



## Understanding Placentitis in Mares



*Dr. Michelle LeBlanc*

Dr. Michelle LeBlanc was a professor at the University of Florida when she conducted a project on Ascending Placentitis, funded by Grayson-Jockey Club Research Foundation. She is now a Theriogenologist at the veterinary firm Rood and Riddle in Lexington, Ky.

**Question:** *Your most recent published research paper deals with Ascending Placentitis. What are the specifics of this condition, and what did your research uncover that had been misunderstood before?*

**Dr. Michelle LeBlanc:** In my opinion, there are four major findings that are important to the veterinary clinician and mare owner.

1. Mares can have placentitis and not show any clinical signs of infection. Four of 16 mares with ascending placentitis

did not exhibit a vulvar discharge or premature udder development.

2. Mares with placentitis—clinical or subclinical—can be identified by measuring plasma progesterin profiles and performing transrectal ultrasonography. If mares are experiencing fetoplacental compromise before the last three weeks of pregnancy then they may exhibit a premature rise or fall in plasma progesterin levels. All 16 infected mares in the model exhibited changes to their progesterin profiles. To determine if there is compromise, four blood samples should be taken a minimum of 48 hours apart. Some of these mares can also be identified by transrectal ultrasonography. Any mare that has had a previous problem pregnancy in late gestation or any mare showing clinical signs of placentitis should be monitored with transrectal ultrasonography and plasma progesterin profiles.

3. The uterus does not contract for days before the mare aborts. It only contracts at the time of premature delivery. Two to four days before the premature delivery the uterine “pressure” may or may not increase. This increase in the “pressure” appears to be associated with the increase in prostaglandins in the allantoic fluid. Clinicians, myself included, had thought that the mare aborts because the uterus begins to contract prematurely and so we had tended to place mares on many drugs that likely do nothing to stop the progression of the disease and may actually harm the mare.

4. The disease is due to an “inflammatory process” that is not

appropriately shut off by the immune system, possibly because the inflammation occurs in the fetal compartment and not in the mare’s body. Bacteria may or may not be recovered from the foal. The organ of predilection is the lung. Aborted foals from mares inoculated with bacteria in this project all showed inflammatory lesions in their lungs and only a few had septicemia. Therefore, treatment protocols need to be directed at (A) stopping bacterial multiplication as this is what feeds the inflammation; (B) stopping the inflammatory process. If the inflammatory process is not stopped quickly, the inflammatory compounds released will induce uterine contractions and rapid delivery of the foal. Furthermore, the inflammatory products adversely affect the fetus and likely interfere with normal maturation and normal development. Further work on treatment modalities need to be performed to identify doses, drugs, and length of treatment needed.

**Question:** *You identify placentitis as the most important cause of premature delivery in foals in the United States. Has this been true historically, or is the problem more common now than in the past?*

**Dr. LeBlanc:** It is difficult to say if the incidence is greater now than it was 20 or 30 years ago as there has not been any additional scientific data on the incidence of placentitis since the early 90s. In those studies the incidence of placentitis was determined by fetal and placental tissues submitted through *continued on page 2*



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the 80s and early 90s to the University of Kentucky's diagnostic laboratory. The incidence was found to be approximately 30%. I believe that we are more aware of the disease and therefore we more closely examine mares in their last trimester of pregnancy. Also, owners will send high risk mares (dripping milk or having vulvar discharge) to a hospital or will quickly send premature or sick foals from suspect mares to neonatal units, so it might appear that the numbers may be increasing.

**Question:** *Is there any regional bias for or against placentitis, and do differing severity patterns of winter/spring weather from year to year have an effect on incidence of the condition?*

**Dr. LeBlanc:** There does not appear to be any regional bias or weather patterns that affect the incidence. Placentitis tends to be most prevalent in older mares that have poor perineal conformation, i.e., the anus is sunken forward, the mare aspirates air even with a Caslick's procedure. However, I am surprised at the number of young mares that will have placentitis. Whether immunosuppression, stress or other factors contribute to the disease is not known.

