Complications associated with intrauterine glass marbles in five mares

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A 15-year-old nulliparous warmblood mare (mare 1) was evaluated for breeding with frozen semen. The mare had retired from competition 3 years previously and had been bred during the previous 2 breeding seasons but had failed to conceive. Palpation per rectum revealed a distended uterus, and transrectal ultrasonography revealed a 10-cm depth of hyperechoic (grade IV) intrauterine fluid. On the basis of these findings, a presumptive diagnosis of pyometra was made. A silicone uterine lavage catheter was inserted transcervically into the uterus, and 21 L of malodorous, mucopurulent fluid was recovered. Subsequent bacteriologic culture and antimicrobial susceptibility testing of a sample of this fluid yielded heavy growth of *Pseudomonas aeruginosa* susceptible to gentamicin and amikacin. After uterine drainage and lavage with approximately 7 L of saline (0.9% NaCl) solution, transrectal palpation and ultrasonography were repeated and revealed a round echogenic foreign body. The mare was sedated with a combination of detomidine hydrochloride (0.02 mg/kg [0.009 mg/lb], IV) and butorphanol (0.02 mg/kg, IV). A hysteroscopic examination was performed, and a colored glass marble was identified at the base of the right uterine horn, surrounded by a small amount of purulent exudate, and adhered to the endometrium. The marble was dislodged with manual massage of the uterus by means of palpation per rectum, and after manual cervical dilation, a 35-mm-diameter marble was retrieved manually. The surface of the marble, which had adhered to the endometrium, was roughened.

The mare was subsequently treated for pyometra for 2 consecutive reproductive cycles with daily uterine lavage (5 to 5 days of treatment/cycle) with approximately 6 L of saline solution and intrauterine infusion of gentamicin (3 g) buffered with an equal volume (30 mL) of 7.8% sodium bicarbonate. Reevaluation the following spring revealed recurrence of pyometra with heavy growth of *Escherichia coli* and Klebsiella spp on bacteriologic culture of a uterine fluid sample, both of which were resistant to gentamicin but susceptible to amikacin on antimicrobial susceptibility testing. The mare was treated with a combination of N-acetylcysteine, Tris-EDTA (8 mM disodium EDTA dehydrate and 20 mM 2-amino-2-hydroxymethyl-1,2-propanediol), and antimicrobial infusions on the basis of results of repeated bacteriologic culture and susceptibility testing of uterine fluid samples for approximately 3 reproductive cycles. Specifically, the initial treatment consisted of drainage of the mucopurulent material (15 L) followed by uterine lavage with saline solution, with a minimum of 6 L of saline solution/lavage procedure or until saline solution that was infused in the mare’s uterus was clear. Following uterine lavage, intrauterine infusion of 20% N-acetylcysteine (30 mL vial) diluted with 90 mL of saline solution was performed. The following day, the uterine lavage procedure was repeated, and intrauterine infusion of 500 mL of Tris-EDTA was performed.

CASE DESCRIPTION
5 mares were evaluated because of reproductive complications following long-term (> 1 year) use of intrauterine glass marbles for estrus suppression.

CLINICAL FINDINGS
3 mares had 1 intrauterine glass marble, and 2 mares had 2 intrauterine glass marbles. On examination, 2 mares had signs of chronic endometritis, and 3 had signs of pyometra. Marbles or glass shards adhered to the endometrium were identified by means of hysteroscopy in 3 of 5 mares. Five of 7 marbles had surface imperfections or were broken.

TREATMENT AND OUTCOME
All patients were treated with uterine lavage and intrauterine and systemic administration of antimicrobials chosen on the basis of results of bacterial culture and susceptibility testing. Two of 5 mares were treated with intrauterine Tris-EDTA. One mare underwent 3 unsuccessful embryo transfer procedures and was subsequently lost to follow-up. One mare was euthanized because of severe vaginal and cervical adhesions and chronic vaginal discharge. Three mares had no apparent signs of reproductive disease at the time of follow-up but were not rebred.

