluids. Only five (7%) of these mares subsequently aborted. This may be related to a decreased exposure to the MRLS insult.

In 2001, because hyperechoic fluids were associated with MRLS, the appearance of this echogenicity was cause for concern. All mares were followed closely by ultrasound, and as pregnancies reached 80 to 90 days, all pregnancies developed echogenicity. While there was concern that this was an indication of exposure to the MRLS insult, it was known that in later pregnancy (150 days plus) hyperechoic fluids were normal.

A study was designed to determine when reproductively normal mares develop echogenic fluids and to determine if the fetal fluids of mares exposed to MRLS differed from the fetal fluids of mares not exposed (3).

One hundred seventy-eight mares that were between 55 and 176 days of gestation were evaluated between July 30, 2001, and August 30, 2001. One hundred four of these mares were in Kentucky, and 74 were in Florida. The results showed that in both the Kentucky and Florida mares the allantoic and amniotic fluids before 85 days are anechoic, and after 85 days both allantoic and amniotic fluids have hyperechoic material.

By mid-June of 2001, echogenic fluids were seen only rarely in pregnancies less than 80 days. In 2002, the number of mares with echogenicity before 80 days also declined by mid-June but remained higher than in 2001. During August 2002, there was an increase in the percentage of mares with echogenicity before 80 days. No EFL was associated with this increased echogenicity.

When MRLS was first identified in 2001, there was an obvious desire to implement treatments or control measures aimed at preventing further abortions. It was very difficult to make reasonable recommendations because the cause of the syndrome was not known.

In my practice, the following treatments were suggested for mares considered at risk:

1. Sulfa-trimethoprim and other broad-spectrum antibiotics—Because bacteria had been cultured from aborted fetuses and placentas.
2. Domperidone—Because some of the late fetal losses (LFL) showed some signs consistent with fescue toxicity (premature placental separation and thickened placentas).
3. Mycotoxin binders—These were used in case there was a fungal pathogen.
4. Flunixin meglumine—This was used for its anti-inflammatory and anti-endotoxin functions.
5. Pentoxifylline—This was recommended for its reagenic properties.

In hindsight, these treatments did not appear to be of any help. Neither Regumate or progesterone was recommended because levels in aborted mares had not indicated a progesterone deficiency.

When considering the cause for MRLS, my clinical impression strongly supports ETC as the cause. In 2002, efforts at prevention were focused on limiting pasture turnout and reducing or eliminating exposure to ETC. Most farms attempted to control caterpillars by either spraying or cutting down cherry trees. When spraying was successful at eliminating caterpillars, MRLS was prevented; however, in many cases sprays were not effective. Farms that cut down all cherry trees reported minimal losses to MRLS. In addition to caterpillar control, limiting turn-out and muzzling were the two most common methods of prevention employed. Many farms were successful at preventing MRLS by limiting turn-out to 2 to 6 hours a day; however, there were farms that limited turn-out that had significant losses. Muzzling mares while on pasture appeared to be close to 100% at preventing MRLS.

I would like to conclude with a short video showing a 63-day pregnancy and the dramatic changes in the allantoic and amniotic fluids that occur following experimental exposure to ETC. These changes occurred over a 24-hour period in a mare that had been tubed with ETC 7 days earlier. These fluids are consistent with fluids from clinical cases of MRLS. I am convinced the ETC plays a direct role in MRLS and now strongly recommend aggressive elimination of the caterpillar.

References

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2. Bryans, J. T. Report on early fetal losses: Department of Veterinary Science, University of Kentucky. 1981.
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Field and Clinical Observations Related to Late Fetal Loss in Mares Affected with Mare Reproductive Loss Syndrome

S. Brown

THE OCCURRENCE OF LATE FETAL LOSSES (LFL) ASSOCIATED with the Mare Reproductive Loss Syndrome (MRLS) ranks second in number of cases affecting the pregnant mare population in the Central Kentucky area in the spring of 2001 and 2002. While staggering and certainly tragic are the losses sustained by area horsemen related to the early fetal losses (EFL), this clinical entity can present with catastrophic outcomes from its effect on both the mare herself and the presenting foal. Managers, owners, and veterinarians were faced with cases numbering more than 500 in the spring of 2001 present from late April through early June. The 2002 season also saw a return of LFL cases but to a lesser degree with approximately 150 suspected cases (information supplied by the University of Kentucky Livestock Disease Diagnosis Center [UKLDDC]). This time frame of occurrence of the LFL cases corresponds with the EFL findings and supports a common insult that most believe is playing a role in this syndrome. The occurrence of these LFL cases has also correlated clinically with the exposure of mares to eastern tent caterpillars (ETC).

