Causes of Early Pregnancy Loss in Mares and Possible Prevention

BY HEATHER SMITH THOMAS

THE FRUSTRATING THING about breeding mares is that sometimes a successful conception does not result in a full-term pregnancy. Often the loss occurs very early in gestation. There are many reasons for early pregnancy loss in mares, and various risk factors. According to Dr. Ahmed Tibary, professor of Theriogenology, Department of Veterinary Clinical Sciences, Washington State University, it's important to check mares early for pregnancy after breeding, and monitor the pregnancy to make sure that it is progressing normally.

The first pregnancy check is usually at about 14 days after ovulation.

"We always recommend a couple of rechecks—one at about 25-28 days and the second one somewhere between 35-50 days, because there is a high incidence of early embryonic death, during the first 50 days of pregnancy," Tibary said. "Seldom would you notice anything unusual in the mare, that early, and might just assume that she's still pregnant."

Dr. Richard Geary and his wife, Cindy, have a veterinary practice, Countryside Veterinary Clinic, in Chester, Idaho, focusing primarily on equine reproduction.

"After I finished veterinary school I worked on my PhD with Gordon Woods, who was a well-known equine reproductive physiologist," Geary said.

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Performing an ultrasound exam

In a normal pregnancy, at about day 38, the developing placenta (around the tiny fetus) starts forming endometrial cups.

"At this point the uterus and the placenta together start to secrete more progesterone, which helps maintain the pregnancy after that," Geary said. "If we can get the pregnancy to that 38-day stage, then the mare will remain pregnant.

"Sometimes we see mares that even at that point don't remain pregnant. Some of them need to be kept on progesterone supplementation until about 100 days. From that point they can usually carry a foal to term without progesterone supplement," he continued.

"After she goes past the 35-day mark—when the endometrial cups are already formed—if she loses the pregnancy she will not come back into estrus," Tibary said.

The endometrial cups are the outgrowths on the placenta that produce the important eCG hormone in the pregnant mare. If these are already formed and producing hormone, the mare may enter a pseudo-pregnancy state which can last up to four months. This can be very disappointing to the owner later, finding out that the mare is actually not pregnant.

"There have been many studies done over the years looking at how many mares failed to foal after they were diagnosed pregnant at 14 days," Tibary said. "There is a wide range of reported incidence of pregnancy loss, depending on the studies—ranging from about 2.5% all the way up to 30%. This tells us that we need to look at the risk factors."

RISK FACTORS

"When we work with a mare to get her bred, we classify her into a certain category—whether she will be easy to get pregnant and maintain the pregnancy or whether she will be at risk of losing the pregnancy," Tibary said. "A simple way of looking at this assumes a young maiden mare in good health, good body development, with no problems settling on the first cycle would have less than 5% chance of losing the pregnancy."

This type of mare would have the least risk for pregnancy loss.

"The other extreme is the aged mare—greater than 18 years of age and one that has had problems with uterine infection, pregnancy loss, or abortion in the past," he said. "This mare would be in the highest risk category."

Then there are many mares somewhere in between. They may have a recent history of weight loss or systemic disease, or even just treatment during the previous cycle for uterine infection. These mares may be at a higher risk of early embryonic death than the healthy maiden mare.

There are many different factors involved.

"When I talk to my students about this I go from the most common causes to the least common or more obscure problems," Tibary said. "When we look at what might cause embryonic loss, we can blame either the uterus (the mare and the uterine environment for that embryo) or we can blame the embryo itself, or the stallion in some instances. There may be some outside environmental factors, as well."

AGE OF MARES

"In the mare herself, the main risk factors we run into are age-related changes to the uterus or even to the quality of the oocyte," Tibary said. "Just as in women, the eggs in an older mare may not be as viable as in a younger individual. Some studies have shown that even when you take young embryos from aged mares and place them in younger mares, those embryos undergo significantly more losses than similar-stage embryos from younger mares. The embryo itself (from the older mare), rather than the uterine environment, can be a factor in early embryonic death."

This goes back to the fact that the oocyte—the egg—from the older mare undergoes a lot of changes that are not compatible with normal development.

"Studies have shown that those changes, and the quality of the oocyte, start showing up in some mares as early as 12 years of age. Definitely by 20 years, most mares will have some problems. In these mares we often see embryonic losses as high as 40 or 50%," Tibary said.

