The Invisible Disease

A major cause of female infertility, endometritis affects up to 15% of broodmares

BY CHRISTA LESTÉ-LASERRE
ANNE M. EBERHARDT PHOTOS

Endometritis is an invisible disease. It affects the delicate lining of a mare's uterus—the endometrium—which can become inflamed and create a hostile environment for sperm, as well as any resulting embryo, to live. Thus, often the only clinical sign of endometritis is not what you do see but what you don't see: a pregnancy. Endometritis is a major cause of female infertility, affecting up to 15% of broodmares. But because it frequently lacks clear clinical signs, it often goes undiagnosed.

The health and soundness of both mare and foal is among the biggest concerns at Thoroughbred breeding and foaling operations

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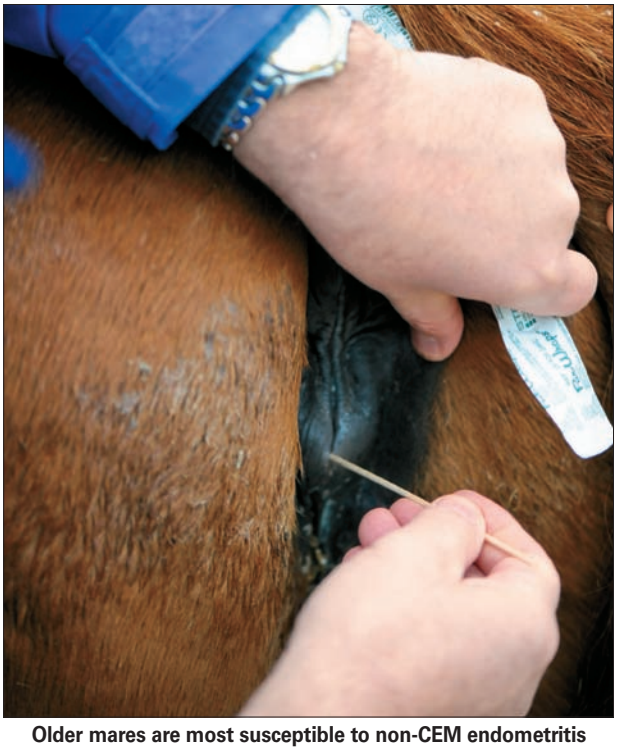
Inflammatory Responses of the Uterus

The mare's uterus is well-protected physically, with the cervix, vestibular-vaginal sphincter (hymen), and vulva lips all serving as effective barriers against contaminants such as feces, urine, and bacteria. However, these contaminants can still enter the uterus during mating, as well as during estrus or veterinary procedures. To clear contaminants and dead sperm after breeding, the uterus sets off a natural inflammatory response. This acute form of endometritis is a healthy, effective cleaning system that summons an army of white blood cells (leukocytes) to attack and kill bacteria and rid the mare of dead sperm. The debris is then expelled from the uterus, which returns to its normal, uninflamed state. In healthy, fertile mares this process takes less than two days, said Dr. Irwin Liu, professor of equine reproduction and theriogenology at the University of California, Davis.



Older mares are most susceptible to non-CEM endometritis

However, mares with a delayed inflammatory response do not react immediately to the contaminants, allowing them to settle in the uterus and, in the case of bacteria, reproduce. The result is enhanced inflammation three or four days later, with secondary infection. Referred to as chronic or persistent endometritis, this is the condition that leads to infertility, said Liu, who, together with Dr. Mats H.T. Troedsson, director of the Maxwell H. Gluck Equine Research Center at the University of Kentucky, recently published a review of equine endometritis diagnosis and treatment.

Mareswithsignsofpersistentendometritis are often called "susceptible mares."

Effects on Fertility

The primary problem associated with endometritis is poor evacuation of the uterus, with retained fluid. Some mares can have as much as two to three centimeters of fluid built up in the uterus. This appears to be related to the myoelectrical activity within the uterus—involuntary muscle spasms and contractions. When the myoelectrical activity functions improperly, the uterus does not react to the semen and bacteria as it should (immediate inflammation of the endometrium). Thus, it does not create the contractions that would expel the fluids.

In fertile mares the vast majority of the fluid is pushed out of the uterus within six to 12 hours of insemination and is gone entirely within 48 hours, according to Dr. Michelle LeBlanc, theriogenologist at Rood & Riddle Equine Hospital in Lexington.

