

# Managing cervical impairment in the mare: a case study



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## Abstract

A 10-year-old Quarter horse mare was presented for breeding management. Mare had no previous reproductive system examination. No apparent problems were noticed during initial reproductive system examination at presentation. Mare was artificially inseminated with cooled transported semen. Minimal uterine fluid accumulation was evident postbreeding and the cervix appeared closed; uterine lavage was performed. Fourteen days postovulation, mare was examined for pregnancy. Large volume of cellular fluid was present in the mare's uterus with no evidence of pregnancy. Endometrial culture and cytology results suggested bacterial endometritis. Therapy included daily large volume uterine lavage, systemic and intrauterine antimicrobials, ecbolic agents, and topical application of butylscopolamine bromide over the cervix. On a subsequent posttherapy estrus, uterus was lavaged before and after insemination and butylscopolamine bromide was applied topically over the cervix to facilitate cervical relaxation and expulsion of uterine fluid. Two bilateral embryonic vesicles were observed during pregnancy diagnosis and 1 was reduced successfully. Mare carried a healthy singleton fetus to term and foaled a healthy colt.

**Keywords:** Mare, cervix, uterus, bacterial endometritis, uterine lavage

## Background

Equine cervix is an important structure that acts as a defense mechanism for the uterus.<sup>1-3</sup> Cervical impairment in the mare is challenging and moderately common in the middle-aged maiden mare. Failure of the cervix to fully dilate in estrus typically results in fluid accumulation in the uterus, especially postbreeding, that may lead to uterine infections and subsequent subfertility. Due to the muscular nature of the cervix, manual dilation can be performed to treat this condition.<sup>4,5</sup> Adjunct treatments include local topical pharmacologic agents, most notably, misoprostol (PGE1) or butylscopolamine bromide (Buscopan®, Boehringer Ingelheim, Vetmedica Inc., St Joesph, MO). Misoprostol aids in cervical ripening in women and many domestic species, and is commonly used in mares.<sup>5</sup> Butylscopolamine bromide causes smooth muscle relaxation and is labeled for parenteral use in spasmodic colic. Topical application for cervical relaxation remains anecdotal. We successfully used butylscopolamine topically for cervical relaxation in the breeding management of a mare that apparently had cervical impairment.

## Case presentation

### History

A 10-year-old Quarter Horse/Paint Horse mare was presented for breeding management. The mare was recently retired from an athletic career due to substantial coffin joint osteoarthritis.

Mare had not been bred previously. To hasten ovulation, mare was maintained under artificial lighting for a period of 3 months prior to presentation.

### Clinical examination

Initial evaluation of the mare revealed an overall good body condition score (6/9). Mammary glands were small and consistent with a nulliparous mare. Perineal conformation was good and the mare had excellent apposition of vulvar lips with no vulvar discharge. Mare's reproductive tract was evaluated via transrectal palpation and ultrasonography. Cervix had moderate tone and uterus had mild tone with a trace of edema of the uterus without intraluminal fluid. Both ovaries had small follicles and a corpus luteum was visualized in the left ovary. It was determined that the mare was in diestrus. Mare was given 250 µg of cloprostenol sodium (Estrumate®, Merck Animal Health, Madison, NJ) intramuscularly to hasten return to estrus. Because the mare was a maiden, there was no indication to perform culture and cytology, as no potential fomites had passed the cervix. Mare's reproductive tract was examined every day via transrectal palpation and ultrasonography. Six days after cloprostenol treatment, a 40 x 35 mm follicle was identified in the left ovary. Edema was noted in the uterus with 5 mm of anechoic intraluminal fluid and the cervix appeared mildly dilated. Mare was given intramuscularly 1.8 mg of deslorelin