Clinically, these mares would present to local horsemen with a definitive set of clinical signs. The mares would show symptoms of restlessness, discomfort, and sweating followed by an intense and explosive presentation with attempts to deliver their respective foals. Most often, individuals would present with premature placental separation with the appearance of the engorged chorioallantoic membrane ("red bag" syndrome). The presentations were mostly compromised by abnormal foal positioning resulting in difficult dystocias with mares in significant distress oftentimes reported to be reluctant to foal in a recumbent position. Some of these mares failed to reach full mammary development or achieve "waxing" prior to these explosive deliveries. Veterinary intervention was often necessitated in these cases so appropriate measures could be implemented to avoid losses for both the mare and foal. If delivered alive, these neonates were compromised as weak, dehydrated, and dysponeic requiring immediate efforts to achieve oxygen supplementation while en route to area referral hospitals. The placentas from these mares were grossly heavy and edematous, weighing as much as 40 pounds, with umbilical cords showing signs of ecchymotic and petechial hemorrhages on their surfaces. Some mares would present with normal deliveries with evidence of amnionitis with yellowing and edematous formations on the placental membranes. Microbiological assays

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routinely yielded evidence of *alpha-hemolytic streptococcus* sp. and *Actinobacillus* sp., among other organisms.

The question to be addressed revolves around the nature of the toxic insult responsible for the pathological processes identified in these mares and their foals. Initially, cases included "red bag" presentations typically associated with exposure to endophyte-infested tall fescue. These mares did not present with prolonged gestations as with fescue toxicosis, and the placentas from these mares were intensely more inflamed than those typically seen with fescue. Thus, attempts at preventative treatment with domperidone resulted in little benefit to these mares in protecting them from the effects of this syndrome.

Pathophysiologically, evidence of LFLs in these mares centered around some common associations. There was an intense placentitis at time of foaling associated with thickened placental membranes. Funisitis associated with the amniotic section of the umbilical cords of these neonates was observed with ecchoymotic and petechial hemorrhage on the surface. Microbiologically, the consistent ability to recover *alpha-hemolytic streptococcus* and *Actinobacillus* sp. from umbilical tissues, lungs, and placentas of affected individuals has become almost a hallmark for defining the clinical entity of LFLs. From these findings, we must attempt to elucidate the nature of the inciting insult and the duration of exposure to cause an abortion. The presence of these microorganisms specific to this condition has caused speculation that an underlying immunologically compromised situation allows the bacteria to flourish as commensals.

Many practitioners in the spring of 2001 and 2002 made numerous attempts to provide useful clinical data by monitoring the development of these cases and in an attempt to identify potential benefits of therapeutic intervention. Ultrasonography, both trans-rectal and trans-abdominal, has been utilized by veterinarians to measure placental thickness and separation at the region of the cervical star, as well as evaluation of fetal parameters such as fetal heart rate to measure fetal stress. Hormonal assays may also be an area of potential benefit to measure placental function. Treatment centered on broad-spectrum antibiotic therapy (trimethoprim-sulfa, nonsteroidal anti-inflammatory drugs [NSAIDs], pentoxyfilline, and vitamin E/selenium) used systemically in supporting the compromised placental unit to improve foal survivability. Future studies of LFL incorporating these monitoring techniques may provide beneficial information to place in the hands of practitioners and horsemen in dealing with these cases.

