Placentitis: Important Facts

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Placental infection (placentitis) during the last 3 to 4 months of gestation is devastating both economically and emotionally because most foals are born prematurely and do not survive unless the infection is identified early and the dam treated appropriately. Unfortunately, many mares do not exhibit classical signs of infection, premature udder development and a vaginal discharge, so infections are commonly missed. Placentitis will occur in 3 to 7% of pregnant mares. Ninety percent of infections are due to bacteria entering the vagina, traveling up to the cervix and penetrating the cervical barrier. Bacteria gain access to the uterus in the cervical star portion of the fetal membranes (Figure 1), where they quickly multiply. Fetal membranes thicken in response to bacterial contamination and eventually separate from the dam’s endometrium at the site of the infection. This results in a decrease in oxygen transfer and nutrients to the fetus and a buildup of toxins within the fetus as blood supply is diminished. The dam responds to this insult with an inflammatory response which consists of white blood cells migrating to the site of the infection, production of pus and release of pro-inflammatory cytokines. While this defense mechanism may block the spread of bacterial infection the pro-inflammatory cytokines stimulate uterine contractions and may induce abortion even though the fetus is not infected. The fetus will respond to a persistent, low grade bacterial placentitis by maturing more quickly in-utero. If the infection is chronic, lasting for 2 to 3 weeks, a foal may be born as early as 310 days and be viable because the stress induces maturation. Unfortunately, not all of the foal’s organs mature at the same rate during a stressful event so most affected foals need significant neonatal care. Inducing parturition in mares with placentitis is not recommended as the foal’s final maturation only occurs in the last 3 to 5 days of gestation and we can’t predict when that will occur in a mare with placentitis. Delivery of a foal before final maturation results in birth of a premature, non-viable foal.

So, what can we do to improve the chances of delivering a viable foal whose dam has placentitis? Early identification followed by appropriate treatment has been shown in experimental models to improve foal survival. Changes in the hormones, progestins and total estrogens and thickening of the placental unit and separation of the fetal membranes from the uterus (most commonly in the region of the cervical region) as seen on ultrasonography are used to identify problems in mares, especially those that exhibit no clinical signs. Progestins are metabolites of progesterone produced by the placental unit from day 120 of gestation until foaling. We are able to measure progestins because they cross react with the progesterone assay used at Rood and Riddle Equine Hospital. In a mare carrying a normal pregnancy, plasma progestins are stable and do not fluctuate, remaining below 10 to 12 ng/ml, until the last 3 weeks of gestation when they begin to rise peaking at levels that exceed 25 ng/ml the day before delivery. The rise in progestins is associated with an increase in fetal adrenal function. Unlike women or other domestic species, the fetal adrenals are unable to produce cortisol, the hormone that stimulates final maturation until the last 3 to 5 days of gestation. The enzyme needed to convert progesterone, (the precursor to cortisol), to cortisol in the fetal adrenals is not produced in adequate amounts until the last week of pregnancy. Therefore, if the fetus is stressed after 260 days of gestation, the fetal adrenals pump out progesterone that is converted to progestins in the placenta. Progestins spill over into the dam’s blood and a change in their concentration indicates fetal stress. We recommend taking 3 blood samples at 48 to 72 h intervals to determine if
Progestins are prematurely rising (before 310 days of gestation)—an indicator of fetal stress—or falling (anytime in the last 3 months)—an indicator of hypoxia, fetal demise or a positive response to treatment—in mares at risk of placental abnormalities. Total estrogens can also be measured. Estrogens rise dramatically in the dam’s blood in mid-gestation and begin to fall around 7 months of gestation. Estrogens are a by-product of the fetal gonads and placenta and are thought to be an indicator of placental blood flow. The horse is unique in that the fetal gonads grow during mid-gestation and then decrease in size in late gestation. Estrogen levels > 1000 ng/ml is associated with a viable fetus. Levels below 500 ng/ml have been associated with a compromised fetus. The test is not conclusive after 10 months of gestation when the gonads are decreasing in size as total estrogens are rapidly falling. Only one blood sample is needed. We recommend that both progestins and estrogens are measured in mares at risk of abortion.