acetate (Sucromate®, Thorne BioScience LLC, Louisville, KY) to induce ovulation and 20 IU of oxytocin intramuscularly 3 times daily, to aid in uterine clearance. Mare was inseminated with 40 ml of cooled transported semen 24 hours after deslorelin treatment. The insemination dose contained  $1.3 \times 10^9$  progressively motile, morphologically normal sperm. Oxytocin treatment was continued every 8 hours for 24 hours after insemination for uterine clearance. Mare's reproductive tract was evaluated 24 hours after insemination via transrectal palpation and ultrasonography. A corpus luteum was identified in the left ovary indicating recent ovulation. A moderate amount of cellular fluid was visualized in the uterus and uterine body (Figures 1). Mare's uterus was lavaged using 5 liters of sterile saline (0.9% NaCl). The initial fluid return was mildly cloudy and was recovered with intravenous oxytocin treatment. It was presumed that the intraluminal fluid accumulation in the uterus was due to lack of cervical dilation and the problem was resolved with uterine lavage. Mare was discharged with plans to return 14 days after ovulation for pregnancy diagnosis.

Mare's reproductive tract was examined via transrectal palpation and ultrasonography at 14 days postovulation for evidence of pregnancy. Multiple small to medium follicles were noted on both ovaries and a corpus luteum was identified in the left ovary. Cervix felt toned and elongated. Mare's uterus was palpably toned and mild edema was identified. Substantial amount (up to 50 ml) of moderately echogenic fluid was detected in the uterine lumen, predominantly in the right uterine horn. Fluid was also noted in the vagina. An embryonic vesicle was not detected. Uterine cytology had marked neutrophilic inflammation with intracellular bacteria. *Streptococcus equi* spp *zooepidemicus* was isolated from a bacterial culture of uterine fluid. Fungal elements were not noted from either uterine cytology or culture. Mare was diagnosed with bacterial endometritis.

## Treatment

Plan for endometritis treatment was multi-faceted; included daily uterine lavage for 5 days, ecbolic agents, and antimicrobial treatment based on culture and sensitivity. Initial uterine lavage, using 5 liters of sterile 0.9% NaCl solution, was performed on the first day. Fluid was infused into the mare's uterus, 1 liter at a time, and effluent recovered. The effluent was initially mucoid and opaque in nature but became watery and more translucent with repeated lavage. Fluid return was adequate during the first 2 days, but became more difficult to recover by the third lavage. Immediately after uterine lavage each day, 5 million IU K+ penicillin reconstituted in 50 ml sterile water was infused into the mare's uterine lumen. Additionally, due to bacterial sensitivity to ceftiofur, the mare was intramuscularly treated with 3.2 gm ceftiofur crystalline free acid (Excede®, Zoetis, Kalamazoo, MI). Despite appropriate lavage therapy and use of ecbolic agents, intraluminal fluid retention persisted on day 3 of treatment, largely due to poor cervical dilation. Digital evaluation of the cervix during uterine lavage on day 3 revealed a poorly relaxed cervix that was tortuous.

On day 4 of treatment, to aid in cervical muscular relaxation, 60 mg (3 ml) of butylscopolamine bromide (Buscopan®) was mixed with 1 ml sterile lubricant and infused into the cervical lumen via a sterile artificial insemination pipette. The mixture was massaged into the cervix, and cervical relaxation was digitally induced immediately after application. Butylscopolamine bromide is a smooth muscle relaxant labeled for use in spasmodic colic episodes, and also has anecdotal evidence of cervical relaxation. This treatment was used with the 2 subsequent uterine lavages. In addition to cervical massage and relaxation, fluid recovery was managed by manipulating the catheter into the base of the horn by deflating the cuff and by using digital guidance in the cervix. Fluid was transrectally massaged to the catheter