As with the other clinical manifestations of MRLS, the LFL cases present all of us, veterinarians, horsemen, and researchers, with a number of perplexing and unexplained questions related to these findings. The timing of these cases, both in season of the year and in association with EFL, makes many ponder if there is a dose-dependent response nature related to the insult or a multifactorial nature that translates into the different clinical scenarios. Some cases with remarkable similarity have been reported earlier in the season. There are reports of LFLs extending into southern hemisphere foaling mares in both 2001 and 2002 during late July and August. Again, is there something unique about these reported sporadic occurrences, and how do they relate to the bulk of normally occurring cases? It will be our endeavor to reach a greater understanding of how all these inconsistencies "fit" into a plausible explanation as we come to fully understand the pathophysiology of MRLS.

Clinical Observations of Mare Reproductive Loss Syndrome in Critical Care Mares and Foals

T. D. Byars and T. L. Seahorn

AT THE END OF APRIL AND THE BEGINNING OF MAY IN 2001, a significant increase in deceased or clinically compromised newborn foals was presented to the University of Kentucky Livestock Disease Diagnosis Center (UKLDDC) or to Central Kentucky equine veterinary neonatal intensive care units, respectively. These pathologic and clinical presentations were observed in an acutely profound increase in caseload numbers with the eventual designation as the Mare Reproductive Loss Syndrome (MRLS). Prodromal signs in mares were inconsistent but varied from being gestational term to within 30 days of foaling, asymptomatic or as depressed and self-isolated in the pastures, having muscle tremors, an implied lack of mammary development due to a rapid onset of foaling, clinical episodes similar to colic, and a rare stiffness that resembled acute laminitis.

The majority of mares lacked clinical signs of an impending foaling and were not identified as "high-risk pregnancies," and agalactia was assessed as present only by the mare's physiological preparation for foaling being acutely compromised. Foalings often occurred without rec-

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ognition of stage one of parturition with a cluster of stage 2 and 3 being most often simultaneous. An increased number of mares foaled while standing. Premature separation of the placenta was common, and fetal membranes were often passed with the foal (placenta privia or "red bag" presentation).

Foals were consistently developed in size and maturity synchronous to the time frame of the gestation. Placentas did not reveal consistent gross abnormalities, with the exception of funisitis found in a significant number of umbilical cords at the UKLDDC. Post-foaling mares were treated with conventional uterine lavage, and a failure to conceive during 2001 was not a feature in this population of mares as opposed to mares experiencing early embryonic losses. The use of prophylactic medications in foaling mares did not provide an apparent resolution in the abnormal foalings from farms experiencing large numbers of losses. These subjective treatments included antibiotics, pentoxifylline, and domperidone.

Clinical signs in the neonates were significantly associated with perinatal asphyxia, requiring resuscitation at birth. Most foals admitted to the intensive care units were dehydrated with signs consistent with the systemic inflammatory response syndrome (SIRS) or sepsis. Hypothermia, tachycardia, and inconsistent respirations were persistently noted in hospital admissions, often with periods of apnea leading to respiratory arrest. Blood cultures were rarely positive, although *alpha Streptococcus* and *Actinobacillus* sp. were the most frequently isolated organisms. Clinical pathology consistently revealed severe dehydration and a neutropenia (400 to 2,500 white blood cells/mm at admission). Surviving foals had relatively higher white cell counts, albeit below normal, or the foal showed a more rapid rise to normal neutrophil numbers during the first 2 days of hospitalization. Hypoglycemia was most present, often below 20 mg/dl. Colostral transfer was consistently inadequate with most immunoglobulin G (IgG) levels approximately 150 mg/dl at 24 hours of age with the use of donor colostrum and, in some cases, following the use of intravenous plasma. The hypoxemic-ischemic (HIE) syndrome occurred in most foals as comatose "sleepers" but rarely with either pre- or post-coma seizure activity. The prognosis for survival was associated with improved blood values and foals exhibiting normal respiratory patterns and rates.

Survivals varied from initially having a high mortality rate to an eventual improved prognosis without noting marked changes in the treatment regimes. Treatments were empirical and subjective principally utilizing routine antibiotics, plasma, fluid therapy, enteral and/or parenteral nutrition, vitamin E, dimethyl sulfoxide (DMSO) or mannitol, anti-inflammatory medications often with single doses of corticosteroids, oxygen supplementation, and intensive nursing care. The variables for survival and differentiation from conventional septic foals included the actual gestational length, a decrease in the "toxic" insult within 1 to 2 days, and the subjective improved clinical care and therapeutics. Surviving foals did not have residual impairment.

