Abortion, defined as the loss of a pregnancy between 150-300 days, has a severe economic impact on the equine industry. Not only is a mare rendered unproductive for that year, but potentially her reproductive efficiency is decreased the next. The incidence of abortion in mares ranges from five to 15% with the upper limit becoming alarming. Older mares that potentially have decreased uterine defense mechanisms and increased fibrosis appear to be at higher risk. Although abortion “storms” are less common than sporadic abortions and noninfectious causes are diagnosed twice as frequently as infectious, when one does occur it is imperative that isolation protocols be implemented immediately. Clinical signs of impending abortion vary considerably from none—in which the mare is found empty during a late-term pregnancy check, or immediately after abortion has occurred—to premature mammary gland development that commonly occurs with placentitis and separation. Care must be taken with mares that are being supplemented with exogenous progesterone since death of a fetus can lead to mummification and retention within the uterus rendering the mare infertile. When abortion occurs mares may present empty with the fetal/placental unit intact close by; with the placenta protruding from the vulva lips and a fetus on the ground; or more frequently with just the placenta protruding and no external evidence of a fetus. The last scenario warrants manual uterine exploration for the fetus that usually is present cranial to a non-dilated cervix. Care should be taken delivering the fetus so as to minimize contamination and exposure of humans and mares to potential pathogens. In addition separating the affected mare from the rest of the herd allows decreased potential exposure to infectious agents that have the highest concentrations in placental tissues and fluids. If a mare aborts in a stall appropriate disinfectants should be applied and the mare turned out into an individual pasture, as long as there are no complications (i.e., retained placenta). If a field is contaminated with placental fluids that section should be roped off so mares remaining in that field are not further exposed. These mares should not be moved or mixed with others on the farm until herpes virus, leptospirosis and equine viral arteritis (EVA) testing is negative. Close monitoring of temperatures, serum titers and pregnancy status should be instituted on exposed mares. The greater the distance in time from abortion the less likely an abortion storm agent is responsible. Since 30% of infectious agents are not etiologically identified, submitting both the fetus and complete placenta for gross and histological examination provides the greatest likelihood for a diagnosis. Examination of the placenta on the farm can provide initial information as to whether there was a placentitis, twins, placental edema/anatomical abnormalities, umbilical cord torsion or fetal diarrhea present. In addition uterine culture, leptospira titers and complete physical examination of the mare may provide immediate answers while histopathology is pending.

**Keywords:** Abortion, equine herpesvirus, equine arteritis virus, leptospirosis, placentitis

The reported causes of abortion and stillbirths in mares change with time, but the differentiation between infectious and noninfectious is still critical in the implications. In a study conducted in central Kentucky during the 1988 and 1989 foaling seasons, placentitis (19.4%) and dystocia-perinatal asphyxia (19.5%) were the two most important causes of equine reproductive loss. Other noninfectious causes of abortion were identified in decreasing frequency as contracted foal syndrome and congenital anomalies (8.5%), twinning (6.1%), improper placental separation (4.7%), torsion of the umbilical cord (4.5%), placental edema (4.3%), bacteremia (3.2%), fetal diarrhea (2.7%) and other placental disorders (6.0%), with a definitive diagnosis not established in 16.9% of the cases. A similar study conducted in the United Kingdom spanning 10 years (1988-1997) concluded that problems associated with the umbilical cord, comprising umbilical torsion (35.7%) and the long cord/cervical pole ischemia disorder (3.1%) were the most common diagnoses of abortion. Twinning (6.0%), intrapartum stillbirth (13.7%) and bacteremia (3.2%) followed as additional non-infectious problems.

Of these noninfectious causes it appears that the ones in which increased knowledge or awareness may have an effect on the outcome includes: twinning, umbilical torsion/pole ischemia and intrapartum/perinatal asphyxia. The use of ultrasonography of the reproductive tract to diagnose pregnancy at an early stage of gestation (11-15 days) has led to a decrease in the incidence of twin abortions. Additionally, most perinatal asphyxiases are associated with relative or absolute fetal oversize, fetal malpresentation, maiden mares and unattended foalings. Increasing observation of mares close to foaling and having the necessary support available to correct dystocias and resuscitate the foal can decrease the incidence of loss. Umbilical torsion occurs between six and nine months. The twisted regions result in vascular compromise to the fetus leading to death. The umbilical cords associated with torsion are long; the mean umbilical cord length is 71.97 ± 21.68 cm as compared to 52.36 ± 14.51 cm for cords.
associated with normal births. The abnormal length of the cord most often involved is the amniotic portion which shows localized edema, hemorrhagic banding and sometimes urachal dilatation between twist. Many foals will remain in utero after death producing autolyzed tissues on presentation. Normal foals have some degree of twisting in utero, but the extent appears to become important when vessels become significantly compressed that the twisting contributes to a lethal outcome. Increased use of fetal monitoring using transabdominal and transrectal ultrasound may have an increased benefit in observing abnormalities or dilatations early. At this time unfortunately there is not much to do unless early termination of the pregnancy is of benefit to the future fertility of the mare.