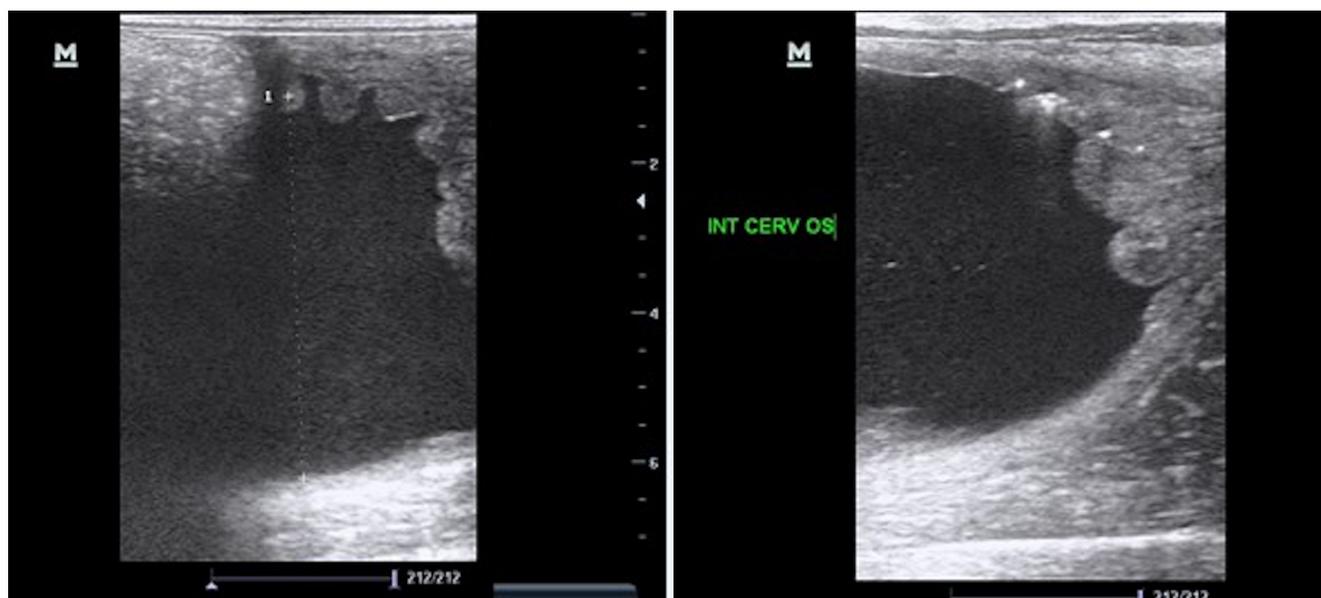


Figure 1. Transrectal ultrasonogram of uterus; note substantial fluid accumulation in the uterine body (right)

tip. The process was repeated on day 5 of treatment and fluid recovery was confirmed by transrectal ultrasonography. Mare was intramuscularly treated with 20 IU of oxytocin 3 times daily for all 5 days of treatment, to aid in uterine evacuation. Ecboic agents were given 4 hours after antimicrobial infusion. Mare received 250 µg of cloprostenol on day 1 of treatment to hasten return to estrus and on day 4 of treatment for of its ecboic potency.

Mare was evaluated 15 days after treatment to determine if the bacterial endometritis had been resolved and for possible breeding management. Mare's reproductive tract was evaluated via transrectal palpation and ultrasonography. Both ovaries were active, and the cervix was toned. Uterus had soft tone palpably, mild edema, and was free of intraluminal fluid. Endometrial cytology had rare degenerate neutrophils but no evidence of bacteria. Endometrial culture had no bacterial growth. Bacterial endometritis that was noted had resolved. Mare was given 250 µg of cloprostenol to hasten return to estrus. On day 3 after treatment, the mare began to exhibit signs of estrus when exposed to a teaser stallion, as evidenced by clitoral eversion, urination, and posturing. Daily evaluation of the mare's reproductive tract revealed mild uterine edema and trace amounts of anechoic intraluminal fluid. Intramuscular 3 times daily oxytocin (20 IU) treatment was initiated.