The MRLS syndrome for foaling mares and their foals should not be considered apparent in individual patients since a pattern of abnormalities must be present in larger numbers for a more definitive diagnosis. In our experience, individual cases could not be separated from the more "routine" septic foals provided annually in a dense population of high-risk mares. The epidemiological appreciation for the consistency of clinical scenarios provided with an abrupt and significant increase in neonatal caseload may be presumptuous for MRLS, but a single patient presentation would not be sufficient to declare MRLS in a foaling mare. However, clinicians should be astute in evaluating severely compromised foals without dysmaturity or obvious placental abnormalities from mares that acutely foal without the conventional stages of parturition as being suspicious for MRLS. The appreciation for a presentation of a peracute and seemingly toxic insult to foaling mares with the respectively clinically ill foals in increased numbers beyond a seasonal norm should signal the preliminary diagnosis of MRLS until other causes have been ruled out. The progressive seasonal increase in survival may be a reflection of a singular environmental insult that decreases in susceptible mares.

Endophthalmitis: A Syndrome Associated with Mare Reproductive Loss Syndrome?

C. Latimer

THIS PRESENTATION WILL SUMMARIZE MY OBSERVATION OF equine endophthalmitis cases in Lexington, Kentucky, during the outbreak of Mare Reproductive Loss Syndrome (MRLS) in 2001 and 2002. The numbers represent my patients only. Twenty-four cases were seen in 2001, and 11 were seen in 2002. Except for the decreased incidence in 2002, no other feature distinguished the two years, so the data are combined.

Two-thirds of the horses presented in the first two weeks of May, with further cases scattered until June 8. Breeds affected seemed to reflect the local population, with Thoroughbreds accounting for 26 of the 35 cases. Males and females were almost equally represented, 19 males, 16 females. Fifteen yearlings and six foals were affected, with one or two horses of 2, 3, 4, 5, 6, 9, 10, and 12 years of age.

Clinical presentation was characterized as an acute onset, unilateral, exudative endophthalmitis. Horses consistently exhibited corneal edema and exudate in the anterior and posterior segments. Variable degrees of pain, periocular swelling, discharge, and hyphema were observed. Diagnosis was based on ophthalmic examination. Bloodwork performed to evaluate status for *Leptospirosis*, *Blastomycosis*, *Histoplasmosis*, equine herpesvirus (EHV), influenza, and *S. equi* was non-diagnostic. Culture and cytology of aqueous and vitreous samples were unproductive. Ultrasound examination revealed a turbid vitreous.

Treatments included systemic and topical antibiotics, anti-inflammatories (NSAIDs and corticosteroids), tissue plasminogen activator, atropine, mycotoxin binders, and cyclosporine. Response to treatment was poor, with 34 of 35 eyes blind and "mid-phthisical." One horse was visual after prolonged systemic corticosteroids and antibiotics, but it is not possible to be certain that this patient was a member of the MRLS/endophthalmitis group, as his symptoms were typical but mild.

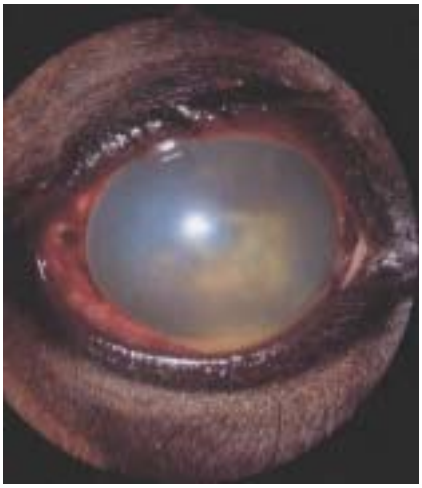

Figure 1. 3-month-old Thoroughbred filly. Corneal edema and anterior chamber debris obscure the iris.

