Reproductive Problems in Mares

BY HEATHER SMITH THOMAS

BROODMARE MANAGEMENT CAN BE CHALLENGING, trying to get every mare safely in foal. There are many reproductive problems frequently encountered and some that are rare, according to Dr. Claire Freeman. She worked in a Thoroughbred practice in Saratoga Springs, N.Y., and abroad in Australia and New Zealand before joining Royal Vista Southwest in Purcell, Okla.

"One thing we must do for successful breeding is time the service appropriately with the mare's ovulation," she said. "Failure to ovulate or poor ovulation timing would be one reason a certain mare does not become pregnant."

However, there are also physiologic, infectious, and anatomic reasons mares might not conceive. Some fertility problems are obvious while others take some effort to figure out.

BREEDING SOUNDNESS EVALUATION

Dr. James Bailey, reproductive specialist (Royal Vista Southwest), says mare owners should always be thinking about the next breeding season and looking at open mares in the fall before they cease cycling.

"Don't wait until they are in anestrus, or the culture results will not yield enough information," he said.

Sometimes the veterinarian must palpate the cervix to check for issues such as a tear from a previous foaling. Any anatomical problems should be ruled out or evaluated at this examination.

"Our typical work-up includes palpation, ultrasound, examination of the cervix, uterine biopsy, and uterine culture," Bailey said. "The culture should check for aerobic bacteria and possibly anaerobic bacteria as well as fungal infections. This may depend on the age of the mare and the problems encountered with her in the past."

COURTESY HEATHER SMITH THOMAS

Dr. James Bailey conducting an ultrasound exam

THE MARE THAT ISN'T CYCLING

A mare can't be successfully bred unless she is cycling and ovulating.

"We start breeding mares prior to the normal physiologic breeding season, so some mares won't be cycling because they are still in anestrus or transitional—if we haven't made changes to their management to cause them to start cycling sooner," Freeman said.

The most common and most effective method to start mares cycling earlier in the year is to put them under lights at least 60 days ahead of breeding season. This can be done with lights in stalls or paddocks or with light masks.

In the northern hemisphere the goal is to start breeding in mid-February. The current industry standard is to expose mares to 16 hours of light per day (natural and artificial as needed), starting about Thanksgiving or in early December.

"It takes about 60 days for the brain to adjust hormonally and for the mare to start cycling," Freeman said. "If she doesn't, she may still be transitional."

Dr. Peter Sheerin, of Nandi Veterinary Associates in New Freedom, Pa., says breeders need to keep in mind that cyclicity in mares is not just light related.

"Other factors include temperature, body condition, and nutrition," he said. "If weather is extremely cold and mares are not protected from the cold, this could slow down their response to light masks."

This could be an issue if the mares are outdoors.

Even with lights some mares are slow to cycle. Mares coming off the racetrack might not start cycling for a while. They need time to let down and get past the stress of an athletic career to make the transition from training and racing.

"If they received some exogenous hormones or other drugs that impact cycling, it will also take some time for those

to clear the system," Sheerin said.

Some mares don't return to normal cyclicity after foaling.

"They may or may not have a foal heat, and then shut down," Sheerin explained. "Many people call this lactational anestrus, similar to what cows do, but in mares it's not truly lactational anestrus. We see this problem in early-foaling mares that were not under lights. They slip into anestrus after they foal because their body realizes it is still winter. One way around this problem is to put pregnant mares under lights, too. This may also shorten gestation length—similar to mares that foal later in the spring."

COURTESY HEATHER SMITH THOMAS

Scanning to check whether a mare is in foal

"Another thing that interferes with cyclic activity is hemorrhagic follicles," Freeman said. "These can prolong the interval before a mare returns to estrus. Instead of the predictable 21-day cycle or 14-to 15-day diestrous period, this may be prolonged because hemorrhagic follicles have luteal-like activity. These follicles do not always respond to treatment with prostaglandin."

It might take time for the follicles to resolve on their own.

Hemorrhagic follicles might occur at the beginning or during the breeding season.

"With some mares, if they start developing hemorrhagic follicles, they keep developing them repeatedly," Freeman explained. "We don't know why. Instead of ovulating the follicle becomes hemorrhagic, and this can be very frustrating.