TIMING OF BREEDING

"There is also another twist regarding aging of the oocytes," Tibary continued. "The aging can be due to the mare's age, but also we need to look at the time elapsed from when the oocyte was ovulated. The longer we wait to breed the mare after she ovulates the higher the risk for poor embryo quality."

The clock is ticking on that oocyte as it waits for fertilization.

"Before the oocyte dies, it is still able to be fertilized, but it may be running out of optimum ability for good development," he said. "We see this happen when people take chances and still breed the mare even if it's been a bit too long after ovulation. Sometimes you end up with a pregnancy at 14 days, but it doesn't continue to develop."

In these instances it may not pay to gamble. It might be better to wait until the next heat cycle to breed the mare, rather than start a pregnancy that will not be viable. You may actually save time by waiting, rather than have the mare become pregnant and lose it and have to start over later.

"This is the frustrating part," he said. "You gamble, and get a positive result at 14 days (you can see the embryo; the mare is pregnant), but then you have to wait, to see if the pregnancy will maintain or not. Usually those embryos from older oocytes are smaller than normal."

UTERINE ENVIRONMENT

"In the uterus we are looking at whether there is inflammation and whether it is acute or chronic," Tibary said. "It is primarily the chronic inflammation that can be the biggest risk factor for loss of pregnancy. This is why every mare going into

the breeding shed should have an endometrial biopsy, particularly if she has any history of infertility or recurrent pregnancy loss. Then we can more accurately determine her chances for allowing the embryo to fix normally (and get enough nutrients from the uterus), and for maintaining pregnancy to term. We look at whether there is scar tissue or fibrosis of the endometrium."

UTERINE CYSTS

"In older mares (and sometimes in younger mares) that have had several pregnancies we may also see uterine cysts," Tibary said. "There is a big debate about whether these cysts are linked to early pregnancy loss. There is some evidence these may affect pregnancy loss. A German study showed when there are large cysts or more than five of them, the risk for losing pregnancy is increased."

Uterine cysts may hinder the movement of the embryo within the uterus, before it fixes and starts attaching.

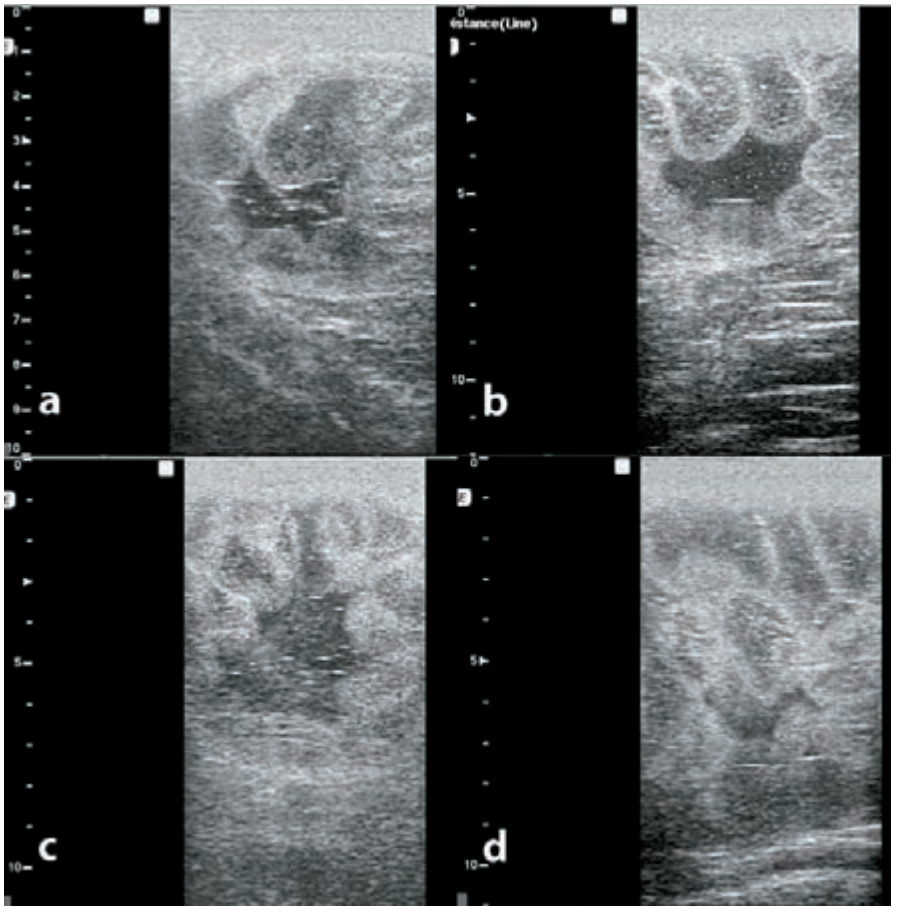
"This movement is required, to signal its existence to the mare (maternal recognition of pregnancy), and maintain the pregnancy," Tibary explained.

