

# Theriogenology Question of the Month

This feature is being sponsored by the American College of Theriogenologists. Readers of the *JAVMA* are invited to submit contributions. Contributions should provide a learning exercise about theriogenology. A specific question should be posed for the readers. The author's answer to the question and a brief discussion should be presented. Possible topics include commonly seen problems in domestic or exotic animals. Herd problems in dairy and beef cattle, sheep, goats, horses, and exotic hoofstock, problems in kennels or catteries, or flock problems in domestic and exotic fowl also are appropriate. Please contact Dr. Craig A. Smith, Assistant Editor (800/248-2862, ext 259, or FAX 847/925-1329), for further details.

## History

A 9-year-old 112-kg female American Miniature horse was admitted because she had been lethargic and inappetent for 24 hours. The mare was nursing a 2-month-old foal and was reported to be pregnant (approx 45 to 50 days of gestation). The mare had been owned for 4 years, during which time she had not had any medical problems. Five months previously, the mare had had a negative result when tested for equine infectious anemia.

Physical examination revealed a lethargic, hypothermic (rectal temperature, 36.6 C) mare that had pale mucous membranes, was tachycardiac (53 beats/min) and tachypneic (24 breaths/min), and had retinal petechiation and minimal borborygmi. The mare was judged to be too small to permit palpation per rectum.

A CBC and serum biochemical analysis revealed anemia (PCV, 14%) and hypoproteinemia (total serum protein [TP], 4.0 g/dl). The number of platelets was low (90,000/ $\mu$ l). Abdominocentesis revealed blood-contaminated peritoneal fluid (PCV, 24%; protein, 5.0 g/dl). Cytologic examination of a sample of peritoneal fluid revealed a large number of nondegenerate erythrocytes, but erythrophagocytosis was not evident. Platelets were detected in the peritoneal fluid. Results of endoscopic examination of the larynx, trachea, and stomach were unremarkable. A diagnosis of recent intra-abdominal hemorrhage was made, but the exact cause of the hemorrhaging was not determined.

The mare was given flunixin meglumine (0.25 mg/kg of body weight, IV, q 12 h). Six hours after admission, rectal temperature had decreased to 34.0 C and

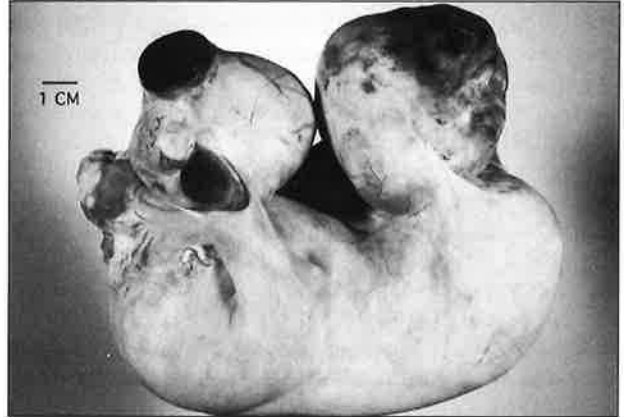


Figure 1—A large ovary containing multiple cystic areas that was found during necropsy of a 9-year-old female American Miniature horse that had internal hemorrhaging. Cystic areas were filled with varying amounts of dark red sanguineous fluid and blood clots.

PCV had decreased to 12%. At that time, 2 L of freshly collected blood was administered. The PCV and TP increased to 21% and 5.8 g/dl, respectively. Twenty-eight hours after admission, an additional liter of blood was administered, which increased the PCV and TP to 24% and 6.8 g/dl, respectively. Thirty-six hours after admission, the mare was markedly improved, and the PCV was unchanged. Forty-eight hours after admission, she was lethargic and, infrequently, became recumbent. The PCV and TP remained unchanged, and she continued to eat and drink. Fifty-six hours after admission, she died unexpectedly during a routine physical examination.

Postmortem examination revealed massive amounts of intra-abdominal hemorrhage. Both ovaries were large (13 × 13 cm in diameter). The external surface of the ovaries consisted of multiple cystic areas (1.5 to 2.5 cm in diameter) and appeared irregularly roughened and dark red (Fig 1). The cysts contained a dark red sanguineous fluid and dark red blood clots. The uterus contained a 6-cm (crown-to-rump length) fetus, which was consistent with a fetal age of 45 to 50 days. The lungs, liver, spleen, endocardium, and adrenal glands all contained areas of acute multifocal hemorrhage.

Histologically, the ovaries contained multiple, irregular, cyst-like structures of various sizes bordered by multiple layers of large, plump, polygonal, granulosa-theca cells, which were surrounded by various amounts of fibrous connective tissue. The centers of the cyst-like structures contained numerous erythrocytes, but there was not any evidence of neoplasia.

## Question

What was the probable cause of death in this mare?  
Please turn the page.

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## Answer

Excessive hemorrhaging from ovarian hematomas on both ovaries.