When fluid remains stagnant in the equine uterus, it weakens the effect of the bacteria-fighting white blood cells, LeBlanc said. It also flattens out the normal folds along the endometrial surface, which is lined with tiny hairlike structures called cilia. When the folds are flattened out, it is much harder for the leukocytes to attack the bacteria, and the cilia become far less effective in sweeping contaminants toward the cervix. Bacteria stick more easily to damaged areas of the endometrium, especially if the protec-

tive mucous blanket has been thinned or eliminated due to persistent inflammation.

Causes

Endometritis is not contagious, except with cases of the sexually transmissible disease contagious equine metritis (CEM). Unlike other forms of equine endometritis, CEM usually produces an obvious vaginal discharge in the mare.

The primary causes of non-CEM endometritis are structural defects of the reproductive tract, inadequate uterine contractibility, and continuous inflammation, according to LeBlanc.

By far the most common group of affected mares includes older ones that have had several foals.

"Repeated foaling and breeding can cause anatomical defects," LeBlanc said.

These include vaginal stretching, incompetent cervix, incompetent sphincter muscles, and poor perineal conformation.

Older mares also might experience a natural phenomenon of aging termed "inflamm-aging," she said. The condition causes increased inflammatory cytokine (mediator) production. The exact impact of inflamm-aging on fertility remains unknown, but researchers are investigating the connection.

Mares that have experienced abortion or a difficult foaling could have a damaged cervix and thus be more susceptible to uterine infections. Cervical malfunction also occurs frequently in older mares (older than 10 years) that have never foaled.

Diagnosis

Occasionally mares will show signs of infection such as frequent heat cycles or, rarely, vaginal discharge. However, many mares have no clinical signs, or signs that only are apparent during certain phases of the heat cycle, and so are said to have "subclinical" endometritis, LeBlanc said.

The most valuable tool in diagnosing endometritis is ultrasound technology, according to Liu.

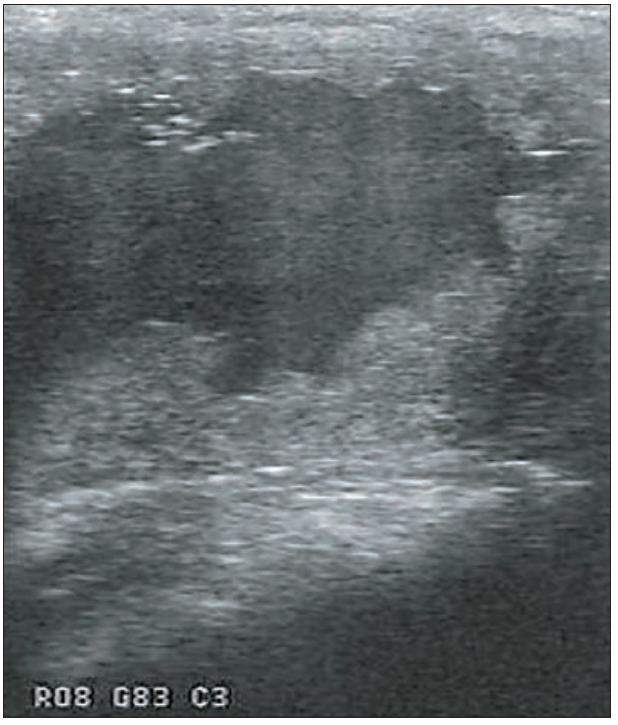
"Since its inception, the use of ultrasonography in reproduction has made a profound impact on our ability to detect the presence of intrauterine fluid in the mare, as well as its severity," he said.

Ultrasound reveals not only the amount of fluid in the uterus, but also provides clues about its character and density. It can reveal differences between susceptible and fertile mares within six to 12 hours after breeding.

Endometrial biopsies are more than twice as accurate in diagnosing infection or inflammation as traditional culture swabs, LeBlanc said. Biopsies also give clues as to the cause of the disease and help the veterinarian determine treatment strategies. However, biopsies can occasionally "miss" the infection site if taken from an unaffected part of the uterus.

Uterine lavage (flushing) is a reliable detection method that also gives specific details about the kind of infection. The lavage procedure involves filling the uterus with sterile fluid and flushing it out, retaining the contents for analysis.