"You hope the problem resolves before breeding season is over and also hope the next time she starts growing a nice big follicle (and you send her to the serving stallion) that it doesn't happen again. Some mares just continue producing hemorrhagic follicles. Some maiden mares have no reason not to get pregnant except they are not ovulating. If they keep forming hemorrhagic follicles (and not ovulating), they are never going to get pregnant."

Another reason a mare might not be cycling could be pathologic, such as a *granulosa* cell tumor on the ovary or some kind of hormone-producing tumor that interferes with the normal cycling process. The tumor must be removed before the mare can be successfully bred. Otherwise, as the tumor becomes more hormonally active, it will cause the normal ovary to stop functioning, making pregnancy impossible.

ERRATIC CYCLES

Sometimes mares cycle erratically due to a uterine infection that causes an inflammation resulting in release of prostaglandin.

"This causes the mare to short cycle herself and come back into heat at an inappropriate time," said Sheerin.

The infection and inflammation must be resolved before the mare can cycle normally.

ENDOMETRITIS

"When evaluating a mare for infertility, we look for things such as endometritis (inflammation of the endometrium, the lining of the uterus), which can be infectious or non-infectious," Freeman said

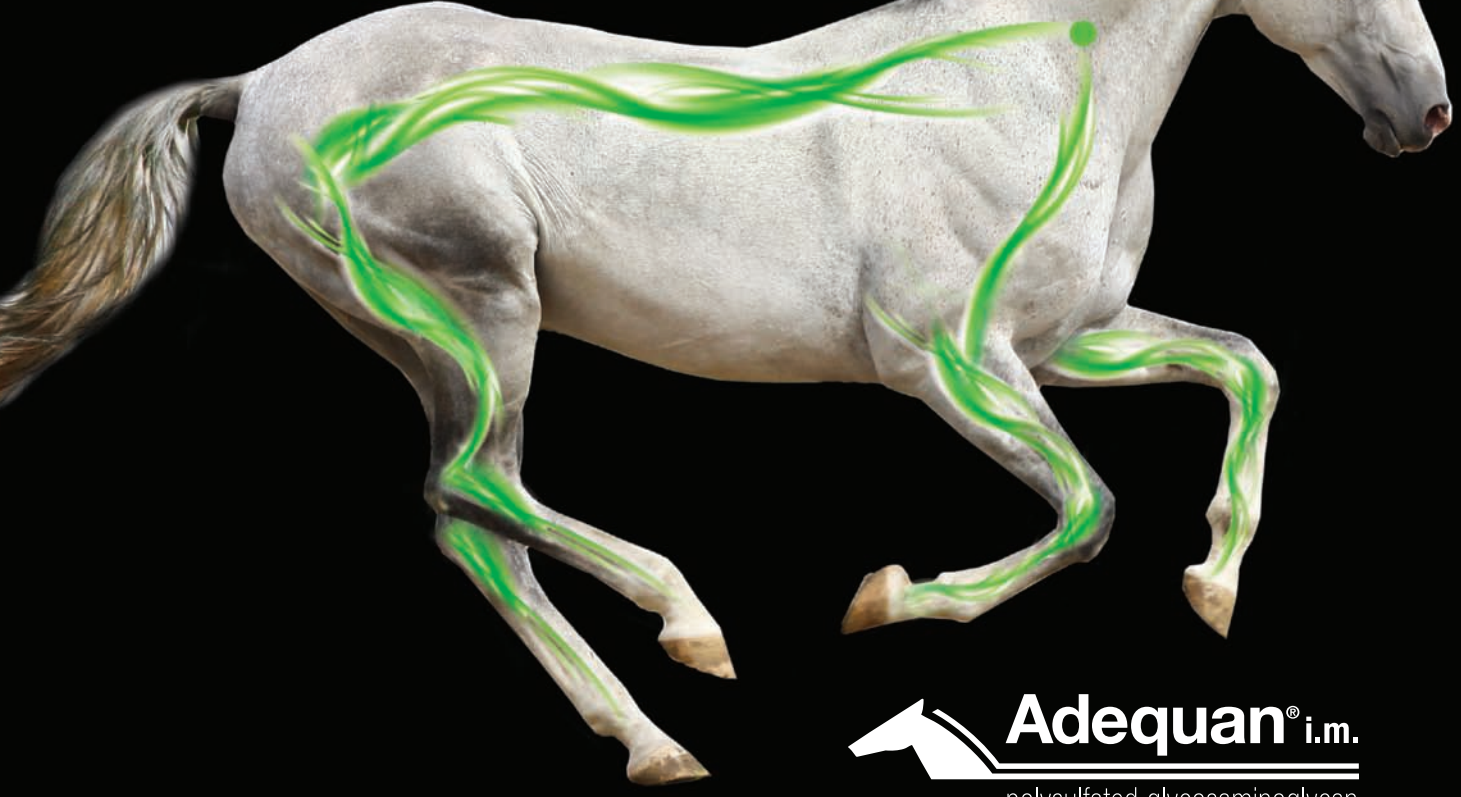
Infectious causes include bacteria and fungi. Bacterial infections are more commonly diagnosed and treated. Fungal endometritis can be stubborn—more difficult to diagnose and to treat.