On day 7 after cloprostenol treatment, 1.8 mg of deslorelin acetate was given to induce ovulation. Butylscopolamine bromide (60 mg in 3 ml) was mixed with 1 ml sterile lubricant and infused into the cervical lumen via a sterile artificial insemination pipette, and uterine lavages with 5 liters of 0.9% NaCl began 24 hours before insemination. Mare was inseminated with 39 ml of cooled transported semen 24 hours after deslorelin treatment. The insemination dose contained  $1.5 \times 10^9$  progressively motile morphologically normal sperm. Six hours after insemination, butylscopolamine bromide was again applied to

the cervix, and a postbreeding uterine lavage was performed. A single dose of cloprostenol was given after lavage, as ovulation had not occurred, to aid in uterine clearance. Morning after insemination, double ovulation was documented on the left ovary. For 3 days following insemination, uterine lavage with 5 liters 0.9% NaCl was performed, with the aid of butylscopolamine bromide applied topically to the cervix. Oxytocin treatment continued 3 times daily throughout the mare's time in hospital. The mare was discharged with an appointment to evaluate for twin pregnancy.

## Outcome

Mare's reproductive tract was examined on day 14 postovulation for evidence of twin pregnancy. Multiple small to medium follicles were noted on both ovaries and 2 corpora lutea were identified on the left ovary. Cervix was toned and elongated and uterus was palpably toned, and no uterine edema or intraluminal fluid was identified. Two embryonic vesicles were located (Figure 2). A 16 mm vesicle was identified in the left uterine horn and a 14 mm vesicle was identified in the right uterine horn. Mare was given intravenously 500 mg flunixin meglumine, 60 mg butylscopolamine bromide, twice 150 mg of xylazine, and orally 20 ml altrenogest (Regumate®, Merck Animal Health, Madison, NJ). After multiple unsuccessful attempts to manually crush an embryonic vesicle, the procedure was discontinued. Mare was hospitalized overnight and a transrectal ultrasonography was performed the following morning. Mare had a 21 mm embryonic vesicle at the base of left uterine horn and an 18 mm embryonic vesicle at the base of right uterine horn. Using the ultrasound transducer, pressure was placed on the right embryonic vesicle until it was visibly flattened and a rapid downward motion applied with a successful embryo crush performed. Free fluid was noted in the base of the right uterine horn. Left uterine horn vesicle remained intact. Mare was given intravenously 500 mg flunixin meglumine and orally 20 ml altrenogest daily for 3 days after embryonic reduction. Mare

