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The occurrence of ovulatory failure during the breeding season can be a significant source of frustration. Although most workers agree that anovulatory follicles are more common early or late in the season, they do sometimes occur during the normal breeding season, especially in older mares. One report examined 737 cycles in 47 mares that were treated repeatedly with CLO and hCG over a 3 year period. The failure of ovulation was more common in the autumn (September/October 22%, November 59%), and approximately 50% of the mares developed an anovulatory follicle during at least one cycle, and 26% experienced them during at least 2 cycles. A tendency for an anovulatory follicle to recur in a mare from one breeding season to the next was noted. Others have reported no effect of season or the highest incidence from May to August, but again found a tendency for some mares to have repeated ovulation failure.

These non-ovulatory follicles have been called hemorrhagic anovulatory follicles (HAF), anovulatory hemorrhagic follicles, hemorrhagic follicles or persistent anovulatory follicles. While the occurrence of these anovulatory follicles is well recognized, the ability to predict their occurrence has eluded us. Using grey-scale B-mode ultrasonography, there are no premonitory signs that can be used to predict that a follicle will fail to ovulate. Typically, an HAF is recognized by the sudden appearance of an abundance of hyperechoic floating specks in the antrum of the follicle. Over the next few days, hyperechoic strands are observed to develop in the antrum and the wall of the follicle thickens as apparent luteal tissue develops. Using Doppler ultrasound, comparing follicles the day before ovulation with those at a similar stage of development that would fail to ovulate; increased vascularity in the apical area (site of impending ovulation) of the follicle was noted in follicles destined to fail to ovulate. This difference was attributed to minimal hemorrhage during ovulation vs. considerable hemorrhage during HAF formation.

The progesterone profile after observation of the formation of an HAF has been described, and in most cases (88%) when an HAF was observed, progesterone was increased. In one report, in 51% of the cases progesterone rose slowly and progressively to > 8 ng/mL, while in 13% it rose rapidly to > 10 ng/mL. In 25% of the HAFs, progesterone reached a plateau of 1 to 4 ng/mL, and in 11% it did not rise above 1 ng/mL. Other studies have reported no significant difference in the concentrations of progesterone or LH between mares that developed an HAF and control mares that ovulated, and only a slightly greater concentration of estrogen in the mares with an HAF was observed 3 d before formation. Other studies have similarly found that concentrations of progesterone in mares with an HAF are elevated to > 1 ng/mL. However in mares which formed a HAF in response to flunixin meglumine administration, the concentration of progesterone on days 5 and 9 after HAF formation was lower than in control mares on corresponding days after ovulation. Consequently, most mares with an HAF will respond to a luteolytic dose of prostaglandin administered at the appropriate interval after for-
formation of the HAF, with a return to estrus and normal ovulation2. However, as discussed below, treating an HAF with a luteolytic dose of CLO may in some cases not be the best course of action, especially in mares prone to forming HAFs.

Similar to the inability to reliably predict the occurrence of an HAF, the etiology remains elusive. Recent work has revealed a relative lack of angiogenic activity in HAFs compared to corpora lutea formed after ovulation5. Other reports have linked the use of cloprostenol (CLO) to induce luteolysis and a return to estrus with an increased risk of formation of HAFs3,7,2,4. In one report,7 the histories of 2 mares that both had an unusually high incidence of HAFs were examined. In these 2 mares, the use of CLO to induce estrus was associated with a high incidence of ovulation failure. Other reports3,4, by the same authors, examined 207 and 7 mares, respectively, over longer periods of time, with a variable number of estrous cycles included for each mare. These authors hypothesized3,4 that the administration of CLO results in a rapid drop in progesterone, which allows LH to rise. If this rise in LH occurs during the development of an immature follicle, before follicular deviation, it could interfere with the intrafollicular metabolism of substances necessary for ovulation and follicular collapse. Similarly, in a model using follicle ablation to induce follicular waves and estrus, the incidence of HAFs was increased and these mares had an earlier rise in LH8. Another report suggested that the use of hCG could contribute to an increased incidence of HAFs9. Alternatively, administration of a prostaglandin inhibitor such as flunixin meglumine can interrupt the ovulatory process, resulting in an increased incidence of HAFs9,2,10. Certain mares appear to be prone to repeated occurrences of HAFs and some researchers feel that conditions such as laminitis may contribute to the occurrence of an HAF1,2,3, which is plausible given the reports linking the use of CLO to HAF formation.

A factor which may play a role but was not described in these reports linking CLO usage and HAF formation is what size follicle was present on the ovaries at the time of CLO ad-

ministration. The status of follicular activity at the time of CLO administration affects the interval to onset of the subsequent estrus and interval to ovulation. It is possible that follicular status at the time of CLO administration may also have a role in the formation of an HAF. Cuervo-Arango and Newcombe (4) propose that the dose of CLO affects the chance of HAF development, with higher doses more likely to result in HAF formation. Therefore in a mare that is prone to HAF development, or when CLO administration to a mare with an HAF is deemed necessary, it would be prudent to use the lowest effective dose possible. Because CLO is more potent and longer acting than the natural tham salt of PGF2α, the effect of administration of PGF2α may not have the same effect as that of CLO. However, no studies have been reported that directly compare administration of CLO with dinoprost tromethamine on the development of HAFs. Alternatively, it may be wise to forego administration of PGF or an analogue and allow the mare to return to estrus on her own, without hormonal intervention. In some cases, waiting a few days longer for a natural estrus may actually result in getting a mare in foal sooner than with hormonal intervention.

REFERENCES


