How to Maximize the Chances of Breeding Successfully From the Older Maiden Mare

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1. Introduction
Reduced fertility associated with fluid accumulation has been recognized for many years in broodmares. This subfertility is caused by an unsuitable environment for the developing conceptus within the uterus, and in some cases, the ensuing endometritis persists and causes early regression of the corpus luteum (CL). Persistent mating-induced endometritis has come to be recognized as a major reason for failure of conception in mares. Recently, it was stated that persistent sperm-induced inflammation may be a more important cause of infertility in susceptible mares than infectious endometritis.1

2. Pathogenesis
It is particularly important to recognize and manage appropriately the older maiden mare. Although they have never been bred before, these mares, in many cases, are susceptible to post-breeding endometritis. Many times, mares that have had a showjumping or dressage career may not be presented to be bred until they are in their teens, and these older maiden mares can be very difficult to get in foal. Many of these mares have some common characteristics that resemble a syndrome. Endometrial biopsy samples reveal glandular degenerative changes and stromal fibrosis (endometrosis) as an inevitable consequence of aging, despite the fact they have not been bred.2 Another common characteristic of these mares is uterine fluid. An older maiden mare often has an abnormally tight cervix that fails to relax properly during estrus; as a result, fluid is unable to drain, and it accumulates in the uterine lumen.3 In many cases, this fluid is negative for bacterial growth and presence of neutrophils (PMNs). After the mare is bred, the fluid accumulation will be aggravated because of poor lymphatic drainage and impaired myometrial contraction compounded by the tight cervix. The amount of intrauterine fluid will vary in individual mares, and it ranges from a few milliliters to more than a liter in extreme cases. Recently, endometrial vascular degeneration has also been considered a contributing factor in the delay in uterine clearance.4 To maximize the fertility of these mares, it is vital that the veterinarian is aware of the possibility of this type of uterine and cervical pathology. Many times, owners assume that the fertility of these mares is comparable to that of young maiden mares; one of the most important aspects of breeding the older maiden mare is to make the owner aware that there is a high possibility that she will have difficulty conceiving.
These mares must be considered highly susceptible and managed accordingly.

3. Diagnosis of the Fluid-Producing Mare

Diagnosis can be difficult, because there may only be subtle changes in the uterine environment that are not readily detected by current diagnostic procedures. Many mares show no signs of inflammation before breeding but will fail to resolve the inevitable endometritis that follows mating. Response to bacterial challenge has been used in a research setting. Demonstration of clearance failure using scintigraphic and other methods based on charcoal clearance has been used to make an accurate diagnosis of a mare that has a clearance problem, but they are difficult to apply in practice.

History of repeat breeding and/or fluid accumulation at the time of breeding is perhaps the most useful indicator of a susceptible mare in practice. Ultrasound detection of uterine luminal fluid has proved useful in identifying mares with a clearance problem. The presence of free intraluminal fluid before breeding strongly suggests susceptibility to persistent endometritis. Generally, if there is >1 cm of fluid during estrus, some attempt should be made to remove it before breeding using oxytocin. If the volume is >2 cm, the fluid may need to be drained and investigated for the presence of inflammatory cells and bacteria. The mare may then need to have a large-volume uterine lavage before breeding. Significant intrauterine fluid present in the early post-breeding period (4–8 h after breeding) may also be an indication of poor uterine clearance. If intrauterine fluid is visible using ultrasonography >18 h after breeding, the mare should be diagnosed with defective uterine clearance. Intrauterine fluid during diestrus is indicative of inflammation and associated with subfertility because of early embryonic death and a shortened luteal phase.

4. Treatment Options for the Older Maiden Mare

The aim of the treatment should be to assist the uterus in physically clearing the normal inflammatory by-products of the response to breeding. Both coitus and artificial insemination can be a source of uterine inflammation. It is well known that spermatozoa are responsible for initiating a marked inflammatory response that leads to a persistent endometritis in susceptible mares. Therefore, susceptible mares should only be bred one time, regardless of whether natural mating or artificial insemination is used.

Within 4 h of mating, the spermatozoa necessary for fertilization are present within the oviduct. The embryo does not descend into the uterus for ~5.5 days; therefore, mares may be treated safely from 4 h post-mating until 2 days post-ovulation, providing that isotonic solutions are used. Progesterone concentrations rise rapidly after ovulation, and it is preferable to avoid treatment involving uterine interference after 2 days post-ovulation. The successful management of older mares should logically require some form of post-mating therapy such as uterine lavage, IV oxytocin, or intrauterine antibiotic infusion. These therapies may be used alone or in combination. For the susceptible mare, treatment should be implemented in the post-breeding period rather than after ovulation. In the period between breeding and ovulation, the susceptible mare frequently accumulates a large volume of fluid, and bacteria are in a logarithmic phase of growth. Therefore, expedient treatment of these mares is critical to fertility.