Infectious agents causing abortion, although overall less common, can be more devastating and produce the most distress among horse owners, managers and veterinarians. Fortunately, improved methods of pre-emptive monitoring, vaccinating, testing, isolating and treating provide a new arsenal with which to combat the diseases. Of infectious agents, bacteria, Leptospira spp., a nocardioform actinomycete and Aspergillus spp. are most frequently associated with placentitis. Equine herpes virus and EVA should also be considered as important potential pathogens in abortions especially when multiple incidences occur.

Bacterial placentitis is most commonly caused by Streptococcus spp. which can be isolated and identified from the placenta and the aborted fetus. Other organisms identified are Escherichia coli, Pseudomonas spp., Klebsiella spp., and Staphylococcus spp. The most common fungus isolated is Aspergillus. These organisms gain access to the placenta and therefore the fetus by three characteristic mechanisms. Ascending infection in which the pathogen enters through the cervix causing destruction of microvilli. The lesion appears to spread from the cervical star region moving cranially to the body of the uterus and fetus. Abortion is due to fetal death from septicemia or by the placental insufficiency that occurs with the loss of microvilli. Differentiation between bacterial and fungal lesions is not possible by visual inspection of the placenta. Hematogenous infection occurs when a mare is bacteremic and the organism becomes seeded within the vasculature of the uterus, placenta and fetus. Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus, Streptococcus and Salmonella abortus equi are other bacteria that can enter the uterus hematogenously. Luckily all of the above are not contagious and will not usually produce abortion storms except for Salmonella (which is transmitted through contamination of pastures with uterine secretions and placental fluids from the mares that aborted). The last means is unidentified and has been attributed to a gram-positive branching bacillus and described as a mucoid placentitis. A nocardioform actinomycete, Crossiella equi and Cattulosimicrobium cellulans have characteristic lesions of an extensive and severe exudative placentitis centered upon the junction of the placental body and horns rather than the cervical star. Although placental lesions are hard to differentiate visually, C. cellulans organisms are absent within chorionic exudates and this bacteria produces prenatal pneumonia and sometimes hepatitis which may be attributed to its motility. In the United Kingdom Enterobacter agglomerans has been identified as another organism that can also produce a mucoid placentitis. How these organisms gain access to the uterus is not known. Clinical signs of placentitis include vaginal discharge and premature lactation; ascending infections are characterized by both and hematogenous and mucoid infections are characterized primarily by premature lactation. In mares that are considered high risk (those that have a history of previous feto-placental compromise, cervical incompetency/lacerations, chronic disease, old age, poor reproductive conformation), monitoring of the uterus and its contents using transrectal and transabdominal ultrasonography and measurement of maternal progestagens and total estrogens, allows early detection of placental and fetal problems (before clinical signs become apparent). These preventative measures in combination enable identification and treatment of a problem early in the course of infection.

For pregnancy to be maintained the fetus needs to develop in a quiet environment, free of infection and inflammation with the placenta providing adequate bloodflow for nutrition and gas exchange. Although bacterial infection initiates disease, based on recent work from an experimental model of ascending placentitis in pony mares, premature delivery may occur secondary to inflammation of the chorion rather than as a consequence of fetal infection. Therefore, therapies are directed at resolving microbial invasion, decreasing inflammation and uterine contractions. Systemic treatment can include antibiotics, exogenous progestagens, anti-inflammatoryatories and tocolytic agents. If a vaginal discharge is present and the cervix open, speculum examination and culture of the exudate contributes to a lethal outcome. Increased use of fetal monitoring using transabdominal and transrectal ultrasound provides identification and sensitivity of the organism allowing local treatment and appropriate systemic treatment to be initiated.