If this trans-uterine embryo migration is hindered, the mare is unable to recognize she's pregnant, the uterus releases prostaglandin F2 alpha (which stimulates the corpus luteum—the source of progesterone) and she returns to estrus.

"The other thing that may happen with cysts is that the embryo may fix near a cluster of cysts or near a large cyst," Tibary said. "Then the fixation is not very solid, and more precarious. Mares have a better chance of maintaining pregnancy if these cysts are removed.

"We do a lot of cyst removal here, either by electro-coagulation, or with laser surgery. This seems to work well, for many mares," he said. "Their success rate for future pregnancies is improved. A study done at Equine Services Surgical Hospital in Kentucky showed when they treated these mares, 60% of the mares that could be followed up got pregnant after the laser surgery, and maintained the pregnancies"

This is something to consider, with a mare that has problems with cysts.



Slides showing post breeding accumulation of fluid

PROGESTERONE DEFICIENCY

The problem most talked about as a cause of early embryonic loss in mares, and the most commonly treated, is progesterone insufficiency. But this cause is very hard to prove. Many people become frustrated with mares and just put them on progesterone. If their history has all the indications they may be at higher risk of losing the pregnancy or they have had loss of pregnancy before, they are generally put on progesterone supplementation, such as Regumate® (altrenogest). People do this in hopes it will help—and it may help in some cases.

"There is not a lot of evidence scientifically that it helps, because it is very hard to design an experiment that would allow us to prove this," Tibary said. "Thus it is a subject of debate, but in equine reproductive practices there are a lot of mares that are put on progesterone. And we do put mares on progesterone any time that they have a situation that may threaten a loss of pregnancy—such as a bout of fever.

"Some studies in England tried to create extra CLs (corpus lutea) so they could reinforce the production of progesterone. This approach showed some positive results, but it is still debatable. Mares were given GnRH at 10 days post-ovulation in the hope that the follicles present at that time would create new CLs that would reinforce the old ones—to help the mare maintain the pregnancy."

Geary says that hormone imbalance is one of the primary reasons for early pregnancy loss.

"The common situation is a mare that lacks sufficient progesterone to maintain pregnancy," he said. "The only way to know that, for sure, is to take a blood

sample and measure the progesterone levels in the mare."

Geary generally puts these mares on progesterone.

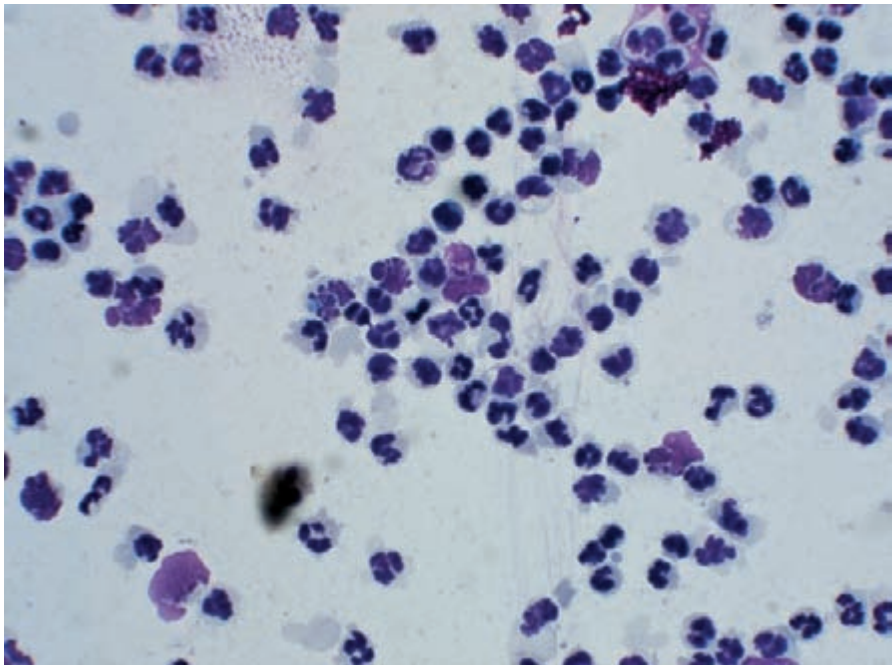
"Typically what happens is the mare shows heat, is covered by the stallion, and at the 14-day ultrasound to check for pregnancy, there is usually no pregnancy because the uterine environment is not sufficient to maintain the embryo—due to low progesterone," he said.