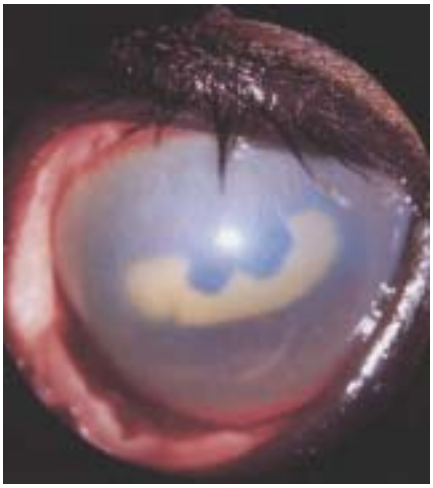

Figure 2. 10-year-old Thoroughbred mare. Typical appearance of the anterior segment. In patients with a visible pupil, the vitreous was noted to be opaque.

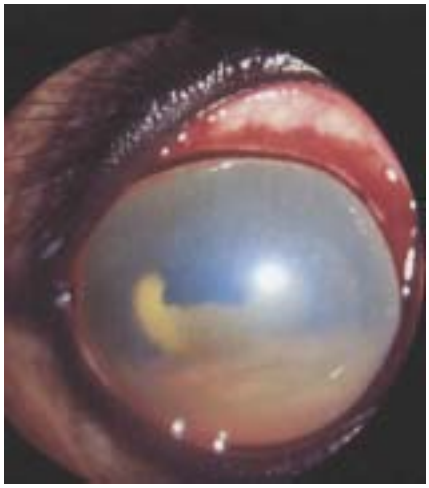

Figure 3. 1-year-old Thoroughbred colt. Some hemorrhage is seen in the anterior segment debris.

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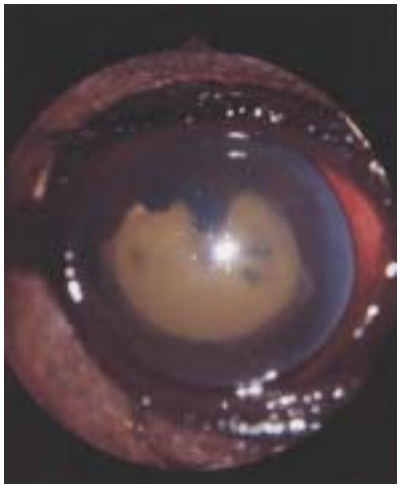

Figure 4. 1-year-old Thoroughbred colt. This colt made some response to initial treatment (e.g., pupillary dilation), but within 48 hours the iris was no longer visible.

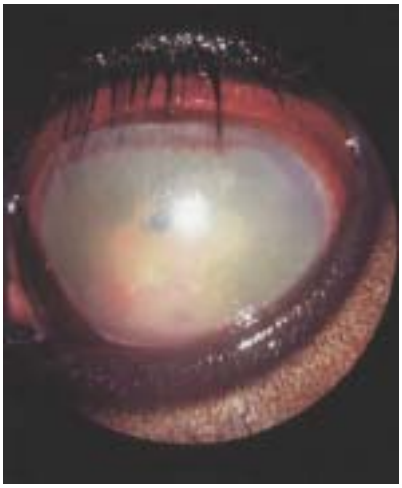

Figure 5. 1-year-old Standardbred filly. Note the limbal vessels, marked corneal edema, and obscured anterior segment.

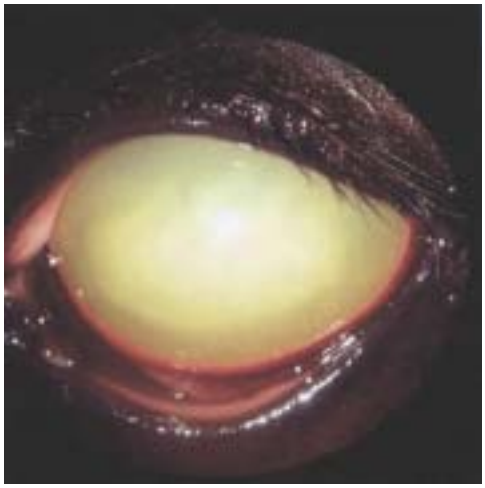

Figure 6. 2-year-old Thoroughbred colt. Uniform corneal edema, xanthochromic diffuse anterior chamber debris, and active limbal vessels are seen.