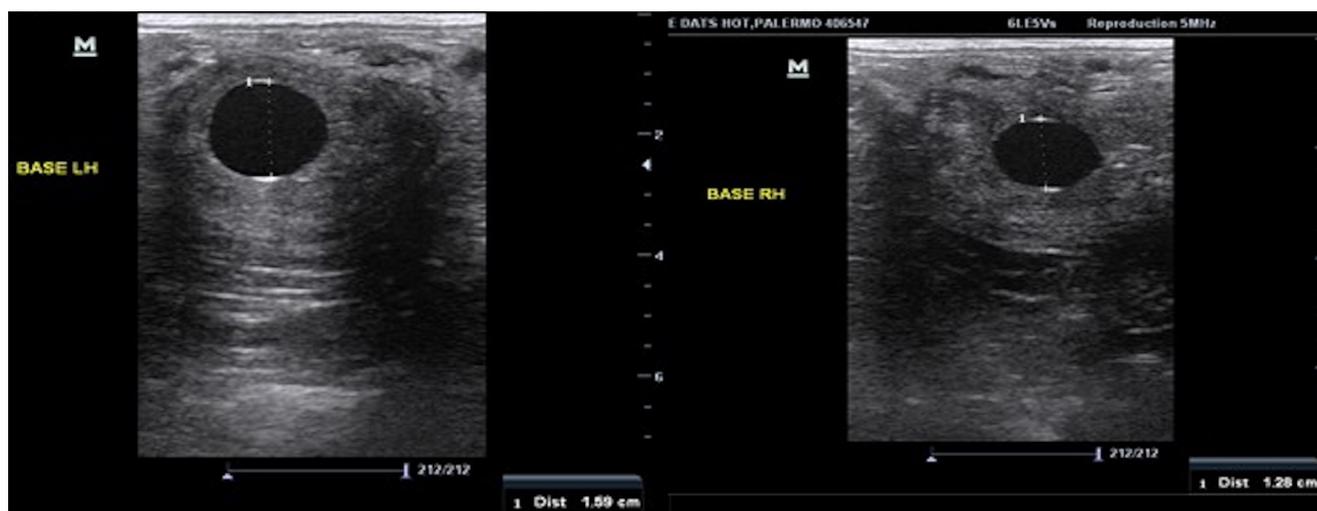


Figure 2. Transrectal ultrasonograms of uterine horns with embryonic vesicles in uterine horns

was discharged with directions to continue 10 ml of once daily oral altrenogest at a dose of 10 ml until the day of next pregnancy diagnosis.

Mare returned 29 days postovulation for pregnancy diagnosis after twin reduction. Transrectal palpation and ultrasonography revealed a good toned uterus and a palpable bulge was noted at the base of left uterine horn. Cervix was closed and a small amount of uterine edema was noted with no intraluminal fluid. Both ovaries had multiple small to medium sized follicles. An embryo, consistent with 29 days of pregnancy, was noted at the base of the left horn. An active embryonic heartbeat was detected. Mare was discharged with the recommendation to continue daily altrenogest treatment until her next pregnancy evaluation.

Mare returned on day 61 postovulation for pregnancy evaluation. Transrectal palpation and ultrasonography evaluation revealed a distinct bulge at the base of the left horn, consistent with 60 days pregnancy; the rest of the uterus, including the left uterine horn and cervix, had a good tone, and there was no evidence of uterine edema. A viable fetus with a heartbeat was visualized. The size and the position of the fetus were as expected for this stage of the pregnancy. Both ovaries were visualized and had small follicles. Altrenogest treatment continued through 120 days of pregnancy. Mare foaled a healthy colt in the spring of 2021.

## Discussion

*Streptococcus equi* spp *zooepidemicus* (*S. zooepidemicus*) is a beta-hemolytic gram-positive cocci, and the pathogen most commonly isolated from the uterus of mares.<sup>6</sup> *S. zooepidemicus* is an opportunistic pathogen and part of the resident flora in the caudal reproductive tract, and endometritis is frequently the result of an ascending infection. Poor anatomic conformation is generally associated with infection, as the bacteria must pass through the 3 anatomical barriers of the mare's reproductive tract, namely, the vulva, the vestibulovaginal sphincter, and the cervix. Furthermore, semen is not sterile, and although most commercial semen extenders contain antibiotics, bacterial contamination during artificial insemination is possible. Any intrauterine procedure may introduce bacterial pathogens into the uterus, despite efforts to maintain sterility.

Treatment of bacterial endometritis consists of appropriate antimicrobial therapy, along with uterine lavages and ecbolic agents. Oxytocin and cloprostenol treatment aid in uterine evacuation by stimulating uterine contractions. The effect is more pronounced and longer lasting with cloprostenol, and effects lasting up to 5 hours. Timing of treatment in relation to ovulation is important, as postovulation cloprostenol treatment was associated with decreased corpus luteum function.<sup>8</sup>

Embryo enters the uterus from the uterine tube between 5 and 6 days postovulation; therefore, the uterine environment must be conducive to maintaining a pregnancy by that point. Intrauterine antibiotic infusions are performed daily for 3 - 7 days, depending on the severity of infection. Uterine lavage is typically performed

for at least during the first 3 days to aid in clearing inflammatory products. Although these procedures are best performed during estrus, they may be continued beyond ovulation if needed, for up to 3 days. Beyond this time uterine defense mechanisms decreases substantially under the influence of progesterone. It is noteworthy that treatment beyond 2 - 3 days postovulation has been associated with decreased pregnancy rates by altering steroid hormone receptors.<sup>8</sup>