**Question:** *Is there a known percentage, or a consensus impression, of the percentage of placentitis cases in which the foal survives and/or has a useful life?*

**Dr. LeBlanc:** This question is difficult to answer as there are no current data (last 10 years) on the incidence of foals entering neonatal units whose dams' had placentitis and there are no data on how these foals do after they have been treated. Clinical impression is that many of these foals do well if they have been stressed in utero from a chronic infection and treated quickly and appropriately after birth. Unfortunately, a sick premature or dysmature foal may enter a neonatal unit and the owner will not know whether or not the mare had placentitis because the placenta "looked normal" and she did not exhibit any signs of placentitis (vulvar discharge or premature udder development).

Two interesting and worrisome findings in our model were that 1) about 20-25% of mares with experimental placentitis will not show clinical signs, i.e., vulvar discharge and/or premature udder development. 2) the placenta will look normal but when it is examined under a microscope it is severely inflamed. Because of these findings, I feel that it is imperative that placentas be submitted for histological examination if a foal is born premature, weak or sick and that the dam's uterus be cultured within 24 hours of foaling.

We also found in our model that if the amniotic fluid (fluid that the foal drinks in utero and is swimming in until birth) contained bacteria the dam's uterus contained the same bacteria. Therefore, culturing the uterus of mares whose foals are born weak, dead or premature can be used as a diagnostic indicator of placentitis. Also, if pathogenic bacteria are recovered a sensitivity pattern can be determined to ensure that the neonatologist has the foal on the appropriate antibiotics.

**Question:** *What does the condition actually entail?*

**Dr. LeBlanc:** The most common cause of placentitis is bacteria ascending through the vagina, the bacteria breaching the cervical barrier, coming in contact with the placenta and multiplying. Most cases of placentitis are due to bacteria or fungi that normally reside in the caudal vagina that gain entry into the cervix. An intriguing question that we were not able to answer is why do some mares lose their cervical plug early? Does this contribute to placentitis? We were not able to induce placentitis in preliminary trials unless we removed some of the plug from the cervix.

Ascending placentitis appears to be most prevalent in older mares that have had many foals. The vestibulo-vaginal fold has been stretched or torn allowing bacteria to enter the anterior vagina and the perineal body (muscles that maintain the vertical relationship between the anus and vulva) may have been torn from a previous birth so there is more contamination of the vulva (even with an

appropriately placed Caslick). However, it will also occur in young mares for unknown reasons. As the bacteria multiply the placental tissue that is near the cervix begins to pull away from the uterine wall and the placental tissue becomes necrotic. The mare may or may not exhibit a vulvar discharge or premature udder development. If the mare is suspect and the caudal aspect of the uterus is evaluated by transrectal ultrasonography a thickening of the placenta and a separation of the placenta from the uterus may be observed.

As the area of compromised placental tissue increases, the oxygen supply to the foal decreases. The diseased placental tissue will release cytokines (inflammatory substances) which generate prostaglandins F2 alpha and prostaglandin E. When the levels of these two prostaglandins reach high concentrations in the allantoic fluid, the uterus begins to contract strongly and the foal is delivered prematurely. In our model, two of 16 foals whose dams received an intra-cervical inoculum of  $1 \times 10^8$  colony forming units of *Streptococcus equi subs zooepidemicus*

were born precociously mature even though their birth dates were 313 and 309 days of gestation. The time from inoculation to delivery in these mares was 20 and 22 days. So it appears that the disease process if slow enough induces changes in the foal such that its time clock for maturation is accelerated. Because some foals are born precociously mature if their dams have placentitis, clinicians treat mares with impending signs of premature delivery in an attempt to save the foal.

**Question:** *Are there various types of placentitis?*

**Dr. LeBlanc:** Bacteria or fungi can enter the uterus either through the cervix (most common) or through the blood (hematogenous; about 10% of cases). There are many types of bacteria or fungi that can cause the disease. Most commonly the disease is caused by bacteria or fungi or yeast that normally reside in the caudal reproductive tract.

**Question:** *If a veterinarian detects existence of the condition, is it practical to induce labor?*

**Dr. LeBlanc:** Labor should never be induced if a mare is showing signs of

premature delivery secondary to placentitis. The equine fetus only matures in the last 5 days of gestation and if it is removed before that time it will die even in the best of neonatal units. What may be most appropriate is to treat the mare for uterine infection and uterine inflammation in an attempt to keep the foal inside its mum for at least 20 days as some of these foals will mature precociously.