Leptospirosis is a zoonotic disease that affects many domestic and wild animals worldwide. Horses are incidental hosts of several leptospiral serovars; only serovar bratislava is suspected to be maintained in horses. Serologic surveys demonstrate that leptospiral infection is common in equine populations. However, most leptospiral infections in the horse are subclinical. Clinical disease produces signs that include recurrent uveitis, fever, hemoglobinuria, jaundice, stillbirth and abortion mainly in the last trimester. The most common serovar/serogroup involved in equine abortion is Leptospira interrogans serogroup pomona serovar kennewicki, but rarely, other serovars (australis, grippotyphosa, bratislava, icterohaemorrhagica, serjroe) have also been isolated.
Which serovar presented is usually dependent on the host in a specific area. Leptospiral infection as a cause of equine abortion has been reported as a diagnosis in 3.1% of cases in Hungary, 2.2-3.3% in the USA, in contrast to a 35% prevalence in North Ireland. In Kentucky the source of equine infection is thought to come from the wild animal population to include raccoons, skunk, deer, opossum, in addition to cattle and swine. The leptospires are shed in the infected animal’s urine contaminating water and feed which are the probable sources of infection for the equine population. Environmental conditions with low-lying swampy areas and stagnant water such as ponds produce higher incidence of disease.

Abortion or stillbirth usually occurs from six months of gestation to term with fetal autolysis present due to death in advance of delivery. The mare usually displays no premonitory clinical signs before delivery, but often has a high antibody titer against one or more leptospiral serovars. The mare is exposed, becomes infected and bacteremic. The organism enters the placenta causing fetal infection with placentitis and funisitis. The gross allantochorion lesions associated with equine leptospirosis consist of nodular cystic allantoic masses, edema, necrotic areas of chorion and necrotic mucoid exudates coating the chorion. The microscopic lesions in the allantochorion are thrombosis, vasculitis, mixed inflammatory cell infiltration of the stroma and villi, cystic adenomatous hyperplasia of the allantoic epithelium, villi necrosis and calcification. The gross and microscopic lesions of the umbilical cord include mild to severe edema, focal to multiple sacculations filled with fluid and coating of the surface with a fibrinous exudate, without visible involvement of the three primary blood vessels. A recent report revealed the surface of the umbilical cord diffusely coated by a dense exudates of mostly nondegenerate neutrophils (funisitis) that were mixed with fibrin. These neutrophils only infiltrated the cord surface and minimally into the Wharton’s jelly. Gross pathologic lesions of the fetus or stillborn foal include icterus and generalized petechial and ecchymotic hemorrhages. Livers are enlarged, mottled and discolored yellow. Edema is evident in the kidney with pale white radiating streaks in the cortex and medulla. Microscopic changes show lesions in the liver and kidney to be the most severe. Liver lesions consist of hepatocellular dissociation, giant cells throughout parenchyma and leukocytic infiltration of the portal triads. The kidneys contain microabscesses with giant cells, dilated tubules, fibrosis and multifocal areas of nonsuppurative interstitial nephritis.

Leptospira sp. can be demonstrated in the allantochorion, umbilical cord, or fetal kidneys by fluorescent antibody tests (FAT), silver staining or immunohistochemistry(IHC). Exposure usually occurs two to four weeks before abortion therefore the affected mares have high serological titers. Serology in the mare and fetus is based on ELISA and microscopic agglutination tests. Positive diagnosis in mares occurs with serum titers of ≥1:6400. The detection of leptospires by FAT is the method of choice for diagnosing leptospirosis in the kidney of aborted fetuses, although IHC has shown to have a 78% sensitivity and 100% specificity when compared to the gold standard method of culture. Culture however, is not practical since it takes six months for leptospires to grow.

Once an abortion has occurred and leptospirosis is suspected, the mare should be isolated so infective urine and uterine fluids will not expose other mares to the pathogen. Mares that have been pastured with the aborted mare should have leptospira titers drawn to try and identify potentially exposed mares so treatment can be initiated and abortion hopefully prevented. The precise titer level at which exposed mares should be treated is debatable with some feeling it is warranted at titers of 1:100 and others treating at 1:6400. Serial serum titers may better identify exposed mares. Sources of infection such as wildlife (skunks for kennewicki and raccoons for grippotyphosa), water and contaminated feed should be identified so further exposure does not occur. Treatment is successful with intravenous oxytetracycline (5 mg/kg) once a day or procaine penicillin G (20,000 IU/kg) intramuscularly twice daily for seven to ten days.

Leptospirosis titers remain high for long periods of time. In addition naturally infected mares shed high numbers of non-host adapted leptospires in urine for up to 14 weeks and therefore mares should not be re-introduced to other mares until shedding has ceased and the mare’s urine is negative on fluorescent antibody or silver stain. To collect the urine, furosemide must be administered and then the second void after administration must be collected since more mucus is present initially and may interfere with testing. Dependent on the concentration of the organisms, false negatives may also be a factor (personal communication with Dr. Debra Williams, University of Kentucky Livestock Disease Diagnostic Center; UKLDDC). Further evidence seen by the UKLDDC suggests that a good way to approximate the time when shedding ceases corresponds to decreasing titers (personal communication with Dr. Mike Donahue). This may be a more practical means of determining persistent shedding since the protocol of collecting the urine sample for FA or silver stain is cumbersome and precise.