"We are usually performing an ultrasound examination of the reproductive tract to see where the mare is in her cycle and might have an indication of endometritis if we see a lot of fluid within the uterus," Freeman said. "However, sometimes infection is only found on a survey culture. In the Thoroughbred industry a culture is often required by stud farms when sending a mare to be served, since we are dealing with live cover and have to worry about the stallion's health as well."

If an infectious condition is discovered, treatment can be targeted accordingly.

"Over the years I've come to prefer use of systemic treatment in conjunction with uterine infusions and/or lavage," Bailey said. "We might keep mares on systemic antibiotics for a 10-day period."

"Recent research suggests some mares develop biofilms with bacterial endometritis, which are difficult to culture and treat," Freeman said. "Sometimes cul-



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LUITPOLD ANIMAL HEALTH

ture of these mares might be negative despite the presence of a biofilm and we need more targeted treatment to break down the biofilm."

Bailey said that often a biopsy will reveal a level of endometriosis not associated with an inflammatory cell picture that indicates bacteria, and the mare has a clean culture.

COURTESY HEATHER SMITH THOMAS

Dr. Claire Freeman conducting an endometrial biopsy

"This inflammatory condition in the uterus is not associated with infection," he said. "This is a common problem and can usually be treated successfully with anti-inflammatory drugs, without antibiotics (which will not correct non-infectious problems). We usually treat these mares with DMSO (dimethyl sulfoxide) and Dexamethasone to try to resolve the uterine inflammation, then do another biopsy in a month to see if we have corrected the condition."

One non-infectious cause of endometritis occurs in some mares after breeding. A normal mare should be able to clear fluid and debris from the uterus within 24 hours. "If you examine a mare more than 24 hours after insemination and she hasn't cleared the fluid yet, this indicates she has delayed uterine clearance or a persistent breeding-induced endometritis," Freeman said. "At that point we generally use uterine lavage or oxytocin to help her evacuate fluid from the uterus. We also wonder why she is having trouble clearing that fluid. Perhaps she's had several foals and has a pendulous uterus and is unable to evacuate fluid mechanically due to gravity. Or perhaps she cannot evacuate fluid because her uterus is not contracting enough to help expel the fluid."

It depends on the mare and the situation, but because Thoroughbred mares carry their own foals, delayed uterine clearance is more common than in embryo donor mares that carry fewer (or no) foals in their lifetime. "When mares have had lots of foals their uterus eventually drops lower in the abdomen and this becomes an issue," Freeman said.

URINE POOLING

"Older Thoroughbred mares that have had several foals and a pendulous uterus are also prime candidates for urine pooling," Freeman said. "These cases can be frustrating and might take several examinations to figure out. I've had some cases in which I was told the mare was pooling urine, but I might not see anything in the uterus at that examination. It depends on where the mare is in her cycle and what her cervix is doing—whether she is in diestrus and the cervix is closed, or in estrus and it is open. If I simply look at a mare at one point in time, it might not give me an accurate picture of what is going on. Owners and breeding farm managers need to realize that we might need to evaluate the mare on more than one occasion to get to the bottom of the issue."

ENDOCRINE PROBLEMS

Another thing to keep in mind, especially in older mares, is the possibility of Cushing's (pituitary pars intermedia dysfunction, or PPID).

"We are still not completely sure how this affects the reproductive cycle, but we know it can hinder fertility," Freeman said. "When trying to get an older mare ready for the next breeding season, especially mares older than 15, it's important to evaluate for signs of PPID, such as the mare's not shedding normally. It's wise to evaluate these mares and do the proper blood testing to know whether you are dealing with that issue."