Oxytocin

Oxytocin is the ideal method of treatment; it is a non-invasive technique and frequently provides early and complete elimination of any intrauterine fluid. The beneficial effect of oxytocin is widely accepted. Oxytocin stimulates uterine contractions in the cyclical, pregnant, and post-partum mare. This therapy was first suggested to promote uterine drainage in mares with defective uterine clearance by Allen. Oxytocin is now widely accepted as an effective therapy in aiding mechanical clearance mechanisms and improving fertility. In a recent study in reproductively normal mares, reported this finding. The dose of oxytocin used by the author in mares ~500 kg is 20 IU given either IV or IM. Smaller mares are given 15 IU of oxytocin.

Recently, a long-acting analogue of oxytocin, carbetocin,* has become available in the United Kingdom and may have an indication where a more prolonged uterine contraction is desired. Preliminary work in the author’s practice has shown it to be safe and effective at inducing uterine clearance. Two IM injections of 0.14 mg carbetocin are given 12 h and 24 h post-breeding in mares with marked uterine edema or free fluid before breeding or in mares with uterine fluid >2 cm deep 12 h post-breeding.

Uterine Lavage

Uterine lavage is a useful tool to aid in the mechanical evacuation of the uterine contents. The technique involves infusing ~1 l of previously warmed (42°C) sterile physiological (buffered) saline or lactated Ringer’s solution into the uterus using a catheter that has been retained within the cervix.
through a cuff. The fluid is then siphoned out of the uterus by gravity flow. This process is repeated two to four times or until the effluent is clear.

The optimum time for uterine lavage therapy in highly susceptible mares was found to be between 4 and 6 h in a study by Knutti et al.17 Eighteen barren mares with a mean age of 15 yr were selected. They had been barren for >1 yr, had been inseminated during more than six estrous periods, had a history of fluid after breeding, and had failed to become pregnant with the standard protocol for management as described above. In nine mares, the standard protocol was repeated (control). In the other nine mares, the standard protocol was performed, but the mare’s uterus was flushed 4–6 h after insemination. Twice as many mares with the early lavage were pregnant compared with the group of mares not lavaged until 18–20 h after insemination. The results of this study correlate with the findings of Brinsko et al.5 that a uterine lavage performed 4 h after insemination does not adversely affect conception rate.

In our practice, known susceptible mares are routinely lavaged the day after breeding. Working on the principle that the longer a foreign particle stays in the uterine lumen, the more PMNs accumulate, earlier treatment should reduce the inflammatory reaction and improve the chances for these susceptible mares to get pregnant. Mares believed to be highly susceptible to endometritis based on history or fluid accumulation should have the lavage performed within 4–6 h.

Prostaglandin Analogues
Prostaglandins are known to be released from the endometrium very early in mares with endometritis.18 The useful role of prostaglandin in increasing myometrial activity and assisting uterine clearance has been shown.19–21 On one hand, Cadario et al.20 and Combs et al.21 showed that the prostaglandin analogue cloprostenol caused increased clearance of radioisotopic fluid in susceptible mares but at a significantly slower rate than that caused by oxytocin. On the other hand, cloprostenol caused the uterus to contract for a longer time (5 h) than oxytocin (45 min). Of the prostaglandins administered (PGF2-alpha, cloprostenol, and fenprostalene), cloprostenol produced the most consistent response. Cloprostenol is indicated in mares that have lymphatic stasis as shown by excessive edema within the endometrium or large lymphatic cysts.22 The suggested dose is 250 µg cloprostenol given at 12 h and 24 h after breeding.4 Cloprostenol should not be given after ovulation to avoid inducing premature luteal regression.4

Intrauterine Antibiotics
The infusion of broad-spectrum antibiotics after breeding is controversial.11,23 In scientific experiments using an endometritis model, it has been shown that saline lavage and uterotonic drugs such as prostaglandin F2-alpha are as effective as antibiotics in eliminating bacteria from the uterus.19 However, this was a controlled experimental-type situation in which a single bacterial species (usually streptococci) was infused into the uterus, and lavage treatment was performed at a fixed time (within 12 h of mating).