**Question:** *When in the pregnancy is it likely that placentitis can be diagnosed?*

**Dr. LeBlanc:** Placentitis is most commonly diagnosed in the last three months of gestation. If it is diagnosed before that time, I am reluctant to treat the mare vigorously as the fetus is still in the stage of organ development. We know from human medicine and from a few cases that we have worked on that these neonates may live but their quality of life (human) or usefulness (horse) will likely be impaired.

**Question:** *What are treatment options at that point?*

**LeBlanc:** Many drugs have been used in mares with placentitis without much scientific basis for *continued on page 4*



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their use. Treatments that have some scientific basis for use include appropriate antibiotics, anti-inflammatory drugs and progestin or progesterone therapy. The antibiotics are used to stop multiplication of bacteria. The anti-inflammatory drugs are used in an attempt to stop the detrimental effects of the cytokines and the oral or injectable progesterone compound is used to block the effects of pro-inflammatory cytokines on the uterine muscles.

**Question:** *Are there preventive approaches that are useful? If so, at what time during the pregnancy would they be best employed?*

**Dr. LeBlanc:** A therapy that is used and appears to have some clinical relevance is the use of broad spectrum antibiotics for 10 days of the month beginning at the fifth or sixth month of gestation in mares that have had a history of placentitis or uterine infections in early pregnancy. This treatment option is used in human medicine with some success. There is empirical evidence that it may also stop the spread of infection in some mares. Many pregnant mares are routinely placed on a progesterone

compound in early pregnancy so its efficacy in preventing placentitis at the dose commonly used is not known. It is likely that mares will need an increased dose of progesterone to block the effects of cytokines on the fetus.

**Question:** *What additional changes in knowledge and reaction to placentitis have been brought about by recent research?*

**Dr. LeBlanc:** The changes in knowledge are presented above. I believe that we are more diligent in examining mares in late gestation and that more veterinarians are using more diagnostics—transrectal ultrasonography in late gestation and progestin profiles—for identifying mares with fetoplacental compromise. I hope that drug use in mares suspected of placentitis will be based on blocking spread of bacteria and inhibiting the inflammatory response as many drugs are used without scientific basis. And finally, that all placentas from mares that foal prematurely be submitted for histopathology to determine the cause of the early delivery as it may appear “grossly” normal to a lay person but it is not normal. I would not be

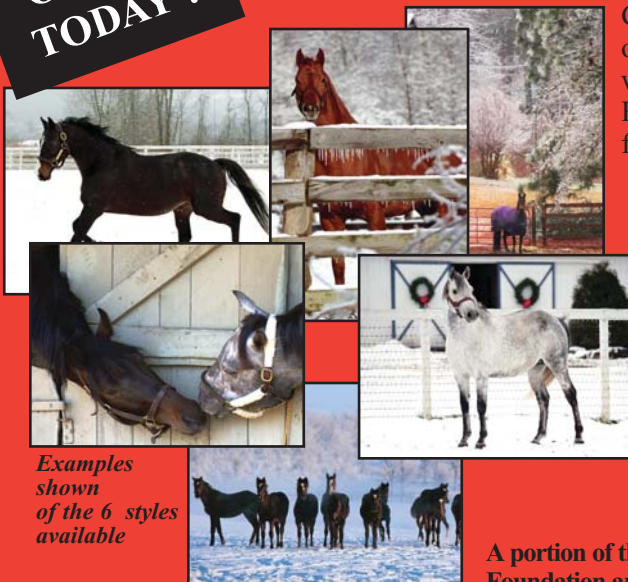
surprised that cause for illness in some sick, premature or dysmature foals is not diagnosed because the placenta is not submitted. The placenta is the house in which the fetus lives for nine to 10 months. Fetal nourishment and waste removal both are functions of the placenta so if the placenta is compromised, so may the foal at birth.

**Question:** *What would you like to see next in the progression of knowledge of placentitis?*

**Dr. LeBlanc:** We need to identify appropriate treatment strategies that will prevent abortion in mares with ascending placentitis. We also need to determine if there are other diagnostic aids for identifying mares in late gestation with fetoplacental compromise. The late gestational period in the mare is extremely difficult and expensive to study because mares do not tolerate instrumentation well and it is expensive to keep a herd of pregnant mares. However, we breed mares to raise a racehorse or performance horse and if the foal is not normal at birth much time, energy and money will have been spent without a viable product to sell or raise.

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