Checking for PPID is becoming more common, especially with Thoroughbreds because owners breed a good mare well into her 20s if they can. You want a valuable mare to produce foals for as long as possible.

"We need to check for any endocrine problems that might affect their ability to cycle normally and get pregnant," she said.

ENDOMETRIAL CYSTS

Endometrial cysts might interfere with ability to carry a pregnancy, and this is a controversial topic.

"We're not sure if aged mares need to have the cysts removed in order to improve fertility," Freeman said. "If you talk to equine veterinarians doing a lot of reproductive work, some of them will tell you these cysts are not a problem at all, and others insist that they are."

The equine embryo migrates around in

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the uterus for a number of days after it comes down through the oviduct, before it attaches. This attachment or fixation, at the base of one of the uterine horns, occurs at day 16 post ovulation.

"The exact mechanism for maternal recognition of pregnancy, which occurs prior to that attachment, is still not known," Freeman said. "There is some thought that embryo migration and contact with the endometrium is a part of that recognition. So some people think that endometrial cysts might interfere with that migration and lead to failure to establish a pregnancy.

"If we ultrasound the mare at day 14 post ovulation and don't see a pregnancy, we are not sure if the embryo was never there (due to fertilization failure) or if it was lost due to failure of maternal recognition of pregnancy. So endometrial cysts, especially in aged Thoroughbred mares, are another issue that might be a factor. The jury is still out on this. I have seen many pregnancies in mares with huge cysts and the pregnancies develop just fine. But if we have evaluated everything else and a mare with cysts still has trouble conceiving, removing them might be something to consider."

LUTEAL INSUFFICIENCY

Another factor that might result in early embryonic death is insufficient progesterone.

"The corpus luteum (the structure formed on the ovary following ovulation) produces progesterone, a hormone that supports the pregnancy during early gestation until the placenta takes over this role. There is some debate regarding what level of progesterone is adequate to support pregnancy," Freeman said.

"We don't know if primary insufficiency (from the corpus luteum that's formed after ovulation) is a real issue because it has not been well documented in the veterinary medical literature. Some people put every bred mare on oral or injectable altrenogest, a synthetic progestin similar to progesterone, in case there is luteal insufficiency. In other situations mares might be started on altrenogest soon after ovulation because in the past they failed to conceive or because they seem to lose their pregnancies early. We don't know for sure that it always helps, but this is a common practice."

EARLY PREGNANCY LOSS

"Most early embryonic deaths (EED) occur prior to about 45 days. This seems to occur more often in older mares.

"We wonder if the oocyte itself, produced by the aged mare, or its DNA, could be damaged and doesn't create as viable an embryo," Freeman said.

PLUGGED OVIDUCT

There are a few mares that don't become pregnant even though everything appears to be normal.

"Culture, cytology, and everything else are normal, but the mare doesn't become pregnant when you breed her," Sheerin said. "You don't know whether it's a stallion issue or a mare issue, so you have to try to figure it out.

"Many diagnoses are made by exclusion. You culture the mare and it's negative. Her cytology, biopsy, reproductive conformation, cervix, etc. are good and everything is normal, but she's not getting pregnant. With that kind of history, we might try an oviduct flush, via endoscope."

There may be something obstructing the oviduct, and sperm can't travel up through it or even if they do, the fertilized egg can't pass down into the uterus.

In a certain number of mares this simple flushing resolves the problem, but it takes a lot of diagnostics (ruling out other problems) to get to the point that you'd decide to try this technique.

"These are mares that typically have been bred on several cycles and are not getting pregnant yet all the diagnostics show everything is normal—and then we try the oviduct flush, and it does the trick," Sheerin said.

GENETIC ABNORMALITY

A less common issue is a genetic abnormality.

"Perhaps the mare is not XY, but is XXY or has some other genetic reason she is not producing normal oocytes and not getting pregnant," Freeman said. "This is rare, but if you've evaluated everything else and done a culture and biopsy, and looked