CLINICAL RELEVANCE
Results of the present small case series suggested that use of intrauterine glass marbles should be discouraged because of the potential for severe reproductive consequences. (J Am Vet Med Assoc 2016;246:1196–1201)
An 11-year-old Quarter Horse mare (mare 2) was referred for reproductive evaluation prior to breeding. The mare had a history of placement of an intrauterine marble 2 years previously. The referring veterinarian had removed the marble 1 year after placement (ie, 1 year prior to referral) and described the retrieved marble as “moth eaten.” The mare was then treated over the following year with altrenogest (0.044 mg/kg [0.02 mg/lb], PO, q 24 h), a synthetic progestin, to suppress estrus during the breeding season and subsequently underwent embryo transfer. The referring veterinarian reportedly observed a small amount of free intrauterine fluid; however, bacteriologic culture yielded scattered growth of *Streptococcus zooepidemicus* and a few colonies of *Bacteroides* sp susceptible to trimethoprim-sulfadiazine, according to antimicrobial susceptibility testing. The mare was sedated with detomidine (0.02 mg/kg, IV) and butorphanol (0.02 mg/kg, IV). Hysteroscopy was performed, which revealed pieces of glass embedded in the endometrium and floating free in the uterine lumen. Attempts to retrieve the glass pieces during the hysteroscopic examination were unsuccessful. An endometrial biopsy specimen was obtained for histologic examination, which indicated mild neutrophilic and chronic lymphoplasmacytic inflammation, consistent with a grade IIB Kenney-Doig classification (10% to 50% chance of conceiving and carrying to term).2 The owner elected not to breed the mare, and no further reproductive evaluation was performed. At the time of final follow-up, the owner reported that the mare was healthy with no apparent signs of reproductive disease.

A 12-year-old nulliparous Hanoverian show horse (mare 3) with a history of intrauterine marble insertion 2 years previously was referred for evaluation of endometritis consistent with a grade III Kenney-Doig classification, which corresponded to an estimated < 10% chance of conceiving and maintaining a pregnancy to term. Because the owner had purchased the mare 3 years previously and was unaware of the presence of the intrauterine glass marble, it was concluded that the marble must have been present for at least 3 years. During that breeding season (1 estrous cycle after the endometrial biopsy), the mare was bred with fresh chilled semen during 4 estrous cycles; these 4 cycles included 3 embryo recovery attempts. The first embryo recovery attempt on postovulation day 8 yielded 1 grade IV (dead or degenerated) embryo with a diameter of 230 µm. The embryo was not transferred to a recipient mare because it was deemed to be nonviable. During the fourth cycle, the recipient mare was not synchronized adequately in relationship to the donor mare’s reproductive cycle (ovulation); therefore, embryo recovery was not attempted. Subsequently, the owner elected to have the mare examined for pregnancy on postovulation day 14, and it was found to be not pregnant. The mare was then lost to follow-up.

An 11-year-old Quarter Horse mare (mare 2) was referred for a reproductive evaluation prior to breeding. The mare had a history of placement of an intrauterine marble 2 years previously. The referring veterinarian had removed the marble 1 year after placement (ie, 1 year prior to referral) and described the retrieved marble as “moth eaten.” The mare was then treated over the following year with altrenogest (0.044 mg/kg [0.02 mg/lb], PO, q 24 h), a synthetic progestin, to suppress estrus during the breeding season and subsequently underwent embryo transfer. The referring veterinarian reportedly observed a small amount of free intrauterine fluid; however, bacteriologic culture of an endometrial biopsy specimen did not yield any growth. During the breeding season after marble removal, the mare was bred 3 times for embryo recovery; on the third embryo recovery attempt, 2 pieces of glass were recovered by the referring veterinarian. The mare was then referred for further evaluation.

On initial evaluation, results of palpation per rectum and transrectal ultrasonography indicated that the mare was in diestrus, with no abnormal uterine fluid or edema present. Results of a vaginal examination were unremarkable. However, during an ultrasonographic examination, hyperechoic areas were evident at the base of the right uterine horn (Figure 1). An endometrial specimen was collected with a double-guarded swab for cytologic examination, bacteriologic culture, and antimicrobial susceptibility testing. Mild inflammation was noted on cytologic examination, and bacteriologic culture yielded scattered growth of *Streptococcus zooepidemicus* and a few colonies of *Bacteroides* sp susceptible to trimethoprim-sulfadiazine, according to antimicrobial susceptibility testing. The mare was sedated with detomidine (0.02 mg/kg, IV) and butorphanol (0.02 mg/kg, IV). Hysteroscopy was performed, which revealed pieces of glass embedded in the endometrium and floating free in the uterine lumen. Attempts to retrieve the glass pieces during the hysteroscopic examination were unsuccessful. An endometrial biopsy specimen was obtained for histologic examination, which indicated mild neutrophilic and chronic lymphoplasmacytic inflammation, consistent with a grade IIB Kenney-Doig classification (10% to 50% chance of conceiving and carrying to term). The owner elected not to breed the mare, and no further reproductive evaluation was performed. At the time of final follow-up, the owner reported that the mare was healthy with no apparent signs of reproductive disease.