Important Questions about This Group of Horses

1. What pathogenesis can explain a 100% unilateral occurrence?
2. Why were yearlings and young horses over-represented in the affected population (15 of 35 yearlings and 28 of 35 <4 years old)?
3. Why did the endophthalmitis cases not have other symptoms of MRLS (pericarditis, EFL, LFL)?
4. Why didn't patients respond to treatment for infection or inflammation?

If these endophthalmitis cases are related to MRLS, as strongly suggested by their temporal occurrence, answers to the above questions may elucidate the pathogenesis of this syndrome.

Clinical Observations of the Pericarditis Syndrome

N. M. Slovis

THE PERICARDIUM OF THE HORSE CONSISTS GROSSLY OF TWO pericardial layers, with appropriate nerves, blood vessels, and lymphatics. The visceral pericardium directly covers the heart surfaces and is sometimes referred mistakenly as the "epicardium." The parietal pericardium is commonly referred to simply and confusingly as the "the pericardium." The parietal pericardium is lined by mesothelial cells, varies in thickness from 1 to 3.5 mm and contains serous fluid that is considered as an ultrafiltrate of the blood plasma (1). The physical effect of the pericardium is to restrict overall heart filling. It helps limit acute cavitary over distension following ruptured papillary muscle, pulmonary hypertension, and acute myocarditis. The pericardium also offers atrial support against ventriculoatrial regurgitation as well as distributing hydrostatic forces over the surface of the cardiac chambers. The mesothelium has cyclooxygenase, prostacyclin synthetase, and lipoxygenase activities. Large amounts of prostacyclin are continually released by the entire pericardial mesothelium into the pericardial cavity in response to pericardial stretching, to increases in myocardial work and loading conditions (1). Prostacyclin influences the tone of the underlying coronary vessels but also has fibrinolytic activity with hemopericardium.

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Pericarditis or inflammation of the pericardium is relatively uncommon in horses; three forms have been described including effusive, fibrinous, and constrictive (2-11). Causes of equine pericarditis include immune-mediated diseases, vasculitis, disease of contiguous structures, trauma, bacterial and viral infection, and neoplasia; however, for many cases, the etiology remains undetermined. While most reports in the literature describe the clinical presentation, treatment. and outcome of a single case, two retrospective studies reported a series of cases, providing relevant prognostic information (10-11).

During the spring of 2001 and 2002, a larger than usual number of cases of fibrinous pericarditis was observed in Central Kentucky. During late April and May of 2001 and 2002, 33 and six horses, respectively, were presented to our clinic with effusive, fibrinous pericarditis. The most common primary complaints were fever, azotemia, colic, weight loss, anorexia, lethargy, tachypnea, and tachycardia. Nineteen of the horses were greater than two years of age, 12 were between one and two years of age, and eight were less than one year of age. Physical examination revealed tachycardia (n = 35), pyrexia (101.5 to 104.8° F) (n = 29), muffled or inaudible heart rate (n = 27), lethargy (n = 24), tachypnea (n = 23), jugular pulses or distension (n = 23). Echocardiograms were performed, and all 39 patients had effusive, fibrinous pericarditis; 18 (45%) of the horses had evidence of right-sided heart failure characterized with pleural effusion and/or ascites.

Diagnostic test results revealed a leukocytosis in 21 cases. Hyperfibrinogenemia was detected in 25 horses. Cardiac troponin I was normal in 3 of 3 horses. Equine viral arteritis (EVA), equine herpesvirus (EHV-1, EHV-2, and EHV-4), and influenza titers were performed, and no significant rise in titers was noted. Polymerase chain reaction (PCR) for EHV-1, EHV-2, and EHV-4 was evaluated on six transtracheal washes (TTW) and were negative. An influenza ELISA test was performed on six TTW samples and was negative. Mycoplasma was submitted for culture in nine pericardial samples and one TTW sample. All were negative. Histoplasmosis titers were measured in three horses and were negative. TTW were performed on six horses. Five of six samples isolated a pathogen consisting of *E. coli* (2), *alpha Streptococcus* (1), *Actinobacillus* and *Pasteurella* (1), *Rhodococcus equi* (1), and *Enterobacillus cancerogenus* (1).