Equine herpesvirus (EHV) 1 was first isolated in 1932 in Kentucky and has been recognized around the world as a major cause of abortion. However, since the use of preventative vaccination the incidence of loss has decreased over the years. Herpesviridae characteristically infect a susceptible host, replicate and establish a lifelong latent infection. This cycle of primary infection with periodic episodes of reactivation and shedding of
uterus and placenta become more susceptible to EHV1 infection as pregnancy proceeds due to local production of progesterone at the uteroplacental junction, resulting in immunosuppression. Transplacental spread of virus occurs at sites of uterine infarction associated with thrombus formation in endometrial arterioles. Virus within the placenta should therefore be concentrated in those areas apposing sites of infarction.

Diagnosis can be made with polymerase chain reaction (PCR) of fresh fetal tissues and paraffin-embedded placenta. Since the virus is transmitted by close contact via aerosol exposure, respiratory secretions, fetal tissues, placenta and uterine fluids from mares that have aborted need to be disposed of and the mare isolated. Virus can be transmitted via organic material on clothes, shoes and material inside stalls, trailers, water buckets or feed. If mares have aborted in the field, the area needs to be isolated from the remaining horses in the field, however those horses should not be moved or mixed with other horses. Horses that have been exposed to infected horses but have not aborted in the field that area needs to be isolated from the remaining horses in the field, however those horses should not be moved or mixed with other horses. Horses that have been exposed to infected horses but have not developed any clinical signs within 21 days of the potential exposure are unlikely to do so.

Vaccination has decreased the incidence of abortion storms dramatically, with most affected mares exposed coming from naïve herds. Initial recommendations to reduce the risk of abortion from EHV1 and 4 included vaccination with a killed virus vaccine at five, seven, and nine months of gestation. Recently increasing the frequency to every two months year round has been suggested on farms with large movements of mares or that have had endemic problems. Modified live virus vaccines have been used during gestation, however at this time it is an off-label use. Immunity to the virus only lasts four to six months so repeated abortions can occur in successive seasons.

The causative agent of the respiratory and abortagenic disease EVA is a small single-stranded RNA virus (Togavirus). Infection is believed to occur by direct contact via nasal droplet spray during the acute phase of infection and by shedding virus in infected stallions’ semen. Susceptible mares are then bred to shedding stallion acquire the disease. Two carrier states exist in the stallion: a short-term state during convalescence (weeks) and a long term chronic condition which may persist for years. The virus persists in the vas deferens, ampullae, seminal vesicles, prostate and bulbourethral glands and appears to be testosterone dependent. Mares do not appear to become carriers and shedders nor do they pass it via the venereal route. Besides abortion, mares and stallions exposed to the virus do not seem to have permanent or future fertility problems.

Clinical signs range from sub-clinical disease only recognized by seroconversion to acute illness and abortion. Signs are variable and include pyrexia; depression; anorexia; edema of the scrotum, ventral trunk and limbs; conjunctivitis; lacrimation; serous nasal discharge and respiratory distress. Adult horses usually make an uneventful recovery after a viremic phase which can persist for up to 40 days after infection. The incidence of abortion is up to 50% of exposed mares. Abortion may occur with or shortly after infection due to myometrial necrosis and edema leading to placental detachment and fetal death. The causative virus can be isolated from both fetus and placenta, especially from placenta, fetal spleen, lung and kidney and fetal/placental fluids. Semen samples with sperm rich fraction should be collected for virus isolation from suspected infected stallions. Antibodies to EAV can be demonstrated by complement fixation (CF) and virus neutralization tests. The CF test is most useful for studying immunity to arteritis during the first four months after exposure, as the titer peaks two to four weeks after infection and decreases below detectable limits after eight months. Virus neutralization antibody titers develop simultaneously with CF titer, are maximal two to four months after infection and remain stable for several years. Previously infected horses are immune to re-infection with virulent virus for up to seven years. A modified live virus (MLV) vaccine is registered for use in some states in the USA. The use of the MLV vaccine does not produce any side effects apart from a short-term abnormality of sperm morphology and a mild fever with no overt clinical signs. Virus can be sporadically isolated from the nasopharynx and blood for to seven to 32 days post-vaccination, so vaccinated horses should be isolated for one month. Horses in contact with and mares served by vaccinated stallions are not infected by EVA. Vaccinated mares bred by positive stallions are protected from clinical infection.
Prevention and control of the disease involves isolation and vaccination of stallions and mares being serviced by infected stallions and maintenance of diligent monitoring of seropositive non-shedding stallions. Stallions shedding the virus should be housed and bred in separate facilities.