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![Figure 1](https://example.com/figure1.png)

**Figure 1**—Transrectal ultrasonographic image of the right uterine horn of an 11-year-old Quarter Horse mare (mare 2) referred for reproductive evaluation prior to breeding. The mare had a history of placement of an intrauterine marble 2 years previously. Note the hyperechoic glass shards (arrows).
metritis. One year after marble placement, the mare exhibited estrous behavior; therefore, a second marble was inserted at the request of the owner, who assumed the first marble had been lost. Six months after the second marble was inserted, the owner requested another (ie, third) marble be placed as the mare continued to exhibit estrous behavior; the owner assumed that the second marble had been lost as well. Six months prior to referral, vulvar discharge was noticed and the mare was treated with ceftiofur hydrochloride (2 mg/kg, IM [0.9 mg/lb], PO, q 24 h for 5 days) and a single injection of dinoprost tromethamine (0.002 mg/kg [0.0009 mg/lb], SC) to induce estrus. During estrus, the referring veterinarian obtained an endometrial swab sample for bacteriologic culture and susceptibility testing, which yielded *Streptococcus zooepidemicus* susceptible to ceftiofur. However, because of ongoing uterine fluid accumulation despite treatment, the mare was referred for further evaluation. On initial examination, palpation per rectum and ultrasonographic examination of the uterus revealed the presence of hyperechoic fluid and 2 spherical hyperechoic structures (Figure 2). Following uterine drainage and lavage with 6 L of saline solution, the mare was sedated with detomidine (0.02 mg/kg, IV) and butorphanol (0.02 mg/kg, IV). A flexible 1.6-m videoendoscope was used to perform hysteroscopy, and 1 large (35-mm-diameter) colored glass marble and a second smaller (25-mm-diameter) white marble were identified. The smaller marble was successfully retrieved with an endoscopic retrieval basket tool inserted via the instrument portal. An initial attempt to manually retrieve the larger marble failed because of a tight cervix. Prostaglandin E2 gel (0.5 mg) was applied topically within and onto the cervix. The next morning, the cervix was manually dilated, and the marble was removed by milking it toward the cervix transrectally with 1 hand, while the fingers of the second hand were placed transvaginally to remove the marble through the cervix. No surface imperfections were evident on the retrieved marbles. The mare was subsequently treated with uterine lavage by means of infusion and drainage of 5 L of saline solution followed by intrauterine infusion of gentamicin (2 g) diluted with an equal volume (20 mL) of 7.8% sodium bicarbonate and sodium penicillin (10 million IU) diluted in 30 mL of sterile water. One month later, a repeated ultrasonographic examination revealed small follicles on both ovaries and no intrauterine fluid. Evaluation of an endometrial swab sample revealed mild inflammation with no growth on bacteriologic culture. Endometrial biopsy was declined by the owner because the mare was not intended for future breeding. The mare successfully returned to showing and was reported to have no apparent signs of reproductive disease 1 year later.