Thirty-eight horses had to have a pericardiocentesis and drain placement to allow evacuation of the pericardial effusion. Thirteen of the horses had pericardiocentesis performed one time, 12 had the procedure performed twice, four had three procedures, and one had the procedure performed five times. The amount of fluid evacuated from the pericardial space ranged from 1 to 22 liters. Laboratory analysis of the fluid in two-thirds of the cases was characterized as a sterile exudate with a cell count ranging from 900 to 28,000 white blood count (WBC)/MM and a total protein count ranging from 3.3 to 5.4 g/dl. A third of the cases had a septic exudate from which *Actinobacillus equuli* (5), *Streptococcus* spp. (2), *Pasteurella multocida* (1), *Staphylococcus aureus* (1), *Acinetobacter* (1), and *Pseudomonas* (1) spp. was isolated.

Treatments consisted of intrapericardial administration of corticosteroids (20 to 50 mg dexamethasone or 100 mg solu-delta-cortef or 30 mg triamcinolone acetonide), antibiotics (ceftiofur, ampicillin, ticarcillin, and/or potassium penicillin), heparin (5,000 IU), hyaluronic acid, and/or streptokinase. All 39 horses were treated with systemic antibiotics (potassium penicillin/gentocin, ceftiofur, tribrissen), NSAIDs (phenylbutazone or flunixin meglumine), corticosteroids (dexamethasone 6 mg to 50 mg intravenous (IV) once a day (SID), furosemide, heparin, colchicine, pentoxifylline, intravenous fluids, vitamin E, and antiulcer medication (omeprazole).

Six horses (15%) died one month to one year after the initial diagnosis of pericarditis. Five were euthanized either because of finances or because of a poor prognosis. Retrospectively, horses less than one year of age were noted to have a poor prognosis for long-term survival. Five of the eight horses less than one year of age were either euthanized or died secondary to pericarditis. Three patients had two or more reoccurrences, while four had one reoccurrence of effusive pericarditis. One of the patients that had one reoccurrence won its maiden allowance race one year after being diagnosed with pericarditis.

A case-control study was undertaken to identify factors associated with an epidemic of equine fibrinous pericarditis (EFP) cases that occurred concurrently with the Mare Reproductive Loss Syndrome (MRLS) (12). Thirty-nine horses that developed EFP during the spring of 2001 and 30 control horses were studied. Distribution of times of diagnosis of EFP was consistent with a point-source epidemic. Results indicated that occurrence of MRLS and EFP were related. Exposure to eastern tent caterpillars (ETC) emerged as the strongest risk factor for development of EFP. Although causality could not be definitively determined for any of the factors studied, results indicate that methods for reducing exposure to ETC would be expected to reduce risk of development of EFP.

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Summary

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I'D LIKE TO GIVE A SHORT SUMMARY AND FINISH OFF WITH some of my thoughts on reproductive physiology and take the liberty in asking some questions and providing some scientific information that maybe supports some of the questions and data that I'll present.

First of all, Dr. Riddle started the session by stating that a similar scenario occurred in 1980-1981. The number of cases was much lower. We didn't have ultrasonography at that time. However, *alpha Streptococcus* and *Actinobacillus* sp. were recovered, similar to what was seen in 2001 and 2002. Four scenarios occurred in 2001 and 2002, the first being early fetal losses (EFL). In 2001, there were approximately 3,500 EFL. This year, although I don't have the exact numbers, it appears it has decreased to less than a third of what was seen in 2001. The second clinical scenario was the late fetal losses (LFL), with the dramatic and severe foal losses occurring over a short time frame. These data were presented by Dr. Brown and Dr. Byars. Last year there were 500 losses, and this year it appears that there were about 150 losses.

There were two scenarios seen in young and older horses. The first was pericarditis, which occurred in animals of all ages, although there were 20 cases in horses less than two years of age. The other was endophthalmitis, which was much more predominant in younger horses than older horses, especially considering the population and ages of the mares and stallions in the area.