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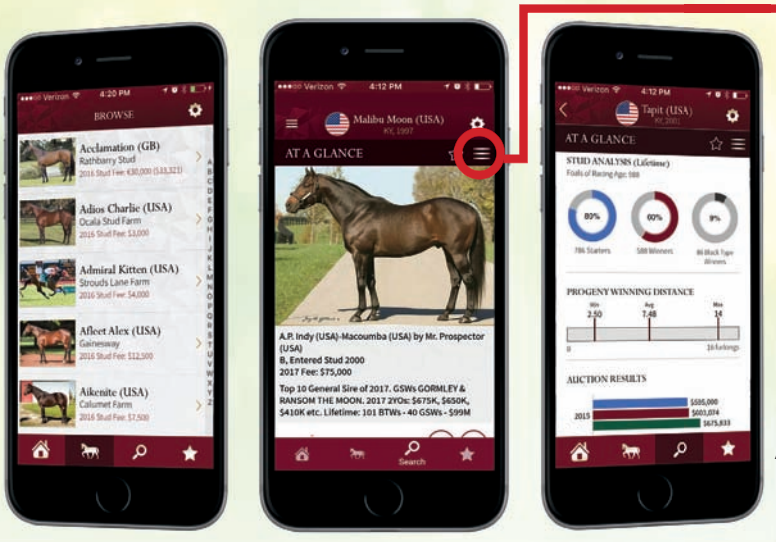

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CULTURES

Some veterinary practices and breeding farms do in-house cultures and sensitivity tests while others send the samples to a diagnostic lab.

"Sending it to a lab is probably the way to go when dealing with a stubborn case," said Dr. Claire Freeman of Royal Vista Southwest in Purcell, Okla. "If, based on history and ultrasound examination, I didn't expect a mare to have a problem, I would do the culture in-house. It might be a barren mare that had an obvious reason for why she didn't get pregnant last year; maybe the stallion had questionable fertility, or she had a late foal and we didn't breed her or only bred her once."

Routine cultures required by a stud farm for service might be performed in-house and checked in 24 or 48 hours.

"These mares usually do not have fluid within the uterus on ultrasound examination," she said. "The mares that have problems—chronically barren, or mares that have uterine fluid on ultrasound—are the ones I might culture in-house for my own interest, but also send to a lab for culture and identification of the pathogen and sensitivity testing.

"If treatment is required for a bacterial infection, I want to make sure I am treating with the appropriate antibiotic. Unfortunately, few labs provide sensitivity data for fungi, but proper identification is also crucial for targeted therapy. It gives me an idea about whether I am dealing with a *Candida* or an Aspergillus, and this may influence my treatment protocol," she said.

It is important for mare owners to understand that cultures are not always accurate indicators of infection.

"There will be some false positives if contaminants are picked up when taking the sample, and some false negatives—if you can't get bacteria to grow on laboratory media," said Royal Vista Southwest's Dr. James Bailey. "A veterinarian must look at the entire clinical picture. Many times we might not get anything to grow, but we are convinced something is there. Sometimes we'll lavage the mare and culture the lavage fluids and have success. It's not always as simple as just pulling a culture and getting all the answers."

—By Heather Smith Thomas

at every other reason why she might not be getting pregnant, this is something to keep in mind."

There are a few mares that have chromosome abnormalities, like equine Turner syndrome, in which a mare is missing one X chromosome (she is XO instead of XX). These mares have a total of 63 chromosomes, rather than 64. This defect can occur in all breeds and is the most common chromosome abnormality. These mares sometimes have smaller body size; small, inactive ovaries; and an under-developed reproductive tract.

Another abnormality is called sex-reversal syndrome, in which the horse has the outward appearance of a mare but is genetically male (XY instead of XX). This defect has been identified sporadically in Thoroughbreds and a few other breeds. These infertile "mares" might be bigger-bodied than most mares and have small, inactive ovaries.

"If a mare is examined in winter, when most mares are in anestrus and have small ovaries, you might not realize she has a genetic problem," Sheerin said. "Then in the spring you'd be waiting and waiting, but she won't come into heat, even after being under lights and use of exogenous hormones to try to get her to cycle. If her ovaries stay tiny, this might be due to a chromosomal defect; a chromosomal analysis would be needed to discover the problem."

If this is the case, she will never be a broodmare.

COURTESY HEATHER SMITH THOMAS

Bailey with a uterine biopsy sample

SUMMARY

Mares are individuals, and they don't read the textbook. Some of them have unique problems.

"When it comes to infertility issues, we have to evaluate every case individually, and utilize diagnostic tools available—palpation, ultrasound, culture, biopsy, blood/endocrine testing, genetic testing, etc.," Freeman said. "In many cases we need to do multiple evaluations; it can be difficult to look at a mare at one point in time and know exactly what the problem is." BH

Heather Smith Thomas is a freelance writer based in Idaho.