Under live mating conditions, there is a mixed bacterial contamination, and lavage cannot always be performed within 12 h. For these reasons, the author prefers to use intra-uterine antibiotics as part of the therapeutic protocol. The treatments have different effects on the uterus: the uterine lavage provides mechanical evacuation of intraluminal fluid and inflammatory products, whereas the single infusion of broad-spectrum antibiotics should prevent any growth of bacteria introduced during insemination or uterine lavage. Furthermore, mares susceptible to post-breeding endometritis have, according to their history, a reduced capacity of uterine clearance and defense mechanisms. Therefore, they cannot be compared with healthy mares used in experiments. Routine administration of intrauterine antibiotics has no negative effect on the pregnancy rate of treated mares.10,23

How to Breed the Mare That Accumulates Fluid
Overall management of such mares must be excellent before breeding.

A. Hygiene
Gynecological procedures should be performed as aseptically as possible. Thorough digital examination of the cervix can identify fibrosis, lacerations, or adhesions that may need treatment before breeding. If feasible, the use of artificial insemination with fresh semen can be helpful to reduce (but not eliminate) the inevitable post-breeding endometritis.

B. Correct Timing of Breeding
Breeding should only occur once and at the optimal time. Mares need very close monitoring of the estrus period by rectal palpation and ultrasonography. Prediction of ovulation is made easier by not breeding these mares too early in the year before they have begun to cycle regularly. The use of ovulation-induction agents is recommended to ensure they are only bred one time. Most stallion spermatozoa are viable at least 48–72 h after mating.24 Early mating allows more time for drainage of fluid through an open estrous cervix and also uses the natural resistance of the tract to inflammation during estrus. It allows sufficient time to flush the mares more than once before ovulation if necessary. Although uterine lavage is possible after ovulation, it is more complicated, because the cervix starts closing. Moreover, the resistance of the tract is reduced, and the uterotonic effect of oxytocin is reduced because of the increasing amount of circulating progesterone.25
C. Ultrasound Evaluation of the Uterus

The ultrasound is used for detection of intraluminal uterine fluid before mating. Even when sterile and free of neutrophils, mares with uterine fluid accumulation before mating have a reduced pregnancy rate when no treatment is performed. If >0.5 cm fluid is detected, administering 10–20 IU oxytocin as an IV bolus can aid in evacuating the uterus. Resolution of intraluminal fluid should be confirmed with a follow-up ultrasound examination. If intraluminal fluid is still visible, oxytocin is repeated. Digitally dilating the cervix can also help. If >2 cm of fluid is present, the uterus is lavaged as described earlier. Antibiotics before breeding should be avoided because of their possible irritant and/or spermicidal action.

D. Correction of Any Conformational Defects

In the normal mare, the vulva provides the first effective barrier to protect the uterus from ascending infection. If the vulval seal is incompetent, aspiration of air and contamination into the vagina can occur. The initial vaginitis may lead to cervicitis and acute endometritis resulting in subfertility. Treatment should be directed at correcting the cause of pneumovagina and concurrently treating the resulting acute endometritis. The former can be done surgically by Caslick’s operation.

E. Post-Breeding Management

Any treatment regimen must be based on the particular individual mare. No standard approach can be given. Susceptibility to endometritis is not an absolute state: failure of the defense mechanisms only needs to be of the degree necessary to slow the process of clearance past a critical point. In mares highly susceptible to post-breeding endometritis, ultrasound examinations of the uterus should begin within 4–8 h of breeding. Examination of all other mares can be performed the day after mating to assess the amount and echogenicity of intrauterine fluid. The first line of defense with mares having <2 cm intraluminal uterine fluid after breeding is administration of oxytocin. Typically, 20 IU of oxytocin are administered every 4–6 h IM. This treatment can easily be accomplished by the stud-farm personnel.

If >2.0 cm of fluid is present in the uterine lumen, uterine lavage is performed. Uterine lavage is followed by administration of 20 IU oxytocin, IV or IM. In cases where the cervix has failed to relax adequately, digital dilation of the cervix with scrupulous attention to cleanliness is indicated. This is followed by infusion of a low volume (25 ml) of water-soluble, broad-spectrum antibiotics instilled through the cervix into the uterus through a sterile irrigation catheter. Further doses of 20 IU of oxytocin are given every 4–6 h.

In mares with lymphatic stasis, the slower release of prostaglandin (cloprostenol; 250 mcg, IM) or carboplatin (0.14 mg, IM) may be useful in addition to oxytocin. The carboplatin or cloprostenol should be given no earlier than 6–8 h after the first oxytocin injection. The mare is reexamined the following day, and oxytocin treatment is repeated if fluid is still present. Only rarely will a second infusion of antibiotics or lavage procedure be performed because of the risk of uterine contamination. The important concept is to treat in relation to breeding and not wait for ovulation.

References and Footnotes


*a*Reprocine, Vetoquinol UK Ltd., Buckingham, UK.

*b*Zent W. Personal communication. 1993.