Even so, some mares with subclinical endometritis will have such varying and vague clinical signs that they will need to be tested several times before the veterinarian arrives at a



COURTESY DR. PETER SHEERIN

An ultrasound image reveals fluid in the uterus that could cause endometritis; the mare will be treated with oxytocin to stimulate the uterus to expel the fluid

positive diagnosis. "Meticulous records are needed…to identify a pattern of subtle abnormalities that repeat cycle after cycle," LeBlanc said.

No conclusions should be made on laboratory results alone, however. An accurate diagnosis requires laboratory data, a physical examination, and a case history of the mare's health and fertility.

Treatment

The kind of treatment plan a veterinarian chooses might vary, depending on what has caused the endometritis, said Liu. But the primary goal remains the same: Improve the function of clearing out the uterus. This generally means increasing uterine contractility.

Medications can be infused directly into the uterus to fight infection, and this is often a first step in fighting endometritis. The technique has proven beneficial in cases of bacterial growth in the uterus, Liu said. However, long-term use of these antimicrobials can lead to the development of fungal endometritis, which must then be treated with an antifungal agent.

The goal of the breeding cycle is a healthy foal

Many practitioners will use diluted disinfectants instead of antimicrobials, but their efficacy is currently in question among researchers, said Liu. Autologous/heterologous or platelet-rich plasma is sometimes infused to help the immune system attack bacteria.

Another common treatment is "chemical curettage"—exposing the uterine lining to chemical agents such as hydrogen peroxide, magnesium sulfate, povodine-iodine solution, and dimethyl sulfoxide, followed by uterine lavage. These agents can cause significant inflammation and enhance the effect of uterine contractions. Many of them probably also kill bacteria. Through this technique, the surface lining of the endometrium is debrided (dead tissue removed) and then regenerates within two to three days after treatment. However, a veterinarian performing this procedure should do so with care to avoid scarring and uterine adhesions.

The success of all these infection-annihilation techniques remains limited so long as the uterus is not being evacuated, according to Liu.

"Regardless of how effective the antimicrobial effect, uterine clearance and optimal uterine contractility are necessary ingredients for a successful outcome," he said.

When mares cannot clear infection on their own, a veterinarian can attempt to clear the uterus artificially, as with uterine lavage. This technique is not only a good diagnostic tool, but also has proved to be an effective treatment option as well, especially when combined with ecbolics, agents that stimulate uterine contraction.

> ***"Repeated foaling and breeding can cause anatomical defects."***
> DR. MICHELLE LEBLANC

Ecbolics—primarily oxytocin and prostaglandin—also are used to enhance labor or induce abortion. They have been shown to effectively treat endometritis by causing stronger contractions to help clear the uterus of debris. However, their use could also present pregnancy risk if used after ovulation, said Liu.

Ideally, a susceptible mare should

Dr. Michelle LeBlanc (right) is a theriogenologist at Rood & Riddle Equine Hospital in Lexington

undergo uterine lavage four hours after mating or insemination, combined with ecbolic treatment if she still has not ovulated by that time, he said. But even if she has ovulated, ecbolics should be considered if lavage alone does not clear the uterus.

A veterinarian should monitor all susceptible broodmares closely using ultrasound during their heat cycles—preferably every day or every other day, to check for fluid, ovulation, and response to treatment, according to LeBlanc. They also should examine the mares using ultrasound 18-24 hours after insemination or mating to evaluate the level of inflammation and fluid buildup.

New Research

Veterinarians have observed that newly approved immune stimulants are useful for treating persistent endometritis. Corticosteroids are also being introduced as a treatment for this disease, and recent study results have been "encouraging," Liu said.

Electroacupuncture is another technique veterinarians are testing clinically as a means to enhance uterine contractions.

At this year's International Symposium on Equine Reproduction, held in July in Lexington, Liu's laboratory revealed evidence that suggests one cause of poor uterine contractility could be compromised uterine blood flow in mares that have had several foals. Finding an effective treatment to increase circulation to the uterus is an ongoing project, he said.

LeBlanc and her colleagues compared scanning electron microscopic images of endometrial cells and their cilia. They compared those of fertile mares to those of susceptible mares, to help researchers better understand the effects of delayed uterine clearance on these cells and cilia.

Further research is still required to confirm efficacy and help researchers understand how these treatments work to fight endometritis.

Excerpted from The Horse: Your Guide to Equine Health Care. Free weekly newsletters at *www.TheHorse.com*

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