Pregnancy losses and clinical disease occurred in late April to early May, and it correlated and was possibly associated with the rise and fall of eastern tent caterpillars (ETC) as they molted and continued to molt and then wandered along the fencelines and onto pastures.

In 2001, the length of time pregnancy loss and clinical disease occurred was approximately three weeks, whereas this year we saw it over five weeks.

So the big questions that we're here trying to answer are: What is the toxin? Where is the toxin coming from? And, if we can identify the toxin, how do we treat it?

Are there any similarities between these clinical syndromes? I believe there are, but I'm sure there will be people who question my thought process.

Is there a relationship between EFL and LFL? There appears to be. From Dr. Riddle's data, it appeared that the greatest losses in his clinical practice occurred between 40 to 80 days of gestation. This is the period of time when the placenta is attaching. The equine placenta attaches between 40 to 100 days of gestation, but it is quite tightly attached by 80 days (1).

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Are the hyperechoic particles in the allantoic fluid and possibly in the amnionic fluid sloughed off cells from the trophoblast or placenta? Are these cells sloughing because placental attachment cannot occur? Is the placenta more susceptible at this period of time, or, as Dr. Riddle said, is it due to the fact that we don't have many mares pregnant between 120 days and nine months gestation during that period of time, so we don't see clinical disease?

However, there are a lot of warmbloods that do not foal until June or July that live in southern Illinois, Ohio, and possibly in North Central Kentucky. Were these mares affected in that time range, because they're not going to foal until June or July?

Is the equine placenta more susceptible to early detachment after nine months of gestation? Dr. Peter Rossdale in Newmarket in the early 1980s did some classic experiments where he looked at effects of oxytocin versus prostaglandin on early detachment of the placenta and birth of the foal. In those studies, he showed that the mare will respond and deliver a foal with one injection of oxytocin as early as 9½ months of gestation. However, she will not respond to repeated injections of prostaglandin in that she will not deliver until the placenta or the fetus is ready. So, in late gestation, is the toxin or the insult causing early detachment of the placenta? This early detachment of the placenta renders the foal in a perilous situation where it's not receiving any more oxygen. We have a hypoxic-ischemic insult, with possible placental detachment, placental edema, and the foal cannot breathe. Delivery of the foal in these mares is dramatic. The mare is trembling, there is premature placental separation, and an explosive birth. Many times the mare delivers while standing. Are the two events related—early fetal and late gestational losses? Are the placentas early in gestation and late in gestation affected either by a toxin that does not allow it to attach in early gestation, whereas in late gestation the toxin induces early and sudden detachment?

The bacteria commonly isolated were *alpha Streptococci* and *Actinobacillus* sp. We rarely see those in early placental problems or in early fetal reabsorptions, nor do we see them late in gestation. So how do these bacteria get in, how are they causing the insult, and are they a primary or a secondary problem? Does the toxin carry the bacteria into the pregnancy late in gestation? Why do we see funisitis? Why do we see amnionitis? Why is primarily a respiratory infection leading to possible pneumonia and death in these foals?

Two syndromes didn't primarily affect pregnant mares, endophthalmitis and pericarditis: Are these immune-mediated diseases? Does the disease occur in younger horses, not because of contact, but because of an immune-mediated complex? Why do dogs get blue eye when they are vaccinated against leptospirosis? From my memory, when I was in small animal practice in the 1970s, it's usually unilateral. Different scenario, but it is a unilateral disease. Is the pericarditis an immune-mediated response to either the toxin or to the bacteria that eventually get into the pericardial sac? I can't answer these questions, and hopefully in the next 48 hours we can come up with some answers.

One last comment about the immune system: Remember that the pregnant mare has a modulated immune response. She goes from a thymus helper-1 (TH-1) pro-inflammatory cytokine response to thymus helper-2 (TH-2), which is an immune-modulated response. So, she is under a more modulated system than a non-pregnant animal that is more apt to respond with a pro-inflammatory cytokine response or the TH-1 response. Is that immune system causing the two different scenarios that we see?

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