An 18-year-old Standardbred mare (mare 4) with a history of 2 previous live foals was referred for evaluation. The last foal had been born by cesarean section 5 years previously because of dystocia. The mare was then retired from breeding and had a glass marble placed in the uterus for estrus suppression. During the 12 months prior to referral, the mare was treated on multiple occasions for endometritis without resolution. Prior to referral, the referring veterinarian identified 2 marbles in the uterus during a transrectal ultrasonographic examination and manually removed an intact colored marble and pieces of a second clear glass marble (Figure 3). On referral,
transrectal ultrasonography indicated that the mare was in estrus with 2 cm of intrauterine fluid present in the uterine body and a 40-mm-diameter follicle on the left ovary. Three small hyperechoic areas, consistent with the presence of glass shards, were identified at the base of the left uterine horn. Vaginal examination revealed dense vaginal and cervical adhesions, presumably secondary to the prior dystocia. Hysteroscopy was performed, and a surgical scar was identified in the right uterine horn. Small (ie, 3- to 5-mm) glass fragments were identified adhered to the uterine wall at the base of the left uterine horn. Following hysteroscopy, a silicone uterine lavage catheter was placed and the uterus was lavaged with 4 L of saline solution. The recovered uterine lavage fluid was filtered through gauze, which revealed fine granular material assumed to be ground glass fragments from the broken marble. The owner declined an endometrial biopsy because the mare was not intended for breeding. The mare underwent repeated uterine lavage with 1 L of Tris-EDTA daily for 3 days during estrus in the next 2 estrous cycles, as performed by the referring veterinarian. Seven months later, vaginal discharge was noted by the owner. Repeated transrectal ultrasonography revealed accumulated intrauterine fluid, and transvaginal examination (visual and manual examination) demonstrated severe vaginal and cervical adhesions that prevented uterine drainage. The owner elected euthanasia.

A 13-year-old Hanoverian mare (mare 5) was evaluated 3 months after purchase because of chronic vaginal discharge. The history included 1 previous live foal. Palpation per rectum and transrectal ultrasonography revealed a large, fluid-filled, pendulous uterus. Vaginal examination revealed purulent discharge and marked mucosal hyperemia. A vaginal swab specimen was submitted for bacteriologic culture and susceptibility testing and yielded Streptococcus dysgalactiae subsp equisimilis susceptible to trimethoprim-sulfadiazine, gentamicin, and penicillin. Ten days later, the mare was administered dinoprost tromethamine (0.002 mg/kg, SC) to induce estrus, a silicone uterine lavage catheter was inserted into the uterus, and 13 L of purulent fluid was subsequently recovered. The uterus was lavaged with 13 L of saline solution, followed by infusion of 1.6 g of gentamicin. The mare was then treated with flunixin meglumine (1.1 mg/kg [0.5 mg/lb], IV) and a 20-day course of trimethoprim-sulfadiazine, gentamicin, and penicillin. After 5 days, transrectal ultrasonography was repeated and an intrauterine foreign body was identified at the base of the left uterine horn. Following hysteroscopy, a silicone uterine lavage catheter was placed and the uterus was lavaged with 4 L of saline solution. The recovered uterine lavage fluid was filtered through gauze, which revealed fine granular material assumed to be ground glass fragments from the broken marble. The owner declined an endometrial biopsy because the mare was not intended for breeding. The mare underwent repeated uterine lavage with 1 L of Tris-EDTA daily for 3 days during estrus in the next 2 estrous cycles, as performed by the referring veterinarian. Seven months later, vaginal discharge was noted by the owner. Repeated transrectal ultrasonography revealed accumulated intrauterine fluid, and transvaginal examination (visual and manual examination) demonstrated severe vaginal and cervical adhesions that prevented uterine drainage. The owner elected euthanasia.

Discussion

Estrus suppression in mares is typically only fully effective and reversible when achieved by means of prolongation of luteal function, with administration of exogenous progesterone, or both. Various intrauterine devices have been used in clinical and experimental settings for estrus suppression in mares. Intrauterine glass marbles have been suggested to suppress estrus by prolonging luteal function, with reported effectiveness ranging from 11% to 41.3%. However, in a recent study of pony mares, intrauterine placement of a borosilicate glass ball (diameter, 35 mm) failed to produce any change in measurable physiologic parameters or behavior. Furthermore, a recent case report suggested that prolonged (> 2 years) use of an intrauterine glass marble may have predisposed a mare to pyometra. Additional reports of the potential adverse effects of intrauterine glass marbles left in place for > 1 year have been published recently. Nonetheless, despite published reports and anecdotally high complication rates, the use of intrauterine glass marbles is still common in practice. There are many other important variables that are likely to influence the rate of complications related to the use of intrauterine marbles. These include the type and quality of the glass marbles, method of sterilization, number of marbles placed, presence of preexisting endometrial disease, and duration of marble placement.