This is generally a malfunction of the corpus luteum; it fails to form on the ovary after ovulation. The corpus luteum is the structure that produces progesterone.

"This is generally an easy fix," he said. "We can inject the mare with progesterone and give things a little boost."

Under normal circumstances, progesterone from the ovary safeguards the pregnancy for the first few weeks. When that source is lacking it must be provided.

"These mares can be put on Regumate—a hormonal product containing progesterone," Geary said. "There are two ways of doing this. You can feed the mare Regumate, or squirt it into the mouth. Or, you can inject a product that is progesterone in oil. This product sometimes causes local soreness and occasionally an abscess at the injection site, but these complications don't happen very often."



Slides of uterine cytology showing inflammation—white blood cells

STRESS FROM DISEASE/INFECTIONS/TEMPERATURE

Systemic disease may also have an impact on whether or not the mare maintains the pregnancy. Any medical situation that is characterized by a very high stress on the mare such as high fever for a few days, or any disease that is linked to the production of endotoxin, will jeopardize the pregnancy.

"All the inflammation, endotoxins, etc. will create an environment that is not compatible with maintenance of the CL function," Tibary said. "The inflammation and fever will usually affect the CL via secretion of prostaglandin.

"There is also the fact that high environmental temperatures and humidity will lead to some loss of pregnancy. This can put the embryo outside the window of healthy temperature.

"I haven't seen this in the U.S. but when I was practicing in the UAE (United Arab Emirates), where the temperature and humidity were very high, we could hardly keep mares pregnant, particularly if the adverse conditions occurred early in the pregnancy," Tibary said.

Stress from adverse heat, systemic infection, severe pain, laminitis, etc. has been shown to cause lower progesterone levels. If the mare colics during early pregnancy, for instance, or undergoes surgery—with the possibility of endotoxemia—this could compromise the quality of the CL and the pregnancy would be at risk.

LACTATION STATUS

Whether or not the mare has a foal at her side and is lactating may also make a difference in her chances for losing the embryo.

"According to one study lactating mares seem to have double the rate of pregnancy loss compared to non-lactating mares," Tibary said. "It's not lactation, per se, that causes this problem, as much as the effect of lactation on the mare. This would include the effect of nutrition and body condition that goes with it. There are some studies from South Africa that have shown that nutrition (quality of energy and protein intake) will affect the maintenance of pregnancy via the quality of the CL and production of progesterone.

If the mare has too much stress trying to maintain herself, feed her nursing foal, and start a pregnancy, the pregnancy gets sacrificed.

FOAL HEAT BREEDING

There is also a lot of discussion about whether breeding at foal heat is less successful than waiting until a later heat.

"Some early studies showed foal heat breeding results in less fertilization and probably more incidence of early embryonic death," Tibary said. "There are some other studies, however, that have shown foal-heat breeding is successful—as long as the mare has not had any complications from foaling.

This must be considered case by case. Some mares will do fine when bred at foal heat, while others need more time to recover from foaling.

NUTRITION

"If a mare is going into her first trimester of pregnancy and losing weight, you also have a higher risk of early embryonic death," Tibary said.

Pregnancy is always a luxury. If the mare's body is having trouble maintaining itself, the pregnancy is often sacrificed.

HOW DO WE KNOW IF A PREGNANCY MAY BE AT RISK?

Breeders often want to know how they might be able to tell if the pregnancy is not viable.

"There are a few indications that sometimes tell us we are dealing with a non-viable pregnancy, though we can't start evaluating the embryo/pregnancy until about 12-14 days after conception, with ultrasound," said Dr. Ahmed Tibary, professor of Theriogenology, Department of Veterinary Clinical Sciences, Washington State University. "I tell my students that doing a pregnancy diagnosis is not just about finding the embryo/vesicle. We also need to pay attention to the health of that vesicle and whether it is of appropriate size for that day of pregnancy."