Ultrasonographic changes in the placental unit may be seen transrectally, especially in the cervical region (Figure 1) or transabdominally in cases of Nocardia placentitis (Figure 2). The placental unit may thicken in response to ascending infection to more than 1.5 cm in diameter. Normal thickness of the uterus and placenta ranges between 0.9 to 1.2 cm in the 10th and 11th months. The fetal membranes may separate from the uterus and pus may be seen swirling between the membranes and uterus. As over 90% of placental cases are due to ascending bacterial infections, most placental lesions are seen transrectally in the area of the cervix. However, in central KY, Nocardia infections are common. This organism resides in the space between the uterus and placenta in the area of the uterine body or at the junction of the uterine body and uterine horn. Nocardia infections cause the placenta to separation from the uterus but the organisms do not cross the placenta so the foal does not become infected. Mares with Nocardia placentitis will usually develop an udder prematurely but will not have a vaginal discharge. The condition is identified by transabdominal ultrasonography. Not all mares with placentitis will exhibit ultrasonographic abnormalities in the placental unit. Fetal heart rate, fetal motion and the clarity of fetal fluids also can be measured by transabdominal ultrasonography and changes in these parameters also indicate fetal compromise.

Treatment must be instituted early if a pregnancy is to be saved and is directed at 1). Stopping spread of the infection; 2). Maintaining uterine quiescence; and 3) blocking production of pro-inflammatory cytokines. If a mare is suspected of having placentitis, a complete physical examination should be performed, transrectal ultrasonography of the placental unit, culture of vaginal discharge (if any is present) and blood drawn for hormonal values. A common treatment for mares includes administration of trimethoprim sulfa orally given to prevent infection, flunixin meglumine (Banamine®) given to block production of pro-inflammatory cytokines and double dose altrenogest (Regumate®) or a long acting progesterone compound given to block pro-inflammatory cytokines thereby decreasing the likelihood of pre-mature uterine contractions. Not all bacteria, however, are sensitive to sulfa drugs so it is best if a vaginal or cervical culture can be obtained. Other drugs that show promise in experimental models include pentoxifylline (Trental®, this drug has tripled in price in 2010 as it is not commonly used in human medicine anymore), aspirin and dexamethasone. Use of these drugs in experimental placentitis in combination with antibiotics and/or Regumate or Banamine improved foal survival. How long should mares be kept on drug combinations? If the problem occurs late in gestation, after 10 months, it is prudent to keep the mare on the antibiotic and progesterone compound until she foals. The other drugs can be given for 3 to 10 days, upon the advice of your veterinarian. If the condition occurs sooner, one needs to consider the long term effects of antibiotics on the mare...
and her fetus. Long term sulfa drugs can induce gastro-intestinal problems in the dam. Gentamicin remains in the fetal compartment much longer than it remains in the dam’s circulation. Prolonged use may damage fetal kidneys. A treatment method that has gained favor in mares that have previously lost their foal to placentitis, although there is not scientific data to support the protocol, is to give these mares, antibiotics and flunixin meglumine, for the first 10 days of the month beginning around the 7th month of gestation. These mares remain on progesterone or Regumate throughout their pregnancy.

If a mare delivers a foal prematurely, the fetal membranes need to be examined closely. The membranes need to be turned inside out because the damage occurs on the side attached to the dam’s uterus (Figures 1 and 2). If there are abnormalities, a veterinarian should be notified immediately even if the foal appears normal as these foals typically don’t show signs of disease for 12 to 72 h, when it is too late to institute successful treatment. Any mare that has placentitis should have a uterine culture taken within 24 h of foaling because most of them will continue to harbor bacteria even if they were treated aggressively during pregnancy. These mares should be treated appropriately and soon after foaling as prolonged uterine infection during pregnancy will hamper their ability to get pregnant and if they do conceive, many will abort in the subsequent breeding season. A close working relationship with your veterinarian is needed to make vital decisions about mares at risk of early delivery, not only to save the foal but to ensure that the mare’s uterus is healthy for subsequent breeding.