Other organisms that have been implicated to a much lesser extent, but should be mentioned, as infectious causes of abortion include; mare reproductive loss syndrome, *Rhodococcus equi*, *Chlamydophila psittaci*, *Neospora* sp., *Borrelia parkeri*, *B. turicatae* and *Ehrlichia risticii*.

Lastly, another syndrome, fescue toxicosis, should be mentioned since it can have a large impact on a foal crop due to environmental contamination. Tall fescue (*Lolium arundinaceum* (Schreb)) a perennial grass is infected with the endophyte *Neotyphodium coenophialum* which produces toxins that when ingested cause severe adverse effects in late term pregnant mares. Reproductive abnormalities include prolonged gestation, late term abortion, premature placental separation, dystocia, traumatic injury to the reproductive tract, thickened placentas, retained placentas, and agalactia. A high incidence of foal mortality results from prolonged gestation, dystocia with anoxia, dysmaturity, weakness, starvation, failure of passive transfer and septicemia.

Multiple toxins are produced by the endophyte in fescue to include peramines, lolines and ergopeptide alkaloids. Ergot alkaloids act as dopamine D2 receptor agonists on prolactin secretory cells of the anterior pituitary (lactotrophs) causing decreased prolactin concentrations producing agalactia and decreased priming of the mammary gland for development; decrease tissue binding of estradiol leading to higher serum concentrations of estradiol 17B; inhibit ACTH secretion lowering cortisol concentrations which controls placental function during late gestation. This compromised placental function leads to decreased circulating progesterone and relaxin; lower progesterone levels fail to stimulate lobulaalveolar growth of the mammary gland, which further complicates agalactia associated with increased estradiol-17B and decreased prolactin; may block corticotrophin releasing hormone (CRH) activity in the foal which stimulates adrenocorticotropic hormone (ACTH) release which causes cortisol release from the adrenal. Fetal cortisol increase signals parturition in the mare, therefore lack of fetal production of CRH, ACTH and cortisol could cause prolonged gestation.

Ergovaline and n-acetyl loline have vasoconstrictive properties which may produce hypoxia causing further placental problems. Ergot alkaloids further interact with dopaminergic mechanisms capable of modifying gut motility and affecting the feeding center of the hypothalamus of mature geldings and yearling horses lowering feed intake and digestibility when ingesting endophyte infected hay.

Signs of fescue toxicosis include: prolonged gestation by 20-27 days (360 ± 4 days); lack of signs of imminent foaling (no mammary gland development, hollowing of the paralumbar fossa, softening of the gluteal muscles or relaxation of the tailhead and vulva); dystocia; placental thickening at the cervical star and uterine body and premature placental separation; retained placenta; agalactia or hypogalactia; decreased fertility; weak or stillborn foals (50-86%); dysmature or hypothyroid foals; reduced daily gains of yearlings without supplementation, and increased sweating in pregnant mares.

Prevention and treatment should start 30 days prior to parturition or as soon as possible if knowledge of continued grazing on endophyte infected fescue. Removing the mare from endophyte infected pasture or hay as soon as possible is imperative and attending the parturition is important due to increased risk of dystocia. Drugs used to aid in fescue toxicosis have included:

1) Domperidone at 1.1 mg/kg of body weight/day per os; if administered after foaling domperidone can be given every 12 hours for several days to ensure optimum milk production. As a DA2 dopamine receptor antagonist it does not cross the blood-brain barrier therefore there is less potential for side-effects. It is effective in resolving pre- and postpartum agalactia and prolonged gestation.

2) Reserpine at 0.01 mg/kg q 24 hours per os. As a Rauwolfian alkaloid it depletes serotonin, dopamine and norepinephrine depots in the brain and other tissues. It is effective in resolving only postpartum agalactia. Unfortunately it crosses the blood brain barrier producing side-effects of sedation and diarrhea; the oral form however has decreased side effects.

3) Sulperide at 3.3 mg/kg/day is a selective DA2 dopamine receptor antagonist. It has a low prevalence of side-effects even though crosses blood brain barrier. This drug resolves agalactia pre-partum although not as effectively as domperidone.

4) Fluphenazine decanoate at a dose of 25 mg IM one time. As a long-acting D2-dopamine antagonist it tranquilizes and may predispose animals to extrapyramidal or Parkinson-like side-effects. It is effective in maintaining systemic relaxin and improving pregnancy outcome, however more studies need to be done to determine its value.
References