This is also the point in time when the veterinarian will check to see if there are twins. Sometimes a pregnancy will be lost when there are twins and they fix on the same side; the chances that you will lose both of them are increased.

"This is one reason we check mares at 14 days," he said. "If there are twins, the embryo can still be moved. It does not stop its migration until day 16. You still have a chance to separate and crush one of the embryos, which allows the other one to develop normally.

"If the vesicle does not stop moving after day 16, this is an indication that there is something wrong," he continued. "The embryo has to fix at the base of the horn by day 16 or it will not survive. Another thing we look for is where the embryo stops. If it fixes in the body of the uterus instead of at the base of a horn, we know that it will likely not be carried to term. It has to fix at the base of one of the horns.

"We also look for presence of edema. If there is a pregnancy but also excessive edema, this tells us there is something wrong with the hormonal environment. If I see a pregnancy on ultrasound, but the uterus on palpation does not feel very toned (nice and tubular) this suggests there is something wrong with either the uterus or the hormonal environment—particularly the level of progesterone," he explained.

"Later on we like to see a proper embryo by day 21 or 22 and by day 25 we need to see a heartbeat. If we do a pregnancy diagnosis at 14 days and everything looks good, we still want to see the mare again at day 25 or 28. Then we can evaluate the presence of fetal heartbeat, growth of the vesicle, etc. The reason we do this is because there are situations in which the vesicle will develop, and be maintained for as long as 30 days, without a proper embryo inside it. These are sometimes called ghost pregnancies. It's just the outer membrane sitting there; the embryo inside it died earlier."

Later ultrasound examination looks at the fluid and membranes.

"We can detect things like a dislodged vesicle, loss of fluid, etc.," Tibary said. "These are methods we use, to indicate whether the pregnancy is viable or not. The clinician may decide to help the pregnancy with progesterone or altrenogest. If I see a good vesicle but the tone is not what I'd like, I may put that mare on altrenogest (synthetic progesterone, such as Regumate®). I like the Altrenogest because it allows me to check the endogenous progesterone of the mare (what she herself is producing) because the test does not cross-react with the synthetic hormone. Now, with Doppler ultrasonography, we can glean even more information about the quality of the pregnancy and the CL (corpus lutea)," he said.

"It is important to follow mares after breeding, to sort out the ones that may be easy and the ones that may be at risk of losing the pregnancy or having complications."

By Heather Smith Thomas

OTHER CAUSES

There are some other causes of pregnancy loss that may be region specific, or specific to a certain year.

"We focus on things such as fescue toxicosis being a problem for late-term pregnancies, but it has been shown that mares on endophyte-infected fescue pastures can also have higher rates of early pregnancy loss," Tibary said. "This is generally due to reduction in the hormone prolactin."

Many breeders assume their mares are safe on fescue pastures until late pregnancy, but this is not always the case. Endophyte-infected fescue pastures should be avoided for broodmares.

Early pregnancy loss has also been associated with the outbreak in Kentucky some years back that was termed MRLS (mare reproductive loss syndrome).

"Those losses are generally later than 50 days, and many of them closer to foaling, but there were some between 80-120 days gestation," he said.

Another interesting thing (and unfortunately there is not a lot of data on this) is that some stallions seem to produce pregnancies that are at higher risk for loss.

"There may be some abnormality in their DNA (chromatin) in the spermatozoa," Tibary said. "These factors are hard to identify, unless we are dealing with stallions that have bred many mares and we have rigorous data on the outcome of breeding." Similarly, in maiden mares that experience repeated pregnancy losses, there may be some individual problems.

"A report that came out a few years ago from University of Kentucky showed some of these mares have normal cycles, they become pregnant when bred, but lose the pregnancy due to a chromosomal abnormality. The embryo or fetus can't get past a certain stage. The chromosomal abnormality leads to a problem in development," Tibary said.

This is a genetic factor that results in pregnancy loss.

"Some of these factors are difficult to identify," Tibary said. "But the bulk of pregnancy losses will be found in aged mares with aged oocytes or aged uteri. When the individual mare has a problem however, it is worth investigating farther."

That particular mare may have a problem that isn't as common, but it affects her ability as a broodmare.

"We don't look at mares as a herd," he said. "Each mare is a special case, with her own unique situation and problems. In other species we have weeded out most of the reproductive problems, but in horses we have selected for other traits than reproduction, and therefore have to deal with various breeding challenges." BH

Heather Smith Thomas is a freelance writer based in Idaho.