## Discussion

Hemoperitoneum is uncommon in horses. Causes of hemoperitoneum include iatrogenic causes (as a result of peritoneal centesis), trauma (severe blunt trauma or penetrating wound), rupture of a uterine artery during parturition, neoplasia (squamous cell carcinoma, adenocarcinoma, hemangiosarcoma, or other neoplasia), diapedesis from vascularly compromised bowel, verminous mesenteric arteritis resulting in artery rupture, pheochromocytoma, or gastric ulcer perforation.<sup>1</sup> When peritoneal fluid contains a large quantity of blood, but erythrophagocytosis is not evident on cytologic examination, hemorrhaging was probably recent. Red blood cells remaining in the abdominal cavity are eventually engulfed by macrophages; thus, erythrophagocytosis is evident on cytologic examination and is indicative of chronic hemoperitoneum.<sup>1</sup>

Mature ovarian follicles are highly vascular and have a hyperemic theca interna layer. Follicular fluid contains a low concentration of fibrinogen and high concentrations of anticoagulants that prevent the ovum from adhering to a clot during ovulation.<sup>3</sup> At ovulation, substantial amounts of blood may accumulate in the follicular cavity, distending the cavity and forming a corpus hemorrhagicum. This hemorrhage can be excessive and result in the formation of an ovarian hematoma.<sup>3</sup>

Ovarian hematomas usually do not have an effect on estrous cycles or pregnancies in mares unless they are sufficiently extensive that they destroy a large portion of the ovarian parenchyma. Ovarian hematomas usually regress during 1 to 2 estrous cycles, but can, at times, become sufficiently large that they persist for several months.<sup>4</sup>

Ovulations during diestrus occur in approximately a fourth of estrous cycles in clinically normal mares. Diestrus ovulations usually are the result of a wave of follicles that develop 10 to 14 days after the original wave of follicles that resulted in estrus and ovulation. Similar diestrus ovulations can occur in pregnant mares for up to 120 days of gestation.<sup>4</sup> There were multiple ovarian hematomas on both ovaries in the mare described here, which resulted from multiple ovulations during pregnancy.

The mare reported here may have had a predisposing clotting disorder, as indicated by the acute multifocal petechial hemorrhages detected in multiple organs. Although she may have had an underlying clotting defect, clinical improvement of the mare and the

administration of freshly collected blood precluded us from performing tests of coagulation. Although this mare was thrombocytopenic, the number of platelets was well above the minimum number (25,000/ $\mu$ l) required to prevent hemorrhage. Thrombocytopenia was probably secondary to increased consumption of platelets associated with active hemorrhage and sequestration of platelets in the peritoneal cavity.<sup>5</sup>

The use of a nonsteroidal anti-inflammatory drug in the mare described here was controversial because of the effects of these drugs on platelet aggregation. Nonsteroidal anti-inflammatory drugs can inhibit platelet aggregation through inhibition of platelet cyclooxygenase, which normally generates large quantities of thromboxane  $A_2$ . This action typically is seen when the drugs are administered at high doses<sup>6</sup>; the lower therapeutic doses that were used in the mare reported here should not have caused a problem.

Retrospectively, perhaps further diagnostic tests could have been performed after the mare had been stabilized to localize the source and cause of the bleeding. Further diagnostic tests could have included ultrasonography (transrectally, transabdominally, or both) and hemostatic function tests. Perhaps even exploratory laparotomy or laparoscopy could have been used to aid us in identifying the source of bleeding as well as allowing for removal of the ovaries to prevent further bleeding. However, it was decided that the risk of surgery was outweighed by the fact that the mare appeared to be improving and that the bleeding appeared to have resolved.

The probable cause of death was exsanguination as a result of bilateral bleeding from ovarian hematomas. Hemorrhage from the ovaries appeared to be a result of normal ovarian activity, because underlying ovarian pathologic conditions were not identified.

## References

1. Parry BW, Brownlow MA. Peritoneal fluid. In: Cowell RL, ed. *Cytology and hematology of the horse*. Goleta, Calif: American Veterinary Publications, 1992;140-141.
2. Roberts SJ. Gestation and pregnancy diagnosis in the mare. In: Morrow DA, ed. *Current therapy in theriogenology*. 2nd ed. Philadelphia: WB Saunders Co, 1986;670-678.
3. Roberts SJ. Infertility in the mare. In: Roberts SJ, ed. *Veterinary obstetrics and genital diseases theriogenology*. 3rd ed. Ann Arbor, Mich: Edwards Brothers, 1986;581-635.
4. Neely DP, Liu IK, Hillman RB. Evaluation and therapy of genital disease in the mare. In: Neely DP, ed. *Equine reproduction*. Nutley, NJ: Veterinary Learning Systems Co, 1983;50-52.
5. Sellon DC. Quantitative platelet abnormalities in horses. *Compend Contin Educ Pract Vet* 1994;16:1335-1347.
6. Lees P, May SA, McKellar QA. Pharmacology and therapeutics of non-steroidal anti-inflammatory drugs in the dog and cat: 1 general pharmacology. *J Small Anim Pract* 1991;32:183-193.