In all 5 mares described in the present report, duration of marble placement exceeded 1 year. Two owners were unaware of the presence of the intrauterine marbles (mares 1 and 5), and it was believed the mares had the intrauterine marbles in place for 3 to 4 years. Severe pyometra was present in both of these mares. One of these mares (mare 1) underwent uterine biopsy and was assigned a grade III Kenney-Doig classification on the basis of results of histologic examination. It is possible that the severe inflammation and fibrosis may have been a result of the presence of the marble. Mares with pyometra may have reduced endometrial prostaglandin release because of extensive loss of endometrial tissue, resulting in prolonged or decreased luteal function. This results in a grave prognosis for carrying a foal to term. Marble adhesion to the uterus and marble fragmentation or disintegration may result in a chronic foreign body-type reaction or irritation, potentially causing pyometra. The resolution of clinical signs, including
chronic vaginal discharge, in 2 mares of this report (mares 3 and 5) after removal of the marbles may support this association.

In the mares described in the present report, 6 of the 7 glass marbles recovered were colored marbles. Colored marbles are typically used for recreational purposes. Colored marbles may include arsenic and lead as well as coloring agents (metal and metal oxides). It could not be verified whether the clear glass marble in mare 4 was composed of borosilicate glass. Glass marbles marketed for intrauterine use are composed of borosilicate glass treated at high temperatures and are therefore comparatively more resistant to thermal shock. However, it has been reported that ion exchange between the surface of the glass marbles and condensed water leads to the formation of hydroxyl ions on the glass surface, which in turn attacks the structure of the glass. None of the commercially available marbles have been tested and approved as medical devices. The use of unapproved intrauterine devices may have consequences regarding professional liability.

All 5 mares described in the present report had signs of chronic inflammation of the uterus on initial evaluation. It is possible that inflammatory mediators may have damaged the surface of intrauterine marbles, resulting in pitting, damage, or disintegration, which was noted in 5 of 7 marbles. Additionally, glass is a porous noncrystalline substance that may be susceptible to disintegration when exposed to strong acid or alkaline solutions and to sterilization procedures such as steam autoclaving. The mare (mare 4) with the clear fragmented marble also had a second intact colored glass marble, which may have resulted in friction or trauma from collision of the marbles. In 1 author's (TC) experience, a healthy mature Standardbred mare had an autoclaved colored glass marble inserted in the uterus for demonstration purposes. Two weeks later, the glass marble was retrieved manually, and it was noted to already have porous imperfections on its surface, suggesting that deterioration may be quite rapid in the uterine environment. However, no clinical signs of endometritis were present in that mare at the time of marble retrieval.

In 2003, Nie et al reported that 90 days of exposure to an intrauterine marble did not cause severe endometritis. In the present report, pyometra or chronic endometritis with hyperechoic intrauterine fluid evident on transrectal ultrasonography was evident in all 5 mares with intrauterine glass marbles present for >1 year. A history of intrauterine marble placement is not always reliably communicated because owners will sometimes change veterinarians and mares are sold. One mare (mare 5) in the present report had a history of dystocia and cesarean section, resulting in vaginal and cervical adhesions, which likely contributed to the pyometra, whereas the other 4 mares in the present report had no other apparent predisposing factors. Whether pyometra resulted from poor insertion technique, improper sterilization, marble damage during sterilization, lack of concurrent intrauterine antimicrobial infusion, or a chronic low-grade foreign body reaction that led to compromise of the physical integrity of the glass could not be determined from this small case series. We suggest that long-term use of intrauterine glass marbles should be discouraged because of the apparent potential for severe reproductive consequences.

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Footnotes

a. Bivona 36F catheter, Partner Animal Health Inc, Iliderton, ON, Canada.
b. Videoscope Olympus GIF-100, 1.6 m length and 1.4 cm diameter, Olympus America, Melville, New York.
c. Mucymost, Hospira Inc, Montreal, QC, Canada.
d. Tricide, Molecular Therapeutics LLC, Athens, Ga.
e. Regumate, Merck Animal Health, Kirkland, QC, Canada.
f. Uterine culture swab, MOFA Global, Iliderton, ON, Canada.
g. Flexible snare and basket retrieval wire basket, 2.3 mm X 2.350 mm, Burtons Medical Equipment Ltd, Tonbridge, Kent, England.
h. Prepidual, Pfizer Inc, New York, NY.
i. Mare-bles, Manufacturer, City, State. Available at: www.glassmarble.com/MareMarbles.html. Accessed Mar 7, 2014.

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