Equine cervix is an important structure that acts as a defense mechanism for the uterus. Mare's cervix is a simple cylindrical structure with no transverse rings. It has a normal length of 5 - 7 cm and a diameter of 2 - 5 cm.<sup>1,3</sup> Cervix has longitudinal mucosal or cervical folds that are continuous with endometrial folds of the uterine body and horns.<sup>2</sup> Mare's cervical canal is lined with simple columnar epithelial cells that consist of alternating nonciliated goblet-like cells that produce mucin, and kinociliated cells that aid in the caudal flow of mucus. Cervix is highly vascularized that ensures a rapid immunological reaction to bacterial invasion.

Hormonally influenced changes in cervical tone and secretions during the estrous cycle are important physical and physiological barriers to protect the uterus and facilitate uterine clearance, fertilization, pregnancy maintenance, and parturition.<sup>3</sup> Cervical changes during the estrous cycle in mares are primarily regulated by steroid hormones. Progesterone tightens and tones the cervix whereas estrogen dilates and relaxes the cervix. Cervix can be best assessed by vaginal speculum examination or by manual digital palpation.<sup>3</sup> During estrus, the cervix should be dilated and loose, allowing uterine clearance. However, in some aged maiden mares, physiologic malfunction or cervical fibrosis may prevent proper dilation. Cervical incompetence typically results in fluid accumulation in the uterus, especially postbreeding that may lead to uterine infections and subsequent subfertility.

Failure of cervical dilation may be congenital or acquired, and mares with this condition frequently accumulate fluid in the uterus. Fluid can become a nidus for infection, and create a hostile environment for conceptus. Cervical adhesions are acquired during parturition. Although suspected age-related fibrosis of the cervix is most commonly encountered in older maiden mares, occasionally, young maiden mares may exhibit inadequate cervical relaxation and patency during estrus.<sup>4</sup> Due to the muscular nature of the cervix, manual dilation can be achieved. However, the dilation may not be long lasting. Adjunct treatments include local topical application of pharmacologic agents,<sup>5</sup> most notably, prostaglandin E1 (misoprostol) or butylscopolamine bromide (Buscopan®). Misoprostol aids in cervical ripening in women and many domestic species, and is commonly used in mares; however, efficacy data are inconsistent. Misoprostol (200 µg) applied intracervically 2 hours before breeding resulted in 6 - 8 hours of cervical dilation<sup>5</sup> and may be effective until 24 hours after treatment.<sup>6</sup> Labelled intravenous butylscopolamine bromide treatment results in smooth muscle relaxation. Although topical use butylscopolamine bromide for cervical relaxation remains anecdotal, it is possible to have a rapid response.

Diligent breeding management is imperative when dealing with subfertile or problem mares. Anatomical issues should be addressed, and endometritis, whether bacterial or sterile breeding induced, must be recognized rapidly and treated appropriately. Approach to management should be multi-modal. Uterine lavage to evacuate fluid and debris from the uterus should be performed. Ecboic agents should be used to aid in continued uterine clearance. Antimicrobial(s) therapy should be initiated as needed, based on endometrial culture and cytology. Identifying and addressing cervical impairment, treating bacterial endometritis, and clearing fluid accumulation in the uterus during breeding management enabled this mare to have a healthy pregnancy.

### Learning points

- Equine cervix is a muscular organ and provides important defense mechanism for the uterus.
- Changes in cervical tone are regulated by steroid hormones of the estrous cycle.
- Failure of the cervix to dilate properly can contribute to poor uterine clearance and subsequent endometritis.
- Whereas manual dilation of the equine cervix is possible, topical application of pharmacological aid in the process.
- Although bacterial endometritis has a good prognosis for future fertility when diagnosed rapidly and managed appropriately, susceptible mares are more prone to recurrence of the condition in subsequent estrous cycles.

### Conflict of interest

None to report.

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